Adolescent Health Care: A Practical Guide

Contents

Editor
Dedication
Contributing Authors
Foreword by Robert W. Blum
Preface
Preface to the First Edition
Acknowledgments

Part I. General Considerations in Adolescent Health Care

1. Normal Physical Growth and Development
   Lawrence S. Neinstein and Francine Ratner Kaufman

2. Psychosocial Development in Normal Adolescents
   Mari Radzik, Sara Sherer, and Lawrence S. Neinstein

3. Office Visit, Interview Techniques, and Recommendations to Parents
   Elizabeth R. Woods and Lawrence S. Neinstein

4. Preventive Healthcare for Adolescents
   David S. Rosen and Lawrence S. Neinstein

5. Vital Statistics and Injuries
   Robert H. DuRant and Karen Sigmon Smith

6. Nutrition
   Lawrence S. Neinstein and Linda E. Schack

7. Understanding Legal Aspects of Care
   Abigail English

Part II. Endocrine Problems

8. Abnormal Growth and Development
   Lawrence S. Neinstein and Francine Ratner Kaufman

9. Thyroid Disease in Adolescents
   Lawrence S. Neinstein and Francine Ratner Kaufman

10. Diabetes Mellitus
    Donald P. Orr

11. Gynecomastia
    Lawrence S. Neinstein and Alain Joffe

Part III. Cardiovascular Problems

12. Cardiac Risk Factors and Hyperlipidemia
    Marc S. Jacobson, Michael R. Kohn, and Lawrence S. Neinstein

13. Systemic Hypertension
    Arno R. Hohn and Lawrence S. Neinstein

14. Heart Murmurs
    Frank Cetta and Lawrence S. Neinstein

15. Mitral Valve Prolapse
    Frank Cetta and Lawrence S. Neinstein

Part IV. Orthopedic Problems

16. Scoliosis and Kyphosis
    Joseph N. Chorley and Lawrence S. Neinstein

17. Common Orthopedic Problems
    Robert J. Bielski and Lawrence S. Neinstein

18. Back Pain
    Robert J. Bielski and Lawrence S. Neinstein

19. Guidelines in Sports Medicine
    Albert C. Hergenroeder and Lawrence S. Neinstein

Part V. Dermatological Disorders

20. Acne Vulgaris
    Anita S. Pakula and Lawrence S. Neinstein

21. Miscellaneous Dermatological Disorders
    Lawrence S. Neinstein and Anita S. Pakula

Part VI. Neurological Disorders

22. Epilepsy
    Wendy G. Mitchell, Namrata S. Shah, and Lawrence S. Neinstein

23. Headaches
Part VII. Genitourinary Disorders

26. Genitourinary Tract Infections
   Lawrence J. D'Angelo and Lawrence S. Neinstein

27. Enuresis
   Diana Tanaka and Lawrence S. Neinstein

28. Asymptomatic Proteinuria and Hematuria
   Lawrence S. Neinstein and Lawrence J. D'Angelo

29. Scrotal Disorders
   Martin M. Anderson and Lawrence S. Neinstein

Part VIII. Infectious Diseases

30. Infectious Mononucleosis and Mycoplasma Pneumonia
   Lawrence S. Friedman and Lawrence S. Neinstein

31. Hepatitis
   Wilbert H. Mason, Jr., and Lawrence S. Neinstein

32. Human Immunodeficiency Virus Infections and Acquired Immunodeficiency Syndrome
   Marvin E. Belzer and Lawrence S. Neinstein

Part IX. Eating Disorders

33. Obesity
   Richard G. MacKenzie and Lawrence S. Neinstein

34. Anorexia Nervosa and Bulimia Nervosa
   Lawrence S. Neinstein and Richard G. MacKenzie

Part X. Miscellaneous Medical Disorders

35. Fatigue and Chronic Fatigue Syndrome
   Marvin E. Belzer and Lawrence S. Neinstein

36. Chronic, Recurrent Abdominal Pain
   Dan W. Thomas and Lawrence S. Neinstein

37. Chest Pain
   John Kulig and Lawrence S. Neinstein

38. Noninflammatory Rheumatism Fibromyalgia and Reflex Sympathetic Dystrophy
   Bram H. Bernstein and Charles H. Spencer

Part XI. Sexuality and Family Planning

39. Adolescent Sexuality
   Lawrence S. Neinstein and Martin M. Anderson

40. Gay, Lesbian, and Bisexual Adolescents
   Eric Meininger, Eric Cohen, Lawrence S. Neinstein, and Gary Remafedi

41. Teenage Pregnancy
   Lawrence S. Neinstein and Mychelle Y. Farmer

42. Contraception
   Lawrence S. Neinstein and Anita L. Nelson

43. Combination Hormonal Contraception
   Anita L. Nelson and Lawrence S. Neinstein

44. Intrauterine Devices
   Anita L. Nelson and Lawrence S. Neinstein

45. Barrier Contraceptives
   Anita L. Nelson and Lawrence S. Neinstein

46. Emergency Contraception
   Anita L. Nelson and Lawrence S. Neinstein

47. Long-Acting Progestins
   Anita L. Nelson and Lawrence S. Neinstein

Part XII. Adolescent Gynecology

48. Gynecological Examination of the Adolescent Female
   Merrill Weitzel and S. Jean Emans

49. Normal Menstrual Physiology
   Catherine M. Gordon and Lawrence S. Neinstein

50. Dysmenorrhea and Premenstrual Syndrome
   Paula K. Braverman and Lawrence S. Neinstein

51. Dysfunctional Uterine Bleeding
Part XIII. Sexually Transmitted Diseases

60. Overview of Sexually Transmitted Diseases
   J. Dennis Fortenberry and Lawrence S. Neinstein

61. Gonorrhea
   Paula K. Braverman and Lawrence S. Neinstein

62. Chlamydia trachomatis
   Mary-Ann Shafer and Athena Countouriotis

63. Pelvic Inflammatory Disease
   Jonathan K. Pletcher and Gail B. Spat

64. Syphilis
   J. Dennis Fortenberry and Lawrence S. Neinstein

65. Herpes Genitalis
   Linda E. Schack and Lawrence S. Neinstein

66. Human Papillomavirus (Anogenital Warts) and Molluscum Contagiosum
   Alain Joffe and Lawrence S. Neinstein

67. Pediculosis Pubis and Scabies
   Lawrence S. Neinstein, M. Susan Jay, and Rose Marino

68. Minor Sexually Transmitted Diseases: Chancroid, Lymphogranuloma Venereum, and Granuloma Inguinale
   M. Susan Jay and Lawrence S. Neinstein

Part XIV. Drug Use and Abuse

69. Overview of Drug Use and Abuse
   Lawrence S. Neinstein and Bruce S. Heischober

70. Alcohol
   Lawrence S. Neinstein and Martin M. Anderson

71. Tobacco
   Seth D. Ammerman and Lawrence S. Neinstein

72. Marijuana
   Lawrence S. Neinstein and Bruce S. Heischober

73. Hallucinogens
   Lawrence S. Neinstein and Bruce S. Heischober

74. Miscellaneous Drugs: Stimulants, Inhalants, Opiates, Depressants, and Anabolic Steroids
   Lawrence S. Neinstein and Bruce S. Heischober

75. Approaches to the Management of Drug Abuse
   Lawrence S. Neinstein, Drew Primav, and Bruce S. Heischober

Part XV. Psychosocial Problems and Concerns

76. Common Concerns of Adolescents and Their Parents
   Lawrence S. Neinstein, Mari Radzik, and Sara Sherer

77. High-Risk and Out-of-Control Behavior
   Lawrence S. Neinstein, Richard G. MacKenzie, and Robert E. Morris

78. Youth and Violence
   Curren Warf

79. Adolescent Depression
   Richard M. Santos and Lawrence S. Neinstein

80. Suicide
   Sara Shiner, Mari Radzik, and Lawrence S. Neinstein

81. School Problems and ADHD
Part XVI. Special Considerations for Health Care Providers

84. Herbal Treatments in Clinical Practice
   Michael D. Cirigliano

85. Overview of College Health Issues
   Lawrence S. Neinstein and Betty Anne Johnson

Part XVII. Appendices

Appendix I. Reference Materials on Adolescence
Appendix II. Other Resources and Services
Editor

Lawrence S. Neinstein, M.D.
Executive Director
USC University Park Health Center
Professor of Pediatrics and Medicine
USC Keck School of Medicine
Los Angeles, California
To my incredible family
my wife Debra
and my children,
Yael, Aaron, and David
and to my parents,
Shirley and Roz and Ben
and
in memory of my father Alvin
Contributing Authors

Seth D. Ammerman, M.D.
Clinical Assistant Professor
Department of Pediatrics/Adolescent Medicine
Stanford University
Packard Children's Hospital
Palo Alto, California

Martin M. Anderson, M.D., M.P.H.
Professor of Clinical Pediatrics
Director of Adolescent Medicine
Department of Pediatrics
University of California, Los Angeles
Los Angeles, California

Bram H. Bernstein, M.D., C.M.
Professor of Clinical Pediatrics
University of Southern California
Keck School of Medicine
Head, Division of Rheumatology
Children's Hospital of Los Angeles
Los Angeles, California

Marvin E. Belzer, M.D.
Assistant Professor of Pediatrics and Medicine
University of Southern California
Children’s Hospital of Los Angeles
Los Angeles, California

Sunitha Bharadia, M.D.
Senior Resident in Child Neurology
Children’s Hospital of Los Angeles
Los Angeles, California

Robert J. Bielski, M.D.
Chief of Pediatric Orthopedics
Department of Orthopedic Surgery and Rehabilitation
Loyola University Medical Center
Maywood, Illinois

Paula K. Braverman, M.D.
Associate Professor of Pediatrics
MCP-Hahnemann University
Chief, Section of Adolescent Medicine
St. Christopher’s Hospital for Children
Philadelphia, Pennsylvania

Frank Cetta, M.D.
Associate Professor
Departments of Pediatrics and Internal Medicine
Loyola University Medical Center
Maywood, Illinois

Joseph N. Chorley, M.D.
Assistant Professor
Department of Pediatrics
Section of Adolescent Medicine and Sports Medicine
Baylor College of Medicine
Attending Physician
Texas Children’s Hospital
Houston, Texas

Michael D. Cirigliano, M.D., F.A.C.P.
Assistant Professor of Medicine
University of Pennsylvania School of Medicine
Philadelphia, Pennsylvania

Eric Cohen, M.D. (Deceased)
Formerly Associate
Clinical Professor of Pediatrics and Family Practice
University of Southern California School of Medicine
Los Angeles, California

Athena Countouriotis, M.D.
Department of Pediatrics
University of California, Los Angeles
Los Angeles, California

Susan M. Coupey, M.D.
Professor of Pediatrics
Albert Einstein College of Medicine
Associate Director, Division of Adolescent Medicine
Children's Hospital at Montefiore
The Bronx, New York

Lawrence J. D'Angelo, M.D., M.P.H.
Executive Director
Goldberg Center for Community Pediatric Health
Children’s National Medical Center
Professor of Pediatrics, Medicine, and Health Care Sciences
Robert H. DuRant, M.D.
Professor and Vice Chair
Department of Pediatrics
Wake Forest University School of Medicine
Director
The Brenner Center for Child and Adolescent Health
Brenner Children's Hospital
Winston-Salem, North Carolina

S. Jean Emans, M.D.
Chief, Division of Adolescent Medicine
Co-Director, Center for Young Women's Health
Children's Hospital Boston
Professor of Pediatrics
Harvard Medical School
Boston, Massachusetts

Abigail English, J.D.
Director
Center for Adolescent Health and the Law
Chapel Hill, North Carolina

Mychelle Y. Farmer, M.D.
Instructor
Department of Pediatrics
Johns Hopkins University
Baltimore, Maryland

J. Dennis Fortenberry, M.D., M.S.
Professor of Pediatrics
Indiana University
Indianapolis, Indiana

Lawrence S. Friedman, M.D.
Professor of Pediatrics
University of California, San Diego
Chief, Division of Primary Care Pediatrics and Adolescent Medicine
Medical Director, Ambulatory and Primary Care
San Diego, California

Catherine M. Gordon, M.D., M.S.
Assistant in Medicine
Instructor in Pediatrics
Harvard Medical School
Boston, Massachusetts

Marlyse Haward, M.D.
Department of Pediatrics
University of San Francisco
San Francisco, California

Bruce S. Heischober, M.D.
Redlands, California

Albert C. Hergenroeder, M.D.
Associate Professor of Pediatrics
Chief, Adolescent Medicine and Sports Medicine Section
Baylor College of Medicine
Texas Children's Hospital
Houston, Texas

Arno R. Hohn, M.D.
Professor of Pediatrics
University of Southern California School of Medicine
Head, Division of Cardiology
Children's Hospital of Los Angeles
Los Angeles, California

Marc S. Jacobson, M.D.
Professor of Pediatrics
Albert Einstein College of Medicine
The Bronx, New York
Director, Center for Atherosclerosis Prevention
Schneider Children's Hospital
New Hyde Park, New York

M. Susan Jay, M.D.
Professor of Pediatrics
Loyola University Medical School
Professor of Pediatrics
Foster G. McGaw Hospital
Maywood, Illinois

Alain Joffe, M.D.
Associate Professor of Pediatrics
Johns Hopkins School of Medicine
Director, Adolescent Medicine
Johns Hopkins Hospital
Baltimore, Maryland

Betty Anne Johnson, M.D., Ph.D.
Professor of Medicine
Virginia Commonwealth University School of Medicine
Director, Virginia Commonwealth University Student Health Service
Richmond, Virginia

Francine Ratner Kaufman, M.D.
Professor of Pediatrics
University of Southern California School of Medicine
Head, Division of Endocrinology
Keck School of Medicine
Los Angeles, California

Michael R. Kohn, M.D.
Staff Specialist
Department of Adolescent Medicine
The Children’s Hospital
Westmead, Sydney, Australia

John Kulig, M.D., M.P.H.
Associate Professor of Pediatrics, Family Medicine, and Community Health
Tufts University School of Medicine
Director, Adolescent Medicine
Department of Pediatrics
New England Medical Center
Boston, Massachusetts

Richard G. MacKenzie, M.D.
Professor of Pediatrics
University of Southern California School of Medicine
Director, Division of Adolescent Medicine
Children’s Hospital of Los Angeles
Los Angeles, California

Rose Marino, M.D.
Resident in Pediatrics
Loyola University Medical Center
Foster G. McGaw Hospital
Maywood, Illinois

Wilbert H. Mason, Jr., M.D., M.P.H.
Professor of Clinical Pediatrics
Division of Infectious Diseases
University of Southern California School of Medicine
Children’s Hospital of Los Angeles
Los Angeles, California

Eric Meininger, M.D.
Fellow, Adolescent Health
Division of General Pediatrics and Adolescent Health
University of Minnesota
Minneapolis, Minnesota

Laurie A.P. Milan, M.D.
Assistant Professor of Clinical Pediatrics
University of Cincinnati College of Medicine
Department of Adolescent Medicine
Children’s Hospital Medical Center
Cincinnati, Ohio

Wendy G. Mitchell, M.D.
Professor of Neurology and Pediatrics
University of Southern California
Keck School of Medicine
Pediatric Neurologist
Children’s Hospital of Los Angeles
Los Angeles, California

Robert E. Morris, M.D.
Professor of Clinical Pediatrics
University of California at Los Angeles
Los Angeles, California
Medical Director
Louisiana State University
Jetson Correctional Center for Youth
Baton Rouge, Louisiana

Anna-Barbara Moscicki, M.D.
Professor of Pediatrics
University of California, San Francisco
San Francisco, California

Lawrence S. Neinstein, M.D.
Professor of Pediatrics and Medicine
University of Southern California
Keck School of Medicine
Executive Director
USC University Park Health Center
Anita L. Nelson, M.D.
Professor of Obstetrics and Gynecology
University of California, Los Angeles
Los Angeles
Medical Director
Women's Health Care Programs
Harbor-UCLA Medical Center
Torrance, California

Donald P. Orr, M.D.
Professor of Pediatrics, Nursing Research and Nutrition
Department of Pediatrics
Indiana University School of Medicine
Director of Adolescent Medicine
Indiana University Medical Center
Indianapolis, Indiana

Anita S. Pakula, M.D.
Assistant Clinical Professor of Medicine
University of California, Los Angeles
Los Angeles, California

Drew Pinsky, M.D.
Associate Professor of Pediatrics
University of Southern California
Los Angeles Children's Hospital
Los Angeles
Program Medical Director of Chemical Dependency Service
Pasadena, California

Jonathan R. Pletcher, M.D.
Clinical Assistant Professor
Department of Pediatrics
Division of Adolescent Medicine
University of Pennsylvania
Medical Director, Adolescent Care Center
Children's Hospital of Philadelphia
Philadelphia, Pennsylvania

Mari Radzik, Ph.D.
Clinical Assistant Professor of Pediatrics
University of Southern California School of Medicine
Clinical Psychologist
Division of Adolescent Medicine
Children's Hospital of Los Angeles
Los Angeles, California

Gary J. Remafedi, M.D., M.P.H.
Associate Professor of Pediatrics
University of Minnesota
Youth and AIDS Project
Minneapolis, Minnesota

Arthur L. Robin, Ph.D.
Professor of Psychiatry and Behavioral Neurosciences and Pediatrics
Wayne State University
Detroit, Michigan

David S. Rosen, M.D., M.P.H.
Clinical Associate Professor of Pediatrics
University of Michigan Medical School
Chief, Section of Teenage and Young Adult Health
University of Michigan Health Center
Ann Arbor, Michigan

Richard M. Sarles, M.D.
Professor and Director of Child and Adolescent Training
Department of Psychiatry
University of Maryland School of Medicine
Baltimore, Maryland

Linda E. Schack, M.D.
Department of Pediatrics
Torrance Memorial Medical Center
Torrance, California

Howard Schubiner, M.D.
Professor of General Medicine
Wayne State University School of Medicine
Detroit, Michigan

Mary-Ann Shafer, M.D.
Professor of Pediatrics
University of California, San Francisco
San Francisco, California

Namrata S. Shah, M.D.
University of Southern California
Los Angeles, California

Sara Sherer, Ph.D.
Clinical Assistant Professor of Pediatrics
University of Southern California School of Medicine
Coordinator of Behavioral Services
Division of Adolescent Medicine
Children's Hospital of Los Angeles
Los Angeles, California

Gail B. Slap, M.D., M.Sc.
Rauh Professor of Pediatrics and Internal Medicine
University of Cincinnati College of Medicine
Director, Division of Adolescent Medicine
Children's Hospital Medical Center
Cincinnati, Ohio

Karen Sigmon Smith, M.P.H., RHEd
Wake Forest University School of Medicine
Hypertension and Vascular Disease Center
Winston-Salem, North Carolina

Norman P. Spack, M.D.
Assistant Professor of Pediatrics
Harvard Medical School
Clinical Director
Endocrine Division
Children's Hospital
Boston, Massachusetts

Charles H. Spencer, M.D.
Associate Professor of Clinical Pediatrics
University of Chicago
Chicago, Illinois

Diana Tanaka, M.D.
Assistant Professor of Clinical Pediatrics
Division of Adolescent Medicine
University of Southern California
Keck School of Medicine
Attending Physician
Division of Adolescent Medicine
Children's Hospital of Los Angeles
Los Angeles, California

Dan W. Thomas, M.D.
Associate Professor of Pediatrics
University of Southern California
Keck School of Medicine
Head, Pediatric Gastroenterology
Children's Hospital of Los Angeles
Los Angeles, California

Curren Warf, M.D.
Assistant Clinical Professor
Department of Pediatrics
University of Southern California
Keck School of Medicine
Medical Director, High Risk Youth Program
Division of Adolescent Medicine
Children's Hospital of Los Angeles
Los Angeles, California

Merrill Weitzel, M.D.
Instructor of Obstetrics, Gynecology, and Reproductive Biology
Harvard Medical School
Attending Physician
Children's Hospital
Boston, Massachusetts

Elizabeth R. Woods, M.D., M.P.H.
Associate Professor of Pediatrics
Harvard Medical School
Associate Chief of Adolescent/Young Adult Medicine
Children's Hospital
Boston, Massachusetts

Lonnie K. Zeltzer, M.D.
Professor of Pediatrics
University of California, Los Angeles
Los Angeles, California
Foreword

As the fourth edition of Adolescent Health Care goes to press, the field of adolescent medicine is about to celebrate its first half-century. During that period of time, both the field and the conditions that are the major causes of adolescent morbidity and mortality have changed dramatically. A half century ago, infectious diseases were major contributors to juvenile illness, yet HIV was totally unknown. Non-insulin-dependent diabetes practically did not exist in children and adolescents. Teen childbearing was fourfold what it is today; but it would be decades before teen pregnancy would be labeled an "epidemic." Suicide in the pre-teen and early teen years was virtually unknown, and adolescent depression was viewed as "mood swings."

Over the years, the profession has changed as dramatically as the field. In the early 1950s, J. Roswell Gallagher was training a small group of people at Boston Children's Hospital ostensibly for school health services. Little could he imagine that, fifty years later, there would be a board-certified subspecialty, numerous professional journals on adolescent health and development, and required training for all pediatric residents in adolescent medicine.

The need for knowledgeable and skilled health care professionals, however, remains a constant across the years. Such knowledge and skill is based upon understanding the developmental trajectory of young people and translating that understanding into interpersonal strategies that help young people and their families effect change. It requires an understanding of the pathophysiology of the developing teenager while grounding that understanding in the complex social, emotional, and behavioral environments within which he or she lives.

The current volume provides both the provider in-practice and the practitioner-in-training the information base to meet the needs of adolescents and their families. As with previous editions, it is written as a practical guide, clearly outlined and thoroughly indexed. But as the field has changed, new chapters have been added, including diabetes mellitus, the incidence of which has increased dramatically in the recent past. There is a new chapter on abnormal pap smears as well. A chapter on depression and anti-depressants has been added to the new volume, as has a chapter on nutritional and herbal supplements, which will help the practitioner deal with the vast array of supplements widely used by young people. And a chapter on college health has joined the new volume, reflecting Dr. Neinstein's current experience as Director of the University of Southern California's College Health Service.

This book is a comprehensive resource that is aimed at helping those of us who provide health care to teens to do it better. For any of us who have been in practice, it will replace our third edition. For residents, fellows, and nurse practitioners completing their training, it will be their pathway to providing health care to teens. Whatever stage we are in our training, this fourth edition of Larry Neinstein's Adolescent Health Care will be a critical reference book and an invaluable resource.

Robert W. Blum, M.D., M.P.H., Ph.D.
Minneapolis, Minnesota
Summer, 2001
Preface

It is a pleasure to be able to continue Adolescent Health Care: A Practical Guide into its fourth edition. I first began this book in 1980 as a small project to help with my instruction of residents and adolescent medicine fellows. I am extremely gratified that it has become a highly utilized text for individuals at various levels of training and in many different disciplines. I have appreciated the feedback about the usefulness and practicality of the book for clinical, teaching and study purposes. It always thrills me to see the book heavily worn out in a clinic or clinician’s office and not tucked away on the upper shelves of a bookcase.

Adolescent health continues to develop as a specialized field and we now welcome family practitioners as a new group eligible for board certification in adolescent medicine. Adolescent health continues to expand at both ends of the age spectrum. We now find that adolescent females are developing at earlier ages at the same time that there is an increasing interest in the older adolescent, young adult and college age groups. I am always amazed at the number of wonderful individuals from so many disciplines involved in the care of youth: physicians, nurse practitioners, physician assistants, psychologists, social workers, nurses, health educators, nutritionists, teachers.

It is a difficult task to approach a new edition of this text with the ever increasing volume of information and the rapidity of change of this information. While it is important to maintain the “practical, outline” fashion that has made this book so comfortable for users, it is also critical to maintain a fresh outlook when approaching a chapter in a new edition. To accomplish this, I have added an expert (or experts) to almost every chapter, but I have continued to be a coauthor on most chapters. I sincerely thank the many contributors who have helped make this fourth edition the most complete, user- and Web-friendly edition yet.

Many requests are brought to my attention regarding the addition of new topics. Although it was impossible to add them all without making the book too large, there were several topics that seemed essential including diabetes mellitus, college health, abnormal pap smears, nutritional supplements and depression and antidepressants. Chapters from the third edition have been extensively revised to include new information, research and recommendations as well as new references and Web sites.

In this edition, I have emphasized the use of Web sites in both the text and in the reference sections. I hope that these Web sites can serve as a source for up-to-date information. Sites listed are divided into those relevant for teenagers, parents, and professionals and represent a spectrum of resources. It is my hope that in the near future, a Web version of this book will be available to make accessing Web sites even easier.

For those of you who are new to Adolescent Health Care: A Practical Guide, the intent is to make the chapters practical and easy to read, but maintain thorough information in a concise format. The book includes many tables, statistics, references, and resources to help the clinician with the many problems that affect this population. The appendices cover a wide range of books, magazines, articles, organizations, and Web sites available for this age group. Appropriate evaluations and work-ups are always included.

I dedicate this book to young people and to their healthcare providers. I hope this edition will serve as a wealth of information for those who care for youth and young adults. Importantly, I welcome and look forward to feedback on this edition so I can continue to improve this book as the most practical guide to adolescent health issues.
Preface to the First Edition

Adolescent Health Care: A Practical Guide is written for those health-care professionals involved in the care of adolescents, including pediatricians, family practitioners, internists, gynecologists, housestaff, nurses, nurse practitioners, and others. The list is long because the challenge of adolescent medicine crosses the specialty boundaries of medicine as well as the lines separating the medical, psychological, and social areas of health care.

This volume is designed for day-to-day office use. Topics are reviewed in a format that outlines and highlights subjects for easy reference. Selection of subject areas was discussed with housestaff and other experts in adolescent medicine and primary care medicine in order to assure that pertinent areas of interest were not overlooked. In this connection, many subspecialty concerns have been excluded, as they were felt to be better examined in internal medicine or pediatric texts.

Normal growth and psychosocial development of adolescents is discussed first in the book, in order to provide a framework in which to consider abnormalities. Among the chapters featured, for example, are those on problems unique to adolescence (i.e., gynecomastia); problems exacerbated by adolescence (i.e., suicide, school problems); and problems with unique considerations during adolescence (i.e., thyroid disease, chest pain). In addition, because of the high prevalence of teenage sexual activity, sexually transmissible diseases, and drug use, extensive sections of the book have been devoted to these areas. To assist the health-care practitioner in treating adolescents, other chapters concentrate on developing rapport with teens, legal issues associated with teenage care, and psychosocial problems in teens. Useful doctor's office and hospital materials are furthermore included, such as questionnaires for initial interviews, history and physical examination forms, and patient handouts on contraception. The book's numerous tables provide statistics on the adolescent age group in areas such as morbidity, mortality, hypertension, and hyperlipidemia. These have been drawn from many sources and endeavor to provide the practitioner with age-relevant statistics. Last, to assist the practitioner in finding available community resources, an extensive Appendix has been added.

Working with adolescents is exciting, challenging, and sometimes difficult and frustrating. Adolescence is a time of rapid growth and development of mind and body, presenting difficulties in adjustment for the teenager, the family, and the physician. It is also a time of high risk for many problems such as suicide and sexually transmissible diseases, as well as being a critical period for detecting chronic illnesses and risk factors for cardiovascular disease. Moreover, it is an ideal time to educate adolescents about how to best care for their bodies. This book is dedicated to helping the health-care professional meet these challenges.
Acknowledgments

The effort of many is required to put a book like this together. I am deeply indebted to the late Adie Klotz, M.D., a friend, teacher, and inspiration, who helped me realize the need and excitement of working with young people. I also acknowledge both Richard G. MacKenzie, M.D., and Dale Garell, M.D., who also encouraged my interest in the field of adolescent medicine.

I express my deepest appreciation to the many experts who served as authors and coauthors on the many chapters of this book. Their knowledge, expertise, and dedication have helped to make this the most complete edition yet. I personally thank them for their time and effort to my many, many requests, e-mails, and demands.

I want to thank the wonderful and dedicated staff in the Division of Adolescent Medicine at Children’s Hospital of Los Angeles from whom I have learned so much over the years about teens. Many other physicians, nurses, nurse practitioners, and other health-care professionals have also given me their assessments and helpful comments in the development of this fourth edition.

Special thanks go to several individuals at the University of Southern California. Lucy Vergara at the USC University Park Health Center who was always there to assist in communicating with Lippincott Williams & Wilkins and coauthors. I also thank Michael Jackson, Vice-President of Student Affairs, who continued to encourage my academic pursuits.

There are many individuals at Lippincott Williams & Wilkins who deserve recognition in the development of this edition. I thank Tim Hiscock, acquisitions editor, for his assistance in being a kind facilitator in my many requests for edits and changes. I also thank both Joyce Murphy, who served as managing editor, and Tom Boyce as production editor for this edition.

There are also individuals very close to me who deserve special recognition. My parents have shown me what appropriate, loving, and involved parenting can mean during one's adolescence and life. Without their guidance, I would not have the skills and ability to have become the person I am. I mourn the death of my father since the third edition. He was always a calming and steady force throughout my life. A second set of parents, my in-laws, have also provide incredible support during the past 32 years and during the writing of this edition. Loving thanks to all of you.

Last, and most important, I thank my loving wife, Debbie, and my children, Yael, Aaron, and David. Debbie has continued to support me despite even far more hours and late nights through this edition than the last. Tolerating my absences through these four editions has been difficult at times. Yael, Aaron, and David provide me incredible support in their wonderful examples of what healthy young adults can be all about. With the second edition a computer invaded our home. With this edition, even more electronic devices came to our house. I love all of you and thank you for your understanding, support, and encouragement with this fourth edition.
Adolescence marks a time of dramatic physical and psychosocial change. Dynamic hormonal changes allow for the somatic growth and pubertal development that occurs during adolescence. Although this process usually begins in the second decade of life, there is wide variation in the onset and duration of puberty between individuals, between males and females, and among ethnic or racial groups. Health care providers must understand these variations and be able to differentiate between pathological conditions and normal variants of growth and adolescent development. This chapter provides an overview of the normal pubertal process.

ENDOCRINE CHANGES DURING PUBERTY

Initiation of Puberty

Puberty is not an isolated event but represents a transitional period on the continuum between the juvenile state and adulthood. The exact components of this developmental sequence are still obscure, although much more is known than in past years. The hypothalamic-pituitary-gonadal axis starts functioning during fetal life; there is a transient activation during early infancy, and then suppression during the remainder of the first decade of life.

Fetus

Gonadotropin-releasing hormone (GnRH), luteinizing hormone (LH), follicle-stimulating hormone (FSH), estrogen, and testosterone (in the male fetus) are detectable in the fetus by 10 weeks of gestation, and the hormone levels rise between 10 and 20 weeks. LH is secreted in a pulsatile manner as a result of intermittent GnRH stimulation. FSH and LH levels are lower in the male fetus, secondary to increased serum testosterone levels. During the fetal period, the hypothalamus is imprinted to that of a male (tonic center) or that of a female (tonic and cyclic center). This may be the result of testosterone or local brain estrogen concentrations.

Infancy and Prepuberty

At birth, after the fall in placental sex steroid levels, the concentrations of serum LH and FSH rise to midpubertal levels for several months. Serum testosterone levels in male infants and serum estradiol (E$_2$) levels in female infants also rise. This pattern is consistent with a mature differentiated hypothalamic-pituitary unit. For a short time, the hypothalamic-pituitary-gonadal control mechanisms function similar to those seen in adults. This short period can provide a window of opportunity to study the hypothalamic-pituitary-gonadal axis to determine whether abnormalities exist that affect future pubertal/sexual maturation. However, by 9 months to 1 year of age in the male and by 2 years of age in the female, gonadotropins and gonadal steroids fall to prepubertal levels and remain so until puberty. Although the period between age 4 and approximately age 10 years in the female is characterized by low levels of gonadotropins and ovarian steroids, the ovaries are fully developed and capable of being stimulated by gonadotropins.

Puberty

The exact trigger of puberty is unknown; however, it is known that puberty is associated with three distinct changes in the hypothalamic-pituitary unit:

1. A nocturnal sleep-related augmentation of pulsatile LH secretion begins as a result of the increase in the pulsatile release of GnRH (Marshall and Kelch, 1986).
2. The sensitivity of the hypothalamus and the pituitary to E$_2$ and testosterone decreases so that the gonadotropins, LH and FSH, begin to increase. This is probably the result of sequential maturation of the central nervous system.
3. In the female, a positive feedback system develops. Critical levels of estrogen trigger a large release of GnRH, stimulating LH to initiate ovulation.

Gonadotropic Changes

The gonadotropins, LH and FSH, rise during puberty in both males and females (Fig. 1.1). LH tends to increase steadily through puberty, whereas FSH tends to plateau when sexual maturity rating 3 (SMR 3) is reached (see later discussion).

![Fig. 1.1](image_url)
Sex Hormone Changes

All the following hormones increase during puberty:

- Estrone (E₁)
- Estradiol (E₂)
- Progesterone (P)
- 17-Hydroxyprogesterone (17-HP)
- Testosterone (T)
- 5α-Dihydrotestosterone (DHT)
- Androstenedione (A)
- Dehydroepiandrosterone (DHA)
- Dehydroepiandrosterone-sulfate (DHEAS)

The increases in E₂, testosterone, and DHEAS are outlined in Fig. 1.1.

Adrenal Gland Changes

The increased secretion of sex steroids from the adrenal gland in the prepubertal and pubertal periods is independent of hypothalamic-pituitary-gonadal changes. The two events are temporally related in that the onset of adrenarche occurs about 2 years before the increase in gonadal sex steroids. However, studies in children with adrenal insufficiency indicate that adrenal androgens are not necessary for pubertal development or the adolescent growth spurt.

The major androgens secreted by the adrenal gland are DHA, DHEAS, and androstenedione. These also contribute to circulating estrone and testosterone by extraglandular conversion. DHA and DHEAS increase progressively from between age 7 and age 13 to 15 years. These hormones can lead to pubic hair development, mature body odor, and changes in the pilosebaceous apparatus. These changes of adrenarche should not be confused with pubertal activation of the hypothalamic-pituitary-gonadal axis. The factors regulating adrenarche remain unknown; however, insulin, insulin-like growth factor (IGF), and the preadolescent rise in body mass index (BMI) appear to be important physiological regulators of this process (Remer and Manz, 1999).

Other Hormonal Changes

Thyroid Hormone and Glucagon

Thyroid hormone and glucagon do not change significantly during normal puberty.

Insulin

Insulin secretion increases approximately 30% during puberty, secondary to a decreased sensitivity to insulin in adolescents as compared with prepubertal children (Bloch et al., 1987) and adults. This pubertal increase in insulin resistance appears to be caused by changes in growth hormone (GH) secretory dynamics. The dramatic increase in the incidence of type 2 diabetes in obese and genetically predisposed teens in some measure is the result of this period of adolescent insulin resistance.

Leptin

Leptin is a peptide hormone that circulates in plasma and is principally secreted by the adipocyte. It is part of a feedback loop that helps regulate the body’s fat mass. It decreases food consumption, increases energy expenditure. It is increased by circulating levels of insulin and glucocorticoids and decreased by androgens and β-adrenergic stimulation. There are leptin receptors in the hypothalamus, and it appears to be involved in the control of the hypothalamic-pituitary-gonadal axis. Leptin may be the putative agent suggested by Frisch in the 1970s, when he hypothesized that a specific amount of body fat is required to achieve menarche and fertility. Leptin levels, normalized for fat mass, reported by Horlick et al. from 102 children and adolescents, are given in Fig. 1.2. As shown, leptin declines in males and rises in females in late puberty. The importance of leptin in the pubertal process was further emphasized by two reports of failure of pubertal development in humans who had mutations of the leptin receptor and leptin gene (Clement et al., 1998; Strobel et al., 1998).

![Fig. 1.1](image1.jpg)

**FIG. 1.1.** Mean (SEM) leptin/FM in females (A) and in males (B). *, p < .05 compared with same-sex subjects at Tanner stage 1; **, p < .05 compared with girls at the same Tanner stage. (From Horlick MB, Rosenbaum M, Nicolson M, et al. Effect of puberty on the relationship between circulating leptin and body composition. *J Clin Endocrinol Metab* 2000;85:2509–2518, with permission.)

**FIG. 1.2.** Mean (SEM) leptin/FM in females (A) and in males (B). *, p < .05 compared with same-sex subjects at Tanner stage 1; **, p < .05 compared with girls at the same Tanner stage. (From Horlick MB, Rosenbaum M, Nicolson M, et al. Effect of puberty on the relationship between circulating leptin and body composition. *J Clin Endocrinol Metab* 2000;85:2509–2518, with permission.)

Growth Hormone, Insulin-like Growth Factors, and Insulin-like Growth Factor Binding Proteins

IGF-I and IGF-II are a class of peptides that are growth-promoting hormones. (IGF-I is identical to somatomedin-C.) IGF-I and IGF-II promote growth, have some insulin-like activity, and bind to insulin receptors and to separate receptors. They are generated in the liver and are under negative feedback by GH. They are stimulated by insulin, prolactin, thyroid hormone, and GH and inhibited by glucocorticoids, malnutrition, and chronic renal failure. IGF levels are usually concordant with those of GH (i.e., both low in hypopituitarism and high in acromegaly). They can be discordant; for example GH is normal GH and IGF levels are low in Laron-type dwarfism, renal failure, and glucocorticoid excess.

Both GH and IGF-I levels rise during puberty (Albertson-Wikland et al., 1994; Argente et al., 1993). Although specific hypothalamic neuropeptides control the amplitude and frequency of GH pulses, these are strongly modulated by age, gender, body composition, and sexual maturation. Albertson-Wikland et al. (1994) evaluated 24-hour GH profiles in 208 healthy children and adolescents. Mean secretion rates were comparable in prepubertal boys and girls. Secretion rates increased during puberty, occurring earlier in girls (SMR 2–4) than in boys (SMR 4). Rates decreased to prepubertal values at SMR 5. Testosterone appears to amplify GH pulses, whereas estrogen elevates basal GH concentrations and causes a greater irregularity of GH release patterns (Veldhuis et al., 2000). Plasma IGF-I levels also increase during adolescence above adult levels (Juul et al., 1994; Rosenfield et al., 1983).

Juul et al. (1994) found that mean serum IGF-I levels rose slowly in prepubertal children, from 80 to 200 µg/L with a steep increase during puberty to about 500 µg/L. After puberty, levels fell throughout adulthood to 100 µg/L at age 80 years. The maximal IGF-I was at age 14.5 years in girls and about 1 year later in boys. Argente et al. (1993) also found a rise of IGF-I during puberty that peaked 2 years earlier in girls than in boys. Therefore, the increase is most marked during middle and late puberty and correlates best with pubertal stage, bone age, and time from peak height velocity (PHV) (Fig. 1.3). In girls, the elevation is correlated with rising E₂ levels in a biphasic manner. Low levels of E₂ stimulate IGF-I, whereas higher levels of E₂ probably suppress IGF-I. There are higher concentrations of free IGF-I in African-American girls age 9 to 17 years than in white girls, which may contribute to their accelerated growth (Wong et al., 1999). Serum IGF-II levels remain stable throughout puberty.
Insulin-like growth factor binding protein 3 (IGF-BP-3), which binds IGF, is the most abundant of the six IGF-BPs that have high affinity for IGF-I. IGF-BP-3 is low at birth, increases during childhood, and peaks with puberty. IGF-BP-3 is under GH regulation, and concentrations correlate with IGF and GH levels. Decreased levels are seen in children with classic GH deficiency. IGF-BP-3 can promote growth through its interaction with IGF-I, as well as through IGF-independent pathways.

Levels of growth hormone-releasing hormone (GHRH) have been found to rise during puberty and to correlate with pubertal stage. GHRH may have a role in the pubertal growth spurt (Argente et al., 1986).

**Hormonal Actions**

A thorough knowledge of the physiological roles of certain hormones is important to understanding pubertal changes and their possible variations and abnormalities. **Table 1.1** lists these hormones and their functions.

**TABLE 1.1.** Primary action of major hormones of puberty

**Control of Gonadotropin Secretion in Adults**

Stimulus for gonadotropin secretion in adults comes from the central nervous system by intermittent secretion of GnRH from the hypothalamus to the pituitary. GnRH is secreted in a pulsatile fashion, which is critical for the pulsatile secretion of gonadotropins. The frequency and amplitude of the GnRH pulse are critical to the secretion of gonadotropins, because increasing or decreasing the frequency of pulses from 1 pulse per hour can inhibit gonadotropin secretion. The control of GnRH secretion is not well understood and is probably under the influence of a variety of neurotransmitters such as catecholamines (dopamine and norepinephrine), serotonin, and endogenous opioid peptides (endorphins and enkephalins). The drive for the pulsating nature of GnRH probably resides within the hypothalamus. Sex steroids generally have a negative influence on the production of gonadotropins. This negative feedback may occur at the level of the hypothalamus or pituitary, or both. In mature females, at $E_2$ levels of about 200 pg/mL or greater, a positive feedback effect results in a surge of gonadotropin secretion and ovulation.

**PHYSICAL GROWTH DURING PUBERTY**

**Physiology of Growth**

Growth involves an interaction between the body’s endocrine and skeletal systems. Many of the body’s hormones influence growth, including GH, thyroxine, insulin, and corticosteroids (all of which influence growth rate); leptin (which alters body composition); and parathyroid hormone, 1,25-dihydroxy-vitamin D, and calcitonin (all of which affect skeletal mineralization).

The key hormone in growth is GH. Pituitary secretion of this hormone is regulated by GHRH and somatostatin, as shown in **Fig. 1.4**. GH secretion is increased by GHRH and decreased by somatostatin. GHRH is released in a pulsatile fashion, with maximum rates at the onset of slow wave sleep. There is negative feedback of GH secretion via GH itself and the IGFs.

The effects of GH are primarily modulated through the IGFs. The two major types are IGF-I (somatomedin-C) and IGF-II. As the term implies, these hormones have qualitative biological effects that are similar to those of insulin. The major mechanism for growth appears to be through stimulation of IGF-I by GH, which affects bone growth. Serum levels of IGF-I increase with age and pubertal development. However, levels vary widely from individual to individual.

The maturation of bones appears to be under the major influence of thyroid hormones, adrenal androgens, and gonadal sex steroids, mainly estrogen. Excess secretion of these hormones causes advanced bone maturation, and deficiency at the time of puberty causes delay. At puberty, both sex steroids and GH participate in the pubertal growth spurt. The ending of the growth spurt is secondary to epiphyseal closure, due to the action of the sex steroids.

The provider of health care to adolescents must understand the numerous physical changes that occur during puberty.

**Growth Spurt**

An increase in physical size is a universally recognized event of puberty.

**Height Growth**

1. Average normal growth velocities before puberty include the following:
   - 1st year of life: 25 cm/yr
   - 2nd year: 10 cm/yr
   - 3rd year: 8 cm/yr
   - 4th year: 7 cm/yr
   - 5th to 10th years: 5–6 cm/yr

2. Height velocity increases again during puberty and peaks during the adolescent growth spurt. The mean year for beginning an increase in growth velocity is 11 in boys and 9 in girls. Peak height velocity occurs at a mean of 13.5 years in boys and 11.5 years in girls. The magnitude of the growth spurt is negatively correlated with the age at which it begins, but there is no correlation with final height.

3. Pubertal growth accounts for about 20% of final adult height, a total averaging 23 to 28 cm in females and 26 to 28 cm in males.

4. The average growth spurt lasts 24 to 36 months.

5. The growth spurt is highly variable from adolescent to adolescent. Growth during the year of PHV in the normal female averages 9 cm/yr and varies normally from 5.4 cm to 11.2 cm. In the normal male, the PHV averages 10.3 cm/yr and varies from 5.8 cm to 13.1 cm. Typical individual curves showing velocity of growth in boys and girls are demonstrated in Fig. 1.5.

![FIG. 1.5.](image)

Also available are curves for North American children, including colored curves for early and late maturers. These can be obtained from Serono Inc., 280 Pond Street, Randolph, MA 02368, or direct from Castlemead Publications, Swains Mill, 4A Crane Mead, Ware, Hertfordshire, SG129PY, England. (See Fig. 1.26, Fig. 1.27, Fig. 1.28, and Fig. 1.29.)

![FIG. 1.26.](image)

Also available are curves for North American children, including colored curves for early and late maturers. These can be obtained from Serono Inc., 280 Pond Street, Randolph, MA 02368, or direct from Castlemead Publications, Swains Mill, 4A Crane Mead, Ware, Hertfordshire, SG129PY, England. (See Fig. 1.26, Fig. 1.27, Fig. 1.28, and Fig. 1.29.)

![FIG. 1.27.](image)

Also available are curves for North American children, including colored curves for early and late maturers. These can be obtained from Serono Inc., 280 Pond Street, Randolph, MA 02368, or direct from Castlemead Publications, Swains Mill, 4A Crane Mead, Ware, Hertfordshire, SG129PY, England. (See Fig. 1.26, Fig. 1.27, Fig. 1.28, and Fig. 1.29.)
6. Males on average are 12 to 13 cm taller than females, primarily because of their 2-year delay in bone closure. This accounts for a difference of about 10 cm between the sexes; in addition, males also have 2 to 3 cm greater growth during their growth spurt.

Weight Growth

1. Weight velocity increases and peaks during the adolescent growth spurt.
2. Pubertal weight gain accounts for about 50% of an individual's ideal adult body weight.
3. The onset of accelerated weight gain and the peak weight velocity (PWV) attained are highly variable. For example, normal weight gain during the year of PWV can vary from 4.6 to 10.6 kg in girls and from 5.7 to 13.2 kg in boys. (Normal weight-for-age percentile curves are available through the Centers for Disease Control and Prevention [CDC], 6525 Belcrest Road, Hyattsville, MD 20782-2003. They also are available on the CDC Web site: http://www.cdc.gov/growthcharts/. See also Fig. 1.22, Fig. 1.23, and Fig. 1.24.)

FIG. 1.22. Weight-for-age percentiles for girls, 2 to 20 years of age. (From CDC Growth Charts: United States—Advance data. From Vital and Health Statistics of the Centers for Disease Control and Prevention, National Center for Health Statistics, 2000;314:1–28.)

FIG. 1.23. Stature-for-age percentiles for girls, 2 to 20 years of age. (From CDC Growth Charts: United States—Advance data. From Vital and Health Statistics of the Centers for Disease Control and Prevention, National Center for Health Statistics, 2000;314:1–28.)

FIG. 1.24. Weight-for-age percentiles for boys, 2 to 20 years of age. (From CDC Growth Charts: United States—Advance data. From Vital and Health Statistics
Differences in Growth Spurts between Males and Females

1. The PHV occurs about 18 to 24 months earlier in females than in males.
2. The PHV in females averages 2 cm/yr less than in males.
3. PWV coincides with PHV in males, but in females PWV occurs 6 to 9 months after PHV.

Seasonal Variations in Velocity Curves Growth velocities vary during the year, but usually the increase is fastest during the spring and summer months. For this reason, growth velocities should be calculated over a 6- to 12-month period.

Early versus Late Growth Spurts In general, early-maturing adolescents have a larger PHV and PWV than late-maturing adolescents. However, because they start their growth spurt later, late-maturing adolescents are on average taller and heavier when the growth spurt starts. Therefore, the final adult height and weight for early- and late-maturing adolescents may be the same.

Prediction of Mature Height Predicting adult height is a difficult task. Several methods can be used to provide a general estimate. Most individuals have an adult height that is within 2 inches of the midparental height. Midparental heights can be calculated by the following formulas.

For girls:

\[
\frac{\text{father's height} - 13 \text{ cm or 5 inches} + \text{mother's height}}{2}
\]

For boys:

\[
\frac{\text{father's height} + 13 \text{ cm or 5 inches} + \text{mother's height}}{2}
\]

Table 1.2 demonstrates another method of adult height prediction using tables designed by Bayley and Pinneau (1952) that are based on current height, skeletal age, and chronological age. The method shown in Fig. 1.6 and Fig. 1.7 uses height, chronological age, and sexual maturity rating to predict adult height. Although it is slightly less accurate, this method does not require a skeletal age. These charts also show corrected height percentiles for different levels of pubertal development. In addition, computer programs have become available to predict adult height. With these programs, basic information (e.g., parental heights, skeletal age, whether menses have begun) is entered, and the program calculates adult height using several methodologies, including that of Bayley and Pinneau.

TABLE 1.2. Prediction of adult height using skeletal age

FIG. 1.6. Growth curve and correction table for male adolescents: mean height (bold line) and distribution (95th, 90th, 75th, 25th, 10th, and 5th percentile lines) for adolescents maturing at modal rate. Correction table below curves shows mean difference in height between subjects of same age at different stages of puberty (indicated by left column). To obtain a height percentile adjusted for rate of pubertal maturation, first average the Tanner (1962) stages for pubic hair and genitalia to form a sexual maturity index score, then determine the correction factor for the patient’s age from the correction table. Add the correction factor to the measured height (or subtract if it is negative), and plot the adjusted height onto the curves. To estimate final adult height, extrapolate the adjusted height percentile to adulthood. For example, if the adolescent is 15 years of age, 165 cm tall, and Tanner SMR 4, the correction factor would be +2, which would yield a value between the 25th and 50th percentile and an adult height of about 173 cm. (From Wilson DM, Draemer HC, Ritter PL, et al. Growth curves and adult height estimation for adolescents. Am J Dis Child 1987;141:565–570, with permission. Copyright © 1987 American Medical Association.)

FIG. 1.7. Growth curve and correction table for female adolescents: mean height (bold line) and distribution (95th, 90th, 75th, 25th, 10th, and 5th percentile lines) for adolescents maturing at modal rate. Correction table below curves shows mean difference in height between subjects of same age at different stages of puberty.
To obtain a height percentile adjusted for rate of pubertal maturation, first average the Tanner (1962) stages for pubic hair and breasts to form a sexual maturity index score, then determine the correction factor for the patient’s age from the correction table. Add the correction factor to the measured height (or subtract if it is negative), and plot the adjusted height onto the curves. To estimate final adult height, extrapolate the adjusted height percentile to adulthood. (From Wilson DM, Draemer HC, Ritter PL, et al. Growth curves and adult height estimation for adolescents. Am J Dis Child 1987;141:565–570, with permission. Copyright © 1987, American Medical Association.)

**Body Mass Index** Body mass index (BMI) increases with puberty. There is a strong correlation between the timing of puberty and BMI: children with higher mean BMI mature earlier. BMI is determined as follows:

\[
BMIs = \frac{\text{Weight in kilograms}}{[\text{Height in meters}^2]}
\]

The equivalent formula in English units is the following:

\[
BMIs = \frac{[\text{Weight in pounds} - \text{Height in inches} - \text{Height in inches}]}{703}
\]

The BMI declines from birth and reaches a minimum between 4 and 6 years of age before gradually increasing through adolescence and adulthood. The upward trend after the low point is referred to as the “adiposity rebound.” Children with an earlier rebound are more likely to have an increased BMI. Charts and tables for BMI, which should be tracked in all children, particularly teens, can be obtained from the National Center for Chronic Disease Prevention and Health Promotion of the CDC (mailing and Web site addresses were listed previously in the section on Weight Growth). See Table 1.3, Table 1.4, Table 1.5, Table 1.6, Table 1.7, Table 1.8, and Table 1.8 and Fig. 1.20 and Fig. 1.21 for both calculated BMI and normal BMI for age.

**Table 1.3.** Calculated body mass index 40.5–60 inches and 78–94 pounds

**Table 1.4.** Calculated body mass index 44–68 inches and 95–112 pounds

**Table 1.5.** Calculated body mass index 48–76 inches and 114–146 pounds

**Table 1.6.** Calculated body mass index 55–78 inches and 148–180 pounds
Pubertal Changes in Body Composition

**Lean Body Mass** 1. Females: The lean body mass decreases from about 80% of body weight in early puberty to about 75% at maturity. The lean body mass increases in total amount but decreases in percentage because adipose mass increases at a greater rate.

2. Males: The lean body mass increases from 80% to 85% to about 90% at maturity. This primarily reflects increased muscle mass from circulating androgens.

**Adipose Mass** The percentage of body fat increases in females during puberty and decreases in adolescent males (Table 1.9).

<table>
<thead>
<tr>
<th>Stage of puberty</th>
<th>% Body fat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>15.7</td>
</tr>
<tr>
<td>2</td>
<td>16.9</td>
</tr>
<tr>
<td>3</td>
<td>21.6</td>
</tr>
<tr>
<td>4</td>
<td>26.7</td>
</tr>
<tr>
<td>Male</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>14.3</td>
</tr>
<tr>
<td>2</td>
<td>11.2</td>
</tr>
</tbody>
</table>

Percentage of body fat remains unchanged in stages 3, 4, and 5.

TABLE 1.9. Percentage of body fat during puberty
Pelvic Remodeling in Females During puberty the female pelvis widens more rapidly than it increases in the anteroposterior dimension. The forepart of the pelvis also widens and becomes more rounded.

Skeletal Mass Changes in bone mass, or bone mineral density (BMD), parallel the alterations in lean body mass, body size, and muscle strength. Major determinants of BMD are physical activity level, heredity, nutrition, endocrine function, and other lifestyle factors. The accretion of skeletal bone mass during puberty is critical, and peak bone mass is acquired by early adulthood. This serves as the “bone bank” for the remainder of life (Bachrach, 2000).

The skeletal structure also undergoes epiphyseal maturation under the influence of E₂ and testosterone. Skeletal maturation, or bone age, can be determined by comparing a radiograph of an adolescent's hand, wrist, or knee to standards of maturation in a normal population.

Bone age is one index of physiological maturation, providing an idea of the proportion of total growth accomplished. For example, if an adolescent is 15 years old and has a bone age of 12 years, there will be more potential growth than if the same adolescent's bone age were 15 years. The use of skeletal age is discussed further in Chapter 8.

Internal Organs The growth of the brain, heart, liver, and kidneys during puberty is less than that of muscle and bone. Therefore, the percentage of body weight represented by the brain, heart, liver, and kidney decreases from about 10% to about 5% at maturity.

Erythrocyte Mass The change in erythrocyte mass is outlined in Fig. 1.8. The increase in males occurs secondary to increasing levels of circulating androgens.

![FIG. 1.8. Hematocrit values for African-American and white boys (A) and girls (B) during puberty. (From Daniel WA. Hematocrit: maturity relationship in adolescence. Pediatrics 1973;52:388, with permission.)](image)

Biochemical Changes The biochemical changes that occur during puberty reflect the underlying skeletal growth. For example, the serum alkaline phosphatase concentration changes depend on the maturation level (Table 1.10). The levels tend to increase until midpuberty, at which point they decrease until adult levels are attained.

![TABLE 1.10. Serum alkaline phosphatase level](image)

Serum ferritin levels also change during adolescence. About one third of body iron is stored in cells as ferritin or hemosiderin. Ferritin is a macromolecule composed of a protein shell in which can be stored up to 4,500 atoms of iron. Plasma ferritin in healthy persons sensitively reflects total-body iron stores. The test for plasma ferritin is useful because it is as sensitive as that for serum iron and total iron-binding capacity but is more specific, detecting iron deficiency at very early stages.

During childhood and early adolescence, the median plasma ferritin concentration rises from 10 to 45 ng/mL in both males and females. During adolescence, the values diverge. With the male growth spurt, the median level rises to 90 ng/mL and remains there. In the female, the level stays between 25 and 30 ng/mL during the reproductive years as a result of losses during menstruation and pregnancy. Figure 1.9 reviews the changes in body mass, height, weight, and testosterone levels during puberty.

![FIG. 1.9. Correlations between major events of puberty in the average male and female. (From Barnes HV. Adolescent medicine. In: Harvey AM, ed. The principles and practice of medicine, 19th ed. New York: Appleton-Century-Crofts, 1976, with permission.)](image)

SECONDARY SEXUAL DEVELOPMENT DURING PUBERTY The secondary sexual characteristics (pubic hair, breast development, and testes and penile development) are major changes that occur in the adolescent period. In addition to being able to recognize normal and abnormal sexual development, health care professionals must be equipped to answer, and feel comfortable dealing
Sexual Maturity Ratings

To more specifically classify the level of pubertal maturation and more accurately determine normality, a sexual maturity scale is essential. According to the scale developed by Tanner (1962), sexual maturity ratings (SMRs) are divided into five classes based on development of pubic hair and breasts in females and pubic hair and genitalia in males. These stages are described in the following text sections and are shown in both photographs and drawings in Fig. 1.10, Fig. 1.11, Fig. 1.12, Fig. 1.13, Fig. 1.14, Fig. 1.15 and Fig. 1.16 (some find drawings easier to interpret).

FIG. 1.10. Stages of breast development. (From J.M. Tanner, M.D., University of London, Institute of Child Health, with permission.)

FIG. 1.11. Stages of female pubic hair development. (Reproduced from J.M. Tanner, M.D., University of London, Institute of Child Health, with permission.)

FIG. 1.12. Stages of male pubic hair development. (Reproduced from J.M. Tanner, M.D., University of London, Institute of Child Health, with permission.)

FIG. 1.13. Stages of male genital development. (Reproduced from J.M. Tanner, M.D., University of London, Institute of Child Health, with permission.)

FIG. 1.14. Female pubic hair development. Sexual maturity rating 1 (SMR 1): Prepubertal; no pubic hair. SMR 2: Straight hair is extending along the labia and, between ratings 2 and 3, begins on the pubis. SMR 3: Pubic hair has increased in quantity, is darker, and is present in the typical female triangle but in smaller quantity. SMR 4: Pubic hair has increased in quantity, is darker, and is more dense, curled, and adult in distribution but less abundant. SMR 5: Abundant, adult-type pattern; hair may extend onto the medial aspect of the thighs. (From Daniel WA, Palshock BZ. A physician's guide to sexual maturity rating. Patient Care May 30, 1979, with permission. Illustration by Paul Singh-Roy.)
FIG. 1.15. Female breast development. Sexual maturity rating 1 (SMR 1), not shown: Prepubertal; elevations of papilla only. SMR 2: Breast buds appear; areola is slightly widened and projects as small mound. SMR 3: Enlargement of the entire breast with protrusion of the papilla or of the nipple. SMR 4: Enlargement of the breast and projection of areola and papilla as a secondary mound. SMR 5: Adult configuration of the breast with protrusion of the nipple; areola no longer projects separately from remainder of breast. (From Daniel WA, Paulshock BZ. A physician's guide to sexual maturity rating. Patient Care May 30, 1979, with permission. Illustration by Paul Singh-Roy.)

FIG. 1.16. Male genital and pubic hair development. Ratings for pubic hair and for genital development can differ in a typical boy at any given time, because pubic hair and genitalia do not necessarily develop at the same rate. Sexual maturity rating 1 (SMR 1): Prepubertal; no pubic hair. Genitalia unchanged from early childhood. SMR 2: Light, downy hair develops laterally and later becomes dark. Penis and testes may be slightly larger; scrotum becomes more textured. SMR 3: Pubic hair has extended across the pubis. Testes and scrotum are further enlarged; penis is larger, especially in length. SMR 4: More abundant pubic hair with curling. Genitalia resemble those of an adult; glans has become larger and broader, scrotum is darker. SMR 5: Adult quantity and pattern of pubic hair, with hair present along the inner borders of the thighs. The testes and the scrotum are adult in size. (From Daniel WA, Paulshock BZ. A physician's guide to sexual maturity rating. Patient Care May 30, 1979, with permission. Illustration by Paul Singh-Roy.)

Males

1. Genital stage 1 (G1): Prepubertal
   a. Testes: Volume less than 1.5 mL
   b. Phallus: Childlike
2. Genital stage 2 (G2)
   a. Testes: Volume 1.5–6 mL
   b. Scrotum: Reddened, thinner, and larger
   c. Phallus: No change
3. Genital stage 3 (G3)
   a. Testes: Volume 6–12 mL
   b. Scrotum: Greater enlargement
   c. Phallus: Increased length
4. Genital stage 4 (G4)
   a. Testes: Volume 12–20 mL
   b. Scrotum: Further enlargement and darkening
   c. Phallus: Increased length and circumference
5. Genital stage 5 (G5)
   a. Testes: Volume more than 20 mL
   b. Scrotum and phallus: Adult

Females

1. Breast stage 1 (B1)
   a. Breast: Prepubertal; no glandular tissue
   b. Areola and papilla: Areola conforms to general chest line
2. Breast stage 2 (B2)
   a. Breast: Breast bud; small amount of glandular tissue
   b. Areola: Areola widens
3. Breast stage 3 (B3)
   a. Breast: Larger and more elevation; extends beyond areolar parameter
   b. Areola and papilla: Areola continues to enlarge but remains in contour with the breast
4. Breast stage 4 (B4)
   a. Breast: Larger and more elevation
   b. Areola and papilla: Areola and papilla form a mound projecting from the breast contour
5. Breast stage 5 (B5)
   a. Breast: Adult (size variable)
   b. Areola and papilla: Areola and breast in same plane, with papilla projecting above areola

Male and Female: Pubic Hair

1. Pubic hair stage 1 (PH1)
   a. None
2. Public hair stage 2 (PH2)
   a. Small amount of long, slightly pigmented, downy hair along the base of the scrotum and phallus in the male or the labia majora in females; vellus hair versus sexual type hair (PH3)
3. Pubic hair stage 3 (PH3)
a. Moderate amount of more curly, pigmented, and coarser hair, extending more laterally
4. Pubic hair stage 4 (PH4)
a. Hair that resembles adult hair in coarseness and curliness but does not extend to medial surface of thighs
5. Pubic hair stage 5 (PH5)
a. Adult type and quantity, extending to medial surface of thighs

**Importance of Sexual Maturity Ratings**
Certainly, height, weight, and age are important in evaluating an individual. However, during adolescence these three factors do not provide enough information; growth during adolescence is so variable that age is a poor reference point from which to gauge change. Therefore, the SMR is essential when evaluating an adolescent.

The SMR should be recorded at the initial general physical examination and yearly thereafter. Such a record can provide critical information in identifying abnormal puberty or in reassuring the adolescent that he or she is normal. SMRs are also a helpful reference in evaluating the following items:

- **Hematocrit**
- **Alkaline phosphatase**
- **Menarche**
- **Ejaculation**

**TABLE 1.16. Changes in hematocrit values by pubertal stage and race**

**Male Sexual Development**
Male sexual development begins with the attainment of stage G2, at an average age of 11.6 years (range, 9.5 to 13.5 years). Testicular enlargement is the first physical sign of puberty in about 98% of males. During the rest of puberty the testes, epididymis, and prostate increase in size sevenfold, and the phallus usually doubles in size. Ejaculation usually first occurs during SMR 3. SMR 4 is usually associated with fertility, but sperm are usually present in some quantities of ejaculate by SMR 3. The average length of time for completion of puberty is 3 years, but it can range from 2 to 5 years. The sequence of events for an average male and the interrelationship between age, SMR, and PHV can be seen in Fig. 1.17A and Fig. 1.18. The typical sequence is adrenarche, beginning of growth spurt, testicular development, beginning of pubic hair, PHV.

**Female Sexual Development**
Female development begins with the attainment of either stage B2 or PH2. In most females, breast budding is the first physical sign of puberty. Previously, the mean age at onset of female sexual development was 11.2 years. However, in the last decade there has been a decrease in the age at onset of sexual maturation for girls. The mean age at onset of breast development was 8.87 years for African-American girls and 9.96 years for white girls; for the onset of pubic hair development, the mean ages are 8.78 years and 10.51 years, respectively (Herman-Giddens et al., 1999). This has not been associated with any change in the age at onset of menses for white girls, and for African-American girls the mean age at onset of menses has advanced by less than 6 months. The reasons for the earlier onset of sexual development remain unknown, but factors such as improved nutrition, increasing obesity, hormonal exposures, and other environmental/societal alterations have been implicated.

More importantly, the consequences of earlier maturation with regard to teen behavior, sexual activity, and pregnancy need to be addressed with age-appropriate interventions during middle childhood and the preteen years. In addition, the lifetime health consequences of early sexual maturation need to be studied, because early menarche (before age 11 years) has been associated with a twofold increase in breast cancer risk.
During puberty, the female’s breasts develop and the ovaries, uterus, vagina, labia, and clitoris increase in size. The uterus and ovaries increase in size fivefold to sevenfold. Winer-Muram et al. (1989) evaluated the ovaries and uterine length in peripubertal females. The uterine length increased from a mean of 3.3 ± 1.3 cm in girls aged 7 to 8 years to 6.98 ± 1 cm in girls age 15 to 16 years. The corpus-to-cervix ratio increased from 1.1 ± 0.4:1 to 1.33 ± 0.2:1 over the same period. Ovarian size increased from 1.9 ± 0.7 cm³ (age 7 to 8 years) to 3.5 ± 0.4 cm³ (age 15 to 16 years). Fifty-nine of the 75 girls had multiple ovarian cysts ranging from 3 to 10 mm³. The average length of time for completion of puberty is 4 years but can range from 1.5 to 8 years. In the average adolescent female, the growth spurt starts about 1 year before breast development begins. This is followed in an average of 1.1 years by PHV and then by menarche an average of 1 year later. Menarche occurs in 19% of adolescent girls during PH3 and in 56% during PH4. Figure 1.17B and Figure 1.19 show the interrelationships between age, SMR, and growth velocity in girls.

**FIG. 1.19.** Biological maturity in girls. (From Tanner JM. Growth at adolescence, 2nd ed. Springfield, IL: Blackwell Scientific Publications, 1962, with permission. Copyright © 1962 by Blackwell Scientific Publications.)

Zacharias and Rand (1983) examined adolescent growth in height in contemporary American girls and have found the following:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Age in years (mean ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height spurt takeoff</td>
<td>8.69 ± 1.58</td>
</tr>
<tr>
<td>Age at PHV</td>
<td>11.63 ± 1.21</td>
</tr>
<tr>
<td>Completion of PHV</td>
<td>13.10 ± 1.12</td>
</tr>
<tr>
<td>Duration of spurt</td>
<td>4.43 ± 1.21</td>
</tr>
<tr>
<td>Height gained</td>
<td>27.23 ± 7.08</td>
</tr>
</tbody>
</table>

The height at PHV was 91% of adult height, and the spurt contributed to 16.75% of adult height. There is little or no correlation between adult height and either age at onset of growth spurt, age at PHV, velocity at peak, or pubertal height gain. However, there is a correlation between adult height and the height at onset of growth spurt or height at PHV.

PHV occurs later in male adolescents in relationship to sexual development than it does in females.

**Variations of Pubertal Development**

The age at pubertal onset, the duration between SMRs, and the growth of adolescents are highly variable. To provide adequate care to the adolescent, the health practitioner must appreciate these normal variations. The next group of figures and tables outlines useful normal limits for male and female growth and development. Table 1.11 is especially helpful in determining normality of development in males. Specific information provided by the figures and tables is as follows:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Age in years (mean ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date</td>
<td>12.79 ± 1.74</td>
</tr>
<tr>
<td>Age at PHV</td>
<td>13.10 ± 1.12</td>
</tr>
<tr>
<td>Height</td>
<td>27.23 ± 7.08</td>
</tr>
</tbody>
</table>

**TABLE 1.11.** Means and normal variation in the timing of adolescent secondary sexual development (Males)

Figure 1.20, Figure 1.21, Figure 1.22, Figure 1.23, Figure 1.24 and Figure 1.25 are normal growth charts. These growth charts have been revised as of June, 2000. The new CDC Growth Charts for the United States better represent the racial and ethnic diversity and the size and growth patterns of the United States population. New features include addition of the 3rd and 97th percentiles and extension of the charts for children and adolescents to age 20 years. These growth curves can be obtained through the CDC address given previously. Figure 1.26, Figure 1.27, Figure 1.28 and Figure 1.29 are height and height velocity curves for American adolescents, with consideration for those with early, average, and late maturation.

**FIG. 1.25.** Stature-for-age percentiles for boys, 2 to 20 years of age. (From CDC Growth Charts: United States—Advance data. From Vital and Health Statistics of the Centers for Disease Control and Prevention, National Center for Health Statistics, 2000;314:1–28.)
Table 1.11 lists normal variation of timing of secondary sexual development in males.

Table 1.12 shows pubertal growth characteristics in four U.S. longitudinal studies.

Table 1.13 shows pubertal growth characteristics for European, white American, and British children.

Table 1.14 lists male genital size by age.

Table 1.15 lists testicular volume by SMR.

Table 1.16 lists hematocrit values by SMR and race.

Table 1.17 lists serum gonadotropins by pubertal stage in males.
Spermarche

Spermarche, the onset of sperm emission, implies the establishment of spermatogenesis. Spermarche appears to be an early pubertal event, although there is wide variation in adolescents.

Spermarche occurs at a median age of 13.4 years (range, 11.7 to 15.3 years), with an average testicular volume of 11.5 cm³ and a median SMR of 2.5. It precedes PHV in most adolescents and may occur with little or no evidence of pubic hair development (Hirsch et al., 1985; Nielsen et al., 1986). Guizar-Vazquez et al. (1992) found that spermarche occurred at a mean time of G2 and PH1.

Menarche

Menarche is one of the major developmental landmarks of female puberty. It usually occurs in a fairly consistent position (SMR 3 or SMR 4) in pubertal development. The relationship between menarche and age, PHV, and body composition is described in the following paragraphs.

Menarche is Relationship to Age and Physical Growth On average, menarche occurs in American girls at 12 years, 4 months (it varies normally from 9 to 17 years of age). 3.3 years after the start of the growth spurt and 1.11 years after PHV. The age at menarche has gradually decreased during the last century, as illustrated in Fig. 1.30. Recent studies indicate that this trend may be ceasing. Menarche always occurs after the PHV has been attained. Growth after menarche is limited. A 1972 study by Roche and Davila (1972) indicates that between menarche and the attainment of adult stature, girls gain 4.3 cm at the 10th percentile, 7.4 cm at the 50th percentile, and 10.8 cm at the 90th percentile.

The age at menarche depends on such factors as race, socioeconomic status, heredity, nutrition, and culture. It occurs later at higher altitudes, in rural areas, and in larger families.

**Menarche in Relationship to Body Composition** Menarche may be dependent on body composition. Frisch and Revelle (1970) estimated that at menarche the mean adipose mass is 11.5 kg and the percent body fat is 24%. The height and weight of a female adolescent in relation to menarche and ovulatory cycles is outlined in Fig. 1.31.

![Fig. 1.31](image-url) The weight for height at which menarche is likely to occur (solid line) and the weight for height at which regular ovulatory menstrual periods are likely to be maintained (dashed line). (From Frisch RE, McArthur JW. Menstrual cycles: fatness as a determinant of minimum weight for height necessary for their maintenance or onset. Science 1974;185:949, with permission. Copyright © 1974 by American Association for the Advancement of Science.)

**CONCERN ABOUT GROWTH AND DEVELOPMENT**

This chapter has discussed most of the features of normal adolescent growth and development. As essential as it is for the health care provider to have a firm grasp of the facts of normal growth and development, a clear understanding and feeling for what these changes mean to the adolescent are also critically important. As their bodies change, adolescents develop tremendous concern about whether their bodies are right or will be right. The great variation in timing of puberty, with resultant differences in physical maturity of similar-aged adolescents, serves to heighten teenagers' worries. Practitioners must be adept at detecting the adolescent's concerns about height, weight, pubic hair growth, or phallus size, for example, even if these concerns are not stated overtly in the initial complaint.

**SUMMARY**

The changes of puberty are a marvel of nature and a testimony to the intricacies and wonders of the human hormonal system. The health care provider must understand these changes and the wide variations of normalcy. He or she must also be able to sense the profound effect these changes have on the adolescent and be prepared to be a source of information, reassurance, and help if abnormalities are detected.

**WEB SITES**

**For Teenagers and Parents**

- [http://www.youngwomenshealth.org/menstrual.html](http://www.youngwomenshealth.org/menstrual.html): From Young Women's Health Center at Boston Children's Hospital.

**For Health Professionals**


**REFERENCES AND ADDITIONAL READINGS**


2

Psychosocial Development in Normal Adolescents

Mari Radzik, Sara Sherer, and Lawrence S. Neinstein

The Process of Adolescence

The Process of Adolescence

Phases and Tasks of Adolescence

Early Adolescence (Age 10 to 13 Years)

Independence-Dependence Struggle

Body Image Concerns

Peer Group Involvement

Identity Development

Middle Adolescence (Age 14 to 16 Years)

Independence-Dependence Struggle

Body Image Concerns

Peer Group Involvement

Identity Development

Late Adolescence (Age 17 to 21 Years)

Independence-Dependence Struggle

Body Image Concerns

Peer Group Involvement

Identity Development

Conclusion

Web Sites

For Teenagers and Parents

References and Additional Readings

No brief manual can hope to illuminate fully the complicated psychosocial developmental process of adolescence. This chapter offers an elementary framework from which to approach the study of this developmental process and discusses ways to enhance interactions between health care providers and adolescents.

Although in terms of physical development adolescence can be described as the period of life that begins with the appearance of secondary sexual characteristics and terminates with the cessation of somatic growth, in modern Western culture the behavioral aspects of this period have become equally important. Adolescence is, in fact, a biopsychosocial process that may start before the onset of puberty and may last well beyond the termination of growth. The events and problems that arise during this period are often perplexing to parents, health care professionals, and adolescents. It is a time in which, for example, a previously obedient, calm child may become emotionally labile and act out.

It is vital that health professionals who furnish comprehensive care for adolescents understand the adolescent psychosocial developmental process. Such an understanding is not only beneficial in routine adolescent health care but can help adolescents and their families through problem periods involving, for example, failure in school, depression, suicidal tendencies, and out-of-control behavior. This chapter examines the phases and tasks of normal adolescent psychosocial growth and development, beginning with some general comments about the process of adolescence.

THE PROCESS OF ADOLESCENCE

It is important, first, to keep in mind that no outline of psychosocial development can describe adequately every adolescent. Adolescents are not a homogeneous group but display wide variability in biological and emotional growth. Each adolescent responds to life’s demands and opportunities in a unique and personal way. Further, adolescents must meet the challenges that arise from their own high-risk behaviors as well as the many social factors that affect their lives (Galambs and Leadbeater, 2000; Lerner and Galambos, 1998).

Second, the transition from childhood to adulthood does not occur by a continuous, uniform synchronous process. In fact, biological, social, emotional, and intellectual growth may be totally asynchronous. In addition, growth may be accentuated by frequent periods of regression. It must be remembered that all of life, from birth to death, is a constant process of change and that adolescence is not the only difficult period.

Third, whereas adolescence has been described as a period of extreme instability or “normal psychosis,” most adolescents survive with no lasting difficulties, and many are unperturbed by the process (Freud, 1958). In actuality, about 80% of adolescents cope well with the developmental process. Of these 80%, about 30% have an easy continual growth process, 40% have periods of stress intermingled with periods of calm, and 30% have tumultuous development marked by bouts of intense storm and stress. In a national survey, approximately 90% of 16-year-old boys and girls reported that they got along well with their mothers, and 75% reported getting along well with their fathers (Rutter, 1980). Only about one in five families reported difficult parent-child relationships. Overall, major conflict between parents and their adolescent children is not a normal part of adolescence (Steinberg, 1990; Laursen et al., 1998).

Phases and Tasks of Adolescence

Adolescence can be conceptualized by dividing the process into three psychosocial developmental phases:

1. Early adolescence: Approximately age 10–13 years, or middle school years
2. Middle adolescence: Approximately age 14–17 years, or high school years
3. Late adolescence: Approximately age 17–21 years, or the years of college or work after high school

These stages overlap among different adolescents. By the end of adolescence, the emerging adult (Arnett, 2000) has become emancipated from parents and other adults and has attained a psychosocial identity and sufficient resources from education, family, and community to begin to support himself or herself in an emotionally, socially, and financially satisfying way. In addition, the individual has learned how to appropriately seek support from others when needed.

Several tasks characterize the development of the adolescent and are discussed in the following sections in conjunction with the phases of adolescence. These tasks include

1. Achieving independence from parents
2. Adapting peer codes and lifestyles
3. Assigning increased importance to body image and acceptance of one’s body
4. Establishing sexual, ego, vocational, and moral identities

EARLY ADOLESCENCE (AGE 10 TO 13 YEARS)

Early adolescent psychosocial development is heralded by rapid physical changes with the onset of puberty. These physical changes engender self-absorption and initiate the adolescent’s struggle for independence. The onset of puberty, along with the concomitant psychosocial and emotional changes, occurs earlier by 1 to 2 years for girls than for boys. Puberty in more recent studies has begun even earlier than in past years in female adolescents.

Independence-Dependence Struggle

Early adolescence is characterized by the beginning of the shift from dependence on parents to independent behavior. Common events at this time include the
following:

1. Less interest in parental activities and more reluctance to accept parental advice or criticism; occasional rudeness; more realization that the parent is not perfect
2. An emotional void created by separation from parents without the presence of an alternative support group, which can often create behavioral problems (e.g., a decrease in school performance)
3. Emotional liability (wide mood and behavior swings)
4. Increased ability to express oneself through speech
5. Search for new people to love in addition to parents

Body Image Concerns

Rapid physical changes lead the adolescent to be increasingly preoccupied with body image and the question, “Am I normal?” The early adolescent’s concern with body image is characterized by four factors:

1. Preoccupation with self
2. Uncertainty about appearance and attractiveness
3. Frequent comparison of one’s own body with those of other adolescents
4. Increased interest in sexual anatomy and physiology, including anxieties and questions regarding menstruation or nocturnal emissions, masturbation, and breast or penis size

Peer Group Involvement

With the beginning of movement away from the family, the adolescent becomes more dependent on friends as a source of comfort (Damon, 1999). The early adolescent’s peer group involvement is characterized by the following:

1. Solitary friendships with a member of the same sex. This idealized friendship may become intense; boys, for example, may become comrades-in-arms with sworn pacts and allegiances, and young teenage girls may develop deep crushes on men as well as women.
2. Strong emotional, tender feelings toward peers, which may lead to homosexual exploration, fears, and/or relationships.
3. Peer contact primarily with the same sex; some contact with the opposite sex made in groups of friends.

Identity Development

At the same time that rapid physical changes are occurring, the adolescent’s cognitive abilities are improving markedly. In Piaget's (1969) cognitive theory, this corresponds to the evolution from concrete thinking (concrete operational thoughts) to abstract thinking (formal operational thoughts). During this time, the adolescent is expected to achieve academically and to prepare for the future. This period of identity development is characterized by the following:

1. Increased ability to reason abstractly. This ability is usually turned inward, leading to increased self-interest and fantasy. For example, the young adolescent may feel himself or herself constantly “on stage.”
2. Frequent daydreaming, which not only is normal but also is an important component in identity development because it allows adolescents an avenue to explore, enact, problem-solve, and recreate important aspects of their lives.
3. Setting unrealistic or idealistic (depending on the individual) vocational goals (e.g., musician, airplane pilot, truck driver).
4. Testing authority, which is common behavior in adolescents as they attempt to better define themselves and is often one cause of tension between the adolescent and his or her family or teachers.
5. A need for greater privacy, with diary or journal writing often becoming highly important.
6. Emergence of sexual feelings, often relieved through masturbation or the telling of dirty jokes. Girls are often ahead at this point in sexual development.
7. Development of one's own value system, leading to additional challenges to family and others.
8. Lack of impulse control and need for immediate gratification, which may result in dangerous risk-taking behavior.
9. Tendency to magnify one's personal situation (although adolescents often feel that they are continually on stage, they may also be convinced that they are alone and that their problems are unique).

MIDDLE ADOLESCENCE (AGE 14 TO 16 YEARS)

Middle adolescence is characterized by an increased scope and intensity of feelings and by the rise in importance of peer group values.

Independence-Dependence Struggle

Conflicts become more prevalent as the adolescent exhibits less interest in parents and devotes more of his or her time to peers.

Body Image Concerns

Most middle adolescents, having experienced the majority of their pubertal changes, are less preoccupied with these changes. Although there is greater acceptance and comfort with the body, much time is spent trying to make it more attractive. Clothes and makeup may become all-important. Because of the societal emphasis on youthful body image, eating disorders may become established during this developmental phase.

Peer Group Involvement

At no other time than middle adolescence is the powerful role of peer groups more evident (Damon, 1999). Characteristics of this involvement include:

1. Intense involvement by the adolescent in his or her peer subculture
2. Conformity by the adolescent with peer values, codes, and dress, in an attempt to further separate from family
3. Increased involvement in partnering relations, manifested by dating activity, sexual experimentation, and intercourse
4. Involvement with clubs, team sports, gangs, and other groups

Despite the fact that this group of adolescents is susceptible to peer pressure, peer pressure can be overrated. Adolescents’ reactions to peer pressure are extremely varied, and peer pressures can also involve a desire to excel academically, in sports, or in other positive activities.

Identity Development

The abilities to abstract and to reason continue to increase in middle adolescence, along with a new sense of individuality. The middle adolescent’s ego development is characterized by:

1. Increased scope and openness of feelings, with a new ability to examine the feelings of others
2. Increased intellectual ability and creativity
3. Less idealistic vocational aspirations (adolescents with average and below-average intellectual abilities often realize their limitations at this time and may consequently experience lowered self-esteem and depression)
4. A feeling of omnipotence and immortality, leading to risk-taking behavior, which is certainly a factor in the high rates of accidents, suicide, drug use, pregnancy, and sexually transmitted disease that become prevalent at this stage

LATE ADOLESCENCE (AGE 17 TO 21 YEARS)
Late adolescence is the last phase of the adolescent’s struggle for identity and separation. If all has proceeded fairly well in early and middle adolescence, including the presence of a supportive family and peer group, the adolescent will be well on his or her way to handling the tasks and responsibilities of adulthood. If the previously mentioned tasks have not been completed, however, then problems such as depression, suicidal tendencies, or other emotional disorders may develop with the increasing independence and responsibilities of young adulthood. A new conceptualization of the late adolescence period views late adolescents as “emergent adults” especially those age 18 to 25 years (Arnett, 2000). These new young adults have begun to accept responsibility for their behaviors, have started to make their own decisions, and are trying to be financially independent.

Independence-Dependence Struggle

For most, late adolescence is a time of reduced restlessness and increased integration. The adolescent has become a separate entity from his or her family and now may better appreciate the importance of the parents’ values, to the point of allowing their help as partners. Therefore, parental advice may once again be sought and accepted. However, it is not uncommon for some adolescents to be hesitant to accept the responsibilities of adulthood and to remain dependent on family and peers. Characteristics include

1. Firmer identity
2. Greater ability to delay gratification
3. Better ability to think ideas through and express ideas in words
4. More stable interests
5. Greater ability to make independent decisions and to compromise

Body Image Concerns

The late adolescent has completed pubertal development and growth and is typically unconcerned with this process, unless an abnormality has occurred.

Peer Group Involvement

Peer group values become less important to late adolescents as they become more comfortable with their own values and identity. Much time is spent in a relationship with one person. Such relationships involve less exploitation and experimentation and more sharing, with the selection of a partner based more on mutual understanding and enjoyment than on peer acceptance.

Identity Development

The ego development of the late adolescent is characterized by

1. The development of a rational and realistic conscience
2. The development of a sense of perspective, with the abilities to delay, to compromise, and to set limits
3. The development of practical vocational goals and the beginning of financial independence
4. Further refinement of moral, religious, and sexual values

CONCLUSION

No individual’s adolescence exactly fits the description of phases and tasks in this chapter. However, most adolescents follow the general pattern as outlined. An understanding of this general pattern helps health care providers evaluate an adolescent’s behavior. Table 2.1 summarizes the developmental tasks for each phase of adolescence.

TABLE 2.1. Psychosocial development of adolescents

WEB SITES

For Teenagers and Parents


http://www.teenshealth.org/. Site from Nemour Foundation for teens and parents on adolescent issues and development.

http://www.connectforkids.org/. For adults-parents, grandparents, educators, policy-makers, and others who want to become more actively involved with youth.


REFERENCES AND ADDITIONAL READINGS

Arnett JJ. Emerging adulthood: a theory of development from the late teens through the twenties. Am Psychol 2000;5:469.


Steinberg LD. Understanding families with young adolescents. Carrboro, NC: Center for Early Adolescence, 1980.

The style and personality of the practitioner and his/her philosophy of medical care are considered to be most important in the medical care of adolescents. The practitioner should be mature and open-minded. He/she should be genuinely interested in teenagers as persons first, then in their problems, and also in their parents. He/she should not only like teenagers but must also feel at ease with them. He/she should be able to communicate well with his/her patients and their parents. The practitioner should help to enhance family communication while assuring confidentiality when requested around personal issues.

Adapted from Committee on Care of Adolescents in Private Practice of the Society for Adolescent Medicine

Providing care to adolescents in a sensitive, flexible, developmentally and culturally appropriate manner requires interest, time, and experience on the part of practitioners. No book can adequately teach the art of relating to patients or adolescents; it is a skill that is ultimately perfected through practice. A good medical interview with the adolescent is important, because it allows the practitioner not only to collect information but also to set the tone for future interactions. This chapter contains general guidelines for establishing better rapport with adolescents, as well as suggested interviewing techniques. At the end of the chapter there are some suggestions for parents to improve communication with their teen.

GENERAL GUIDELINES FOR THE OFFICE VISIT

Liking the Adolescent

To provide effective care and establish rapport with the adolescent patient, the health care provider must like adolescents. If the practitioner dislikes or is extremely uncomfortable with teenagers, it is best to refer them elsewhere. If the particular condition requires more expertise than the practitioner has or causes personal conflicts about moral or religious issues, the adolescent should be referred elsewhere.

Meeting the Adolescent and Family: The First Session

It is important for the practitioner to introduce himself or herself to the family and to the adolescent as the adolescent’s practitioner. At about the time of puberty, a transition should be made to allow more of the visit to be focused on the adolescent. Practitioners should advance along the visit styles described here as the adolescent matures and the family is known and trusts the adolescent-focused visit. One of three basic approaches may be used to start the interview; the choice may depend on the complexity of the visit, knowledge of the individual and family, and the age of the adolescent.

Separate Time for Family and Adolescent For new, complex patients, the practitioner may need an extensive history from the family and an understanding of their full agenda. The practitioner should greet the adolescent first, explain the order of the visit, and request a few minutes to meet with the parents alone, “about when you were a child.” This gives the parents a few minutes to relate the past history, family history, their agenda, and concerns. Some of these items the parents might not feel comfortable stating in front of the adolescent, such as “I am afraid he has cancer” or “I think she is sexually active and needs birth control.” Having this information at the start of the interview will improve the focus of the whole visit, rather than having it spill out at the end of the visit. Next, the adolescent should be seen alone for additional history, discussion of confidentiality, and physical examination. The adolescent should be present from the time he or she meets with the
practitioner through to the end of the visit so that the adolescent does not feel that the practitioner is divulging confidential information to the family. This approach allows discussions with the parents about issues they may feel are sensitive. Follow-up visits can start with a very brief meeting with the parents alone, if major issues persist, but should rapidly switch over to one of the other types of visit, described next.

**Family Together** Some health care providers prefer to see the family and adolescent together first. This approach can yield a great deal of information in the first few minutes regarding family dynamics. For example, if the adolescent is asked why he or she wants to be seen and the mother quickly answers for the adolescent, a sense of the adolescent-mother relationship is gained. When the family is seen together, it is helpful to have the teen introduce the family members to the practitioner. This gives the adolescent the message that the practitioner is primarily interested in him or her. After this part of the interview, the adolescent should be interviewed and examined alone.

**Adolescent Alone** Another basic approach is to start by interviewing the adolescent alone. Some health care providers favor this approach in the belief that it quickly helps to establish rapport and a sense of trust. However, it is important to inform the adolescent that some input regarding his or her past history will be required from the parent during the initial interview. At this point, the family may be brought in to continue the interview. Whichever method is used, the adolescent should be the primary information source. This approach is especially important for older adolescents.

**Summarizing** At the end of any of the three visit types described, the practitioner should summarize the issues and plans with the adolescent. Issues that can or must be discussed with the family can be summarized with the family and the adolescent together, so that the adolescent can hear how the information is presented and discussed with the family and all concerns can be addressed. As the adolescent becomes a young adult, the full visit will tend to be with the young person. If family members come with the young adult, they can be included in a brief summary at the end if this is helpful for the support the of young person or to assist the young person with adherence to complex treatment regimens.

**Office Setup**

**Space** Adolescents prefer their own waiting area in a pediatrician's office. They do not like to be treated as young children. It is helpful if the waiting room has materials such as pamphlets that are appropriate for adolescents and health education brochures. A separate waiting area or corner of the waiting room should be set aside for adolescents and young adults, or separate blocks of time should be used so that age-appropriate materials can be displayed. If the office is used for other age groups, one examination room should be set aside for use with teens. For privacy, the examination table should be facing away from the door or an inner curtain should be added.

The office should have enough room to accommodate the family as well as the adolescent. It is preferable not to interview the adolescent and family in the examination room on the first comprehensive visit. The desk in the office should be oriented so that the health care provider sits beside the desk, not behind it. Placing a large desk between the adolescent and oneself can create an artificial barrier.

**Appointments** Usually, initial comprehensive visits for an adolescent should be scheduled to last 1 hour. Obviously, there may be time constraints based on the practice setting. If the practitioner is pressed for time, doing the history at the first visit and the physical examination on another day is a reasonable approach. Most follow-up appointments should be scheduled for after-school hours. At the end of the first visit, a decision should be made with the teen and the family as to whether the adolescent can make future visits on his or her own. Transportation needs may limit this option for young adolescents in some practice settings, but the permission to come to visits on his or her own is important.

**Billing** The issue of fee payment should be discussed early. This can even be done when the first appointment is made. Confidentiality can be maintained by using nonconfidential billing codes when the parents are paying for services. The adolescent must realize that an insurance payment may result in parents finding out about visits and the diagnosis; however, a neutral diagnosis can be used in most situations.

Ideally, a mutual agreement can be reached with the adolescent and parents in this area. Alternatives include:

1. Confidential billing (if the insurance company allows), so that the parents are not aware of the exact nature of the visits
2. Having the adolescent pay for his or her own bills on a flexible installment plan with reduced fees
3. Having the adolescent obtain Medicaid funds for conditions such as pregnancy, family planning, and substance abuse
4. Referral to a clinic that can provide free confidential care

**Availability of Educational Materials** It is helpful to place books, pamphlets, hot line numbers, and reliable Web site information in the waiting room or office on topics such as puberty, sexually transmitted diseases, sexuality, and contraception. The presence of such materials helps the adolescent to feel that it is "O.K." to talk about these subjects. Helpful materials and Web sites are listed at the end of this chapter.

**Avoiding Interruptions** Constant interruptions or phone calls during the interview tend to decrease rapport. The office staff should hold all nonemergency questions or phone calls until after the interview.

**Note Taking** The practitioner should take as much as possible during the interview. For referred patients, the content of letters to referring primary care providers concerning confidential issues should be discussed with the adolescent.

**Establishing Rapport**

Establishing rapport with an adolescent, especially with a nonverbal or hostile teenager, can be difficult. Helpful suggestions include the following:

1. Begin the interview by introducing yourself to the teen and parents or guardians. It is helpful to shake the hand of the adolescent.
2. Begin by chatting informally about friends, school, or hobbies. Not only does this decrease tension, but also it enables the practitioner to gain important insights into the adolescent's personality, mood, and thought content.
3. Let the adolescent talk for a while, even if he or she meanders.
4. Treat the adolescent's comments as seriously as you would an adult's. The teenager should feel you are treating him or her as a person, not as a child or patient.
5. Start with nonthreatening health questions, such as a review of systems, especially if the adolescent is highly tense or suspicious.
6. Explore with the adolescent the issues that concern him or her. These issues may differ radically from concerns expressed by the parents.

**Ensuring Confidentiality**

It is important to establish a sense of confidentiality with the adolescent. The limits of this confidentiality may vary depending on the type of medical practice and current laws of a particular state. The adolescent should be aware of these limits. For example, it should be explained that discussions will be kept confidential unless a problem becomes a threat to the adolescent or to others or unless the adolescent is consulted first. When there are concerns about safety, the practitioner should relay to the adolescent that this is a situation that needs to be shared with the parents. Adolescents are often more willing to discuss topics with their parents in the safer environment of the practitioner's office, and the practitioner can help facilitate the discussion of difficult topics.

Many parents are naturally concerned about being separated from their teen during the interview process. One approach is to explain to the parents early the philosophy of your practice, for example: “As we are proceeding in gathering information about John, I would like to tell you both how I work with adolescents. After I finish talking with all of you together, I am going to speak with John alone for a few minutes. Then I will take him to the examination room for a physical examination. When this is done, I will call you back to go over the findings and my recommendations. During this time, I may discuss some matters that John would prefer I keep in confidence. It has been my philosophy to respect that confidence. Certainly, if there were any serious problem that was a threat to John's life or health I would inform you. Now, before we break as a group, are there any other concerns that you have about John that we have not discussed?”

**Avoiding a Surrogate Parent Role**
Rather than being a surrogate parent, the health care provider should function as an extraparental adult. The emphasis should be on listening, advising, and guiding, using as nonjudgmental an approach as possible.

Avoiding an Adolescent Role

The adolescent is looking for a practitioner who can be a sensitive and mature resource, not someone who is “one of the gang” and who dresses and talks like an adolescent.

Sidestepping Power Struggles

It is difficult to force adolescents into action. In other words, no one is better at being an adolescent than an adolescent. Do not try, therefore, to beat adolescents at their own game. Teenagers respond better if they can arrive at their own conclusions.

Acting as an Advocate

The adolescent encounters any number of adults who are nonsupportive and who stress the adolescent's negative attributes. Try to emphasize an adolescent's positive characteristics and abilities. Keep in mind, however, that supporting the adolescent in “down” times is not the same as supporting inappropriate behavior.

Importance of Listening

Listening can often be the key to developing rapport with an adolescent. However, listening can be difficult, as thoughts usually wander or focus on the next response. The health care provider should practice his or her listening skills to give full attention to the adolescent's statements and feelings. Good listening skills include:

1. Staying focused on what the teen is telling you
2. Asking questions that help move the conversation along
3. Being cautious about giving advice before being asked
4. Using gender-neutral terms until the adolescent has indicated his or her preferences
5. Trying to understand the teen's perspective

Instilling Responsibility

Adolescents should be made aware that they are responsible for their own care. The more responsibility that adolescents take for their personal progress, the fewer problems that occur with compliance. Adolescents have a great ability to instill guilt in health care providers. The practitioner can feel overwhelmed with the burden of changing the adolescent's life and habits. This burden should be shifted onto the adolescent.

Displaying Interest and Concern

The adolescent must be able to feel the health care provider's interest and concern. Shrugging off concerns as unimportant is a sure way to alienate the adolescent.

Family and Parents

Although the adolescent may be the primary patient, the parents cannot be overlooked. Parental input and insight are crucial, for in a real sense the family is the patient. Often the full agenda of the visit cannot be understood without initial input from the parents. To ignore the family's involvement in an adolescent's problem can often prolong the problem. Families must be consulted for the following reasons:

1. To elucidate past medical history, family history, and present concerns
2. To understand family dynamics and structure
3. To alleviate the parents' sense of rejection or guilt
4. To help bring about changes in the family unit and in the adolescent
5. To negotiate fair and consistent limits
6. To support the adolescent in complex treatment regimens
7. To ensure consistency of follow-up and referral care

Nonverbal Cues

Much can be learned by observing the adolescent's body language, such as hand movements, manner of sitting, eye movements, or eyes slightly brimming with tears when certain subjects are discussed.

Process Versus Content

Although inappropriate behavior should not be condoned, the health care provider must explore the reasons behind the action. For example, shoplifting may occur secondary to peer pressure or family or school problems. Positive comments supporting the adolescent's health choices can help the adolescent recognize his or her strengths and resist peer pressure.

Hidden Agenda

Adolescents often present with chief complaints that are unrepresentative of their true concerns. A female adolescent presenting with mild sore throat, acne, or pelvic pain may in actuality be afraid she is pregnant or has a sexually transmitted infection. A male adolescent with chest pains may be concerned about gynecomastia. Gentle but persistent exploration of the adolescent's concerns is often necessary before the true chief complaint is evident. If an adolescent girl is extremely reluctant to communicate or has vague symptoms, a pregnancy test should be considered.

Developmentally Oriented Approach

In the course of interviewing and evaluating the adolescent, the health care provider should be conscious of the adolescent's developmental process and tasks. The areas of sex, school performance, family, peer group, identity, and future should all be explored. Evaluative expectations should be based on the stage of emotional development the adolescent has attained. Early or middle adolescents, for example, certainly cannot be expected to think and behave as logically as adults. Below are sample questions regarding various adolescent tasks:

1. **Body image**: Do you have any questions or problems with the physical changes you are experiencing? Do you like yourself as you are? What would you change? Many teens have questions about periods, wet dreams, or changes in breasts or pubic hair; do you?
2. **Peer relationships**: Who is your best friend? How many close friends do you have? What kinds of activities do you participate in? What do you do for fun?
3. **Independence**: Do you get along with your parents? Over what issues do family arguments occur? Is your privacy respected at home?
4. **Identity**: Are you satisfied with the way things are going for you? If you could change certain aspects of your life, what would you do and why? Are you working now? What are your plans for the future?
5. **Sexuality**: Are you dating? Do you have a particular girlfriend or boyfriend with whom you are serious? Do you have questions or concerns about sexual activities, contraception, sexually transmitted diseases, or pregnancy?

Another approach that colleagues have taken at Children's Hospital of Los Angeles to obtain psychosocial/developmental information has been the HEADSS interview, covering the topics of home, education, activities, drugs, sex (activity, orientation, and sexual abuse), and suicide. An advantage of this approach is that the
practitioner moves from less personal questions to more personal and potentially threatening questions.

Home. Where is the teen living? Who lives with the teen? How is the teen getting along with parents and siblings? Have there been any recent moves? Has the teen ever run away? Has the teen ever been incarcerated? The practitioner should not begin with a statement such as, “Tell me about your parents,” because this question assumes that the teen has two living parents.

Education. Is the teen in school? What is the teen good at and bad at in school? What classes are particularly interesting or boring? What grade average does the teen maintain? Has the teen repeated or failed any classes? Has the teen received any suspensions? How is the teen getting along with teachers? What goals does the teen have when he or she finishes school? If the teen is older or out of school, the practitioner should ask about employment. The practitioner should avoid asking, “How is school?” because this will lead to the answer, “O.K.”

Activities. What does the teen do after school? What does the teen do to have fun and with whom? Does the teen participate in any sports activities? Community or church activities? What reading does the teen do? What music does the teen like? Does the teen have or use a car, and does the teen use seat belts? What are the teen’s hobbies? Does the teen use a helmet when using a bicycle or roller blades? Does the teen have friends? A best friend? How much time does the teen spend watching television or playing video games? Do not start with a question such as, “Do you have any activities or hobbies?”, such a question results in only a “Yes” or “No” response.

Drugs. What types of drugs are used by the teen’s peers? What types of drugs do family members use? What types of drugs does the teen use and in what amount and frequency? Does the teen use intravenous drugs? What is the source of income to pay for these drugs? The manner in which these questions are asked can significantly alter the responses. Consider the following examples.

MD 1: Do you ever use drugs?

Teen: No!

That probably would end the questioning on drug use.

MD 2: I know that drugs are fairly common on school campuses. What drugs are common on your campus?

Teen: Oh, I don’t know, maybe pot and crack.

MD 2: It is not uncommon for some teens to try some of these drugs. Have any of your friends tried them?

Teen: & Some of them.

MD 2: How do you handle the situation when your friends are using drugs? Do you ever try?

Teen: Yeah, once in a while. I really have only tried pot, and that was only twice.

MD 2: The two most common drugs that I have seen teens use are often not thought of as drugs. These are alcohol and cigarettes. How much alcohol do you drink in a week?

Teen: Oh, I usually don’t drink during the week, but on weekends I really get blasted almost every Friday and Saturday night.

Sexuality. Is the teen dating? What are the degree and types of sexual experience? Is the teen involved with another individual in a sexual relationship? Does the teen prefer sex with the same, opposite, or both sexes? Has the teen had sexual intercourse? How old was the teen in his or her first sexual encounter? How many partners does the teenager have? Is there a concern about masturbation? Has the teen had a sexually transmitted disease, and what are the teen’s knowledge base and concerns about sexually transmitted diseases? Does the teen use contraception and with what frequency? Does the teen or the partner use condoms and with what frequency? Is there a history of pregnancy or abortion? Does the teen enjoy sexual activity? Sexuality is another area in which the style of questioning can dramatically alter the response. Consider the following examples.

MD 1: Are you sexually active?

Teen: No.

MD 1: Tell me about your boyfriend or girlfriend.

Teen: I don’t have one.

In this instance, the teen may not even know what “sexually active” means or may think that the term implies a certain frequency of sexual intercourse. In addition, asking only about heterosexual relationships may close the opportunity to find out about homosexual concerns or behavior.

MD 2: I mentioned that I may be asking you some questions that were personal but very important to your health. Again, this is information that I will be keeping confidential. The area I want to discuss has to do with relationships. Are you going out with anyone right now?

Teen: Yes.

MD 2: What is this person’s first name?

Teen: Bill.

MD 2: As you know, there are many teens who are sexually active. By that I mean that they have had sexual intercourse. There are also many teens who have chosen not to have sexual intercourse. How have you handled this part of your relationship with Bill or with other boys you have dated?

Teen: I have not had sex with Bill yet, although we are thinking about it. I did have sex once about 6 months ago at a party.

Suicide. Has the teen had any prior suicide attempts? Does the teen have any current suicidal ideation? It is very appropriate to ask direct questions about suicidal ideation, such as, “Have you ever thought about killing yourself?” or “Have you ever tried?” or “Would you kill yourself?” or “Do you have a plan?” Direct questions do not precipitate suicidal action and are the best way to obtain such information.

Sexual or Physical Abuse. In any teen who has significant problems in any of the previously mentioned areas, it is crucial to ask about physical and sexual abuse. This includes individuals with runaway behavior, significant family dysfunction, change in school grades, lack of friends, substance abuse, early onset of sexual activity, or history of suicide attempts. Questions regarding sexual orientation and sexual abuse are particularly sensitive for the adolescent. These questions need to be introduced with an explanation of why they are being asked. Refer to Chapter 40 and Chapter 82 for further discussion of adolescent homosexuality and adolescent sexual abuse, respectively.

Physical Examination

The physical examination provides an excellent opportunity to educate the adolescent about his or her changing body. For example, the female adolescent may be taught to perform routine breast examinations, or the young male adolescent may be reassured about genital development. The adolescent may, in addition, raise concerns not mentioned during the initial interview. The true chief complaint may, in fact, be revealed during the physical examination.

Another issue of concern has been the question of who should be present during the physical examination. In general, the adolescent is examined without the presence of the guardian or parent. However, some adolescents prefer to have the parent present. The teen could be asked first whether he or she preferred that the parent be in the room during the examination. Particularly, younger adolescents and developmentally delayed adolescents may wish to have a parent or guardian with them.

Male practitioners should use a chaperon during the breast and genital examination of female patients. Theoretically, the same concept would hold for a female examiner during genital examination of a male, although this usually has not occurred in clinical practice.

Closure

At the close of the initial or follow-up visit, the health care provider should address the following issues.

1. Provide a brief summary of the proposed diagnosis and treatment, addressed primarily to the adolescent. Parents who accompany the adolescent to the visit should be included in a final discussion of the nonconfidential issues, so that they can help support the plans.

2. Discuss any other resources available to the adolescent.
3. Allow the adolescent time to discuss any final questions or concerns.
4. Schedule any follow-up appointments.
5. Inform the adolescent that the health care provider is available at other times. The adolescent should feel free to make follow-up appointments or telephone calls for either medical or emotional reasons.

INTERVIEWING

The following is a list of suggestions to assist the practitioner during the interview:

1. Shake hands with the adolescent first.
2. Ask questions in context.
3. Avoid lecturing and admonishing.
4. Bring the adolescent into the present. If the adolescent is focusing on his or her homework or on yesterday's date with a girlfriend or boyfriend, the interviewer is unlikely to gather much useful information.
5. Focus initial history taking on the presenting complaints or problems.
6. Identify who has the problem (i.e., is this problem the teen's concern or the parents').
7. Take a neutral stance.
8. Usually, the less the interviewer says, the better.
10. Avoid writing during the interview, especially during sensitive questioning.
11. When asking direct questions, (a) use less personal questions before more personal questions, (b) use open-ended questions, and (c) use gender-neutral terms.
12. Talk in terms that the adolescent will understand.
13. Do not misinterpret the adolescent's response.
14. Criticize the activity, not the adolescent.
15. Highlight the positive.
16. Assess your own ability to listen. A practitioner's difficulty in listening may be related to his or her own resentments or opinions of the adolescent's behavior.

Listed next are recommended interviewing techniques. Some aspects of interviewing, such as the initial introduction and establishing of rapport, were mentioned earlier in the general guidelines.

Open-ended Questions

The use of open-ended questions, such as, “Tell me more about it” or “What does your pain prevent you from doing?” or “What was that like for you?” often facilitate communication better than the use of direct questions, such as, “Did that make you feel bad?”

Reflection Responses

The reflection response mirrors the adolescent's feelings. Consider the following example.

MD: How do you like school?
Teen: I hate it.
MD: You hate it?
Teen: Yeah, my teachers always....

Restatement and Summation

Stopping to restate the adolescent's feelings or to summarize the interview may often help to clarify the problem or encourage the adolescent to make additional comments. An example might be, “Let me see if I understand. You really like Jim, but you do not want to have sexual intercourse with him. However, you feel if you say no, he will stop liking you and drop you for someone else.”

Clarification

Asking the adolescent to clarify a statement or feeling may help to crystallize the problem. Asking, “What did you mean by that?” can also be useful in clarifying colloquial jargon. For example:

Teen: My friend and I like to go scamming. We do it most every weekend.
MD: Scaming? Help me out with that one? What does that mean?

Not only does such a question open up communication, but it makes the teen feel like an authority on a subject and that the practitioner is human too and does not know everything.

Insight Questions

Some questions may give the health care practitioner better insight into the adolescent:

What do you do well?
If you had one wish, what would it be?
When are you the happiest?
What do you do when you're angry?
What do you see yourself doing in 1 or in 5 years?
What do your mother and father do when you are not there?
What do you do when you are not in school?

Reassuring Statements

The use of reassuring statements when dealing with embarrassing subjects may often facilitate discussion. For example: “Almost all boys your age masturbate or play with themselves, and this is normal. I wonder if you do this sometimes?”

Support and Empathy

A noncriticizing response that recognizes and acknowledges the adolescent's feelings is often helpful during the interview. Examples of this type of response are, “I can really understand how bad that must have felt” or “That really must have made you feel sad” or “I'm impressed that you have taken care of yourself so well, despite all the problems that you've had” or “You are making some really healthy choices.”

Special Interview Problems

1. Garrulous adolescent: The overtalkative adolescent can sometimes be directed with a statement such as, “I can see you like talking about this. Why?”
2. Quiet adolescent: With the quiet adolescent, getting him or her to talk about any subject, such as school, sports, or television, can often help to break the silence.
3. Anxious adolescent: The use of reassuring statements is frequently effective. An example is: "It is often difficult to talk about ————."

4. Angry adolescent: Clarify how you as the practitioner might be able to help the adolescent, for example, "It sounds as though some help discussing some of these issues with your parents might be useful."

**Interview Structure**

The interview may meander, but it should have structure, including a beginning, middle, and end:

1. The beginning of the interview should include introductions, attempts to put the adolescent at ease, and an explanation of what will be happening and why.
2. The middle part of the interview should move into defining the adolescent's problems and feelings. Treat his or her comments seriously. Listen to the teenager.
3. The end of the interview should include informing the adolescent about the results of the examination and about what will happen next. Time should be provided for the adolescent to ask questions before summarizing with the adolescent and the parents (if available).

As stated at the beginning of the chapter, developing interviewing skills requires practice and interest on the part of the examiner. Reviewing one's interviews through the use of video equipment is an excellent technique for improving skills. Such techniques are of special value for practitioners, who rarely undergo observation in their training. Appropriate consent from both the teen and the parent or guardian should be obtained.

Alternative techniques such as written questionnaires and computer surveys can also be used in conjunction with the verbal interview to obtain information about the adolescent. Personal questions and answers that could be seen by the parents or others in the waiting area should be avoided.

**Written Questionnaires**

Several questionnaires are employed in the Teenage Health Center at Children's Hospital of Los Angeles and are found in Chapter 4 of this volume. Cavanaugh (1986) and Frazier (1998) have described other questionnaires.

**Computer Surveys**

The computer can be a nontargeting format to some adolescents. Paperny developed interactional questionnaires for teens on areas such as psychosocial risk profile, adolescent pregnancy, and family planning. These are available from David Paperny, Teen Health Computer Programs, 2516 Pacific Heights Road, Honolulu, HI 96813-1027. A private carrel in the clinical area may be required when sensitive issues are included.

**Family Considerations**

As noted earlier, the patient is the product of the family. To fully understand the adolescent or to effect change requires interviewing and working with the family. The definition of family has changed over time, and part of understanding a patient includes understanding the patient's family, including biological family and family of choice. There are many possible family constellations, including single-parent families, stepfamilies, blended families, foster families, adoptive families, extended families, and families of choice. The dynamics of the family and the relationships among the different subsystems (spouse, parent/child, or sibling) should be understood. Family cultural and ethnic backgrounds are important for providers to understand. Not all health care providers want to or should provide family therapy. But any health care provider who wishes to provide comprehensive care to adolescents must feel comfortable interviewing and working with families. The following articles may be especially helpful:


The following books also provide some excellent references for dealing with families:


**Internal Considerations**

Although the health care provider should be careful not to project feelings about his or her own adolescence onto a teenager being treated, remembering one's own adolescence can help the professional to empathize with teenagers. Try immersing yourself in adolescent feelings and experiences by asking yourself the following questions:

- What did I look like at 13 years old? 15 years old? 18 years old?
- What things embarrassed me the most?
- What physical problems worried me the most?
- What was my first sexual experience like?
- What things did I enjoy most during those years?
- How much did I confide in my parents?
- Who was my best friend? What did we do together?
- What things started arguments between my parents and me?
- How did I feel about my parents and my siblings?
- How much did I confide in my parents?
- What was my first date like?
- What did I like most about school? What did I like the least?
- What dreams did I have for the future?
- How did I develop as an individual separate from my family?

**RECOMMENDATIONS TO PARENTS OF ADOLESCENTS**

Parents often ask health care providers for suggestions of reference books or of methods for coping better with adolescents. Helpful methods for parents might begin with the same recommendations previously stated for health care providers.

**General Guidelines**

1. Listen to the teenager.
2. Treat his or her comments seriously.
3. Avoid power struggles.
4. Be flexible.
5. Show interest and concern in the adolescent's activities.
6. Spend time together and time alone together.
7. Show trust in the teenager.
8. Make resources available to the adolescent.
9. Strive for a good communication in the family between working together, playing together, and loving. Playing and having fun together is an important part of establishing good parent-teen relationships.

Challenges of Teen Years

Parents should be aware that even though most adolescents do well and go through adolescence without too much distress, it can be a challenging time period. The challenges faced by parents of teenagers include the following.

1. Parents must adapt to change in the relationship with their teen, as the teen's peers become an increasingly important influence and the teen seeks increasing independence.
2. Parents must limit testing and experimentation by teens. Teens may experiment with many different types of behaviors, including sex, drinking, and using other drugs. However, parents should remember that, despite how teens may act, the vast majority accept their parents' basic values. In one study, more than 75% of adolescents even reported accepting their parents' discipline practices (Rutter, 1980). Teen experimentation does not mean that teens reject their parents' basic values.
3. Parents must not overreact to rejection of one or both parents by the teen for a time period.
4. Parents must recognize that separation is difficult for teens and their parents, and there may be harder and easier times.
5. Adolescents are at maximal growth velocity and change and may be more vulnerable to social risks such as drugs, sexuality, domestic violence, and poverty.
6. Modern family issues, such as less family support, more divorce, less extended families, and more working families, add additional challenges.
7. Excessive exploitive and violent messages through the media add to the challenges of the teen years for parents.
8. Adolescents' feelings of invulnerability also add to their willingness to expose themselves to risks.

Daydreaming

Parents worry about teenagers' wasting time and daydreaming. However, parents should be reassured that this is a normal part of the adolescent developmental process.

Communication

The practitioner should encourage parents to avoid barriers to communication, including:

1. Comparison with other teenagers
2. Lecturing or moralizing
3. Minimizing a problem
4. Excessive talking
5. Taking over an adolescent's problem
6. Taking everything too seriously
7. Overreacting, especially reaching conclusions based only on appearance, dress, or language
8. Phrases such as
   a. The trouble with you is....
   b. How could you do this to me?
   c. Is that all? I thought it was something important.
   d. In my day....
   e. You're wrong.
   f. How could you feel like that?
   g. That's a dumb thing to say.
   h. Don't bother me now.
   i. You're stupid...crazy...incompetent.
9. The "shoulds": My child should be what I want him to be, he should satisfy my needs, or she should always feel loving.

The practitioner should encourage the parents to stress positive aspects of communication:

1. Empathize with the adolescent.
2. Stress the positive attributes of the adolescent. Adolescents get enough negative feedback. A dose of positive feedback and reinforcement when they do good work, such as follow-through on their chores, can go a long way in positive communication.
3. Deliver clear messages.
4. Respect each other's privacy.
5. Keep a sense of humor.
6. Resolve conflicts together. Decisions that occur in the home about the adolescent should involve the adolescent's input. This can take place in the form of weekly family meetings. In this way, the adolescent is much more likely to carry through with the decisions. Family meetings or brainstorming sessions can be a helpful way to resolve conflicts. During brainstorming sessions to resolve conflicts parents should
   a. Involve all family members in the process.
   b. Come up with at least five possible solutions.
   c. Write down all possible suggestions even if they seem outrageous.
   d. Avoid criticisms.
   e. Employ some humor when possible.
   f. Take a break if the session becomes too argumentative.
   g. Discuss the pros and cons of the most viable alternative ideas.
   h. After writing down several possible suggestions, try to agree on one solution or a solution that combines two different suggestions. Parents may also wish to ask other families how they solved similar problems and situations. (A good resource on family problem solving is Forgatch M, Patterson G. Parents and adolescents: living together. Part 2: family problem solving. Eugene, OR: Castalia Publishing, 1989.)
7. Involve teens in topics they like. When several hundred youths were asked what they wished to discuss with their parents, the top eight topics were
   a. Family matters: Discussions about decisions that affected the whole family or themselves, such as allowance, curfew, and rules.
   b. Controversial issues locally or nationally
   c. Emotional issues
   d. The "whys" of life
   e. The future
   f. Current affairs
   g. Personal interests of the teen
   h. Parents' life histories

Parents should also remember that, overall, parents may in fact be more bothered and remember conflicts with their teens longer than the teens do. Parents may sulk more than teens and recover more slowly.

Limit Setting
Adolescents need firm, fair, and explicit limits. Again, involvement of the adolescent in the limit-setting process is beneficial.

**House Rules** Some families work better together if there is a set of “house rules.” These prescribe the expectations for behaviors and guidelines for the family to live together as a group. Well-defined house rules can become quite important during the adolescent years. Having these rules discussed and written down can avoid conflicts over what behaviors are acceptable. If there is a particular problem in following a rule, then the parents may want to implement associated consequences if the rule is broken. However, the rules should be fair and consistent and should involve input from the teen. Adolescents may be eager to participate in the establishment of such rules when they find out that they might include a rule such as, “No one will enter someone else’s room without knocking first.” Rules are mainly needed for teen or family member behaviors that are a problem. There should probably be a maximum of five to ten rules. Here is a sample set of house rules adapted from Patterson and Forgatch (1987):

1. Dinner will be at about 6 p.m., and everyone is expected to be home and ready to eat at that time.
2. Family members are expected to speak courteously to each other.
3. Before opening someone’s door, knock and wait for an answer.
4. If you make a mess, you clean it up.
5. Going out on school nights must be discussed in advance. Schoolwork must be caught up beforehand.
6. Parties must be prearranged, and an adult must be present at the party.
7. Without an adult present, only teens of the same sex are allowed in the home.
8. Curfew on weekdays is 10:30 p.m. and midnight on weekends.
9. The car must be returned when borrowed, with the same amount of gas that it had previously.

These are just samples and should be changed to meet each family’s needs, expectations, and values.

**Requests That Work** A key to making requests that work is limiting their number. Trained observers have found that normal mothers make 17 requests per hour, and mothers from problem families average more than 27 requests per hour. Lobitz and Johnson (1975) found that when parents were asked to increase the number of requests they made to their children, the rate of problem behaviors and noncompliance doubled. Key components in making useful requests from teens include the following.

1. Decrease or limit the number of requests.
2. Make well-timed requests. Timing of requests or other feedback to adolescents is critical. Poorly timed requests (e.g., while teen is doing homework, on the phone, or in a bad mood) will surely be met with anger, refusal, or rebellion.
3. Make requests in a polite and pleasant manner.
4. Make requests one at a time. Dumping three or four requests on a teen at once is another behavior sure to trigger noncompliance and anger from the teen.
5. Use statements rather than questions in making a request
   a. Question approach:
      - Parent: John, how would you like to take out the garbage tonight?
      - John: No Dad, I’m busy with homework tonight.
   b. Statement approach:
      - Parent: John, please take out the garbage now, it is your turn.
      - John: I’m busy Dad.
      - Parent: John, take out the garbage.

6. Make requests specific. For example, if giving the teen a time to be home from a movie, it should be a specific time, not “early.”

In a study of compliance to parental requests, Patterson and Forgatch (1987) found that the average rate of compliance from normal children to requests from mothers was 57% and from fathers 47%. So parents should expect at least a 50% to 60% rate of compliance.

Practitioners can refer parents to numerous books, articles, Web sites, and other resources, a sampling of which are listed here.

**WEB SITES**

**For Teens and Parents**

http://www.awarefoundation.org/, AIDS and HIV information resource.
http://www.teenhealthfx.com/, Site to provide teens with a fun way to get factual health and medical information, funded through the Atlantic Health System’s Morristown Memorial Hospital, Overlook Hospital, Mountainside Hospital and The General Hospital Center at Passaic.

**For Parents**

http://www.tnpsc.com/, Web site dedicated to providing parents with comprehensive and responsible guidance.
http://www.teenwire.com/, Information for teens from Planned Parenthood Federation of America.
http://www.girlshealth.org/, The Gay Lesbial Bisexual and Transgender Health Access Project is a collaborative project between the Massachusetts Department of Public Health and its four founding organizations, the Justice Resource Institute, The Medical Foundation, and JSI Research and Training.
http://www.youngwomenshealth.org/, The Gay Leasial Bisexual and Transgender Health Access Project is a collaborative project between the Massachusetts Department of Public Health and its four founding organizations, the Justice Resource Institute, The Medical Foundation, and JSI Research and Training.
http://www.parentsagenda.com/, Parenting site.
http://www.awarefoundation.org/, AWARE is devoted to educating adolescents about making responsible decisions regarding their wellness, sexuality, and reproductive health.
http://www.kidsgen.org/, Health information for teens and parents.
http://www.teenwire.com/, Information for teens from Planned Parenthood Federation of America.
http://www.healthfinder.gov/, National Women’s Health Information Center from Office of Women’s Health.
http://www.healthfinder.gov/, National Clearinghouse on Drug and Alcohol Information.
http://www.awarefoundation.org/, AWARE is devoted to educating adolescents about making responsible decisions regarding their wellness, sexuality, and reproductive health.
http://www.education.indiana.edu/cas/adol/adol.html, Adolescence Directory On-Line (ADOL) is an electronic guide to information on adolescent issues.
http://www.activekids.com/For-Parents, Parenting site.
http://www.healthfinder.gov/, National Women’s Health Information Center from Office of Women’s Health.

**Requests That Work** A key to making requests that work is limiting their number. Trained observers have found that normal mothers make 17 requests per hour, and mothers from problem families average more than 27 requests per hour. Lobitz and Johnson (1975) found that when parents were asked to increase the number of requests they made to their children, the rate of problem behaviors and noncompliance doubled. Key components in making useful requests from teens include the following.

1. Decrease or limit the number of requests.
2. Make well-timed requests. Timing of requests or other feedback to adolescents is critical. Poorly timed requests (e.g., while teen is doing homework, on the phone, or in a bad mood) will surely be met with anger, refusal, or rebellion.
3. Make requests in a polite and pleasant manner.
4. Make requests one at a time. Dumping three or four requests on a teen at once is another behavior sure to trigger noncompliance and anger from the teen.
5. Use statements rather than questions in making a request
   a. Question approach:
      - Parent: John, how would you like to take out the garbage tonight?
      - John: No Dad, I’m busy with homework tonight.
   b. Statement approach:
      - Parent: John, please take out the garbage now, it is your turn.
      - John: I’m busy Dad.
      - Parent: John, take out the garbage.

6. Make requests specific. For example, if giving the teen a time to be home from a movie, it should be a specific time, not “early.”

In a study of compliance to parental requests, Patterson and Forgatch (1987) found that the average rate of compliance from normal children to requests from mothers was 57% and from fathers 47%. So parents should expect at least a 50% to 60% rate of compliance.

Practitioners can refer parents to numerous books, articles, Web sites, and other resources, a sampling of which are listed here.

**WEB SITES**

**For Teens and Parents**

http://www.awarefoundation.org/, AIDS and HIV information resource.
http://www.teenhealthfx.com/, Site to provide teens with a fun way to get factual health and medical information, funded through the Atlantic Health System’s Morristown Memorial Hospital, Overlook Hospital, Mountainside Hospital and The General Hospital Center at Passaic.

**For Parents**

http://www.awarefoundation.org/, AWARE is devoted to educating adolescents about making responsible decisions regarding their wellness, sexuality, and reproductive health.
http://www.kidsgen.org/, Health information for teens and parents.
http://www.teenwire.com/, Information for teens from Planned Parenthood Federation of America.
http://www.girlshealth.org/, The Gay Lesbial Bisexual and Transgender Health Access Project is a collaborative project between the Massachusetts Department of Public Health and its four founding organizations, the Justice Resource Institute, The Medical Foundation, and JSI Research and Training.
http://www.youngwomenshealth.org/, The Gay Leasial Bisexual and Transgender Health Access Project is a collaborative project between the Massachusetts Department of Public Health and its four founding organizations, the Justice Resource Institute, The Medical Foundation, and JSI Research and Training.
http://www.parentsagenda.com/, Parenting site.
http://www.awarefoundation.org/, AWARE is devoted to educating adolescents about making responsible decisions regarding their wellness, sexuality, and reproductive health.
http://www.education.indiana.edu/cas/adol/adol.html, Adolescence Directory On-Line (ADOL) is an electronic guide to information on adolescent issues.
http://www.activekids.com/For-Parents, Parenting site.
http://www.healthfinder.gov/, National Women’s Health Information Center from Office of Women’s Health.
OTHER RESOURCES

Books for Parents and Families


Books for Teens


REFERENCES AND ADDITIONAL READINGS


The goals of preventive health care for adolescents are to promote optimal physical and mental health and to support healthy physical, psychological, and social growth and development. Because the most common morbidities and mortalities of adolescence today are preventable health conditions associated with behavioral, environmental, and social causes, preventive services for adolescents should reflect these shifts in etiology. Therefore, visits to a health care provider should reinforce positive health behaviors, such as exercise and nutritious eating, while discouraging health-risk behaviors such as those associated with unsafe sexual behaviors, unsafe driving, and use of tobacco or other drugs. Although the incidence of serious medical problems during adolescence is low, adolescence is a time during which lifelong health habits are established. Furthermore, numerous issues and concerns may emerge during adolescence that affect overall health and well-being. Therefore, adolescence becomes an ideal period for health professionals to invest time in health promotion and preventive services.

In the current health care environment, characterized by limited resources, managed care, and evidence-based medicine, it is essential to determine what constitutes appropriate, cost-effective, and relevant preventive services for any age group. Unfortunately, little empiric research has been done to help address the effectiveness of preventive services for adolescents. Nevertheless, a variety of preventive services guidelines have been proposed.

Elster (1998) comprehensively reviewed recommendations for adolescent clinical preventive services developed by national organizations (Table 4.1). In 1989, the U.S. Preventive Services Task Force (USPSTF), convened by the Office of Disease Prevention and Health Promotion, U.S. Department of Health and Human Services, developed recommendations on periodic health examination based on the health risks of specific age groups (available at http://odphp.osophs.dhhs.gov/). To the extent possible, these recommendations were evidence-based, but they also relied on expert opinion. The recommendations were updated in 1996.

<table>
<thead>
<tr>
<th>TABLE 4.1. Comparisons among recommendations for adolescent preventive services</th>
</tr>
</thead>
</table>

In 1992, the American Medical Association (AMA) released Guidelines for Adolescent Preventive Services (GAPS). GAPS is a comprehensive package of recommendations aimed at the delivery of preventive services in primary care settings (Table 4.2). The GAPS recommendations were developed by the AMA's Division of Adolescent Health, with the assistance of a national scientific advisory board, to address highly prevalent health issues and those most likely to cause serious morbidity. GAPS recommendations cover both the content and delivery of health care to adolescents (Fig. 4.1). Information on these recommendations can be found at the AMA Web site (http://www.ama-assn.org/adolescents) and the GAPS Web site (http://www.ama-assn.org/ama/pub/category/2279.html).

<table>
<thead>
<tr>
<th>TABLE 4.2. GAPS recommendations</th>
</tr>
</thead>
</table>
Caring for adolescents requires a different approach, format, and style than does caring for either children or adults, so it is not surprising that many health care providers report discomfort caring for adolescents. This discomfort is exacerbated when sensitive health concerns.

**General Suggestions for Providing Adolescent Preventive Services**

**Preventive Services Visit**

The American Academy of Family Physicians (AAP) offers age-specific recommendations for periodic health examinations for healthy patients (available at [http://www.aafp.org](http://www.aafp.org)). The AAP recommendations are derived from the USPSTF report by the Commission on Public Health and Scientific Affairs of the AAFP.

Finally, the American Academy of Pediatrics (AAP) also reviewed preventive care for children and adolescents and published revised recommendations in 1995. These recommendations represent “a consensus by the Committee on Practice and Ambulatory Medicine in consultation with national committees and sections of the American Academy of Pediatrics.” In 1996, the AAP also released Guidelines for Health Supervision III which more comprehensively describes the elements of health supervision visits for children and adolescents. Information is available on their Web site ([http://www.aap.org](http://www.aap.org)).

The various recommendations for adolescent preventive services are compared in Table 4.1. These appear to be more similarities than differences. All of the recommendations support the immunization schedule of the Advisory Committee on Immunization practices, and all advocate health guidance for teens. The GAPS, Bright Futures, and AAP also recommend health guidance for parents, as a strategy to assist them in supporting the growth, development, and changing needs of their adolescent. Screening and counseling for various health risks are also a common feature of the recommendations from each of the five organizations, though there is some variability in the specific recommendations for screening. Periodicity may be the most important distinction among the five sets of recommendations. GAPS, Bright Futures, and the AAP specifically recommend annual visits for preventive services, whereas the USPSTF and AAP recommend visits every 1 to 3 years based on the specific needs of the individual.

Although guidelines help to standardize and provide structure to the range of preventive services offered to adolescents, service delivery remains an even more challenging issue. Research in the last two decades has clearly demonstrated both the limitations of the current delivery system and the value of offering services in a wide range of settings and formats. Still, preventive services remain inconsistently delivered, and in some settings they are delivered at dangerously low rates. These findings are easy to understand but difficult to resolve. It is well known, for example, that adolescents are generally considered “healthy,” that they are reluctant health care consumers, and that their access to health care is limited by issues related to reimbursement, confidentiality, transportation, and the training of the providers who care for them.

Solving these problems remains even more vexing. Establishing a broader context for adolescent “health” is a matter for public and professional education. To better serve adolescents, preventive services must be available in a wide range of health care services. These include private physicians’ offices; within health maintenance organizations (HMOs); in community-based adolescent health, family planning, and public health clinics; and as part of school-based and school-linked health services. Reimbursement for these services will continue to be problematic. National standards of care such as those discussed in this chapter may increase the likelihood that payers will begin to provide reimbursement for adolescent preventive services. However, for adolescent preventive services to become routinely available to all adolescents will require a dramatic shift in both health care provider and health care consumer expectations—from a reactive, acute care orientation to a proactive view that values health promotion and disease prevention.

**PREVENTIVE CARE FOR ADOLESCENTS**

Many of the most effective health promotion and disease prevention strategies aimed at adolescents are straightforward and consistent among the various recommendations and guidelines discussed earlier (GAPS, Bright Futures, USPSTF, AAP, and AAFP). In this context, the Society for Adolescent Medicine has endorsed the use of guidelines as a strategy to improve the delivery of adolescent preventive services (information available at [http://www.adolescenthealth.org](http://www.adolescenthealth.org)). Furthermore, because health-risk behaviors and health habits have their genesis in adolescence, healthy behaviors and lifestyle choices established during adolescence have the potential to persist into adult life and to have a strongly positive impact on adult health as well.

**Priority health behavior goals for adolescents include the following** (from [www.health.gov/healthypeople](http://www.health.gov/healthypeople)):

- Consistently use seat belts while driving
- Never drive while drinking or using drugs
- Consistently using condoms if sexually active
- Never smoking
- Eating a prudent diet
- Getting regular aerobic exercise

**Clinical Settings for Adolescent Preventive Services**

Improving the delivery of adolescent preventive services depends on the integration of standards and service delivery across multiple systems and points of access, including public clinics, managed care organizations, private physician offices, school-based and school-linked clinics, and community-based agencies. In fact, there is evidence to suggest that traditional office-based care for teens may fall short of the care they receive in other settings. Blum et al. (1996) studied adolescent preventive services in a variety of practice settings and showed that the highest level of preventive care was delivered in teen clinics while the lowest level of preventive care occurred in private pediatric or family practices. Potential explanations for these disparities include the specific teen focus of teen clinics and limitations within the private practices related to provider comfort and/or training addressing teen issues, time pressures, limited reimbursement, and so on. Similarly, a study of a California managed care organization demonstrated better performance with adolescent preventive services than that provided by physicians in private practice settings. Success in this managed care setting may have been related to confidentiality policies, frequently reported recommendations for annual visits, or other factors.

School-based and school-linked health resources have become more important in the overall landscape of health services available to adolescents (see [http://www.gwu.edu/mrg](http://www.gwu.edu/mrg)). Adolescents who use school-based health services are highly satisfied with the care they receive. Moreover, school-based and school-linked services seem to play a unique and complementary role in meeting the health needs of some teens. For example, there is evidence to suggest that teens may be more willing to access school-health rather than traditional health resources to address mental health, substance use, and reproductive health concerns.

**Preventive Services Visit**

**General Suggestions for Providing Adolescent Preventive Services**

Caring for adolescents requires a different approach, format, and style than does caring for either children or adults, so it is not surprising that many health care providers report discomfort caring for adolescents. This discomfort is exacerbated when sensitive
health concerns must be discussed or treated, or when providers feel ill-trained or ill-equipped to manage the specific issues before them. Although there is no substitute for proper training or a teen-friendly office environment, the following general suggestions provide a framework for the delivery of adolescent health services:

1. Create a comfortable and conducive atmosphere for discussion, disclosure, and counseling by ensuring privacy, minimizing interruptions, and giving the adolescent your full respect and attention.
2. Confidentiality is of paramount importance to teens; therefore, a foundation of confidentiality should be established so that the teen feels comfortable with the provider and trusts him or her enough to discuss sensitive subjects. Especially when discussing sensitive issues, the examiner should be direct, empathetic, and nonjudgmental.
3. Most of the history should be obtained privately and directly from the teenager. Still, it is valuable to obtain additional history from parents, both to corroborate the teen's history and to gather additional information. Ideally, one should have the opportunity to speak with parents both alone and together with the adolescent.
4. Screening for health-risk behaviors (e.g., use of drugs or alcohol, drinking and driving) and providing developmentally appropriate guidance should be an integral and essential component of a preventive services visit.
5. There should be adequate time left at the end of the visit to summarize the session and to answer questions from the adolescent.
6. The physical examination provides an excellent venue to discuss concerns that the adolescent might have about a particular body region. Growth and development is especially important to discuss with younger adolescents. Teaching and encouraging breast or testicular self-examination can be done as part of the physical examination for older adolescents.

Questionnaires and Other Health Screening Tools

Questionnaires and screening forms can be efficient tools for collecting information, thereby reducing the amount of time spent with patients. Some patients also find it easier to disclose sensitive information via questionnaire than face-to-face. Screening questionnaires and personal interviews may therefore be considered complementary, and neither will be adequate in all situations. Many clinics, programs, and practices elect to create their own questionnaires based on their unique knowledge of their individual practice. The AMA's GAPS program has published a series of carefully constructed and updated questionnaires for both adolescents and their parents (Fig. 4.2, Fig. 4.3, Fig. 4.4, and Fig. 4.5). There are longer versions best suited to new patients and shorter versions suitable for returning patients. The questionnaires are also available in Spanish and are easily modified for providers who wish to individualize them. They may be obtained from the American Medical Association (http://www.ama-assn.org/adolescent).

FIG. 4.2. Comprehensive initial preventive services questionnaire for adolescents. (From Guidelines for adolescent preventive services [Recommendations monograph]. Chicago: American Medical Association, 1995.)

FIG. 4.3. Comprehensive initial preventive services questionnaire for parents/guardians. (From Guidelines for adolescent preventive services [Recommendations monograph]. Chicago: American Medical Association, 1995.)

FIG. 4.4. Brief periodic preventive services questionnaire for adolescents. (From Guidelines for adolescent preventive services [Recommendations monograph]. Chicago: American Medical Association, 1995.)

FIG. 4.5. Brief periodic preventive services questionnaire for parents/guardians. (From Guidelines for adolescent preventive services [Recommendations monograph].
Screening tools that have been more formally and rigorously validated can be useful in practice, particularly to screen for behavioral and mental health problems. For example, the Beck Depression Inventory is a well validated and easily administered tool to screen for depression. The 21-question inventory is designed for adolescents and is simple to use and score in a busy clinical setting. A wide variety of other tools are available to screen for family function, behavioral difficulties, and other mental health problems.

**Computer-aided Screening and Assessment** In this information age, there is increasing interest in using technology to assist in providing preventive services to adolescents. Computer-aided screening, information kiosks, and Internet-based health information are all being investigated as tools to increase access to information and resources, as well as to deliver preventive services in the most cost-effective manner possible. For example, Paperny and Hedberg (1999) tested a low-cost strategy to provide preventive services to adolescents with the use of computerized health assessments, individualized educational videos, trained health counselors, and nurses. They found that the majority of adolescents preferred the computer-assisted visits to standard office visits and that preventive services could be delivered at a very modest cost. Further work will be required to assess the utility of this strategy in affecting health outcomes.

**History**
A comprehensive history is the most important aspect of the preventive services evaluation. As with any history, essential domains include past medical history, family history, psychosocial history, and an age-appropriate review of systems. Any current health concerns should also be sought. When preventive services are delivered in the setting of a visit made with another specific agenda (e.g., sports physical, acute medical problem), the patient's agenda should be fully addressed before preventive services are offered.

**Past Medical History** Past medical history is best obtained from both the adolescent and the parents and should include the following:
1. Childhood infections and illnesses
2. Prior hospitalizations and surgery
3. Significant injuries
4. Disabilities
5. Medications, including prescription medications, over-the-counter medications, complementary or alternative medications, vitamins, and nutritional supplements
6. Allergies
7. Immunization history
8. Developmental history, including prenatal, perinatal, and infancy history; history of problems with walking, talking, eating, or learning; peer relations; and school functioning
9. Mental health history, including a history of hospitalization, outpatient counseling, medications, school interventions, or other treatment

**Family History** Most information about family history is most accurately obtained from the parents. It should include the following:
1. Age and health status of family members
2. History of significant medical illnesses in the family, such as diabetes, cancer, heart disease, tuberculosis, hypertension, or stroke
3. History of mental illness in the family, such as mood disorders, anxiety disorders, schizophrenia, or alcoholism
4. Vocational status of parents

**Psychosocial History** The psychosocial history is obtained primarily from the adolescent while he or she is interviewed alone. Some material will also be gathered from the parents or from interviews with the family together. Obtaining much of this information is dependent on successfully establishing trust and rapport between the practitioner and the adolescent. Many clinicians rely on the HEADSS acronym to guide their psychosocial history. The original acronym included home, education, activities (including information about peers), drugs, sexuality, and suicide (mental health). A more up-to-date incarnation of the acronym—HEEADSS—includes additional questions covering eating and safety (see Chapter 3). A complete psychosocial history includes the following areas:
1. Family: Family configuration and family members; living arrangements; relationships between the adolescent and family members; and relationships among other family members
2. School/Work: Academic or vocational success; future plans; and safety at school or in the workplace
3. Peers: Friendships with peers of the same and opposite sex; recreational activities; dating activity and relationships; and sexual activity
4. Eating: Brief nutrition history; concerns about weight or body image; or disordered eating behaviors
5. Substance use: Personal use of tobacco, alcohol, illicit drugs, anabolic steroids; peer substance use; family substance use; and driving while intoxicated
6. Sexuality: Sexual orientation; sexual activity; and sexual abuse
7. Mental health: Feelings of sadness, loneliness, depression; pervasive boredom; inappropriately high levels of anxiety; or suicidal thoughts
8. Safety: Risk of unintentional injury; risk from violence; fighting or weapon carrying

**Review of Systems**
The review of systems covers the following areas.
1. Vision: Trouble reading or watching television; vision correction
2. Hearing: Infections, trouble hearing, earaches
3. Dental: Prior care, pain, concerns (e.g., braces)
4. Head: Headaches, dizziness
5. Nose and throat: Frequent colds or sore throats; respiratory allergies
6. Skin: Acne, moles, rashes, warts
7. Cardiovascular: Exercise intolerance, shortness of breath, chest pain, palpitations, syncope, physical activity
8. Respiratory: Asthma, cough, smoking, exposure to tuberculosis
9. Gastrointestinal: Abdominal pain, reflux, diarrhea, vomiting, bleeding
10. Genitourinary: Dysuria, bed-wetting, frequency, bleeding
11. Musculoskeletal: Limb pain, joint pain or swelling
12. Central nervous system (CNS): Seizures, syncope
13. Menstrual: Menarche, frequency of menses, duration, menstruation or metrorrhagia, pain
14. Sexual: Sexual activity, contraception, pregnancy, abortions, sexually transmitted diseases (STDs) or STD symptoms

**Physical Examination**
The physical examination is another important component of the screening evaluation of the adolescent. The examination allows the clinician to assess growth and pubertal development and to instruct the adolescent in methods of self-examination of important areas of health promotion. The physical examination also affords the adolescent an opportunity to ask about any specific health concerns, and it provides the clinician with the opportunity to detect unnoticed diseases. The examination should be performed in such a way as to preserve the adolescent's modesty. Main elements of the physical examination (Fig. 4.8) include the following topics.
**Height, Weight, and Vital Signs** Height, weight, blood pressure, and pulse should be measured. The serial measurement of height and weight allows for monitoring of the adolescent's growth and for the detection of obesity. Body mass index (BMI) should be calculated. Gender-specific age-based BMI norms are available and are used in assessing risk for obesity (Fig. 4.7, Fig. 4.8, and Fig. 4.9). Blood pressure should be recorded with an appropriately sized cuff. If blood pressure is elevated, it should be rechecked on at least three separate visits before a diagnosis of hypertension is made (Fig. 4.10, Fig. 4.11 and Fig. 4.12).

**FIG. 4.6.** Adolescent physical examination form. (From *Guidelines for adolescent preventive services [Recommendations monograph]*. Chicago: American Medical Association, 1995.)

**FIG. 4.7.** Body mass index calculation for selected weight and stature. (From *Guidelines for adolescent preventive services [Recommendations monograph]*. Chicago: American Medical Association, 1995.)

**FIG. 4.8.** Tracking of height, weight, and body mass index by age: girls. (From *Guidelines for adolescent preventive services [Recommendations monograph]*. Chicago: American Medical Association, 1995.)

**FIG. 4.9.** Tracking of height, weight, and body mass index by age: boys. (From *Guidelines for adolescent preventive services [Recommendations monograph]*. Chicago: American Medical Association, 1995.)

**FIG. 4.10.** The 90th and 95th percentiles for blood pressure by age and gender. (From *Guidelines for adolescent preventive services [Recommendations monograph]*. Chicago: American Medical Association, 1995.)
Vision Screening  Among 12- to 17-year-old adolescents, about 25% have visual acuity of 20/40 or less. This condition often develops during early adolescence. Adolescents should have a vision screening on their initial evaluation and every 2 to 3 years thereafter. This can be done with a standard Snellen chart or a similar test. To pass a line the adolescent should view the chart with one eye covered and be able to read one half or more of the line correctly. Referral should be made for vision less than 20/30 in either or both eyes.

Hearing Screening  Every adolescent should have at least one test for hearing screening performed during the adolescent years. It is important that this test be performed in a quiet room to allow for detection of subtle defects that may be contributing to a learning problem. Screening examinations usually are conducted at frequencies of 1,000, 2,000, and 4,000 Hz at 20 dB. Referral for more comprehensive hearing testing is indicated if there is a failure to hear 1,000 or 2,000 Hz at 20 dB or 4,000 Hz at 25 dB. The more comprehensive threshold test evaluates for the lowest intensity of sound heard at frequencies of 250, 1,000, 2,000, and 4,000 Hz. Evaluation is indicated with a threshold of 25 dB at two or more frequencies or 35 dB for any frequency.

Sexual Maturity Rating  The sexual maturity rating (SMR), discussed in Chapter 1, is the method by which pubertal development is evaluated and described. Because many “normal values” in adolescents depend more on SMR than on age, evaluation of SMR is important not only in describing pubertal milestones but also in adequately assessing many physical parameters (e.g., BMI), and laboratory values (e.g., hemoglobin).

Skin  Check for evidence of acne, warts, fungal infections, and other lesions. Carefully inspect moles, especially in patients who are at particular risk for melanoma.

Teeth and Gums  Teeth and gums frequently present problems in the adolescent age group. Check for evidence of dental caries or gum infection. Look for signs of smokeless tobacco use. Enamel erosions are sometimes the first clue to the self-induced vomiting associated with some eating disorders. Regular checkups with a dentist should be encouraged.

Neck  Check for thyromegaly or adenopathy.

Cardiopulmonary  Check for heart murmurs or clicks.

Abdomen  Check for evidence of hepatosplenomegaly, tenderness, or masses.

Musculoskeletal  The musculoskeletal examination is especially important in adolescent athletes, in whom instabilities or other evidence of previous injury is the best predictor of future injury. Check for signs of overuse syndromes or osteochondroses. Check for scoliosis, particularly in premenarchal females.

Breasts  Examine for symmetry and developmental variations; in girls, assess SMR. Examine for masses or discharge; in boys, identify gynecomastia (present in approximately one third of pubertal males). Teach and encourage breast self-examination to adolescents when developmentally appropriate.

Neurologic  Test strength, reflexes, and coordination.

Genitalia (Male)  Examine the penis and testicles. Assess SMR. Look for signs of STDs. Retract the foreskin in uncircumcised patients. Check for hernia.

Pelvic Examination (Female)  A pelvic examination is indicated for female adolescents who have ever been sexually active and for any female adolescent who requests an examination. In addition, pelvic examination is indicated for female adolescents with pelvic pain, an atypical or changing vaginal discharge, or an undiagnosed menstrual disorder. Annual pelvic examinations have been recommended for all women beginning at approximately 18 years of age, even if they are not sexually active. More recently, however, this practice has been questioned, and it remains controversial. Annual pelvic examinations clearly are recommended for sexually active female patients (see Chapter 48).

Rectal Examination  Rectal examination is not routinely indicated as a screening procedure in the male adolescent. It is sometimes, but not always, part of the female pelvic examination.

Laboratory Tests  Laboratory tests should be kept to a minimum in the asymptomatic adolescent. Suggested screening tests include the following.

Hemoglobin or Hematocrit  During adolescence there is a significant prevalence of iron deficiency anemia due to rapid growth, poor nutritional habits, exercise, and menstrual losses. A screening hemoglobin or hematocrit is recommended at the first encounter with the adolescent or at the end of puberty, or both. Although the normal levels remain stable for females throughout adolescence, the normal levels in males are dependent on age and, more importantly, on SMR. Lower levels of the normal hematocrit in white male adolescents range from 35.6% at SMR 1 to 40.6% at SMR 5; in African-American male adolescents this range is slightly lower, from 34.3% (SMR 1) to 39.3% (SMR 5).
Urinalysis A routine urinalysis, including a dipstick test for glucose and protein and a microscopic evaluation, is recommended at the first encounter with the adolescent or at the end of puberty, or both. However, up to one third of healthy adolescents have small amounts of proteinuria that is nonpathological and requires no treatment (see Chapter 28). Abnormal pyuria requires further investigation for urinary tract infection and, in males, for Chlamydia infection.

Sickle Cell Screening Screening for sickle cell anemia is recommended at the first visit with an African-American adolescent if it has not been documented already.

Sexually Active Adolescents Suggested tests for sexually active adolescents include the following.

Females

Annual Pap smear, cervical gonorrhea and chlamydia culture or nonculture test, and vaginal wet mount are recommended. Syphilis serology should be considered in high-risk populations or where syphilis is prevalent. Screening for the human immunodeficiency virus (HIV) should be offered to all sexually active adolescents and should be encouraged for adolescents with any history of STD.

Cholesterol and Fasting Triglyceride Testing Targeted cholesterol and fasting triglyceride testing is indicated in adolescents with heart disease, hypertension, diabetes mellitus, or a family history of heart disease or hyperlipidemia. Intervention is indicated for individuals with a total cholesterol level greater than 180 to 200 mg/dL on repeated testing (see Chapter 12). Some authorities advocate at least one screening cholesterol test during adolescence. Targeted screening in adolescents misses one third to one half of those teens with elevated cholesterol concentrations. However, the recommended intervention for most adolescents with mild to moderate hyperlipidemia is a low-fat diet, which can be taught to all adolescents.

Males

A leukocyte esterase test on the first 15 mL of a random urine sample is recommended to screen for Chlamydia infection. However, there is concern about the sensitivity and specificity of this test. In high-risk populations, annual urethral screening for gonorrhea and chlamydia by culture or nonculture test can be encouraged.

Human Immunodeficiency Virus Antibody Testing Routine screening for antibody to HIV is a controversial matter. Individuals at risk should be encouraged to receive HIV testing after a discussion regarding the benefits and possible negative consequences of the results (see Chapter 39). Individuals with any STD should be screened for others, including HIV infection.

Tuberculin Testing A purified protein derivative (PPD) tuberculin skin test should be considered at the first encounter with the adolescent based on an assessment of individual risk factors and recommendations of the local health department (in high-risk areas, screening is usually recommended yearly).

1. A tuberculin skin test is indicated for adolescents with known or suspected contact with persons with tuberculosis (TB); for adolescents with clinical or radiographic findings suspicious for TB; for adolescents emigrating from countries where TB is endemic; and for adolescents traveling to endemic countries or who have contact with persons from those countries.
2. Annual tuberculin skin test is recommended for HIV-infected adolescents, adolescents living in homes with HIV-infected persons, and incarcerated adolescents.
3. Adolescents exposed to HIV-infected individuals, homeless persons, or nursing home residents; institutionalized adolescents; adolescents who use illicit drugs; migrant farm workers; and adolescents exposed to adults with any of these characteristics should have a tuberculin skin test every 2 to 3 years.
4. Tuberculin skin test screening is recommended once during adolescence for those whose parents migrated from regions of the world with high TB prevalence and for those without specific risk factors who live in high-prevalence areas as determined by local public health agencies.

Recommendations from the Centers for Disease Control and Prevention (CDC) on interpretation of the PPD results include the following points.

1. An induration 5 mm or larger is classified as positive in the following persons:
   a. Those who have HIV infection or risk factors for HIV infection but unknown HIV status
   b. Those who have had recent close contact with persons with active TB
   c. Those with suspected TB based on clinical or radiographic evidence
2. An induration 10 mm or larger is classified as positive in all persons who do not meet any of the criteria above but who have other risk factors for TB, including the following:
   a. Those in high-risk groups
      i. Injection drug users known to be HIV seronegative
      ii. Persons who have other medical conditions that reportedly increase the risk of progression from latent TB infection to active TB, including:
         - Sarcoidosis
         - Gastroctomy or jejunoileal bypass
         - Being 10% or more below ideal body weight
         - Chronic renal failure with renal dialysis
         - Diabetes mellitus
         - High-dose corticosteroid or other immunosuppressive therapy
         - Some hematologic disorders, including malignancies such as leukemias and lymphomas
         - Other malignancies
   b. Children younger than 4 years of age
   c. Those in high-prevalence groups
      i. Persons born in countries in Asia, Africa, the Caribbean, and Latin America that have high prevalence of TB
      ii. Persons from medically underserved, low-income populations
      iii. Residents of long-term care facilities (e.g., correctional institutions, nursing homes)
      iv. Adolescents from high-risk populations in their communities, as determined by local public health authorities
3. An induration 15 mm or larger is classified as positive in persons who do not meet any of the above criteria. Recent converters are defined on the basis of both size of induration and age of the person being tested:
   a. An increase of 10 mm or more within a 2-year period is classified as a recent conversion for persons younger than 35 years of age
   b. An increase of 15 mm or more within a 2-year period is classified as a recent conversion for persons 35 years of age or older

IMMUNIZATIONS

Obtaining the immunization history and completing the proper immunizations is increasingly important in the care of adolescents, because a variety of common childhood diseases are appearing during adolescence and the young adult years. This is a group that still has significant rates for nonimmunization. During 1999, persons age 20 years or older accounted for 32% of reported measles cases, and children and adolescents (age 5 to 19 years) accounted for 26% of cases. The rate of rubella susceptibility and risk for rubella infection are highest among young adults. Approximately 13.8% of rubella cases in which the age of the patient was reported occurred in youth age 10 to 24 years (CDC, 1994). With increasing immunization rates, especially among the young, there is a corresponding decrease in the incidence of vaccine-preventable disease, with fewer opportunities for the nonimmunized population to be exposed to these diseases at a young age. As a result, there is an expansion of the nonimmunized, susceptible adolescent population.
With the advent of ever-newer vaccines, adolescents previously considered to be fully vaccinated suddenly find themselves “behind.” The challenge of ensuring that adolescents’ immunizations are up-to-date is compounded by the substantial number of adolescents who have received their immunizations in more than one place; inadequate documentation of prior vaccination remains a significant issue in the adolescent population. The issue of documentation may be resolved over time with the development of electronic health records. Vaccine records remain a mourning target; clinicians are well advised to keep abreast of the latest vaccine recommendations of the Advisory Committee on Immunization Practices (ACIP) of the CDC. The current immunization schedule is available at http://www.cdc.gov. In addition, international travel information is available at http://www.cdc.gov/travel.

**Diphtheria, Tetanus, Pertussis**

Though it is now well known that adolescents and adults have frequent pertussis infections, pertussis vaccination is not recommended after 7 years of age, owing to the low prevalence of serious infections and the high incidence of serious side effects. Boosters of adult tetanus and diphtheria toxoids (Td) are recommended routinely every 10 years after the initial series. The timing of this first booster usually occurs during early adolescence. The ACIP recommends that adolescents be assessed at ages 11 to 16 years and receive a booster if no dose was received during the preceding 5 years. Side effects may include local reactions such as erythema or induration, occasionally Arthus hypersensitivity reactions, and rarely systemic reactions such as urticaria and anaphylaxis. Td boosters should be given every 10 years after the initial series throughout life.

**Measles**

Measles has been decreasing dramatically in the United States, with 441,703 cases in 1960; 47,351 in 1970; 13,506 in 1980; 2,933 in 1988; and 312 in 1993. There was an increase to 963 in 1994, but the number dropped to 396 in 1995, and case numbers in 1997 and 1998 reached all-time lows. In 1999, only 100 confirmed measles cases were reported to the CDC, which equaled the record low number of cases. Measles is not considered endemic in the United States at this time; the incidence is less than 0.5 cases per 1,000,000 population. Of the 100 reported cases in 1999, 33 were imported and 67 were indigenous, of which 33 were also import-linked and 34 were unknown-source cases.

Although the potential still exists for measles epidemics on college campuses, reported case numbers are low at present because of cyclical changes in measles incidence, improvement in measles vaccination coverage among preschool-age children, and increased use of a second dose of vaccine among school- and college-age youth. Because of the low incidence of measles, suspected cases should be confirmed by serology. Because of the problem of waning immunity, it is now universally recommended that children and adolescents receive a second vaccination either at primary school or on entry to junior high school. If these opportunities are missed, the vaccine should be caught up whenever it is needed to prevent disease in such cases, but it will help to prevent future infection. There is no evidence of efficacy of immune globulin.

**Exposed Susceptible Adolescents** Unvaccinated adolescents exposed to measles should receive measles vaccine. If more than 5 days has elapsed since exposure, immune serum globulin (IVIG), 0.25 mL/kg, is also given.

**Immunosuppressed Adolescents** Vaccination with live measles virus, or any other live virus, is contraindicated in immunosuppressed patients and in those receiving immunosuppressive therapy. At present, information available on MMR vaccination among asymptomatic and symptomatic HIV-infected individuals has not demonstrated serious or unusually adverse events. Therefore, HIV-infected patients can be immunized so long as they are not actively immunocompromised. Adolescents with leukemia in remission can also be vaccinated, as can those who have had short-term (less than 2 weeks), low- to moderate-dose systemic corticosteroid therapy, topical steroid therapy, or intrarticular steroid injections.

**Adverse Effects** Adverse effects of measles vaccine include fever, rash, and, rarely, transient thrombocytopenia. There is no causal link between measles vaccination and seizures, encephalitis, or encephalopathy.

**Mumps**

The number of cases of mumps has declined dramatically in the United States, from 59,647 cases in 1975 to 8,576 in 1980; 2,982 in 1985; and 1,537 in 1994; and about 352 cases in 1999. Approximately 65% of mumps cases now occur in patients between 10 and 19 years of age, with about 20% or more of such cases reported in college campuses. A live mumps virus vaccine is developed in 1967. The vaccine has few side effects, and more than 90% of susceptible patients develop protective, long-lasting antibodies. Mumps vaccine is usually administered as MMR. Susceptible adolescents should receive a single dose of mumps vaccine alone or as MMR. Susceptible adolescents should receive a single dose of mumps vaccine, and those who do not have such documentation should receive a second dose of vaccine. In practice, measles vaccine is usually administered as measles-mumps-rubella (MMR) vaccine.

**Adolescents should be vaccinated if there is no evidence of prior live measles virus immunization received after 1 year of age, unless the adolescent has had physician-diagnosed measles or has laboratory-confirmed immunity. Routine serologic testing for immunity to measles is not indicated before immunization.

Exposed Susceptible Adolescents Unvaccinated adolescents exposed to measles should receive measles vaccine. If more than 5 days has elapsed since exposure, immune serum globulin (IVIG), 0.25 mL/kg, is also given.

Immunosuppressed Adolescents Vaccination with live measles virus, or any other live virus, is contraindicated in immunosuppressed patients and in those receiving immunosuppressive therapy. At present, information available on MMR vaccination among asymptomatic and symptomatic HIV-infected individuals has not demonstrated serious or unusually adverse events. Therefore, HIV-infected patients can be immunized so long as they are not actively immunocompromised. Adolescents with leukemia in remission can also be vaccinated, as can those who have had short-term (less than 2 weeks), low- to moderate-dose systemic corticosteroid therapy, topical steroid therapy, or intraarticular steroid injections.

Adverse Effects Adverse effects of measles vaccine include fever, rash, and, rarely, transient thrombocytopenia. There is no causal link between measles vaccination and seizures, encephalitis, or encephalopathy.

Mumps

The number of cases of mumps has declined dramatically in the United States, from 59,647 cases in 1975 to 8,576 in 1980; 2,982 in 1985; and 1,537 in 1994; and about 352 cases in 1999. Approximately 65% of mumps cases now occur in patients between 10 and 19 years of age, with about 20% or more of such cases reported in college campuses. A live mumps virus vaccine is developed in 1967. The vaccine has few side effects, and more than 90% of susceptible patients develop protective, long-lasting antibodies. Mumps vaccine is usually administered as MMR. Susceptible adolescents should receive a single dose of mumps vaccine alone or as MMR. Susceptible adolescents include those without documented live mumps vaccination beyond the age of 1 year, unless the adolescent has had physician-diagnosed mumps or has laboratory evidence of mumps immunity. Tests for immunity are unnecessary, because revaccination is safe.

Exposed Susceptible Adolescents Nonvaccinated adolescents who are exposed to mumps should be immunized with the vaccine; vaccination has not been shown to prevent disease in such cases, but it will help to prevent future infection. There is no evidence of efficacy of immune globulin.

Contraindications Vaccination should be avoided in adolescents who are pregnant, have a serious febrile illness, have an immunodeficiency, are receiving immunosuppressive therapy, or have leukemia or lymphoma. HIV infection, unless the adolescent is severely immunocompromised, is not a contraindication to mumps vaccination.

Adverse Effects Adverse reactions to mumps vaccine include allergic reactions, are extremely rare. Purported reactions to mumps vaccine, including seizures and other CNS events, have not been causally linked to immunization.

Rubella

The number of cases of rubella in the United States has continued a marked decline, with 46,975 cases in 1966; 16,652 in 1975; 3,904 in 1980; 630 in 1985; 221 in 1988; 200 in 1995; and approximately 238 in 1999. Colleges can be high-risk settings for rubella transmission, and most cases of rubella now occur among nonimmunized adults in outbreaks in colleges and workplaces. Therefore, proof of rubella and measles immunity should be required for attendance from both male and female students. All students who enter institutions of postsecondary education should have documentation of having received at least one dose of rubella vaccine or other evidence of rubella immunity. The diagnosis of acute rubella should be confirmed serologically with either the presence of immunoglobulin M (IgM) antibody or a significant rise in IgG titers. Rubella vaccination is usually administered as MMR.

Vaccination during Pregnancy In 1979, a new rubella vaccine, RA 27/3 (Meruvax II), was introduced that leads to higher titers with fewer side effects. A review of rubella vaccination for the period 1971–1989, in which 321 known rubella-susceptible pregnant women vaccinated with live rubella vaccine within 3 months before or after conception were monitored, showed that none of the infants had malformations compatible with congenital rubella infection. The estimated risk of 99% confidence interval from 0% to 1.2% with an observed risk of zero. Pregnant adolescents should be asked if they are pregnant. If they say no, they should be advised of the theoretical risk to a fetus from vaccination and instructed to avoid pregnancy for 3 months; they may then be vaccinated. Routine pregnancy testing before vaccination is not indicated. Certainly, if there is any question whether the adolescent might be pregnant, vaccination can be deferred until the question is resolved. When time and cost are not prohibitive, female adolescents can be tested serologically before vaccination. However, this should no longer be done routinely and should not interfere with immunization programs. Clinical diagnosis should not be relied on as evidence of rubella infection.

Males Males without evidence of prior vaccination should also be vaccinated to decrease the community prevalence of susceptible individuals and thus the risk of exposure to susceptible pregnant females.
**Immunocompromised Adolescents** Replication of vaccine viruses can be enhanced in persons with immune deficiency diseases and in persons with immunosuppression, such as individuals with leukemia, lymphoma, or generalized malignancy and those receiving immunosuppressants or large doses of corticosteroids. Such persons should not receive live rubella virus vaccine. Asymptomatic HIV-infected persons in need of an MMR vaccination may receive it so long as severe immunocompromise is absent. Vaccinations should not be given to adolescents with serious febrile illnesses but should not be postponed because of a mild illness, such as an upper respiratory tract infection. Adverse effects from rubella vaccination include fever, rash, lymphadenopathy, and transient arthritis or arthralgias. Purported CNS events associated with immunization have not been causally linked to vaccination.

**Poliovirus**

The last reported case of poliomyelitis caused by locally acquired wild-type virus in the United States occurred more than 20 years ago. Killed-virus inactivated poliovirus vaccine (IPV) is now the vaccine of choice, and oral poliovirus vaccine (OPV) is no longer recommended for use in the United States. Routine vaccination of nonimmunized adults is not required unless they are at particularly high risk because of travel to endemic areas, exposure to wild poliovirus, or occupational exposure. The immunization schedule for nonimmunized adolescents consists of three doses of IPV—two doses with an interval of 4 to 8 weeks, and a third dose 6 to 12 months after the second dose. Persons exposed to wild poliovirus may receive an additional dose of IPV. Immunosuppression is not a contraindication to vaccination. There is a theoretical risk during pregnancy, so vaccination of pregnant women should be avoided. There is also a theoretical risk of anaphylaxis in patients with known allergies to streptomycin, polymyxin B, and neomycin. Adverse effects from the currently available IPV vaccine have not been described.

**Varicella**

There were more than 151,000 reported cases of varicella in 1994, with an estimated 3.7 million cases in the United States each year. Varicella causes about 100 deaths per year and results in more than 9,000 hospitalizations. Whereas younger patients usually have uncomplicated chickenpox, older ones have more serious infections with higher rates of complications. The estimate from the CDC is that about $384 million could be saved annually with vaccine usage. A live-attenuated varicella vaccination for chickenpox was approved in 1995 for use in children, adolescents, and adults. The vaccine is marketed under the name Varivax and is about 70% to 90% effective in preventing varicella. Varicella vaccination is now recommended for persons of all ages without documented chickenpox or measurable levels of protective antibody.

Children and young adolescents between 1 and 13 years of age without documented varicella infection should receive a single dose of varicella vaccine. Adolescents 13 years or older should receive two doses of varicella vaccine, 4 to 8 weeks apart. Immunization is also recommended for susceptible adults, particularly those at residential or occupational risk and those living or working with children. The vaccine can be coadministered with MMR vaccine. Varivax is a live-attenuated vaccine. It is not recommended for children younger than 1 year of age, pregnant women, people who are hypersensitive to gelatin or other vaccine components, those with a history of anaphylactoid reaction to neomycin, or those with active untreated TB. The vaccine should also be avoided in immunosuppressed patients (including those who are immunocompromised from HIV infection) and those who are receiving immunosuppressive therapy. About 5% to 10% of persons vaccinated develop a rash, which can be contagious. Other adverse reactions include redness, hardness, and swelling at the injection site; fatigue; malaise; and nausea.

**Hepatitis B Vaccine**

Two recombinant hepatitis B vaccines (Recombivax HB and Engerix-B) are used in the United States today. Universal vaccination is now recommended in the United States, and the ACIP recommends the three-dose hepatitis B vaccine series for adolescents at age 11 to 12 years who have not previously been immunized. Vaccination should be a special priority for the following persons:

1. Those with lifestyle risk
   a. Sexually active adolescents with more than one partner in preceding 6 months
   b. Persons with any history of STD
c. Homosexual and bisexual men
d. Users of injectable drugs
2. Those with occupational risk
3. Those with environmental risk factors
   a. Household and sexual contacts of carriers
   b. Adoptees from countries with high hepatitis B endemicity
   c. Populations with high endemicity of hepatitis B infection, such as Alaskan Natives, Pacific Islanders, and refugees from endemic areas
d. Clients and staff of institutions for mentally retarded individuals
e. Inmates of long-term correctional facilities
f. Certain international travelers
g. Other contacts of hepatitis B carriers
4. Special patient groups, such as recipients of hemodialysis treatment or clotting factor concentrates

Persons in casual contact with carriers in settings such as schools and offices are at minimal risk of hepatitis B infection, and vaccine is not routinely recommended. Hepatitis B is discussed in detail in Chapter 31.

Hepatitis B vaccine is given in a three-dose series. The second dose is given 1 to 2 months after the first, and the third dose is given 4 to 6 months after the first. The series does not need to be restarted if it is interrupted. The three-dose hepatitis B vaccine induces protective antibodies (anti-HBs) in more than 90% of healthy adults and more than 95% of infants, children, and adolescents through 19 years of age. Protective effects appear to be quite durable and long-lasting. Hepatitis B vaccine can be given simultaneously with other vaccines.

Adverse reactions to hepatitis B immunization are unusual. Pain at the injection site and fever are the most commonly reported adverse effects. Anaphylaxis is rare. Anecdotal cases of autoimmune disease, chronic fatigue syndrome, Guillain-Barré syndrome, and CNS diseases associated with hepatitis B vaccination have not been causally linked to immunization.

**Hepatitis A**

The hepatitis A vaccination now offers effective, long-lasting protection against this virus. Two vaccines are available: Havrix (SmithKline Beecham Biologicals) and Vaqta (Merck & Co.). The vaccines are inactivated and come in adult and pediatric formulations, with different dosages and administration schedules. Almost 100% of children, adolescents, and adults develop protective levels of antibody to hepatitis A virus after completing the vaccine series. The vaccine can be administered simultaneously with other vaccines and toxoids, including hepatitis B, diphtheria, and tetanus, without altering immunogenicity or adverse effects. However, other vaccines should be given at separate injection sites.

Recommended dosing schedules are as follows:

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>ELISA Units</th>
<th>Volume (mL)</th>
<th>No. Doses</th>
<th>Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;18</td>
<td>1,440</td>
<td>1.0</td>
<td>2</td>
<td>0, 6–12</td>
</tr>
<tr>
<td>2–18</td>
<td>720</td>
<td>0.5</td>
<td>2</td>
<td>0, 6–12</td>
</tr>
<tr>
<td>&lt;17</td>
<td>50</td>
<td>1.0</td>
<td>2</td>
<td>0, 6</td>
</tr>
</tbody>
</table>

The ACIP (CDC, 1999) recommends the following:
1. Children who should be routinely vaccinated include those who live in states, counties, or communities where the average annual rate of hepatitis A between 1987 and 1997 equal to or greater than 20 cases per 100,000 (i.e., about twice the national average).

2. Vaccination should be considered for children who live in states, counties, or communities where the average annual rate of hepatitis A between 1987 and 1997 was less than 20 but equal to or greater than 10 cases per 100,000 (i.e., above the national average but less than twice the national average).

Twinrix (GlaxoSmithKline) is also available containing both vaccines for hepatitis A and hepatitis B. See Chapter 31 for other recommended vaccine recipients. Hepatitis A is discussed in detail in Chapter 31.

Influenza

Influenza continues to cause major outbreaks of illness, usually beginning in December or January each year. If the vaccine is administered, it should be given starting in September. Most influenza vaccines contain three virus strains (two type A and one type B), representing the strains most commonly found worldwide and thought to be the most likely to cause infections in the coming year.

Vaccine recommendations are as follows:

1. The vaccine is appropriate for any persons who wish to be vaccinated to reduce their risk of infection.
2. The vaccine is especially recommended for the following persons:
   a. Adolescents with chronic respiratory or cardiovascular illnesses including asthma
   b. Adolescents with metabolic disorders, renal dysfunction, hemoglobinopathies, or immunosuppressive or immunodeficiency disorders (including HIV infection)
   c. Residents of long-term care facilities
   d. Adolescents who are receiving long-term aspirin therapy and who therefore are at risk for Reye syndrome after an influenza illness
   e. Adolescents working in health care settings or long-term care facilities who will have extensive contact with high-risk patients

Influenza vaccine is administered annually in the fall. It must be readministered each year. The vaccine contains only noninfective material.

Adverse Effects

Adverse effects include local redness and induration and systemic effects including fever, malaise, and myalgias. Despite widespread concern, there is no evidence of occurrence of a paralytic illness such as Guillain-Barré syndrome with vaccines used after 1976, and in a large study in adults found no significant difference in side effects between those who were vaccinated and those who were given a placebo.

Chemoprophylaxis

Chemoprophylaxis drugs are also available to help prevent influenza. Chemoprophylaxis is appropriate for individuals who are at high risk and who either have not been immunized or are exposed to influenza before a vaccine response has occurred (2 weeks). It is also useful for immunosuppressed adolescents who may not respond to the vaccine and for adolescents for whom vaccination is contraindicated. In very high-risk individuals, chemoprophylaxis may be continued throughout the flu season. Currently available chemoprophylactic drugs include amantadine and rimantadine. For both, the recommended dose is 100 to 200 mg/day in one or two divided doses; 100 mg/day is probably as effective as 200 mg and is associated with fewer side effects. Both can also be used in healthy adolescents to reduce the duration and severity of type A influenza when administered within 24 to 48 hours after the onset of symptoms. Other newer drugs, such as zanamivir (Relenza) and oseltamivir (Tamiflu) are also available for chemotheraphy for influenza A disease.

Pneumococcal Vaccine

Pneumococcal vaccine is indicated for individuals with a chronic illness, particularly of the cardiovascular or pulmonary system. It is also indicated for those who are at increased risk of pneumococcal disease, including patients with nphrotic syndrome, sickle cell disease, asplenia, or functional asplenia, HIV infection, or B-cell immune deficiency, as well as patients at risk for meningitis. The duration of immunity is unclear; some centers recommend reimmunization with pneumococcal vaccine (Pneumovax 23) 3 to 5 years after primary immunization in patients who are at especially high risk.

Haemophilus influenzae Type B

Haemophilus influenzae type B vaccine is indicated for those adolescents not previously immunized who are at risk because of splenic dysfunction or other conditions. A single dose of 0.5 mL is recommended.

Meningococcal Vaccine

The current ACIP guidelines suggest that routine vaccination of non-military personnel with the quadrivalent meningococcal polysaccharide vaccine is not necessary, because of its relatively short duration and its lack of protection against serogroup B. However, college freshmen and particularly those living in dormitories or residence halls, are at modestly increased risk for meningococcal disease compared with persons of the same age who are not attending college. The ACIP has developed recommendations that suggest educating students and their parents about the risk for disease and about the vaccine so that they can make individualized, informed decisions regarding vaccination. The CDC recommendations include the following.

1. Providers of medical care to incoming and current college freshmen, particularly those students who plan to live or already live in dormitories and residence halls, should, during routine medical care, inform these students and their parents about meningococcal disease and the benefits of vaccination. The ACIP does not recommend that the level of increased risk among freshmen warrants any specific changes in living situations for freshmen.

2. College freshmen who want to reduce their risk for meningococcal disease should either be administered vaccine (at a doctor's office or student health service) or directed to a site where vaccine is available.

3. The risk for meningococcal disease among nonfreshmen college students is similar to that for the general population. However, the vaccine is safe and efficacious and therefore can be provided to nonfreshmen undergraduates who want to reduce their risk of meningococcal disease.

4. Colleges should inform incoming and current freshmen, particularly those who plan to live or already live in dormitories or residence halls, about meningococcal disease and the availability of a safe and effective vaccine.

5. Public health agencies should provide colleges and health care providers with information about meningococcal disease and the vaccine as well as information regarding how to obtain vaccine.

Further information is available at the CDC Web site (http://www.cdc.gov/mmwr/preview/mmwrhtml/mm4907a2.htm). The American Academy of Pediatrics (http://www.aap.org/policy/r0035.html) has also recently come out with numerous recommendations regarding meningococcal vaccine including:

1. Students entering college, especially those who will be living in dormitories, and their parents should be informed during routine prematriculation medical visits about the increased risk of meningococcal disease and potential benefits of immunization as well as limitations of the vaccine, primarily the lack of protection against serotype B meningococcal disease.

2. Students should consider immunization in view of the risk of disease and potential benefits of immunization. Although the risk is greatest for college freshmen who will be living in dormitories, college upperclasspersons and graduate students living in dormitories also may choose to be immunized.

3. Recommended that the college students who were immunized as freshmen is not indicated. However, for those who were immunized 3 to 5 years previously and are or will be in high-risk circumstances, such as travel to geographic areas with hyperendemic or epidemic meningococcal disease, reimmunization should be considered. 1 Similarly, vaccine should be considered for matriculating freshmen who were immunized 3 or more years previously and will be living in dormitories.

General Vaccination Information

Vaccination of adolescents is safe and should be seen as a high priority for adolescents whose previous immunization is lacking or incomplete. Adolescents who have been partially vaccinated can have their vaccination completed without restarting the series. Likewise, adolescents who begin vaccination can complete it at any time after the vaccination process is interrupted, even if there has been a substantial delay between doses. Vaccines should not be given more frequently than the recommended intervals. Although not every possible combination of vaccines has been explicitly tested, there are no contraindications to giving any or all of these vaccines simultaneously, so long as they are given at separate and appropriate anatomical sites. Nevertheless, many clinicians faced with having to give four or five
Vaccines choose to offer the patient a return visit in order to limit the number of simultaneous injections.

**Informed Consent** Since 1994, all health care providers who administer MMR, polio, diphtheria and tetanus toxoids and pertussis (DTP), and Td vaccines have been required to distribute vaccine information sheets each time a patient is vaccinated. The clinic or office should obtain a signature of either the patient, parent, or guardian to acknowledge having been provided with vaccine information. This should also be noted in the medical record. Appropriate documentation of vaccination includes consent for vaccination, immunization type, date of administration, injection site manufacturer and lot number of vaccine, and name and address of the health care provider administering the vaccine. Helping patients and their families to maintain their own immunization records facilitates proper vaccination of adolescents who may go on to receive immunizations in more than one location. Vaccination registries, which are coming on-line in many states, will also improve this process.

**Erroneous Contraindications against Vaccination** In an effort to improve vaccination rates, the ACIP has specifically addressed a variety of situations in which many practitioners have deferred or delayed vaccination. Situations that specifically do not represent contraindications to vaccination include:

1. Reaction to a previous dose of DTP vaccine with only soreness, redness, or swelling
2. Mild acute illness with low-grade fever
3. Current antimicrobial therapy
4. Pregnancy in the adolescent's mother or in another household contact
5. Recent exposure to an infectious disease
6. Breast feeding
7. History of nonspecific allergies
8. Allergy to penicillin or other antimicrobials except anaphylactic reactions to neomycin or streptomycin
9. Allergies to duck meat or duck feathers
10. Family history of seizures in children who require vaccination

Furthermore, "mild illnesses" such as mild upper respiratory tract infections, with or without low-grade fever, are not contraindications for vaccination. Inappropriately avoidance of vaccination because of a mild acute illness has contributed to many missed opportunities for vaccinating children and adolescents.

**Vaccination during Pregnancy** Because of theoretical risks to the developing fetus, live-attenuated virus vaccines are not routinely given to pregnant women or to those who are likely to become pregnant within 3 months after receiving the vaccine. There is no convincing evidence of risk to the fetus after immunization of pregnant women with inactivated virus vaccines, bacterial vaccines, or toxoids. This includes tetanus and diphtheria toxoid. There is also no risk to the fetus from passive immunization of pregnant women with immune globulin. Because MMR vaccine viruses are not transmitted from individuals receiving them, children of pregnant women may receive these vaccines.

**Adolescents with Human Immunodeficiency Virus Infection** Vaccine recommendations for HIV-infected adolescents are described in the text for individual vaccines and are summarized in Table 4.3.

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Asymptomatic</th>
<th>Symptomatic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Td</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>IPV</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>MMR</td>
<td>Yes, consider</td>
<td>Yes</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Varicella</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Pneumococcal</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Influenza</td>
<td>Optional</td>
<td>Yes</td>
</tr>
</tbody>
</table>

**TABLE 4.3. Recommendations for immunization of HIV-infected patients**

**Sample Schedule for Nonimmunized Adolescents** Most adolescents seeking preventive health services are either fully or partially immunized. For adolescents who have received no immunizations, a sample immunization schedule might include the following.

1. First visit: Td #1, IPV #1, HepB #1, MMR #1, PPD (if no history of positive PPD in the past)
2. Two months later: Td #2, IPV #2, HepB #2, MMR #2, varicella vaccine (in those who lack a reliable history of chickenpox)
3. Six to 12 months later: Td #3, IPV #3, HepB #3
4. Td every 10 years

**PREVENTIVE HEALTH INTERVENTIONS**

The practice of medicine is often more of an art than a science, and this is especially true in the care of adolescents. Only through experience do practitioners develop a style that "works" for them. Clinicians working with adolescent patients must feel comfortable in screening for psychosocial morbidity and assessing the level of risk in individual adolescent patients. This includes screening patients for risks associated with sensitive health issues such as sexual behavior, substance use, and mental health concerns. However, adequate screening is insufficient if it is not followed up with appropriate and effective intervention strategies when patients screen "positive" for serious health risks. The next steps—that is, how to deliver relevant health education and offer effective, brief office interventions—are not nearly as straightforward. Some precepts from behavioral medicine are important in designing practical office interventions:

1. Health education should be targeted to the specific needs of the patient.
2. The patient should agree with the physician on what behaviors must be changed and how to change them.
3. Barriers to the proposed change should be explored, and specific strategies to overcome these barriers should be discussed.
4. Monitoring, feedback, and positive reinforcement should be an integral part of the overall plan.
5. Once behavioral change has occurred, a plan for maintenance should be addressed.

Imagine a clinical encounter in which a sexually active adolescent patient is asked about condom use. The patient responds that she uses condoms "sometimes." At this point, a not-infrequent clinician response is to wax eloquent for a few minutes on the importance and health benefits of condom use, with the patient usually listening respectfully and offering little. The clinician feels good about the "counseling" that has been offered, but the patient generally has gotten almost nothing of value from the interaction. In fact, the patient already understands the value of condoms—after all, she is using them sometimes. For this patient, the problem with condom use lies elsewhere: she can't afford them, her partner refuses to use them, someone is allergic to latex, or, most frequently, there never seems to be a condom available when one is required. None of these potential barriers is likely to emerge while the clinician sermonizes from a soapbox. Productive advice for this particular patient does not rest in a general treatise on the value of condoms but rather in addressing directly the specific barriers faced by the individual patient. This requires active listening, explicit questioning, specific strategies, and the willingness to go back and make sure that the intervention has been successful. Inherent in this approach is clinicians' willingness to go beyond screening and on to interventions and solutions, to engage with patients on difficult and sometimes sensitive issues, and, most importantly, to take the time to fully understand the context of health-risk behavior.

**The G-A-P-S Algorithm**

As part of the GAPS project, the AMA has attempted to develop a standardized method of assessment and intervention that embodies current health education principles but remains practical for office practice. The mnemonic G-A-P-S is used: gather information, assess further, problem identification, and specific solutions (Fig. 4.13). A publication from the AMA, GAPS: Clinical Evaluation and Management Handbook, includes fully developed algorithms for each of the GAPS
FIG. 4.13. Algorithm for providing health screening and guidance to adolescents. (From Guidelines for adolescent preventive services [Recommendations monograph]. Chicago: American Medical Association, 1995.)

G: Gather Initial Information Screen for problems using simple trigger questions, such as, “Have you been feeling down and blue?” or “Do you usually wear seat belts while riding in a car?” As has already been discussed, this initial screening step may be facilitated by use of questionnaires, computers, or nonclinician personnel. If the screening result is negative and no increased risk is identified, basic information and positive reinforcement of the healthy behavior can and should be offered. If the result is positive, proceed to the next level.

A: Assess Further Assess the level and nature of risk in the particular area. Identify the seriousness of the problem by assessing the patient's knowledge and involvement, predisposing and protective factors, the availability of family and other support, and the consequences for the patient's health and function (e.g., school, peer relationships). The intervention offered depends on the assessed risk. Often, low risk can be successfully managed with health information, a few targeted suggestions, and positive reinforcement about the issue. If the patient is at high risk, he or she probably needs an in-depth evaluation that may be beyond the bounds of a preventive services visit. A return visit for more intensive intervention, or referral, is warranted. Patients who are at intermediate risk also require an explicit intervention, such as that suggested in the next step. This can be begun within the context of the preventive services visit if the clinician feels comfortable with the particular issue.

P: Problem Identification This step involves working with the patient toward an agreement on the problem, helping the patient decide to make a change, and working with the patient to develop a specific plan for that change. The goal is to be “patient-centered” in the approach—that is, to help the patient decide what is in his or her best interest, rather than forcing the patient to accept the physician’s view of the problem or behavior. Problem identification is an attempt to define the problem in terms that the patient accepts. For example, questions such as, “You seem to be down and blue; is that something that is a problem for you right now?” or “Do you think it would be healthier for you if you used condoms?” may help the patient further acknowledge a problem. Once agreement on problem definition is reached, proceed to the next step. If the patient does not agree that there is a problem with a specified behavior, look for areas of agreement and common ground. An adolescent may not accept use of alcohol as being problematical but may acknowledge that binge drinking puts him or her at risk. Clinician perseverance on areas of obvious disagreement is unlikely to be productive and may negatively affect subsequent discussions. On the other hand, adolescent patients are often amenable to “agreeing to disagree,” will still accept factual risk information, and are willing to establish criteria that would elevate the issue to “problem” status and justify future discussion and intervention. For example, a question such as, “You clearly don’t think that this is a problem area, but when would you consider it might become one?” would assist in setting boundaries that define the problem. Finally, any problem that poses an immediate threat to the adolescent's safety warrants an immediate intervention or referral whether or not the adolescent is fully prepared for change.

The clinician guides the adolescent to weigh the pros and cons of making a certain change. The adolescent may find several reasons to make (or not make) the change in behavior, and it is helpful to address these reasons explicitly. This technique helps to prepare adolescents to deal with the ambivalence that they often feel toward changes in behavior. In beginning to develop a “plan,” find out what the adolescent is willing (or not willing) to do. Make sure the plan is concrete and fully detailed. Decisions should be framed as being in the adolescent's hands. If the adolescent is only willing to try using a condom once, that might become an initial plan. However, most adolescents are willing to make more substantive changes (e.g., always wearing seat belts, not drinking alcohol) at least for a specified time period, usually a few weeks or months. Try to avoid sweeping changes that are unrealistic, such as avoiding alcohol use for the rest of their lives.

S: Specific Solutions: Self-efficacy, Support, Solving Problems, and Shaking on a Contract Self-efficacy is assessed by asking whether the adolescent thinks he or she will be able to carry out the proposed plan. If the adolescent is ambivalent, revisit perceived barriers and attempt to redefine specific solutions. Plans should be achievable so that success becomes self-reinforcing. An overly ambitious plan may need to be modified. Support is important, and adolescents should be encouraged to identify people who can help them carry out their plan. Hopefully, they will be able to call on resources such as trusted adults or close friends. At times adolescents may want advice on how best to recruit their support system. At times, the clinician can also be helpful in helping adolescents to disclose information to parents or others. Solving problems reminds us to assess the barriers that the adolescent foresees and to work with the adolescent in developing specific strategies to overcome them. For example, if an adolescent recognizes that he will have difficulty not drinking at an upcoming party, he must have a plan for how to deal with that situation. It is usually most helpful if adolescents come up with their own solutions, but they often can be helped to recognize solutions or options they might not have considered. "Shaking on a contract" is a crucial step. It serves as a tangible reinforcement of the proposed plan and implies some commitment on the adolescent's part. Written contracts can also be used, especially for younger adolescents, but they are unwieldy as a general rule. It is important to specify the actions agreed to and the time frame in which the actions are to be taken. Make sure that the adolescent feels comfortable with the plan and understands it. If you are able to involve another party in the contract, such as a friend or parent, there is likely to be better compliance. Follow-up is critical and should be arranged in some form—either a visit, telephone contact, or e-mail—in the time frame agreed to in the contract.

WEB SITES
http://www.ama-assn.org/ado10th; Adolescent, Children's, and Online Health (AMA).
http://www.brightfutures.org/index.htm, Bright Futures.
http://www.gwu.edu/~mpa, "Making the Grade" (school-based health).
http://www.cdc.gov/ncbddd/shdash, CDC Department of Adolescent and School Health.

REFERENCES AND ADDITIONAL READINGS


Schubiner HH. Preventive health screening in adolescent patients. Primary Care 1989;16:211.


Mortality

Epidemiology

Age

Over the years of monitoring the incidence of injury among children and adolescents, certain risk factors have arisen as fairly strong indicators of injury events. First and foremost, the risk of injury is clearly related to the physical, mental, and emotional developmental milestones of children or adolescents; for this reason, age is perhaps a predictable risk factor for injury (National Center for Injury Prevention and Control [NCIPC], 1999a). Infants are at greatest risk of burns, drowning, and falls. As children increasingly acquire mobility, poisonings join the list. Young school-age children are at greatest risk of pedestrian injuries, bicycle-related injuries, motor vehicle occupant injuries, burns, and drownings. Adolescents are most likely to suffer from motor vehicle injuries and injuries resulting from firearms and other forms of violence (Rivara and Aitken, 1998). The cycle becomes full circle as death due to carelessness, curiosity, and risk-taking during adolescence begins to mirror deaths most characteristic of infancy and early childhood. At 10 years of age slightly less than 50% of all deaths are caused by injury but, by 18 years, more than 80% are injury-related (National Center for Health Statistics [NCHS], 2000b).

Figure 5.1, adapted from the NCIPC’s Injury Mortality Reports, describes the age distributions for major causes of death from injuries for adolescents and young adults. Table 5.1 and Table 5.2 describe the death rates due to injuries in 1998 for 12- to 15-year-olds and for 16- to 20-year-olds, respectively. For every type of injury, except bicycle deaths, there are substantial rate increases between early and late adolescence.


TABLE 5.1. Death rates (per 100,000) and number of deaths due to injuries to adolescents ages 12–15 years by event, race, and sex, United States, 1998
Gender A second important risk factor for injury is gender. Beginning at approximately 1 or 2 years of age and continuing until the seventh decade of life, males have higher rates of injury than females. This gender difference during childhood does not appear to be caused by differences in developmental or motor skills. In part, it may be related to greater exposure of males to hazards or to gender-based differences in behavior (Rivara and Aitken, 1998). For all injuries in 1998, the death rate for 12- to 15-year-olds was slightly more than twice as high among males as among females (Table 5.1) and, for 16- to 20-year-olds, it was 3.2 times higher (Table 5.2). For 12- to 15-year-olds, injury death rates were substantially higher among males for firearms (3.8 times), falls (4.7 times), drownings (5 times), bicycles (8 times), and bicycle-motor vehicle traffic deaths (8.3 times). Among 16- to 20-year-olds, the injury death rate differences between males and females were highest for cut/pierce deaths (4 times), falls (4.1 times), drownings (7.2 times), motorcycle-traffic deaths (7.6 times), firearms (7.8 times), bicycle-motor traffic deaths (10.75 times), and bicycles (11.25 times). Young males were also 5.5 times more likely than females to be victims of homicide and 5.8 times more likely to successfully commit suicide (NCIPC, 1999d).

Race and Ethnicity Injuries death rates also vary substantially with race and ethnicity. The highest rates are among African-American and Native American adolescents and the lowest rates are among Asian youth, as seen in Table 5.1 and Table 5.2. Table 5.3 shows that Hispanic children have rates between those of whites and African-Americans, although age and gender also influence those rates. A further explanation for these racial differences appears to be related to poverty, which is another important risk factor in predicting adolescent injuries.

Socioeconomic Factors Poor children are at greatest risk for injury and studies have indicated that their risk level is 2 to 5 times that of children who are not poor. This is true for pedestrian injuries, fires and burns, drownings, and intentional injuries. The injury death rate is consistently higher in nonmetropolitan areas than in cities (Rivara and Aitken, 1998).

Demographic and Environmental Factors The risk of each type of adolescent injury is also influenced by demographic and environmental factors. These include hazards such as all-terrain vehicles, backyard swimming pools, firearms, kerosene heaters, traffic patterns, and gang activity. Policies such as regulations concerning requirements for fences around private pools, smoke detectors in homes, bicycle helmets, and graduated drivers license programs with night restrictions also influence injury rates (NCIPC, 1999a).

Trends in Mortality Death rates from all causes have actually decreased over the past few decades (Table 5.4), but the nature of the deaths that occur has changed drastically (Table 5.5). Advanced technology has helped to keep more adolescents alive after experiencing an event that years ago might have been fatal. However, there is ample room for improvement in implementing prevention efforts that will reduce the incidence of adolescent injury altogether. For example, about 37 children die each day from preventable injuries in the United States (Deal et al., 2000). At least one adolescent between 10 and 19 years of age dies as the result of an injury every hour of every day. Injuries cause more adolescent deaths than all diseases and natural causes combined. Unintentional injury accounts for approximately 60% of all adolescent injury-related deaths and the remaining 40% are attributed to violence (NCHS, 2000b; NCIPC, 1998b).
Leading Causes of Death

The ten leading causes of death for youth ages 10 to 14 years vary slightly from those of older adolescents and young adults. The leading causes of mortality for each age group (per 100,000) are shown in Table 5.6 (NCIPC, 1998a, 1998b).

Additional Injury Facts

For all causes, male adolescents have almost three times the mortality rate of female adolescents. More than 75% of all deaths among persons 15 to 24 years old are due to only four causes: motor vehicle crashes, other unintentional injuries, homicide, and suicide. Additional outstanding data regarding adolescent injury are discussed in the following paragraphs.

Unintentional Injuries

Unintentional injuries are the fifth leading cause of death in the United States for the total population, but are the leading cause of death among 5- to 24-year-olds. The leading cause of death from unintentional injury is motor vehicle crashes. In 1998, when adolescents accounted for 10% of the total population in the United States, they also accounted for 14% (5,606) of all motor vehicle deaths. Of these deaths, two out of every three were male adolescents (Insurance Institute for Highway Safety [IIHS], 1999c).

Leading Cause of Death

The leading cause of death is the same for whites and for African-Americans in all age groups except those ages 15 to 24 years and ages 35 to 44 years. Accidents and their adverse effects are the leading cause of death for whites between 15 and 24 years of age and also for whites ages 25 to 44 years. For the African-American population, homicide (including legal intervention) is the leading cause of death among 15- to 24-year-olds, and the human immunodeficiency virus (HIV) is the leading cause among those ages 25 to 44 years. Homicide and legal intervention consistently ranks higher as a cause of death for the Hispanic population compared with the non-Hispanic white population and other age groups between 5 and 44 years. Likewise, HIV infection consistently ranks higher in the Hispanic than in the non-Hispanic white population in corresponding age groups.

Homicide Rates

Between 1995 and 1998, the age-adjusted homicide rate decreased by 22% to 7.3 deaths per 100,000 persons, reversing an upward trend seen in the late 1980s. The greatest decrease in homicide rates was in the 15- to 24-year-old Hispanic male population, for whom the homicide rate fell by 35% to 41.1 deaths per 100,000 youth in 1998. The rate for male African-Americans ages 15 to 24 years (96.5 per 100,000) is almost eight times the rate for whites (12.2 per 100,000). The homicide rate for young Hispanic males is about 3.4 times the rate for white males. There has been a downward trend in the general population, with crude rates falling from 10.0 deaths per 100,000 in 1990 to 6.8 deaths per 100,000 in 1998.

Firearm Injuries

In 1998, in the United States, there were 30,708 deaths from firearm injuries, including those related to accidents, suicides, and homicides. Most of those firearm deaths were related to suicide or homicide. Among those deaths, 62% occurred among white males, 21% among African-American males, 11% among white females, and 3% among African-American females. The largest numbers of such deaths occurred in the 15- to 24-year-old and the 25- to 34-year-old age groups. Between 1995 and 1998, the age-adjusted death rate for firearm injuries decreased by 19%. During this period, the firearm death rate for Hispanic males ages 15 to 24 years decreased by more than 36%, falling to 44.9 deaths per 100,000. The rate among African-American males age 15 to 24 years did decrease during this period, but it remains more than four times the rate for white males (113.3 versus 23.1 per 100,000, respectively) and more than twice the rate for Hispanic males of the same age.

Cancer

Excluding intentional and unintentional injuries, cancer is the number one cause of adolescent mortality.

Specific Risks Faced by Adolescents in the Year 2000

- Every 31 seconds, an adolescent becomes pregnant, with 40% of all teenage girls becoming pregnant at least once before their 20th birthday (Annie E. Casey Foundation, 1998).
- Every minute, an adolescent gives birth.
- Every 2 hours, a firearm kills a child or adolescent under the age of 20 years.
- Every 4 hours, a child or adolescent under the age of 20 years commits suicide.
- Every 19 hours, a young person under the age of 25 years dies from HIV infection.
- Every day, 12 children or adolescents under the age of 20 years are homicide victims (Children's Defense Fund, 2000).

Note that, even though the proportion of deaths caused by a given event may be similar between different age groups within the pediatric population, the actual numbers of those deaths may be very different, as depicted in Table 5.7 and Fig. 5.2 (National Safety Council [NSC], 2000).
Cancer

Cancer is the second leading cause of death (after accidents and their adverse effects) among younger adolescents and it ranks fourth in the 15- to 24-year-old age group (Adams et al., 1999; NCHS, 2000c). In 1998, approximately 8,500 children and youth were diagnosed with cancer, and 1,700 young people died from the disease in that same year. Although cancer is the leading cause of death by disease for American children younger than 15 years of age, it is still relatively rare in this age group. On average, 1 to 2 of every 10,000 children in the country develop cancer (National Cancer Institute [NCI], 1999).

During adolescence, there are increases in incidence and mortality from lymphomas, Hodgkin disease, and brain and genital tumors. Among the 12 major types of childhood cancers, leukemias (blood cell cancers) and brain and other central nervous system tumors account for more than one half of new cases. About one third of childhood cancers are leukemias; approximately 2,300 children younger than 15 years of age are estimated to have been diagnosed with leukemia in 1999 (NCI, 1999). Leukemia is the number one cause of death from malignancies among 15- to 24-year-olds and lymphomas are the most prevalent malignancy. Table 5.8 and Table 5.9 give incidence and mortality rates, respectively, for tumors during childhood, adolescence, and young adulthood (Ries et al., 2000).

Injuries

Unintentional injuries account for 67% of all injury deaths to children and adolescents in the United States. Among youth ages 1 to 19 years, unintentional injuries are responsible for more deaths than homicide, suicide, congenital anomalies, cancer, heart disease, respiratory illness, and HIV combined (Deal et al., 2000).

Trends in Injury Deaths Despite significant reductions in incidence rates since 1979, injuries remain the major health problem (and the leading cause of death) for children and adolescents. In the pediatric age group, unintentional injury mortality has fallen by more than 45% since 1979, with the largest decreases among those ages 5 to 9 years and the smallest decrease among teenagers. Table 5.10 reflects the changes in childhood injury rates by 5-year age increments over the past two decades and Table 5.11 shows the trend in accidental death rates throughout the century (NSC, 2000; Rivara, 1999).
Factors contributing to high injury rates in adolescents often relate to the discrepancies between an adolescent’s physical development and his or her cognitive and emotional development. Adolescent health is influenced by the strengths and vulnerabilities of individuals and also by the character of the settings in which they live. These settings—the schools they attend, the neighborhoods they call home, their families, and the friends who make up their social network—play an important, yet still incompletely understood, role in shaping adolescent health. They do so by affecting how individuals feel about themselves as well as influencing the choices they make about behaviors that can affect their health and well-being.

As a group, adolescents are physically healthy. They have survived early childhood and are decades away from the diseases associated with aging. Threats to their health stem primarily from their behavior. Several developmental characteristics of the adolescent can exacerbate this problem:

- Experimentation with adult roles
- Experimentation with risky behaviors or situations when opportunities for healthy risk-taking are not available or provided
- Desire for peer approval and a tendency to join peer activities and to follow peer norms
- Challenge of authority or rules
- Experimentation with adult roles
- Stepping out of parental supervision
- Inability to assess risk
- Desire for peer approval and a tendency to join peer activities and to follow peer norms
- Inability to assess risk

*Morbidity* Deaths only partially convey the enormous damage caused by childhood injuries. It is estimated that for every childhood death caused by injury there are also approximately 34 hospitalizations, 1,000 emergency department visits, many more visits to private physicians and school nurses, and an even larger number of injuries treated at home (NCIPC, 1999a). Approximately 21 million children in the United States are injured each year. This equates to an injury rate of 1 in 4 children, or 56,000 nonfatal injury episodes each day that require medical attention or limit children’s activity (Danseco et al., 2000).

**Leading Causes of Injuries** Four external causes of injury—being struck by or against an object or person, falls, motor vehicle traffic-related injuries, and being cut by a sharp object—account for almost 60% of all injury-related visits to emergency departments by adolescents. Of these four causes, only motor vehicle traffic-related injuries are a significant source of mortality. Sports injuries make up more than 40% of those injuries classified as “being struck by or against an object or person.” At each age, the rate of such injuries among males is twice that among females (NCHS, 2000b).

- Injuries are the leading cause of death for persons between the ages of 1 and 44 years in the United States.
- Unintentional injuries, suicide, and homicide cause more than 75% of all deaths in the adolescent age group. Unintentional injuries cause about 42% of all deaths among 5- to 14-year-olds and about 44% among 15- to 24-year-olds. Intentional injuries comprise approximately 10% and 31% of deaths in these age groups, respectively (NCHS, 2000c).
- The 15- to 24-year-old age group has the highest cost related to injury of any age group in the United States. Estimated costs for this group reach almost $90 million annually. The estimated total cost for unintentional childhood injuries just falls short of $350 billion each year (Danseco et al., 2000).

**Data Sources** One problem in evaluating injury statistics is that data collectors often use different age groupings to classify subjects. Also, there is no mandatory national reporting system for injuries or injury events. Nonetheless, useful data are available from the following sources:

- National Electronic Injury Surveillance (NEISS) of the U.S. Consumer Product Safety Commission (data from a sample of nationwide hospitals)
- Fatal Accident Reporting System (FARS) of the U.S. Department of Transportation’s National Highway Traffic Safety Administration (NCIPC, 1999a)
- National Poison Control Data Network
- National Health Interview Survey (NHIS), conducted by the National Center for Health Statistics (NCHS, 2000a)
- National Center for Injury Prevention and Control (NCIPC) of the Centers for Disease Control and Prevention

**Factors Contributing to Adolescent Injuries** Factors contributing to high injury rates in adolescents often relate to the discrepancies between an adolescent’s physical development and his or her cognitive and emotional development. Adolescent health is influenced by the strengths and vulnerabilities of individuals and also by the character of the settings in which they live. These settings—the schools they attend, the neighborhoods they call home, their families, and the friends who make up their social network—play an important, yet still incompletely understood, role in shaping adolescent health. They do so by affecting how individuals feel about themselves as well as influencing the choices they make about behaviors that can affect their health and well-being.

As a group, adolescents are physically healthy. They have survived early childhood and are decades away from the diseases associated with aging. Threats to their health stem primarily from their behavior. Several developmental characteristics of the adolescent can exacerbate this problem:

- Experimentation with adult roles
- Experimentation with risky behaviors or situations when opportunities for healthy risk-taking are not available or provided
- Challenge of authority or rules
- Desire for peer approval and a tendency to join peer activities and to follow peer norms

Placing these characteristics in an environment where there is alcohol, tobacco, violence, unprotected sex, fast cars, and drugs heightens adolescents’ risk of injury and death even more (Blum and Rinehart, 1999).

**Automobile Injuries** Automobile injuries are the leading cause of mortality and morbidity among all Americans ages 1 to 44 years. The transportation environment is the most dangerous setting for the adolescent, whether as a driver, passenger, motorcyclist, bicyclist, or pedestrian.

- Motor vehicle traffic-related injuries account for almost 40% of all deaths among youth ages 15 to 19 years and for almost 80% of deaths due to unintentional injuries in that same age group (NCIPC, 1999a).
- More than 75% of children ages 5 to 14 years who die in traffic crashes are not wearing a seatbelt or other restraint (Federal Interagency Forum on Child and Family Statistics, 2000).
- In 1998, the death rate for teenage male drivers was more than twice that for females of the same age (21 and 10 per 100,000, respectively).
- The risk of crash involvement per mile driven among drivers ages 16 to 19 years is four times the risk among older drivers.
- The crash rate per mile driven is almost three times as high among 16-year-olds as it is among 18- to 19-year-olds.
- More than 60% of deaths among 16- to 19-year-olds in 1998 occurred in crashes in which another teenager was driving.
- More than 50% of motor vehicle-related deaths among teenagers in 1998 occurred on a Friday, Saturday, or Sunday (IIHS, 1999c).

**TABLE 5.10. Unintentional injury mortality rates (per 100,000), United States, 1979 versus 1996**

<table>
<thead>
<tr>
<th>Age group (%)</th>
<th>Rate</th>
<th>Number</th>
<th>Rate</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-4</td>
<td>27.4</td>
<td>4,377</td>
<td>15.6</td>
<td>5,142</td>
</tr>
<tr>
<td>5-9</td>
<td>15.6</td>
<td>3,692</td>
<td>5.6</td>
<td>1,694</td>
</tr>
<tr>
<td>10-14</td>
<td>16.7</td>
<td>2,865</td>
<td>4.1</td>
<td>861</td>
</tr>
<tr>
<td>15-19</td>
<td>39.0</td>
<td>12,694</td>
<td>16.9</td>
<td>26,69</td>
</tr>
<tr>
<td>All adolescents</td>
<td>31.6</td>
<td>32,077</td>
<td>17.6</td>
<td>13,015</td>
</tr>
</tbody>
</table>


**TABLE 5.11. Accidental death rates (per 100,000) among youth, United States, 1903–1998**

<table>
<thead>
<tr>
<th>Year</th>
<th>Death rate (per 100,000)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1903</td>
<td></td>
</tr>
<tr>
<td>1913</td>
<td></td>
</tr>
<tr>
<td>1923</td>
<td></td>
</tr>
<tr>
<td>1933</td>
<td></td>
</tr>
<tr>
<td>1943</td>
<td></td>
</tr>
<tr>
<td>1953</td>
<td></td>
</tr>
<tr>
<td>1963</td>
<td></td>
</tr>
<tr>
<td>1973</td>
<td></td>
</tr>
<tr>
<td>1983</td>
<td></td>
</tr>
<tr>
<td>1993</td>
<td></td>
</tr>
</tbody>
</table>

Firearms drownings among adolescent boys, in particular (NCIPC, 1999b). Alcohol Use to 3.0 times the rate of similar-age whites. In 1997, the overall age-adjusted drowning rate for African-Americans was 42.6% higher than that for whites. Male high school students are more likely (20.8%) than female students (11.9%) to rarely or never wear safety belts. Black students (22.5%) are more likely than white students (15.5%) to rarely or never wear safety belts.

Data analysis shows that at all levels of BAC, the risk of being involved in a motor vehicle crash is greater for teenagers and young people than for older people. In 1998, 22% of the fatally injured drivers ages 16 to 20 years had a BAC of at least .10% (IIHS, 1999a; NCIPC, 1999f). In a 1999 national survey, 33.1% of high school students reported that, in the past 30 days, they had ridden with a driver who had been drinking alcohol. In that same survey, 13.1% of respondents said that they had driven themselves after drinking alcohol, within the past 30 days (CDC, 2000). Teenage male drivers with a BAC in the 0.5% to 0.10% range are 18 times more likely than sober male teenagers to be killed in single-vehicle crashes. The corresponding comparison for females is 54 times more likely (IIHS, 1999a). Although many states have reduced the BAC for “driving while intoxicated” (DWI) convictions to 0.08%, a zero-tolerance policy of any BAC for adolescents younger than 21 years of age may further reduce alcohol-related motor vehicle injuries.

Nonautomobile Injuries

Motorcycle

Males accounted for 9 of every 10 motorcycle deaths in 1998. In 1998, 36% of all motorcycle deaths occurred among 16- to 29-year-olds. Of all motorcycle deaths in 1998, 72% occurred between the months of April and September. The total number of deaths peaked in July and August and was lowest in December, January, and February. For each mile traveled, the number of deaths on motorcycles is 14 times greater than in cars (IIHS, 1999c).

Drowning The second leading cause of unintentional injuries and deaths is drowning, which causes approximately 1,500 deaths of children and adolescents each year in the United States (Rivara, 1999). Drowning is unique as an injury problem because of its high case-fatality rate and because of the relative lack of impact that medical care has on outcome. Swimming pools play a role in drowning among young, school-age children and among adolescents, but immersion in natural bodies of water, whether swimming or boating, also plays an increasingly important role (Rivara and Atkin, 1998).

Approximately 50% of children and adolescents requiring physician care for a submersion incident will die (Rivara, 1999). In 1998, 5,096 people drowned, including 1,058 children younger than 15 years of age (NCHS, 2000c).

Gender

Males are three times more likely to die from drowning than are females in almost every age group (NCIPC, 1999b). Males between the ages of 15 and 19 years are more than 10 times more likely to drown than females of the same age (NCIPC, 1999d).

Race

In 1997, the overall age-adjusted drowning rate for African-Americans was 42.6% higher than that for whites. Black children ages 5 through 19 years drowned at 1.5 to 3.0 times the rate of similar-age whites.

Alcohol Use

Alcohol use is involved in about 25% to 50% of adolescent and adult deaths associated with water recreation. It is also a major contributing factor in up to 50% of drownings among adolescent boys, in particular (NCIPC, 1999b).

Firearms Firearms are the third leading cause of death due to unintentional injuries in the adolescent age group. In 1998, 3,792 children and adolescents younger than 20 years of age died from firearms. This represents a 10% reduction from the 4,223 youth who died from firearms in 1997 and a 35% decrease since 1994. Table 5.12 shows the 1998 rates of firearm mortality based on age, sex, and race.

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Sex</th>
<th>Rate per 100,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-4</td>
<td>Male</td>
<td>0.57</td>
</tr>
<tr>
<td>5-14</td>
<td>Male</td>
<td>0.12</td>
</tr>
<tr>
<td>15-24</td>
<td>Male</td>
<td>0.07</td>
</tr>
<tr>
<td>25-34</td>
<td>Male</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Adolescents and young adults have the highest rate of unintentional firearm-related fatalities, with males between the ages of 20 and 24 years having the highest risk (NCHS, 2000c). Among adolescents 15 to 19 years old, one in every four deaths is caused by a firearm (NCIPC, 1999d). The data for 1998 shows that firearm deaths had decreased by 19% for all ages since 1995. Among adolescents ages 15 to 24 years, there was a 27% decrease in the firearm death rate between 1995 and 1998 (NCHS, 2000b). More than 85% of all firearm-related deaths occur in males (Rivara, 1999).
• It is estimated that there are approximately three nonfatal firearm injuries for every death associated with a firearm.
• More than 70% of homicides are committed with a firearm.
• Firearm assaults on family members and other intimate acquaintances are 12 times more likely to result in death than are assaults with other weapons (NCIPC, 1999c).
• In 1999, 4.9% of high school students in a national survey reported having carried a gun to school within the past 30 days (CDC, 2000).

Bicycle Accidents

In 1998, 761 bicyclists were killed in crashes with motor vehicles. This is 8% less than in 1997 and represents a 24% reduction since 1975.
In 1998, 30% of bicycle deaths were among riders between the ages of 5 and 15 years (National Highway Traffic Safety Administration [NHTSA], 2000).
About seven times as many bicycle deaths occur among males as compared to females (IHHS, 1999c).
Bicycle deaths are most likely to occur in the summer and between the hours of 3 p.m. and 9 p.m. (IHHS, 1999b).
Bicycle tire puncture is the most common cause of head injuries sustained while bicycling.
Only 25% of all children between the ages of 5 and 14 years wear a helmet when riding. The percentage drops when teenagers are involved (NCIPC, 1999g).
Head injuries account for 67% of bicycle-related emergency department visits, 33% of hospitalizations, and 75% of bicycle-related deaths.
Motor vehicle collisions are responsible for approximately 33% of all bicycle-related brain injuries and 90% of bicycle fatalities.
Bicycle helmets decrease the risk of head injury by 85% and brain injury by 88% (Rivara and Aitken, 1998).
In 1999, more than 85% of all high school students reported riding a bicycle within the preceding 12 months also reported never or rarely wearing a bicycle helmet (CDC, 2000).

Skateboards Skateboarding has experienced intermittent periods of popularity since the 1960s. Along with this popularity, there have been concomitant increases in numerous types of injuries. Most documented cases occur in boys between the ages of 10 and 14 years, with injuries ranging from minor cuts and abrasions to multiple fractures and, in some cases, even death. Head injuries account for approximately 3.5% to 9% of all skateboarding injuries and fractures of both upper and lower extremities account for 50% of all musculoskeletal traumas. Not surprisingly, 33% of those injured on skateboards experience some form of trauma within the first week of participating in the sport. Despite traffic legislation, 65% of injured adolescents sustain injuries on public roads, footpaths, and parking lots. Skateboard injuries are expected to rise with the increasing number of participants, high-tech equipment, and renewed advertising (Fountain and Meyers, 1996).

All-Terrain Vehicles Almost 3,000 deaths have been associated with use of all-terrain vehicles (ATVs) since 1985. The risk of death, approximately 0.8 to 1.0 per 10,000 ATVs, has remained fairly steady for the past 10 years. Presently, about 54,500 emergency department visits each year are related to use of ATVs. Children younger than 16 years of age account for 47% of the injuries and more than 36% of deaths, while those younger than 12 years represent 15% of all deaths related to ATVs. Risk factors for injury include rider inexperience, intoxication with alcohol, excessive speed, and lack of helmet use. Head injuries account for most ATV-related deaths. Other nonfatal injuries include head and spinal trauma, abdominal injuries, abrasions, lacerations, and fractures (American Academy of Pediatrics [AAP] Committee on Injury and Poison Prevention [CIPP], 2000a).

Personal Watercraft The use of personal watercraft (PWC) has increased dramatically during the past decade, as have the speed and mobility of the watercraft. A similar dramatic increase in PWC-related injury and death has occurred simultaneously. The number of PWC-related fatalities was over 11 times greater (57) in 1996 than in 1987 (5). Preliminary data for 1997 show at least 83 PWC-related deaths. In many states, persons under 16 years of age are not legal operators of PWCs. Nonetheless, 7% of all injuries occur in children 14 years-old and younger and 27% occur in those under the age of 17 years. The most common types of PWC-related injuries are head trauma, lacerations, and fractures (AAP CIPP, 2000b).

Poisoning In 1998 alone, more than 2.2 million human exposures to poison were reported to poison control centers in the United States (Litovitz et al., 1999). Each year, almost 900,000 visits to emergency departments occur because of poisonings (NCIPC, 1999c). Most poisonings happen in the home and involve children. In 1999, 92% of all poisonings occurred in the home and 53% involved children younger than 6 years of age. Even though young children are at particular high risk for unintentional ingestion because of their developmental status, Fig. 5.3 shows that the percentage of unintentional deaths due to poisoning actually increases with age in the adolescent population (NCIPC, 1998a).

Debates continue regarding the relative importance of poverty, race, and age on the rates of unintentional injuries. In general, children who are injured are more likely to be poor, black, or Hispanic. Additional studies are needed to determine the extent to which injuries are associated with specific behaviors (CDC, 2000).

Common household items are often the cause of poisonings. The top five substances involved in poisonings among children younger than 6 years of age are cosmetics, cleaning substances, pain relievers or analgesics, plants, and cough and cold preparations. For children between the ages of 10 and 14 years, about 80% of all poisoning deaths are from substances other than medications. In contrast, medications are the cause of 58% of all poisoning deaths among adolescents ages 15 to 19 years. The most lethal substances for children of all ages are stimulants and street drugs, cardiovascular drugs, and antidepressants (Grossman, 2000b).

School Environment Because children and adolescents spend much of their day at school, it follows that many of the injuries they sustain occur there. In fact, between 33% and 50% of all child and adolescent injuries happen on school grounds. Playground accidents are the most common source of childhood injury at schools, particularly in the lower grades. However, most such injuries are minor and do not require medical attention outside of the school nurse (Hudson et al., 1999).

Schools and athletic fields increase with age and grade level. A large number of those injuries involve the improper use or malfunctioning of equipment (Knight et al., 2000).

Sports Injuries Approximately 45 million youth engage in scholastic and organized sports in the United States each year (Marsh and Daigneault, 1999). Data from the National Federation of State High School Associations show that between 1988 and 1998 participation in boys’ high school sports increased by about 10% while participation in girls’ sports rose almost 40% (Powell and Barber-Foss, 2000). Such participation results in about 750,000 sports-related injuries each year that require hospital-based care. In total, 81% of all participants, totaling more than 3 million injuries annually that result in time lost from sports (Marsh and Daigneault, 1999). Male athletes account for 84% of all adolescent sports-related injuries, despite the fact that rates are often higher among females, because fewer girls participate (Cheng et al., 2000). Within any given season, it is estimated that 48% of all adolescent athletes sustain at least one injury (Patel and Nelson, 2000). Of all adolescent sports injuries, 17% occur while participating in one of six sports: football, basketball, baseball or softball, soccer, bikini, or skating. The event-based injury rate for adolescent sports is 25.0 per 1,000 adolescents and the most common mechanisms are falls and being struck by or against objects. Table 5.13 shows the percentages of injury types and body locations within those six high school sports. Hospitalization is required in 2% of all sports-related injury visits; of those cases, 51% involve other persons, 12% are equipment-related, and 8% involve poor field or surface conditions (Cheng et al., 2000).
adolescent suicide (AAP COA, 2000). Because there is little chance for rescue. Firearms in the home, regardless of whether they are kept unloaded or stored locked up, are associated with a higher risk of

The most common method among adolescents who attempt suicide is the ingestion of pills. Firearms, used in more than 60% of all adolescent suicides, are the

**Method**

The most common method among adolescents who attempt suicide is the ingestion of pills. Firearms, used in more than 60% of all adolescent suicides, are the leading cause of death for male and female adolescents who successfully take their own lives. More than 90% of suicide attempts involving a firearm are fatal because there is little chance for rescue. Firearms in the home, regardless of whether they are kept unloaded or stored locked up, are associated with a higher risk of adolescent suicide (AAP COA, 2000).
The true number of deaths from suicide may actually be much higher than indicated, because some of these deaths are recorded as "accidental" (AAP COA, 2000).

**Suicide Attempts**

In a national survey of high school students in 1999, 19.3% reported having seriously considered attempting suicide during the 12 months preceding the survey. Overall, female students (24.9%) were significantly more likely than male students (13.7%) to have considered suicide. More serious ideation was reported by 14.5% of students nationwide who, during the preceding 12 months, had made a specific plan to attempt suicide. Female students were more likely to devise these plans than were male students (18.3% versus 10.9%). In reality, 8.3% of high school students attempted suicide at least once within the previous 12 months. More female than male students actually made an attempt to take their own life (10.9% versus 5.7%). Of all students who reported unsuccessful suicide attempts, 2.6% sustained an injury, poisoning, or overdose that had to be treated by a doctor or nurse (CDC, 2000).

**Homicide**

Homicide continues to be a major public health problem in the United States, particularly for young African-American males. Homicide remains the number two cause of death in the 15- to 24-year-old population and the number one cause of death among African-American males ages 15 to 24 years. The homicide rate among African-American male adolescents increased by 135% between 1950 and 1990. The rate peaked at 138.3 per 100,000 in 1990 and subsequently decreased by 30% to a rate of 96.5 per 100,000 in 1998. Still, the current rate is eight times that of white males and more than twice that of Hispanic males in the same age group. Of all deaths in the African-American male adolescent population, 52% are attributable to homicide. Firearms are involved in about 68% of all homicides but play a part in only 46% of homicides among African-American male adolescents (Adams et al., 1999; NCHS, 2000c).

**Recovery from Injuries: Consideration in the Adolescent**

It is clearly evident that children and youth grow and mature at accelerated rates, both physically and psychologically, during the adolescent years. Maturation results in physiological changes that affect performance, health status, and the healing process. Young people lack the experience and maturity to make appropriate decisions about how to respond to certain situations, and this may impede a timely and successful recovery after serious injury. Peer pressure heightens during adolescence and influences individuals to aspire to being and doing what it is they think others expect of them. It is not uncommon for adolescents to push themselves psychologically and physically beyond their limits. The adolescent developmental process confounds the recovery period in many ways. Significant differences exist between how young people adapt and recuperate from serious injury and how older adults do. For example:

1. A lack of knowledge exists in the medical field regarding the recovery process from trauma in adolescents.
2. It is often difficult to distinguish between developmental issues of adolescents and problems secondary to the injury, such as irritability or poor judgment.
3. Expectations of friends and family may fail to adjust to changes resulting from the injury.
4. Mental changes including impaired judgment, decreased attention span, irritability, short-term memory loss, and memory deficits make it difficult for adolescents to adhere to a treatment regimen.
5. Adolescents who experience athletic injuries and must discontinue sports participation may suffer depression or other psychological symptoms (Marsh and Daigneault, 1999).

**Prevention of Injuries**

Most unintentional injury deaths of children can be prevented. The three key approaches to injury prevention are education, environment and product changes, and legislation or regulation. Education can serve to promote changes in individual behaviors that increase the risk of injury and/or death. Environment and product modifications can make the adolescent's physical surroundings, toys, equipment, and clothes less likely to facilitate an injury. Legislation and regulation are among the most powerful tools to reduce adolescent injury, but they also require the most energy and concentrated efforts on the part of individuals and groups on each level of the socio-ecological model.

Successful reductions in future rates of childhood and adolescent injury will require the dedication of individuals to implement what we know works, the determination of communities to create environments where children can grow up safely, and public and private dollars to support injury prevention research and disseminate effective interventions. In addition, the four areas that have stymied injury prevention efforts of the past and continue to impede progress must be addressed and overcome if rates of adolescent injury are to be effectively managed:

1. The absence of reliable data on nonfatal injuries to allow proper targeting of interventions
2. The lack of training to prepare a multidisciplinary group of professionals to enter the field of injury prevention
3. Inadequate funding for injury research and prevention, given the magnitude and cost of the unintentional injury problem
4. The lack of coordinated prevention efforts by public and private agencies (Deal et al., 2000)

The following lists indicate some of the measures that may be taken to reduce injuries to adolescents.

**Motor Vehicle Injuries**

1. Adopt graduated licensing laws.
2. Impose a curfew to keep teenage drivers off the streets during late night and early morning hours.
3. Have parents impose restrictions and limitations of driving privileges on their teenage children.
4. Adopt laws restricting the number and age of passengers carried by teenage drivers (Chen et al., 2000; Grossman, 2000a).
5. Promote administrative license revocation that authorizes police to confiscate the licenses of drivers who either fail or refuse to take a chemical test for alcohol.
6. Promote primary safety belt laws that allow police to stop vehicles if the occupants are not using safety belts.
7. Strictly enforce the zero-tolerance laws for BAC in drivers younger than 21 years of age.
8. Strictly enforce the underage drinking laws.
9. Evaluate strategies to limit access to alcohol and promote safety belt use among teenagers.
10. Evaluate the separate components of graduated licensing systems to determine which ones are most effective (NCIPC, 1999f).

**Bicycle Injuries**

1. Make bicycle helmets mandatory for all riders.
2. Impose bicycle curfews to keep riders off the streets after dark.
3. Disseminate injury control recommendations on bicycle helmets.
4. Conduct proper bicycle helmet checks similar to child safety seat checkpoints.
5. Distribute written materials addressing all traffic laws and rules of the road in communities and schools.
6. Advise against riding double and freestyle stunts riding.

**Drownings**

1. Encourage swimming lessons at an early age.
2. Educate parents about the dangers of leaving children unattended in the bathtub or around swimming pools.
3. Establish a buddy system and never swim alone.
4. Educate people about the dangers of mixing alcohol with swimming or boating.
5. Mandate and enforce legal limits for BAC during water recreation activities.
6. Eliminate advertisements that encourage alcohol use during water recreation.
7. Require fencing around all public and private pools.
8. Restrict the sale of alcohol at water recreation facilities (NCIPC, 1999b).
9. Always wear a personal flotation device while boating in open water (Grossman 2000a).
Personal Watercraft Injuries

1. Require a PWC operator’s license for 16- to 20-year-olds.
2. Restrict adolescents younger than 16 years of age from operating a PWC unless accompanied by an adult.
3. Require PWC driver education for all operators.
4. Require helmets and life jackets for all riders.

Sports Injuries

1. Make the preparticipation athletic examination a requirement for all participants.
2. Encourage weight training and aerobic conditioning before the start of the season.
3. Provide medical coverage for all athletes at sporting events.
4. Appoint only coaches who have been properly trained and certified in youth sports.
5. Ensure that all athletes are properly hydrated throughout sporting events.
6. Appoint only officials who have been properly trained and certified in youth sports.
7. Ensure that all playing equipment, fields, and surfaces are safe and approved for youth sport participation.
8. Document the proper use of sport-specific protective equipment and distribute such items to all participants and their parents before play begins.
9. Check for proper safety equipment before approving players for participation in practice sessions or games.
10. Mandate the attendance of a certified emergency medical professional at all sporting events.
11. Arrange team composition based on body size and skills, not just chronological age (Cheng et al., 2000).

Suicide

Adolescents at higher risk of suicide commonly have a history of depression, a previous suicide attempt, a family history of psychiatric disorders, family disruption, or certain chronic or debilitating physical disorders or psychiatric illness. Alcoholism, alcohol use, and other substance use also indicate a high risk for suicidal tendencies. Psychosocial problems and stresses such as conflicts with parents, breakup of a relationship, school difficulties or failure, legal difficulties, social isolation, and physical ailments are also commonly reported or observed in young people who attempt suicide.

1. Document the risk factors for suicide attempts and disseminate this information to parents and teachers.
2. Ask questions about depression, suicidal thoughts, and other risk factors associated with suicide during routine history taking and analysis in adolescents.
3. Advocate for health insurance plans that ensure that adolescents have access to preventive and therapeutic mental health services that adequately address their needs (AAP COA, 2000).
4. Recommend that guns be removed from the home or, if present, that they be kept unloaded and locked in a combination safe, separate from bullets or shells (Grossman, 2000a). Placing cable or trigger locks on locked guns is an added safety feature.

Homicide

1. Encourage advocacy to institute a skills-building violence prevention and conflict resolution curriculum in the schools, from kindergarten through grade 12.
2. Provide education regarding conflict resolution, negotiation, and anger management skills among adolescents.
3. Advise parents to limit their adolescents’ viewing of violence in the media and witnessing or experiencing violence in the home and neighborhood (NCIPC, 1999e).
4. Encourage parents to remove guns from the home or, if guns are present, to keep them unloaded and locked in a combination safe, separate from bullets or shells (Grossman, 2000a). Placing cable or trigger locks on locked guns is an added safety feature.

MORBIDITY

Although the mortality rates for adolescents are low compared with those for adults, there is significant morbidity among teenagers. Table 5.14 lists the morbidity rates for selected diseases among adolescents during 1998 and Table 5.15 lists acute conditions in adolescents as reported in the 1996 National Health Interview Survey (CDC, 1998; Adams et al., 1999). Much like adolescent injury deaths, many of the diseases that are contracted by adolescents are a direct result of their health-related behaviors and lifestyle choices. For example, sexually transmitted diseases (STDs) are more prevalent among adolescents than in any other population group, and poor decisions lead adolescents to continually pass such diseases on to others (CDC, 1998).

### Table 5.14.
Morbidity of selected notifiable diseases in children, adolescents, and young adults, United States, 1998

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute respiratory infections</td>
<td>7.2</td>
<td>17.0</td>
<td>27.2</td>
<td>18.2</td>
<td>14.3</td>
<td>12.5</td>
<td>11.4</td>
<td>10.0</td>
<td>9.1</td>
<td>8.3</td>
<td>7.0</td>
</tr>
<tr>
<td>Influenza</td>
<td>1.9</td>
<td>5.1</td>
<td>6.5</td>
<td>7.1</td>
<td>5.9</td>
<td>4.7</td>
<td>4.4</td>
<td>4.1</td>
<td>3.6</td>
<td>3.1</td>
<td>2.6</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>3.5</td>
<td>7.0</td>
<td>8.5</td>
<td>8.5</td>
<td>8.4</td>
<td>7.8</td>
<td>7.5</td>
<td>7.1</td>
<td>6.6</td>
<td>6.6</td>
<td>6.0</td>
</tr>
<tr>
<td>Poliomyelitis</td>
<td>1.0</td>
<td>0.3</td>
<td>0.2</td>
<td>0.1</td>
<td>0.1</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Pertussis</td>
<td>1.0</td>
<td>2.0</td>
<td>3.0</td>
<td>3.0</td>
<td>3.0</td>
<td>3.0</td>
<td>3.0</td>
<td>3.0</td>
<td>3.0</td>
<td>3.0</td>
<td>3.0</td>
</tr>
<tr>
<td>Tetanus</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
</tr>
<tr>
<td>Malaria</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Mumps</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Rubella</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Rickets</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Hemophilia</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Scurvy</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
</tbody>
</table>

### Table 5.15.
Rates (per 100) of acute conditions per year, by age and type of condition, United States, 1996

<table>
<thead>
<tr>
<th>Year</th>
<th>Condition</th>
<th>Rate (per 100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1996</td>
<td>Acute respiratory infections</td>
<td>7.2</td>
</tr>
<tr>
<td>1996</td>
<td>Influenza</td>
<td>1.9</td>
</tr>
<tr>
<td>1996</td>
<td>Pneumonia</td>
<td>3.5</td>
</tr>
<tr>
<td>1996</td>
<td>Poliomyelitis</td>
<td>1.0</td>
</tr>
<tr>
<td>1996</td>
<td>Pertussis</td>
<td>1.0</td>
</tr>
<tr>
<td>1996</td>
<td>Tetanus</td>
<td>0.1</td>
</tr>
<tr>
<td>1996</td>
<td>Malaria</td>
<td>0.0</td>
</tr>
<tr>
<td>1996</td>
<td>Mumps</td>
<td>0.0</td>
</tr>
<tr>
<td>1996</td>
<td>Rubella</td>
<td>0.0</td>
</tr>
<tr>
<td>1996</td>
<td>Rickets</td>
<td>0.0</td>
</tr>
<tr>
<td>1996</td>
<td>Hemophilia</td>
<td>0.0</td>
</tr>
<tr>
<td>1996</td>
<td>Scurvy</td>
<td>0.0</td>
</tr>
</tbody>
</table>

Hospitilizations and Outpatient Visits

According to the Healthcare Cost and Utilization Project, hospitalizations for youth between the ages of 1 and 17 years represented 5.23% of the total number of hospitalizations in the United States in 1997. Table 5.16 and Table 5.17 provide additional data regarding childhood and adolescent medical visits and hospitalizations (Schappert and Nelson, 1999).
TABLE 5.16. Number and percentage distribution of office visits by ten most frequent principal reasons and principal diagnoses for ages 15 to 24 year, United States, 1995–1996

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Percentage of Visits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease and disorders of the respiratory system</td>
<td>20.23</td>
</tr>
<tr>
<td>Pregnancy, childbirth, and the puerperium</td>
<td>12.05</td>
</tr>
<tr>
<td>Diseases and disorders of the digestive system</td>
<td>11.96</td>
</tr>
<tr>
<td>Diseases and disorders of the musculoskeletal system</td>
<td>7.17</td>
</tr>
<tr>
<td>Diseases and disorders of the nervous system</td>
<td>6.98</td>
</tr>
<tr>
<td>Mental diseases and disorders</td>
<td>6.58</td>
</tr>
<tr>
<td>Endocrine, nutritional, and metabolic diseases and disorders</td>
<td>5.63</td>
</tr>
<tr>
<td>Diseases and disorders of the ear, nose, throat, and mouth</td>
<td>5.54</td>
</tr>
<tr>
<td>Infectious and parasitic diseases</td>
<td>3.07</td>
</tr>
<tr>
<td>Injuries, poisonings, and toxic effects of drugs</td>
<td>2.95</td>
</tr>
</tbody>
</table>

Data Sources

The National Health Interview Survey (NHIS) is a multistage probability sample survey conducted annually by interviewers at the Bureau of the Census for the NCHS. Data are collected during in-home interviews of the civilian noninstitutionalized U.S. population. The objectives of the survey are to present national estimates on the following (NCHS, 2000a):

1. Incidence of acute conditions
2. Percent of medically attended acute conditions
3. Number of disability days
4. Episodes of persons injured and associated activity restriction
5. Persons with activity limitation due to chronic conditions
6. Restricted activity days associated with acute and chronic conditions
7. Physician contacts and short-stay hospitalizations
8. Prevalence of chronic conditions and respondent-assessed health status

The National Health and Nutrition Examination Survey (NHANES) is another survey conducted by the NCHS. Data collection is unique in that it combines a home interview with health tests, which are done in a Mobile Examination Center. The goals of this research are as follows (NCHS, 2000a):

1. To estimate the number and percentage of persons in the U.S. population and designated subgroups with selected diseases and risk factors
2. To monitor trends in prevalence, awareness, treatment, and control of selected diseases
3. To monitor trends in risk behaviors and environmental exposures
4. To analyze risk factors for selected diseases
5. To study the relationship between diet, nutrition, and health
6. To explore emerging public health issues and new technologies
7. To establish a national probability sample of genetic material for future genetic testing

The National Longitudinal Study of Adolescent Health (Add Health) focuses on forces that influence adolescents’ behavior, in particular those residing in the various contexts of their lives: families, friendships, romantic relationships, peer groups, schools, neighborhoods, and communities. The study collects data to use in exploring the influences of both the individual attributes of adolescents and the attributes of their various environments on health and health-related behavior. Areas that are addressed include

Diet
Physical activity
Health service use
Morbidity
Injury
Violence
Sexual behavior
Contraception
Sexually transmitted infections
Pregnancy
Suicidal intentions/thoughts
Substance use/abuse
Runaway behavior

Data are also collected on such attributes as height, weight, pubertal development, mental health status (focusing on depression, the most common mental health problem among adolescents), and chronic and disabling conditions. Data are gathered from adolescents themselves, from their parents, and from school administrators. Already-existing databases provide information about neighborhoods and communities. With data from so many sources, new types of analyses are possible, involving both separate and joint effects of surroundings and circumstances on behavior and health status. The Add Health study is longitudinal, including a baseline in-school survey, an in-home survey 6 months later, and a third interview 1 year after the initial survey. Instead of relying on respondents’ memories and reconstruction of past events, it is thus possible to measure directly the influence of their experiences at one time on their behavior (and its consequences) at another.

An additional in-home survey has also recently been completed (Blum and Rinehart, 1999).

With technical assistance from the CDC, state members of state departments of education conduct the Youth Risk Behavior Survey (YRBS) every 2 years. Staff can add or delete questions in the core questionnaire to better meet the needs and interests of their state or local school district. School-based surveys were last conducted in 1999 among high school students nationwide, with the next survey planned for the spring of 2001. The goals of the YRBS are as follows:

1. To determine the prevalence and age at initiation of health-risk behaviors
2. To assess whether health-risk behaviors increase, decrease, or remain the same over time
3. To allow researchers to examine the occurrence of health-risk behaviors among young people
4. To provide comparable national, state, and local data
5. To monitor progress toward the Healthy People 2000 and Healthy People 2010 objectives and the National Education Goals (National Center for Chronic Disease Prevention and Health Promotion [NCCDPHP], 2000a)

Some of the outstanding statistics reported by the 1999 YRBS are presented in Table 5.18. Corresponding data from the 1998 Alternative High School Youth Risk Behavior Survey can be seen in Table 5.19. To understand how adolescent trends in risk-taking behavior have changed, Table 5.20 reports statistics from throughout the past decade.

Additional statistics of particular notability include the following:

- Nationwide, 37.7% of high school students had been treated by a doctor or nurse for injuries sustained while exercising, playing sports, or being physically active during the 12 months preceding the survey.
- During the 30 days preceding the survey, 13.1% of students nationwide had driven a vehicle at least once after drinking alcohol.
- Nationwide, 4.0% of students had been treated by a doctor or nurse for injuries sustained in a physical fight at least once during the 12 months preceding the survey. An estimated 105.9 incidents of physical fighting had occurred per 100 students on at least 1 day during that same 12-month period.
- During the 12 months preceding the survey, 8.8% of students nationwide had been hit, slapped, or physically hurt on purpose by their date, boyfriend, or girlfriend. Nationwide, 8.8% of students had even been forced to have sexual intercourse when they did not want to.
- Nationwide, 5.2% of students had missed at least 1 day of school during the 30 days preceding the survey because they felt unsafe at school or when traveling to and from school.
- Nationwide, 23.5% of all students younger than 18 years of age who reported current cigarette use had purchased their cigarettes themselves in a store or gas station during the 30 days preceding the survey.
- More than one fourth (26.7%) of students had used marijuana at least once during the 30 days preceding the survey, 4.0% had used a form of cocaine, and 4.2% had used inhalants.
- Nationwide, 36.3% of all students had had sexual intercourse during the 3 months preceding the survey, and 6.3% of students reported that they had been
pregnant or had gotten someone else pregnant. A large majority (90.8%) of students had been taught in school about acquired immunodeficiency syndrome (AIDS) or HIV infection.

- Nationwide, 40.4% of students had eaten less food, fewer calories, or foods low in fat to lose weight or to avoid gaining weight during the 30 days preceding the survey. Another 7.6% had taken diet pills, powders, or liquids without a doctor's advice, and 4.8% had vomited or taken laxatives to lose weight or to avoid gaining weight (CDC, 2000).

The trends that develop in regard to certain behavior patterns of various population-based groups become the basis for defining priority areas and setting health objectives for future years. Some of the National Health Objectives outlined in Healthy People 2010 that specifically relate to adolescents and young adults are listed here (NCCDPHP, 2000b; U.S. Department of Health and Human Services, 2000).

1. **Dental health**
   a. Reduce the proportion of adolescents with dental caries experience in permanent teeth.
      - Baseline: 61% in 1994
      - Target: 51% in 2010
   b. Reduce the proportion of adolescents with untreated decay in permanent teeth.
      - Baseline: 20% in 1994
      - Target: 15% in 2010

2. **Education**
   a. Increase the proportion of middle, junior high, and senior high schools that provide comprehensive school health education to prevent health problems in the following areas: unintentional injury, violence, suicide, tobacco use and addiction, alcohol or other drug use, unintentional pregnancy, HIV/AIDS and STD infection, unhealthy dietary patterns, inadequate physical activity, and environmental health.
      - Baseline: 28% in 1994
      - Target: 70% in 2010
   b. Increase the proportion of young adults who have received formal instruction before turning 18 years old on reproductive issues, including all of the following: birth control methods, safer sex to prevent HIV, prevention of STDs, and abstinence.
      - Baseline: 64% in 1995
      - Target: 90% in 2010
   c. Increase the proportion of the nation's public and private schools that require daily physical education for all students.
      - Baseline: 17% of middle and junior high schools and 2% of high schools in 1994
      - Target: 25% of middle and junior high schools and 5% of high schools in 2010

3. **Mortality**
   a. Reduce deaths of adolescents ages 10 to 14 years.
      - Baseline: 21.8 per 100,000 in 1998
      - Target: 16.8 per 100,000 in 2010
   b. Reduce deaths of adolescents ages 15 to 19 years.
      - Baseline: 69.7 per 100,000 in 1998
      - Target: 43.2 per 100,000 in 2010
   c. Reduce deaths of adolescents ages 20 to 24 years.
      - Baseline: 93.8 per 100,000 in 1998
      - Target: 67.3 per 100,000 in 2010
   d. Reduce the rate of suicide attempts by adolescents.
      - Baseline: 12-month average of 2.6% in 1997
      - Target: 12-month average of 1.0% in 2010

4. **Physical activity**
   a. Increase the proportion of adolescents who engage in vigorous physical activity that promotes cardiorespiratory fitness 3 or more days per week for 20 or more minutes per occasion.
      - Baseline: 64% in 1997
      - Target: 85% in 2010
   b. Increase the proportion of adolescents who engage in moderate physical activity for at least 30 minutes on 5 or more days per week.
      - Baseline: 20% in 1997
      - Target: 30% in 2010
   c. Increase the proportion of adolescents who participate in daily physical education classes at school.
      - Baseline: 27% in 1997
      - Target: 50% in 2010
   d. Increase the proportion of trips made by walking for youth ages 5 to 15 years.
      - Baseline: 28% in 1995
      - Target: 55% in 2010
   e. Increase the proportion of trips made by bicycling for youth ages 5 to 15 years.
      - Baseline: 2.2% in 1995
      - Target: 5.0% in 2010
   f. Reduce the proportion of children and adolescents who are overweight or obese.
      - Baseline: 11% in 1994
      - Target: 5% in 2010

5. **Sexual behavior**
   a. Increase the proportion of adolescents who abstain from sexual intercourse or use condoms if currently sexually active.
      - Baseline: 85% in 1997
      - Target: 95% in 2010
   b. Increase the proportion of adolescents ages 15 to 19 years who never engaged in sexual intercourse before age 15 years.
      - Baseline: 81% of girls and 79% of boys in 1995
      - Target: 88% in 2010
   c. Increase the proportion of adolescents who have never engaged in sexual intercourse.
      - Baseline: 62% of girls and 2.57% of boys in 1995
      - Target: 75% in 2010
   d. Reduce the proportion of adolescents and young adults with Chlamydia infection.
      - Baseline: 12.2% of females ages 15 to 24 years seen in STD clinics in 1997
      - Target: 3.0% of females ages 15 to 24 years seen in STD clinics in 2010
   e. Reduce the incidence of gonorrhea.
      - Baseline: 123 new cases per 100,000 in 1997
      - Target: 19 new cases per 100,000 in 2010
   f. Reduce the incidence of AIDS among adolescents and young adults.
      - Baseline: 19.5 new cases per 100,000 in 1998
      - Target: 1.0 new case per 100,000 in 2010
   g. Increase the proportion of sexually active unmarried adolescents 15 to 17 years of age who use contraception that both effectively prevents pregnancy and provides barrier protection against disease.
      - Condoms
      - Baseline: 68% of females and 72% of males in 1995
      - Target: 75% of females and 83% of males in 2010
      - Condoms and hormonal method
      - Baseline: 6% of females and 8% of males in 1995
      - Target: 9% of females and 11% of males in 2010
   h. Increase contraceptive use at last intercourse by unmarried adolescents age 15 to 17 years.
      - Condoms
      - Baseline: 38% of females and 70% of males in 1995
6. Substance use
   a. Increase the proportion of adolescents not using alcohol or any illicit drugs during the past 30 days.
      - Baseline: 77% in 1997
      - Target: 89% in 2010
   b. Increase the proportion of adolescents not using marijuana during the past 30 days.
      - Baseline: 9.4% in 1997
      - Target: 0.7% in 2010
   c. Reduce the proportion of adolescents who report riding, during the previous 30 days, with a driver who had been drinking alcohol.
      - Baseline: 37% in 1997
      - Target: 30% in 2010
   d. Reduce the proportion of high school seniors who report engaging in binge drinking during the past 2 weeks.
      - Baseline: 32% in 1998
      - Target: 11% in 2010
   e. Reduce the proportion of adolescents ages 12 to 17 years engaging in binge drinking during the past month.
      - Baseline: 8.3% in 1998
      - Target: 3.0% in 2010
   f. Reduce steroid use among adolescents.
      - Baseline: 1.2% in 8th and 10th grades and 1.7% in 12th grade in 1998
      - Target: 0.4% in 8th, 10th, and 12th grades in 2010
   g. Reduce the proportion of adolescents who use inhalants.
      - Baseline: 4.4% in 1997
      - Target: 0.7% in 2010
   h. Increase the average age at first use of substances by adolescents.
      - Baseline: 13.1 (alcohol) and 13.7 (marijuana) in 1997
      - Target: 16.1 (alcohol) and 17.4 (marijuana) in 2010
   i. Increase the proportion of high school seniors who report never having used substances.
      - Baseline: 19.9% (alcohol) and 46% (marijuana) in 1998
      - Target: 29.0% (alcohol) and 56% (marijuana) in 2010
7. Tobacco use
   a. Reduce cigarette smoking by adolescents.
      - Baseline: 36% in 1997
      - Target: 16% in 2010
   b. Reduce the use of spit tobacco among adolescents.
      - Baseline: 9% in 1997
      - Target: 1% in 2010
   c. Increase the age at first-time use of tobacco products by adolescents and young adults.
      - Baseline: 12 for ages 12 to 17 years and 15 for ages 18 to 25 years in 1997
      - Target: 14 for ages 12 to 17 years and 17 in 2010 for ages 18 to 25 years in 2010
   d. Increase adolescent tobacco use cessation attempts by adolescent smokers.
      - Baseline: 73% in 1997
      - Target: 84% in 2010
8. Violence
   a. Reduce physical fighting among adolescents.
      - Baseline: 36.6% in 1997
      - Target: 33.3% in 2010
   b. Reduce weapon carrying by adolescents on school property.
      - Baseline: 8.5% in 1997
      - Target: 6.0 % in 2010

Demographics

As demonstrated in Table 5.21 and Table 5.22, the adolescent population is, once again, on the rise. The number of white, black, and Hispanic children under the age of 18 years has been increasing steadily since 1985. However, the proportion of youth who live with both parents has decreased with the rise in total population. Single parents are raising an increasing number of young people. Additional details regarding family composition are included in Table 5.22 (United States Census Bureau, 2000).

![Table 5.21: Actual and projected number of adolescents, United States (in thousands)](image)
Trends in Office-based Ambulatory Care

The number of ambulatory care office visits has remained relatively stable since 1989. The total number of visits for all ages increased only 3.3% from 1989 to 1995–1996, and the visit rate per person decreased only slightly, from 2.8 in 1989 to 2.7 in 1995–1996. In general, females, whites, and older adults have higher visit rates than males, blacks and other races, and young people. Table 5.23 displays the number of office visits in 1995–1996 by medical specialty and patient age. For that period, visit rates for persons ages 15 to 24 years were the lowest of any age group. Between 1989 and 1995–1996, the percentage of visits to generalists decreased and visits to pediatricians and medical and surgical specialists increased. In 1989, 20.8% of all visits were made to general and family practice physicians, a significant decrease from the 30.5% recorded in 1985 (Schappert and Nelson, 1992, 1999). However, in the 1990s, visits to general and family practitioners began to increase again, accounting for 25.6% of all visits in 1995–1996. The current strong emphasis on primary and managed care, together with changing reimbursement rates of health insurance, will quickly turn these numbers back around. Table 5.24 reviews health insurance coverage by age throughout the 1990s. Adolescents were the least likely to have medical insurance to cover visits to any of these medical professionals (Schappert and Nelson, 1999).

TABLE 5.23. Number of office visits and percentage distribution, by medical specialty and patient's age, United States, 1995–1996

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Total Person Visits</th>
<th>Total Percent of All Visits</th>
<th>Pediatrician</th>
<th>General Practitioner</th>
<th>Medical and Surgical Specialist</th>
<th>Other Specialties</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–4</td>
<td>1,234,567</td>
<td>100</td>
<td>34.5%</td>
<td>65.5%</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>5–14</td>
<td>1,234,567</td>
<td>100</td>
<td>34.5%</td>
<td>65.5%</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>15–24</td>
<td>1,234,567</td>
<td>100</td>
<td>34.5%</td>
<td>65.5%</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>25–64</td>
<td>1,234,567</td>
<td>100</td>
<td>34.5%</td>
<td>65.5%</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>65+</td>
<td>1,234,567</td>
<td>100</td>
<td>34.5%</td>
<td>65.5%</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

TABLE 5.24. Health insurance coverage status by selected characteristics, United States, 1990–1997

WEB SITES

http://www.childstats.gov/. This Web site offers easy access to federal and state statistics and reports on children and their families, including population and family characteristics, economic security, health, behavior and social environment, and education. Reports of the Federal Interagency Forum on Child and Family Statistics include America’s Children: Key National Indicators of Well-Being, the annual federal monitoring report on the status of the nation's children, and Nurturing Fatherhood.

http://www.ahrq.gov/data/hcup/hcupnet.htm. From the Agency for Healthcare Research and Quality, a tool for identifying, tracking, analyzing, and comparing statistics on hospitals at the national, regional, and state level.


http://www.cdc.gov/nccdphp. Statistics and information on chronic diseases from National Center for Chronic Disease Prevention and Health Promotion.


http://www.cdc.gov/nchs, Portal for national statistics from the National Center for Health Statistics.

http://www.cdc.gov/nicip/niciphtm.htm. Statistics and searching tool from the National Center for Injury Prevention and Control; click either data or facts for information.

http://www.cdc.gov/nchs/about/major/ahcd/ahcdf1.htm. Data from the National Center for Health Statistics on ambulatory care.


http://www.aecf.org/. Annie E. Casey Foundation Web site, which strives to provide the best available data and analysis on critical issues affecting struggling families and at-risk kids.


http://www.futureofchildren.org/. The Future of Children is published twice annually by The David and Lucile Packard Foundation, Los Altos, California; its primary purpose is to disseminate timely information on major issues related to children’s well-being.


http://www.childtrends.org/. Child Trends is a nonprofit, nonpartisan research organization that studies children, youth, and families through research, data collection, and data analysis.


REFERENCES AND ADDITIONAL READINGS


Blum RW, Rinehart PM. Reducing the risk: connections that make a difference in the lives of youth. Minneapolis, MN: Division of General Pediatrics and Adolescent Health, University of Minnesota, 1999.


Nutrition is an essential component of total adolescent health care. Two important changes occurring during adolescence can cause a crisis in a teenager's nutritional needs. First, growth in height, weight, and body components is greater and more rapid than at any other time except infancy. Second, an adolescent's eating habits may change from regular meals prepared at home to irregular meals, skipped meals, and nutrition-poor snacks and fast-food meals. Adolescents have been found to have the highest prevalence of any age group of unsatisfactory nutrition. Practitioners should assess nutritional status and provide appropriate nutritional counseling as part of health supervision visits. The Food Guide Pyramid is a helpful educational tool that can be used to assist teenagers in improving their diets.

**POTENTIAL NUTRITIONAL PROBLEMS**

**Risk Factors**

1. Increased nutritional needs during adolescence are related to several factors.
   a. Adolescents gain 20% of their adult height.
   b. Adolescents gain 50% of their adult skeletal mass.
   c. Caloric and protein requirements are maximal.

2. Increased physical activity of adolescents makes proper nutrition essential.

3. Poor eating habits contribute to nutritional problems.
   a. Missed meals are common.
   b. High-sugar snacks of low nutritional value are popular. A study of 460 teenage girls (Wyshak, 2000) found that almost 80% consumed soft drinks, most of which were sugar-containing cola drinks. The same study found an association between carbonated beverage consumption and history of bone fracture.
   c. Peer pressure leads to erratic eating behavior.
   d. The adolescent's family may exhibit poor eating habits, and meal preparation may be inadequate.
   e. Many meals are obtained from vending machines or fast-food restaurants. Table 6.1 lists the fat and sodium contents of popular fast foods and ice cream snacks, many of which approach or exceed 50% of their calories from fat. Physicians and patients can access nutritional information on fast foods on the Internet at [http://www.fastfoodfacts.com](http://www.fastfoodfacts.com) or on the Web site of the Minnesota Attorney General's Office, [http://www.ag.state.mn.us/](http://www.ag.state.mn.us/) (click on Fast Food Facts in the "Featured on our Site" box).

4. Special considerations or stresses may be present.
   a. Sports
   b. Menstruation
   c. Teenage pregnancy
   d. Substance abuse
   e. Special diets (i.e., vegetarian)

All of these factors contributed to the findings of the Food and Drug Administration's Ten State Nutritional Survey in the 1960s (U.S. Department of Health, Education and Welfare, 1972); the National Health and Nutrition Examination Survey (NHANES) during 1971–1974 (National Center for Health Statistics [NCHS], 1979); and the NHANES III study in 1988–1994 (NCHS, 1994) all of which concluded that the highest prevalence of unsatisfactory nutritional status occurs in the adolescent age group. Of particular note were deficiencies of calcium, iron, riboflavin, thiamine, and vitamins A and C. 

**Associated Difficulties**

1. Iron deficiency: 5% to 8% prevalence during adolescence.
2. Obesity: 11% to 15% prevalence during adolescence. NHANES III data show that the prevalence of overweight individuals continues to increase: 12.3% of male adolescents, 10.7% of female adolescents, highest percentages among Mexican-American males (15%) and black females (16.3%).
3. Dental caries: Increased by consumption of high-sugar snacks. However, the cumulative number of carious permanent teeth decreased to 57.2% of individuals younger than 18 years of age between NHANES I and NHANES III.
4. Deficiencies in protein, minerals, and vitamins during pregnancy.

**DIETARY ASSESSMENT**

Assessing the dietary status of an adolescent should form part of the comprehensive health evaluation. This becomes even more important if a nutritional deficit is
suspected, if a chronic illness is present, or if the teenager is pregnant. Nutritional assessment can include dietary, anthropometric, clinical, and laboratory data.

**Dietary Data**

Dietary information can be obtained from a food record kept by the teenager, a dietary history obtained from a nutritionist, a 24-hour recall, or a diet questionnaire. Figure 6.1 is an example of a diet questionnaire for adolescents. Often, sample screening questions are quicker and easier; examples include:

1. Do you feel that your weight is too much, too little, or about right?
2. Have you recently lost or gained weight, or have you stayed the same?
3. Are there any foods that you have eliminated from your diet?
4. How many meals do you usually eat in a day?
5. Tell me everything you have eaten in the last 24 hours.
6. Are you on a diet?
7. What is the most you have ever weighed, and what would you like to weigh?
8. Are you comfortable with your eating habits?
9. Do you ever eat in secret?

Questions specifically useful in screening (sensitivity and specificity for disordered eating) in older adolescents and young adults include the following (Anstine and Grinenko, 2000):

1. How many diets have you been on in the past year? (two or three diets, 88% sensitivity and 63% specificity; four or five diets, 69% sensitivity and 86% specificity).
2. Do you feel you should be dieting? (often, 94% sensitivity and 67% specificity; usually, 87% sensitivity and 82% specificity).
3. Do you feel dissatisfied with your body size? (often, 96% sensitivity and 61% specificity; usually, 88% sensitivity and 74% specificity).
4. Does your weight affect the way you feel about yourself? (often, 97% sensitivity and 61% specificity; usually, 91% sensitivity and 74% specificity).

Each of these questions appears to have a very high correlation with the score on the EAT-26. The Eating Attitudes Test is a widely used standardized measure of symptoms characteristic of eating disorders.

**Anthropometric Measurements**

**Weight** Weight is a short-term measurement of nutrition. Use a balance-beam scale and have the teen remove shoes and heavy clothing. Weight-for-age charts are available as part of the growth charts published by the NCHS at [http://www.cdc.gov/growthcharts/](http://www.cdc.gov/growthcharts/). Slide presentations on growth charts and changes from NHANES I to NHANES III are available at [http://128.248.232.56/CDCGrowth/presentation/](http://128.248.232.56/CDCGrowth/presentation/). See also Fig. 1.22 and Fig. 1.24 in Chapter 1.

An estimate of ideal weight in postpubertal male adolescents of medium build is 106 pounds plus 6 pounds for each additional inch over 5 feet. For girls, the equivalent ideal weight is 100 pounds plus 5 pounds for each additional inch over 5 feet.

**Height** Height is a long-term indicator of nutrition. A wall-mounted Stadiometer is most accurate. Have the teen remove shoes and stand with heels touching the wall. Height-for-age charts are also available on NCHS growth charts.

**Weight for Height** Weight for height is a good indicator of obesity in preadolescents. These data are available on NCHS growth charts only for preadolescents. However, weight-for-age and height-for-age charts are included in Chapter 33 for adolescents age 12 to 17 years.

**Body Mass Index** The Expert Committee on Clinical Guidelines for Overweight in Adolescent Preventive Services (Himes and Dietz, 1994) recommends screening adolescents by using the body mass index (BMI). The BMI is equal to the weight (W, in kilograms) divided by the square of the height (H, in meters), or BMI = W/H^2. The BMI is easily determined, is highly reliable, and has a correlation of 0.7 to 0.8 with body fat content in adults; it also correlates well with body fat content in children and adolescents. In adolescents, a BMI exceeding the 85th percentile for age and gender has been suggested as one definition for overweight or for risk of being overweight. Values in adolescents are listed in Fig. 1.20 and Fig. 1.21 in Chapter 1. BMI-for-age charts may also be obtained in the Centers for Disease Control and Prevention Web site: [http://www.cdc.gov/growthcharts/](http://www.cdc.gov/growthcharts/).

**Skin Fold Measurements** The skin fold measurement is helpful in evaluating the adipose tissue component and degree of obesity. Formulas for calculating percent body fat with skin fold measurements are included in Chapter 33. However, although skin fold thickness is a more direct measure of adiposity than BMI and correlates well with body fat content in both adults and children, this technique requires training and has lower intraobserver and interobserver reliability than height and weight measurements used to calculate BMI.

**Midarm Circumference Measurement** The midarm circumference measurement evaluates muscle and adipose tissue and is a good indicator of nutritional status. It is predominantly a research technique and is not used frequently in clinical practice. Midarm circumference should be measured on the nondominant arm at a midpoint between the tip of the olecranon process and the tip of the acromion, with the arm relaxed at the side. The measurement should be taken without compressing the arm. Values less than 90% of standard indicate nutritional depletion. Table 6.2 shows standard midarm circumference measurements for adolescents.

---

**Fig. 6.1. Diet questionnaire for adolescents.** (Adapted from Fomon S. Nutritional disorders of children: prevention, screening, and follow-up [DHEW Publication (HSE) 78-5104]. Rockville, MD: U.S. Department of Health, Education, and Welfare, Health Services Administration, 1976.)

---

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>Sex</th>
<th>10th</th>
<th>25th</th>
<th>75th</th>
<th>90th</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td>Male</td>
<td>23.6</td>
<td>26.4</td>
<td>30.7</td>
<td>36.7</td>
</tr>
<tr>
<td>16</td>
<td>Male</td>
<td>23.6</td>
<td>26.4</td>
<td>30.7</td>
<td>36.7</td>
</tr>
<tr>
<td>17</td>
<td>Male</td>
<td>23.6</td>
<td>26.4</td>
<td>30.7</td>
<td>36.7</td>
</tr>
<tr>
<td>18</td>
<td>Male</td>
<td>23.6</td>
<td>26.4</td>
<td>30.7</td>
<td>36.7</td>
</tr>
<tr>
<td>19</td>
<td>Male</td>
<td>23.6</td>
<td>26.4</td>
<td>30.7</td>
<td>36.7</td>
</tr>
</tbody>
</table>

Source: [BMI for adolescents and measurement of midarm circumference in adolescents](http://www.cdc.gov/growthcharts/).
**TABLE 6.2.** Midarm circumference measurements in adolescents

**Waist-Hip Ratio** The waist-hip ratio (WHR) is useful in young adults. The WHR is equal to the circumference of the waist divided by the circumference of the hips. Its reliability is similar to that of the BMI, and it may be a better predictor of the sequelae associated with adult obesity. A WHR greater than 1.0 in adult men or 0.8 in adult women has been shown to predict complications from obesity, independent of BMI. It should be noted that the WHR has not been evaluated in all ethnic groups.

**Clinical Evaluation**

The clinical evaluation includes examination of skin, eyes, lips, tongue, gums, teeth, hair, and nails. The following is a list of clinical findings and possible nutritional causes.

1. **Skin**
   - **Pallor:** Iron deficiency
   - **Follicular hyperkeratosis:** Vitamin A deficiency or excess
   - **Xanthoma:** Hyperlipidemia
   - **Petechiae:** Vitamin C deficiency

2. **Eyes**
   - **Night blindness:** Vitamin A deficiency
   - **Angular palpebritis:** Riboflavin, niacin deficiencies

3. **Lips**
   - **Angular stomatitis, cheilosis:** Riboflavin, niacin deficiencies

4. **Tongue**
   - **Glossitis:** Niacin, folic acid, vitamin B₁₂, or vitamin B₆ deficiencies
   - **Papillary atrophy:** Riboflavin, niacin, folic acid, vitamin B₁₂, or iron deficiencies
   - **Loss of taste:** Zinc deficiency

5. **Gums**
   - **Soft, spongy, or bleeding:** Vitamin C deficiency

6. **Teeth**
   - **Excessive dental caries:** Diet high in refined sugar

7. **Hair**
   - **Dry, dull, and brittle:** Protein-calorie malnutrition

8. **Nails**
   - **Brittle with frayed borders:** Malnutrition, iron or calcium deficiency
   - **Concave or eggshell (free edge curved sharply outward):** Vitamin A deficiency

9. **Other signs of general malnutrition**
   - **Muscle wasting**
   - **Delayed sexual maturation**
   - **Amenorrhea**
   - **Hepatomegaly**

**Laboratory Tests**

Laboratory tests helpful in assessing nutritional status include hemoglobin, hematocrit, ferritin, serum protein, and albumin.

**Nutritional Requirements**

The Recommended Dietary Allowances (RDAs) for adolescents are reviewed in *Table 6.3* and *Table 6.4*. These are based on the recommendations of the Food and Nutrition Board of the National Academy of Sciences. In the past, the RDAs served as the benchmark of nutritional adequacy in the United States. However, scientific knowledge regarding the roles of nutrients has expanded dramatically since the inception of the RDAs. This has led to the development of the Dietary Reference Intakes (DRIs). This project has been divided into seven nutrient groups:

**TABLE 6.3.** Recommended Dietary Allowances for adolescents

**TABLE 6.4.** Recommended Dietary Allowances (light face type) and adequate intake (bold face type) values, by age

Calcium, vitamin D, phosphorus, magnesium, and fluoride
Folate and other B vitamins
Antioxidants (e.g., vitamin C, vitamin E, selenium)
Macronutrients (e.g., proteins, fats, carbohydrates)
Trace elements (e.g., iron, zinc)
Electrolytes and water
Other food components (e.g., fiber, phytoestrogens)

DRIs apply to healthy populations only; they are used to refer to several types of reference values:

- **Recommended Dietary Allowance (RDA):** This is the dietary intake level that is sufficient to meet the nutrient requirements of almost all healthy individuals (97% to 98%) of North Americans.
- **Adequate Intake (AI):** This is the value based on observed or experimentally determined approximations of nutrient intake by a group—used when RDA cannot be determined.
- **Estimated Average Requirement (EAR):** This is the intake value that is estimated to meet the requirement defined by a specified indicator of adequacy in 50% of an age- and gender-specific group. At this level of intake, the remaining 50% of the specified group would not have its needs met.
- **Tolerable Upper Intake Level (UL):** This is the maximum level of daily nutrient intake that is unlikely to pose risks of adverse health effects to almost all of the individuals in the group for whom it is designed.

**Energy Requirements**

Energy requirements are determined by basal metabolic rate, growth needs, and level of activity. Energy is provided by fat (which supplies 9 kcal/g), carbohydrates (4 kcal/g), and protein (4 kcal/g). Alcohol (7 kcal/g) can also be a significant source of calories. Diets in teenagers should probably contain no more than 30% of calories from fat. Suggested caloric intakes are listed in Table 6.3, but these will vary widely according to body size and activity level.

**Protein**

Protein requirements increase during adolescence by about 10 g/day, to 1 g/kg in males and 0.8 g/kg in females. Most teenagers' diets exceed the RDA for protein.

**Minerals**

**Iron**

There is an increased need for iron in both males and females during adolescence, in males because of the increase in muscle mass and blood volume and in females because of menstrual losses. High-iron foods include lean red meats, spinach, green vegetables, and fortified cereals. Nonheme iron, which is present in plant sources, is less bioavailable, but its absorption can be enhanced by concurrent intake of vitamin C.

**Calcium**

Skeletal growth causes an increased need for calcium, to about 400 mg/day, during adolescence. Many adolescents have inadequate calcium intakes, possibly in part because of the substitution of carbonated beverages for milk. It is highly likely that current high levels of soft drink consumption are replacing the drinking of milk. Data from the U.S. Department of Agriculture Continuing Surveys of Food Intakes by Individuals indicate a drop in milk intake among adolescent girls, from 72% drinking milk on a given day in 1977–1979, to 57% in 1994. In addition to dairy products, calcium is found in tofu, sardines, and dark-green leafy vegetables.

**Zinc**

Daily needs increase from 10 to 15 mg during adolescence. Zinc is needed for adequate growth, sexual maturation, and wound healing. Good food sources of zinc include lean meats, seafood, eggs, and milk.

**Vitamins**

Vitamin requirements increase during adolescence, especially for vitamin B₁₂; folate; vitamins D, A, C, and E; thiamine; niacin; and riboflavin. It has been shown that supplements of antioxidant vitamins (A, C, E, and β-carotene) probably reduce the risk of cardiovascular disease and certain cancers, but there is no current recommendation to prescribe them routinely.

**GUIDELINES FOR NUTRITIONAL THERAPY**

**General Recommendations**

1. Stress to the adolescent the effects of dietary changes on current lifestyle: appearance, muscle development for sports, feeling energetic, and so on.
2. Use the Food Guide Pyramid ([Fig. 6.2](#)) to recommend the appropriate number of daily servings from each food group.

![Fig. 6.2](#)

**FIG. 6.2.** Food guide pyramid; a guide to daily food choices. (From U.S. Food and Drug Administration. *FDA consumer special issue on food labeling* [S/N 017-017-01200360-5]. Washington, DC: U.S. Government Printing Office, 1993. Black-and-white reproducibles suitable for producing office handout material may be ordered from the U.S. Food and Drug Administration [HFI-40], 5600 Fishers Lane, Rockville, MD 20856, 301-443-3220.)

3. Encourage teenagers to be aware of the comparative nutritional values of fast foods and to read food labels ([Fig. 6.3](#)).

![Fig. 6.3](#)


4. Suggest that teenagers exercise at least 3 days a week, for a minimum of 20 min/day.
5. Simplify good nutrition concepts by recommending the following to adolescents and their families:
   a. Eat a variety of foods.
   b. Maintain a healthy weight.
   c. Choose foods low in saturated fat and cholesterol.
      - Broil or bake instead of frying foods.
      - Select leaner cuts of meats.
      - Substitute low-fat or nonfat milk for whole-milk dairy products.
      - Use more polyunsaturated fats.
   d. Eat more fruits, vegetables, and grains.
   e. Use sugar and salt sparingly.
      - Avoid presweetened cereals and products.
      - Keep sugar bowl and salt shaker off the table.
      - Drink fruit juices or water instead of soft drinks or fruit drinks.
      - Decrease intake of candy, cookies, and pie.
      - Avoid salty and smoked meats.
   f. Eat meals together as a family. In a 2000 study by Gillman et al., eating family dinner was correlated with improved nutritional intake in early adolescence.

Special Conditions

Vegetarian Diets

Adolescents may be vegetarian for reasons of health or because of ecological, economic, religious, or philosophical beliefs. Teens who are vegetarians should be supported and encouraged, because their diets are likely to be more healthful than that of the typical adolescent. Nutritional counseling may be of benefit to ensure adequate intakes of vitamins and minerals and to determine the need for supplements.

Types of Vegetarians

Semivegetarians eat milk products and limited seafood and poultry but no red meat.
Lactovegetarians consume milk products but no eggs, meat, fish, or poultry.
Ovolactovegetarians consume milk products and eggs but no meat, fish, or poultry.
Ovovegetarians consume eggs but no milk products, meat, fish, or poultry.
Vegans consume vegetable foods only and no foods of animal origin (i.e., no eggs, milk products, meat, fish, or poultry).

Further information is available from the Vegetarian Resource Center on their Web site: http://www.vrg.org/.

Supplemental Needs of Vegetarians

Vitamins: Semivegetarians, lactovegetarians, and ovolactovegetarians have no need for supplements if attention is paid to dietary composition. Ovovegetarians and vegans may need supplemental riboflavin and vitamins D and B₁₂.

Protein: Adequate protein intake has been a traditional concern for vegetarians; however, vegetarians usually meet or exceed protein requirements. There is also mounting evidence that the practice of eating complementary proteins in the same meal is unnecessary.

Minerals: There is no uniform need for supplements, but vegetarians are at increased risk for iron and zinc deficiencies.

Pregnancy

During pregnancy, daily caloric needs increase from 2,200 to 2,500 kcal/day. Weight gain during pregnancy should range from 25 pounds for an overweight teen to 40 pounds for an underweight teen. Teen should be counseled against dieting during pregnancy. A prenatal vitamin supplement should be prescribed, to include 1 mg of folate. Dietary counseling can be one of the most important interventions for a pregnant adolescent to ensure a healthy delivery and a healthy baby.

Athletes

Risk for Iron and Zinc Deficiency

Both male and female adolescent athletes are at risk for iron deficiency. Athletes (especially menstruating females and those involved in endurance sports such as distance running) should be screened for low hemoglobin or hematocrit levels. Serum ferritin can be helpful in determining loss of iron stores and need for supplementation. Ferritin levels lower than 12 µg/L correspond to completely depleted iron stores, and levels between 12 and 35 µg/L indicate partially depleted iron stores. For the athlete who is not anemic but has low iron stores, 50 to 100 mg of elemental iron daily (ferrous gluconate, 240 or 325 mg twice daily, or ferrous sulfate, 325 mg daily or twice daily) should be recommended. For the anemic athlete, 100 to 200 mg of elemental iron daily (ferrous gluconate, 325 mg three times daily, or ferrous sulfate, 325 mg twice daily) should be given. Repeat laboratory measurements should be performed after 2 to 3 months of therapy. Athletes with iron deficiency anemia may also be zinc deficient. Education regarding good dietary sources of zinc and iron should be provided.

Sodium and Potassium

Athletes need increased intake of sodium and potassium, but this requirement will generally be met as they increase their calorie intake.

Calories

The active athlete who engages in 2 hr/day of heavy exercise needs 800 to 1,700 extra calories per day beyond the recommended minimum for age, sex, height, and weight. The approximate distribution of calories, according to the American Dietetic Association, should be carbohydrates, 55% to 60%; proteins, 12% to 15%; and fats, 25% to 30%.

Hydration

Attention must be given to hydration before and during activity:
- The athlete should drink 10 to 16 ounces of cold water 1 to 2 hours before exercise.
- Repeat 20 to 30 minutes before exercise.
- Drink 4 to 6 ounces of cold water every 10 to 15 minutes during exercise.
- Cold fluids are preferable because gastric emptying is more rapid.
- Plain water can be used for exercise periods of less than 2 hours.
- Sports drinks may be used to provide carbohydrates for longer events. Fructose-containing solutions should be avoided, because fructose is less well absorbed than sucrose or glucose and can cause gastrointestinal upset.

Weight Restrictions

Avoid any major weight restrictions during the adolescent growth spurt. Alterations in diet to cause rapid weight gain or loss should be discouraged. Eating disorders are prevalent among female athletes, especially those involved in running, swimming, diving, gymnastics, or dance. Therefore, carefully question all female athletes regarding body image, desired weight, and amenorrhea. The female athlete triad (amenorrhea, disordered eating, and osteoporosis) should be suspected in an athlete with secondary amenorrhea.
Carbohydrate Loading

Diets that are chronically high in carbohydrate are not recommended. For optimal performance, the athlete should train lightly or rest 24 to 36 hours before competition. On the day of competition, the athlete may consider a high-carbohydrate, low-fat meal 3 to 6 hours before an event and an optional snack 1 to 2 hours before the event. Foods high in carbohydrates (60% to 70%) have also been recommended after competition to replace glycogen stores. However, Hawley et al. (1995) pointed out that a diet of 5,000 cal/day that is only 45% carbohydrate is sufficient to restore muscle glycogen within 24 hours. An initial “depletion phase” consisting of vigorous workouts and low-carbohydrate eating before competition also is no longer recommended.

Ergogenic Nutritional Supplements

 Branched-chain amino acids (BCAAs), creatine, and carnitine are among the substances being used by some athletes to improve performance.

The rationale for use of BCAAs is that they supply muscle tissues with extra substrate, thereby improving performance. However, studies do not support improved performance with ingestion or infusion of BCAAs.

Creatine phosphate provides phosphate for muscle energy storage in the form of adenosine triphosphate (ATP) via adenosine diphosphate (ADP). Data indicate that creatine ingestion does increase muscle creatine and does improve performance for exercise of very short duration (i.e., 15 to 30 seconds). Less benefit is seen in the more highly trained athletes. There is no improvement in exercise endurance. In conclusion, creatine may improve short-duration, high-intensity exercise, and adverse effects have not been noted.

The rationales for use of carnitine are that it has a glycogen sparing effect as a result of increased fatty acid oxidation, it may increase availability of acetyl-Coenzyme A used in the Krebs cycle, and it may increase pyruvate oxidation and prevent lactic acid accumulation. Most studies do not support improved performance.

Teen athletes who are considering the use of nutritional supplements should note that research subjects may represent a narrow group (e.g., male collegiate athletes), that the effects of long-term supplement use have generally not been studied, and that laboratory results may not transfer to on-the-field results. In addition, supplements can be quite costly. Most athletes can maximize their performance via consistent, appropriate training and attention to adequate nutrition rather than relying on supplement use.

WEB SITES

For Teenagers and Parents

http://www.mayoclinic.org/, Nutrition section from Mayo Clinic.
http://www.bcm.tmc.edu/crc/index.htm, Baylor University nutrition research center for children.
http://www.fitness.com/, Exercise and nutrition site for teens.
http://www.foodsafety.gov/, U.S. Food and Drug Administration site on nutrition and food safety.

For Health Professionals

http://www.nal.usda.gov/8001/pv/pmap.htm, Food Pyramid from USDA.
http://www.americanheart.org/, American Heart Association diets.
http://www4.nas.edu/IOM/IOMHome.nsf/Pages/Food+and+Nutrition+Board, Food and Nutrition Board home page with sections on RDIs.

REFERENCES AND ADDITIONAL READINGS


Himes JH, Dietz WH. Guidelines for overweight in adolescent preventive services recommendations from an expert committee. The Expert Committee on Clinical Guidelines for Overweight in


Wherever a health care practitioner treats an adolescent, it is essential for the practitioner to have a clear understanding of the legal framework within which care is to be provided. Because many adolescents are minors—younger than 18 years in almost all states—their legal status differs from that of adults. Therefore, the laws related to their health care have distinct aspects based on their age and legal status.

For adolescents who are age 18 years or older, the governing laws are the same as those for other adults. For adolescents who are minors, the laws may be different. The issues that arise most frequently in providing health care to adolescents who are minors fall into three specific areas:

1. Consent: Who is authorized to give consent and whose consent is required?
2. Confidentiality: Who has the right to control the release of confidential information about the care, including medical records, and who has the right to receive such information?
3. Payment: Who is financially liable for payment and is there a source of insurance coverage or is public funding available that the adolescent can access?

LEGAL FRAMEWORK

Over the past three decades, the legal framework that applies to the delivery of adolescent health care has evolved in several significant ways. First, the courts have recognized that minors, like adults, have constitutional rights, although there has been considerable controversy concerning the scope of those rights. Second, all states have enacted statutes to authorize minors to give their own consent for health care under specific circumstances. Third, the financing of health care services for all age groups and income levels is undergoing major change, at an increasingly rapid pace, which has had and will continue to have a significant impact on adolescents’ access to health care.

Constitutional Issues

Beginning with In re Gault in 1967, in which the U.S. Supreme Court stated that “neither the Fourteenth Amendment nor the Due Process Clause is for adults alone,” the Court has held repeatedly that minors have constitutional rights. The Gault decision, which accorded minors certain procedural rights when they are charged by the state with juvenile delinquency offenses, was followed by others recognizing that minors also had rights of free speech under the First Amendment ( Tinker v. Des Moines Independent School District, 1969) and that they had privacy rights (Planned Parenthood of Central Missouri v. Danforth, 1976; Carey v. Population Services International, 1977). Although the Supreme Court subsequently rendered decisions that were more equivocal about the scope of minors’ constitutional rights, the basic principles articulated in the early cases still stand.

The area of most frequent constitutional litigation—and the greatest controversy—has been the rights of minors with respect to reproductive health care, particularly abortion. The early cases, Carey and Danforth, clearly established that the right of privacy protects minors and adults and encompasses minors’ access to contraceptives and the abortion decision. However, the history of constitutional litigation with respect to abortion has been complex. After the decision in the Danforth case, which held that parents do not have an arbitrary veto power with respect to the abortion decisions of their minor daughters, the U.S. Supreme Court decided a series of cases over the next two decades—beginning with Bellotti v. Baird in 1979 and continuing more recently with Planned Parenthood of Southeastern Pennsylvania v. Casey in 1992—addressing parental notification and consent issues related to abortion. The import of these cases has been that although a state may enact a mandatory parental involvement requirement for minors who are seeking abortions, it must also, at minimum, establish an alternative procedure, usually known as a “judicial bypass.” In the bypass proceeding, a minor must be permitted, without parental involvement, to seek a court order authorizing an abortion: If she is mature enough to give an informed consent, the court must allow her to make her own decision; and if she is not mature, the court must determine whether an abortion would be in her best interest. Many, but not all, states have enacted such parental involvement or judicial bypass statutes, some of which have been implemented, although others have been enjoined by the courts.

State and Federal Statutes

Although the constitutional litigation concerning minors’ rights in the reproductive health care arena has attracted significant attention, most of the specific legal provisions that affect adolescents’ access to health care are contained in state and federal statutes or in “common law” decisions of the courts. These provisions cover a broad range of issues related to consent, confidentiality, and payment and are critical in defining the parameters of what practitioners in the adolescent health field are legally permitted and required to do. Thus, practitioners providing services to adolescents must develop a familiarity not only with the general constitutional principles that have evolved in recent decades, but also with federal laws and state laws that apply in their own states.

CONSENT

The law generally requires the consent of a parent before medical care can be provided to a minor. There are, however, numerous exceptions to this requirement. In many situations, someone other than a biologic parent—such as a foster parent, a juvenile court, a social worker, or probation officer—may be able to give consent in the place of the parent. Moreover, in emergency situations, care may be provided without prior consent to safeguard the life and health of the minor.

Highly significant for the adolescent health care practitioner, however, are the legal provisions that authorize minors themselves to give consent for their care. These provisions are typically based on either the status of the minor or the services sought. (See the Appendix at the end of this chapter, which sets forth some of these provisions.)

All states have enacted one or more provisions that authorize minors to consent to certain services. These services most frequently include contraceptive services; pregnancy-related care; diagnosis and treatment of sexually transmitted diseases, human immunodeficiency virus, or acquired immunodeficiency syndrome, and reportable or contagious diseases; examination and treatment related to sexual assault; counseling and treatment for drug or alcohol problems; and mental health treatment, particularly outpatient care. Not all states have statutes covering all of these services. Some of these statutes contain age limits, which most frequently fall between the ages of 12 and 15 years.

Similarly, all states have enacted one or more provisions that authorize minors who have attained a specific status to give consent for their own health care. Pursuant to these provisions, the following groups of minors may be authorized to do so: emancipated minors, those who are living apart from their parents, minors serving in the armed forces, married minors, minors who are the parents of a child, high school graduates, and minors who have attained a certain age. Moreover, in a few states, explicit statutes authorize minors who are “mature minors” to consent for care. Few states have enacted all of these provisions and laws are frequently amended; thus, practitioners are advised to consult their state laws and to ensure they have current information.
THE MATURE MINOR DOCTRINE AND INFORMED CONSENT

Even in the absence of a specific statute, however, “mature minors” may have the legal capacity to give consent for their own care. The mature minor doctrine emerged from court decisions addressing the circumstances in which a physician could be held liable in damages for providing care to a minor without parental consent. Pursuant to the doctrine, in most states, there is little likelihood that a practitioner will incur liability for failure to obtain parental consent in situations in which the minor is an older adolescent (typically at least the age of 15) who is capable of giving an informed consent and in which the care is not high risk, is for the minor’s benefit, and is within the mainstream of established medical opinion. During the past few decades, diligent searches have found no reported decisions holding a physician liable in such circumstances solely on the basis of failure to obtain parental consent when nonnegligent care was provided to a mature minor who had given informed consent. The basic criteria for determining whether a patient is capable of giving an informed consent are that the patient must be able to understand the risks and benefits of any proposed treatment or procedure and its alternatives and must be able to make a voluntary choice among the alternatives. These criteria apply to minors, as well as adults. Again, however, laws do vary from state to state and practitioners must become familiar with local requirements.

PRIVACY AND CONFIDENTIALITY

There are numerous reasons why it is important to maintain confidentiality in the delivery of health care services to adolescents. Possibility the most important is to encourage adolescents to seek necessary care and provide a candid and complete health history, but additional reasons include supporting adolescents’ growing sense of privacy and autonomy and protecting them from the humiliation and discrimination that could result from disclosure of confidential information.

The confidentiality obligation has numerous sources in law and policy. They include the federal and state constitutions; federal statutes and regulations (such as those that pertain to medical privacy in general, Medicaid, family planning programs, federal drug and alcohol programs, maternal and child health programs, or community and migrant health centers); state statutes and regulations (such as medical confidentiality statutes, medical records statutes, privilege statutes, professional licensing statutes, or funding statutes); court decisions; and professional ethical standards. The federal government has recently issued extensive regulations on medical privacy that affect the care of adolescents and adults, which are of critical importance. It is also possible that Congress will enact federal privacy legislation that would affect adolescents, so practitioners should monitor ongoing developments carefully.

Because these varied provisions sometimes conflict or are less than clear in their application to minors, practitioners must have some general guidelines to follow—or questions to ask—when developing their understanding of how to handle confidential information. Confidentiality protections are rarely, if ever, absolute, so practitioners must understand what may be disclosed (based on their discretion and professional judgment), what must be disclosed, and what may not be disclosed. In reaching this understanding, practitioners may ask questions; a few of the most relevant questions include the following:

- What information is confidential (because it is confidential information that is protected against disclosure)?
- What information is not confidential (because such information is not protected)?
- What exceptions are there in the confidentiality requirements?
- What information can be released with consent?
- What other mechanisms allow for discretionary disclosure?
- What mandates exist for reporting or disclosing confidential information?

In general, even confidential information may be disclosed as long as authorization is obtained from the patient or another appropriate person. Often, when minors have the legal right to consent to their own care, they also have the right to control disclosure of confidential information about that care. This is not always the case, however, because there are a number of circumstances in which disclosure over the objection of the minor might be required: if a specific legal provision requires disclosure to parents, if a mandatory reporting obligation applies, as in the case of suspected physical or sexual abuse, or if the minor poses a severe danger to him or herself or to others.

When the minor does not have the legal right to consent to care or to control disclosure, the release of confidential information must generally be authorized by the minor or, if the minor is not capable of providing consent (or guardianship), by someone with legal authority to act on the minor’s behalf. In general, an authorized person must be someone who has the legal authority to consent (or guardianship) for the minor. Some statutes require that the authorized person be someone who is related to the minor (e.g., a parent or legal guardian). In other cases, the designated authorized person may depend on the circumstances of the case. For example, in some states, the authorized person may be anyone who is legal authorized to provide care for the minor or someone who is related to the minor by blood or marital relationship. In many cases, the authorized person will be the minor’s legal guardian. In other cases, the authorized person will be the person who is responsible for the minor’s care. The authorized person must be someone who is able to give valid consent for the minor’s care.

There are some federal and state health care funding programs that enable minors to obtain confidential care with little or no cost to them. Most notable is the federal privacy legislation that would affect adolescents, so practitioners should monitor ongoing developments carefully.

WEB SITES

http://www.adolescenthealthlaw.org/. The Center for Adolescent Health & the Law is a national organization that supports laws and policies that promotes the health of adolescents and their access to health care.
http://www.healthy.org/. The National Health Law Program is a national public interest law firm that seeks to improve health care for low-income families and children, minorities, and people with disabilities.
http://www.youthlaw.org/. The National Center for Youth Law is a national nonprofit law office serving the legal needs of children and their families.
http://www.abanet.org/child/home.html. The American Bar Association Center for Children and the Law is a national project of the American Bar Association that works to improve children’s lives through advances in law, justice, knowledge, practice, and public policy.
http://www.class.org/. The Center for Law and Social Policy is a national nonprofit organization with expertise in law and policy affecting the poor.
http://www.hhs.gov/ocr/hippa/. The office for civil rights in HHS is the agency charged with implementing the new federal medical privacy regulations.
REFERENCES AND ADDITIONAL READINGS


In re Gault, 387 US 1 (1967).


APPENDIX

The Appendix Table is the most recent compilation by the Alan Guttmacher Institute (AGI) on state statutes relating to an unmarried and unemancipated minor's authority to consent to health services. The AGI periodically reviews state laws pertaining to minors' authority to consent to medical care and make other important decisions without their parents' knowledge or permission. The AGI, in this current version, expanded its review to consider state court decisions and attorneys' general opinions that affect young people's access to confidential services. This review was conducted in July 2000.

More information is available from the AGI at the following Web addresses:

http://www.agi-usa.org/sections/youth.html
http://www.agi-usa.org/sections/law.html
http://www.agi-usa.org/pubs/b_minor_00.pdf

Please note that neither this chapter nor the Appendix represents legal advice. Health care practitioners are reminded that laws change that may affect court decisions, statutes, and court decisions may be subject to differing interpretations. It is the responsibility of each health care professional to be familiar with the current relevant laws that affect the health care of adolescents. In difficult cases involving legal issues, advice should be sought from someone with state-specific expertise.

For detailed information about each state's minor consent laws, see English et al., 2001. This 200-page monograph contains summaries of each state's minor consent statutes with citations. It is available in hard copy by request from the Center for Adolescent Health & the Law (info@adolescenthealthlaw.org) or through the center's Web site (http://www.adolescenthealthlaw.org).

APPENDIX TABLE. Minors’ right to consent to health care and to make other important decisions

<table>
<thead>
<tr>
<th>State</th>
<th>Contraceptive Prenatal care</th>
<th>STD/HIV services</th>
<th>Treatment for alcohol and/or drug abuse</th>
<th>Outpatient mental health services</th>
<th>General medical health services</th>
<th>Abortion/Drop out services (of school)</th>
<th>Medical/Placing care for child for adoption</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alabama</td>
<td>NL</td>
<td>MC</td>
<td>MC</td>
<td>MC</td>
<td>PC</td>
<td>MD</td>
<td>PC</td>
</tr>
<tr>
<td>Alaska</td>
<td>MC</td>
<td>MC</td>
<td>NL</td>
<td>MC</td>
<td>PC</td>
<td>MD</td>
<td>MC</td>
</tr>
<tr>
<td>Arizona</td>
<td>NL</td>
<td>MCI</td>
<td>MC</td>
<td>MC</td>
<td>PC</td>
<td>MD</td>
<td>MC</td>
</tr>
<tr>
<td>Arkansas</td>
<td>MCI</td>
<td>MCI</td>
<td>NL</td>
<td>NL</td>
<td>PC</td>
<td>MD</td>
<td>MC</td>
</tr>
<tr>
<td>California</td>
<td>MCI</td>
<td>MCI</td>
<td>MCI</td>
<td>MCI</td>
<td>PC</td>
<td>MD</td>
<td>MC</td>
</tr>
<tr>
<td>Colorado</td>
<td>MCI</td>
<td>MCI</td>
<td>MCI</td>
<td>MCI</td>
<td>PC</td>
<td>MD</td>
<td>MC</td>
</tr>
<tr>
<td>Connecticut</td>
<td>MCI</td>
<td>MCI</td>
<td>MCI</td>
<td>MCI</td>
<td>PC</td>
<td>MD</td>
<td>MC</td>
</tr>
<tr>
<td>Delaware</td>
<td>MCI</td>
<td>MCI</td>
<td>MCI</td>
<td>MCI</td>
<td>PC</td>
<td>MD</td>
<td>MC</td>
</tr>
<tr>
<td>Dist. of Columbia</td>
<td>MCI</td>
<td>MCI</td>
<td>MCI</td>
<td>MCI</td>
<td>PC</td>
<td>MD</td>
<td>MC</td>
</tr>
<tr>
<td>Florida</td>
<td>MCI</td>
<td>MCI</td>
<td>MCI</td>
<td>MCI</td>
<td>PC</td>
<td>MD</td>
<td>MC</td>
</tr>
<tr>
<td>Georgia</td>
<td>MCI</td>
<td>MCI</td>
<td>MCI</td>
<td>MCI</td>
<td>PC</td>
<td>MD</td>
<td>MC</td>
</tr>
<tr>
<td>Hawaii</td>
<td>MCI</td>
<td>MCI</td>
<td>MCI</td>
<td>MCI</td>
<td>PC</td>
<td>MD</td>
<td>MC</td>
</tr>
<tr>
<td>Idaho</td>
<td>NL</td>
<td>MCI</td>
<td>MCI</td>
<td>MCI</td>
<td>PC</td>
<td>MD</td>
<td>MC</td>
</tr>
<tr>
<td>Illinois</td>
<td>MCI</td>
<td>MCI</td>
<td>MCI</td>
<td>MCI</td>
<td>PC</td>
<td>MD</td>
<td>MC</td>
</tr>
<tr>
<td>Indiana</td>
<td>NL</td>
<td>MCI</td>
<td>MCI</td>
<td>MCI</td>
<td>PC</td>
<td>MD</td>
<td>MC</td>
</tr>
<tr>
<td>Iowa</td>
<td>MCI</td>
<td>MCI</td>
<td>MCI</td>
<td>MCI</td>
<td>PC</td>
<td>MD</td>
<td>MC</td>
</tr>
<tr>
<td>Kansas</td>
<td>MCI</td>
<td>MCI</td>
<td>MCI</td>
<td>MCI</td>
<td>PC</td>
<td>MD</td>
<td>MC</td>
</tr>
<tr>
<td>Kentucky</td>
<td>MCI</td>
<td>MCI</td>
<td>MCI</td>
<td>MCI</td>
<td>PC</td>
<td>MD</td>
<td>MC</td>
</tr>
<tr>
<td>Louisiana</td>
<td>NL</td>
<td>MCI</td>
<td>MCI</td>
<td>MCI</td>
<td>PC</td>
<td>MD</td>
<td>MC</td>
</tr>
<tr>
<td>Maine</td>
<td>MCI</td>
<td>MCI</td>
<td>MCI</td>
<td>MCI</td>
<td>PC</td>
<td>MD</td>
<td>MC</td>
</tr>
<tr>
<td>Maryland</td>
<td>MCI</td>
<td>MCI</td>
<td>MCI</td>
<td>MCI</td>
<td>PC</td>
<td>MD</td>
<td>MC</td>
</tr>
<tr>
<td>Massachusetts</td>
<td>NL, MCI</td>
<td>MCI</td>
<td>MCI</td>
<td>MCI</td>
<td>PC</td>
<td>MD</td>
<td>MC</td>
</tr>
<tr>
<td>Michigan</td>
<td>NL</td>
<td>MCI</td>
<td>MCI</td>
<td>MCI</td>
<td>PC</td>
<td>MD</td>
<td>MC</td>
</tr>
<tr>
<td>Minnesota</td>
<td>MCI</td>
<td>MCI</td>
<td>MCI</td>
<td>MCI</td>
<td>PC</td>
<td>MD</td>
<td>MC</td>
</tr>
<tr>
<td>Mississippi</td>
<td>MCI</td>
<td>MCI</td>
<td>MCI</td>
<td>MCI</td>
<td>PC</td>
<td>MD</td>
<td>MC</td>
</tr>
<tr>
<td>Montana</td>
<td>MCI</td>
<td>MCI</td>
<td>MCI</td>
<td>MCI</td>
<td>PC</td>
<td>MD</td>
<td>MC</td>
</tr>
</tbody>
</table>
Nebraska: NL; MC; MC; NL; NL; NL; PN; MD; NL = 14

Nevada: NL; NL; MC; MC; NL; NL; MD; NL = 14

New Hampshire: NL; NL; MC; MC; NL; NL; MD; NL = 14

New Jersey: NL; NL; MC; MC; NL; NL; MD; NL = 14

New Mexico: NL; MC; NL; MC; NL; NL; MD; NL = 14

New York: NL; MC; NL; MC; NL; MC; NL; NL = 14

North Carolina: MC; MC; MC; NL; NL; NL; NL; NL = 14

North Dakota: NL; NL; MC; MC; NL; NL; NL; NL = 14

Ohio: NL; NL; MC; MC; NL; NL; NL; NL = 14

Oklahoma: MC; MC; MC; NL; NL; NL; NL; NL = 14

Oregon: MC; NL; NL; MC; MC; NL; NL; NL = 14

Pennsylvania: NL; MC; MC; MC; NL; NL; NL; NL = 14

Rhode Island: NL; NL; MC; MC; NL; NL; NL; NL = 14

South Carolina: MC; NL; NL; MC; NL; NL; NL; NL = 14

South Dakota: NL; NL; MC; MC; NL; NL; NL; NL = 14

Tennessee: MC; MC; MC; MC; NL; NL; NL; NL = 14

Texas: NL; MC; MC; NL; MC; MC; NL; NL = 14

Utah: NL; MC; MC; NL; NL; NL; NL; NL = 14

Vermont: NL; MC; MC; MC; NL; NL; NL; NL = 14

Virginia: MC; MC; MC; MC; MC; NL; NL; NL = 14

Washington: NL; NL; MC; MC; NL; NL; NL; NL = 14

West Virginia: NL; NL; MC; MC; NL; NL; NL; NL = 14

Wisconsin: NL; NL; MC; MC; NL; NL; NL; NL = 14

Wyoming: MC; NL; MC; NL; NL; NL; NL; NL = 14

Total PMCD: 26; 28; 51; 46; 21; 22; 3; 34; 11; 30; 35

Total PC/PN: 0; 0; 0; 0; 0; 2; 3; 11; 8; 0; 5

Total NL/NA: 25; 0; 2; 0; 6; 30; 27; 17; 8; 0; 11

Note:

1. In all but four states, the age of majority is 18. In AL and NE, it is 19, and in PA and MS, it is 21; however, in MS 18 is the age of consent for health care. STD, sexually transmitted disease; HIV, human immunodeficiency virus; MC, minor explicitly authorized to consent; MD, minor allowed to decide; PC, parental consent explicitly required; PN, parental notice explicitly required; NL, no law or policy found.

2. All states require minors to attend school until a certain age, beyond which the young person or, in a few states, the parents may decide whether the minor will stay in school.

3. Minor must be at least 12.

4. State officially classifies HIV/AIDS as an STD or infectious disease, for which minors may consent to testing and treatment.

5. Doctor may notify parents.

6. Minor must be at least 16.

7. Minor may consent if a parent; also if married in DE, KY, ME, MD, MN, MS, MO and NV; also if married or pregnant in CO, FL, IL, MA, MT, NY and OK.

8. Law has been blocked by court action.

9. Law does not distinguish between minor and adult parents.

10. Includes abortion.

11. Includes surgery.

12. Any minor who is mature enough to understand the nature and consequences of the proposed medical or surgical treatment may consent.

13. Involvement of both parents is required.

14. Minor may not drop out.

15. Minor parent must have a court-appointed guardian.

16. Law explicitly authorizes minor to consent to HIV testing and/or treatment.

17. Law does not apply to HIV treatment.

18. Minor may consent if a child or doctor believes minor will suffer “probable” health hazard if services not provided; in IL also if minor is referred by doctor, clergyman or Planned Parenthood clinic; in CO and MS also if minor is referred by a doctor, clergyman, family planning clinic, school of higher education or state agency.

19. Minor must be at least 15.

20. Applies to minors younger than age 16.

21. Includes an alternative to parental involvement or judicial bypass. In MD the law provides for a physician bypass but does not have a judicial bypass.

22. A minor who is pregnant or, in DE, FL, GA, IN, MD and OK, has a child may marry without parental consent; in FL, KY and OK, the marriage must be authorized by a court; in IN and MD a minor must be at least 15.

23. Minor must be at least 13.

24. Minor must be at least 14.

25. Includes surgery.

26. Minor may drop out if employed and in MA, MO and NE is 14, in HI is 15, in IA also it has completed the sixth grade; in NE also if has completed the eighth grade. Otherwise a minor may drop out at 16 in these states.

27. Teens need judicial authorization.

28. The state's medical consent statutes allow “any person of ordinary intelligence and awareness” to consent to hospital, medical, surgical or dental care. Although a later section authorizes parent consent for a minor child, the attorney general's office “frequently” interprets the law as authorizing minors to consent. (R. Hardin, deputy attorney general, personal communication to P. Donovan, 27.

29. Minor may consent if she has ever been pregnant.

30. Minor may consent if she has ever been pregnant.

31. Includes an alternative to parental involvement or judicial bypass. In MD the law provides for a physician bypass but does not have a judicial bypass.

32. A minor who is pregnant or, in DE, FL, GA, IN, MD and OK, has a child may marry without parental consent; in FL, KY and OK, the marriage must be authorized by a court; in IN and MD a minor must be at least 15.

33. Minor must be at least 13.

34. Minor must be at least 14.

35. Includes surgery.

36. Minor may drop out if employed and in MA, MO and NE is 14, in HI is 15, in IA also if has completed the sixth grade; in NE also if has completed the eighth grade. Otherwise a minor may drop out at 16 in these states.

37. Teens need judicial authorization.

38. The state's medical consent statutes allow “any person of ordinary intelligence and awareness” to consent to hospital, medical, surgical or dental care. Although a later section authorizes parent consent for a minor child, the attorney general's office “frequently” interprets the law as authorizing minors to consent. (R. Hardin, deputy attorney general, personal communication to P. Donovan, 27.

39. Minor may consent if she has ever been pregnant.

40. Minor may consent if she has ever been pregnant.

41. Includes an alternative to parental involvement or judicial bypass. In MD the law provides for a physician bypass but does not have a judicial bypass.

42. Minor may consent to pregnancy testing and diagnosis.

43. Law allows minors to consent when parent or guardian is not “immediately available.”

44. Parent must be shown the informed consent form for an HIV test before the minor signs it.

45. Minor may consent if she has ever been pregnant.

46. Minor must be at least 16 or have completed eighth grade, whichever occurs later.

47. After eighth grade, court determines whether the minor or the parents can make the decision.

48. May require the consent of a minor parent's parent.

49. Minor may consent if she has ever been pregnant.

50. Minor parent must have a court-appointed guardian.

51. Includes an alternative to parental involvement or judicial bypass. In MD the law provides for a physician bypass but does not have a judicial bypass.

52. Includes an alternative to parental involvement or judicial bypass. In MD the law provides for a physician bypass but does not have a judicial bypass.

53. Minor may consent if she has ever been pregnant.

54. Providers rely on State v. Kloos, which held that minors have the same constitutional rights as adults, to provide confidential contraceptive services and prenatal care to minors.

55. Includes an alternative to parental involvement or judicial bypass. In MD the law provides for a physician bypass but does not have a judicial bypass.
Chapter 1 described the numerous and varied normal physical changes of adolescence. Sometimes, however, an adolescent's growth falls outside the range of normal. For example, the adolescent may be too short, too tall, or possibly not as sexually developed as his or her peers. These are areas of enormous concern to adolescents and their family, and the health care provider, consequently, must have a clear understanding of how to evaluate and manage these problems.

**Delayed Puberty**

**Definition**

In general, two standard deviations (SDs) above and below the mean are used to define the range of normal variability. An adolescent who falls above or below these limits deserves a careful evaluation for hypothalamic, pituitary, or gonadal dysfunction, or undiagnosed chronic illness. 

Chapter 1 is helpful in determining guidelines for evaluation. Further guidelines are listed next.

**Male Guidelines** A male adolescent may be considered to have delayed puberty if

1. Genital stage 1 (G1) persists beyond the age of 13.7 years, or pubic hair stage 1 (PH1) persists beyond the age of 15.1 years.
2. More than 5 years have elapsed from initiation to completion of genital growth.
3. The following sexual maturity ratings (SMRs) persist past the listed guidelines:
   - G2 > 2.2 years
   - 3G > 1.6 years
   - G4 > 1.9 years
   - PH2 > 1.0 year
   - PH3 > 0.5 year
   - PH4 > 1.5 years

**Female Guidelines** A female adolescent may be considered to have delayed maturation if

1. Breast stage 1 (B1) persists beyond the age of 13.4 years, PH1 persists beyond the age of 14.1 years, or there is failure to menstruate beyond the age of 16 years.
2. More than 5 years have elapsed between initiation of breast growth and menarche.
3. The following SMRs persist past the listed guidelines:
   - B2 > 1.0 year
   - B3 > 2.2 years
   - B4 > 6.8 years
   - PH2 > 1.3 years
   - PH3 > 0.9 year
   - PH4 > 2.4 years

These general guidelines must be taken in the context of the teen's family history as to growth and pubertal development, his or her previous growth pattern, and with regards to the review of systems and physical examination.

**Differential Diagnosis**

The differential diagnosis of delayed puberty can be divided between those processes associated with short stature and those associated with normal stature.

**Pubertal Delay without Short Stature**

1. Constitutional delay of puberty
2. Acquired gonadotropin deficiency
   a. Central hypothalamic-pituitary tumors: Craniopharyngioma, hypothalamic glioma, astrocytoma, pituitary adenomas
   b. Head trauma
   c. Central nervous system (CNS) infections: Viral encephalitis, tuberculosis
   d. Histiocytosis X
   e. Sarcoidosis
3. Isolated gonadotropin deficiency
   a. Kallmann syndrome
   b. Other disorders with luteinizing hormone (LH) and follicle-stimulating hormone (FSH) deficiency
4. Acquired gonadal disorders
   a. Infections: Gonorrhea, tuberculosis, viral
   b. Trauma
   c. Postsurgical removal
5. Congenital gonadal disorders
   a. Klinefelter syndrome
   b. Anorchism
   c. Pure gonadal dysgenesis
   d. Enzyme defects in androgen and estrogen production

6. Androgen-receptor defects
   a. Complete (previously referred to as “testicular feminization”)
   b. Incomplete (previously referred to as a variety of syndromes, including Reifenstein syndrome)

7. Chronic diseases
   a. Congenital or acquired heart disease
   b. Asthma
   c. Inflammatory bowel disease
   d. Celiac disease
   e. Juvenile rheumatoid arthritis
   f. Systemic lupus erythematosus
   g. Anorexia nervosa
   h. Hyperthyroidism
   i. Galactosemia (in girls)

Pubertal Delay with Short Stature

1. Constitutional delay of puberty and normal variant short stature
2. Panhypopituitarism
   a. Congenital
   b. Acquired
      • Infectious: Viral, tuberculosis
      • Posttraumatic
      • Central tumors
      • Sarcoidosis
      • Histiocytosis

3. Congenital syndromes
   a. Turner syndrome: Girls
   b. Noonan syndrome: Boys or girls
   c. Mixed gonadal dysgenesis
   d. Prader-Willi syndrome
   e. Laurence-Moon-Bardet-Biedl syndrome
   f. Alström syndrome

4. Glucocorticoid excess

5. Chronic diseases
   a. Chronic heart disease
   b. Asthma
   c. Inflammatory bowel disease
   d. Celiac disease
   e. Juvenile rheumatoid arthritis
   f. Tuberculosis
   g. Chronic renal failure
   h. Renal tubular acidosis
   i. Sickle cell anemia
   j. Hypothyroidism
   k. Diabetes mellitus
   l. Systemic lupus erythematosus
   m. Anorexia nervosa
   n. Cystic fibrosis
   o. Infection with human immunodeficiency virus (HIV)
   p. Use of stimulants for attention deficit disorder

Evaluation of Delayed Puberty

Most adolescents with delayed maturation have constitutional delay of puberty. However, this diagnosis is made by excluding other causes. Following is a discussion of the evaluation of the adolescent with delayed puberty, including criteria for a provisional diagnosis of constitutional delay of puberty.

**History**

1. Growth record: This is important in determining the timing and form of any deviations from the norm. Examples of growth charts in various disease states are provided in Fig. 8.1, Fig. 8.2, Fig. 8.3, Fig. 8.4, Fig. 8.5, Fig. 8.6 and Fig. 8.7.

![Fig. 8.1. Constitutional delay of puberty in girls 2 to 20 years of age (National Center for Health Statistics percentiles). (Adapted from National Center for Health Statistics, NCHS growth charts, 2000. www.cdc.gov/growthcharts.)](Fig. 8.1. Constitutional delay of puberty in girls 2 to 20 years of age (National Center for Health Statistics percentiles). (Adapted from National Center for Health Statistics, NCHS growth charts, 2000. www.cdc.gov/growthcharts.)
FIG. 8.2. Catch-up growth in girls 2 to 20 years of age, with prematurity or deprivation states (National Center for Health Statistics percentiles). (Adapted from National Center for Health Statistics, NCHS growth charts, 2000. www.cdc.gov/growthcharts.)

FIG. 8.3. Low height and low weight in girls 2 to 20 years of age with familial short stature, primordial short stature, or constitutional delay of puberty (National Center for Health Statistics percentiles). (Adapted from National Center for Health Statistics, NCHS growth charts, 2000. www.cdc.gov/growthcharts.)

FIG. 8.4. Decreased height and markedly decreased weight in girls 2 to 20 years of age with chronic illness states (National Center for Health Statistics percentiles). (Adapted from National Center for Health Statistics, NCHS growth charts, 2000. www.cdc.gov/growthcharts.)

FIG. 8.5. Markedly decreased height and decreased weight in girls 2 to 20 years of age with hypopituitary states, metabolic disorders such as rickets, or hypothyroidism (National Center for Health Statistics percentiles). (Adapted from National Center for Health Statistics, NCHS growth charts, 2000. www.cdc.gov/growthcharts.)

FIG. 8.6. Decreased height and increased weight in girls 2 to 20 years of age with Cushing syndrome and hypothyroidism (National Center for Health Statistics percentiles). (Adapted from National Center for Health Statistics, NCHS growth charts, 2000. www.cdc.gov/growthcharts.)
FIG. 8.7. Markedly decreased weight in girls 2 to 20 years of age with anorexia nervosa (National Center for Health Statistics percentiles). (Adapted from National Center for Health Statistics, NCHS growth charts, 2000. www.cdc.gov/growthcharts.)

2. Family history: Obtaining the family history will determine whether there is a history of late puberty in other family members. The heights of parents, siblings, and grandparents should be ascertained, measured if possible, as well as the age at menarche of the mother and the adolescent's sisters. Also helpful are questions such as Was the father small as a teenager in relation to his classmates, and at what age did he start to shave? Most patients (more than 60%) with constitutional delay of puberty have a positive family history.

3. Review of systems: This helps to rule out any chronic systemic illness. Particular attention should be given to CNS and gastrointestinal (GI) symptoms.

4. Nutritional history and eating habits: This helps to discount a problem of chronic malnutrition.

Physical Examination A complete physical examination is indicated for the adolescent with delayed puberty, but the following areas are of particular importance:

1. Nutritional status (if indicated, include skin fold thickness).
2. Body measurements, including height, weight, body mass index, arm span, and upper/lower (U/L) body-segment ratios.
   a. U/L ratio: Determined by measuring the height from the top of the head to the symphysis pubis and dividing by the height from the symphysis pubis to the floor. Normally, the ratio is 1.7 at birth, 1.0 at 10 years of age, and 0.9–1.0 in adulthood. Adult African-American individuals tend to have longer limbs, so the U/L ratio is closer to 0.85–0.9. There are no standards in Asian and American-Indian populations, but these individuals tend to have shorter limbs and therefore would tend to have a higher normal U/L ratio than white populations.
   b. Hypothyroidism: The U/L ratio will remain greater than 1.0. Most patients with a chondrodysplasia will also have an abnormally high U/L ratio.
   c. Hypogonadism: The U/L ratio will be close to 0.9 or less. A normal ratio will be found in growth hormone (GH) deficiency, constitutional delay of puberty, and chronic illness states.
3. SMR: It is critically important to evaluate the SMR to determine whether puberty has started, as well as for longitudinal follow-up.
4. Thyroid: Check for evidence of goiter. Absence of goiter can be seen with hypothyroidism.
7. Abdomen: Check for abdominal distention as a sign of a malabsorptive disease and check for evidence of liver or spleen enlargement as a sign of a chronic systemic disorder.
8. Pelvic examination: An external vaginal examination should be performed on all girls, and if amenorrhea is a problem, a complete pelvic examination is indicated. As indicated later, a pelvic ultrasound can be performed if needed to determine the presence of müllerian structures (uterus and tubes) and to visualize ovaries.
9. Neurological examination: This will help to eliminate from consideration any intracranial pathology. Ophthalmoscopic and visual-fields examination is done to rule out abnormalities of the optic nerves and to look for evidence of intracranial hypertension.

Laboratory Tests

1. Complete blood cell (CBC) count: Check for evidence of anemia or leukocytosis.
2. Urinalysis: Check for evidence of renal disease and with specific gravity for diabetes insipidus.
4. A serum chemistry profile should include measurements of glucose, creatinine, calcium, phosphorus, serum albumin, protein, and liver function tests.
5. Bone age: Determination of bone age is an essential part of the evaluation for delayed puberty. Delayed bone age will be seen in adolescents with hypopituitarism, hypothyroidism, chronic illness, and constitutional delay of puberty. Normal or delayed bone age may be seen in patients with Turner syndrome. Bone age is also helpful when used in conjunction with height age and chronological age. Height age is determined by locating the corresponding age at which the patient's height would be equal to the 50th percentile. Table 8.1 describes typical relationships between bone age, height age, and chronological age for various causes of delayed puberty and short stature.

<table>
<thead>
<tr>
<th>Causes of delayed puberty</th>
<th>Bone age vs. height age (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skeletal</td>
<td>-4 to +2 SD</td>
</tr>
<tr>
<td>General hypopituitarism</td>
<td>-3 to +2 SD</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>-1 to +2 SD</td>
</tr>
<tr>
<td>Constitutional delay</td>
<td>0 to +2 SD</td>
</tr>
<tr>
<td>Hypogonadism</td>
<td>0 to +2 SD</td>
</tr>
<tr>
<td>Chronic illness</td>
<td>0 to +2 SD</td>
</tr>
<tr>
<td>Systemic</td>
<td>0 to +2 SD</td>
</tr>
</tbody>
</table>

6. Central imaging studies such as magnetic resonance imaging (MRI), computed tomography (CT), or lateral skull x-ray study: The lateral skull x-ray is of such limited value that it should not be performed. If a central process is considered, a cranial CT or MRI should be performed.
7. Hormone levels: Check adjusted thyroxine (T4) level and thyroid-stimulating hormone (TSH) level.
8. Insulin-like growth factor I (IGF-I) and IGF-binding protein 3 (IGF-BP-3): These hormones have been described in Chapter 1. IGFs are a family of insulin-like peptide growth factors. They are under the control of GH secretion and act to increase the growth of skeletal tissues. IGF-I levels reflect GH activity but can be influenced by various other factors and conditions, including malnutrition, liver disease, or renal impairment. The correlation with growth is not exact. For example, a teen may grow normally but have a low IGF-I. Usually a high-normal IGF-I concentration excludes GH deficiency. IGF-BP-3 can also be measured as a reflection of GH and IGF-I sufficiency.
   a. Normal levels (IGF-I, IGF-BP-3): Levels vary with age. They are lowest during infancy and increase throughout childhood to peak values during puberty. When IGF-I levels are interpreted, they should be interpreted as to bone age, if it is markedly different from chronological age.
   b. Low levels: Levels of IGF-I and IGF-BP-3 can be low in patients with GH deficiency, malnutrition, chronic illness states, hypothyroidism, resistance to endogenous GH, and errors in GH structure.

Additional Tests

Other tests are necessary in some evaluations, particularly if the diagnosis of constitutional delay of puberty is in doubt. These tests could include the following:

1. Karyotype: A karyotype is particularly useful in ruling out Turner syndrome in short girls.
2. Upper GI tract series, small-bowel follow-through, and barium enema series: These tests are indicated if history or laboratory findings suggest inflammatory
3. Celiac panel: Helps to assess for this form of malabsorption.
4. Pelvic ultrasound: A pelvic ultrasound can be performed to determine the presence of the müllerian structures, such as the uterus and tubes. The ultrasound can also be used to visualize the ovaries and to determine ovarian dimensions.
5. Gonadotropin levels: High levels suggest gonadal failure, whereas low levels suggest hypothalamic-pituitary failure. Polyclonal assays are now discriminating in the low range to help differentiate gonadotropin deficiency from constitutional delay of puberty. FSH levels elevated for the degree of pubertal development after 9 years of age can be seen in patients with Turner syndrome and can be used as a screening test before obtaining a karyotype.
6. GH measurements: Because a single fasting level is insufficient to diagnose GH deficiency, stimulation tests are necessary. Listed here are several commonly used tests. A normal response is a GH level of more than 7–10 ng/mL after stimulation. GH deficiency has been classically defined as a lack of an increase in serum GH to 7 ng/mL or more in response to two pharmacological stimulation tests in children growing at a subnormal rate. Of these tests, either the L-Dopa, the glucagon, or the clonidine test is probably the best outpatient screening tool, and the combined insulin tolerance and arginine infusion test is probably the most reliable to confirm the diagnosis of GH deficiency. However, the administration of insulin to induce hypoglycemia must be done with caution.
   a. Sleep: Test GH level 1–2 hours after onset of sleep. This is difficult to obtain in clinical practice.
   b. Exercise: Test GH level before and after 15 minutes of vigorous stair climbing. This is an unreliable screen because of the inability to quantitate exercise.
   c. Arginine: Test GH levels before and at 30-minute intervals for 3 hours after glucagon (1 mg) is given intramuscularly or subcutaneously. This test can also be used to assess cortisol secretion.
   d. Insulin: Test GH levels before and at 15-minute intervals for 1 hour after regular insulin (0.1 U/kg of body weight) is given intravenously. This test requires constant monitoring for severe hypoglycemia, and intravenously administered glucose should be readily available to terminate the test if necessary. Cortisol response to hypoglycemia can also be done.
   e. L-Dopa with or without propranolol: After an overnight fast, administer L-Dopa (500 mg) plus propranolol (0.75 mg/kg [up to 40 mg]). Serum is drawn for determination of GH levels 60 minutes and 90 minutes later.
   f. Arginine infusion: L-Arginine monohydrochloride (0.5 g/kg [up to a maximum of 30 g]) is given intravenously over 30 minutes. GH is measured at 0, 15, 30, 50, 90, and 120 minutes after the start of the arginine infusion. This test is an excellent confirmatory test.
   g. Clonidine: A dose of 0.1–0.15 mg/m² can be given orally, and GH is measured at 0, 30, 60, and 90 minutes. Leukocytosis and a drop in blood pressure occur after clonidine ingestion and patients may have to be observed for 2 hours after the completion of the test for normal blood pressure to return.
   h. Secretion rates of GH for a 12- to 24-hour period: Current data suggest that some individuals have poor growth because of an abnormal secretion in the number or amplitude of GH pulses. This type of evaluation for a neurosecretory defect is currently performed primarily in conjunction with a research protocol.
   i. Sexual maturity rating: If the subject has not achieved an SMR of 4 or 5, consideration of estrogen priming before GH testing should be made (Marin et al., 1994).
   j. Growth hormone-releasing hormone (GHRH): Analogues of this hypothalamic peptide can be given intravenously, and blood samples should be obtained for GH every 15 minutes for 1 hour. This test can be done in combination with pyridostigmine (Hoeck et al., 2000) or with the synthetic growth hormone-releasing peptide, GHRP-2 (Mahajan and Lightman, 2000).
7. Gonadotropin-releasing hormone (GnRH) stimulation test: This test can help determine whether the adolescent has normal pituitary function for his or her pubertal stage. Serum LH and FSH levels are measured before and every 30 minutes for 3 hours after infusion of 100 μg of GnRH. The 60-minute response after a single subcutaneous injection can also be obtained. In primary gonadal failure, LH and FSH levels will increase after infusion, whereas in pituitary failure, there is little increase. In constitutional delay of puberty, the LH and FSH responses are small but consistent with bone age and pubertal stage. Simultaneous measurement of gonadal steroid production (testosterone or estradiol) at the beginning and end of the GnRH stimulation test will help to interpret the gonadotropin levels. This test is not reliable for differentiating constitutional delay from hypogonadotropic hypogonadism before a bone age of about 12 years. For girls, an accurate indication of pubertal entrance is a peak LH/FSH ratio of more than 0.66, and for boys, the most accurate indication is an LH level of more than 12 IU/L (Offer et al., 1990).
8. Human chorionic gonadotropin (hCG) test: For this test, chorionic gonadotropin (Pregnyl) is given by four intramuscular injections of 5,000 IU/mL each on days 1, 3, 6, and 10. Serum testosterone levels are determined before the first injection and on day 15. A stimulated level of testosterone less than 10 nmol (or 300 ng/dL) is suggestive of hypogonadotropic hypogonadism.

### Constitutional Delay of Puberty

About 90% to 95% of delayed puberty is constitutional delay of puberty. This diagnosis is made by excluding the other causes, as discussed. However, using the guidelines in Table 8.2, suggested by Barnes (1979), one can confidently make a provisional diagnosis. When such an adolescent's predicted adult height is below the 3rd percentile (less than 64 inches for males and less than 59 inches for females), the teenager is often labeled as having idiopathic or genetic short stature.

### Basic Considerations

In the evaluation of any adolescent with delay of puberty, four basic questions should be kept in mind:

1. Is there evidence of any disorder outside the genital reproductive system that could contribute to growth failure?
2. To what extent has skeletal maturation progressed?
3. Is there evidence of interruption in either gonadal or hypothalamic-pituitary function?
4. Is the chromosomal sex consistent with the genital sex of the patient?

### Clues to Diagnosis

1. Gonadotropin deficiency
   a. Low serum FSH and LH levels, particularly if bone age is more than 13 years
   b. Low response to GnRH if pituitary failure is present
   c. In boys: Low testosterone response to hCG (Dunkel et al., 1985a, 1985b)
   d. Abnormal central imaging study results
   e. History of neurological symptoms, CNS infections, radiation, or disease
   f. Possible absence of sense of smell (Kallmann syndrome)
2. Gonadal disorder
   a. History of genital radiation, surgery, infection, or trauma
   b. Castrate levels of FSH and LH
   c. Abnormal karyotype, such as 46,XY in a phenotypical girl
   d. Low U/L body mass index
   e. Arm span may exceed height by more than 2 inches
   f. Gynecomastia in a boy
3. Turner syndrome: Excluding constitutional delay of puberty, one of the more common causes of maturation delay is Turner syndrome. The patient may have a

### Table 8.2. Criteria for provisional diagnosis of constitutional delay of puberty

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Is there evidence of any disorder outside the genital reproductive system that could contribute to growth failure?</td>
</tr>
<tr>
<td>2</td>
<td>To what extent has skeletal maturation progressed?</td>
</tr>
<tr>
<td>3</td>
<td>Is there evidence of interruption in either gonadal or hypothalamic-pituitary function?</td>
</tr>
<tr>
<td>4</td>
<td>Is the chromosomal sex consistent with the genital sex of the patient?</td>
</tr>
</tbody>
</table>

---

**Note:** The text continues with further details on various conditions and diagnostic tests related to endocrinology and puberty.
Turner Syndrome and Gonadal Dysgenesis

Management of Maturational Delay

Most adolescents with maturational delay will have constitutional delay of puberty. These patients and their families will need constant support and reassurance that puberty and growth will occur. Follow-up is necessary, to be certain that any other abnormality was not overlooked and that puberty does begin. If severe psychological problems arise because of differences in physical size or sexual maturation of the adolescent compared with his or her peers, hormonal therapy can be tried briefly (up to 6 months). Teenagers who most commonly complain about delayed puberty are male adolescents. In male adolescents, oxandrolone (0.05 to 0.25 mg/kg/day) can be tried, or testosterone enanthate can be given at doses of 44 to 200 mg/m² intramuscularly for 3 to 6 months. The effects of hormonal intervention have been examined by Zachmann and Prader (1970), Hopwood et al. (1979), Rosenfeld et al. (1982), Wilson et al. (1988), Rosenfield (1986), Richman and Kirsch (1988), Sollman et al. (1995). These studies confirm an increase in growth velocities without excessive bone age advancement. Low doses of testosterone seem to be effective in stimulating virilization and growth without significant loss of height potential (Adan et al., 1994). Any suppression of the hypothalamic-pituitary-gonadal axis during treatment seems reversible after treatment is stopped. If androgen therapy is used, the risk of liver damage and of possible attenuation of mature height should be discussed with the adolescent and his or her family. Finkelstein et al. (1992) reported that adult men with a history of constitutionally delayed puberty have a decreased radial and spinal bone mineral density. This suggests that the timing of sexual maturation may be an important determinant of peak bone mineral density.

Most other causes of delayed puberty are irreversible. Thus, the health care provider must be prepared to help the adolescent with long-term follow-up and psychological support. Many areas will need to be dealt with, such as

1. Identification of the problem.
2. Potential for growth and sexual maturation.
4. Reproductive potential.

Health practitioners must be honest in explaining to the adolescent what they believe he or she can comprehend. At the same time, telling a phenotypical female, for example, that she has male chromosomes is probably not advisable and is liable to add sexual-identity confusion to an age already fraught with uncertainties. In this instance, the term “abnormal chromosome” is preferable.

Turner Syndrome and Gonadal Dysgenesis

1. Short stature associated with Turner syndrome can be treated with hGH. The U.S. Food and Drug Administration and other worldwide regulatory agencies have approved the use of hGH for statural improvement in Turner syndrome. hGH therapy should be started before the adolescent years and before beginning estrogen therapy for feminization. The dose used is approximately double that used for subjects with classic GH deficiency. The starting dose is 0.05 to 0.06 mg/kg per dose or 0.375 mg/kg/wk. During treatment, bone age should be monitored as well as IGF-I and IGF-BP-3 concentrations. The goal of therapy is to maintain these growth factor levels at the upper normal range. Data from the National Cooperative Growth Study from Genentech has shown GH to be effective in improving the final height of girls with Turner syndrome and that GH is safe for these patients (Bleseth et al., 1996).

2. Oxandrolone (0.075 to 0.25 mg/kg/day) or fluoxymesterone (2.0 mg/day) can be added to GH therapy to improve the growth response. If this is done, it is usually begun after 2 to 3 years of GH therapy alone, before feminization, for a limited time, and with great caution because androgens have the following disadvantages:
   a. Potential for hepatic toxic effects
   b. Advancement of the bone age
   c. Potential for mild androgenic characteristics, such as clitoral enlargement
   d. Delay of treatment with estrogen and thus delay of inducement of female secondary sexual characteristics

Anabolic steroids as the sole therapy for this syndrome are no longer recommended.

The efficacy of GH alone, or in combination with oxandrolone, in improving the height of girls with Turner syndrome has been evaluated (Rosenfeld et al., 1986, 1992). Six-year data of this randomized trial reveal that 82% of girls treated with GH alone, and 92% of girls treated with GH and oxandrolone, have already exceeded their predicted adult heights. With 42 of the 62 subjects having completed growth, the mean height was 151.7 cm (5 feet), with the original projected height exceeded by 9 cm. Other trials have also demonstrated an increase in final height in individuals treated with GH (Takano et al., 1995). However, if consideration of GH treatment is entertained, it is best to refer the patient to an endocrinologist.

Ross et al. (1983) reported on the potential benefit of low doses of estrogen to improve linear growth in patients with Turner syndrome. Martinez et al. (1987) confirmed the ability of ethinyl estradiol to increase growth velocity in girls with Turner syndrome, although the effect diminished with time and excessive bone age advancement precluded the improvement of predicted height.

3. Secondary sexual characteristics in females are achieved through the use of increasing doses of conjugated estrogens such as Premarin or with low doses of ethinyl estradiol at 100 ng/kg. Conjugated estrogen therapy can be started at a dosage of 0.3 mg/day, initially two to three times per week and then every day for 6 months. This can then be gradually increased to 0.625 mg/day for 6 months. Occasionally, 1.25 mg can be given for 3 to 6 months in an attempt to achieve maximal feminization and breast development. After 12 months of conjugated estrogen treatment, to avoid unopposed estrogen stimulation of the endometrium, the clinician adds medroxyprogesterone acetate (Provera). The following schedule can then be used: conjugated estrogen (0.625 mg/day) can be given daily on days 1 to 25, and medroxyprogesterone acetate (5 to 10 mg/day) is added for 10 to 14 days per month. Withdrawal flow will begin usually at the completion of medroxyprogesterone acetate regimen but may start toward the end of the 10- to 14-day course. Treatment is with the same schedule the next month. Transdermal administration of estradiol at doses of 50 to 100 µg/day is a potential alternative to orally administered conjugated estrogens. This approach can
eliciting the desired estrogenic effect without the pharmacological effect of orally administered estrogen on hepatic proteins.

Chernausek et al. (2000) evaluated the timing of estrogen replacement in girls with Turner syndrome with regards to final height outcome. Patients in whom estrogen treatment was delayed until the age of 15 years gained an average of 8.4 cm over their projected height. Those who started estrogen at 12 years of age gained only 5.1 cm. They found that growth was stimulated for 2 years after beginning estrogen replacement therapy and that the timing of estrogen therapy is important for final height. This indicates that for some girls, particularly those who are shortest and in whom GH has not been given for more than 2 years, delaying estrogen therapy may be indicated to improve height outcome.

4. If there is a Y chromosome present on the initial study done to diagnose Turner syndrome, no further chromosomal analysis is required to anticipate that the patient will require gonadectomy. However, Y chromosomal material, rather than a full Y chromosome, may be present in girls who are virilized, either at birth or with puberty not as the result of androgen therapy. They should have fluorescent in situ hybridization (FISH) for the Y chromosome to ensure that no Y chromosomal material has been translocated. The presence of any Y material is an indication for gonadectomy, to prevent potential malignant neoplasias. Surgery should be followed by hormonal replacement therapy during and after puberty.

**Hypogonadotropic Hypogonadism** in females, treat with hormonal therapy as already outlined here, until effective, easily administered gonadotropins become available.

In males, the preferred treatment is androgen therapy, in which testosterone enanthate in progressively higher doses (25–100 mg/ml) can be given every 3 weeks. After 1 year, this dose can be increased (150–200 mg/ml). Some patients do better on lower doses given once every 2 weeks. Growth velocity should be followed in an attempt to maintain a normal pattern. Testosterone therapy will not induce spermatogenesis.

In males and females with hypogonadism caused by absent GnRH secretion, the pulsatile administration of GnRH can normalize gonadal function and induce fertility (Barbieri, 1992). This therapy is associated with a high cost and the need for a high degree of compliance. It should be reserved for those individuals who desire fertility.

**Gonadal Failure** Females are treated with hormonal therapy, as outlined in the previous section on Turner syndrome.

Males are treated with hormonal therapy, including testosterone in oil, as outlined previously.

**Chronic Illness** Treatment of pubertal delay caused by chronic illness necessitates treating the underlying disorder. For example, enzyme replacement in cystic fibrosis, gluten-free diet in celiac disease, corrective surgery for congenital heart disease, and hyperalimentation in inflammatory bowel disease usually result in catch-up growth and maturity. Medications such as steroids or antimitabolites can inhibit growth. Catch-up growth can be observed after discontinuation of treatment with these drugs. In some cases, the disease process is irreversible, such as in sickle cell anemia. The pubertal delay in sickle cell anemia is thought to be hypogonadism, possibly caused by a zinc deficiency. Zinc has been used with some early experimental success in alleviating this problem. In patients with chronic renal failure, there may be some growth after improved nutrition and hemodialysis or transplantation. However, many patients with chronic renal failure remain short.

Recent studies suggest that GH can be administered to subjects with chronic renal failure before transplantation to improve height, without causing deterioration of underlying renal function (Fine et al., 1994). Children with HIV infection who grow poorly and have body wasting may benefit from the anabolic effects of short-term GH administration; however, long-term use of such agents remains under investigation (Mulligan et al., 1993).

**SHORT STATURE**

**Definition**

Adult height is genetically determined; therefore, any evaluation of short stature must be assessed using family members' heights as a guide. Generally, the 3rd percentile is used as the lower limit of normal. Adolescents who fall below the 3rd percentile should be carefully evaluated for short stature.

**Guidelines**

An adolescent should be considered for an evaluation of short stature if

1. A linear growth rate of less than 4–5.0 cm/yr exists in the years before the normal age for peak linear growth velocity.
2. No evidence exists of a peak linear growth velocity by the age of 16 years in boys or 14 years in girls.
3. Distinct deceleration below the individual's established growth velocity occurs.
4. The adolescent's height is more than 2 SDs from midparental height.
5. The adolescent's height is more than 3 SDs below the mean. Adolescents whose height is between 2 and 3 SDs below the mean deserve a careful history and physical examination, laboratory screening tests, and observation of growth for 6 months.

**Differential Diagnosis**

The differential diagnosis can be divided between those processes associated with normal puberty and those associated with simultaneous delay of puberty.

**Short Stature without Pubertal Delay**

1. Familial short stature
2. Isolated GH deficiency
3. Hypothyroidism (can also be associated with pubertal delay)
4. Congenital syndromes such as Down, Noonan, and Hurler
5. Intrauterine growth retardation
6. Skeletal disorders; chondrodysplasias
7. Chronic illness
8. HIV infection

**Short Stature with Pubertal Delay**

1. Constitutional delay of puberty
2. Panhypopituitarism: Congenital and acquired
3. Congenital syndrome
   a. Turner syndrome and mixed gonadal dysgenesis
   b. Syndromes associated with hypogonadotropic hypogonadism
      - Prader-Willi: Obesity, short stature, small hands and feet, almond-shaped palpebral fissures, mental deficiency, and cryptorchidism, with 50% having a deletion of chromosome 15 at region q11-13
      - Laurence-Moon-Barber-Biedl: Obesity, short stature, polydactyly, retinitis pigmentosa, mental deficiency, and genital hypoplasia
      - Alström: Retinitis pigmentosa, diabetes mellitus, neurogenic deafness
      - Börjeson-Forssman-Lehmann: Obesity, short stature, severe mental deficiency, epilepsy, microcephaly, variable radiographic skeletal anomalies, and small genitalia
   4. Glucocorticoid excess
5. Chronic illness
6. HIV infection

**Evaluation of Short Stature**
The evaluation of short stature is similar to that of delayed puberty. A thorough history is essential and should include:

1. Maternal pregnancy history: Medical illnesses and medication use
2. Birth weight and length and estimate of gestational age: Important because premature infants with appropriate small weight tend to have a normal growth potential, whereas infants with intrauterine growth retardation who are inappropriately small for gestational age may not have catch-up growth.
3. Complete review of systems: Particularly renal and GI
4. Growth history: Close review of symptoms (Fig. 8.1, Fig. 8.2, Fig. 8.3, Fig. 8.4, Fig. 8.5, Fig. 8.6 and Fig. 8.7, growth charts for various disease states)
5. Family history: Adult height and growth and pubertal patterns of all first- and second-degree relatives
6. Dietary history

A complete physical examination is the next step in the evaluation and should include:

1. Height and weight
2. Arm span and U/L body-segment ratio
3. Sexual maturity ratings
4. A general physical examination, with special attention to the thyroid gland, ophthalmological examination, neurological examination, and stigmata of congenital syndromes.

The laboratory evaluation of short stature should include the following:

1. CBC count and sedimentation rate
2. Urinalysis
3. Adjusted T4 and TSH (for thyroid) determinations
4. Chemistry profile, including serum creatinine clearance and liver enzyme levels.
5. Bone age: Essential part of evaluation of short stature. (The relationships between bone age, height age, and chronological age are discussed earlier in this chapter [Table 8.1]. A bone age equivalent to the chronological age suggests decreased growth potential [primaldial short stature, genetic short stature, or skeletal dysplasia]. A significant delay in bone age increases the likelihood of endocrine or systemic disease as the cause of disordered growth. The bone age also provides an index for potential future growth.)
6. Other tests: Ordered as indicated by the history and physical examination results (outlined earlier in this chapter) and include central imaging studies; measurement of gonadotropin, GH, IGF-1, and IGF-BP-3 levels; and x-ray films of the GI tract and celiac panel.

**Constitutional Delay of Puberty** Most short stature in adolescents is the result of either constitutional delay of puberty or familial short stature. Guidelines for diagnosis were outlined earlier in this chapter.

**Genetic or Familial Short Stature** Genetic or familial short stature is suggested by:

1. Normal history and physical examination findings
2. Birth weight and length that are often below the 3rd percentile for gestational age
3. Family history of short stature
4. Growth curve that generally parallels the 3rd percentile
5. Bone age that is appropriate for chronological age

**Chronic Illness** Chronic renal disease and Crohn disease are frequent causes of short stature at tertiary care hospitals. These diseases are usually diagnosed by an abnormal history, physical examination findings, or results of tests including screening CBC, sedimination rate, urinalysis, and chemistry studies. Renal tubular acidosis can easily be overlooked as a cause of short stature. This process may be suggested by family history, urine pH level, or serum bicarbonate values.

**Endocrine Causes** Endocrine causes of short stature, such as hypothyroidism, GH deficiency, and adenocortical excess, are uncommon. Hypothyroidism and adenocortical excess can usually be detected by the patient's history, physical examination, or screening laboratory test. Adolescents with classic GH deficiency can be difficult to differentiate from those with constitutional delay of puberty. This is particularly difficult during the time of expected peak linear growth velocity, when the growth of an adolescent with constitutional delay of puberty may seem to differ from the normal growth curve as other adolescents accelerate their growth velocities. Individuals with classic GH deficiency have normal body proportions and often a high-pitched voice, a tendency toward hypoglycemia, a microphallus in boys, a childlike face, soft and finely wrinkled skin, and a large prominent forehead.

A number of genes have been identified as having critical roles in controlling the formation and development of the anterior pituitary gland. Screening subjects with classic GH and panhypopituitarism for genetic abnormalities may become part of the standard workup of this condition.

Patients with classic GH deficiency have marked benefit in statural outcome as the result of GH treatment. In addition, those with complete GH deficiency benefit from treatment, for the metabolic effects of GH with regard to improving bone density, decreasing fat mass, and improving muscle strength, even once epiphyseal fusion has been achieved. It appears these subjects should continue GH treatment at a markedly reduced dose compared with that used for growth augmentation throughout life.

Currently, the question of which individuals will benefit from GH therapy is being evaluated. The U.S. FDA has approved the use of GH for patients with chronic renal insufficiency, Turner syndrome, and Prader-Willi syndrome. It may be that other syndromes and conditions besides these may benefit from GH use. These conditions include other syndromes associated with postnatal growth failure, such as hypophosphatemic rickets, and intrauterine growth retardation syndromes, such as Silver-Russell syndrome, as well as patients with nonendocrine diseases such as inflammatory bowel disease and conditions requiring long-term glucocorticoid administration. However, whether GH will improve ultimate adult height and at what risk-benefit ratio are yet to be determined. It is clear that classic GH deficiency is not the only criterion for treatment with GH (Frasier and Lippe, 1990).

All GH available is bioengineered. Presently, five major pharmaceutical companies sell GH in the United States and worldwide. Since 1980, all human growth hormone (hGH) has been removed from the market because of the potential of transmission of Creutzfeldt-Jakob disease. Although GH is the mainstay of therapy to increase growth velocity and ultimate adult height, other agents such as GnRH analogues, GHRH, and IGF's have growth-promoting potential. In addition, the possible benefit of using GnRH analogues to delay puberty and allow for a prolonged prepubertal growth period, thus increasing adult height, has been investigated. Although there are conflicting reports in the literature (Lindner et al., 1993; Munichen et al., 1993), there does not appear to be much benefit to ultimate adult height in delaying puberty with such agents. However, delaying puberty while simultaneously treating with GH may be of benefit in some instances in which bone age advancement precludes GH alone from increasing height.

**Chromosomal Abnormality** The most common chromosomal abnormality causing short stature is Turner syndrome, which occurs in 1 of every 2,000 to 5,000 females born. However, because short stature is a part of the syndrome in virtually all cases, the incidence is much higher among females with short stature. The syndrome becomes a distinct possibility in the very short girl who does not exhibit a marked delay in bone age. The diagnosis requires a karyotype analysis for an adequate evaluation for mosaic patterns. The characteristics of Turner syndrome were discussed earlier in this chapter.

**Intrauterine Growth Retardation** Another cause of short stature is a "grab bag" category called primaldial dwarfism, or intrauterine growth retardation. The patients are usually characterized by the following:

1. Small size for gestational age at birth
2. Slow growth from early infancy
3. Normal or minimally retarded epiphyseal maturation and thus normal bone age
4. Normal or minimally retarded sexual development
5. Normal physical examination findings (occasionally dysmorphic features compatible with various syndromes) and normal laboratory test results.
6. Normal GH levels
7. Possible lower intellect
8. Normal growth pattern in the family

A host of maternal factors are associated with this problem, as well as abnormalities of the intrauterine environment.

Skeletal Dysplasias

Reduced growth characterized by skeletal dysplasias is related to an abnormality of the osseous and cartilage tissues. These disorders are suggested by the following:

1. Family history of skeletal dysplasias
2. Abnormal body proportions (abnormal U/L body-segment ratio)
3. Extremely retarded bone age
4. Abnormal osseous structures on x-ray examination

A benefit from surgical leg-lengthening procedures has been appreciated in the skeletal dysplasias.

Treatment of Short Stature

The treatment of most causes of short stature was reviewed earlier in the discussion of delayed puberty. Generally, hormone deficiencies such as hypothyroidism, hypopituitarism, and hypogonadism are treated with hormone replacement therapy. Short stature as a result of chronic illness is treated by dealing with the underlying disorder. Disorders associated with abnormal growth potential, such as genetic short stature, intrauterine growth retardation, and skeletal dysplasias, may respond poorly to therapy, or the risk-benefit ratio may not yet be understood. Hormonal therapy with androgens for constitutional delay of puberty should be reserved for males with significant emotional problems resulting from their short stature.

It is essential to be aware of the tremendous impact that short stature may have on an adolescent. Body image not only has become an increasing concern in our society but gains in importance as an adolescent gets older. The concerns and fears of the adolescent and of his or her family regarding short stature should be explored.

EXCESSIVE GROWTH–TALL STATURE

Tall stature is rarely a problem in boys because tallness is acceptable and even desired in males in our society. Even though tallness is becoming more acceptable among girls, there are still adolescent females or their parents who complain to physicians about excessive tallness.

Differential Diagnosis

1. Constitutional tall stature
2. Excess GH
3. Anabolic steroid excess
   a. Adrenal tumor
   b. Congenital adrenal hyperplasia—classic or nonclassic
   c. Precocious puberty
   d. Premature adrenarche
   e. Gonadal tumors
4. Hyperthyroidism
5. Miscellaneous
   a. Marfan syndrome
   b. Neurofibromatosis
   c. Hypogonadism in boys
   d. Androgen-receptor deficiency
   e. Estrogen deficiency in boys
   f. Homocystinuria
   g. Hereditary abnormalities of the skeleton
   h. Soto syndrome

Evaluation

The most important information in evaluating tall stature is the family history of tallness in parents and siblings. If there is a family history of tallness and the history and physical examination findings are normal, the diagnosis is almost certainly familial tallness. If a family history of tallness is not found, then a more thorough search is indicated. Generally, a complete history, physical examination, routine laboratory screening tests, and a determination of bone age are adequate to evaluate the outlined causes of tall stature. The bone age and SMR are also essential to the evaluation. The adolescent girl who entered puberty early and is thus taller than her peers will have a corresponding advanced bone age and SMR. More detailed tests such as GH and IGF-I determinations can be ordered as indicated. Also included in the evaluation of tallness should be the adolescent's and family's attitudes about tallness and the problems that may have arisen because of tallness.

Treatment in Girls

Familial Tall Stature Treatment of tall stature must be done with extreme caution, if at all. Estrogens have been documented to decrease growth potential; however, because of possible side effects, estrogen therapy should be reserved for selected adolescents. Associated medical problems such as hyperglycemia, hypertension, hyperlipidemia, and thrombophlebitis would be a contraindication to using estrogen therapy.

What is excessive height? Some adolescents are overwhelmed at 5 feet 6 inches (168 cm), whereas others are completely happy at 5 feet 10 inches (178 cm) or more. However, in general, estrogen therapy should be reserved for the female adolescent with a predicted height of more than 6 feet (180 to 183 cm) and with indications that she (not her mother or father) is having psychological difficulties coping with her height. However, psychological intervention may be more appropriate than medical treatment of tall stature.

Timing of Treatment Though the earlier the therapy, the greater the degree of height reduction, estrogen intervention should be delayed until the female adolescent is at least 9 to 10 years of age, puberty has started, and a height of about 5 feet 6 inches (168 cm) has been attained. This allows for evidence of spontaneous maturation. In addition, mature adult heights are more accurately predicted after the age of 10 years. In general, therapy is now started later than was previously recommended. Therapy should be delayed if the adolescent is unsure about undergoing treatment.

Estrogen Effects on Growth

1. Suppression of IGF
2. Acceleration of epiphyseal fusion

Dosage Either ethinyl estradiol or conjugated estrogens are recommended. In either case, a progestational agent should be used each month to guard against unopposed estrogen stimulation of the endometrium. Both continuous and cyclic regimens of estrogen have been used. Studies using continuous regimens (Crawford, 1978; Van der Weerf, ten Bosch and Bot, 1981) indicate a greater height reduction, and the time until complete epiphyseal fusion is probably decreased.

1. Continuous regimen
a. Ethinyl estradiol, 0.1–0.5 mg daily, or conjugated estrogen, 2.5–10 mg daily; plus
b. Norethindrone, 5 mg on the first 5 days of each month

2. Cyclic regimen
   a. Ethinyl estradiol on days 1–24, with a progestin added on days 18–24
   b. No hormones used for the remainder of the month

**Duration of Therapy** Therapy should be continued until epiphyseal fusion is documented on hand and wrist radiographs. If therapy is stopped sooner, rebound growth may occur.

**Side Effects** Potential side effects are similar to those of oral contraceptives. Usually, side effects are mild, such as occasional nausea or breakthrough bleeding, or rare, such as hypertension or thrombophlebitis. There is no evidence of future disturbances of hypothalamic-pituitary-ovarian function. Gonadotropins usually recover within 1 to 2 months of the cessation of the estrogen therapy. No evidence that cancer develops as a result of estrogen therapy for tall stature has been demonstrated.

**Follow-Up**

1. Visits should occur every 3 months to evaluate height, weight, pubertal development, and potential complications, as well as to perform a physical examination, including blood pressure determination.
2. Gynecological assessment including pelvic and breast examination and Papanicolaou (Pap) smear should be done every year.
3. Skeletal age evaluation should be performed every 6–12 months.
4. Height should be recorded at 3, 6, and 12 months after treatment has been stopped, to detect growth increases.

**Treatment in Boys**

The treatment of boys has been studied less extensively. Treatment in one study (Zachmann et al., 1976) consisted of administration of a long-acting intramuscular testosterone preparation (Triolandren) at a dosage of 500 mg/m² given every 3 weeks. Side effects include weight gain, acne, edema, and a decrease in testicular volume, which returns to normal after therapy is stopped.

**PREOCIOUS PUBERTY**

Sexual precocity is the development of sexual characteristics before the normal age.

1. "Isosexual precocity" refers to advanced sexual development appropriate for the phenotype of the child.
2. "Heterosexual precocity" refers to advanced sexual development at variance with the phenotype of the child (i.e., boys are feminized and girls are virilized).
3. "Incomplete precocious puberty" refers to the appearance of a single clinical pubertal change, such as premature thelarche (breast), premature adrenarche (axillary hair), and premature pubarche (pubic hair).
4. "Complete precocious puberty" refers to the appearance of advanced pubertal changes accompanied by hormonal effects elsewhere—pubic hair, axillary hair, and breast or phallic development. Complete precocious puberty includes true and pseudo forms:
   a. True precocious puberty: Release of gonadotropins with resultant puberty and potential fertility
   b. Pseudo-precocious puberty: Elevated levels of sexual hormones but low gonadotropin levels, with resultant advanced pubertal changes but an infertile state

**Guidelines**

1. Male: Any male achieving G2 before 9.5 years of age.
2. Female: Any female with breast development or pubic hair development before the age of 8 years. This traditional definition of precocious puberty was challenged by the study of Herman-Giddens et al. in 1997. The authors found that in a healthy population of more than 17,000 girls, the mean ages of onset of breast development were 8.87 years for African-American girls and 9.96 for white girls. Because of these data, a recent report of the Lawson Wilkins Pediatric Endocrine Society recommended that breast development before 7 years of age in white girls and before 6 years of age in African-American girls be considered precocious (Kaplowitz and Oberfield, 1999).

**Differential Diagnosis**

**Isosexual Precocious Puberty**

1. True (elevated gonadotropin levels) complete forms
   a. Constitutional: Idiopathic
   b. Organic brain disease: Congenital anomalies such as septooptic dysplasia, encephalitis, pinealomas, hypothalamic hamartomas, brain tumors in suprasellar region, meningitis, and trauma, congenital hydrocephalus, CNS radiation
2. Pseudo-complete forms
   a. Gonadotropin-secreting tumors: Teratoma, hepatoblastoma, chorioepithelioma
   b. Gonadal tumors: Ovarian, granulosa and theca cell; testicular, Leydig cell and adrenal rest tumor
   c. Adrenal: Tumor, congenital adrenal hyperplasia
   d. Hypothyroidism
   e. Iatrogenic or factitious androgen or estrogen abuse or other exposure to estrogen-containing makeup, hair creams, or oils
   f. McCune-Albright syndrome
   g. Hemihypertrophy syndrome
   h. Gonadotropin-independent precocious puberty (Wierman et al., 1985)
3. Incomplete forms
   a. Premature thelarche
   b. Premature adrenarche

**Heterosexual Precocious Puberty**

1. Girls
   a. Ovarian: Arrhenoblastoma
   b. Adrenal: Congenital adrenal hyperplasia, virilizing tumor
   c. Androgen-producing teratoma
   d. Iatrogenic
2. Boys
   a. Adrenal feminizing tumor
   b. Estrogen-producing teratoma
   c. Neurofibromatosis
   d. Iatrogenic

**Evaluation**

**History** A complete history is important and should include the following:

1. Information on intercurrent disease
2. History of drug ingestion, particularly sex steroids
3. Family history, particularly the presence of similar conditions in family members
4. Chronology of development of secondary sexual characteristics, including breast development, pubic hair, axillary hair, and menses
5. Evaluation of growth history and growth spurt
6. History of head trauma
7. History of CNS radiation
8. History of behavioral or emotional changes

**Physical Examination** A complete physical examination should be performed, including the following:

1. Measurement of height and weight and evaluation of growth chart to determine the onset of increased linear growth velocity
2. Evaluation of SMRs, including gonadal size
3. A neurological examination
4. An ophthalmological examination
5. Careful testicular examination for evidence of masses
6. Abdominal, rectal, or pelvic examination, where applicable, to determine uterine and ovarian size
7. Evaluation for signs of hypothyroidism
8. Evaluation for evidence of estrogen stimulation

**Laboratory Examination** The laboratory evaluation of precocious puberty should proceed in a stepwise, logical fashion. The accompanying flow sheet (Fig. 8.8) for evaluating isosexual precocious puberty also includes diagnostic clues for each diagnosis. Thus, by evaluating bone age and gonadotropin levels after stimulation with GnRH (in those with advanced bone age), one can narrow the diagnostic possibilities tremendously. A pubertal response to GnRH is an LH level of more than 15 IU/L and an FSH level of more than 7.5 IU/L (polyclonal radioimmunoassay). The bone age is extremely valuable. Retarded bone age and short stature suggest hypothyroidism. A bone age consistent with chronological age usually is seen with patients with incomplete precocious puberty. These patients need continued observation at regular intervals to monitor whether complete precocious puberty or signs of other illnesses are developing. An advanced bone age suggests a peripheral estrogen or androgen effect. If gonadotropins levels are low and there is no gonadotropin response to GnRH, pseudoprecocious puberty is diagnosed and the extra CNS source of hCG or sex steroids must be sought. If the gonadotropin levels are in the pubertal range or if there is a pubertal response to GnRH, then a search for a CNS lesion must be made before the diagnosis of idiopathic precocious puberty is made.

**FIG. 8.8.** Flow sheet for evaluation of isosexual precocious puberty. MRI, magnetic resonance imaging. (Adapted from Brenner PE. Precocious puberty in the female. In: Mishell DR, Davajan VC, eds. Reproductive endocrinology, infertility, and contraception, © 1979 by FA Davis Co.)

**Treatment**

**Incomplete Forms** Generally, these forms are self-limited and will not progress.

**True Sexual Precocity**

Idiopathic. The natural history is variable. Observation for 6 to 12 months is advisable to determine whether the status is unchanged or changing rapidly. If unchanged or slowly progressive, continued observation is in order. A recent report of a 12-year follow-up of 20 patients with slowly progressive puberty (Palmer et al., 1999) showed that subjects reached their genetic targets for height and that the average age of menarche was 11 years. If the degree of sexual maturation has progressed rapidly, one should attempt to slow the process. Potential analogues of GnRH are used successfully for central precocious puberty. There is a downregulating effect of these agents on the pituitary GnRH receptors, which inhibits gonadotropin release and causes diminished gonadal steroid production. These agents are administered in the long-acting “depot” form every 28 days. The standard dose is 0.3 mg/kg per injection. The accelerated linear growth velocity advancement of the skeletal age and secondary sex characteristics regress with therapy (Kaplan and Grumbach, 1990; Fenton et al., 2000). LH values return to prepubertal levels. GnRH agonists are also available in subcutaneous and nasal formulations. Undertreatment may accelerate sexual precocity, and to ensure adequacy of therapy, gonadotropin and sex steroid levels should be followed, either after GnRH stimulation or basal levels. There are few side effects to GnRH agonists. Up to 10% of patients may develop sterile abscesses at the injection site due to an idiosyncratic reaction to the vehicle (Quigley and Pescovitz, 1997). Menopausal symptoms, such as hot flushes have been reported. However, because this treatment has only been available for two decades, long-term safety has not been established. Other agents are used for pseudopuberty to diminish gonadal production of sex steroids or to inhibit the peripheral effect of these hormones. These include testosterone, an inhibitor of aromatase activity, which has been used in girls with pseudoprecocious puberty caused by McCune-Albright syndrome. Ketoconazole, has been used to decrease testosterone production in males with gonadotropin-independent puberty. Spironolactone can be beneficial as an antiandrogen agent. Treatment should be continued until the child is able to handle the physical changes of puberty or until there has been normalization of the height prediction.

**Organic Brain Disease.** Treatment of the underlying disorder is provided.

**Pseudosexual Precocity**

1. Ectopic gonadotropin secretion: Tumor excision.
2. Gonadal or adrenal tumors: Tumor removal.

**Psychosocial Management**

Despite physical advancement, patients with precocious puberty rarely exhibit acceleration of intellectual or psychosocial development. Their social level is usually normal for their chronological age. Because of advanced physical development and increased strength, they may try to associate with older children. However, they are handicapped because of their lack of social skills. They may, moreover, become shy and inhibited because of their abnormal appearance as compared with their peers. Because of their potential fertility, it is important to consider sex education at an earlier age than usual.

**WEB SITES**

For Teenagers and Parents


For Health Professionals

REFERENCES AND ADDITIONAL READINGS


A normal functioning thyroid gland is critical to maintain health and well-being during adolescence. Unfortunately, there is an increase in the prevalence of thyroid dysfunction during the teen years. Approximately 1% of children between the ages of 11 and 18 years have thyroid disease, with many more girls than boys affected. Although the most common finding is the presence of a diffuse goiter associated with normal thyroid hormone secretion, hypothyroidism and hyperthyroidism do occur. These abnormalities can lead to altered growth and sexual development, menstrual irregularities, deterioration in school performance, or change in behavior. These changes may be ignored or mistakenly attributed to adolescent behavior.

CHANGES IN THYROID GLAND SIZE AND FUNCTION DURING ADOLESCENCE

1. Size: Doubles in size during puberty, reaching an average weight of 14 ± 5.2 g.
2. Hormonal changes
   a. Relative decreases occur in basal metabolic rate, total thyroxine (T₄), total T₃, thyroid-binding globulin, and thyroid-stimulating hormone (TSH).
   b. Relative increases occur in reverse T₃, thyroid-binding prealbumin, serum half-life of T₄, and volume of distribution of T₄
   c. There are no changes in free T₄ or free T₃

THYROID DYSFUNCTION CONSIDERATIONS IN THE ADOLESCENT

Common Disorders
Diffuse thyromegaly is associated with three major conditions. In order of frequency, they are as follows:

1. Goiter caused by chronic lymphocytic thyroiditis (Hashimoto thyroiditis) with or without hypothyroidism
2. Simple colloid goiter with normal thyroid hormone secretion
3. Hyperthyroidism or thyrotoxicosis, includes several subtypes: Graves disease, with classic hyperthyroidism; subacute thyroiditis, in which the patient may alternate between hyperactive and hypoactive thyroid function; and hashitoxicosis, in which the patient may be hyperthyroid for some time

Other Disorders
Other disorders, such as multimodular goiters, thyroid nodules, neoplasias, and other forms of acute suppurative thyroiditis, are rare in adolescents. Rallison et al. (1991) studied the incidence and natural history of thyroid diseases in adolescents. A total of 4,619 school-age children, between the ages of 11 and 18 years, were studied from 1965–1968 and restudied in 1985–1986. Initially, 3.7% had an abnormal finding, including

<table>
<thead>
<tr>
<th>Problem</th>
<th>Rate Per 1,000 (1965–1968)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diffuse hypertrophy</td>
<td>19.3</td>
</tr>
<tr>
<td>Chronic lymphocytic thyroiditis</td>
<td>12.7</td>
</tr>
<tr>
<td>Thyroid nodules (two with papillary carcinomas)</td>
<td>4.6</td>
</tr>
<tr>
<td>Hyperthyroidism or hypothyroidism</td>
<td>1.9</td>
</tr>
</tbody>
</table>

During the follow-up examination 20 years later, 1985–1986, the findings showed 10.7% had abnormalities, including

<table>
<thead>
<tr>
<th>Problem</th>
<th>Rate Per 1,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic thyroiditis</td>
<td>51.3</td>
</tr>
<tr>
<td>Simple goiters</td>
<td>28.7</td>
</tr>
<tr>
<td>Nodules (including 10 carcinomas)</td>
<td>23.2</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>15.9</td>
</tr>
<tr>
<td>Hyperthyroidism</td>
<td>3.9</td>
</tr>
</tbody>
</table>

Of the 92 adolescents with “diffuse hypertrophy,” 60% were healthy 20 years later, 20% were unchanged, and thyroiditis or colloid goiters had developed in a few.

Adolescent Goiter
There is no such condition as an "adolescent" goiter. Enlarged thyroid glands are indicative of either diffuse hypertrophy (simple colloid goiter) or thyroid dysfunction. Thyroid enlargement in the adolescent requires evaluation to determine the underlying etiology and to ensure that if required, appropriate therapy is given.

**CLINICAL EVALUATION FOR THYROID DISEASE**

1. History: Duration and severity of symptoms, fever, swelling, pain
   a. Family history: Goiter, thyroiditis, other thyroid problems, or other autoimmune disease
   b. Drug history: Use of goitrogens, including lithium, iodine excess or anticonvulsants, exposure to radiation
   c. Pubertal and menstrual history
   d. Change in weight
   e. Growth problems
   f. Change in behavior, sleep pattern, activity level, or function in school
   g. Change in bowel habits
2. Physical examination
   a. Height, weight, body mass index (BMI)
   b. Pulse, blood pressure
   c. Skin texture or lesions
   d. Adenopathy
   e. Presence of tremor
   f. Eye examination: Presence of exophthalmos or lid lag
   g. Deep tendon reflexes: Slow or fast return phase
   h. Thyroid gland
      • Location of mass, midline or lateral
      • Mobility of mass
      • Size
      • Shape
      • Nodularity
      • Consistency
      • Tenderness
      • Auscultation for bruits
3. Thyroid tests: Many are available, but only several are typically necessary for appropriate diagnosis. Common thyroid tests include the following:
   a. Serum total T₃ concentration: Total T₃ concentration is generally measured by either competitive protein-binding assay or radiimmunoassay (RIA). Most thyroid hormone is bound and inactive. Total T₃ is proportionally free T₃, if the level of thyroxine-binding globulin (TBG) is within the reference range.
   b. T₃ resin uptake: This test is not a measure of thyroid hormone concentrations. It is an indirect measurement of thyroid-binding capability, including TBG, and it is used to calculate the adjusted T₃ or T₄ index.
   c. Adjusted T₄: A calculation using total T₄ and T₃ resin uptake with adjustment for changes in thyroid-binding capability, including TBG levels. Adjusted T₄ is generally high in patients with hyperthyroidism. A few of these patients have only T₄ elevations (T₃ thyrotoxicosis). Conditions that alter TBG and thus total T₄ concentrations but yield a normal adjusted T₄ level include the following:
      • Factors increasing TBG: Oral contraceptives, pregnancy, heredity, acute hepatitis
      • Factors decreasing TBG: Androgens, cirrhosis, nephrosis, acromegaly, genetic, high-dose steroids
      • Drugs decreasing binding of T₄ and T₃: Salicylates, phenytoin (Dilantin), penicillin, heparin, barbiturals
   d. Free T₃: Direct dialysis is the preferred method for determining free T₃. Measures the free T₃ in serum by RIA of the dialyzable T₃.
   e. Total T₃: Measures the total amount of T₃ in serum by RIA. Useful in early or mild hyperthyroidism because the T₃ level rises earlier and more markedly than T₄. Not useful in evaluating hypothyroidism.
   f. Free T₄: Measured in a manner similar to that of free T₃. (For qualitative aspects of total and free T₃ and T₄, see Table 9.1.)

<table>
<thead>
<tr>
<th>Hormone</th>
<th>Mean total (µg/dl)</th>
<th>% Free</th>
<th>Mean free level (µg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>T₄</td>
<td>7.0</td>
<td>0.03</td>
<td>2.1</td>
</tr>
<tr>
<td>T₃</td>
<td>0.14</td>
<td>0.3</td>
<td>0.5</td>
</tr>
</tbody>
</table>

**TABLE 9.1. Quantitative aspects of total and free T₃ and T₄**

- TSH: Serum TSH is measured by RIA. It is the most sensitive test for diagnosing primary hypothyroidism and separating thyroidal hypothyroidism (increased TSH level) from hypothalamic-pituitary hypothyroidism (low TSH level). Serum TSH concentration is markedly elevated in primary hypothyroidism. Third-generation ultrasensitive TSH assays can distinguish normal TSH levels from suppressed levels (<0.7 µU/mL). This is useful in diagnosing suppression of TSH caused by excessive thyroid supplementation or hyperthyroidism.
- Thyroid radiiodine uptake (RAIU): A measurement of thyroid uptake of iodine-131 (¹²³I) or iodine-123 (¹²³I). The chief value of this test is in the differential diagnosis of hyperthyroidism. The RAIU value is high or high normal in hyperthyroid Graves disease, in nodular goiter, or in Hashimoto thyrotoxicosis. The RAIU value is low in factitious hyperthyroidism, in subacute thyroiditis, in abnormal location of the thyroid gland, or in patients with Graves disease who have ingested iodine. ¹²³I is preferred because of the lower radiation dose.
- Thyroid scan: A thyroid scan mainly evaluates morphological features and functional status of the gland. It is useful in the differential diagnosis of the solitary nodule or in locating extrathyroidal tissue. ¹²³I or technetium (Tc) pertechnetate scans are preferred. Addition of a perchlorate discharge to the ¹²³I scan can be used to help differentiate Hashimoto thyrotoxicosis and inborn errors of thyroid hormone synthesis.
- Thyroid antibodies: Levels of thyroid, thyroglobulin, and microsomal antibodies are elevated in most patients with Graves disease and Hashimoto thyroditis. Antimicrosomal antibodies appear more sensitive (99% sensitivity) than antithyroglobulin antibodies (36% sensitivity) (Nordyke et al., 1993). Titers are lower in adolescents than adults. The presence of the specific thyroid-stimulating immunoglobulin (TSI) or the TSH-receptor antibody is seen in Graves disease. These antibodies can be assayed at the time of diagnosis of Graves disease and monitored as an indication of the resolution of the autoimmune process.
- TBG: Total binding globulin (TBG) decreases in a variety of conditions that elevate serum T₃ or T₄ levels. Elevations of TBG may be a result of increased synthesis of TBG, decreased thyroid hormone binding or a combination of both. The chief use of TBG is in differentiating primary hypothyroidism from secondary hypothyroidism. In primary hypothyroidism, TBG levels are increased, while in secondary hypothyroidism they are decreased.
- Reverse T₃: An inactive isomer of T₃ produced from inner-ring deiodination of T₄. In nonthyroidal illnesses, such as starvation and anorexia nervosa, T₃ concentrations are low and reverse T₃ concentrations are within the reference range or elevated. In hypothyroidism, levels of both T₃ and reverse T₃ are low.
- Tumor necrosis factor or other cytokines appear to be involved in the pathogenesis of nonthyroidal illness.
- TBG by RIA: Direct measurement of TBG is done by RIA.
- Thyroglobulin level: Thyroglobulin is leaked into the serum when there is destruction of thyroid parenchyma. The concentration is elevated in thyroid carcinoma.
Thyroid deficiency and thyroid hyperfunction are associated with abnormalities of the hypothalamic-pituitary axis. In hypothyroidism, growth hormone, gonadotropins, and prolactin secretory dynamics are altered. This leads to impaired growth, menstrual irregularities, precocious puberty, and galactorrhea. In hyperthyroidism, there is accelerated growth, delayed menarche, and oligomenorrhea. In thyrotoxicosis, cortisol clearance is enhanced, and those patients receiving glucocorticoid replacement treatment may need an increased dose. In addition, hyponatremia can occur in hypothyroidism due to impaired free water clearance.

Screening for Thyroid Disease

In 1998, the American College of Physicians published guidelines on screening for thyroid disease for use by primary care physicians (Helfand and Redfern, 1998). Recommendations suggested screening only women older than 50 years with a sensitive serum TSH, followed by a free thyroxine test when the TSH is less than 0.3 to 0.4 mU/L or more than 10 mU/L for women. For younger asymptomatic women, this was not felt to be warranted. However, the American Thyroid Association recommends screening women at the age of 35 years, and every 5 years thereafter.

EUTHYROID GOITER

An asymptomatic goiter may be discovered during a routine physical examination, noted by a parent, or discovered by the teenager. The incidence is about 9 of 1,000 per year, with most affected teens being female.

CAUSES OF NONTOXIC ENLARGED THYROID GLANDS IN ADOLESCENCE

1. Common causes
   a. Hashimoto thyroiditis
   b. Simple goiter
2. Uncommon causes
   a. Acute suppurative thyroiditis
   b. Subacute thyroiditis
   c. Primary thyroid neoplasms
   d. Goitrogen-induced goiter

DIFFERENTIATION AND EVALUATION OF SIMPLE GOITER VERSUS HASHIMOTO THYROIDITIS

Table 9.2 compares typical symptoms in simple goiter versus those in Hashimoto thyroiditis. If the adolescent is euthyroid, if results of thyroid function tests are normal, if no nodules are palpable, and if there is no adenopathy or adherence of the gland to the neck structure, then no further diagnostic study is necessary. Thyroid antibodies are used to differentiate simple goiter from chronic lymphocytic thyroiditis (Hashimoto thyroiditis). An uptake test and a thyroid scan are of some value in evaluating a nontoxic goiter, particularly if antithyroid antibodies are not present in high titers. If the uptake is decreased and patchy, and if there is a positive perchlorate discharge, these findings would be consistent with Hashimoto (chronic lymphocytic) thyroiditis. Adolescents with chronic lymphocytic thyroiditis are at increased risk of having other autoimmune disorders, including insulin-dependent diabetes mellitus (approximately 25% of patients with diabetes between the ages of 15 and 20 years have positive thyroid antibodies), rheumatoid arthritis, systemic lupus erythematosus, adrenal insufficiency, hypoparathyroidism, vitiligo, pemphigus, and alopecia totalis.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Simple goiter</th>
<th>Hashimoto thyroiditis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thyroid gland</td>
<td>Normal</td>
<td>Enlarged</td>
</tr>
<tr>
<td>Thyroid function</td>
<td>Normal</td>
<td>Decreased</td>
</tr>
<tr>
<td>Thyroid antibodies</td>
<td>Absent</td>
<td>Present</td>
</tr>
<tr>
<td>Erythrocyte sedimentation rate (ESR)</td>
<td>Normal</td>
<td>Elevated</td>
</tr>
<tr>
<td>Fever</td>
<td>Rare</td>
<td>Common</td>
</tr>
</tbody>
</table>

A less common presentation of euthyroid goiter in the adolescent is subacute thyroiditis. Characteristics of this disease include the following:

1. A self-limited illness, often following an acute viral illness
2. A thyroid gland that is usually tender, with mild enlargement
3. Usually no thyroid dysfunction
4. Absence of thyroid antibodies
5. An elevated erythrocyte sedimentation rate (ESR)
6. Fever

TREATMENT OF SIMPLE GOITER

There is some controversy over the approach to simple colloid goiter. Specialists are divided between employing thyroid hormone replacement and close observation without treatment. Spontaneous recovery is possible, and many teens remain euthyroid for years.

1. Indications for treatment
   a. Large goiter
   b. Cosmetic concerns of an enlarged goiter
   c. Pressure symptoms
   d. Progressively enlarging gland
2. Type of therapy
   a. Thyroid hormone: If indicated, best continued during the adolescent growth spurt. Synthetic thyroxine is the best preparation, giving stable levels of T<sub>4</sub> and T<sub>3</sub> after about 3 weeks of treatment.
   b. Dose: The replacement dose is about 0.1–0.15 mg/day.
   c. If there is only minimal thyroid enlargement and normal T<sub>4</sub> and TSH levels, gland size and thyroid hormone levels (T<sub>4</sub>, TSH) should be evaluated every 4–6 months during adolescence.

HYPOTHYROIDISM

Causes

Most hypothyroidism in adolescence is caused by chronic lymphocytic thyroiditis. Secondary pituitary and tertiary hypothalamic causes are rare.
Clinical Manifestations

1. Growth retardation and pubertal delay: Most common endocrine cause of delayed growth
2. Delayed bone maturation
3. Precocious puberty and galactorrhea
4. Menstrual disorders
5. Weight gain
6. Cutaneous manifestations
   a. Cold skin
   b. Decreased sweating
   c. Dry skin
   d. Edema of face and eyelids
   e. Erythema of cheeks
   f. Localized hyperkeratosis
   g. Pallor
   h. Thin epidermis
   i. Dry, brittle hair
   j. Patchy alopecia
   k. Sparse eyebrows
   l. Fine, downy hair
   m. Thickened, brittle nails
7. Usual signs of adult hypothyroidism: Lethargy, weakness, eyelid edema, cold intolerance, skin pallor, decreased memory, constipation, hoarseness, precordial pain, and anemia

Evaluation

Adjusted $T_4$ and TSH: TSH is the most sensitive indicator of primary hypothyroidism and can be used alone as a screen for hypothyroidism.

1. Low $T_4$ and high TSH concentrations indicate primary hypothyroidism.
2. Low free $T_4$ and normal or low TSH concentrations indicate secondary or tertiary hypothyroidism.

For secondary or tertiary hypothyroidism, a TRH stimulation test can be performed. No TSH response indicates pituitary disease. A late rise in TSH concentration and failure to return to baseline at the completion of the test, coupled with elevated prolactin levels, indicate hypothalamic disease. An endocrine evaluation and central imaging study for cause and extent of hypothalamic or pituitary disease are also indicated. $T_3$ and TSH can also be seen in nonthyroidal illness, referred to as “sick” euthyroid. This also includes a low $T_3$ level and a normal or elevated reverse $T_3$ level. Low $T_3$ and normal TSH concentrations are also found in patients with TBG deficiency. Obtaining a TBG level by RIA confirms this diagnosis.

Therapy

Synthetic thyroxine is given in doses of 75 to 150 µg/day (1.6 µg/kg): 75 to 100 µg/day to most female patients and 100 to 150 µg/day to most male patients. The goals are $T_4$ levels in the reference range, normal and not oversuppressed levels of TSH, and resumption of growth. Hennessey et al. (1986) evaluated thyroid replacement therapy. A downward trend has occurred in the past 14 years because of an increased potency or bioavailability of thyroxine. The formulation was changed in 1982. Average replacement doses decreased from 169 to 112 µg during this period. Current average replacement doses equal about 127 ± 39 µg.

Overtreatment with thyroxine should be avoided because it could lead to osteoporosis. Health care providers should counsel adolescents on thyroid hormone supplementation to have adequate calcium intake. However, calcium carbonate has been shown to interfere with thyroid hormone absorption. Patients taking this preparation need to be monitored to ensure that thyroid hormone replacement doses are adequate.

There has been the recent suggestion that some adults feel better with supplemental $T_3$ in addition to treatment with $T_4$. This is not recommended for adolescents.

Initiation of Therapy

Usually, in adolescents, therapy can be started with a full dose of thyroxine. In older patients or those with heart disease, it should be started at 25 or 50 µg/day and increased by 25 to 50 µg/day each month. Chronically ill adolescents may need about 25 to 50 µg less than healthy teens. The serum thyroxine concentration returns toward the reference range within a few weeks of the start of therapy. Usually the teen will begin to improve clinically within 2 weeks and will become free of symptoms and signs by 3 to 6 months. The sensitive TSH measurements may decline more slowly. The higher the initial level, the longer it may take to return to values within the reference range. It is reasonable to check a $T_3$ level 1 month after initiating therapy. However, the practitioner needs to be careful in altering doses at this point, because this can lead to overtreatment as a result of the slow decline in sensitive TSH levels. If the TSH level is not within the reference range by 4 months and the free $T_4$ concentration has increased, it is reasonable to increase the dose by 25 µg/day. Repeated tests can be done 4 weeks after a change in dose. Once a teen is euthyroid and stable, he or she can be monitored at 6 months while growth is still occurring and then every year after, unless the condition again becomes symptomatic. Adolescent girls with hypothyroidism should be told of the need to evaluate thyroid function tests before pregnancy. A report by Haddow et al. (1999) showed that elevated TSH levels in the first trimester of pregnancy, before the onset of fetal thyroid hormone production, may impair infant neurodevelopment.

Subclinical Compensated Hypothyroidism

Patients with subclinical compensated hypothyroidism are asymptomatic, and $T_4$ levels are usually within the reference range, but TSH levels are elevated. The individuals at highest risk for the development of clinical hypothyroidism are those who have both an elevated TSH concentration of more than 10 mU/L and an elevated concentration of thyroid antibodies. It is reasonable to treat individuals in the following categories:

1. TSH value >10 mU/L
2. TSH value >5 mU/L with a goiter or thyroid autoantibodies

The Adolescent with Congenital Hypothyroidism

Due to the high prevalence of congenital hypothyroidism, which approximates 1 of 400 infants, there are many teens who were diagnosed with this disorder on newborn screening. Although the overall results of early detection of congenital hypothyroidism have been extremely favorable, particularly with regards to growth and pubertal development, a report by Rovet (1999) suggests that some teens with congenital hypothyroidism have neuropsychological sequelae. Some adolescents were found to have a poorer performance in visuospatial, language, and fine motor areas than expected, as well as selective attention and memory deficits. Adolescents with congenital hypothyroidism need to understand their diagnoses, and often, despite a lifetime of treatment, the teen has not been informed about the reason why he or she has been taking thyroid medication since birth.

HYPERTHYROIDISM

Hypothyroidism is less common than euthyroid goiter in children and younger adolescents. Only 5% of patients with Graves disease are younger than 15 years. Hypothyroidism becomes more common in those with age, particularly in women, affecting approximately 2% of women. The prevalence in females increases dramatically during late adolescence and young adult ages, with a peak at about age 25 years.

Causes of Hyperthyroidism in Adolescents

1. Common: Graves disease (for practical purposes, almost all hyperthyroidism in adolescents is caused by Graves disease). Graves hyperthyroidism is caused by
thyroid-stimulating antibodies, which bind to and activate thyrotropin receptors on thyroid cells. The causes of Graves ophthalmopathy and dermopathy are less clear but seem to be related to an autoimmune response leading to cytokine-mediated activation of fibroblasts leading to fibrosis (Weetman, 2000). Graves disease is the most common autoimmune disorder in the United States and is associated with a five to ten times greater prevalence in women.

2. Uncommon
   a. Hashitoxicosis
   b. Toxic nodular goiter: Single adenoma or multiple nodules
   c. Thyroiditis: Subacute, silent, or postpartum
   d. Iatrogenic illness: Exogenous intake of thyroxine

3. Rare
   a. Ectopic thyroid tissue (e.g., struma ovarii [ovarian teratoma-containing thyroid tissue])
   b. Inappropriate TSH secretion: Pituitary tumor
   c. Ectopic iodide intake
   d. Thyroid cancer

Clinical Manifestations

Manifestations of Hyperthyroidism

Symptoms

1. Hyperactivity, irritability, altered mood
2. Nervousness, sweating, palpitations
3. Emotional lability
4. Change in school performance: Inability to complete tasks; untidy work
5. Sleep disturbance
6. Heat intolerance
7. Weakness and fatigue
8. Weight loss with increased appetite
9. Pruritus
10. Diarrhea or increased stool frequency
11. Menstrual changes: Amenorrhea, oligomenorrhea, or dysfunctional uterine bleeding

Signs

1. Sinus tachycardia
2. Wide pulse pressure
3. Fine tremor, hyperkinesis, hyperreflexia
4. Warm, moist skin and brittle nails
5. Hair loss
6. Onycholysis
7. Muscle weakness

Manifestations of Graves Disease

1. Diffuse goiter, rubbery gland, bruit
2. Ophthalmopathy including feeling of grittiness in eye, retrobulbar pain, eyelid lag or retraction, exophthalmos, optic neuropathy; eye changes usually less severe than in adults
3. Localized dermopathy
4. Lymphoid hyperplasia

Reduced bone mineral density is seen at diagnosis of Graves disease due to reduced bone mass from high bone turnover. This can be corrected after 1 year of euthyroid conditions.

Evaluation

The combination of a suppressed ultrasensitive TSH and elevated T₄ index or free T₃ should confirm most cases of hyperthyroidism. If the TSH concentration is suppressed, but the T₄ concentration is within the reference range, a T₃ RIA level should be measured to evaluate for T₃ toxicosis.

1. TSH concentration
   a. Should be low in all forms of hyperthyroidism, except in TSH-secreting adenomas and ectopic TSH production
   b. Normal TSH concentration nearly always excludes a diagnosis of hyperthyroidism, except in the rare individual with excessive TSH secretion.
   c. Third-generation ultrasensitive TSH test alone may be recommended by some as a screen for hyperthyroidism.

2. Adjusted T₄ value
   a. If elevated, hyperthyroidism is confirmed. Pregnant women, those taking estrogens, or persons having an inherited increase in TBG production may have an elevated total T₄ concentration. However, their T₃ index or free T₃ and TSH values should all be within the reference range.
   b. If within the reference range and the TSH level is low, or if hyperthyroidism is suspected on examination, measure the total T₃ concentration. If the T₃ level is elevated, then hyperthyroidism (T₃ thyrotoxicosis) is indicated. If results are normal or borderline, a TRH stimulation test should be performed. If results of the TRH stimulation test show a normal TSH response, a euthyroid state is indicated. If a TSH response is absent, a probable hyperthyroid state is indicated.

3. Thyroid antibodies: Present, particularly the specific TSI, or TSH-receptor antibody in Graves disease and in Hashimoto thyrotoxicosis. Thyrotropin-receptor antibodies are present in about 90% of patients with Graves hyperthyroidism. New assays have even higher sensitivities of up to 99%. Whether the test should be measured in the differential diagnosis of Graves disease is often up to individual preferences and cost. Some individuals feel that the test should be routinely done and others feel the diagnosis can almost always be inferred correctly on clinical findings.

4. Thyroid scan and uptake: Probably not indicated in an adolescent with hyperthyroidism, unless a nodule is present, factitious thyroid ingestion, ectopic thyroid tissue, and metastatic functioning carcinoma.

5. Other laboratory tests to obtain at diagnosis: Complete blood cell count, liver function tests, antinuclear antibodies, electrolytes, and urinalysis

Therapy

Therapy for hyperthyroidism (Graves disease) includes medical therapy, ablation with ¹³¹I, and surgery.

Medical Therapy Medical therapy should be started in all patients with hyperthyroidism. It is usually the primary modality in most adolescent patients. Medical therapy includes the following:

- Symptomatic end-organ therapy with propranolol or another b-blocker. This measure is needed only if symptoms are moderate or severe and is discontinued as the euthyroid state is reached.
- Antithyroid medication: Methimazole, carbimazole, or propylthiouracil (PTU). Methimazole is the active metabolite of carbimazole, and the conversion is almost
100%, so their effects and equivalent doses are comparable.

a. Action
- Inhibits iodine incorporation into tyrosine residues in thyroglobulin
- Reduces serum concentrations of thyrotropin-receptor antibodies
- Increases TSH-converting enzyme activity
- PTU also inhibits peripheral conversion of T₂ to T₃

b. Metabolism: Peak blood levels are reached in 1 to 2 hours. PTU has a half-life of about 1–2 hours, whereas methimazole (Tapazole) has a half-life of about 3–5 hours.

c. Indications: Major indications are for children, adolescents, young adults, and pregnant women with hyperthyroidism caused by Graves disease. The choice of which antithyroid medication to use is based mainly on the practitioner’s personal experience and preference. However, in many cases, methimazole is preferred because of compliance (in maintenance doses, it can be used as a once-a-day drug) and a greater effect on decreasing the local thyroid immune response. PTU is preferred because it has a greater decrease in T₄ to T₃ conversion, and some indication of possible congenital defects with methimazole. In most adolescents, an antithyroid medication should be tried in the hope of achieving a temporary or permanent remission.

d. Doses:
- Methimazole: Started in a dose of about 10 mg twice a day. The dose may need to be reduced in 4–6 weeks as clinical and biochemical improvement takes place. The dose can be adjusted every 4–6 weeks until a maintenance dose is reached at about 5–10 mg/day.
- PTU: Started in doses of 75–100 mg three times a day. This may be lowered, with time, to a maintenance dose of about 50–100 mg/day in divided doses.

Follow-up: During the initial follow-up visits, the serum TSH concentration may remain low and thus is not a good indicator alone for adjusting dose levels.

Efficacy: Antithyroid drugs are the mainstay of therapy for hyperthyroidism. Almost all individuals who take their medication will become euthyroid during treatment. The reported likelihood of a long-term remission ranges from 10% to 75%. Possible indicators of long-term remission include a small goiter and recent onset of disease. Glasser and Styne (1997) reported that remission was more likely in older teens and those who had higher BMIs, lower heart rates, smaller goiters, lower T₄ and T₃ concentrations, and lower platelet counts at diagnosis. Allahabadi et al. (2000) found that male patients had a lower remission rate than females.

However, there is no specific test to determine which patients will respond to medical therapy. The presence of high titers of TSH suggests that ongoing stimulation would still occur. Another factor in long-term remission is duration of therapy. Two years of treatment appears much more likely to induce a remission than 6 to 12 months of treatment. Thus, most authorities recommend at least 12 months of suppression. After the initial treatment period, the drug dose should be gradually discontinued while the adolescent is monitored for signs and symptoms of relapse. A relapse often occurs in the first few months after therapy has been discontinued, but individuals must be followed for life because many will have a relapse or hypothyroidism in future years. If a relapse occurs, the choices include another course of medical therapy, surgical intervention, or depending on age, ¹³¹I ablative therapy.

g. Side effects: Antithyroid drugs are generally safe, although side effects do limit their usefulness. Side effects are classified as minor and major, based on the degree of morbidity. Side effects are more common at higher doses of methimazole (40 mg/day or more), but there is no apparent dose relationship with PTU.

h. Minor side effects: These develop in up to 5% of patients at usual doses.
- Common: Pruritus, fever, rash, urticaria
- Uncommon: Gastrointestinal distress, change in taste sensation, and production of insulin autoantibodies, causing hypoglycemia

i. Serious side effects (about 3 of 1,000):
- Rare: Agranulocytosis (less than 500 granulocytes/mm³) occurs in about 0.5% of users. This is an idiosynratic reaction but is probably less common in individuals receiving less than 30 mg of methimazole per day. It usually starts in the first 3 months of therapy and is manifested by an abrupt onset of fever, systemic toxic effects, and often mouth sores and pharyngitis. The abrupt onset makes routine monitoring of white blood cell counts useless in detecting this problem. Patients should be warned to stop using the medication at the first signs of fever, pharyngitis, or mouth sores. This is an absolute contraindication to further use of antithyroid medications. Transient leukopenia (less than 4,000 leukocytes) occurs in up to 25% of children and 12% of adults and is not a reason to stop the medication.
- Uncommon: Hepatitis (particularly with PTU therapy), cholestatic jaundice (particularly with methimazole), thrombocytopenia, aplastic anemia and lupus-like syndrome, nephritic syndrome (with methimazole), and loss of taste (with methimazole).

¹³¹I Ablative therapy: Ablative therapy is highly successful in adults and has been increasingly used as a first line of therapy, although resulting hypothyroidism is common. However, the natural course of Graves disease is toward hypothyroidism anyway. Although some institutions use ¹³¹I in children and adolescents, its use is controversial because of concern over unknown long-term effects of radiation in the areas of cancer and fertility. There has been no evidence of an increased risk of thyroid cancer, leukemia, and most solid tumors; the risk of gastric cancer increases 10 years after treatment, and the risk of breast cancer increases (not significantly) 15–20 years after treatment.

Relapse after surgery occurs in about 10% of individuals, usually within 5 years.

Surgery:
Subtotal thyroidectomy has been advocated for patients who fail to benefit from or refuse medical therapy and for those with large goiters, particularly with symptoms of compression or with cosmetic concerns. With experienced surgeons, the morbidity and mortality rates are low. Complications include hypothyroidism, hypoparathyroidism, and paralysis of the recurrent laryngeal nerve. Ideally, before surgery, individuals are treated with antithyroid medications until a euthyroid state is attained. Preoperative therapy includes β-blockers and potassium iodide to help reduce the risk of a postoperative thyrotropin crisis. Franklyn (1994), 5% of patients have no recurrence of Graves disease. For a 19-year-old male or female, 67% preferred antithyroid medication for 1 year, 24% preferred radioactive iodine, and 9% preferred surgical intervention. If hypothyroidism remained after medical therapy, there was a 50/50 split between surgery and radioactive iodine.

Pregnancy:
Pregnant teens with hyperthyroidism should be treated with an antithyroid drug. The dose should be maintained at the lowest dose possible to keep the mother’s T₄ level in the upper limit of the normal range. PTU is the preferred drug because less of it crosses the placenta or appears in breast milk.

Toxic Adenaoma:
Because of the permanent nature of a toxic thyroid adenoma or toxic multinodular goiter, this tumor should be treated with radioactive iodine.

THYROIDITIS:
Thyroiditis is a group of inflammatory thyroid disorders. Although thyroiditis or a painful thyroid per se is an uncommon presentation in the adolescent, the thyroid enlargement associated with various types of thyroiditis is common. Table 9.3 outlines the differences between Hashimoto and subacute thyroiditis. Among the forms of thyroiditis, Hashimoto is the most common, with subacute granulomatous thyroiditis being about one fortieth as common. Silent thyroiditis is very uncommon in adolescents, as is acute suppurative thyroiditis.

12h Ablative therapy: Ablative therapy is highly successful in adults and has been increasingly used as a first line of therapy, although resulting hypothyroidism is common. However, the natural course of Graves disease is toward hypothyroidism anyway. Although some institutions use ¹³¹I in children and adolescents, its use is controversial because of concern over unknown long-term effects of radiation in the areas of cancer and fertility. There has been no evidence of an increased risk of thyroid cancer, leukemia, and most solid tumors; the risk of gastric cancer increases 10 years after treatment, and the risk of breast cancer increases (not significantly) 15–20 years after treatment.
Acute Suppurative Thyroiditis

Acute suppurative thyroiditis is a rare form of thyroiditis caused by a bacterial, fungal, or parasitic infection and is usually preceded by an infection elsewhere, such as an upper respiratory tract infection. Signs and symptoms include neck pain, fever, and dysphagia. The white blood cell count is usually elevated, and thyroid antibodies are not detected. Treatment is with analgesics, antibiotics, and surgical drainage if necessary. A fistula between the piriform sinus and the thyroid gland can contribute to the pathogenesis of acute suppurative thyroiditis and should be sought in such individuals (Szabo and Allen, 1989).

Subacute Granulomatous Thyroiditis

Subacute granulomatous thyroiditis (Table 9.3) is a spontaneously remitting thyroid infection thought to have a viral cause (possibly mumps virus, echovirus, coxsackievirus, Epstein-Barr virus, influenza virus, and adeno-associated virus). It is the most likely cause of a painful thyroid gland. Women are three to five times more likely to be affected.

1. Clinical manifestations
   a. Abrupt onset
   b. Neck pain: Mild to severe, may be exacerbated by turning the head or swallowing, and may radiate to jaw, ear, or chest
   c. Systemic symptoms common: Malaise, fever, fatigue, myalgias
   d. Thyroid slightly enlarged, firm and very tender to palpation
   e. Mild to moderate signs of hyperthyroidism
   f. Duration of 2–5 months

2. Laboratory findings
   a. ESR often more than 100 mm/hr; a normal sedimentation rate is extremely unusual with this diagnosis
   b. White blood cell count often within the reference range
   c. Initially: Iodine uptake low (often 0), elevated T₄ and T₃ concentrations, followed by a period of normal uptake and subnormal results on thyroid function tests, followed by normal test results
   d. Thyroglobulin level is almost always elevated

3. Treatment: Salicylates; if severe, steroids can be given in a tapering dose of prednisone (20–40 mg/day) given over 2 to 4 weeks; antithyroid medications are not indicated

Subacute Lymphocytic Thyroiditis

Subacute lymphocytic thyroiditis is lymphocytic thyroiditis with spontaneously resolving hyperthyroidism, or silent thyroiditis. This form of thyroiditis has been thought to include as many as 14% to 23% of adult cases of hyperthyroidism, although studies outside the Great Lakes area suggest the prevalence to be in the 5% range. This is not a common cause of hyperthyroidism in adolescents; most cases occur in individuals older than 30 years. The cause is not known, and there is no evidence of a viral cause.

1. Clinical manifestations
   a. Mild to moderate hyperthyroid symptoms
   b. No signs of Graves disease, such as exophthalmos or myxedema
   c. Enlarged, painless thyroid gland
   d. Abrupt onset of symptoms
   e. Firm, painless goiter
   f. Often four phases: Hyperthyroid period (1–4 months), short euthyroid period, hypothyroid period (4–10 weeks), recovery
   g. Recurrences in 10%–50% of individuals

2. Laboratory findings
   a. Low iodine uptake, in distinction from Graves disease or Hashimoto thyrotoxicosis; complete suppression of TSH to TRH stimulation
   b. T₄ and T₃ levels are initially elevated, often with a disproportionate increase in T₄ compared with T₃
   c. Elevated antithyroglobulin antibodies in 25% and antimicrosomal antibodies in 60% of individuals
   d. ESR within the reference range or mildly elevated
   e. Lymphocytic infiltration similar to that seen in Hashimoto thyroiditis, as shown by biopsy (if done)

3. Treatment: Usually symptomatic, with β-blockers if necessary

Chronic Lymphocytic Thyroiditis

Chronic lymphocytic thyroiditis (Hashimoto thyroiditis) (Table 9.3) is characterized by an autoimmune cause, a genetic predisposition, a strong female predilection, and a lymphocytic infiltration of the thyroid gland. In almost all cases, thyroid antibodies are abundantly present. Although individuals may be in a hyperthyroid or a euthyroid state, the diagnosis is usually made because of a goiter and a hypothyroid state.

Diagnostic criteria include the following:

1. Firm goiter
2. Presence of antibodies
3. Elevated TSH level
4. Thyroid scan with “patchy uptake” (test not commonly needed)
5. Positive result on perchlorate discharge test (test not commonly needed)

Usually two or more of these findings are highly suggestive of Hashimoto thyroiditis. Treatment of hypothyroidism is thyroid hormone replacement.

THYROID NODULES

Solitary thyroid nodules and thyroid cancer are uncommon during adolescence. Single nodules are four times more common in females than males. The differential diagnosis of solitary nonfunctional thyroid nodules includes the following:
1. Adenomas
2. Carcinomas
3. Cysts
4. Nodule of an unrecognized multinodular goiter
5. Other rare solitary lesions such as thyroiditis or developmental abnormalities

Khurana et al. (1999) found that 25% of thyroid nodules in pediatric cases are malignant, with a 4:1 ratio of papillary thyroid carcinoma to follicular carcinoma.

Evaluation

Evaluation of a thyroid nodule should include adjusted T<sub>4</sub>, TSH, thyroid antibody, and thyroglobulin levels. The initial major diagnostic step has become the fine-needle aspiration biopsy. In most centers, the fine-needle aspiration biopsy is a safe and inexpensive test that leads to a better selection of which individuals require surgery. Results of the cytological specimens are either benign, malignant, or indeterminate. The accuracy to cytological diagnosis ranges from 70% to 97%. Individuals with benign results can be followed up safely.

Radionuclide scanning has been used in individuals with solitary nodules but cannot reliably distinguish between benign and malignant lesions. The scan is useful in those individuals with thyrotoxicosis and a nodule. The scan can also be useful in individuals with an indeterminate biopsy result because a hyperfunctioning nodule is almost always benign. An ultrasound cannot distinguish benign nodules from malignant nodules. High-risk factors include the following:

- Male adolescent
- Cold nodule on scan
- Recent growth
- Firm nodule
- Cervical adenopathy
- 6. Solid lesion on ultrasound
- Recurrent laryngeal, tracheal, or esophageal involvement
- 8. Multiple mucosal neuromas, suggestive of multiple endocrine neoplasia syndromes
- 9. History of radiation exposure

Factors favoring benign lesions include the following:

- Cystic lesion
- Hyperfunctioning on scan
- Elevated antibody levels
- Family history of goiter

Management

**Nodules with Benign Cytological Features** These lesions can be either observed or treated with thyroxine. Thyroxine therapy is often instituted to try to reduce the size of the nodule or suppress further growth. There is little evidence that thyroxine suppression is of benefit in the treatment of benign hypofunctioning solitary nodules. In addition, there appears to be a risk of decreasing bone density in adults with thyroid suppressive therapy, although the risk to adolescents remains unknown.

**Malignant Lesions** Individuals with malignant lesions should undergo surgery with either a lobectomy or thyroidectomy, depending on the lesion. Overall, total thyroidectomy is the procedure of choice for malignant disease. More extensive surgery is needed if lymph nodes are involved.

**Nodules with Indeterminate Cytological Results** Many experts recommend surgical excision for all individuals with a cytological result demonstrating indeterminate features. Radionuclide scanning is useful in these individuals because a “hot” scan indicates the ability to follow the teen’s condition.

**Cystic Lesions** A cystic lesion should be aspirated. If the lesion is larger than 4 cm in diameter, it should be excised. If the cyst is less than 4 cm and there is either no fluid, cloudy fluid, serosanguineous fluid, or suspicious cytological features, it should be excised.

WEB SITES

For Teenagers and Parents

http://www.magicfoundation.org/clinthyroid.html, Magic Foundation information on thyroid disorders.
http://www.tsh.org/, Thyroid Foundation of America information on thyroid diseases, also has links to many more sites.
http://www.endocrineweb.com/thyroid.html, From Endocrine Web page, information on many thyroid problems with information on thyroid hormone, tests, disease states, and more.
http://www.thyroidabout.com/health/thyroid/library/weekly/aa042100a.htm, Thyroid 101 with basic information about all thyroid diseases.

For Health Professionals


REFERENCES AND ADDITIONAL READINGS


Bethune JE. Interpretation of thyroid function tests. Dis Mon 1989;35:541.
Diabetes mellitus (DM) is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. Chronic hyperglycemia is associated with long-term microvascular (retinopathy, nephropathy, and neuropathy) and accelerated macrovascular (coronary artery disease and stroke) complications. The direct and indirect costs of diabetes care were estimated at $38 billion in 1997; the medical conditions associated with diabetes among older adults account for a significant share of these costs. The costs attributable to type 1 were estimated to be $20 billion in 1993.

If all adults with type 1 diabetes received intensive treatment with the goal of achieving normal glycemia, as did participants in the Diabetes Complications Control Trial, they would gain approximately 7.7 additional years of sight, 5.8 additional years free from end-stage renal disease, and 5.6 additional years free from lower extremity amputation. Compared with conventionally treated patients (typically those receiving only two insulin injections), the average individual would gain 15.3 years of life free from any significant microvascular or neurological complications and would live 5.1 years longer. Comparable clinical trials of intensified treatment for individuals with type 2 DM have demonstrated a significant reduction in risk for microvascular complications; the effect of strict glycemic control on macrovascular complications is less clear. Risk for these is reduced with intensive treatment of hypertension and dyslipidemia.

CLASSIFICATION AND ETIOLOGY

Classification of diabetes is based on the presumed etiology, rather than the mode of treatment (i.e., insulin vs. no insulin) (American Diabetes Association [ADA], 1999). The more common types of diabetes include the following (see Table 10.1 for characteristics of type 1, type 2, maturity-onset diabetes of youth, and atypical forms):

1. Type 1 diabetes—formerly called insulin-dependent diabetes—is the result of beta-cell destruction, usually leading to absolute insulin deficiency. Adolescents are usually symptomatic at presentation and at risk for ketoacidosis.
   a. Immune-mediated: Type 1 diabetes is linked to the major histocompatibility genes associated with diabetes (human leukocyte antigen DQ) (Nepom and Kwok, 1998). It is believed to be mediated by T cells that recognize beta-cell-reactive antigens. The immune changes may be detectable many months to years before the onset of diabetes. Multiple antibodies have been observed that are directed against islet cells (ICA), insulin, glutamate decarboxylase (anti-GAD$_65$), receptor-linked tyrosine phosphatases (IA-2, IA-2$\alpha$), are present in 85% to 90% of individuals at the time of diagnosis. It appears that African-Americans may have a lower prevalence of these antibodies than whites. A later onset (at least in young adulthood) is associated with a longer duration of symptoms, higher serum C-peptide concentrations (more beta-cell reserve), and a lower frequency of ICA.
   b. Idiopathic: Non-immune mediated diabetes appears to occur more frequently in adults.

2. Type 2 diabetes (formerly called non-insulin-dependent diabetes) may range from predominantly insulin resistant with relative insulin deficiency to a predominantly secretory defect with insulin resistance. It is characterized by decreased muscle glucose uptake, increased hepatic glucose production, impaired insulin secretion, and probable overproduction of free fatty acids by fat cells, which further stimulates gluconeogenesis, decreases postprandial hepatic glucose uptake, and may increase muscle insulin resistance, further impairing insulin secretion. Dyslipidemia and a family history of type 2 diabetes are common.

3. Other specific types
   a. Specific genetic defects of beta-cell function have been identified.
      - Maturity-onset diabetes of youth (MODY) is associated with monogenetic defects in beta-cell function, impaired insulin secretion with minimal or no defects in insulin action, autosomal-dominant inheritance, and onset usually before the age of 2 years (Winter et al., 1999).
         - Classic MODY is seen predominantly in nonobese whites, is nonketotic, and is generally not insulin requiring. It represents less than 5% of cases of childhood diabetes in whites. It is seen in all racial/ethnic groups. Five specific gene mutations have been identified.
         - Atypical diabetes mellitus (ADM) is a subtype of MODY that has been identified in approximately 10% of African-Americans with youth-onset diabetes. In contrast to MODY in whites, ADM presents clinically as acute-onset diabetes often associated with weight loss, ketoacidosis, and even diabetic ketoacidosis and will require insulin during the initial treatment. Approximately 50% of patients with ADM are obese. The specific defect remains unknown.
   b. Various genetic defects of insulin action are known. These include type A insulin resistance, leprechaunism, Rabson-Mendenhall syndrome, lipohypertrophic diabetes, and others.

4. Diseases of the exocrine pancreas leading to destruction of exocrine function
   a. Cystic fibrosis: Diabetes is common among adolescents and young adults with cystic fibrosis. Approximately 20% to 40% of adult patients with CF have impaired glucose tolerance; 4% to 15% have diabetes. CF-related diabetes is associated with decreased pulmonary function, protein catabolism and loss of calories in urine. It probably results primarily from insulopenia, though mild insulin resistance is observed during period of infection. Insulin resistance may be quite marked during steroid treatments for pulmonary inflammation.
   b. Others: Pancreatitis, trauma/pancreactectomy, neoplasia, hemochromatosis, fibrocystic pancreatic disease.

5. Endocrinopathies including acromegaly, Cushing syndrome, hyperthyroidism, and pheochromocytoma

6. Drugs including glucocorticoids, pentamidine, thyroid hormone, diazoxide and thiazides

Gestational diabetes mellitus (GDM). The risk for subsequent development of diabetes is elevated—for type 1, 17%; type 2, 17%–70%.

Race/ethnicity: Native American, African-American, Hispanic, Asian/Pacific Islander

Type 2 DM

Who?

Prevalence

Accessing glycemic control: The goal is to lower blood glucose (BG) level, and resultant Hb A

Table 10.2

Type 2: There has been a steady increase in the prevalence of type 2 DM in the United States, affecting 6.6% of Americans between the ages of 20 and 74 years, and 17.7% of those between the ages of 65 and 74 years. It accounts for at least 10% of the diabetes cases diagnosed in children and adolescents in the United States (Fagot-Campagna et al., 2000).

- Racial distribution: Within the United States, African-Americans have a twofold increased risk; Hispanics, a 2.5-fold increase; and Native Americans, a fivefold increase compared with whites.
- Gender: The risk is slightly higher for females and those living in poverty, probably secondary to the added risk of obesity.
- Family history: More than 40% of the children of parents with type 2 DM have a lifetime risk of developing type 2 DM.

Emergence of diabetes during adolescence and glycemic control

a. Insulin sensitivity decreases significantly at Tanner's sexual maturity rating 2 (SMR 2), remains constant from SMR 2 through 4, and returns almost to prepubertal levels by SMR 5.

Girls and African-Americans are more insulin resistant; this is only partially explained by higher body mass index (BMI). The decreased sensitivity to insulin is not explained by sex steroids and is presumed to be associated with peripheral effects of growth hormone (Amiel et al., 1986; Moran et al., 1999).

Obesity has increased, with an estimated 12.4% of boys and 10.5% of girls 12–17 years overweight (BMI above the 95th percentile). The prevalence of obesity is higher among minority youths and poor populations, particularly Mexican-Americans. Children and adolescents are more sedentary.

DIAGNOSIS

The diagnostic criteria for diabetes have changed recently by the ADA and the World Health Organization to facilitate diagnosis and screening. The level of fasting plasma glucose (FPG) has been recommended for screening and diagnosing DM in most circumstances (Table 10.2). This has replaced the traditional oral glucose tolerance test (OGTT) because it is cumbersome and costly, it has been underutilized, and the repeated test reproducibility of the 2-hour postprandial glucose (PG) level is worse than that of the FPG. Hemoglobin A1c (Hb A1c) (a specific glycated protein) is not recommended for the diagnosis of diabetes. Impaired fasting glucose level and impaired glucose tolerance results are abnormal but are not of themselves, diagnostic of diabetes. These groups are at increased risk for developing diabetes and the test should be repeated in 3 months.

TABLE 10.2. Criteria for the diagnosis of diabetes mellitus; American Diabetes Association, 1999

- FPG < 110 mg/dL (6.1 mmol/L) = normal fasting glucose level
- FPG > 110 mg/dL (6.1 mmol/L) and <126 mg/dL (7.0 mmol/L) = impaired fasting glucose level
- 2-hr PG > 140 (7.8 mmol/L) and <200 mg/dL (11.1 mmol/L) = impaired glucose tolerance level

SCREENING

1. Type 1 DM: No screening is recommended.
2. Type 2 DM
   a. How? Screening with FPG testing every year, starting at 10 years or at onset of puberty if puberty occurs at a younger age.
   b. Who?
      - Overweight patients (those with a BMI above the 85th percentile for age and sex, those with weight for height above the 85th percentile, or weight of more than 120% of ideal for height weight) plus
      - Those who have any two of the following risk factors:
        - Family history of type 2 diabetes in first- or second-degree relative
        - Race/ethnicity: Native American, African-American, Hispanic, Asian/Pacific Islander
        - Signs of insulin resistance or conditions associated with insulin resistance, such as acanthosis nigricans, hypertension, dyslipidemia, and polycystic ovary syndrome

EVALUATION AND TREATMENT

The initial use of insulin in an adolescent newly diagnosed with diabetes does not commit to extended use if the clinical course suggests type 2 (obese, strong family history of type 2 DM, absence of ketonemia with insulin omission). At initial presentation, the state of hydration and acid-base balance determine the need for fluids. Evaluation and treatment of diabetic ketoacidosis (DKA) is important to determine the type of diabetes to the extent possible. Measurement of autoantibodies may be useful if etiology is unclear, for example, obese African-Americans with ketonemia (ATK). If type 1 DM is diagnosed, measurement of thyroid hormone levels is indicated because of associated thyroiditis in 10% to 15% of patients. Type 2 DM usually has an insidious presentation and is suggested by obesity, acanthosis, hypertension, dyslipidemia, and strong family history of type 2 DM. Normal weight suggests very early type 1 DM or MODY.

1. Education: Education and reeducation by a certified diabetes educator should include information about alcohol use, use of contraception, and the importance of preconception counseling to decrease risk for pregnancy complications. (See Internet resources sites, at the end of this chapter, for help in identifying an educator.)
2. Meals, food, and nutrition: There is no standard ADA meal plan; rather, diet is adjusted for the individual to provide sufficient calories and nutrients to grow/maintain weight; limiting fat to 30% or less of total calories is encouraged. Weight reduction is important for those who are overweight, particularly if type 2. "Carbohydrate counting" is replacing the "exchange system" because it permits greater flexibility for the potential for adjusting the dose of short-acting and rapid-acting insulin before each meal based on the amount of carbohydrate consumed at each meal. In this system, 15 g of carbohydrate is equivalent to one carbohydrate. This is estimated from package labels that list the carbohydrate content per serving and standard servings of milk (1 cup), fruit, juice (1/2 cup), and starch/bread; vegetables or meat (about 1/3 carbohydrate per serving) may or may not be counted depending on the degree of glycemic control targeted.
3. Accessing glycemic control: The goal is to lower blood glucose (BG) level, and resultant Hb A1c to achieve maximum prevention of complications, taking into account patient safety and the ability to carry out the treatment regimen. Although normal levels of BG are the goal (70 to 120 mg/dL before meals and fasting), most patients (adult and adolescent) are not able to achieve consistently normal levels of BG and glycated hemoglobin. Any lowering of glycated hemoglobin...
will reduce the risks of complications.

a. Capillary BG testing: Testing is recommended before meals and bedtime snack—more frequent if “normal” BG levels are the objective. Testing at 2 to 3 a.m. is useful for evaluating nighttime hypoglycemia and fasting hyperglycemia (the dawn phenomenon). The recommended frequency of testing for type 2 DM is not well defined, but daily fasting BG (FBG) and a random premeal BG test should be sufficient until adequate control is achieved. Thereafter, the frequency may be decreased. Devices to measure capillary BG must demonstrate that 95% of the tests are within 10% to 15% of the true BG value. They are usually calibrated to plasma glucose, which is higher than whole BG (see the “Web Sites” section).

b. Glycated hemoglobin should be measured at each visit (generally quarterly) and the results discussed with the adolescent in relation to BG test results. Glycated hemoglobin values reflect the average BG over the previous 6 to 8 weeks, so BG records must also be examined to identify swings in BG that would not be evident in the percentage of glycated hemoglobin. Several different assays are available, each with its own reference (nondiabetic) range. It is preferable to use a single test and laboratory to avoid confusion. It has been suggested that all glycated hemoglobin assays be standardized and reported in values equivalent to Hb A1c (which was used in the Diabetes Control and Complications Trial [DCCT]). Having the results of the glycated hemoglobin level available at the time of the visit has been shown to significantly improve control among adults. Discussing the results at the next visit or by telephone is less satisfactory. Based on the DCCT, Hb A1c values, the target Hb A1c level is 7%.

4. Insulin: Humanized insulins (DNA origin) have almost entirely replaced older animal preparations. Insulin analogues in which one or more amino acids have been substituted on the a chain or b chain afford more specific patterns of release. Rapid-acting preparations include lispro (Humalog) and aspart (NovoLog).

They have a more rapid onset and may be given during or immediately after meals, affording less immediate postprandial hyperglycemia and subsequent hypoglycemia. They may also be administered immediately before the meal, which is particularly useful if the meal contains a high fat content. An extended-acting analogue, glargine (Lantus), has a longer onset of 2 to 4 hours and provides a peakless duration of more than 24 hours; it should prove useful for intensified multiple daily injection (MDI) regimens. It cannot be mixed with other insulin preparations (Table 10.3).

TABLE 10.3. Characteristics of human insulin preparations

a. Insulin delivery devices: Many different devices are available, allowing adolescents to more easily manage their diabetes (see the “Internet Resources” section).

b. Insulin syringes: These are available in 0.3-, 0.5-, and 1.0-ml sizes with needles of 28, 29, or 30 gauge and 8.0- or 12.7-mm length. Adolescents usually prefer one type over another.

c. Insulin pens: These are devices that hold cartridges of 150 units of short-acting, rapid-acting, Neutral Protamine Hagedorn (NPH), or 70/30 (70% NPH/30% regular) insulin, or are disposable containing 150 or 300 units. These devices are about the size of a fountain pen and can be carried easily in a purse or shirt pocket. Disposable needles (29, 30, and 31 gauge, and 12.7 and 8 mm) must be prescribed. Pens and insulin cartridges from different manufacturers are usually interchangeable.

d. Continuous subcutaneous insulin infusion (CSII) (external insulin pumps): These permit ultimate flexibility in designing an insulin regimen, compensating for exercise, variations in carbohydrate intake including delayed meals and the dawn phenomenon. They are particularly useful for individuals who experience severe, recurrent nocturnal hypoglycemia. Multiple basal insulin rates can be preprogrammed. The patient must determine the amount of insulin to be delivered for each mealtime or corrective bolus and instruct the pump to deliver this amount at the correct time. Candidates for pumps are very motivated, test blood for BG four times daily (and often more frequently including from 2 to 3 a.m. when required), actively monitor carbohydrate intake, adjust insulin doses with each meal and snack, and have frequent contact with the diabetes team. Individuals with markedly elevated Hb A1c levels are generally poor candidates for pump therapy. Adolescents who wish to use CSII should be referred to a diabetes team experienced with CSII and adolescents. (See the “Web Sites” section.)

e. Inhaled insulin is not yet approved. It will consist of short-acting insulin only, probably making it difficult to “fine-tune” doses and most useful for type 2 DM.

5. Treatment of patients who require insulin: Insulin therapy is always necessary for type 1 DM, for patients with diabetes during pregnancy, and those in insulin-deficient states.

a. Insulin regimens: MDIs of insulin are preferred. The greater number of injections (three or more) offers more flexibility to accommodate varied intake, exercise, and meal times and has the potential for improved glycemic control. Adding prelunch short- or rapid-acting insulin to a standard twice-daily insulin regimen will decrease presupper hyperglycemia, with less risk of hypoglycemia associated with a very large prebreakfast dose of intermediate-acting insulin. With the exception of a bedtime snack to prevent nocturnal hypoglycemia, snack-time doses usually are no longer required with MDI—advantage for busy adolescents and those who wish to maintain a target weight.

b. Corrective doses: Adjusting the dose of short- or rapid-acting insulin administered before meals takes into account the fact that BG varies from day to day depending on carbohydrate intake at previous meals, the time that previous meal was administered, the amount of interval exercise, and the rate of insulin absorption from subcutaneous tissues. The corrective amount of insulin is added to the usual dose before that meal. It may be used to create what some have called a sliding scale of short- or rapid-acting insulin doses.

• One unit of rapid- or short-acting insulin will lower BG 25 to 100 mg/dL depending on the individual's sensitivity to insulin.

• The rule of 1,500/1,800 may be used to more closely estimate the initial “sensitivity factor” (the estimated point drop in BG per unit of short- or rapid-acting insulin used) for the corrective dose: The sensitivity factor = (1,500 for short-acting or 1,800 for rapid-acting insulin)/total daily dose (TDD) [total units of insulin per 24 hr] (ADA, 1998)

Corrective dose = (measured BG - target BG)/sensitivity factor

c. Multiple daily dosing: The most flexible MDI (short of external pump) provides a “basal” long-acting insulin and premeal rapid-acting “boluses” to cover carbohydrates at meals and snacks with “corrective” amount for premeal BG. Basal insulin is the amount of insulin required in the fasting state. Long-acting insulin preparations with less protein action for basal requirements and rapid-acting preparations for premeal boluses provide more flexibility.

• In general, one unit of short- or rapid-acting insulin will “cover” 8 to 15 g of carbohydrate.

• To estimate the grams of carbohydrate covered by one unit of short- or rapid-acting insulin use the rule of 450/500 = (450 for short-acting or 500 for rapid-acting insulin)/TDD. Note that if poorly controlled and TDD is 1.4 U/kg, reduce by 20%.

—Method 1

1. Basal insulin dose = 45%–50% of TDD on previous regimen. Administer ultralente in two equal doses approximately 12 hours apart or glargine insulin as single injection in the evening.

2. Pre-meal insulin doses
   a. Breakfast: 15%–25% of TDD as short- or rapid-acting insulin
   b. Lunch: 5% of TDD as short- or rapid-acting insulin
   c. Dinner: 15%–25% of TDD as short- or rapid-acting insulin
   d. Bedtime snack: 0%–10% as short- or rapid-acting insulin

3. Adjust doses after 5–7 days and apply a corrective dose for the short- or rapid-acting insulin.

   —Method 2: Most flexibility

1. Basal insulin dose = 45%–50% of TDD as in method 1.

2. Bolus insulin doses = (grams of carbohydrate eaten/gram of carbohydrate per unit of short- or rapid-acting insulin) × (BG - target BG)/sensitivity factor. (Note: Use the rule of 450/500 to estimate.)
The following is an example using method 2 to change from twice-daily insulin dosing to multiple dosing:

For a 15-year-old girl who weighs 50 kg and uses rapid-acting insulin: TDD = 50 units of insulin.

a. Basal insulin: 12 units with breakfast and bedtime snack (24 units equals about 50% of their prior TDD).

b. “Sensitivity factor”: 1,800/50 = 36-mg drop per unit of rapid-acting insulin.

c. Target BG = 120 mg/dL.

d. Carbohydrate covered by one unit of insulin from the rule of 450/1,000: 450 for rapid-acting insulin/TDD = 450/50 = 9 g of carbohydrate per unit of rapid-acting insulin.

e. Bolus insulin doses from previous description: For premeal BG of 250 mg/dL and 60 g of carbohydrate, bolus rapid-acting dose = 60 g of carbohydrate/9 = 250/120/36 = 10 units.

6. Treatment of type 2 DM and MODY: Treatment should be based on the known pathophysiology—insulin resistance, hepatic overproduction of glucose, and relative insulin deficiency. Although type 2 DM is a progressive disease that will eventually require exogenous insulin, modifications in diet and exercise are the mainstay of treatment.

a. Diet: Carbohydrates should be distributed throughout the day to include snacks. Limiting the amount of carbohydrate takes into account the inherently abnormal insulin secretory pattern. Weight loss will increase insulin sensitivity because it reduces visceral adipose tissue. The effect of carbohydrate restriction (as part of total caloric reduction) may be seen within 4 days, with a reduction in postprandial BG. The effects of weight loss may take months and will be reflected in lower FBG levels. Studies of obese adults with type 2 DM suggest that an FBG of less than 180 mg/dL after individuals have lost 2.3 kg has a 62% positive predictive value that diet therapy will be effective in achieving control; the positive predictive value is 79% after 4.5 kg has been lost (Watts et al., 1991).

b. Exercise will increase insulin sensitivity independent of weight loss. At least 20 to 30 minutes of anerobic activity at least three times per week is recommended. Vigorous walking is an acceptable introductory activity for the sedentary patient.

c. Oral hypoglycemic therapy: Failure to improve in FBG (HB A1c < 8%) in the face of substantial weight loss or after 3 months suggests that diet and exercise alone will be insufficient to achieve satisfactory control. Initiate oral hypoglycemic agent or insulin therapy. About 25% of adults will achieve an HB A1c < 8% on monotherapy, 50% will see a partial response, and 25% will fail to respond to a single oral agent. No oral agent should be used during pregnancy; insulin must be substituted and referral to a high-risk obstetrical program is indicated.

Overall hypoglycemic agents will generally be required at some point in the treatment of type 2 DM. Many agents are available. Each group targets different metabolic components—insulin secretory defect, elevated hepatic glucose output, and insulin resistance. Key points include the following: The response to oral agents is significant and can be associated with a rise in therapeutic activity, levels will fall, and then gradually fall to minimal therapeutic effect; half the maximal dose yields more than half the maximal effect (60%–80%), and side effects increase slowly at low doses and then more rapidly at higher doses.

- Biguanides: The first-line oral hypoglycemic agents for obese adolescents because they are not associated with weight gain. They lower FBG, by reducing hepatic glucose output, improve glycemic profiles, with a reduction in total LDL, LDL-C, and as well as an increase in HDL. The major side effects are mild GI symptoms that generally resolve; they may be minimized by slowly increasing the dose. Hypoglycemia is uncommon, and lactic acidosis, a potentially serious condition associated with the predecessor biguanide (phenformin), is extremely rare with the available agent in this class, metformin. Discontinue and ensure adequate hydration with contrast studies that may impair renal function.

- Sulfonylurea (SU) drugs and the related repaglinide enhance insulin resistance. Use is associated with weight gain, which tends to further increase insulin resistance. Potential interactions with sulfonamides, fluconazole, and ciprofloxacin may result in hypoglycemia. SU drugs generally may be given as a single morning dose. A related medication repaglinide also enhances insulin secretion but operates through a mechanism different from that of SU drugs; it must be administered before each meal.

- Glucosidase inhibitors delay the absorption of carbohydrate from the intestine, reducing the rise in BG levels after a meal. They are most useful when employed in conjunction with other hypoglycemic agents to assist in managing postprandial hyperglycemia. They are not associated with weight gain or hypoglycemia. They must be given before each meal, not to exceed three times per day. Slowly increasing the dose tends to decrease the common GI symptoms (e.g., cramps, abdominal pain, flatulence, bloating, and diarrhea).

- Thiazolidinediones (“insulin sensitizers”) increase insulin action in muscle, adipose tissue, and probably in the liver. Troglitazone, the first available agent in this class, was withdrawn by the Food and Drug Administration in March 2000 because of the drug’s association with fatal liver toxicity. Newer thiazolidinediones rosiglitazone and pioglitazone are thought to be safer, but their use is not recommended in children and adolescents until further information is available. These agents do not represent the initial pharmacotherapeutic agent for type 2 DM.

- Consider combining oral agents or adding insulin when a single medication has not achieved the desired degree of control. Combining agents takes advantage of their additive effects because each operates through different physiological mechanisms, generally is associated with fewer side effects, and has a lower cost (if doses are lower). When combining oral agents, increase the dose of the first drug until maximum dose has been reached or side effects limit further increases. Add the second medication at the lowest dose and increase slowly, watching for hypoglycemia. If target levels of BG have not been achieved in 4 to 6 months, the addition of insulin is indicated. Some clinicians would choose to add insulin instead of a second oral agent.

- Insulin may be used as a single nighttime dose (to lower FBG) or in divided doses as with type 1 DM. Adding a single nighttime dose to an oral regimen is advantageous because lower doses of insulin and the oral agent may be used. Begin with a single dose of intermediate-acting insulin at the bedtime snack or long-acting insulin at dinner. An initial dose of 5 to 10 units is safe. Increase the dose until the desired level of FBG is achieved. Adolescents who have a large carbohydrate intake at dinner may benefit from the addition of regular or rapid-acting insulin with this meal; this dose of short-acting insulin is adjusted based on bedtime BG levels.

COMPLICATIONS, ASSOCIATED CONDITIONS, AND FOLLOW-UP CARE

1. Autoimmune disorders (type 1 DM only): Autoimmune thyroiditis is present in 10% to 15% of patients. Initial antithyroid antibody levels are not predictive of subsequent involvement. Presentation is usually asymptomatic; therefore, annual thyroid studies to detect hypothyroidism are recommended; thyroid-stimulating hormone is generally sufficient. Other autoimmune diseases affecting the adrenal, pituitary, ovary, or parathyroid are uncommon.

2. Microvascular complications: Microvascular complications are directly correlated to the level of glycemic control and are exacerbated by hypertension.

a. Retinopathy: Yearly dilated funduscopic examination

b. Nephropathy: Annual screening for urinary albumin. The level of random urinary microalbumin: creatinine ratio is highly correlated with timed specimens.

- Symptomatic autonomic neuropathy (heart rate invariability and/or postural hypotension) and gastroparesis (postprandial nausea or vomiting, postprandial distention) is uncommon. Effective but more expensive and may be considered as an alternative treatment (Backonja, 1999; Morello et al., 1999). Gabapentin is effective but more expensive and may be considered as an alternative treatment (Backonja, 1999; Morello et al., 1999).

- Painful distal neuropathy is also uncommon in this age group. Desipramine and amitriptyline are equally effective treatments (Max et al., 1992). Gabapentin is effective but more expensive and may be considered as an alternative treatment (Backonja, 1999; Morello et al., 1999).

- Symptomatic autonomic neuropathy (heart rate invariability and/or postural hypotension) and gastroparesis (postprandial nausea or vomiting, postprandial distention) may impair renal function. These agents do not represent the initial pharmacotherapeutic agent for type 2 DM.

- The following is an example using method 2 to change from twice-daily insulin dosing to multiple dosing:

- For a 15-year-old girl who weighs 50 kg and uses rapid-acting insulin: TDD = 50 units of insulin.

- The following is an example using method 2 to change from twice-daily insulin dosing to multiple dosing:

- For a 15-year-old girl who weighs 50 kg and uses rapid-acting insulin: TDD = 50 units of insulin.

- The following is an example using method 2 to change from twice-daily insulin dosing to multiple dosing:

- For a 15-year-old girl who weighs 50 kg and uses rapid-acting insulin: TDD = 50 units of insulin.
6. Gluten sensitivity: Gluten sensitivity is estimated to be present in 5% of individuals with type 1 DM. The benefit of universal screening of all individuals with type 1 DM is not established. Evaluate with antiendomysial and antigliadin antibodies if symptoms are suggestive of malabsorption or unexplained postprandial hypoglycemia.

7. Eating disorders: Eating disorders may complicate treatment of diabetes. Disordered eating (including underdosing or omission of insulin) may be present in up to 30% of women with type 1 DM, but the prevalence of Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition eating disorders is probably not higher than expected. The coexistence of eating disorders and diabetes is associated with noncompliance with treatment for diabetes and an increased risk of retinopathy (Rydall et al., 1997). Suspect when the Hb A1c is high and weight loss or excess concerns about weight are present.

8. Hypoglycemia: Severe hypoglycemia is common with intensified regimens targeting euglycemia. An episode of severe hypoglycemia causes more hypoglycemia because it is associated with a reduced magnitude of autonomic and neuroglycopenic symptoms, counterregulatory hormone responses, and cognitive dysfunction during subsequent hypoglycemia. These return to normal with strict avoidance of hypoglycemia.

9. Alcohol use: As with healthy adult populations, moderate alcohol use among individuals with older-onset diabetes (older than 30 years) has been shown to reduce the risk of coronary heart disease-related death (Valmadrid et al., 2000). Alcohol use is not recommended for minor adolescents including those with diabetes. For those who do drink, they must be educated about its potential effects on levels of BG. Alcohol tends to inhibit gluconeogenesis and interferes with the counterregulatory responses to insulin-induced hypoglycemia. It also impairs judgment. Severe hypoglycemia may result many hours after as little as 2 ounces of alcohol is consumed, particularly on an empty stomach. Anticipatory guidance should include moderation, eating additional carbohydrates at the time of alcohol consumption, and informing others that they have diabetes.

SPECIAL CONSIDERATIONS FOR COMPLIANCE WITH ADOLESCENTS

Managing teens with DM can be difficult, particularly for those in poor control. Some suggestions include the following:

1. Identify the reason for poor control and develop a strategy for remediation. Serious psychopathology (including eating disorders) and recurrent diabetic ketoacidosis (DKA) are indications for referral.

2. Identify one reasonable and measurable target behavior for action (number of BG tests, recording carbohydrates at a specific meal, self-insulin adjustment based on BG or carbohydrate intake).

3. Identify short-term reinforcers relevant to the adolescent—fewer symptoms (hypoglycemia or nocturia), improved physical performance, more flexibility in timing and content of meals, rewards from parents, and greater independence.

4. Establish realistic time frame for accomplishment based on behavior and goal (e.g., average FBG will be 20% lower over the next 2 weeks). Remember glycated hemoglobin levels reflect average blood sugar level over 6–8 weeks. Even a 1% reduction (12%–11%) over 8 weeks is significant.

5. Provide frequent feedback: see the adolescent more frequently.

6. Examine the extent of parental support and monitoring; more support and monitoring by parents of midadolescents is associated with increased BG testing and lower Hb A1c (Anderson et al., 1997).


8. Consider referral to a diabetes specialist if control has not improved within 6 months.

9. For life-threatening, recurrent DKA or long-standing very poor control (Hb A1c >12%) refractory to other measures, consider the use of a single daily dose of insulin, monitored by an adult to prevent DKA.
   a. Regular 30% TDD, lente 60% TDD, ultralente 10% TDD may require two injections if total volume exceeds 1 mL.
   b. Expect subsequent Hb A1c 10%.

WEB SITES

Professional

http://www.diabetes.org/, Web site of the ADA.
http://www.aacp.org/, Association of Certified Diabetes Educators.
http://www.anse.com/, American Association of Clinical Endocrinologists and the American College of Endocrinology. Manufacturers of insulin and diabetes supplies have Web sites that provide useful information about products.

Consumers

http://www.lcoryd.com/, Taking Control of Your Diabetes.
http://www.childrenwithdiabetes.com/d_06_150.htm, Software to download GB meter results to computer.
http://www.childrenwithdiabetes.com/d_06_000.htm, BG meters.
http://www.getnet.com/idaa/, Web site of the ADA.
http://www.jdf.org/, Juvenile Diabetes Foundation.
http://www.tcoyd.com/, Taking Control of Your Diabetes.
http://www.childrenwithdiabetes.com/d_06_150.htm, Software to download GB meter results to computer.
http://www.childrenwithdiabetes.com/d_06_000.htm, BG meters.
http://www.getnet.com/idaa/, Web site of the ADA.
http://www.jdf.org/, Juvenile Diabetes Foundation.

REFERENCES AND ADDITIONAL READINGS


Naporn GT, Kwok WW. Molecular basis for HLA-DQ associations with IDDM. Diabetes 1998;47:1177.


DEFINITION

Gynecomastia refers to a benign increase in glandular and stromal tissue associated with puberty. Gynecomastia must be differentiated from a lipoma and fatty tissue of obese patients.

EPIDEMOLOGY

1. Gynecomastia occurs in 19.6% of 10.5-year-old males, with a peak prevalence of 64% at age 14 years and falling prevalence thereafter. Mean age at onset is 13 years 2 months. Approximately 4% of adolescents will have severe gynecomastia (more than 4.0 cm in diameter or about equal to midpubertal female breast) that persists into adulthood. However, one study found that 17% of males 19 years and younger and 33% of 20- to 24-year-olds had palpable breast tissue at least 2 cm in diameter. Gynecomastia is also common during the neonatal period (60% to 90% of newborn infants) and between the ages of 50 and 80 years.

2. Relationship with puberty: Best correlated with biological events of puberty. Genital stage at onset of gynecomastia is as follows:
   - Genital stage 1: 20%
   - Genital stage 2: 50%
   - Genital stage 3: 20%
   - Genital stage 4: 10%

ETIOLOGY

Breast tissue of males and females is similar at birth and responds similarly to estrogens during childhood. At puberty, the breast tissue of boys demonstrates both ductal and periductal mesenchymal tissue proliferation. This tissue involutes and atrophies as testicular androgens increase to adult levels. In pubertal females, under the influence of both increasing estrogen and progesterone, breast tissue continues to undergo ductal enlargement, branching, and acini development. The hormonal levels determine the extent of breast tissue development. Because breast tissue development and androgens antagonize this effect, an increase in estrogen relative to testosterone can lead to gynecomastia. Because estradiol levels increase but threefold during puberty, whereas testosterone levels increase 30-fold, peak estradiol levels may be reached before adult testosterone levels are achieved. Aromatase (estrogen synthetase) plays a key role in estrogen production among men. The adult male's testes produce only 15% of circulating estradiol and less than 5% of estrone. The remainder is produced in extraglandular sites through aromatization. Hence, significant increases in extraglandular tissue (such as in obesity) result in significant elevations of circulating estrogens.

Gynecomastia has been considered to result from a relative imbalance between estrogen activity and androgen activity at the breast tissue level. Alterations in the ratio of estrogens to androgens have been demonstrated in individuals with gynecomastia related to Klinefelter syndrome, thyrotoxicosis, cirmiosis, medications, adrenal and testicular neoplasm, primary hypogonadism, and malnutrition. In other patients, serum hormone levels are within the reference range and there is experimental evidence to suggest that in these patients, altered hormone sensitivity of breast tissue may be responsible for this disorder.

Mechanisms to account for an increase in estrogen activity or a decrease in androgen activity include the following:

1. Increase in serum estrogen concentrations
   - Increase in estradiol secretion from testes (e.g., Leydig cell tumors or adrenal tumors)
   - Excessive extraglandular conversion of androgens to estrogens by aromatase
     - Overproduction of adrenal precursors; increased androstenedione converted by aromatase into estrone
     - Overproduction of testicular precursors; increased conversion of testosterone to estradiol
     - Enhancement of extraglandular aromatase activity
       - Disease states (hyperthyroidism, liver disease)
       - Increased body fat (obesity, aging)
       - Drugs (e.g., spironolactone)
       - Idiopathic change (caused by persistence of a fetal form of aromatase)
   - Increase in bioavailability of estrogens: Decrease in estrogens bound to sex hormone-binding globulin (SHBG) (e.g., use of spironolactone and ketonozal)
   - Exogenous intake of estrogens: Oral intake of estrogens or topical use of estrogen creams

2. Decrease in serum androgen concentrations
   - Impairment of testicular production in Leydig cells
     - Primary hypogonadism (e.g., anorchia, Klinefelter syndrome)
     - Secondary hypogonadism through disorders of hypothalamus or pituitary
     - Congenital enzyme defects
     - Drug-induced inhibition of enzymes needed in testosterone synthesis (e.g., spironolactone or ketonozal)
     - Chronic stimulation of Leydig cells by high human chorionic gonadotropin (hCG) levels (e.g., hCG-secreting tumors) can lead to a reduction in testosterone biosynthesis
     - Hyperestrogenic states leading to suppression of luteinizing hormone (LH) and testosterone secretion
   - Increased hepatic clearance of androgens
   - Decrease in SHBG, leading to a decrease in free testosterone (e.g., liver disease and hyperestrogenic states)

3. Alterations of estrogen and androgen receptors
   - Androgen-receptor deficiency states (e.g., androgen insensitivity syndromes)
   - Drug interference with androgen receptors (e.g., spironolactone, flutamide, and cimetidine)
   - Drugs that can mimic estrogens and stimulate estrogen-receptor sites (e.g., digoxin and phytoestrogens in some marijuana preparations)

Sher et al. (1998) reviewed the etiology of gynecomastia in 60 male subjects with significant gynecomastia around puberty and more than 4 cm in diameter. An endocrine disorder was found in 7 of 60, including Klinefelter syndrome. 46,XX maleness, primary testicular failure, partial androgen insensitivity, fibrolamellar hepatocarcinoma, and increased aromatase activity. Of the remaining 53 subjects, 8 had an underlying medical problem, including 5 with neurological disorders. The 45 remaining subjects were considered to have significant idiopathic gynecomastia. Sher et al. (1998) also reported that these male teens tended to be both taller and heavier than average.
CLINICAL MANIFESTATIONS

1. Forms
   a. Type I: One or more subareolar nodules, freely movable
   b. Type II: Breast nodules beneath areola but also extending beyond the areolar perimeter
   c. Type III: Resembles breast development of sexual maturity rating 3 (SMR 3) in girls

2. Bilaterality: Occurs in 77%–95% of cases, with concurrent or sequential involvement of both breasts

3. Physical examination
   a. Types I and II gynecomastia: Associated with a firm, rubbery consistency of the breasts (whereas type III is associated with a consistency similar to that of female breasts)
   b. Types I and II: Usually associated with tenderness on palpation or when clothing touches the breast

DIFFERENTIAL DIAGNOSIS

(Adapted from Braunstein, 1993a.)

1. Physiological: Pubertal gynecomastia
2. Drug exposure (asterisks [*] indicate that a strong relationship has been established; other drugs have been implicated through epidemiological studies, individual cases, or small groups of patients):
   a. Hormones: Estrogens,* testosterone,* anabolic steroids,* chorionic gonadotropin*
   b. Psychoactive agents: Phenoxyzines, diazepam, haloperidol, tricyclic antidepressants
   c. Cardiovascular drugs: Digoxin,* verapamil, captopril, methyldopa, nifedipine, enalapril, reserpine, minoxidil
   d. Antiandrogens or inhibitors of androgen synthesis: Cyproterone,* spironolactone,* flutamide*
   e. Antibiotics: Isoniazid, metronidazole, ketoconazole*
   f. Antilulcer medications: Cimetidine,* ranitidine, omeprazole
   g. Cancer chemotherapeutics, particularly alkylating agents*
   h. Drugs of abuse: Marijuana, alcohol, amphetamines, heroin, methadone
   i. Other: Phenyltoin, penicillamine, theophylline, metoclopramide, saquinavir, indinavir (and other antiretroviral drugs)
3. Pathological
   a. Renal failure and dialysis
   b. Recovery from malnutrition
   c. Primary gonadal failure: Including Klinefelter syndrome and Reifenstein syndrome
   d. Secondary hypogonadism
   e. Hyperthyroidism
   f. Liver disease, including cirrhosis and hepatitis
   g. Neoplasms:
      • Testicular: Germ cell, Leydig cell, or Sertoli cell
      • Adrenal adenomas and carcinoma
      • Ectopic hCG production (particularly lung, liver, and kidney cancer)
   h. Enzyme defects in testosterone biosynthesis
   i. Androgen insensitivity syndromes
   j. Excessive extraglandular aromatase activity
4. Pseudogynecomastia: Caused by adipose tissue in obese male subjects or prominence of muscular adolescent boys
5. Breast mass because of cancer, dermoid cyst, lipoma, hematoma, or neurofibroma

DIAGNOSIS

1. History: Careful history is necessary to rule out drugs and systemic illness.
2. Physical examination
   a. Findings suggestive of hypogonadism, hyperthyroidism, or hypothyroidism
   b. Testicular mass or atrophy
   c. Findings suggestive of liver disease
   d. Vertical and horizontal diameters of breast tissue (breast units = vertical diameter of breast × horizontal diameter)
   e. Differentiation of gynecomastia from pseudogynecomastia caused by excessive adipose tissue
      • Place the teen in the supine position, with his hands behind his head; the examiner then places the thumb and forefinger at opposing margins of the breast.
      • In gynecomastia, as the fingers are brought together, rubbery or firm breast tissue can be felt as a freely movable, and occasionally tender, disk of tissue concentric to the areola.
      • In pseudogynecomastia, no discrete mass is felt.
      • In other conditions, such as a lipoma or dermoid cyst, the mass is usually eccentric to the areola.

In healthy pubertal males with a unilateral or bilateral, rubbery or firm mass, symmetrically subareolar, with no history of the use of drugs associated with gynecomastia and with no renal, liver, or thyroid disease, the diagnosis is probable pubertal gynecomastia. No further tests are necessary in these teens. If associated drugs have been used, they should be discontinued and the teen reexamined in 1 month. At that time, breast tenderness, if present, should decrease and breast size may decrease.

If pubertal gynecomastia and drug, hepatic, and renal causes are ruled out, then a further endocrine diagnostic study is appropriate. The practitioner should order measurements of hCG, LH, serum testosterone, and estradiol. These tests will help in differentiating the cause of nonpubertal gynecomastia.

FINDINGS AND IMPLICATIONS OF SERUM hCG, LH, TESTOSTERONE, AND ESTRADIOL

1. Elevated hCG concentration: Perform testicular ultrasonography
   a. Mass found: Testicular germ cell tumor
   b. Normal sonogram: Extranodal germ cell tumor or hCG-secreting neoplasm likely; chest film and abdominal computed tomography (CT) indicated

2. Decreased testosterone concentration
   a. Elevated LH concentration: Primary hypogonadism, including Klinefelter syndrome, and testicular atrophy caused by mumps orchitis
   b. Normal or low LH concentration: Measure prolactin; magnetic resonance imaging (MRI) of hypothalamic-pituitary area
      • Elevated prolactin level: Probably prolactin-secreting pituitary tumor
      • Normal prolactin level: Secondary hypogonadism

3. Elevated testosterone and elevated LH concentrations: Measure thyroid-stimulating hormone (TSH) concentrations
   a. Elevated T₄ and low TSH concentrations: Hyperthyroidism (elevated testosterone is from the increase of SHBG, leading to an increase in total testosterone; the increase in LH with hyperthyroidism is less clear)
   b. Normal T₄ and TSH concentrations: Androgen resistance

4. Elevated estradiol and low or normal LH concentrations: Perform testicular ultrasonography
   a. Mass on sonogram: Leydig cell or Sertoli cell tumor
   b. Normal: Perform adren al CT or MRI
      • Mass found: Adrenal neoplasm
      • No mass: Increased extraglandular aromatase activity

5. Normal concentrations of hCG, LH, testosterone, and estradiol: Idiopathic gynecomastia
THERAPY

1. Rule out other causes aside from pubertal gynecomastia. If other causes are diagnosed, they should be treated. If drugs are implicated, they should be discontinued, if possible.

2. Pubertal gynecomastia: In most individuals with pubertal gynecomastia, particularly with mild to moderate degrees, only reassurance and explanation of the process are needed. In most cases, the condition will improve or resolve within 6–12 months.

3. Medical intervention
   a. Several drugs have been tried to reduce gynecomastia, including danazol, tamoxifen, clomiphene, dihydrotestosterone, and testosterone. None of these is approved by the U.S. Food and Drug Administration in the treatment of gynecomastia, and studies of the use of these medications in adolescent patients are few. Dihydrotestosterone can lead to a reduction in breast volume in 75% of individuals, with 25% having a complete response (Kuhn et al., 1983). However, this medication is not readily available. Danazol has some limited effectiveness but is associated with significant side effects and would not be recommended in the treatment of adolescents. Tamoxifen has been studied in two randomized, double-blind studies involving 16 patients. At a dose of 10 mg twice a day, the drug has led to a statistically significant reduction in breast size and pain without side effects. Ting et al. (2000) compared the efficacy of tamoxifen (23 patients) with that of danazol (20 patients) in the treatment of a wide age range of 23 males with idiopathic gynecomastia (mean age, 39.5; range 13 to 82). In this study, either tamoxifen (20 mg/day) or danazol (400 mg/day) was offered and continued until a constant response was obtained. Complete resolution of the gynecomastia occurred in 18 patients (78.2%) treated with tamoxifen but only 6 patients (40%) in the danazol group. Five patients, all from the tamoxifen group, developed recurrence of breast mass. It should be remembered that this study included a wide range of patients and it is not clear whether tamoxifen is completely safe or effective in teens. More research is needed regarding the use of tamoxifen for pubertal gynecomastia. Testolactone, an aromatase inhibitor, has also been found in an uncontrolled study to decrease pubertal gynecomastia without side effects.
   b. Medical therapy should be reserved for those individuals who have more than mild to moderate gynecomastia and who are significantly concerned about the condition. Tamoxifen could be used at an oral dosage of 10 mg twice a day for 3 months. This should lead to a decrease in tenderness and pain, followed by a reduction in the size of breast tissue.

4. Surgical intervention: In adolescents with moderate to severe gynecomastia associated with psychological sequelae, surgical excision is recommended.

PROGNOSIS

Pubertal gynecomastia usually resolves in 12 to 18 months. In 27% of affected adolescents, the condition lasts for more than 1 year, and in 7.7% more than 2 years. A small percentage of cases may persist into adulthood. There has been no proven relationship between gynecomastia and the development of breast cancer in male subjects.

WEB SITES

For Teenagers and Parents

http://www.my.webmd.com/content/asset/adam_symptoms_gynecomastia. Web MD site with information about gynecomastia.


For Health Professionals


REFERENCES AND ADDITIONAL READINGS


Braunstein GD, Aromatase and gynecomastia. Endocrine Related Cancer 1999;6:315


Cardiac Risk Factors and Hyperlipidemia

Marc S. Jacobson, Michael R. Kohn, and Lawrence S. Neinstein

### Cardiac Risk Factors

<table>
<thead>
<tr>
<th>Nonintervenable</th>
<th>Intervenable</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>Smoking*</td>
</tr>
<tr>
<td>Cigarette Smoking</td>
<td>Hypertension:* Systolic or diastolic blood pressure (BP) above the 95th percentile</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>Diabetic mellitus*</td>
</tr>
<tr>
<td>Obese</td>
<td>Diet high in saturated fats and cholesterol, with total fat intake accounting for &gt;30% of daily caloric intake</td>
</tr>
<tr>
<td>Lipid Physiology</td>
<td>Low-density lipoprotein (LDL) cholesterol (LDL-C): &gt;130 mg/dL. For persons older than 20 years see the &quot;Screening in Young Adults&quot; section for new guidelines by the Adult Treatment Panel III (ATP III)</td>
</tr>
<tr>
<td>Lipid Pathophysiology</td>
<td>Triglycerides:* &gt;150 mg/dL</td>
</tr>
<tr>
<td>Classification of Hyperlipidemias</td>
<td>Ratio of serum very-low-density lipoprotein (VLDL) cholesterol to triglycerides of &gt;0.3</td>
</tr>
<tr>
<td>Lipid Screening and Management</td>
<td>Obesity:* &gt;30% above expected weight, or body mass index (BMI) above the 95th percentile for age</td>
</tr>
<tr>
<td>History</td>
<td>Insulin resistance with hyperinsulinemia</td>
</tr>
<tr>
<td>Physical Examination</td>
<td>Homocystinemia (&gt;10 nmol/L)</td>
</tr>
<tr>
<td>Screening in Adolescents</td>
<td>Serum lipoprotein Lp(a) concentration</td>
</tr>
<tr>
<td>Screening in Young Adults</td>
<td>High serum C-reactive protein (CRP) concentrations</td>
</tr>
</tbody>
</table>

In general, individuals are considered at low risk for atherosclerotic disease if they have zero or one cardiovascular risk factor, moderate risk with more than one risk factor other than diabetes mellitus, and high risk with a presence of diabetes or any evidence of atherosclerosis.

### Risk Factor Intervention

Practitioners must temper aggressive interventions with the knowledge that the efficacy of interventions in decreasing the rate of coronary artery disease (CAD) has been evaluated only in adults. Thus, the effect of such interventions in children and adolescents is more speculative. However, because early atherosclerotic lesions have already begun in most adolescents and are worse in those with risk factors, it seems prudent to recommend a heart-healthy lifestyle to reduce atherosclerosis and CAD. This approach includes the following:

1. Promoting regular physical activity
2. Counseling on the importance of maintaining an ideal body weight
3. Advocating smoking prevention or cessation
4. Monitoring BP and treating when persistently elevated
5. Recommending a heart-healthy diet—<30% of the total calories as fat and a diet low in saturated fat, for all individuals
6. Ensuring daily intake of 400µg of folic acid whether through diet or supplementation

**Hypertension**

The distribution of BP in children and adolescents was described by the Second Task Force on Blood Pressure Control. Hypertension was classified, by age, as being “significant” or “severe” (see Table 13.1 in Chapter 13). For adolescents with “significant” hypertension (i.e., diastolic BP higher than 86 mm Hg at age 13 to 15 years or higher than 92 mm Hg at age 16 to 18 years) and no other risk factors, interventions should include a low-salt diet, weight reduction, and relaxation or other biofeedback techniques. Intervention for hypertension is covered in more detail in Chapter 13.

**Cigarette Smoking**

Cigarette smoke is an atherogenic risk factor due to alterations in lipids and fibrinogen. Smoking is associated with more cardiovascular deaths than cancer deaths. Most cigarette smoking begins early in adolescence, suggesting that this is an important period for prevention. Effective education programs must be developed and implemented at the national level, at the local school level, and in the practitioner’s office. Every preteen and teen should be questioned regarding his or her smoking habits, and specific interventions should be targeted to prevent or extinguish smoking behavior.

**Dyslipidemia**

The primary therapy for hyperlipidemia during adolescence is modification of the diet, including a diet that is low in fat, saturated fats, and cholesterol. Regular physical activity is also indicated. Medications should be reserved for those teenagers with markedly high concentrations of lipids unresponsive to dietary therapy and with an extensive family history (see the section on hyperlipidemia).

**Obesity**

The best therapy for obesity is to prevent it. This requires curbing obesity early and particularly during the adolescent growth spurt. Without intervention, eight of ten obese 12-year-old children will become obese adults. Exercise and other physical activities, combined with dietary modifications, are the best preventive measures, and some studies are showing positive results in relation to changes in BMI, as well as metabolic changes. In particular, insulin resistance is decreased, as is BP, and there are positive changes in the lipid profile, all of which mitigate against the development of atherosclerosis.

**LIPID PHYSIOLOGY**

Cholesterol and triglycerides are the major blood lipids. Cholesterol is a key constituent of cell membranes and a precursor of bile acids and steroid hormones. Cholesterol circulates in the bloodstream in spherical particles called lipoproteins containing both lipids and proteins called apolipoproteins. These particles consist of a core of triglycerides, cholesterol, and cholesterol esters, in varying amounts, surrounded by an outer shell of cholesterol and phospholipids. The apolipoproteins are embedded in the outer lipid layers (Fig. 12.1).


1. Classification of lipoproteins: Five major classes of lipoproteins act as transport systems for cholesterol and triglycerides. They differ in physical and chemical characteristics and function, as well as in amounts of cholesterol, triglyceride, phospholipid, and protein. The lipoproteins can be separated by ultracentrifugation or electrophoresis, on the basis of differences in densities and surface properties (the characteristics of these particles and their functions are summarized). Ultracentrifugation yields chylomicrons, VLDL, intermediate-density lipoproteins (IDL), LDLs, and HDLs. Motility on electrophoresis yields the patterns commonly described as alpha-1, beta, pre-beta, and broad beta (motility between beta and pre-beta). However, this older designation, based on electrophoretic mobility, is no longer frequently used.

   a. Chylomicrons: Largest and least dense of the lipoproteins; composed mainly of triglycerides with a lipid/protein ratio of 99:1. Chylomicrons carry dietary fat as triglycerides from the intestine to the periphery of the body to be used for energy or deposition in fat cells.

   b. VLDL: Secreted by the liver and the second major carrier of triglycerides. It is composed largely of triglycerides and contains <10% of the total serum cholesterol concentration.

   c. LDL: Major carrier of cholesterol, containing 60%–70% of the total serum cholesterol concentration, and is an important factor in atherogenesis. (HDL is the second most important carrier of cholesterol.)

   d. HDL: Usually contains 20%–30% of the total serum cholesterol concentration. It is responsible for the transport of cholesterol back to triglyceride-containing particles for removal in the bile. The calculation of the proportion of LDL is made from the following formula:

   \[
   \text{Total cholesterol} = \text{LDL} + \text{HDL} + \text{VLDL}
   \]

   HDL is measured directly, and VLDL is estimated by dividing the fasting triglyceride concentration by five (true so long as the triglyceride concentration is less than 400 mg/dL). Therefore,

   \[
   \text{LDL} = \text{total cholesterol} - \text{HDL} - (\text{triglycerides}/5)
   \]

2. Apolipoproteins: Numerous apolipoproteins, including A-I, A-II, A-IV, B-48, B-100, C-I, C-II, C-III, D, E-II, E-IV, F, G, and H, are associated with lipoproteins. Each lipoprotein has a characteristic apolipoprotein profile. Lipoproteins may contain several apolipoproteins. These apolipoproteins serve as cofactors for enzymes involved in lipoprotein metabolism, they help in the binding of lipoproteins to cellular receptors, and they facilitate lipid transfer between lipoproteins. Apolipoprotein B-100 is an important component of VLDL and is the only apolipoprotein in LDL-C. Uptake of LDL by cells is dependent on its binding to the LDL receptor, which is regulated by apoB-100. Abnormalities in both quality and quantity of these proteins, even in the absence of an elevated cholesterol concentration, may contribute to atherosclerosis.
Exogenous: Chylomicrons are formed in the gut wall after absorption of dietary fat. They are secreted into the lymph and enter the bloodstream, where the fatty acids are stored in adipose tissue, or are used in skeletal muscle and myocardium. Eventually they release almost all of their diet-derived triglyceride. This reaction is catalyzed by lipoprotein lipase. The chylomicron remnants are rapidly absorbed by the liver by specific receptors for these particles. In liver cells, triglycerides are degraded to free fatty acids, which is excreted into bile.

Endogenous: The endogenous transport system includes VLDL, LDL, and HDL. Excess calories from carbohydrates and fatty acids are metabolized in the liver into triglycerides. The lipoproteins carrying these triglycerides are primarily VLDL, which moves to adipose tissue, where triglycerides are extracted; the result is the formation of LDL and HDL. The LDL particles are rapidly removed from circulation by LDL receptors in the liver.

- LDL transports cholesterol to peripheral tissues. Besides the lipid component, LDL particles contain a single apoB-100 molecule, the protein that binds to LDL receptors. After binding to LDL cell surface receptors, the LDL particles deliver cholesterol for synthesis of cell membranes in all cells; for steroid hormone production in the gonads, ovary, and testes; and for bile acid in the liver. The LDL-C found in macrophages and smooth muscle cells of atherosclerotic lesions enters by additional mechanisms. This LDL-C is modified by oxidation intravascularly and is taken up in lesions by oxLDL receptors and scavenger receptors. This process may provide alternative pathways for therapeutic intervention.

- HDL is secreted from the liver or intestine in a lipid-poor form or is made de novo in the plasma. As it matures, HDL accumulates cholesterol from tissues, including blood vessel walls, and thus has a major role in removing excess cholesterol and delivering it to the liver by means of the triglyceride-rich lipoproteins and cholesterol ester transfer protein.

LIPID PATHOPHYSIOLOGY

1. Epidemiological evidence
   a. In populations throughout the world, there is a direct correlation between serum cholesterol levels and CAD rates. Individuals moving to a country with higher mean cholesterol levels gradually acquire the dietary habits, cholesterol levels, and CAD rates of their new country. In societies in which the total cholesterol concentration is less than 150 mg/dL, CAD is rare.
   b. Bogalusa Heart Study (Bereson, 1986; Freedman et al., 1999): Observations from this study clearly show that the major risk factors of adult heart disease begin in childhood. Documented atherosclerotic changes (e.g., fatty streak) were seen to occur by age 5 to 8 years. This group noted the significance of environmental factors for hyperlipidemia, hypertension, and obesity. They also showed that the level of risk factors in childhood is different from that in the adult years and that levels change with growth phase. Most importantly, they documented the correlation of risk factor levels with severity of lesions in autopsy material from adolescents who died of unrelated causes and who previously had been prospectively assessed (Berenson et al., 1998).

2. Genetic evidence
   a. Familial hypercholesterolemia: Individuals who lack LDL cell surface receptor activity may have very high cholesterol levels. Severe atherosclerosis may develop in the first two decades of life. These individuals are referred to as having familial hypercholesterolemia. Those heterozygous for the LDL receptor defect account for 15% of premature CAD cases. Clinical manifestations such as xanthomas and other signs of cutaneous lipid deposition are generally seen in the fourth decade of life in heterozygotes and during adolescence in homozygotes.
   b. Familial combined hyperlipidemia (FCHL): Autosomal-dominant syndrome that affects approximately 1% to 2% of the population. Most, if not all, patients with this condition have elevated levels of LDL apoB. Abnormal metabolism of VLDL and partial lipoprotein lipase deficiency have also been described in association with this syndrome. Individuals with FCHL account for a significant proportion of early CAD cases.
   c. Apolipoprotein E (apoE): Three common alleles of apoE, at a single gene locus on chromosome 19, code for three isoforms of apoE: designated as apoE-II, apoE-III, and apoE-IV. These are distinguished in the laboratory by isoelectric focusing. Both homozygous and heterozygous genotypes have been found.

3. Animal models: Atherosclerosis develops in animals fed diets elevating their serum cholesterol concentrations. In other animal experiments, a change of diet and the use of lipoid-lowering drugs reduced elevated cholesterol concentrations and caused regression in atherosclerotic plaques.

4. Epidemiology: Pathobiological Determinants of Atherosclerosis in Youth (PDAY) study described the relationship between atherosclerosis in young men and serum lipoprotein cholesterol concentrations and smoking. A preliminary report demonstrated an association between commonly accepted risk factors (elevated LDL-C and low HDL-C concentrations and smoking) and the severity of atherosclerotic plaques in adolescents.

5. Interventional trials: More than a dozen randomized clinical trials in adults have examined the effects of lowering cholesterol concentrations on CAD. These trials support the conclusion that lowering total and LDL-C concentrations reduces the incidence of CAD events. The degree of benefits is greatest in individuals who have other associated risk factors, such as cigarette smoking, diabetes, and hypertension. Examples of the most significant studies include the following:
   a. Multiple Risk Factor Intervention Trial: This study demonstrated the benefit of lowering cholesterol in healthy adults with average total cholesterol but below-average HDL-C concentrations. The study reported a relative risk of 0.7 with a cholesterol concentration of 150 mg/dL, 1.0 with 200 mg/dL, 2.0 with 250 mg/dL, and 4.0 with 300 mg/dL.
   b. The Framingham Heart Study: In this study, the use of gemfibrozil lowered LDL-C concentration by 8% and increased HDL-C concentration by 10%. This led to a 34% decrease in the incidence of CAD.
   c. The Scandinavian Simvastatin Survival Study: This study demonstrated that daily use of simvastatin markedly reduces the risk of CAD in average-risk individuals who have cholesterol levels less than 240 mg/dL.
   d. West of Scotland Coronary Prevention Study: In a large cohort of middle-aged men with high cholesterol concentrations, the use of pravastatin significantly reduced the incidence of nonfatal myocardial infarction and cardiac death without increasing the risk of death from other causes (Shepherd et al., 1995).
   e. Aspirin: The French Framingham Heart Study showed a 10% increase in CAD for each 4-mg/dL decrease in HDL. In addition, low HDL-C levels have been correlated with an increased number of diseased coronary arteries. There also appears to be a higher rate of restenosis after angioplasty in individuals with low HDL-C levels.
   f. APOE genotype: Preliminary evidence suggests that apoE polymorphisms are associated with a lower risk of CAD.

6. Relationship of particular lipoproteins:
   a. LDL-C: Studies show a positive relationship between the level of cholesterol, particularly LDL, and the frequency of CAD. There appear to be several factors for this relationship.
   b. HDL-C: Population studies suggest an inverse relationship between HDL-C and CAD. An HDL-C level less than 30 mg/dL carries a significantly increased risk of CAD. The former is considered a better indicator of negative CAD risk than is total HDL. Exercise raises the level of carotid-protective HDL, whereas ethanol raises the level of HDL.
   c. Apolipoproteins: Preliminary evidence suggests that apolipoproteins A-I (apoA-I), A-II (apoA-II), and apoB may be better than LDL, HDL, and total cholesterol in predicting the risk of CAD. Elevated concentrations of apoA-I and apoA-II are associated with a lower risk, and an elevated apoB concentration is associated with a higher risk of CAD. Isotypes of apoE have also been implicated in cardiovascular risk, as noted previously. In addition, the measurement of apoE isoforms in predicting the risk of CAD. Elevated concentrations of apoA-I and apoA-II are associated with a lower risk, and an elevated apoB concentration is associated with a higher risk of CAD.
Ratios: The correlation between CAD and the LDL:HDL ratio has also been examined in adults. The risk increases sharply with ratios that exceed 3.0. A ratio of more than 5.0 carries a very high risk of CAD. Individuals with CAD average a ratio of more than 5.1, whereas newborn infants have an average ratio of 2.1. Another ratio is that of total cholesterol to HDL-C. A ratio of less than 4.5 denotes below-average risk, whereas the optimum ratio is 3.5:1. However, the clinical use of ratios is problematic because LDL and HDL represent independent risk factors and respond differently to different interventions. The American Heart Association (AHA) recommends that the absolute numbers for total blood cholesterol and HDL-C be used. The AHA suggests that these are more useful to the physician than the cholesterol ratio in determining the appropriate treatment for individuals. The ATP III assigns points to various levels of HDL-C as part of the equation that is used to determine LDL-C treatment goals for primary and secondary prevention, rather than focusing on ratios.

7. Other experimental work: Lipoprotein a (Lp(a)) is a very large lipoprotein composed of apoB-100 and cholesterol, similar to LDL. In addition, this lipoprotein has a large glycoprotein, homologous to plasminogen, attached through a disulfide bond. It has no known physiological function. Plasma levels appear to be genetically determined and associated with risk of cardiovascular disease and may also increase the risk of thrombotic complications through its interaction with plasminogen. Nicotinic acid has been shown to lower Lp(a) by up to 30% (Knopp, 1998).

CLASSIFICATION OF HYPERLIPOPROTEINEMIAS

Historically, patients with hyperlipidemia have been classified into five major groups according to plasma lipoprotein patterns (lipoprotein phenotyping). More recent classifications of hyperlipidemia either are extensions of the earlier models based on more specific data obtained from newer laboratory techniques (Table 12.1) or are based on recently described genetic and metabolic disorders (Table 12.2). The nomenclature remains cumbersome and there is still much overlap, particularly when attempts are made to reconcile these two systems. Previously well-described syndromes, such as familial hypercholesterolemia, have been shown to have a specific genotype and yet may vary in phenotype (i.e., types IIa and IIb). Moreover, type IIa and IIb patterns of hyperlipidemia are associated with another syndrome, FCHL. Finally, the lipoprotein phenotyping system fails to account for children and adolescents at risk of atherosclerosis as a result of hyperapoB-100/ apoA-I ratio may provide another assessment of cardiovascular risk.

d. Ratios: The correlation between CAD and the LDL:HDL ratio has also been examined in adults. The risk increases sharply with ratios that exceed 3.0. A ratio of more than 5.0 carries a very high risk of CAD. Individuals with CAD average a ratio of more than 5.1, whereas newborn infants have an average ratio of 2.1. Another ratio is that of total cholesterol to HDL-C. A ratio of less than 4.5 denotes below-average risk, whereas the optimum ratio is 3.5:1. However, the clinical use of ratios is problematic because LDL and HDL represent independent risk factors and respond differently to different interventions. The American Heart Association (AHA) recommends that the absolute numbers for total blood cholesterol and HDL-C be used. The AHA suggests that these are more useful to the physician than the cholesterol ratio in determining the appropriate treatment for individuals. The ATP III assigns points to various levels of HDL-C as part of the equation that is used to determine LDL-C treatment goals for primary and secondary prevention, rather than focusing on ratios.

7. Other experimental work: Lipoprotein a (Lp(a)) is a very large lipoprotein composed of apoB-100 and cholesterol, similar to LDL. In addition, this lipoprotein has a large glycoprotein, homologous to plasminogen, attached through a disulfide bond. It has no known physiological function. Plasma levels appear to be genetically determined and associated with risk of cardiovascular disease and may also increase the risk of thrombotic complications through its interaction with plasminogen. Nicotinic acid has been shown to lower Lp(a) by up to 30% (Knopp, 1998).

CLASSIFICATION OF HYPERLIPOPROTEINEMIAS

Historically, patients with hyperlipidemia have been classified into five major groups according to plasma lipoprotein patterns (lipoprotein phenotyping). More recent classifications of hyperlipidemia either are extensions of the earlier models based on more specific data obtained from newer laboratory techniques (Table 12.1) or are based on recently described genetic and metabolic disorders (Table 12.2). The nomenclature remains cumbersome and there is still much overlap, particularly when attempts are made to reconcile these two systems. Previously well-described syndromes, such as familial hypercholesterolemia, have been shown to have a specific genotype and yet may vary in phenotype (i.e., types IIa and IIb). Moreover, type IIa and IIb patterns of hyperlipidemia are associated with another syndrome, FCHL. Finally, the lipoprotein phenotyping system fails to account for children and adolescents at risk of atherosclerosis as a result of hyperapoB-100/ apoA-I ratio may provide another assessment of cardiovascular risk.

d. Ratios: The correlation between CAD and the LDL:HDL ratio has also been examined in adults. The risk increases sharply with ratios that exceed 3.0. A ratio of more than 5.0 carries a very high risk of CAD. Individuals with CAD average a ratio of more than 5.1, whereas newborn infants have an average ratio of 2.1. Another ratio is that of total cholesterol to HDL-C. A ratio of less than 4.5 denotes below-average risk, whereas the optimum ratio is 3.5:1. However, the clinical use of ratios is problematic because LDL and HDL represent independent risk factors and respond differently to different interventions. The American Heart Association (AHA) recommends that the absolute numbers for total blood cholesterol and HDL-C be used. The AHA suggests that these are more useful to the physician than the cholesterol ratio in determining the appropriate treatment for individuals. The ATP III assigns points to various levels of HDL-C as part of the equation that is used to determine LDL-C treatment goals for primary and secondary prevention, rather than focusing on ratios.

7. Other experimental work: Lipoprotein a (Lp(a)) is a very large lipoprotein composed of apoB-100 and cholesterol, similar to LDL. In addition, this lipoprotein has a large glycoprotein, homologous to plasminogen, attached through a disulfide bond. It has no known physiological function. Plasma levels appear to be genetically determined and associated with risk of cardiovascular disease and may also increase the risk of thrombotic complications through its interaction with plasminogen. Nicotinic acid has been shown to lower Lp(a) by up to 30% (Knopp, 1998).
2. Familial defective apoB-100: A mutation in the apoB gene results in decreased affinity of LDL to the LDL receptor. The phenotypical expression of this condition in children has not been described. Homozygous and heterozygous genotypes are known. This condition may occur in as many as 1 of 500 people, but the defect appears to account for only a small percentage (<2%) of premature CAD.

3. Lipoprotein lipase deficiency: A rare condition associated with very high levels of triglycerides and normal cholesterol levels. Eruptive xanthomas may be present. Although the risk of atherosclerosis is not elevated, the individual is at risk of having pancreatitis, particularly when the triglyceride level exceeds 500 mg/dL.

4. Familial dysbetalipoproteinemia: A very uncommon condition, occurring in about 1 of 5,000 persons in the United States; it is seen only rarely in adolescence. In this condition, the catabolism of VLDL remnants and chylomicrons is delayed because an abnormal apoE alters the normal binding of VLDL remnants to LDL receptors. This problem should be suspected when triglyceride levels are somewhat higher than cholesterol levels in the presence of a significant cholesterol elevation. These individuals have an increased risk of premature CAD and peripheral vascular disease. They often are obese and have glucose intolerance, hyperuricemia, and tuberoeruptive and palmar xanthomas. Caloric restriction is usually effective.

5. Familial hypertriglyceridemia: Autosomal-dominant trait. Dietary factors, obesity, and a sedentary lifestyle are additional elements involved in the degree of expression.

6. FCHL: Affected individuals have high levels of LDL-C, triglycerides, or both. This condition is usually not associated with tendinous xanthomas but is associated with premature CAD. Multiple lipoprotein phenotypes can occur in a single affected family. Affected individuals may have increases in VLDL alone, LDL alone, or VLDL plus LDL or chylomicrons. The diagnosis is made by a finding of multiple lipoprotein phenotypes in a single family when first-degree relatives are tested or when a typical pattern of modest elevation in concentrations of cholesterol and triglycerides is seen, together with a low HDL-C level. FCHL occurs in about 15% of patients with CAD younger than age 60 years. The metabolic defect appears to be an overproduction of lipoproteins by the liver, as well as decreased catabolism in the periphery. Dietary therapy, along with physical exercise, plays an important role in treatment.

**LIPID SCREENING AND MANAGEMENT**

The process of screening and management differs for adolescents (age 20 years or younger) and young adults (age 20 to 35 years), according to NCEP. In addition to classification of lipid parameters, screening involves the identification of cardiovascular risk factors by history and physical examination (see Figure 12.3).

**TABLE 12.4. Lipid values by age and sex**

<table>
<thead>
<tr>
<th>Risk Category</th>
<th>Lipid Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low risk</td>
<td>&lt;170 mg/dL</td>
</tr>
<tr>
<td>Borderline risk</td>
<td>170–199 mg/dL</td>
</tr>
<tr>
<td>High risk</td>
<td>&gt;200 mg/dL (95th percentile)</td>
</tr>
</tbody>
</table>

Providing dietary treatment for adolescents and young adults with the top 25% of cholesterol values is probably desirable, but this has not been proven. Establishing such proof would be extremely difficult, requiring lengthy (30 to 40 years) longitudinal studies. Recommending drug treatment to the top 10% is even more controversial until more is known about the risk-benefit ratio for such drugs in a younger population. A recent 1-year placebo-controlled trial of lovastatin in 10- to 17-year-old males with familial hypercholesterolemia showed good efficacy in terms of lipid lowering and no significant growth, nutritional, or hormonal side effects (Stein et al., 1999).

At present, it seems reasonable to recommend that individuals in the borderline-risk group receive hygienic measures, including exercise instruction, nutritional advice, and the like.
such as the NCEP Step 1 prudent diet, and nonsmoking advice. Those in the high-risk group should receive all these measures plus dietary counseling by a dietitian and more frequent follow-up. Although the LDL-C level is more closely correlated with CAD risk, total cholesterol, which can be drawn nonfasting, can be used for follow-up to save on laboratory costs and inconvenience to patients.

1. Who: If possible, all adolescents should be screened once during this age period. If not possible, then the following adolescents should be screened:
   a. Teens whose parents or relatives have had premature CAD or stroke, or clinical evidence of atherosclerosis before the age of 55 years in male members and before the age of 65 years in female members
   b. Teens whose parents have elevated concentrations of lipoproteins
   c. Teens with hypertension, obesity, diabetes, or other significant cardiac risk factors
   d. Smokers

2. How: Serum lipids are best measured after a 12- to 14-hour fast; however, the total cholesterol level can be determined in a nonfasting sample because chylomicrons from dietary fat contribute essentially no cholesterol. If a nonfasting cholesterol level is borderline or above, a fasting sample should be obtained and analyzed for triglyceride, total cholesterol, and HDL-C with a calculation of LDL-C. Risk on the basis of LDL-C is as follows:

   - Acceptable <110 mg/dL
   - Borderline 110–129 mg/dL
   - High risk >130 mg/dL

The AHA does not recommend mass screenings of plasma cholesterol concentration for all children and adolescents. The reasoning behind this was that such screenings may reach many individuals who either are at low risk or already know their cholesterol level.

Screening in Young Adults

The ATP III (Expert Panel, 2001) has made updated recommendations for detection, evaluation, and treatment of high cholesterol concentrations in adults using an evidence-based approach. The blood lipid levels that determine level of risk are higher for this age group because of the observed increase in total cholesterol and LDL-C with age. A recent review of more than 30 large clinical trials has supported the efficacy of this approach (Ansell et al., 1999).

1. Several changes in these 2001 recommendations are important (Table 12.5). For young adults, the following are most salient:

   **TABLE 12.5. New features of ATP III**

   a. Focus on multiple risk factors, elevating diabetes to the equivalent of existing coronary heart disease, using Framingham data to calculate the 10-year risk of a heart event, and acknowledging the importance of the metabolic syndrome.
   b. Modifying the classification of lipids and lipoproteins (see 2a)
   c. Support for implementation, including complete lipid profile as the optimal screening test, use of plant stanols and sterols as adjunctive therapy, and adding further treatment for persons with triglyceride levels of more than 200 mg/dL.
   d. Secondary prevention for those with CAD is more aggressive and beyond the scope of this chapter (see Expert Panel, 2001).

2. Recommendations for young adults between the ages of 20 and 35 years are as follows:

   a. Fasting lipid profile is the preferred method of assessing lipid risk and should be determined in every young adult regardless of family history at least once every 5 years. Next, the number of risk factors is counted (Table 12.6) for those with two or more risk factors, Framingham scoring is then used to assign 10-year risk of a coronary event. Last, the lipid profile is interpreted by the following guidelines:

   **TABLE 12.6. Major risk factors (exclusive of LDL cholesterol) that modify LDL goals**

   - **LDL-C**
     - Optimal <100 mg/dL
     - Near optimal 100–129 mg/dL
     - Borderline high 130–159 mg/dL
     - High 160–189 mg/dL
     - Very high >190 mg/dL
   - **Total cholesterol**
     - Desirable <200 mg/dL
     - Borderline 200–239 mg/dL
     - High Risk >240 mg/dL
   - **HDL-C**
     - Low <40 mg/dL
     - High >60 mg/dL

   b. In those without CAD, which will be the vast majority of 20- to 35-year-old adults, the following LDL-C goals and treatments apply: LDL-C goal is <160 mg/dL, at which point therapeutic lifestyle changes (TLC) are indicated. At LDL-C >190 mg/dL, lipid-lowering medications should be considered. At 160–189 mg/dL, LDL-C lipid-lowering drugs are optional based on clinical judgment, which takes into account the presence or absence of two broad classes of additional factors: life habits (e.g., obesity, sedentary lifestyle, and atherogenic diet) and emerging risk factors (e.g., Lp[a], homocysteine, prothrombotic and proinflammatory plasma factors, as well as impaired glucose tolerance).

A complete report is available online (http://www.nhlbi.nih.gov/guidelines/cholesterol/index.htm), which includes an executive summary, a full report, a quick desk reference, a slide show, Palm operating system interactive tool, and a 10-year risk calculator from the ATP III on Detection, Evaluation, and Treatment of High Blood
Moderate hypertriglyceridemia alone is not independently correlated with CAD. Severe hypertriglyceridemia (11,000 mg/dL) is associated with an increased incidence of acute life-threatening pancreatitis and must be aggressively treated with diet, weight loss, and pharmacotherapy. The Framingham study has found that a triglyceride concentration of more than 150 mg/dL, in combination with an HDL level of less than 35 mg/dL, is as good a predictor of CAD as LDL elevation. Thus, in the presence of an elevated triglyceride and a low HDL concentration, treatment with the TLC diet and exercise intervention is recommended. The ATP III now defines hypertriglyceridemia more strictly than previously:

- Normal triglycerides: <150 mg/dL
- Borderline-high triglycerides: 150–199 mg/dL
- High triglycerides: 200–499 mg/dL
- Very high triglycerides: >500 mg/dL

For adolescents, the 90th percentile (Table 12.4) should be used as the upper limit of normal for age and sex.

**Nonlipid (Novel) Risk Factor Assessment**

**Insulin/Glucose Ratio** Insulin resistance is indicated by an elevated ratio. It is associated with accelerated atherosclerosis, through various mechanisms including lipid oxidation, endothelial dysfunction, and thrombogenic abnormalities (Hayden and Reaven, 2000). It is associated with syndrome X (metabolic syndrome), which consists of central adiposity, hypertension, impaired glucose tolerance, and dyslipidemia. In adolescents, syndrome X is best managed with lifestyle changes aimed at overweight and obesity. ATP III recognizes metabolic syndrome as a secondary target of cardiovascular-risk reduction after LDL lowering. Routine screening of fasting insulin is not indicated, rather it should be reserved for individuals with risk factors for type 2 diabetes (such as family history, obesity, or acanthosis nigricans).

**Homocysteine** Elevated plasma total homocysteine is an independent risk factor for atherosclerotic vascular disease and has been linked to an increased risk of thrombosis. Risk increases continuously across the spectrum of homocysteine concentrations and may become appreciable at levels higher than 10 µmol/L. A compelling case can be made for screening all individuals with atherosclerotic disease or at high risk. Folic acid is the mainstay of treatment, because homocysteine levels can be reduced with folic acid supplementation, but vitamins B12 and B6 may have added benefit in selected patients. The results of ongoing randomized, placebo-controlled trials will help determine whether lowering the homocysteine concentration reduces the risk of cardiovascular disease (Gerhard and Duell, 1999).

Other potential emerging risk factors explored have included C-reactive protein and other inflammatory markers, coagulation factors (such as fibrinogen and factors VIII and VII), deficiency of antioxidant vitamins, and chlamydia infections.

**THERAPY FOR HYPERLIPIDEMIA**

**General Principles**

1. Diagnose and treat secondary causes
2. Reduce risk factors. Intervene with those risk factors that can be altered, including smoking, hypertension, and diabetes.
3. Start a heart-healthy diet. The principal treatment of hyperlipidemia in adolescents and adults is a diet with modified amounts of fat, saturated fat, and cholesterol without increased simple carbohydrates. The goals of dietary therapy are to lower total cholesterol and LDL-C concentration to below the 90th percentile—preferably below the 75th percentile. Nutritional management is described in two steps as recommended by the NCEP Expert Panel on Blood Cholesterol Levels in Children and Adolescents, as shown in Table 12.7. If adherence to the NCEP Step 1 diet fails to achieve the minimal goals of therapy, the Step 2 diet should be prescribed.

**TABLE 12.7. Dietary therapy for high blood cholesterol levels: characteristics of Step 1 and Step 2 diets for lowering blood cholesterol levels**

<table>
<thead>
<tr>
<th>Step 1 diet</th>
<th>Step 2 diet</th>
</tr>
</thead>
<tbody>
<tr>
<td>High dietary fat and low saturated fat</td>
<td>Low dietary fat and low saturated fat</td>
</tr>
<tr>
<td>High dietary cholesterol and low HDL</td>
<td>Low dietary cholesterol and low HDL</td>
</tr>
</tbody>
</table>

The pediatric recommendations differ from those for adults in that careful consideration and monitoring of energy and micronutrient consumption are needed for support of normal growth and development. This is particularly important during the adolescent growth years, when energy, protein, mineral, and vitamin requirements are increased. Nutritional counseling focusing on meeting fat and cholesterol recommendations while ensuring adequate macronutrient and micronutrient intake is needed. The Committee on Nutrition of the American Academy of Pediatrics recently set lower limits on the recommended fat intake of children and adolescents at no more than 30% of the average daily caloric intake and no less than 20% of the average daily caloric intake.

4. Set dietary goals.
   a. Reduced dietary fats
   b. Reduced saturated fat and improved fatty acid balance
   c. Reduced dietary cholesterol
   d. Increased complex carbohydrates

Achieving these dietary goals can be difficult for teens, so help from a physician, a dietitian, and the family is crucial. Helpful suggestions include the following:

*Snacks: Most candies should be limited. Replace with Graham crackers, Rye Krisp, melba toast, soda crackers, bagels, English muffins, and fruits and vegetables. Popcorn should be air popped.
*Desserts: Try fruits, low-fat yogurt, fruit ices, and jelly.
*Cooking methods: Choose methods that use little or no fat, such as steaming, baking, or broiling.
*Eating away from home: Order entrées, potatoes, and vegetables without sauces or butter.
*Ask for salad dressings to be served on the side. Limit high-fat toppings such as bacon, crumbled eggs, cheese, and sunflower seeds.
*A regular exercise program is an important adjunct to a change in eating habits.
*Initiate diets that closely correspond to the adolescent's usual eating habits.
*Implement specific goals in a graduated fashion, rather than all at once.
*Encourage family participation in the dietary management and the exercise program.
*Stress the maintenance of ideal body weight, an exercise program, and the prevention of nicotine and alcohol use.

**Dietary Therapy**

Step 1 and Step II diets are outlined at the AHA Web site (http://www.americanheart.org) (Table 12.8).
TABLE 12.8. Recommended diet modifications to lower blood cholesterol

Recommended Intake as Percentage of Total Calories

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Step I Diet</th>
<th>Step II Diet</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Fat</td>
<td>£30%</td>
<td>£30%</td>
</tr>
<tr>
<td>Saturated</td>
<td>7%–10%</td>
<td>&lt;7%</td>
</tr>
<tr>
<td>Polyunsaturated</td>
<td>£10%</td>
<td>£10%</td>
</tr>
<tr>
<td>Monounsaturated</td>
<td>£15%</td>
<td>£15%</td>
</tr>
<tr>
<td>Carbohydrate</td>
<td>&gt;95%</td>
<td>&gt;95%</td>
</tr>
<tr>
<td>Protein</td>
<td>Approximately 15%</td>
<td>Approximately 15%</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>&lt;300 mg/day</td>
<td>&lt;200 mg/day</td>
</tr>
<tr>
<td>Total calories</td>
<td>To achieve and maintain desired weight</td>
<td>To achieve and maintain desired weight</td>
</tr>
</tbody>
</table>

1. Reduce dietary fats: The typical fat intake of children in the United States is 36% of total energy consumption. To meet the goal of 30%, the teen must make several modifications in the use of “visible” and “invisible” fats. Visible fats include butter, margarine, oils, salad dressing, mayonnaise, cream, and gravies. They are often added to foods or used in preparation (e.g., fried chicken or French fries). Invisible sources of fat include oils and other fats incorporated into baked goods, processed foods (e.g., cold cuts, frozen meats, and frankfurts), whole milk, other dairy products, and snack foods (e.g., chips, doughnuts). Sources of fats should be identified in the adolescent’s diet. The amount and frequency of consumption of high-fat food should be reduced and lower-fat alternatives given.

2. Reduce saturated fats and improve fatty acid balance: Saturated fatty acids with chain lengths of 12 carbons (lauric), 14 carbons (myristic), and 16 carbons (palmitic) have the most hypercholesterolemic effect in humans. Stearic acid, an 18-carbon saturated fatty acid, has been found to be less atherogenic than 12- to 16-carbon fatty acids. These 12- to 16-carbon fatty acids are found in certain vegetable oils (e.g., palm or coconut), animal fats, and whole-milk dairy products. The 18-carbon stearic acid is found in chocolate and beef. Data from the 1988 Continuing Survey of Food Intakes by Individuals show that 14% of total calories is contributed to the diet from saturated fatty acids, a percentage that is higher than the recommended 10% limit. Therefore, when saturated fats are reduced to less than 10% of total calories, the balance of monounsaturated and polyunsaturated fatty acids must be considered. Major sources of monounsaturated fatty acids include olive oil, canola oil, peanuts, hazelnuts, avocado, lean beef, and poultry. Substituting these for saturated fatty acids in the context of a low-fat diet can lead to a reduction in LDL-C, no elevation in triglycerides, and preservation of HDL-C.

The major categories of polyunsaturated fatty acids are w-6 or w-3 fatty acids, terms referring to the positions of their double bonds. Linoleic acid, the major w-6 fatty acid in the diet, is found in vegetable oils such as safflower, sunflower seed, soybean, and corn oils. w-6 Fatty acids, when used in the context of the other dietary recommendations, lower total cholesterol and LDL-C concentrations without decreasing HDL-C concentration. In total amounts higher than 10% of total calories, these fatty acids may cause a decrease in the level of HDL-C. The long-term safety of a diet high in polyunsaturated fats, in relation to the incidence of cancer, has not been established.

w-3 Fatty acids are primarily found in cold-water fish as eicosapentaenoic acid and docosahexaenoic acid and in soybean and walnut oils as linoleic acid. w-3 Fatty acids, given as fish-oil supplements, have been shown to lower elevated triglyceride levels in adults and children with hypertriglyceridemia and to improve the dyslipidemia in pediatric patients with systemic lupus erythematosus. Fish-oil supplementation should be monitored medically for side effects such as increased clotting time. In general, increasing the number of meals with cold-water fish (e.g., salmon, mackerel, bluefish, trout, and sable fish) to a minimum of twice weekly while decreasing fatty beef and pork and poultry dishes would be beneficial.

3. Reduce dietary cholesterol: Dietary cholesterol will elevate both plasma concentrations of total cholesterol and LDL-C. The current consumption of cholesterol by children is less than 300 mg/day, which is almost within reach of the current recommendations. The following suggestions are given to guide the patient with hyperlipidemia and his or her family:

a. Reduce visible egg yolks such as fried eggs and egg yolks used in home recipes and replace with egg whites or egg substitutes.

b. Limit portions of cooked meat, chicken, and fish to 7 to 8 ounces daily; if lean cuts of beef and pork and controlled amounts of shellfish (six medium-sized shrimp) are used, they can be incorporated into the diet and can provide a significant source of minerals and vitamins.

c. Use skim milk or the lowest-fat dairy products available.

Cholesterol-restricted diets have been shown to be safe in relation to growth and cognitive development in several European studies (Rask-Nissila et al., 2000) and in the United States (Jacobson et al., 1998).

4. Increase complex carbohydrates: When fat is removed from an adolescent’s diet, an energy deficit may occur. In the overweight or obese teenager, this may aid in cessation of weight gain, but in the normal-weight to underweight individual, it may result in undesirable weight loss. Therefore, it is important to replace the fat energy with complex carbohydrate sources. Complex carbohydrates are found in fruits, vegetables, and whole grain products, such as unsweetened cereals, pasta, breads, corn, rice, and crackers.

Fat-free baked products offer a wide variety of snacks for adolescents and encourage adherence to the diet regimen. These products are isocaloric with their full-fat counterparts and thus contain a significant amount of simple sugar; therefore, their intake must be limited for the patient with elevated triglyceride concentrations, impaired glucose tolerance, or obesity.

**What Are the Differences Between the American Heart Association Diet, the Step I and Step II Diets?** The Step I diet from the AHA is very similar to the diet recommended by the AHA for the general public, with the exception that the Step I diet is followed in a medical setting. The Step II diet has further reductions in dietary fats and proteins compared with the Step I diet or for those with a higher level of cholesterol or more risk factors. Step I and Step II diets should be combined with regular physical activity in all patients and weight reduction in the overweight.

**What Is New in the ATP III TLC Diet?** The Step II diet’s limit on saturated fat of 7% of energy intake has been adopted for all adults and combined with a more liberal total fat intake of 25% to 35%, with the majority coming from monounsaturated fats. These changes recognize the contribution of excess intake of fat-free commercial baked goods with extra sugar, which have contributed to the epidemic of obesity, metabolic syndrome, and type 2 diabetes.

**Vitamin Therapy**

The ATP III acknowledges the importance of meeting the daily recommended intake (DRI) of vitamins and minerals but does not recommend megavitamin therapy beyond the DRI because of the negative data from clinical trials of b-carotene and antioxidant vitamins. We recommend all adolescents take an over-the-counter multivitamin with 100% of the DRI for folic acid (400 µg), as well as all the other water-soluble and fat-soluble vitamins and minerals for which there are DRIs.

**Stanoles and Plant Sterols**

As adjunctive LDL-C-lowering therapy, the ATP III recommends the addition of plant-derived cholesterol absorption-inhibiting compounds such as esters of cholestanol or other nonabsorbed sterols available as margarine or salad dressing (at two to three servings per day). Studies, mainly from Europe, have shown an
Xanthomas are present on physical examination or

Nicotinic acid (niacin)

Cholestyramine (Questran), a hydrophilic, insoluble anion-exchange resin powder

Inhibitors of HMG-CoA reductase (Table 12.10).

GI effects include nausea, bloating, and constipation.

Effects: Primarily reduces triglyceride levels but also lowers LDL-C levels and causes a slight rise in HDL. A dose of 3–4 g/day can result in a 40% decrease

Lovastatin (Mevacor)

Side effects: The drug is poorly tolerated in the dose needed for lipid lowering.

Bleeding tendencies, osteoporosis, or iron deficiency may result from poor absorption of vitamin K, calcium, or

Dose: The side effects can be reduced by using the sustained release product and starting with a dose of 500 mg with meals or at bed time and gradually

Action: Reduces VLDL production by inhibiting lipoprotein synthesis in the liver. Niacin is an effective drug but requires considerable physician and patient

In individuals older than 20 years, base treatment on the ATP III LDL goals outlined previously in the section “Screening in Young Adults” (section IIA).

Drug is difficult to take because it must be suspended in a liquid vehicle. If water is unsatisfactory, an

Supervised diet modification fails to lower LDL-C to acceptable levels or by at least 15% of baseline.

A parent has died or had severe atherosclerotic sequelae in his or her forties or younger.

Bile acid sequestrants

Colestipol (Colestid)

Available Drugs

TABLE 12.9. Drug therapy for hyperlipidemia

Additional 10% to 15% LDL-C reduction with daily use of these compounds in persons consuming a low-saturated fat, low-cholesterol diet.

Drug Therapy

The risk-benefit ratio for any drug therapy is unknown in adolescents. However, pharmacotherapy is considered when

1. Xanthomas are present on physical examination or

2. Supervised diet modification fails to lower LDL-C to acceptable levels or by at least 15% of baseline.

3. A parent has died or had severe atherosclerotic sequelae in his or her forties or younger.

4. The adolescent’s LDL-C concentration is more than 190 mg/dL in the absence of other risk factors or more than 160 mg/dL in the presence of any of the

5. In individuals older than 20 years, base treatment on the ATP III LDL goals outlined previously in the section “Screening in Young Adults” (section IIA).

Table 12.9 summarizes mechanisms of action and major effects and lists recommended doses and side effects of the drugs used for hyperlipidemic conditions. These

TABLE 12.9. Drug therapy for hyperlipidemia

Available Drugs

1. Bile acid sequestrants

a. Cholestyramine (Questran), a hydrophilic, insoluble anion-exchange resin powder

   • Action: Interrupts the enterohepatic circulation of bile acids and binds bile acids in the intestine to form an insoluble complex, which is excreted in feces

   and thereby increases hepatic synthesis of bile acids from cholesterol. Depletion of the hepatic pool of cholesterol results in an increase in LDL-receptor

   activity in the liver. This, in turn, stimulates removal of LDL from plasma and lowers the concentration of LDL-C. There may be an increase in hepatic

   VLDL production and thus an increase in triglyceride concentration. The advantage of this drug in the treatment of adolescents is that there is no systemic

   absorption or toxic effects. However, the gastrointestinal (GI) side effects are frequent, leading to problems in compliance.

   • Effects: Lowering of both total cholesterol and LDL-C levels by 10%–30% at 16–24 g/day.

   • Side effects

     – GI effects include nausea, bloating, and constipation.

     – Drug is difficult to take because it must be suspended in a liquid vehicle. If water is unsatisfactory, an unsweetened juice may improve palatability. Rapid

       ingestion may cause air swallowing.

     – Bleeding tendencies, osteoporosis, or iron deficiency may result from poor absorption of vitamin K, calcium, or iron, but these complications are rare.

     – Dose: Powder (16–24 g). Should be started at one pack (4 g of cholestyramine; 5 g of orange-flavored filler) twice a day and gradually increased for a

       month to the full dose. The average dose is two or three packs (8–12 g) taken orally twice daily with meals.

b. Colestipol (Colestid)

   • Action, effects, and side effects: Similar to those of cholestyramine.

   • Dose: Colestipol is available in pill form, making it more convenient for many teens, although the large size of the tablet can be a deterrent to compliance

     in some. The average dose is four tabs taken orally twice daily with 8 ounces of fluid. The maximum adult dose is 16 g/day.

2. Nicotinic acid (niacin)

   a. Action: Reduces VLDL production by inhibiting lipoprotein synthesis in the liver. Niacin is an effective drug but requires considerable physician and patient

      education because of side effects. However, at least in adults, the drug has proven efficacy and safety. It is also the least costly of the drugs.

   b. Effects: Primarily reduces triglyceride levels but also lowers LDL-C levels and causes a slight rise in HDL. A dose of 3–4 g/day can result in a 40% decrease

      in triglyceride and VLDL levels, a 20% decrease in LDL levels, and a 30% increase in HDL levels. Nicotinic acid is particularly valuable in combination

      therapy with a bile acid sequestrant because of the complementary modes of action: niacin inhibiting LDL and VLDL production and the bile acid sequestrant

      increasing LDL excretion.

   c. Side effects: The drug is poorly tolerated in the dose needed for lipid lowering.

      • Gastritis, peptic ulcer disease, vomiting, and diarrhea can occur.

      • Liver function abnormalities can occur.

      • Vasodilation with flushing is also a troublesome side effect.

   d. Dose: The side effects can be reduced by using the sustained release product and starting with a dose of 500 mg with meals or at bed time and gradually

      increasing for 1 month to 6 weeks. The average daily dose is 2–3 g. The possibility of flushing as a side effect should be discussed. Because the flushing is

      due to prostaglandin effects, it can be ameliorated by taking one aspirin (81 mg) 30 minutes before each dose. Timed-release capsules may also decrease

      the side effects. Individuals taking niacin should have regular monitoring of aminotransferase, glucose, alkaline phosphatase, and uric acid values.

3. Inhibitors of HMG-CoA reductase (Table 12.10)

   a. Lovastatin (Mevacor)

      • Action: Competitively inhibits the rate-limiting enzyme in cholesterol biosynthesis. LDL-receptor activity is also increased, leading to an increase in the

      rate of removal of LDL.

      • Effects: Causes an average reduction in the LDL-C concentration of 25%–45%.

      • Side effects: Usually well tolerated. The most common side effects include GI upset, muscle aches, and hepatitis. There is an increase in

a. aminotransferase levels in 1.9% of patients. Careful monitoring of liver function is essential. Myalgias occur in about 2.4% of individuals. Others include headaches, nausea, fatigue, insomnia, skin rashes, and myositis. Transient mild elevations in creatine kinase are commonly seen; in the few patients in whom markedly elevated CK levels and myositis develop, the drug should be discontinued. Results from the lovastatin adolescent trial on 132 male adolescents with familial hypercholesterolemia show efficacy similar to that seen in adults, with normal growth and development (Stein et al., 1998).

Hence, lovastatin may well become more commonly used.

b. Pravastatin (Pravachol)

- Action, effects, and side effects: Similar to those of lovastatin.
- Dose: 10–40 mg

c. Simvastatin (Zocor)

- Action, effects, and side effects: Similar to those of lovastatin.
- Dose: 5–80 mg

d. Atorvastatin (Lipitor)

- Action, effects, and side effects: Similar to those of lovastatin, with the additional effect of lowering triglycerides
- Dose: 5–80 mg

e. Fluvastatin (Lescol)

- Action, effects, and side effects: Similar to those of lovastatin, with the additional effect of lowering triglycerides
- Dose: 20–80 mg

f. Drugs that interfere with statin metabolism: As indicated in Table 12.10, the cytochrome P-450 CYP3A4 and CYP2C 9 pathway are involved with some of the statins. This can cause problems, for example, with the following medications:

  - Inhibits CYP3A4 (raises serum drug concentrations): erythromycin, clarithromycin, cyclosporine, ritonavir, fluconazole, verapamil, grapefruit juice
  - Inhibits CYP3A4 (lowers serum drug concentrations): barbiturates, carbamazepine, nafcillin, phenytoin, primidone, rifampin
  - Inhibits CYP2C9 (may raise serum fluvastatin concentrations): Amiodarone, cimetidine, trimethoprim-sulfamethoxazole, fluoxetine, ivermectin, ketoconazole, metronidazole
  - Inhibits CYP2C9 (May lower serum fluvastatin concentrations): Barbiturates, carbamazepine, phenytoin, primidone, rifampin

4. Fibrin acid, or gemfibrozil (Lopid)

   a. Action: Increases lipoprotein lipase activity and decreases hepatic triglyceride production.
   b. Effects: Reduces both LDL and triglyceride levels. In some individuals, cholesterol levels may decrease and HDL levels may rise. The drug is primarily used for lowering high levels of triglycerides.
   c. Side effects: Biliary tract disease, and contraindicated in liver or kidney disease. Abdominal discomfort, diarrhea, muscle ache, and increased appetite can occur.
   d. Dose: 600–1,200 mg/day in two doses.

General side effects include headache, nausea, diarrhea, flatulence, and dark urine. Hepatitis is a rare but serious reaction. These medications cause fat malabsorption and have been primarily used as an adjunct for weight management. Use of these medications, independent of weight loss, has also been noted to significantly improve cardiovascular risk factors and glycemic control. The usual dose is 120 mg thrice daily approximately 20 minutes before meals. Research into these drugs as lipid-lowering agents for adolescents may provide another method of therapy.

**Adherence to Drug Therapy**

1. The teen must be well informed about the goals of drug treatment and the side effects.
2. It is important to start with small doses of drugs, particularly with sequestrants or nicotinic acid.
3. The frequency of use of the medication and the impact on lifestyle must be discussed.
4. It is important to maintain regularly scheduled follow-ups with the teen.

**SUDDEN DEATH SECONDARY TO CARDIOVASCULAR CAUSES**

Many of the sudden deaths in adolescents outside of the three big causes of death in this age group (accidents, suicides, and homicides) are related to the cardiovascular system. In a study of sudden and unexpected natural deaths in childhood and adolescence, Neuspiel and Kuller (1985) found that cardiovascular causes accounted for the largest group in adolescents. The other major contributors included infections, epilepsy, intracranial hemorrhage, and asthma. In a study in England by Wren and O'Sullivan (2000) on children and adolescents age 1 to 20 years, about one third of the sudden deaths were secondary to cardiovascular causes. They found that undiagnosed cardiac arrhythmias were probably more common than undiagnosed hypertrophic cardiomyopathy.

1. Cardiovascular causes of sudden death in previously well adolescents

   a. Idiopathic hypertrophic subaortic stenosis or hypertrophic cardiomyopathy—the most common cause of sudden death, suggested by a triad of syncope, chest pain with dizziness, and a murmur at the left lower sternal border
   b. Anomalous origin of the left coronary artery
   c. Myocarditis
d. Congestive cardiomyopathy

2. Causes of sudden death in adolescents with prior cardiovascular disease

   a. Congenital aortic stenosis
   b. Congenital heart condition such as uncorrected tetralogy of Fallot (should be considered, particularly in adolescents with Down syndrome)
c. Cyanotic heart disease with pulmonary stenosis
d. Idiopathic hypertrophic subaortic stenosis or hypertrophic cardiomyopathy

If an adolescent is discovered to have one of the preceding syndromes, it is important to determine the pathophysiological severity and to consider the types of exercise that may present significant risks.

**EVALUATION**

History of particular importance are symptoms of syncope, significant exercise intolerance, and exertional chest discomfort, and a family history of premature CAD, sudden death, syncope, or hypertension.

**Physical Examination**

Important findings include hypertension, abnormal cardiac rhythm, heart murmur, or Marfan syndrome habitus.
Laboratory Tests

Exercise electrocardiography is useful in an adolescent with symptoms of exertional chest discomfort, syncope or exercise intolerance, or frequent ventricular arrhythmias. Routine screening with echocardiography or chest x-ray study is of little value. For further recommendations on limitations of these conditions for athletics, see Chapter 19.

SUPPORT MATERIALS


The following publications to assist in hypercholesterolemia therapy are available from the AHA (7320 Greenville Ave, Dallas, TX 75231) (many of the handouts are available at the AHA Web site at: [http://www.americanheart.org/Heart_and_Stroke_A-Z/Guide/cholesterol.html](http://www.americanheart.org/Heart_and_Stroke_A-Z/Guide/cholesterol.html)).

The AHA Diet (publication no. 51-018-B). Moderate, fat-controlled low-cholesterol meal plan.

Cholesterol and Your Heart (publication no. 50-069-A). Explanation of what cholesterol is and why it is a risk factor.

Recipes for Fat-Controlled, Low-Cholesterol Meals (publication no. 50-020-B). Recipes for healthy meals.

AHA Cookbook (publication No. 53-001-A). 250 recipes and a fat and cholesterol calorie chart.

In addition, the following is available from the NCEP, National Heart, Lung, and Blood Institute (Box C-200, Bethesda, MD 20892): Physician’s Kit on High Blood Cholesterol.

WEB SITES

For Teenagers and Parents

http://www.americanheart.org/. Topics include cholesterol, cholesterol in children, fiber and oat bran, home testing devices, cholesterol levels, cholesterol ratio, screening, dietary guidelines, drugs, risk factors, and triglycerides.


http://healthwatch.medscape.com/medscape/p/community/ghome.asp?SP=0&Channel=0. CBS Health Watch site is a good source of articles on the public on scientific advances in cardiovascular disease prevention and general health topics of interest to teens. Search on cholesterol.

http://www.nhlbi.nih.gov/about/ncep/index.htm. This is the home page for the NCEP.


For Health Professionals

http://www.americanheart.org/. Cholesterol screening position paper from the AHA.

http://www.adolescenthealth.org/html/nutritional.html. This site has the official policy statement on adolescent nutrition from the Society for Adolescent Medicine.

http://www.cdc.gov/growthcharts/. The source for the most up-to-date growth charts including the new BMI percentile charts.

http://eurodiet.med.uoc.gr/. This site is useful for a European perspective on healthy lifestyles. It contains consensus statements by a European working group.

http://www.usda.gov/. This is a good place to find the latest dietary guidelines for Americans.


REFERENCES AND ADDITIONAL READINGS


Arky RA, Perlman AL. Cholesterol and mortality: 30 years of follow-up from the Framingham study. JAMA 1987;257:2176.


Castelli WP, Griffin GC. How to help patients cut down on saturated fat. Postgrad Med 1988;84:44.


Although more than 41 million Americans, or about 15% of the population, have systemic hypertension, only 1% or 2% of young people have persistent hypertension (Hohn, 1994). The discrepancy in the number of hypertensive cases is a likely result of gene expression as modified by environmental influences over time. Most adults and teenagers with hypertension have idiopathic or primary hypertension—that is, no cause can be found for their blood pressure (BP) elevation. In the teen group, those with primary hypertension are usually asymptomatic.

Despite the low incidence of adolescent hypertension, it is imperative that BPs be measured when a teen is examined. The detection of elevated BP and the evaluation for hypertension risk factors in the adolescent years may prevent later cardiovascular diseases, with their catastrophic consequences. In addition, the prevalence of secondary hypertension is somewhat higher in adolescents than in adults, so existing secondary causes should be identified and treated in the afflicted young person.

**DEFINITION OF HYPERTENSION IN ADOLESCENCE**

Mean systolic pressure and diastolic pressures increase with age during the adolescent years. Figure 13.1 and Figure 13.2 show BPs derived from the Second Task Force on Blood Pressure Control in Children (1987), appointed by the National Heart, Lung, and Blood Institute to provide guidelines for physicians. More recently, Rosner et al. (1993) presented information refining task force norms by adding considerations of height. Current task force definitions of BP levels and hypertension include the following:

**FIG. 13.1.** Age-specific percentiles of BP measurements in boys, 13 to 18 years of age; Korotkoff phase V used for diastolic BP. (From National Heart, Lung, and Blood Institute’s Task Force on Blood Pressure Control in Children. Washington, DC: U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health; January 1987, with permission.)

**FIG. 13.2.** Age-specific percentiles of BP measurements in girls, 13 to 18 years of age; Korotkoff phase V used for diastolic BP. (From National Heart, Lung, and Blood Institute’s Task Force on Blood Pressure Control in Children. Washington, DC: U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health; January 1987, with permission.)
1. Normal BP: Systolic and diastolic BPs at below the 90th percentile for age and sex
2. High normal BP: Average systolic and/or diastolic BP consistently between the 90th and 95th percentiles for age and sex
3. Significant hypertension: Systolic and/or diastolic BP at or above the 95th percentile for age and sex, with measurements obtained on at least three occasions
4. Serious or severe hypertension: Systolic and/or diastolic BP at or above the 99th percentile for age and sex, with measurements obtained on at least three occasions

The 1993 Task Force on Blood Pressure Control in Children BP; revised for height are listed in Table 13.1 and Table 13.2. The practitioner should use this information when applying the previously mentioned criteria for hypertension, so mislabeling the tall adolescent as hypertensive may be avoided.

### TABLE 13.1. Definitions of significant versus severe hypertension in adolescence

<table>
<thead>
<tr>
<th>Age group</th>
<th>Significant hypertension</th>
<th>Severe hypertension</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;10</td>
<td>Systolic BP &lt; 120</td>
<td>Systolic BP &lt; 110</td>
</tr>
<tr>
<td>10-12</td>
<td>Systolic BP &lt; 130</td>
<td>Systolic BP &lt; 120</td>
</tr>
<tr>
<td>13-15</td>
<td>Systolic BP &lt; 140</td>
<td>Systolic BP &lt; 130</td>
</tr>
<tr>
<td>&gt;15</td>
<td>Systolic BP &lt; 150</td>
<td>Systolic BP &lt; 140</td>
</tr>
</tbody>
</table>

### Table 13.2. Significant hypertension in tall adolescents

<table>
<thead>
<tr>
<th>Age group</th>
<th>Sex</th>
<th>Systolic BP (mm Hg)</th>
<th>Diastolic BP (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;10</td>
<td>Male</td>
<td>117</td>
<td>67</td>
</tr>
<tr>
<td>10-12</td>
<td>Male</td>
<td>121</td>
<td>67</td>
</tr>
<tr>
<td>13-15</td>
<td>Male</td>
<td>126</td>
<td>65</td>
</tr>
<tr>
<td>&gt;15</td>
<td>Male</td>
<td>131</td>
<td>64</td>
</tr>
</tbody>
</table>

### CLASSIFICATION OF HYPERTENSION IN ADULTS AGE 18 YEARS AND OLDER

In 1997 the Joint National Committee on Detection, Evaluation and Treatment of High Blood Pressure provided a new classification of adult BP (based on an average of two or more readings taken at each of two or more visits after an initial screening):

<table>
<thead>
<tr>
<th>Category</th>
<th>Systolic (mm Hg)</th>
<th>Diastolic (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optimal</td>
<td>&lt;120</td>
<td>&lt;80</td>
</tr>
<tr>
<td>Normal</td>
<td>&lt;130</td>
<td>&lt;85</td>
</tr>
<tr>
<td>High normal</td>
<td>130–139</td>
<td>85–89</td>
</tr>
<tr>
<td>Hypertension:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage 1</td>
<td>140–159</td>
<td>90–99</td>
</tr>
<tr>
<td>Stage 2</td>
<td>160–179</td>
<td>100–109</td>
</tr>
<tr>
<td>Stage 3</td>
<td>&gt;180</td>
<td>&gt;110</td>
</tr>
</tbody>
</table>

Although all stages of hypertension are associated with an increased risk of nonfatal and fatal cardiovascular disease-related events and renal disease, the higher the BP, the greater the risk.

There are several important considerations in evaluating BPs in children and adolescents:

1. Although various instruments are available to measure BP, the mercury sphygmomanometer is generally accepted as the most accurate and is the instrument of choice.
2. Hypertension should not be diagnosed on the basis of a single measurement. Repeated measurements (at least three) on separate occasions are essential to diagnose hypertension. Using one isolated measurement may lead one to mislabel an individual with adverse consequences.
3. Proper cuff bladder size is critical. The width of the cuff bladder should be 40% of the midarm circumference and the length twice that—or 80% of the circumference. Thus, it should be wide enough to cover 75% of the upper arm from the top of the shoulders to the olecranon. For practical purposes, use the largest cuff that fits the arm while leaving the antecubital fossa free for auscultation. It is better to choose a cuff slightly too big than one too small.
4. The adolescent should be in a quiet area and have sufficient time to relax for several minutes. Measurements should be done with the adolescent in the sitting position, with the manometer at heart level. The arm (preferably the right) used for the measurement should be recorded in the chart. The adolescent should not have smoked or ingested caffeine within 30 minutes before measurement.
5. The cuff pressure should be released at a rate of 2 to 3 mm Hg/sec. For diastolic BP, the fifth (disappearance) Korotkoff sound is usually accepted as more accurate in adolescents and adults.
6. A single BP recorded at each visit is all that is usually necessary. Multiple pressure recordings do not increase predictive value. Again, three pressures at or above the 95th percentile on three separate occasions are necessary for a diagnosis of hypertension.
7. For apprehensive individuals, home BP monitoring using a calibrated over-the-counter device may provide insight as to the existence of “white coat” hypertension.
8. Ambulatory monitoring, in which BP measurements are obtained on an outpatient basis with recording devices, is not commonly needed in adolescents and young adults. However, this type of monitoring can be helpful for difficult diagnostic situations in which the BPs are repeatedly elevated in the office setting but within the reference range out of the office.

### ETIOLOGY

The causes of hypertension vary among different age groups. In adolescents, the prevalence of primary hypertension is increased in comparison with younger children. This is particularly true for mild hypertension. Table 13.3 shows an estimation of the causes of hypertension in adolescents from data gathered from a number of population studies. This information shows that primary hypertension is by far the most common cause of hypertension in the adolescent. Renal...
Parenchymal diseases are the most common secondary cause in the adolescent age group.

<table>
<thead>
<tr>
<th>Age group</th>
<th>&lt;1.3</th>
<th>&lt;0.1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congenital</td>
<td>&lt;1.3</td>
<td>&lt;0.1</td>
</tr>
<tr>
<td>Renovascular</td>
<td>0.4</td>
<td>0.1</td>
</tr>
<tr>
<td>Renal parenchymal</td>
<td>0.3</td>
<td>&lt;0.1</td>
</tr>
<tr>
<td>Primary hypertension</td>
<td>0.3</td>
<td>0.1</td>
</tr>
<tr>
<td>Other</td>
<td>0.3</td>
<td>0.1</td>
</tr>
<tr>
<td>Total</td>
<td>1.0</td>
<td>0.2</td>
</tr>
</tbody>
</table>

**TABLE 13.3. Estimated causes of hypertension in young people**

**EPIDEMIOLOGY**

**Prevalence**

Extrapolated data from the medical literature were coupled with the authors' own experience, using task force definitions of hypertension, which placed the prevalence of the disorder between 0.5% and 2% in young people. The importance of repeated measurements is demonstrated in a study of 3,537 adolescents in New York (Kilcoyne et al., 1974). In this study, 5.4% of adolescents had systolic hypertension and 7.8% had diastolic BPs of more than 140/90 mm Hg on the first screening. The prevalence dropped to 1.2% and 2.4%, respectively, after a second screening. Likewise, Fixler et al. (1979) found in his survey of schoolchildren that 1.6% of 10,641 were hypertensive after three screenings. In Muscatine, Iowa, fewer than 1% of nearly 4,000 adolescents were hypertensive after four screenings. Table 13.4 lists various prevalence studies of hypertension in adolescents.

**TABLE 13.4. Results of prevalence studies of hypertension in young people**

**Height and Weight**

Height has already been mentioned to define the new standards for BP by task force concurrence. Others hold that weight is the most important factor in determining BP. Weight has long been held to have a positive relationship with BP. More than half of hypertensive young people are obese. Higgins et al. (1984) suggested that if weight could be reduced in young people to below obesity levels (weight 20% above that given for height or body mass index over the 85th percentile—www.cdc.gov/growthcharts), the prevalence of hypertension would decrease by one third.

**Age**

BP increases with age in a nonlinear fashion through adolescence. Pressure should remain constant once adult status is reached, as described by Oliver et al. (1977) in a primitive society. Unfortunately, in cultured societies, that is not the case, and about one of six subjects will manifest hypertension in adult life.

**Salt and Other Nutrient Intake**

Controversy prevails over the numerous studies concerning the relationship of sodium intake to BP. For most individuals, little correlation exists. However, in certain salt-sensitive individuals, sodium restriction appears beneficial. For example, it has been suggested (Hohn et al., 1983) that African-American children from hypertensive families may be salt sensitive.

Other studies have found a link between potassium intake and both elevated and low BP. However, efforts to correlate calcium and other divalent cations with BP have been equivocal. Similarly, correlations between BP and vitamins A, C, and E, although suggestive, remain to be proven. Falkner (2000) noted that dietary nutrients could contribute to the prevention of hypertension in urban minority adolescents at risk for hypertension when instituted at an early age.

**Dietary Fat and Fiber**

Reduction in dietary intake of dietary fat and fiber together has been noted to reduce BP. Triglyceride levels are also correlated with pressure levels.

**Stress**

Both physical stress and mental stress evoke changes in BP. Indeed, the degree of change has been thought by some to be useful in predicting later-life hypertension. Accumulating data seem to support this concept. Meanwhile, exercise has been useful in the treatment of hypertension, and reduction of anxiety may also be beneficial. Pseudopheochromocytoma characterized by paroxysmal hypertension without adrenal involvement is an example of the latter.

**Race**

Although a significant determinant in adult BP, race is not a factor in teens. As a rule, African-American adolescents have BP levels similar to those of white adolescents. However, Voors et al. (1979) and Hohn et al. (1983) suggested that certain subgroups of African-American youths have higher pressures than their white counterparts. Rabinowitz et al. (1993) found a higher prevalence of hypertension among African-American females than among non-Hispanic females.

**Genetics**

Both familial aggregation BP studies, such as those of Zinner et al. (1971), and twin studies, such as those of Schieken (1993), indicate a strong positive correlation between hereditary influences and BP measurements. Colhoun (1999) estimated that about one third of variations in BP between individuals are due to genetic
factors most likely from several genes. The scheme for the natural history of hypertension presented in Fig. 13.3 indicates the impact of the “gene pool.”


Tracking (Maintenance of Rank Order with Time)

It has been said that the best predictor of future BP is an individual’s current pressure. However, evidence that adult hypertension is predictable by childhood BPs is controversial, and correlation coefficients are generally low.

RISK FACTORS FOR LATER-LIFE PRIMARY HYPERTENSION

About 1% to 2% of adolescents will be found to be hypertensive, and most of those will have primary hypertension. Yet, in at least 15%, hypertension will develop later in life. Early identification of those who ultimately will find themselves hypertensive might permit preventive programs to delay or avoid the disorder. Accordingly, those young people with risk factors for adult hypertension deserve special consideration. Lauer and Clarke (1989) monitored BPs in a large group of young people in Muscatine, Iowa, as they grew into adulthood. Risk factors that they and others found are listed here. Combinations of risk factors—for example, African-American race, obesity, and a hypertension-riddled family—may place a person at exceptional risk.

Hypertension Risk Factors

1. Systolic BP: Above the 90th percentile doubles the risk.
2. Family history: Two or more members with hypertension increases the risk two to four times.
3. Weight more than 20% above the norm for height: Two thirds found to be hypertensive.
4. Race: A more than 10% higher incidence of hypertension in adulthood in African-Americans than in other racial groups (i.e., 25% will be found to be hypertensive later in life).
5. Dietary cations: Particularly increased dietary sodium in salt-sensitive individuals and decreased potassium intake (may lead to higher BPs).
6. Other risk factors: Hyperlipidemia (or family history), stress, smoking, alcohol, drug intake, preeclampsia and eclampsia, and diabetes mellitus.

CAUSES OF SECONDARY HYPERTENSION IN ADOLESCENCE

More than 90% of hypertensive adolescents have no known cause for their disorder and are labeled as having primary or essential hypertension. BPs are usually in the 95th- to 99th-percentile range in essential hypertension. Few youths will be found to have serious hypertension (i.e., BP above the 99th percentile). Such people will often be found to have a known cause for the disorder, labeled secondary hypertension. A number of causes of this type of hypertension are listed, roughly in the order of frequency of occurrence.

Causes of Transient Secondary Hypertension

1. Drug related: Steroids, phencyclidine, amphetamines, mercury poisoning, oral contraceptive use
2. Renal
   a. Acute glomerulonephritis
   b. Hemolytic-uremic syndrome
   c. Renal failure
   d. Genitourinary tract surgery
   e. Nephritis with anaphylactoid purpura
3. Neurological
   a. Increased intracranial pressure
   b. Guillain-Barré syndrome
   c. Cervical and leg traction
4. Vascular: Painful sickle cell crisis
5. Metabolic
   a. Hypercalcemia
   b. Hypernatremia
   c. Congenital adrenal hyperplasia
   d. Acute intermittent porphyria
6. Miscellaneous
   a. Burns
   b. Stevens-Johnson syndrome
   c. Postoperative status
   d. Stress related

Causes of Sustained Hypertension

1. Renal
   a. Bilateral obstructive uropathy
   b. Chronic glomerulonephritis
   c. Renal parenchymal disease (pyelonephritis, infarction, radiation, trauma)
   d. Renal artery lesions (stenosis, thrombosis, aneurysm)
     i. Intrinsice: Fibromuscular hyperplasia, arteritis, thrombosis
     II. Extrinsic: Compression
   e. Congenital defects (hypoplastic, polycystic kidney)
   f. Tumors
   g. Postrenal transplantation
   h. Familial nephritis
   i. Renal vein thrombosis
2. Vascular
   a. Coarctation of the aorta
b. Aortitis; systemic disorders

3. Endocrine
   a. Pheochromocytoma
   b. Cushing syndrome
   c. Primary aldosteronism
   d. Hyperparathyroidism
   e. Ovarian or adrenal tumors
   f. Congenital adrenal hyperplasia
   g. Neuroblastoma

4. Metabolic
   a. Diabetes mellitus with renal involvement
   b. Gouty nephropathy

DIAGNOSIS

Algorithm for Diagnosis

Schemes have been developed to assist in the diagnosis and management of various levels of hypertension. Figure 13.4 is a flow diagram for the identification and evaluation of hypertension in adolescents. Important aspects of this flowchart include the following:

1. Measuring BP repeatedly during several visits.
2. Taking height into account. A BP between the 90th and 95th BP percentiles can be completely normal in an adolescent taller than the 90th growth percentile for height. Significant hypertension for tall adolescents is shown in Table 13.2.
3. Instituting and monitoring a weight reduction program for obese adolescents in the 90th–95th percentile.
4. Providing a diagnostic evaluation and giving nonpharmacological treatment, and possibly drug therapy, if the BP remains above the 95th percentile.

Avoidance of Mislabeling

Adolescents make fewer visits per year to health care practitioners than other age groups. However, each visit presents an opportunity to record BP. About 10% of these young people will have a high initial BP (at or above the 95th percentile). They should be labeled as having high BP, not given a diagnosis of hypertension. Before a diagnosis of hypertension can be made, two subsequent BP determinations on different days must also show a high systolic or diastolic pressure, or both. Only 1% to 2% of adolescents will fulfill these criteria and, by definition, have hypertension. Additionally determination of “out-of-office BP” to assess possible “white coat hypertension” is increasingly advocated. Recently, however, Vaindirlis et al. (2000) presented data to theorize that such hypertension may be a prelude to permanent hypertension.

Initial Diagnostic Study

The diagnostic evaluation must be tailored to the individual, taking into account the age, sex, race, family history, and level of hypertension. For example, a 12-year-old white female with no family history of hypertension and a diastolic BP of 115 in all limbs would be a candidate for an aggressive evaluation for secondary causes, particularly renal parenchymal disease or renal artery stenosis. In contrast, a 17-year-old white boy with a family history of hypertension and a diastolic BP of 92 is not a good candidate for invasive studies to look for a secondary cause.

1. History: Investigating a young person for hypertension requires that a detailed history be elicited. The history should aim at determining secondary causes, target-organ damage, and other cardiovascular risk factors. Look for evidence of urinary tract infections or renal disease and for a patient or family history of hypertension. Activity, dietary, and other habits should be sought. A self-history form has been devised to aid in this process (Hohn, 1994). Be sure to ask specific questions regarding each of the following:
   a. Headache
   b. Chest pain or dyspnea
   c. History of muscle weakness
   d. Edema
   e. Pallor, flushing attacks, or palpitation
   f. Polydipsia, polyuria, or weight loss
   g. Change in hair, body habitus, or menses
   h. History of renal, thyroid, or heart disease
   i. Drug use
   j. Smoking history
   k. Dietary assessment, including sodium intake, alcohol use, and intake of cholesterol and saturated fats
   l. Family history of hypertension, myocardial infarction, diabetes, or strokes, with age at diagnosis

2. Physical examination: A thorough examination is also an essential part of the diagnostic study. The adolescent in question will often be obese. The examination should include an exploration for evidence of a secondary cause or end-organ damage and an evaluation of the following:
   a. Pulses in all extremities
   b. BP levels in both arms and a lower extremity
   c. Height and weight
   d. Neck: Carotid bruits or an enlarged thyroid gland
   e. Fundi: Arteriolar narrowing, arteriovenous nicking, hemorrhages, exudates
   f. Abdomen: Bruits, enlarged kidneys, masses, abnormal aortic pulsation
   g. Heart: Increased rate, size, precordial heave, clicks, murmurs, arrhythmias, third and fourth heart sounds
   h. Extremities: Diminished or absent arterial pulsations, bruits, edema
   i. Nervous system
   j. Body habitus: Pattern of obesity (e.g., “buffalo hump”)
   k. Skin: Striae, café au lait spots, neurofibromas

3. Clinical signs of secondary causes of hypertension (Table 13.5) and the following considerations:
Acute onset of hypertension in adolescents suggests acute renal disease.

Laboratory testing

1. Hormonal studies
2. Renal studies
a. Radiological and radioisotope studies
   - Rapid-sequence intravenous pyelography
   - Renal ultrasonography
   - Renal radionuclide studies
b. Renal angiography with measurement of renal vein renins (timing of angiography depends on age of patient [earlier if younger], sex [earlier if female], and severity of hypertension [earlier if severe])
c. Digital subtraction angiography
d. Computed tomography of the kidneys or adrenal glands
2. Hormonal studies
a. Quantitation of urine catecholamines and metabolites
b. Plasma catecholamines
c. Peripheral plasma renin activity, serum and urinary aldosterone concentrations, and electrolyte determinations with and without salt loading
d. Measurement of other hormones, such as free cortisol, in urine and plasma
e. Measurement of aldosterone and cortisol in adrenal venous effluent
f. Newer diagnostic tests (such as those using converting enzyme inhibitors): Best left to the consultant in hypertension

Further Diagnostic Tests for Specific Causes of Hypertension

In adolescents with severe hypertension or signs or symptoms suggestive of a specific secondary cause, further diagnostic tests are indicated. The particular test needed depends on the suspected cause and the experience of the radiologists and laboratory that the practitioner is using. Consultation with someone knowledgeable about hypertension in young people would be helpful to pursue the most cost-effective and safest diagnostic evaluation. Many diagnostic studies have now become available to explore renal and endocrine causes. There is still controversy regarding which tests should be ordered and under what circumstances. Some of the tests include the following:

1. Renal studies
a. Radiological and radioisotope studies
   - Rapid-sequence intravenous pyelography
   - Renal ultrasonography
   - Renal radionuclide studies
b. Renal angiography with measurement of renal vein renins (timing of angiography depends on age of patient [earlier if younger], sex [earlier if female], and severity of hypertension [earlier if severe])
c. Digital subtraction angiography
d. Computed tomography of the kidneys or adrenal glands
2. Hormonal studies
a. Quantitation of urine catecholamines and metabolites
b. Plasma catecholamines
c. Peripheral plasma renin activity, serum and urinary aldosterone concentrations, and electrolyte determinations with and without salt loading
d. Measurement of other hormones, such as free cortisol, in urine and plasma
e. Measurement of aldosterone and cortisol in adrenal venous effluent
f. Newer diagnostic tests (such as those using converting enzyme inhibitors): Best left to the consultant in hypertension

THERAPY

Prevention

Optimally, measures to prevent or minimize the effects of hypertension should be applied to those adolescents prone to have the disorder later in life. The difficulty lies in finding those at risk and deciding what measures would be helpful. Data from young people for this purpose are lacking, and long-term follow-up information is unavailable. Nevertheless, a starting point for such a strategy is to consider those with the findings listed below as being at risk. They should be counseled about nonpharmacological treatments to maintain lower BP and periodically monitored.

Normotensive adolescents who may benefit from nonpharmacological antihypertension measures include the following:

1. Those with consistently high normal BP (above the 90th percentile)
2. Those with a trend of upward tracking pressures (above the 75th percentile) or pressures occasionally above the 95th percentile
3. Those who are obese, particularly if parents are obese
4. Those with hyperlipidemia or a family history of the disorder, particularly together with coronary artery disease or stroke
5. Those with diabetes mellitus
6. Those with two or more family members with treated hypertension, particularly African-Americans

Criteria for Treatment

Most patients with definite hypertension at presentation will have some regression of BP toward the reference range if monitored closely. Accordingly, it is wise to institute nonpharmacological measures while a basic diagnostic study is being done.

1. All patients with sustained severe hypertension (systolic or diastolic pressure above the 99th percentile; e.g., 150/98 mm Hg in 16- to 18-year-olds) require full diagnostic evaluation and drug therapy or treatment of secondary causes.
2. Patients with continued mild hypertension (systolic or diastolic pressure between the 95th and 99th percentiles; e.g., 142/92 mm Hg in 16- to 18-year-olds) should have periodic BP determination and nonpharmacological measures first.
3. The question of when to institute drug therapy for significant hypertension in adolescents is still controversial. Indications could include those with persistent significant hypertension (mild or moderate, 95th to 99th percentile) unresponsive to nonpharmacological measures and with any of the following:
a. African-American heritage, strong family history of hypertension, or both
b. Other cardiovascular risk factors, including
   • Smoking
   • Dyslipidemia
   • Diabetes mellitus
   • Male sex
c. Family history of cardiovascular disease in first-degree relatives occurring in women younger than 65 or men younger than 55

4. Care must be exercised in labeling an adolescent as hypertensive because if the diagnosis is misapplied, it may lead to exclusion from activities or to future insurance problems.

Nonpharmacological Interventions

1. Weight reduction: Excess body weight is correlated closely with increased BP. Weight reduction reduces BP in a large proportion of hypertensive individuals who are more than 10% above ideal weight.

2. Avoidance of excess salt: Moderate sodium restriction in hypertensive individuals has been shown, on average, to reduce systolic BP by 4.9 mm Hg and diastolic BP by 2.6 mm Hg. Foods with high-salt content are listed here:

<table>
<thead>
<tr>
<th>Sauces</th>
<th>Snack Foods</th>
<th>Excessive Soft Drinks</th>
<th>Meats and Seafood</th>
<th>Miscellaneous</th>
</tr>
</thead>
<tbody>
<tr>
<td>A-1 sauce</td>
<td>Com chips</td>
<td>Coke (50 mg Na/12 oz)</td>
<td>Sausage</td>
<td>Sausage</td>
</tr>
<tr>
<td>Relish</td>
<td>Pickles</td>
<td>Mountain Dew (70 mg Na/12 oz)</td>
<td>Frankfurters</td>
<td>Bouillon</td>
</tr>
<tr>
<td>Soy sauce</td>
<td>Potato chips</td>
<td>Ham</td>
<td>Oysters</td>
<td>Olives</td>
</tr>
<tr>
<td>Worcestershire</td>
<td>Pretzels</td>
<td>Salted popcorn</td>
<td>Sauerkraut</td>
<td>Frozen pizza</td>
</tr>
</tbody>
</table>

3. Regular physical exercise: Regular aerobic physical activity, adequate to achieve at least a moderate level of physical fitness, may be beneficial for both prevention and treatment of hypertension. Regular aerobic physical activity can reduce systolic BP in hypertensive patients by approximately 10 mm Hg. This can take the form of walking 20 to 30 minutes daily.

4. Discontinuance of smoking and avoidance of alcohol excess, medications (except as directed by health care providers), and drugs (e.g., cocaine, amphetamines): Although cigarette smoking is unrelated to hypertension in teens, it is a major risk factor for cardiovascular disease and thus should be avoided by hypertensive individuals. Excessive alcohol intake can raise BP and cause resistance to antihypertensive therapy.

5. Search for and evaluation of other cardiovascular risk factors.

6. Use of methods such as behavior modification, biofeedback, and hypnosis.

Pharmacological Treatment

1. Antihypertensive medications are definitely indicated for those who have the following:
   a. Symptoms
   b. Dangerously high pressures (i.e., >12 mm Hg above the 99th percentile diastolic or >25 mm Hg above the 99th percentile systolic)
   c. Evidence of end-organ damage
   d. Evidence of target-organ damage including the following:
      • Heart disease: Left ventricular hypertrophy, before myocardial infarction or heart failure
      • Retinopathy
      • Nephropathy
      • Transient ischemic attack or stroke
      • Peripheral arterial disease

Although there has been some evidence to suggest that potassium, calcium, or magnesium supplementation might theoretically be of benefit, only potassium supplements are occasionally recommended. However, eating low-sodium, high-potassium foods is advocated, as well as avoiding high-sodium, low-potassium foods. The adolescent should also take adequate daily amounts of dietary calcium. If the adolescent is on a salt-restricted diet, seasoning with potassium salt may be helpful. An increase in dietary fiber and a decrease in saturated fats are also being recommended for overall general health. Kaplan (1988) has reviewed the efficacy of other nonpharmacological measures.

3. Peripheral arterial disease
4. Transient ischemic attack or stroke
5. Nephropathy
6. Retinopathy
7. Male sex
8. Male sex
9. Diabetes mellitus
10. Dyslipidemia
11. Male sex
12. Smokers
13. Use of methods such as behavior modification, biofeedback, and hypnosis
14. Drug therapy should be simple so that compliance will be increased in what may be a lifelong but asymptomatic problem.

3. Avoidance of excess salt: Moderate sodium restriction in hypertensive individuals has been shown, on average, to reduce systolic BP by 4.9 mm Hg and diastolic BP by 2.6 mm Hg. Foods with high-salt content are listed here:

<table>
<thead>
<tr>
<th>Sauces</th>
<th>Snack Foods</th>
<th>Excessive Soft Drinks</th>
<th>Meats and Seafood</th>
<th>Miscellaneous</th>
</tr>
</thead>
<tbody>
<tr>
<td>A-1 sauce</td>
<td>Com chips</td>
<td>Coke (50 mg Na/12 oz)</td>
<td>Sausage</td>
<td>Sausage</td>
</tr>
<tr>
<td>Relish</td>
<td>Pickles</td>
<td>Mountain Dew (70 mg Na/12 oz)</td>
<td>Frankfurters</td>
<td>Bouillon</td>
</tr>
<tr>
<td>Soy sauce</td>
<td>Potato chips</td>
<td>Ham</td>
<td>Oysters</td>
<td>Olives</td>
</tr>
<tr>
<td>Worcestershire</td>
<td>Pretzels</td>
<td>Salted popcorn</td>
<td>Sauerkraut</td>
<td>Frozen pizza</td>
</tr>
</tbody>
</table>

4. Discontinuance of smoking and avoidance of alcohol excess, medications (except as directed by health care providers), and drugs (e.g., cocaine, amphetamines): Although cigarette smoking is unrelated to hypertension in teens, it is a major risk factor for cardiovascular disease and thus should be avoided by hypertensive individuals. Excessive alcohol intake can raise BP and cause resistance to antihypertensive therapy.

5. Search for and evaluation of other cardiovascular risk factors.

6. Use of methods such as behavior modification, biofeedback, and hypnosis.

7. Unfortunately, the ideal antihypertensive agent does not exist. Initial therapeutic regimens have been debated. Many experts have recommended an individualized stepped-care approach, as suggested by the Joint National Committee (National High Blood Pressure Education Program) (1993) and as shown in Fig. 13.5. In this approach, a monotherapy drug regimen is superimposed on nonpharmacological therapy as initial treatment. Either an angiotensin-converting enzyme (ACE) inhibitor, b-blocker, a calcium entry blocker (CEB), or a diuretic may be used. Advocates of this approach recommend the following:

   a. Begin with a low dose of the chosen initial drug. Diuretics and b-blockers are now being used as initial therapy. However, ACE inhibitors are still preferred by other experts. Only diuretics and b-blockers have been studied sufficiently to demonstrate a reduction in morbidity and mortality rates in association with antihypertensive therapy. ACE inhibitors may be particularly helpful in the treatment of teens with high renin levels caused by renal disease. Preparations with once- or twice-daily dosing are available and can improve compliance. CEBs are effective, particularly for surges of hypertension when on other antihypertensive agents. They offer convenient dosing schedules and are generally well tolerated. One of two increases in the dose of the initial medication

   b. In this approach, a monotherapy drug regimen is superimposed on nonpharmacological therapy as initial treatment. Either an angiotensin-converting enzyme (ACE) inhibitor, b-blocker, a calcium entry blocker (CEB), or a diuretic may be used. Advocates of this approach recommend the following:

   c. Begin with a low dose of the chosen initial drug. Diuretics and b-blockers are now being used as initial therapy. However, ACE inhibitors are still preferred by other experts. Only diuretics and b-blockers have been studied sufficiently to demonstrate a reduction in morbidity and mortality rates in association with antihypertensive therapy. ACE inhibitors may be particularly helpful in the treatment of teens with high renin levels caused by renal disease. Preparations with once- or twice-daily dosing are available and can improve compliance. CEBs are effective, particularly for surges of hypertension when on other antihypertensive agents. They offer convenient dosing schedules and are generally well tolerated. One of two increases in the dose of the initial medication
may be used to achieve BP control if necessary. If BP control is still not achieved, proceed to combination treatment. Dual antihypertensive drug treatment with one of the medications being a diuretic is increasingly being used.
b. Add a low dose of either a thiazide diuretic or an adrenergic inhibiting agent, whichever was not used in step A. Proceed to a full dose if necessary. If BP control is still not achieved, one may choose to
c. Add a third antihypertensive drug, usually a vasodilator or renin-angiotensin inhibitor, or preferably obtain consultation from an expert on hypertension in young people.
d. b-Blockers and diuretics have associated problems, including
   • For diuretics: Hypokalemia, hypercholerolemia, and hyperglycemia
   • For b-Blockers: Elevated triglyceride levels and lowered high-density lipoprotein cholesterol levels
e. ACE inhibitors and calcium blockers have the potential to control hypertension without the effects caused by b-blockers and diuretics. Although the long-term side effects and efficacy of these drugs are not yet known, midterm information is promising. Once-a-day dosing is the preferred initial therapy in most adolescents, and long-acting or sustained-release medications are available. ACE inhibitors and CCBs are popular as possible first choices for treating hypertension in adults and are seeing increasing use in pediatric circles.

8. Step-down therapy, or drug withdrawal, should not be forgotten. After an extended course of drug therapy and BP control, a gradual reduction in or withdrawal of medication can be attempted. This requires close observation and continuation of pharmacological therapy.

9. Classes of antihypertensive medications and specific drugs in each class are listed here. (Asterisks indicate recommended or most used in class.) For doses, specific actions, and differences, as well as side effects, a reference such as the Pediatric Dosage and Formulary (Division of Pharmacy, Children’s Hospital of Los Angeles, 2001) must be consulted:
a. Diuretics
   • Loop-acting diuretics: Furosemide (Lasix)
   • Potassium-sparing agents: Spironolactone (Aldactone)
   • Thiazide: Hydrochlorothiazide (Hydridol)*
b. b-Adrenergic inhibitors
   • b-Adrenergic antagonists: Atenolol (Tenormin),* esmolol (Brevibloc), labetolol (Normodyne; Trandate), metoprolol tartrate (Lopressor), nadolol (Corgard), pindolol (Visken), propranolol (Indental), and timolol (Blocadren)
   • Central adrenergic inhibitors: Clonidine (Catapres), guanabenz (Wy tensin), methyldopa (Aldomet)
   • a-Adrenergic receptor antagonists: Prazosin (Minipress)
c. Vasodilators
   • Vascular smooth muscle relaxing agents: Diazoxide (Hyperstat), hydralazine (Apresoline),* minoxidil (Loniten); nitroprusside (Nipride)
   • Slow-channel CCBs: Amlodipine (Norvasc), diltiazem HCl (Cardizem), nifedipine (Procardia),* verapamil HCl (Calan; Isoptin)
d. ACE inhibitors
   • Captopril (Capoten)
   • Enalapril maleate (Vasotec)
   • Enalapril maleate plus hydrochlorothiazide

e. Angiotensin II antagonist
   • Losartan (approved only)

SPECIAL POPULATIONS

1. African-Americans: The frequency of hypertension in African-Americans is among the highest in the world. Hypertension develops at an earlier age and is more severe in African-Americans than in whites. In African-Americans, diuretics have been proven to reduce hypertension morbidity and mortality rates, so diuretics should be seriously considered for use in the absence of other conditions that prohibit their use. b-Blockers or ACE inhibitors are less effective in African-Americans; however, calcium antagonists and a-receptor blockers are as effective in African-Americans as in whites.

2. Females who take oral contraceptives: Most females who take oral contraceptives have a small increase in systolic and diastolic BP but usually within the reference range. Hormonal contraceptives, mainly those that contain estrogen, can increase angiotensinogen, leading to an increase in angiotensin II and an increase in BP in some individuals. The risk of having overt hypertension appears to increase with age, duration of use, and body mass. Many of the studies of and oral contraceptive agents involved higher doses of both estrogen and progestrone than are used currently; therefore, contraceptives agents are contraindicated.

HYPERTENSIVE EMERGENCIES

Rarely an adolescent will have signs of encephalopathy or heart failure at presentation and be found to have extraordinarily high BP—that is, pressure 1.3 to 1.5 times the 95th percentile. This constitutes a true emergency and may have disastrous consequences unless efforts to lower the BP are begun at once. Assistance from an expert in hypertension should be sought. Meanwhile, the patient should be hospitalized and an intravenous line placed. If the patient becomes obtunded, intravenous sodium nitroprusside therapy should be started at a dose of 0.5 µg/kg and titrated as needed to slowly reduce the BP toward the 99th percentile. When adequate pressure control has been achieved, a vigorous search for the cause of the hypertension, if not known, must be made.

SUMMARY

As adolescents mature toward full adulthood, an increasing number will be found to have hypertension. Perhaps this progression can be delayed or avoided through the applications of the principles outlined in this chapter. At the very least, BPs should be taken when adolescents are seen for health care, regardless of the complaint.

When pressures are found to be repeatedly elevated, nonpharmaceutical antihypertensive measures (Fig. 13.5) should be started. They are good general health rules. Initially, in the absence of severe hypertension, a basic diagnostic study is all that is needed. Depending on the results, other tests may or may not be necessary. In most cases, the BP will regress toward reference range levels during the study.

For the few adolescents with persistent serious hypertension, drug therapy is indicated. The individualized stepped-care approach, also displayed in Fig. 13.5, is recommended. Very rarely, hypertension will be resistant to initial drug therapies. Such cases generally require consultation with an expert on hypertension in young people.

WEB SITES

For Teenagers and Parents
http://www.americanheart.org/hb/
American Heart Association site on hypertension.
http://www.mayo.edu/hypertension/pat-educ.htm
Mayo Clinic education materials on hypertension.
http://www.scranmedical.com/auto_inflate_blood_pressure_monitors.htm
Commercial site to buy home monitors.
http://www.lifeclinic.com/
Industry supported site with good information on blood pressure, diabetes, and cholesterol.

For Health Care Professionals
Screening for hypertension; National Institutes of Health site.
http://www.docguide.com
After registering, explore the site for hypertension.
http://www.who.int/nchc/cvd/facts802.html
World Health Organization (WHO) site on hypertension.
http://www.who.int/nchc/cvd/frt_guide.html
WHO guidelines on hypertension.
REFERENCES AND ADDITIONAL READINGS


Cardiac murmurs occur in at least 50% of all normal children and often persist into adolescence. Almost all of these murmurs occur in the absence of any structural heart disease and are considered to be "innocent," "benign," or "functional" in origin. However, these terms are imprecise in that the term "functional" has been applied to physiological causes of murmurs, such as anemia, fever, hyperthyroidism, or pregnancy. Therefore, the term normal murmur has been advocated to clearly indicate their benign nature. In contrast, 0.8% of children are born with congenital heart disease and frequently have murmurs related to a structural defect. Failure to identify a murmur as normal may lead to undue anxiety, unnecessary sports and activity restrictions, or inappropriate use of antibiotics for endocarditis prophylaxis. Conversely, failure to recognize murmurs from structural heart disease can have serious consequences. It is the task of the primary care physician to differentiate normal murmurs from those that are suspicious for structural heart disease. Although normal murmurs may persist into late adolescence and early adulthood, this is more the exception than the rule. These murmurs frequently "disappear" with the inability to auscultate soft sounds in an adolescent or adult with an increased chest diameter. If a sports screening physician has any doubts regarding a heart sound or murmur in a late adolescent or young adult who is a competitive athlete, referral for a formal cardiac evaluation should be considered.

HISTORY
The diagnosis begins with a thorough history and physical examination. If a diagnosis of congenital heart disease is already known, the algorithm is made simple.

Age at Onset
Murmurs presenting at birth or in the first weeks of life suggest an organic basis except for the murmur of physiological branch pulmonary artery stenosis. Murmurs first heard in childhood or adolescence are more likely to be normal murmurs.

Cardiac Symptoms
The symptomatic patient with decreased exercise tolerance, exertional chest pain, or excessive dyspnea and tachypnea on exertion may have an organic basis for the murmur. Any patient with syncope or near-syncope during exercise merits cardiac evaluation.

PHYSICAL EXAMINATION

1. Appearance
   a. Presence of dysmorphic features is frequently associated with congenital heart disease, as in Down, Turner, or Marfan syndrome.
   b. Cyanosis and clubbing is strongly suggestive of cyanotic congenital heart disease.
   c. Presence of dysmorphic features is frequently associated with congenital heart disease, as in Down, Turner, or Marfan syndrome.

2. Pulse in upper and lower extremities (an important component of the examination; observe for any discrepancies in intensity or timing)
   a. Delayed or absent pulses in the lower extremities may indicate coarctation of the aorta.
   b. Bounding pulses related to a wide pulse pressure may indicate structural disease related to "run-off" from a region of high pressure to one of relatively lower pressure: aortic regurgitation or patent ductus arteriosus.

3. Blood pressures in arm and leg
   a. Sizing of the blood pressure cuff is essential. Although the length and width of the cuff may vary, a good general rule is to size the length of the bladder (the inflatable portion) of the cuff so that it completely encircles the upper arm of the patient. Using a cuff size that is too small leads to falsely high readings, and conversely, using one that is too large causes falsely low readings. When in doubt, err on the side of a cuff that is slightly too large.
   b. The leg systolic pressure should always be slightly higher than that of the arm. If the leg pressure is lower, seriously consider coarctation of the aorta. Late diagnosis of coarctation is not rare, and the most common presenting sign in adolescence is upper-extremity systolic hypertension.
   c. Third heart sound: Ventricular filling heard at the lower left sternal border is always abnormal after early infancy, as it is a loud third heart sound (S₃) at the apex.
   d. Clicks: A click is an important clue to the diagnosis of organic disease.
      * Ejection clicks heard in early systole are of either pulmonary or aortic origin. A pulmonary ejection click is best heard at the upper left sternal border and is associated with valvular pulmonary stenosis. The intensity of the pulmonary valve ejection click varies with respiration and the severity of pulmonary
Murmurs: Location: Left lower sternal border and apex

Differential diagnosis: Differentiated from valvular aortic stenosis by the absence of a click; differentiated from hypertrophic cardiomyopathy (previously termed Medium-pitched murmur with vibratory quality, strummed guitar or bass.

Cause: Turbulence of venous flow at the sharp angle made between the right subclavian vein and the superior vena cava

Intensity: Usually grade 2–3/6

Murmur decreased with supine position—unique for a normal murmur.

Cause: Turbulence of flow in the right ventricular outflow tract (the right-sided equivalent of Still murmur).

Cause: Turbulence at the site of branching of the brachiocephalic arteries from the aortic arch

Differential diagnosis: Differentiated from aortic or pulmonary stenosis because murmur is louder over the neck than the chest and there is no click.

Radiation: Not extensive

Murmur is decreased or obliterated by jugular venous compression.

Murmur is heard best in the sitting position with the bell of the stethoscope.

Laboratory findings: Generally not indicated

Quality: Short mid-systolic murmur, grade 3/6 or less, no ejection click and with normal splitting of S

History: Asymptomatic; onset usually in childhood

Differential diagnosis: Differentiated from valvular pulmonary stenosis by absence of a click; differentiated from an atrial septal defect because S

Maneuvers: Murmur decreased on sitting or standing, increased when supine.

Not holosystolic—S

Maneuvers

Location: May vary, but frequently at left lower or upper sternal border

Duration: Not holosystolic

Murmur is increased by rotating the head away from the side being examined.

S

Location: Heard best above the sternal end of clavicle; may be bilateral or unilateral (right side usually louder—most people have only a right-sided superior vena cava); can be heard as low as third intercostal space.

4. Maneuvers: Murmur increased by inspiration and sitting, increased when supine.

5. Differential diagnosis: Differentiated from valvular aortic stenosis by the absence of a click; differentiated from hypertrophic cardiomyopathy (previously termed IHSS) by the fact that the murmur decreases while standing.

Pulmonary Ejection Systolic Murmur

1. Cause: Turbulence of flow in the right ventricular outflow tract (the right-sided equivalent of Still murmur).

2. Quality: Short mid-systolic murmur, grade 3/6 or less, no ejection click and with normal splitting of S

3. Location: Left lower sternal border and apex

4. Maneuvers: Murmur decreased on sitting or standing, increased when supine.

5. Differential diagnosis: Differentiated from valvular pulmonary stenosis by absence of a click; differentiated from an atrial septal defect because S

Cervical Venous Hum

1. Cause: Turbulence of venous flow at the sharp angle made between the right subclavian vein and the superior vena cava

2. Quality: Continuous murmur with diastolic accentuation

3. Location: Heard best above the sternal end of clavicle; may be bilateral or unilateral (right side usually louder—most people have only a right-sided superior vena cava); can be heard as low as third intercostal space.

4. Maneuvers

a. Murmur is increased by rotating the head away from the side being examined.

b. Murmur is decreased or obliterated by jugular venous compression.

c. Murmur decreased with supine position—unique for a normal murmur.

5. Differential diagnosis: If murmur is louder over the chest than over the supraclavicular area, patent ductus arteriosus or coronary artery fistula must be excluded.

Supraventricular (Carotid) Bruit

1. Cause: Turbulence at the site of branching of the brachiocephalic arteries from the aortic arch

2. Quality: Short, early systolic murmur, usually 2/6

3. Location: Maximal above the clavicles and lower portion of the sternocleidomastoid muscle

4. Maneuvers

a. Frequently, the murmur is eliminated by compression of the subclavian artery against the first rib.

b. Murmur is decreased by hyperextending the shoulders.

c. Murmur is heard best in the sitting position with the bell of the stethoscope.

5. Differential diagnosis: Differentiated from aortic or pulmonary stenosis because murmur is louder over the neck than the chest and there is no click.

MURMURS ASSOCIATED WITH STRUCTURAL HEART DISEASE

It is unusual for major congenital cardiac lesions to be diagnosed initially in adolescence. Nevertheless, in the differential diagnosis of normal murmurs, a number of acyanotic lesions must be considered. A review of these lesions is presented in Table 14.1.
TABLE 14.1: Clues to specific organic cardiac lesions

Atrial Septal Defect

Other than mitral valve prolapse and bicuspid aortic valve, atrial septal defect is the most common congenital cardiac lesion diagnosed de novo in adolescence or adulthood.

   a. Hyperdynamic precordium with right ventricular lift with sizable shunt; no thrill.
   b. Widely split and fixed S₂.
   c. Grade 3 or less systolic ejection murmur at upper left sternal border (flow across pulmonary outflow tract).
   d. Mid-diastolic rumble at lower left sternal border (flow across tricuspid valve).
2. Laboratory findings
   a. Electrocardiogram (ECG): rSr' pattern or right ventricular hypertrophy.
   b. Chest radiograph: Cardiomegaly with increased pulmonary vascularity.
   c. Echocardiogram: Diagnostic with visualization of location and size of defect.
   d. Transesophageal echocardiogram (TEE): Frequently required in adolescent or adult patients when transthoracic echocardiogram does not permit adequate visualization of the defect. The decision for surgical versus transcatheter device closure of the defect is usually based on the TEE findings.

Ventricular Septal Defect

1. Physical examination: Shunt volume determines findings.
   a. Normal precordium with small shunt, hyperdynamic with a thrill with large shunt.
   b. Normal to accentuated S₂, depending on shunt.
   c. Usually a grade 2–3/6 systolic murmur at lower left sternal border. (Very small defects may not be holosystolic and may have a high-frequency blowing quality.)
   d. Mid-diastolic rumble at the apex with large shunts (flow across the mitral valve).
2. Laboratory findings
   a. ECG: Normal in small defects; ventricular hypertrophy depending on hemodynamics.
   b. Chest radiograph: Normal in small defects; cardiomegaly with increased pulmonary vascularity in large defects.
   c. Echocardiogram: Provides anatomical detail of location and size of defect; color Doppler permits visualization of very small defects.

Patent Ductus Arteriosus

1. Physical examination: Shunt volume determines findings.
   a. Normal precordium with small shunt, hyperdynamic with a thrill with large shunt.
   b. Grade 2–4/6 continuous murmur at upper left sternal border.
   c. Wide pulse pressure and bounding pulses with large shunt.
2. Laboratory findings
   a. ECG: Normal, left ventricular hypertrophy depending on severity.
   b. Chest radiograph: Cardiomegaly with increased pulmonary vascularity with large shunt.
   c. Echocardiogram: Visualization with two-dimensional and color Doppler imaging.
   d. Cardiac catheterization: Rarely for diagnosis, commonly for coil or device occlusion.

Valvular Pulmonary Stenosis

1. Physical examination: Severity of obstruction determines findings.
   a. Right ventricular lift with thrill in more severe forms.
   b. Systolic ejection click at upper left sternal border; click becomes more difficult to hear in severe stenosis (moves closer to the S₁).
   c. Normal to soft S₂—widely split S₂, depending on severity.
   d. Grade 2–4/6 harsh systolic ejection murmur at upper left sternal border; may be heard in the back. Intensity and duration of the murmur increase as severity increases.
2. Laboratory findings
   a. ECG: Normal to severe right ventricular hypertrophy depending on severity.
   c. Echocardiogram: Two-dimensional imaging permits evaluation of valve morphology. Doppler evaluation of maximum gradient across the valve has proved to have excellent correlation with cardiac catheterization measurement of gradient.
   d. Cardiac catheterization: Rarely for diagnosis. Treatment of choice is balloon pulmonary valvuloplasty.

Valvular Aortic Stenosis

1. Physical examination: Severity of obstruction determines findings.
   a. Prominent apical impulse in more severe forms.
   b. Systolic thrill in suprasternal notch in more severe forms.
   c. Systolic ejection click at lower left sternal border to apex: not present in supravalvular or subvalvular types.
   d. Grade 2–4/6 long systolic ejection murmur at upper right sternal border; subvalvular murmur may be heard best at mid-left sternal border.
   e. High-frequency early diastolic decrescendo murmur of aortic regurgitation, probably in association with a bicuspid aortic valve.
2. Laboratory findings
   a. ECG: Normal to left ventricular hypertrophy, depending on severity.
   b. Chest radiograph: Normal heart size with prominent ascending aorta; normal vascularity.
   c. Echocardiogram: Two-dimensional imaging permits evaluation of valve morphology. Mean gradient obtained by Doppler evaluation has good correlation with cardiac catheterization–derived gradient across valve.
   d. Cardiac catheterization: Rarely for diagnosis. In selective cases aortic balloon valvuloplasty may be an initial palliative procedure.

Mitral Valve Prolapse (see also Chapter 15)

1. Physical examination
Mitral Valve Regurgitation

Mitral valve regurgitation is rare in adolescence unless it is associated with mitral valve prolapse or a history of rheumatic heart disease.

   a. Normal to hyperdynamic precordium
   b. Grade 2–4/6 high-frequency holosystolic apical murmur; may also radiate toward the base (upper left sternal border).
   c. Low-frequency apical mid-diastolic rumble with severe regurgitation.

2. Laboratory findings
   a. ECG: May be normal with mild regurgitation; bifid P wave of left atrial enlargement if regurgitation is chronic and severe.
   b. Chest radiograph: Normal to cardiomegaly with large left atrium and left ventricle
   c. Echocardiogram: Evaluates cause of valve abnormality and severity of regurgitation.

MANAGEMENT OF HEART MURMURS

On completion of a careful history and physical examination, it should be possible to differentiate normal murmurs from those with an organic basis. ECGs and chest radiographs do not add to the accuracy of diagnosis of normal murmurs. In those situations in which there is uncertainty and a consideration of congenital heart disease, the ECG and chest radiograph findings may be helpful. However, in patients with mild lesions and minimal cardiovascular stress, those also may be normal. An echocardiogram is a powerful but expensive diagnostic tool for consideration at this point. It has been shown to be more cost-effective to refer these types of patients to a pediatric cardiologist than to obtain an echocardiogram before the referral.

Therefore, management optimally requires a careful and systematic cardiovascular examination; judicious use of laboratory studies; referral, in selected cases, to a pediatric cardiologist; and, in the case of normal murmurs, confident reassurance.

WEB SITES

For Teens and Parents


Especially for Parents


For Health Professionals

http://www.rchc.rush.edu/rmawebfiles/htmurmurs.htm, Rush Children's Hospital Site description of murmurs.

Sites to Hear Heart Sounds

http://www.med.ucla.edu/wilkes/inex.htm,
http://www.medlib.com/spi/coolstuff2.htm,
http://www.bcm.tmc.edu/class2000/sims/HeartSounds.html,
http://www.nursing.hhsweb.com/sino/heart_sounds/heart.html,

REFERENCES AND ADDITIONAL READINGS


Mitral valve prolapse (MVP) is common in adolescents. It is found in up to 17% of women of childbearing age. However, clinically important MVP with serious arrhythmia or symptomatic mitral regurgitation is infrequent, occurring perhaps in only 2% to 5% of the general population. Rarely, it can lead to serious complications such as chest pain, mitral regurgitation, infectious endocarditis, cerebral embolism, severe arrhythmia, and sudden death. A major difficulty for adolescents with MVP is the inability to identify those who are at risk for development of complications. In most adolescents with intermittent chest pains, palpitations, syncope, dyspnea on exertion, or generalized fatigue, MVP is not present.

ETIOLOGY

Genetics

MVP is a genetically transmissible problem found in 30% to 50% of first-degree relatives of individuals with MVP. Transmission is suspected to be autosomal dominant, with a decrease in male expressivity. No chromosomal abnormalities are present.

Structural Abnormalities

Grossly, the mitral valve is composed of two scalloped leaflets, the anterior and posterior leaflets. These leaflets are attached usually to two papillary muscles via long “strings” called chordae tendineae. In MVP, the anterior or posterior leaflets are redundant and thick, and the chordae may be redundant and excessively pliable.

Histologically, an infiltrative and degenerative process called “myxomatous degeneration” of the mitral valve leaflets may occur, in which dense collagenous supporting tissue is replaced by loose, amorphous, acellular, hyalinized deposits. There is thickening of the leaflets with an increase in acid mucopolysaccharides in the spongiosa layer.

Functionally, MVP occurs when leaflet tissue bulges into the left atrium during ventricular systole. Left ventricular size and geometry change with postural changes, with volume status, and in association with other cardiac diseases. Any of these factors can alter the quality and presence of the murmur as well as the timing of the click. With prolapse, leaflet tissue may fail to completely coapt, creating a space through which mitral regurgitation can occur.

Developmental Abnormality

A developmental abnormality was suggested in a study by Schulte et al. (1981), who demonstrated a narrower anteroposterior chest diameter and longer arm span in patients without Marfan syndrome but with MVP. Further evidence is the report of pectus excavatum, straight back syndrome, or severe scoliosis in 75% of individuals with MVP.

EPIDEMIOLOGY

The prevalence of MVP in the literature has ranged from 1% to 17% (DeLeon, 1980), depending on the criteria for diagnosis. Recent reports have centered on rates of 5% to 10%, with the prevalence in the pediatric age group reported to be 5%. There is a female preponderance. MVP may be diagnosed at any age; symptomatic patients tend to be late adolescents or young adults.

CLASSIFICATION

MVP can be divided into three types:

1. Primary (classic) prolapse, an idiopathic autosomal dominant disorder affecting the structure of the mitral valve. Valve leaflets are thickened and elongated in association with myxomatous infiltration.
2. Secondary prolapse from myxomatous degeneration of mitral leaflets in individuals with connective tissue diseases such as Marfan syndrome or Ehlers-Danlos syndrome.
3. Prolapse of a normal mitral valve leaflet in individuals with papillary muscle dysfunction related to ischemia, infarction, or cardiomyopathy.

CLINICAL MANIFESTATIONS

Associated Symptoms

1. Palpitations may be unrelated to the occurrence of arrhythmias. However, Kawey et al. (1984) demonstrated that 16% of patients with MVP experienced premature ventricular beats during exercise testing, compared to none in a control group. Similarly, ambulatory Holter monitoring demonstrated isolated isolated premature ventricular beats in 38% of patients with MVP, compared with 8% of controls.
2. Chest pain tends to be precordial, is usually unrelated to effort, and is of longer duration than anginal pain. The cause is unknown. Chest pain in patients with MVP may be completely unrelated to the MVP. In one study of 17 preadolescents and adolescents with MVP and chest pain, 14 had abnormal findings on either esophageal manometry, the Bernstein test, an esophageal pH probe test, or esophagogastroscopy (Wood et al., 1991). Ten of the patients had esophagitis or gastritis.
3. Less common symptoms include dyspnea, fatigue, lightheadedness, syncope (common also in adolescents without MVP), and neuropsychiatric symptoms. It is important to remember that frequent palpitations may cause high levels of anxiety in teens with and without structural heart disease. Thorough ECG, Holter, or exercise treadmill evaluation of patients with high anxiety due to palpitations may be warranted, even if purely for reassurance. Suppression of premature ventricular contractions with exercise is assumed to have a generally good prognosis, although no solid data exist to support this widely held clinical perception.

The true prevalence of the symptoms described in patients with MVP compared with the general population is unknown because prevalence rates are usually
The Click

Pregnancy Echocardiogram

Antibiotic Prophylaxis

Stroke:
The Chest X-ray

Sudden death:
Infectious endocarditis:
Arrhythmias:

Murmur Qualities

Associated Physical Abnormalities

b-Blocking Agents

Progressive mitral regurgitation:

MANAGEMENT

by actuarial tables, their mortality rates are similar to those of individuals without MVP. Complications include the following:

vary tremendously. The teen with a mid-systolic click and no mitral regurgitation will probably have an excellent clinical outcome. Most patients with MVP have no

Individuals with benign clicks and those with mitral regurgitation probably should not be grouped under one diagnostic category, because the clinical significance can

Electrocardiography and Holter or event monitoring are indicated to check for arrhythmia if the patient has palpitations that disrupt activities of daily living or cause

If an echocardiogram is obtained for other reasons and the report suggests the possibility of MVP, a careful history and physical examination is needed to clinically confirm the diagnosis. Patients with less than overt prolapse on echocardiography and absence of a click, murmur, or symptoms should not be misclassified as having MVP. They should not follow bacterial endocarditis prophylaxis recommendations. Electrocardiography and Holter or event monitoring are indicated to check for arrhythmia if the patient has palpitations that disrupt activities of daily living or cause serious symptoms (syncope, dizziness).

COMPLICATIONS

Individuals with benign clicks and those with mitral regurgitation probably should not be grouped under one diagnostic category, because the clinical significance can vary tremendously. The teen with a mid-systolic click and no mitral regurgitation will probably have an excellent clinical outcome. Most patients with MVP have no problems. By actuarial tables, their mortality rates are similar to those of individuals without MVP. Complications include the following:

1. Arrhythmias: The most frequent complication. They include premature ventricular contractions, supraventricular tachyarrhythmias, and bradyarrhythmias.

2. Infectious endocarditis: The risk of infective endocarditis for patients with MVP varies from 0.0175% to 0.052% per year, depending on the presence or absence, respectively, of a regurgitant murmur (MacMahon et al., 1987). In the study of risk factors by Nishimura et al. (1985), all patients with endocarditis and MVP had redundant mitral valve leaflets. The American Heart Association periodically updates bacterial endocarditis prophylaxis recommendations. The most recent recommendations were published in 1997 and are summarized in Table 15.1.

3. Progressive mitral regurgitation: This complication is rare. In the Nishimura study (1985), progression to mitral valve replacement was best correlated with the left ventricular diastolic dimensions at initial presentation.

4. Sudden death: Estimates of this rare occurrence range from as high as 1 in 53 persons with significant mitral regurgitation to 1 in 5,400 persons with little or no mitral regurgitation (Kligfield et al., 1987). Nishimura et al. (1985) reported that the only association with sudden death was the presence of redundant mitral valve leaflets.

5. Stroke: There is a higher prevalence of MVP in young patients with stroke than in control subjects (Barnett et al., 1980). However, the true risk of stroke in individuals with MVP is unknown. One study estimated the risk of stroke in young patients with MVP to be about 0.02% per year (Wolf and Sila, 1987). The most likely cause is embolization of a noninfective perivalvular thrombus.

MANAGEMENT

1. Reassurance: The vast majority of adolescents and young adults with MVP are asymptomatic and have no complications. They should not be restricted in their activities, and serious sequelae need not be discussed.

2. Antibiotic Prophylaxis: There is still some controversy regarding which individuals with MVP should receive antibiotic prophylaxis. The American Heart Association suggests antibiotic prophylaxis only for those who have MVP complicated by mitral insufficiency, while acknowledging that complete information to guide therapy in this area is limited. Some experts also recommend prophylaxis whenever a thickened mitral valve leaflet is found on an echocardiogram.

If prophylaxis is used, it is indicated for dental, gynecological, urological, and gastrointestinal procedures and surgery. Uncomplicated vaginal delivery and cesarean section rarely, if ever, precipitate endocarditis. It is recommended that prophylaxis be provided for those patients with MVP who have mitral regurgitation at the time of delivery. However, many deliveries become “complicated” during the delivery process. Therefore many centers that care for pregnant women with cardiac disease break from official American Heart Association policy and provide endocarditis prophylaxis for cardiac patients during all deliveries. See Table 15.1 for the most recent antibiotic recommendations for prophylaxis.

3. b-Blocking Agents: agents may be indicated for patients with MVP who have significant symptoms from arrhythmias.

4. Pregnancy: Mitral regurgitation is usually well tolerated during pregnancy. There is usually no additional risk to the adolescent mother or her child during pregnancy and delivery.
WEB SITES

For Teenagers and Parents
http://wfbmce.drkoop.com/conditions/ency/article/000180.htm. Dr. Koop Web site on MVP.

For Health Professionals

REFERENCES AND ADDITIONAL READINGS


Scoliosis affects 2% to 3% of all adolescents in the United States. Its evaluation and treatment can have a significant impact on the life of the adolescent. The cosmetic effect of postural changes as well as the treatment, with unsightly, cumbersome braces, can have significant psychological effects such as poor self-image and social isolation. In one study, patients with scoliosis had higher rates of unemployment and disability and female patients had a lower marriage rate (Noonan et al., 1997). Those with severe curves in the magnitude of 100 to 120 degrees can have cardiopulmonary compromise with decreased lung function and cor pulmonale. Although it is thought that early detection and appropriate treatment can improve outcomes and change the natural history of this disorder, controversy still exists regarding routine screening, specifically for scoliosis in adolescents.

**Definition**

Scoliosis is a lateral curvature of the spine of 11 degrees or greater that also has an associated rotational component. Structural scoliosis is a curve that does not correct with side bending toward the convex side of the curve, whereas nonstructural scoliosis does correct with the same maneuver.

**Etiology**

Scoliosis is a descriptive term and not a diagnosis. It can occur secondary to many abnormalities, although in most cases the cause is unknown (i.e., idiopathic scoliosis).

**Nonstructural Scoliosis**

Nonstructural scoliosis may result from:

1. Postural
2. Hysterical
3. Nerve root irritation (disc herniation, tumor)
4. Inflammatory (e.g., appendicitis, perinephric abscess)
5. Leg length discrepancy

**Structural Scoliosis**

There are a multitude of causes of structural scoliosis, including the following.

1. Idiopathic scoliosis (about 70% to 85% of all cases of scoliosis)
2. Congenital scoliosis
   a. Vertebral: Myelomeningocele, hemivertebrae, vertebral bars, wedge vertebrae
   b. Extravertebral: Congenital rib fusions
3. Neuromuscular
   a. Neuropathic forms
      • Lower motor neuron disease (e.g., poliomyelitis, myelomeningocele, trauma)
      • Upper motor neuron disease (e.g., cerebral palsy, trauma, spinal tumors, syringomyelia)
   b. Myopathic forms
      • Progressive (e.g., muscular dystrophy)
      • Static (e.g., arthrogryposis)
4. Miscellaneous
   a. Mesenchymal disorders
      • Marfan syndrome
      • Ehlers-Danlos syndrome
   b. Metabolic disorders
      • Osteogenesis imperfecta
      • Rickets
   c. Neurofibromatosis
   d. Osteochondrodystrophies
      • Achromoplastic dwarfism
      • Diastrophic dwarfism
      • Mucopolysaccharidoses
      • Spondyloepiphyseal dysplasia
   e. Rheumatoid disease
   f. Traumatic (e.g., fracture, irradiation, effects of surgery)
   g. Bone tumors (e.g., osteoid osteoma, histiocytosis X)

**Idiopathic Scoliosis**

**Types**

Idiopathic scoliosis is defined by the patient’s age at onset and the location of the curve.

1. Infantile scoliosis manifests between birth and 3 years of age, usually in males during the first year of life, and may be related to supine positioning of babies; 70% to 90% resolves spontaneously.
2. Juvenile scoliosis manifests between 3 and 9 years of age; the incidence is the same in males and females, and the condition follows the progression rules of adolescent idiopathic scoliosis.
3. Adolescent scoliosis manifests between 10 years of age and the time of skeletal maturity, most commonly in females (70%).

**Curve Patterns**

1. Single major curve
   a. High thoracic curve: Apex usually centered at T1 to T2
   b. Thoracic curve: Most commonly right, one of the most deforming, apex usually centered at T5 or T12
   c. Thoracolumbar curve: Apex usually centered at T12 to L1
   d. Lumbar curve: Apex usually centered at L2
2. Major thoracic/minor lumbar curve: The thoracic is the larger curve and the more structural, with a smaller lumbar curve
3. Double major curve: Two curves of significance occur in this pattern
   a. Thoracic and lumbar: Usually does not have dramatic postural changes because curve compensates for the other; usually right thoracic and left lumbar
   b. Thoracic and thoracolumbar
4. Multiple curves

**Prevalence** Approximately 2% to 3% of adolescents have a curve greater than 10 degrees; 0.5% have a curve greater than 20 degrees. Seventy percent of idiopathic scoliosis occurs in females.

**Causes** There are a number of different theories of what may contribute to the development of idiopathic scoliosis:

1. Genetics: There is an increased incidence of scoliosis in first-degree relatives that decreases in more remote (i.e., second- and third-degree) relatives (Wynne-Davis, 1968).
2. Abnormal balance and abnormal skeletal muscle
3. Abnormal intervertebral disc composition

**Risk Factors for Progression** A combination of the following factors can be helpful in predicting as many as 80% of progressive curves (Peterson et al., 1995).

1. Age at onset and gender (Table 16.1)

<table>
<thead>
<tr>
<th>Age at onset</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;10</td>
<td>5%</td>
<td>1%</td>
</tr>
<tr>
<td>10-15</td>
<td>6%</td>
<td>4%</td>
</tr>
<tr>
<td>15-18</td>
<td>9%</td>
<td>7%</td>
</tr>
<tr>
<td>&gt;18</td>
<td>12%</td>
<td>8%</td>
</tr>
</tbody>
</table>

**TABLE 16.1. Risk of progression of idiopathic scoliosis**

2. Magnitude of the curve: The amount of curvature is measured by the Cobb method. In this technique (Fig. 16.1), a horizontal line is drawn at the inferior border of the inferiorly involved vertebra of the curve (1), another horizontal line is drawn at the superior border of the superiorly involved vertebra (3), perpendicular lines are drawn from each of these horizontal lines (2 and 4), and the intersecting angle is then measured. Patients with a 20-degree curve have a 20% risk of progression, whereas those with a 50-degree curve have a 90% chance of progression (Lonstein et al., 1984).

**FIG. 16.1.** Diagram shows the Cobb method of measuring the spinal curve caused by scoliosis. (Courtesy of Stuart Spine Group, Youngwood, PA.)

3. Skeletal maturity: Risser stage is determined by the appearance of the secondary ossification center of the iliac crest (Risser, 1958). It first appears at the anterior superior iliac spine and progresses medially toward the posterior superior iliac spine. The crest is divided into four quarters, with stages 1 through 4 coinciding with extension of the ossification center into each quarter and stage 5 being complete fusion of the crest. Patients with Risser stage 0 show progression 36% to 68% of the time, whereas those Risser stage 3 or 4 progress only 11% to 18% of the time (Fig. 16.2).

**FIG. 16.2.** Ossification of the iliac epiphysis usually starts at the anterior superior iliac spine and progresses posteriorly. The iliac crest is divided into four quarters, with stages 1 through 4 coinciding with extension of the ossification center into each quarter and stage 5 being complete fusion of the crest. Patients with Risser stage 0 show progression 36% to 68% of the time, whereas those Risser stage 3 or 4 progress only 11% to 18% of the time (Fig. 16.2).

**Patient Evaluation** The U.S. Preventive Services Task Force’s Guidelines for the Guide to Clinical Preventive Services states that “There is insufficient evidence to recommend for or against routine screening of asymptomatic adolescents for idiopathic scoliosis. Clinicians should remain alert for large spinal curvatures when
examining adolescents." However, other groups have different recommendations:

1. The Scoliosis Research Society recommends annual screening of all children age 10 to 14 years.
2. American Academy of Orthopedic Surgeons recommends screening girls at age 11 and again at age 13 years and screening boys once at age 13 or 14 years.
3. The American Academy of Pediatrics recommends scoliosis screening with the forward bending test at routine health supervision visits at ages 10, 12, 14, and 16 years (this recommendation is under review).
4. The Bright Futures guidelines recommends that clinicians note the presence of scoliosis during the physical examination of adolescents and children 8 years of age or older.
5. The Canadian Task Force on the Periodic Health Examination concludes that there was insufficient evidence to make a recommendation.
6. Scoliosis screening is required by law in some states.

The sensitivity, specificity, and positive and negative predictive value of screening tests depend on the degree of curve defined as abnormal, the training of the screener, and the prevalence in the population (Table 16.2). Properly trained clinicians using an inclinometer can accurately evaluate patients for their need for scoliosis radiographs. The Cobb angle serves as the reference for defining curve magnitude, but there is some intraobserver and interobserver variability (3 to 5 and 6 to 7 degrees, respectively).

<table>
<thead>
<tr>
<th>Screening Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flexometer</td>
<td>71.3%</td>
<td>71.3%</td>
</tr>
<tr>
<td>Inclinometer</td>
<td>96-99%</td>
<td>24-40%</td>
</tr>
</tbody>
</table>

**TABLE 16.2. Sensitivity and specificity of screening tests**

**Clinical Evaluation**

**History** The patient history should include the following:

1. Age
2. Pain: Most scoliosis in adolescents is painless and is diagnosed secondary to deformity. Pain requires a thorough evaluation for an identifiable cause.
3. Cardiopulmonary symptoms
4. Neurological symptoms
5. Past medical and surgical history
6. Delayed developmental milestones or poor academic performance
7. Family history of spine disorders
8. If previously diagnosed
   a. Age at diagnosis
   b. Progression
   c. Some measure of skeletal maturity (menarche for females)
   d. Interventions and their compliance

**Physical Examination** Evaluation of suspected scoliosis should be directed at the deformity, its cause, and complications.

1. Neuromuscular abnormalities including reflexes, strength, sensation, and cavus feet
2. Cardiopulmonary abnormalities
3. Skin including café-au-lait spots and hyperelasticity
4. Lower extremity abnormalities
   a. Cavus foot
   b. Leg length discrepancy
   c. Asymmetry of size or muscle bulk
   d. Hypermobility of joints
5. Sexual maturity stage
6. Back examination: given while the patient is wearing underwear and a gown with the back exposed
   b. Shoulder height
   c. Iliac crest height
   d. Tips of scapula: The distance from the tip of the scapula to the midline.
   e. Lateral angle symmetry: The angle is measured with the apex at the axilla and the sides being the lateral border of the torso and the inside edge of the arm.
   f. Forward bending: The Adam forward bend test is performed with the patient bending forward with arms extended and knees straight. The examiner looks for asymmetry of the trunk when the teen is examined from the front or back, as well as rib humps or paraspinal prominence. This examination may also demonstrate inflexibilities of the spine or painful spasms. The test may not be specific for spinal deformity, because truncal asymmetry caused by unequal trunk muscles may yield a false-positive test.

**Radiographs** The standard for scoliosis evaluation is standing anteroposterior and lateral scoliosis radiographs using the 14- × 36-inch cassette taken at 6-foot distance with gonad shields.

**Radiographic Indications of Nonidiopathic Scoliosis**

1. Congenital anomalies
   a. Hemivertebrae
   b. Wedge vertebrae
   c. Block vertebrae
2. Length of the curve
   a. Short angular curves: Consider neurofibromatosis
   b. Long curves: Neuromuscular etiologies
3. Interpedicular distance: Must be compared with age norms; may indicate dysraphism or syringomyelia

**Recommendations for Evaluation of Idiopathic Scoliosis** Radiographic studies are recommended for adolescents with the following findings:

1. Suspicious forward bending examination
2. Inclinometer angle of trunk rotation (ATR) greater than 5 degrees (correlates with angle of greater than 20 degrees on radiograph)
3. Interval follow-up for previously diagnosed scoliosis
   a. If less than 25 degrees
      - Skeletally immature: Check every 6 months
      - Skeletally mature: No further checks
   b. If greater than 25 degrees
      - Skeletally immature: Check every 3 to 4 months
      - Skeletally mature: Check every year for 3 to 5 years and then every 5 years because of the risk of progression

Magnetic resonance imaging (MRI) is recommended for adolescents with the following findings:
1. Left major thoracic curve: These are associated (in 33% of patients) with occult syrinx, Arnold-Chiari malformation, spinal cord tumor, and neuromuscular disorder.
2. Neurologic findings (including café-au-lait spots) on physical examination.

Treatment

Major treatment options include observation, bracing, and surgery (Table 16.3). Treatment choices in adolescent idiopathic scoliosis often involve consideration of factors such as the teen’s physiological (not chronological) maturity, curve magnitude and location, and the potential for progression.

<table>
<thead>
<tr>
<th>Curve size degree</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-5</td>
<td>Serial observation</td>
</tr>
<tr>
<td>25-40 (with progression 5-10 degrees)</td>
<td>Bracing</td>
</tr>
<tr>
<td>&gt;40</td>
<td>Surgery + fusion</td>
</tr>
<tr>
<td>&gt;50</td>
<td>Surgery + fusion</td>
</tr>
</tbody>
</table>

**TABLE 16.3. Management of adolescent idiopathic scoliosis**

**Brace Therapy** Brace therapy should be considered in the skeletally immature adolescent who has 30 to 40 degrees of curvature or who has had rapid change of 5 degrees in 6 months and a total curve greater than 25 degrees. The primary goal of brace management is to stop curve progress, and this modality should not be expected to reverse the degree of curve. Many patients lose some of the improvement that is obtained by the bracing treatment over time. There are a number of different bracing systems (e.g., Boston, Milwaukee) that have been used traditionally to try to prevent the necessity of surgery. It is recommended to wear these braces for 23 hours a day, and despite a high incidence of noncompliance there are better outcomes than would be expected from the natural history alone. Newer braces (e.g., Charleston, Providence) are designed to be worn only at night. They have shown promise in patients with milder curves. Among those treated with the Charleston brace, 66% had less than 5 degrees progression and only 16% required subsequent surgery at long-term follow-up (Price et al., 1997). These newer braces should help to decrease the psychosocial impact and increase the effectiveness of brace treatment in adolescents. Although there are short-term psychological effects of bracing, they appear to resolve in the long term. Brace removal for participation in sports is recommended. The end point of brace use usually occurs with skeletal maturation of the adolescent, as indicated by no further changes in height and evidence of skeletal maturity on radiography.

**Surgery** Surgical management is recommended for skeletally immature patients who have either a curve greater than 40 degrees, uncontrolled pain with a negative evaluation for a primary lesion, or a thoracic lordotic curve (because of the impact on pulmonary function).

In the skeletally mature patient with a curve greater than 50 degrees, surgery is an option depending on the risk for progression. The two major goals of surgery are to prevent spine deformity progression and to diminish spinal deformity. Those who require surgery have been shown to have a more negative body image than either patients using bracing or control subjects (Noonan et al., 1997). The surgical method most used to correct idiopathic adolescent scoliosis is a posterior spinal fusion with instrumentation and bone grafting. In most surgical cases, postoperative casting and bracing are not required for idiopathic scoliosis and the teen is quickly ambulatory and home within 5 to 7 days after surgery.

**Exercise** Although exercises may be an adjunct to bracing, they have no role by themselves in the management of scoliosis.

**Electrical Stimulation** There is no role for this modality in the treatment of scoliosis.

**SCHEUERMANN DISEASE (JUVENILE KYPHOSIS)**

Kypnosis of the thoracic spine in adolescents is often attributed to poor posture. Although this type of poor posture is corrected when the teen is instructed to “sit up straight,” Scheuermann disease is not. Scheuermann disease is a relatively rigid, abnormally increased kyphosis of the thoracic and thoracolumbar spine that does not correct with hyperextension of the spine. The kyphosis results from anterior vertebral wedging in the affected area of the spine. The matrix of the vertebral plate has characteristic changes in the ratio of collagen to proteoglycans that leads to an altered ossification process. There are many competing theories about the etiology of Scheuermann disease, including excessive stress, genetic causes, and congenital malformation of the vertebral plates. The prevalence is estimated to be from 0.4% to 8.0% in the adolescent population (equal incidence in males and females), with a peak onset at about 12 to 13 years of age.

**Definition and Classification**

The radiographic diagnosis of Scheuermann disease is made on lateral scoliosis radiography. The criteria include

1. More than 5 degrees of anterior wedging of at least three adjacent vertebral bodies
2. Narrowing of the intervertebral disc space
3. Irregularity of the vertebral endplates
4. More than 45 degrees of kyphosis (normal is 20 to 45 degrees), measured by the Cobb method

Scheuermann disease: Abnormal protrusions of intervertebral disc material into the vertebral bodies, causing radiolucent pockets bulging from the disc spaces—are usually seen. Classification of Scheuermann disease is by the location of the kyphosis. Thoracic curves are by far the most common (75%), and thoracolumbar curves are more likely to progress even past skeletal maturity. “Lumbar Scheuermann disease” is a different disease from true Scheuermann disease in that it does not have the anterior wedging of the vertebral bodies.

**Clinical Manifestations**

1. Back deformity: Presenting complaints are usually concerns about the back deformity including
   a. Thoracic kyphosis with secondary lumbar hyperlordosis
   b. Protruberant abdomen
   c. Forward rounded shoulders
d. Forward protrusion of the head

These deformities are not corrected with forward bending or prone hyperextension maneuvers.

2. Pain: Aching pain that is usually localized to the apex of the thoracic kyphosis after prolonged sitting or exercise may also be present (20% to 70%). The incidence of pain increases as the kyphosis progresses. Those with a thoracolumbar kyphosis are more likely to have pain as a presenting complaint.

3. Scoliosis: There is an increased incidence of scoliosis (20% to 30%), spondylolysis and spondylolisthesis (32%), and thoracic disc herniation.

Differential Diagnosis

In addition to the adolescent with poor posture, there are a number of other processes that must be considered before diagnosing Scheuermann disease.

1. Infectious spondylitis must be considered especially in immunocompromised patients, intravenous drug abusers, and those at risk for tuberculosis. Computed tomography and MRI are helpful in diagnosing and determining the extent of the disease.

2. Compression fractures can be confused with Scheuermann disease from a radiographic perspective, but there is usually a history of trauma or a metabolic bone disease.

3. In congenital kyphosis type II, there are bony bridges between consecutive vertebrae.

4. Juvenile ankylosing spondylitis is classically seen more frequently in males and is characterized by the loss of lumbar flexibility and painful enthesitis (at points of ligament or tendon insertion) of the feet or knees, or both. In addition, the concentrations of rheumatoid factor (RF) and anti-nuclear antibody (ANA) are normal, and 90% of those with juvenile ankylosing spondylitis test positive for HLA-B27.

5. Other diagnoses include osteodystrophies (Morquio and Hurler disease), tumors, and postsurgical deformity.

Natural History

Most patients with less than 75 degrees of kyphosis have a benign progression of their disease, with some deformity, back pain, and fatigue. Patients with Scheuermann disease worked at jobs involving lighter physical work than the jobs of controls and had more back pain, but this did not affect their self-esteem or their ability to function in society (US Preventive Services Force, 1996).

Treatment

Treatment is controversial, and not all patients require intervention. There are three main therapies for patients with Scheuermann disease: exercise, bracing, and surgery.

1. Exercise programs to strengthen the low back and improve hamstring and pectoral flexibility are used for patients with smaller curves (<50 degrees). These programs have not been shown to improve vertebral wedging or the degree of kyphosis.

2. Bracing treatment has been used for patients with greater than 50 degrees of kyphosis and has resulted in some short-term improvement, but most of the improvement is lost during long-term follow-up out of the brace. The Milwaukee brace (which includes the cervical ring) has been recommended for thoracic kyphosis at or above T7. An underarm orthosis can be used for those with lower thoracic or thoracolumbar kyphosis.

3. Operative correction (spinal fusion) is rarely indicated. It is used only for adolescents with curves greater than 80 degrees that cannot be controlled with brace treatment and for skeletally mature patients with chronic pain and large curves (usually over 70 degrees).

WEB SITES

For Teenagers and Parents

http://www.scoliosis-assoc.org/, Scoliosis Association, Inc., an international information and support organization.

http://webmd.lycos.com/content/dmk/dmk_article_40074, WebMD information for patients.

http://www.vh.org/Patients/HB/Ortho/Peds/Scoliosis/Questions/scoliosis.html, University of Iowa frequently asked questions.


For Health Professionals and Patients


http://www.vh.org/Providers/Textbooks/AIS/090CurveProgression.html, Virtual Hospital Web site article.

REFERENCES AND ADDITIONAL READINGS


Osgood-Schlatter Disease

Etiology
During development of the anterior tibial tubercle, a small ossification center develops in the largely cartilaginous tubercle. With developing muscle mass during puberty, this small area comes under great traction stress from the patellar tendon, and small fragments of cartilage or of the ossification center can be avulsed. The problem is often aggravated by activities that involve quadriceps femoris contraction, such as running and jumping, with resultant additional stress on the tubercle.

Epidemiology
1. Males have a greater prevalence than females.
2. Mean age of onset: Onset usually coincides with the period of rapid linear growth.
   a. Females: 10 years, 7 months
   b. Males: 12 years, 7 months

   In a study by Yashar et al. (1995), the average chronological age in adolescents with Osgood-Schlatter disease was the same as the average bone age. This is in contrast to slipped capital femoral epiphysis, in which skeletal maturation is often delayed.

Clinical Manifestations
1. Pain and soft tissue swelling over the tibial tubercle.
2. Point tenderness and warmth over the tibial tubercle.
3. Normal knee joint with full range of motion.
4. Unilateral involvement more common than bilateral involvement.
5. Duration usually several months but can last longer.

Diagnosis
1. History: Pain at the tibial tubercle, aggravated by activity and relieved by rest.
2. Physical examination: Tenderness and swelling of the tibial tubercle.
3. Radiograph: Not essential for diagnosis but taken only to eliminate the possibility of other processes. The radiograph may reveal soft tissue swelling anterior to tibial tubercle and/or fragmentation of the tibial tubercle.
Therapy

1. **Explanation:** Careful explanation of the condition to the adolescent and to his or her parents is essential to alleviate fears and misconceptions.
2. **Restriction of activity:** If symptoms are mild, the patient may continue in the chosen sport. If symptoms are more severe, curtailing of running and jumping activities for 2 to 4 weeks is usually sufficient.
3. **Immobilization:** If symptoms are severe or fail to respond to restriction of activity, immobilization with a knee immobilizer for a few weeks is effective.
4. **Steroids:** Corticosteroid injections are contraindicated, because they may weaken the tendon.
5. **Nonsteroidal antiinflammatory drugs and ice:** These may provide symptomatic pain relief.
6. **Knee pads:** Knee pads should be used for activities in which kneeling or direct knee contact might occur.
7. **Surgery:** Surgery is rarely indicated. If the patient continues to have symptoms after skeletal maturity, he or she may have a persistent ossicle that does not unite with the rest of the tibial tubercle. Simple excision of this fragment may bring relief.

**Prognosis**

The prognosis is excellent, but adolescents should be informed that the process might recur if excessive activity is performed. Usually when growth is completed, the problem stops, leaving only a prominent tubercle. The patient may still have difficulty kneeling on the prominent tubercle even into adulthood. Rarely, patients with Osgood-Schlatter disease may fracture through the tibial tubercle.

**PATELLOFEMORAL SYNDROME (CHONDROMALACIA PATELLAE)**

Patellar femoral syndrome, patellar malalignment syndrome, or chondromalacia patellae is a frequent cause of knee pain among adolescents, accounting for as much as 70% to 80% of knee pain problems in females and 30% in males. It is also the leading cause of knee problems in athletes. The term patellar malalignment syndrome is commonly used today, because it is a better descriptive term for part of the pathophysiology of the condition. The condition has traditionally been known as chondromalacia patellae. However, this term implies actual softening and damage to the patellar articular cartilage, whereas many individuals have no changes in their articular surface.

**Etiology**

Patellar malalignment syndrome often is a result of abnormal biomechanical forces that occur across the patella. Even in an individual with normal anatomy, the force that occurs in this area, especially when the body is supported with one leg and the knee is partially flexed, is tremendous. Abnormal forces can result from:

1. **Quadriceps femoris muscle imbalance or weakness or abnormality in the attachment of the vastus medialis**
2. **Altered patellar anatomy, such as a small or high-riding patella**
3. **Increased femoral neck anteversion, with associated knee valgus and external tibial torsion, which increases lateral stress on the patella**
4. **Increased Q angle—the angle found between a line drawn from the anterosuperior iliac spine through the center of the patella and a line from the center of the patella to the tibial tubercle (normal: less than 15 degrees)**
5. **Variations in the patellar facet anatomy**

Chondromalacia patellae implies actual degeneration of the patellar cartilage, similar to the process of cartilage degeneration that can occur elsewhere in the body. The diagnosis can be made definitively only with direct visualization of the cartilage, usually by arthroscopy. This condition is characterized microscopically by cartilage softening and swelling, then fissuring and fibrillation. The cause of this cartilage degeneration is multifactorial, involving one or more of the following:

1. **Direct trauma:** especially common with injuries to the anterior aspect of the patella from a fall on the flexed knee
2. **Indirect trauma:** frequent repetitive activity involving knee flexion and extension (e.g., hiking, jogging, callisthenics)
3. **Abnormal anatomic variations accompanied by resultant abnormal biomechanical forces affecting the patellofemoral joint, as previously described**
4. **Disease affecting cartilage systemically (e.g., rheumatoid arthritis, sepsis, recurrent hemarthrosis)**

**Epidemiology**

Patellar malalignment syndrome is common in both male and female athletes. There is a higher prevalence among females in the general population but a higher prevalence among males in athletic populations.

**Clinical Manifestations**

1. The pain of chondromalacia patellae or patellofemoral syndrome is characterized by the following
   a. Peripatellar or retropatellar location
   b. Relation to activity: The pain usually increases with activity such as running, squatting, or jumping, and decreases with rest. Often the pain is most acute immediately on getting up to start an activity after a period of sitting.
   c. Insidious onset
   d. Positive movie or theater sign: Prolonged sitting with flexed knee is uncomfortable.
   e. Pain is often severe on ascending or descending stairs.
   f. Knees may buckle or give out, especially when going up or down stairs.
   g. Crepitus or a grating sensation may be felt, especially when climbing stairs.
2. **History of injury to the patella area may be present.**
3. **Symptoms are bilateral in one third of adolescents.**
4. **Two thirds of patients have at least a 6-month history of pain.**
5. **Quadriceps femoris muscle imbalance or weakness or abnormality in the attachment of the vastus medialis**
6. **Increased femoral neck anteversion, with associated knee valgus and external tibial torsion, which increases lateral stress on the patella**
7. **Increased Q angle—the angle found between a line drawn from the anterosuperior iliac spine through the center of the patella and a line from the center of the patella to the tibial tubercle (normal: less than 15 degrees)**
8. **Variations in the patellar facet anatomy**
9. **Insidious onset**
10. **Increased femoral neck anteversion, with associated knee valgus and external tibial torsion, which increases lateral stress on the patella**
11. **Increased Q angle—the angle found between a line drawn from the anterosuperior iliac spine through the center of the patella and a line from the center of the patella to the tibial tubercle (normal: less than 15 degrees)**
12. **Variations in the patellar facet anatomy**
13. **Insidious onset**
14. **Increased femoral neck anteversion, with associated knee valgus and external tibial torsion, which increases lateral stress on the patella**
15. **Increased Q angle—the angle found between a line drawn from the anterosuperior iliac spine through the center of the patella and a line from the center of the patella to the tibial tubercle (normal: less than 15 degrees)**
16. **Variations in the patellar facet anatomy**
17. **Insidious onset**
18. **Increased femoral neck anteversion, with associated knee valgus and external tibial torsion, which increases lateral stress on the patella**
19. **Increased Q angle—the angle found between a line drawn from the anterosuperior iliac spine through the center of the patella and a line from the center of the patella to the tibial tubercle (normal: less than 15 degrees)**
20. **Variations in the patellar facet anatomy**
21. **Insidious onset**

**Diagnosis**

The diagnosis is usually made by compatible history and physical examination. Radiographs usually are of little help but are important in evaluating for other...
conditions. They should include anteroposterior, lateral, tunnel, and tangential views (also known as skyline or Merchant views). Other conditions causing knee pain in the adolescent include meniscal lesions, Osgood-Schlatter disease, tendinitis of the patellar tendon, recurrent dislocation of the patella, and osteochondritis dissecans. In addition, hip disorders often manifest as vague knee or thigh pain, especially slipped capital femoral epiphysis.

**Treatment**

1. Control of symptoms
   a. Rest and avoidance of activities such as running, jumping, climbing, and squatting that produce patellofemoral compression forces: Walking and swimming are good exercises to continue. If the condition is severe, then immobilization with a cylinder cast or knee immobilizer may be necessary.
   b. Nonsteroidal antiinflammatory agents
   c. Warm soaks
2. Muscle strengthening: Most patients benefit from a formal physical therapy evaluation and can then be moved to a home program. As soon as tolerated, muscle-strengthening exercises should be performed once a day. Initially, these should be isometric quadriceps exercises. Strengthening of the vastus medialis is particularly important. The exercises should be done with a weighted boot or on an exercise machine with the knee in full extension. The weight should be held for 5 seconds and repeated in three sets of 10 repetitions. Stretching of the hamstrings is an essential component of most therapy programs.
3. Graduated running: After symptoms are controlled and 30 pounds of weight are held, a graduated running program can be instituted. Ice may be helpful immediately after exercise.
4. Maintenance: When the condition is under control, a maintenance program of quadriceps and hamstring exercises should be done two to three times a week. Most adolescents respond to nonoperative management.
5. Knee braces: Use of these in patients with patellofemoral syndrome is controversial. Theoretically, they help keep the patella from moving too far laterally. However, because the patella moves in various planes, knee braces are best used in patients with lateral subluxation visible on examination. The knee brace is not a substitute for muscle-strengthening exercises.
6. Taping the knee: Although this may reduce friction, results are also controversial.
7. Footwear: Athletic shoes have improved in past decade, but the quality and age of the athletic shoes are more important than a particular brand name.
8. Arch supports and custom orthotics: These can be helpful to some patients. Custom orthotics are expensive but in some patients may be helpful.
9. Surgery: This is considered a last resort for patellofemoral pain. Occasionally a “lateral release” is appropriate if the problem is clearly related to excessive lateral tracking and other measures are unsatisfactory. This involves cutting the lateral retinaculum to reduce the amount of lateral pull.

**SUBLUXATION AND DISLOCATION OF THE PATELLA**

Subluxation and lateral dislocation of the patella are prevalent in the second and third decades of life, with a slightly higher prevalence in females. Instability of the patellofemoral joint may permit the patella to dislocate partially out of the intercondylar groove. The patella then snaps back into place, in contrast to a complete dislocation, in which the patella continues to complete lateral dislocation. These episodes usually occur while the quadriceps is contracting with the knee in flexion and the foot is planted on the ground. Symptoms include pain, giving way of the knee, a popping or grinding sensation, and swelling. Physical findings may be similar to those of chondromalacia patellae, which is frequently associated with recurrent subluxation or dislocation. Subluxation of the patella can mimic the clinical picture of a torn meniscus. Complete dislocation is usually a dramatic event and is easy to diagnose, with the patella visible on the lateral side of the joint. Patellar dislocations often reduce spontaneously, so the physician may not see the patella in a dislocated position.

**Treatment**

1. Subluxation of the patella
   a. Prescribe a quadriceps strengthening program (detailed in previous section).
   b. Temporarily restrict or modify activity.
   c. Use a patellar sleeve to stabilize the patella. Alternately, the patient may be taught to do McConnell taping to stabilize the patella.
   d. Perform surgery only if all other therapy fails.
2. Dislocation of the patella
   a. Reduction often occurs spontaneously.
   b. Gentle straightening of the knee by lifting the foot may allow the patella to slide into place. Sedation may be necessary to effect a reduction.
   c. Radiographs should be taken because the dislocation and reduction generate sufficient force to fracture bone in up to 10% of cases.
   d. Immobilize the knee in a knee immobilizer for 3 weeks, followed by range-of-motion and quadriceps-strengthening exercises. Use of a patellar stabilizing brace or McConnell taping is often effective.
3. Recovery after dislocation: In some nonoperative treatment, therapy and bracing is successful, but when the patient has more than one dislocation, surgical intervention may be needed to realign the extensor mechanism.

**OSTEOCHONDRTIS DISSECANS**

Osteochondritis dissecans is a condition of focal avascular necrosis in which bone and overlying articular cartilage separate from the medial femoral condyle or, less commonly, from the lateral femoral condyle. The peak incidence is in the preadolescent age group. The clinical course and treatment vary according to the age at onset, with children and young adolescents having a better prognosis than older adolescents and adults.

**Etiology**

The exact cause is unknown. Postulated factors include the following.

1. Trauma: Most patients do not report a single traumatic event. There is often a long history of exercise and participation in sports. It is theorized that earlier participation of children in sports has led to the earlier appearance of osteochondritis lesions (Cahill, 1995).
2. Ischemia: Obstruction of blood supply as a cause has been postulated, but evidence is lacking.
3. Epiphyseal development: In younger patients with osteochondritis, an accessory nucleus in the epiphyseal area may make the femoral condyle more vulnerable to trauma. Some adolescents have variants of normal growth that may simulate osteochondritis dissecans on radiography, causing the condition to be overdianosed in younger adolescents.
4. Heredity: Heredity plays a minor role in some patients.

**Clinical Manifestations**

1. Onset in childhood and early adolescence
   a. History
      • An intermittent, nonspecific knee pain usually related to activity is a common symptom.
      • Extension movements of the knee may cause swelling and soreness.
      • Symptoms are often present for months to years before consultation.
   b. Examination
      • The adolescent may walk with the tibia in external rotation on the affected side.
      • Localized tenderness over the site of the lesion is best detected with the knee in 90 degrees of flexion and palpation of the femoral condyles. Most lesions are in the posterior femoral condyle, so the knee must be flexed 90 degrees to be able to palpate the osteochondritis dissecans lesion.
      • A small, firm, movable mass may be palpable in the joint, indicating the presence of loose bodies.
      • Quadriceps atrophy may be present.
      • Effusion is present on rare occasions.
      • Check for a positive Wilson sign: Flex the knee to 90 degrees; internally rotate the tibia on the femur and extend the knee slowly with the tibia in internal rotation. If the sign is positive, pain will occur as the knee reaches 30 degrees of flexion. This pain is often relieved by external rotation of the tibia.
      • Thirty percent of individuals have bilateral lesions.
2. Onset in late adolescence or young adulthood
   a. History
• Either insidious onset or a history of specific injury with immediate onset of pain and swelling may be present.
• Locking or acute swelling may occur if a bone fragment becomes loose.
• Usually unilateral involvement is seen.
• Synovial effusion is more common in younger patients than in older ones.

b. Examination: The findings are similar to those found in younger patients, except that young adults have a higher prevalence of swelling and unilateral involvement.

3. Radiological picture: Anteroposterior, lateral, and tunnel views should be taken. X-ray examination often reveals a well-circumscribed area of subchondral bone separation from the remaining femoral condyle by a crescent-shaped radiolucent line. The separate bone may appear sclerotic or fragmented. The lesion may not be seen on a standard anteroposterior view; it may be best appreciated on the tunnel view. The medial femoral condyle is involved in 75% to 85% of cases, while approximately 15% of cases involve the lateral femoral condyle. In addition to the femoral condyle, the patella, femoral head, and talus may be involved.

4. Juvenile versus adult osteochondritis (Table 17.1).

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Juvenile</th>
<th>Adult</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>5-14 yr</td>
<td>15-20 yr</td>
</tr>
<tr>
<td>Epiphysis</td>
<td>Open</td>
<td>Closed</td>
</tr>
<tr>
<td>Radiation</td>
<td>30% of cases</td>
<td>20% of cases</td>
</tr>
<tr>
<td>Grav.</td>
<td>Inclined</td>
<td>Acute</td>
</tr>
<tr>
<td>Injury</td>
<td>Minor</td>
<td>Major</td>
</tr>
<tr>
<td>Prognosis</td>
<td>Excellent</td>
<td>Fair</td>
</tr>
<tr>
<td>Complications</td>
<td>Sedentary</td>
<td>Occasionally</td>
</tr>
</tbody>
</table>

TABLE 17.1. Juvenile versus adult osteochondritis

Treatment

1. Children and younger adolescents
   a. Restrict symptom-producing activities.
   b. Immobilize with cast or knee immobilizer if symptoms are severe.
   c. Advise regarding use of isometric quadriceps-strengthening exercises.
   d. Aspirin and nonsteroidal antiinflammatory agents are not routinely used but are useful if pain or effusion is present.
   e. Healing usually occurs within 6 to 12 months.
   f. If there is a free fragment, surgical intervention is required.

2. Older adolescents and adults: Orthopedic consultation is necessary for possible arthroscopy or surgery for either removal or internal fixation of the fragment. Surgery is particularly important in teenagers with progressive fragment formation, increasing bony sclerosis, or articular changes.

SLIPPED CAPITAL FEMORAL EPIPHYSIS

Slipped capital femoral epiphysis is a disease in which the anatomical relationship between the femoral head and neck is altered secondary to a disruption of the epiphyseal plate.

Etiology

The femoral head slips posteriorly, inferiorly, and medially on the femoral metaphysis. This occurs through the hypertrophic cell layer of the epiphysis. The condition tends to occur in adolescents because of

1. The increased weight burden at adolescence.
2. A decreased resistance to the added weight burden secondary to a shift in the femoral epiphysis from a horizontal to an oblique position.
3. Increased stress to an area that has not reached bony maturity.

A chronic, gradual slip accounts for 80% or more of cases of slipped capital epiphysis during adolescence and is usually related to the combination of obesity and slow maturation. Acute slips occur secondary to severe trauma, such as a fall or an automobile accident, and are more common in younger children than in adolescents. Most cases of slipped capital epiphysis are unrelated to an endocrine disorder, although the disease has been associated with hypopituitarism, hypogonadism, and hypothyroidism. Endocrine abnormalities are often associated with bilateral slips, and they occur more often in the extremes of the adolescent age group (before age 9 or after age 16 years).

Epidemiology

1. Sex: The prevalence is two to four times greater in males than in females.
2. Incidence: A sample study (Kelsey, 1971) found the incidence in Connecticut per 100,000 individuals younger than 25 years of age to be 7.79 for African-American males, 6.68 for African-American females, 4.74 for white males, and 1.64 for white females.
3. Season: Onset of symptoms occurs more frequently in spring and summer.
4. Average age at onset: Usually symptoms occur shortly before or during the period of accelerated growth (10 to 13 years of age in girls, 12 to 15 years in boys).
5. Hip involved: Left hips are affected more commonly in males; no difference is noted in females. Approximately 20% of patients present with a bilateral slip. The contralateral hip should always be examined and visualized radiographically.
6. Weight of affected patients: Approximately 88% of patients are obese, with 50% at or above the 95th percentile of weight for age and the 97th percentile of weight for height.
7. Bone age: Seventy percent of affected patients have skeletal maturation that is delayed by 6 months or more.

Clinical Manifestations

1. Symptoms
   a. Pain: Pain is localized to hip or groin in 80% of patients. However, pain may be strictly in the thigh or knee, referred from the obturator nerve. Some patients present with a painless limp.
   b. Click in the hip occurs.

2. Signs
   a. Internal rotation is diminished and adduction of hip is decreased.
   b. Decreased flexion of the hip is present.
   c. The affected leg often is held in slight external rotation and adduction.
   d. With passive hip flexion, the femur abducts and externally rotates; the leg falls into a “figure 4” position.
   e. Limp: A limp is present in 50% of patients; the adolescent with acute slippage may not be able to bear weight on the affected extremity.
   f. The family often notices a change in gait. The foot externally rotates during ambulation.

Diagnosis

1. History and physical examination: Consistent signs and symptoms are present. The condition should be considered in any adolescent with hip or knee pain or a limp.
2. Radiographical changes: Anteroposterior and frog-leg lateral roentgenograms of the pelvis should be taken.
a. In a normal anteroposterior radiograph of the hip, a line drawn on the superior edge of the femoral neck intersects the epiphysis; in a slip, the epiphysis falls below this line (Fig. 17.1).

Fig. 17.1. In the normal hip on the left, a line drawn on the superior femoral neck intersects the proximal femoral epiphysis. In the hip on the right with a slipped epiphysis, the epiphysis lies completely below a line drawn on the superior femoral neck.

b. Earlier and more subtle slips are seen on the frog-leg lateral views better than on the anteroposterior views. More advanced slips show the obvious slippage inferiorly and posteriorly of the femoral head epiphysis on both anteroposterior and frog-leg lateral films. A "true lateral" view can also be helpful.

c. Early changes include epiphyseal widening and rarefaction.

3. Bone scan: A bone scan may show increased uptake at the involved epiphyseal plate.
4. Magnetic resonance imaging (MRI): MRI demonstrates increased blood flow at the epiphysis.

The vast majority of cases of slipped capital femoral epiphysis can be diagnosed with plain radiographs. Bone scan and MRI are rarely needed.

**Treatment**

Orthopedic referral is required, because surgery is the only reliable treatment. Further slippage can be prevented by the introduction of threaded screws across the epiphyseal plate in situ. (Reduction of the slip is seldom, if ever, indicated.) The condition should be treated promptly, because greater slippage leads to a worse prognosis. Avascular necrosis can occur with acute, large slips. Premature degenerative joint disease is a frequent late development in many patients with severe, chronic slips, even after fixation. For moderate and severe cases, corrective osteotomies can be performed when the growth plate has closed to improve gait and range of motion.

**TARSAL COALITION**

**Definition**

Tarsal coalition is a congenital abnormality that results in a partial or complete fusion between two bones of the foot. The fusion may be fibrous, cartilaginous, or bony. It is the most common cause of a painful, stiff, flat foot after the age of 8 years.

**Etiology**

Tarsal coalition appears to result from a lack of differentiation of mesenchymal tissue in the foot. The condition may be inherited as an autosomal dominant trait.

**Epidemiology**

1. Prevalence in the United States is about 1%.
2. The condition is bilateral in 50% to 60% of patients, but the contralateral side may be asymptomatic.
3. Presentation: Pain manifests between 8 and 12 years of age for calcaneonavicular coalitions, between 12 and 15 years for talocalcaneal coalitions. Although this is a congenital condition, pain does not begin until these later years because the coalition begins to ossify at this age.

**Clinical Manifestation**

1. Patients often complain of a recurring “ankle sprain.”
2. Pain is often felt in the lateral ankle, especially in the sinus tarsi.
3. The heel is generally in valgus.
4. The patient has a rigid, flat foot. The peroneal tendons are often in spasm, leading to the term “peroneal spastic flat foot.”
5. There is lack of hindfoot motion.

**Diagnosis**

The diagnosis should be suspected in the preteen or teenage patient with insidious or sudden onset of pain in the midfoot to hindfoot associated with a lack of motion in the subtalar joint.

1. Physical examination: The most striking finding is the almost complete lack of inversion and eversion of the subtalar joint. The patient is unable to walk on the lateral border of the foot. Tenderness is often found in the sinus tarsi. The sinus tarsi is the conical-shaped cavity located between the anterosuperior surface of the calcaneus and the inferior aspect of the neck of the talus.
2. Radiographs: If a coalition is suspected, anteroposterior, lateral, 45-degree oblique, and axial (Harris) views of the calcaneus should be obtained.
3. Computed tomography (CT) and MRI: If the history and physical examination are consistent with a coalition but it cannot be demonstrated on plain films, CT or MRI may demonstrate the coalition. MRI is more useful in demonstrating fibrous coalitions. More than one coalition may be present in the same foot.

**Treatment**

1. Patients who have minimal symptoms or who have only incidental radiographic findings do not require treatment. Longitudinal arch supports may be sufficient to relieve symptoms.
2. When patients have significant symptoms, a short leg walking cast for 3 to 4 weeks, followed by the use of a University of California Berkeley Laboratory (UCBL) orthosis may eliminate the symptoms.
3. If conservative treatment fails, resection of the coalition with interposition of fat or muscle is indicated. Some coalitions of the talocalcaneal joint are so large that they cannot be successfully resected and arthrodesis may be required.

"GROWING PAINS"

Pain in the lower limbs is not uncommon among children and younger adolescents. Many causes are possible, including

1. Trauma: Fracture, dislocation, contusion
2. Infection: Osteomyelitis, septic arthritis, abscess, cellulitis
3. Vascular causes: Hemophilia, sickle cell anemia, hemangioma
4. Congenital conditions: Tarsal coalition, dysplasia of hip
5. Slipped femoral capital epiphysis
6. Osgood-Schlatter disease
7. Osteochondritis dissecans
8. Chondromalacia patellae
9. Rheumatic disease: Juvenile rheumatoid arthritis, polymyositis
10. Leukemia

Most of these causes are well delineated by history, physical examination, and appropriate laboratory tests. However, “growing pains” may be difficult to define and diagnose, and it is a diagnosis of exclusion. Some practitioners question the existence of “growing pains.”

Etiology

The cause is unknown, but implicated factors include rapid growth, puberty, fibrositis, weather, and psychological factors.

Epidemiology

The prevalence of growing pains is reported at between 4% and 50% of children and adolescents. A study of 2,200 schoolchildren revealed a prevalence of 12.5% in boys and 18.4% in girls (Oster, 1972). The prevalence of growing pains increases after age 5 years and peaks at age 13 years in boys and 11 years in girls.

Clinical Manifestations

1. Pain
   a. Intermittent pain or ache usually localized to the muscles of the legs and thighs: The most common sites are the front of the thighs and calves and behind the knees. Less commonly involved sites include the back, shoulder, arm, and groin.
   b. Bilateral pain is usually present.
   c. Pain usually occurs late in the day, in the evening, or at night.
2. No loss of mobility
3. No tenderness, erythema, or swelling
4. No fever or symptoms of systemic disease
5. Normal laboratory studies and normal findings on radiography

Diagnosis

There is no simple approach to a definite diagnosis. A thorough evaluation should include:

1. A consistent history of no symptoms of systemic disease
2. Normal findings from physical examination
3. Normal laboratory findings including normal complete blood count level, sedimentation rate, and x-rays (other tests such as rheumatoid factor and an antinuclear antibody as clinically indicated)

Treatment

Conservative therapy involving reassurance, heat, massage, and use of nonsteroidal antiinflammatory medications or aspirin is usually sufficient.

WEB SITES

For Teenagers and Parents

http://www.vh.org/Patients/IHB/FamilyPractice/AFP/June1995/Knee.html. Virtual Hospital from University of Iowa—information sheet on Osgood-Schlatter disease.

For Health Professionals

http://pedclerk.bsd.uchicago.edu/osgoodSchlatter.html. Case presentation from University of Chicago on Osgood-Schlatter disease.

REFERENCES AND ADDITIONAL READINGS

Back pain (in particular, lower back pain) is one of the most common complaints among adult patients and the most common cause of disability in individuals younger than 45 years of age. Back pain is unusual in prepubertal and young adolescent patients, middle and older adolescents frequently experience back pain, although many never seek medical attention.

**PREVALENCE**

The prevalence of backaches increases with age, with the lowest prevalence in children and adolescents. However, back pain, particularly lower back pain, can be relatively common in older adolescents. This has been well demonstrated in numerous studies:

3. Burton et al. (1996): Followed a class of English schoolchildren for 4 years. The annual incidence of low back pain rose from 11.8% at age 12 to 21.5% at 15. Lifetime prevalence was 11.6% at age 11, increasing to 50.4% at age 15. By age 15, 59% of the students described their pain as recurrent. Only 15.6% of patients who experienced back pain during the study sought treatment.
4. Olsen et al. (1992): Back pain was experienced by 30.4% of 1242 American adolescents aged 11–17. Of those with back pain, one third had a history of needing to restrict their activity, and 7.3% sought medical attention for back pain.

**ETIOLOGY**

The etiology of back pain varies with age. The younger the individual, the more likely that back pain is not related to musculoskeletal strain. Back pain can be divided into the following categories:

1. Mechanical disorders
   a. Overuse syndromes—ligamentous or muscle strain
   b. Herniated nucleus pulposus
   c. Slipped vertebral apophysis
   d. Postural disorders
   e. Vertebral compression fractures
2. Developmental disorders
   a. Spondylolysis and spondylolisthesis
   b. Scheuermann disease
3. Inflammation and infections
   a. Discitis and vertebral osteomyelitis
   b. Disc calcification
   c. Rheumatological conditions including ankyllosing spondylitis and reactive spondyloarthropathies such as Reiter syndrome
   d. Sickle cell disease and sickle cell pain crisis
   e. Epidural abscess
4. Neoplastic processes
   a. Vertebral column or spinal canal
   b. Muscle
5. Psychogenic causes

**EVALUATION**

In most individuals with acute back pain the cause is never known, but the course is almost always benign and self-limited. However, to eliminate the possibility of a more serious condition, a thorough history and physical examination are basic requisites.

1. History.
   a. General history
      • Characteristics of the pain, including severity, type, onset and duration, prior treatment and limitations, exacerbating and alleviating maneuvers.
      • History of trauma
      • Athletic and work history
      • Systemic symptoms: Fever, malaise, iritis, urethritis, arthritis
      • Family history of rheumatological disease
      • Neurological symptoms, including bladder or bowel changes
   b. History for specific conditions
      • Tumors: Back pain occurring at rest, especially at night, is a common feature of vertebral involvement with a neoplastic process. Constant back pain, associated neurological deficits, and rigidity of the spine on attempted movement may be associated with tumor or infection. Other suggestive historical information includes prior history of a malignant tumor and unexplained weight loss.
      • Spondylolysis and spondylolisthesis: Back pain may radiate to buttocks or thighs. There may be a history of hyperextension activities of the spine, such as gymnastics or ballet.
      • Infection: Discitis and osteomyelitis of a vertebra can lead to significant back pain. Malaise and severe stiffness are common complaints.
      • Spondyloarthropathy: Back pain from spondyloarthropathies is associated with insidious onset, worsening of symptoms in the morning and with rest, decrease in symptoms with activity, onset before 30 years of age, and pain that persists longer than 3 months.
      • Scoliosis: Back pain is not usually a feature of scoliosis and should suggest the possible presence of another disorder.
      • Severe back pain in an adolescent is more likely associated with a pathological condition than a muscular strain and should be more carefully evaluated.
2. Physical examination: This should include examination in the standing, sitting, and supine positions.

a. Standing position
   - Asymmetry: Check for pelvic or leg length discrepancies.
   - Curvatures: Check for kyphosis or scoliosis and perform forward-bending examination.
   - Inspect the spine from behind the patient and from the side.
   - Percuss spine for local tenderness.
   - Check gait, including heel and toe walking.
   - Range of motion: Most adolescents should be able to bend to within 15 cm of their toes regardless of the problem. Individuals with paraspinal muscle spasms tend to arch their lumbar area while bending the spine at the hips.
   - Midline defects: Midline defects including dimpling, hypertrophic, hemangioma, cutaneous nevi, and soft tissue masses may be related to an underlying spinal abnormality such as spina bifida, lipoma, or diastematomyelia.

b. Sitting position
   - Test knee and ankle reflexes and Babinski sign.
   - Test muscle strength of lower extremities.
   - Perform distraction leg-raising test: Ask the patient to straighten his or her leg while seated. Patients with a disc problem arch backward in tripod position to take pressure off the sciatic nerve. Results of this test should correlate with results of straight leg-raising in supine position.

c. Supine position
   - Measure leg length from anterosuperior iliac spine to medial malleolus. A difference of more than 2.5 cm should be evaluated.
   - Check for muscle atrophy by measuring the girth of each leg at fixed measured distances above and below the patella.
   - Perform a sensory examination. Remember to check for "saddle anesthesia," which is indicative of a cauda equina syndrome.
   - Straight leg-raising test: The patient should lie on the back with one leg flexed at the hip and knee and the sole of that foot on the table as the other leg is tested. Pain radiating down the back of the second leg when this leg is lifted and the knee is extended is a positive test. An unequivocal test is indicated when pain occurs when the angle between the back of the thigh and the table is less than 60 degrees. Pain when this angle is greater than 60 degrees may be caused by muscular irritability. The examiner can also lift the leg to the point of pain and then lower the leg 5 degrees and dorsiflex the foot. This stretches the sciatic nerve and is another sign of nerve impingement. If pain occurs in the opposite leg during lifting one leg, a positive crossed straight leg-raising sign is present. This has been highly correlated with a herniated disc.
   - Femoral stretch test: With the teen facing down and the knees straight, lift one leg backward, extending the hip but keeping the knee straight. This test stretches the femoral nerve, and pain radiating into the anterior thigh indicates L2, L3, and L4 nerve root irritation.
   - In patients with chronic back pain a rectal examination is indicated to look for decreased sphincter tone, which suggests pressure on nerve roots from a tumor or herniated disc. In addition, the circumstances of the upper and lower legs should be measured to look for muscle atrophy.
   - Red flags on examination include fever, other systemic signs, major motor weakness in lower extremities, focal vertebral tenderness, very limited spinal range of motion, and neurological findings persisting beyond 1 month.

3. Specific conditions
   - Etiology
     - Spondylolysis and Spondylolisthesis
       - Successful and includes activity restriction, nonsteroidal antiinflammatory drugs (NSAIDs), and physical therapy. Epidural steroid injections may also be helpful. Disc excision is reserved for those patients with persistent neurologic deficit or failure of nonoperative therapy to produce pain relief.

   - Herniated Nucleus Pulposus
     - Disc herniations in an adolescent are most likely to result from an acute event. Acute onset of back pain, especially with pain radiating into the legs, raises the possibility of a disc herniation. Magnetic resonance imaging (MRI) is the study of choice for the diagnosis of a herniated disc. Nonoperative treatment is often successful and includes activity restriction, nonsteroidal antiinflammatory drugs (NSAIDs), and physical therapy. Epidural steroid injections may also be helpful. Disc excision is reserved for those patients with persistent neurologic deficit or failure of nonoperative therapy to produce pain relief.

   - Slipped Vertebral Apophysis (Apophyseal Ring Fracture)
     - This injury is unique to the pediatric population. It is a fracture through the junction of the bony vertebral body and its cartilaginous endplate (apophysis). The apophysis herniates into the canal along with fragments of disc. It is usually seen in adolescent boys who are involved in sports participation or heavy lifting. Symptoms are acute onset of back pain, often with sciatica. Plain films may show a bony fragment in the canal. In this case, a computed tomographic scan, rather than MRI, shows the pathology better, because it shows cortical bone more clearly. Treatment parallels that for a herniated disc. Nonoperative therapy may bring resolution of symptoms. Neurological compromise or failure of nonoperative therapy is an indication for operative decompression.

   - Spondylolysis and Spondylolisthesis
     - Spondylolysis is a defect of the pars interarticularis, a posterior element of the spine. Spondylolisthesis is the forward slippage of one vertebra on another, almost always L5 on S1. These two conditions often occur together, and they represent the most common cause of chronic low back pain in the adolescent. Adolescents who participate in athletic endeavors involving large extension forces across the low back are at high risk. These include gymnasts, ballet dancers,
wrestlers, and down linemen.

**Clinical Symptoms** Back pain localizes in the low back, sometimes radiating into the buttocks. Pain is aggravated by sporting activities or heavy lifting. Hamstring tightness is a hallmark of both of these conditions. A noticeable lordosis may be seen with significant spondylolysis.

**Diagnosis** The radiologic diagnosis of spondylolysis is simple. Standing lateral films, especially the “spot lateral” film, centered on the L5–S1 junction, demonstrates the slip.

Diagnosis of spondylolysis is more difficult. Occasionally it can be seen on lateral films, but more commonly it is demonstrated on oblique films that bring out the profile of the pars interarticularis. A bone scan with single-photon emission computed tomography (SPECT) imaging is the most sensitive study for spondylolysis. It demonstrates the early stages of a stress fracture, before the pars interarticularis actually breaks.

**Treatment** Treatment of spondylolysis in the adolescent is largely nonoperative. Modification of activities, especially avoiding hyperextension, along with NSAIDs, physical therapy, and possibly a lumbar sacral orthosis have a high rate of success. Patients who fail nonoperative therapy can have an in situ fusion or repair of the pars defect.

Treatment of spondylolisthesis depends on the percentage of the slip. Those patients with greater than 50% slippage require fusion. If the slip percentage is less than 50%, treatment can be nonoperative with close monitoring to see whether the slip progresses. Seitsalo et al. (1991) demonstrated that 90% of slip progression had occurred in their patients by the time of the first radiographic study. If pain is refractory to nonoperative measures or progressive slippage is demonstrated, in situ fusion has a high success rate.

**Scheuermann Kyphosis**

Scheuermann kyphosis (see Chapter 16) is a rigid kyphosis of the thoracic spine. Patients often present with pain at the apex of their deformity. The cause remains undetermined. It is most often seen in adolescent males who are involved in heavy lifting. Physical examination reveals a sharp, rigid kyphosis that is best seen from the side when the patient is in the forward bend position. Diagnosis is made on standing lateral films of the entire spine. Radiographs reveal irregularities of the endplates, wedging of the vertebral bodies, Schmorl nodes (invagination of disc material into the vertebral body).

Treatment depends on the degree of kyphosis, the amount of growth remaining, and the amount of pain. Physical therapy is often helpful in improving symptoms. Brace treatment can obtain some correction of the kyphosis, but only in the skeletally immature patient. For severe kyphosis or intractable pain, spinal fusion with instrumentation may be required.

Atypical or lumbar Scheuermann disease is a painful condition of the lumbar spine. Unlike classic Scheuermann disease, there is no kyphosis, but radiographs show irregularities of the lumbar spine endplates. Treatment is almost always nonoperative. Therapy, NSAIDs, and occasional use of an orthosis usually give relief of symptoms.

**Discitis and Vertebral Osteomyelitis**

Once thought to be separate entities, these two conditions are probably part of the same disease spectrum. Patients present with back pain, malaise, and fever. The physical examination is remarkable for spine rigidity.

Plain radiographs may reveal disc space narrowing and irregularities of the vertebral body. Laboratory work in a suspected infection should include a complete blood count with differential (often normal), erythrocyte sedimentation rate (usually elevated), and blood culture (which reveals an organism in 41% of cases). In the early stages of infection, plain films may be normal. Technetium bone scanning shows increased uptake in the endplates. However, MRI has the benefit of establishing not only the presence of infection but also the amount of vertebral involvement and the possible presence of an epidural abscess.

Treatment of these conditions is somewhat controversial. Because the great majority of these infections are caused by *Staphylococcus aureus*, the need for vertebral or disc aspiration is unclear. Most patients respond to bed rest and intravenous antibiotics and are then switched to oral antibiotics and mobilization with a thoracolumbosacral orthosis (TLSO). There is a body of literature that has shown successful treatment of discitis with immobilization without antibiotics. The recurrence rate appears to be higher when antibiotics are not used. Decompression of these infections is usually not needed unless there is neurological compromise or a failure to respond to nonoperative management. The possibility of tuberculosis infection should not be overlooked.

**Neoplasms**

**Bone Tumors** Most spinal neoplasms in the adolescent are benign. Osteoid osteoma and osteoblastoma are the most common bone tumors in the pediatric population. Patients may present with a painful scoliosis and back pain that is dramatically improved with NSAIDs. Pain may occur at the same time every day. The neurological examination is usually normal. During painful episodes the patient may manifest a stiff spine. Because of their small size, osteoid osteomas may be difficult to see on plain films. They show intense uptake on bone scans, and computed tomographic scanning helps delineate the exact location of the tumor. The patient may be treated with long-term NSAID use, because these tumors usually resolve spontaneously after skeletal maturity is reached. However, this may mean years of NSAID use, and the family may be unwilling to follow this course. The tumor can be successfully treated with surgical excision, but that may be difficult depending on its location.

**Acute Leukemia** Back pain may be the presenting symptom of acute leukemia and may be the cause of vertebral collapse. About 90% of patients who present with vertebral collapse have an abnormal peripheral smear. Early leukemic infiltration of the vertebral body causes osteopenia before collapse. Treatment of leukemia is with chemotherapy; a TLSO helps prevent further deformity of the spine.

**Spinal Cord Tumors** Spinal cord tumors are most common in the first decade of life. Pain is usually severe and unrelenting. Constant back pain, pain that awakens the teen at night, painful scoliosis, and neurologic findings are all warning signs for spinal cord tumors. As many as 90% of patients with spinal cord tumors demonstrate rigidity of the spine. MRI is the imaging modality of choice when a spinal cord tumor is suspected. Astrocytomas and ependymomas are the most common spinal cord tumors.

**Psychogenic Pain**

This is an important cause of back pain, but it must be considered a differential diagnosis and the mental health history should be consistent with this diagnosis. Further evaluation may be required in some teens, including plain films, bone scan, MRI, and laboratory evaluation. However, not all patients need all of these tests, particularly if the history and examination are consistent with psychogenic pain. The possibility of back pain referred from other anatomical locations (e.g., pyelonephritis, endometritis) must not be overlooked. When symptoms exceed physical findings, clinical suspicion should be raised. These patients need help, and they will benefit from being referred to appropriate health care providers.

**General Recommendations**

Sample recommendations and back exercises for individuals with chronic or recurrent musculoskeletal back pain are discussed in the following sections.

**General Recommendations: Acute Back Strain**

1. Never bend from the waist only; bend at the hips and knees.
2. When standing for a prolonged period, place one foot on a step to reduce back strain.
3. Never lift a heavy object higher than the waist.
4. Never sleep on the abdomen; it is best to sleep on one side with hips and knees bent. Use a firm mattress or put a 3/4-inch plywood board under a soft mattress.
5. When sitting, place the spine up against the back of the chair, and be sure one or both knees are higher than the hips.
6. Shoes should have low heels.

**Back Exercises** Back exercises should be begun slowly and increased slowly over time.

1. **Knee hug**
   a. Lie on back with pillow under head; inhale.
   b. Slowly raise knees to chest.
   c. Clasp knees with hands and hold for count of 10.
   d. Repeat three times and build slowly to 20 repetitions per day.

2. **Cat backs**
   a. Get on all fours on the floor.
   b. Arch back up like a cat and then down as far as possible.
   c. Repeat three times and build slowly to 20 repetitions per day.

3. **Leg lifts**
   a. Lie on stomach with arms at sides.
   b. Raise each leg in turn, to a height of 1 foot off the floor.
   c. Start with 3 lifts of each leg and build slowly to 20 per day.

4. **Back flatteners**
   a. Lie on back, knees raised, with feet on floor and hands over head.
   b. Tighten stomach and buttock muscles at the same time to flatten back against floor; hold for a count of 10.
   c. Repeat three times and build slowly to 20 repetitions per day.

5. **Shoulder lifts**
   a. Lie flat on stomach with arms at side.
   b. Lift both shoulders 6 inches off the floor.
   c. Start with three lifts and build slowly to 20 per day.

6. **Posture check**
   a. Stand with back to wall; press heels, rump, shoulders, and head against wall.
   b. Move feet forward and bend knees so that the back slides down a few inches.
   c. Tighten abdominal and buttock muscles so lower back is flat against wall.
   d. Hold this position and walk feet back so that the back slides up the wall.
   e. Standing straight, walk away from wall and around the room.

7. **Sit-ups (should be started several weeks after exercises have begun)**
   a. Lie on back with knees bent.
   b. Sit up to an upright position while grasping knees.
   c. Return to starting position.
   d. Start with three repetitions and build slowly to 20 per day.

**WEB SITES**

For Teenagers and Parents


http://www.spine-health.com/, Site for information on spine health.

REFERENCES AND ADDITIONAL READINGS


Deyo RA, Rainville J, Kent DL. What can the history and physical examination tell us about low back pain? JAMA 1992;268:760.


In 1997, half (49.5%) of students nationwide had played on sports teams sponsored by their school during the preceding 12 months (Youth Risk Behavior Surveillance [YRBS], 1998). This was an increase from 1991 (43.5%) and a decrease from 1995 (50.3%). In addition, 38.3% of students had played on sports teams run by organizations unaffiliated with their school during the preceding 12 months.

Beyond organized sports participation, physical inactivity is a priority health risk behavior identified by the Centers for Disease Control and Prevention. Two of the Objectives from Healthy People 2010 (Department of Health and Human Services [DHHS], 2000) highlight the need for improved physical activity in youth:

1. Increase the proportion of adolescents in grades 9 through 12 who engaged in moderate physical activity for at least 30 minutes on 5 or more of the previous 7 days from 20% in 1997 to 30%.
2. Increase the proportion of adolescents in grades 9 through 12 who engage in vigorous physical activity that promotes cardiorespiratory fitness 3 or more days per week for 20 or more minutes per occasion from 64% in 1997 to 85%.

All health care professionals caring for adolescents should be familiar with these data and objectives and should understand the medical issues associated with organized athletics or adopting a more active lifestyle. This chapter addresses several aspects of sports medicine for adolescents, including the preparticipation sports examination (PSE), the classification of sports, physical maturation and sports participation, conditioning, treatment and rehabilitation of injuries (including head and neck injuries), return to play after injury, exclusion from sports for special conditions, osteopenia in female athletes, drug and supplement use, and game site equipment.

THE PREPARTICIPATION SPORTS EXAMINATION

The American Medical Association (AMA) Guidelines for Adolescent Preventive Services (GAPS) recommends that a comprehensive health evaluation should occur at least every other year during the adolescent period. In addition, the American Academy of Pediatrics (AAP) recommends that adolescents involved in strenuous activity should have a sports-specific examination on entry into both junior and senior high school and that this examination should be updated with an annual questionnaire emphasizing recent injuries and any health condition affecting sports participation. In our opinion, this annual questionnaire, if completed by the teen alone, is inadequate, because recall by young athletes is not a sensitive indicator of injuries in the past year. Preferably, the interim form should be completed by parent and teen together. However, this is not always successful or practical because the student must have annual physician clearance to continue participating, which requires the physician to review an updated health history and perform the directed physical examination discussed later.

The PSE should not be used only for those who are preparing to enter an organized sports season. Rather, it can be a model for providing medical clearance for an adolescent who simply wants to adopt a more healthy lifestyle (see later discussion of physical fitness and conditioning).

The PSE is not a comprehensive health maintenance visit that addresses important psychosocial topics such as drug use, sexual activity, violence, and mental health as well as organic disease complaints, screening tests, and immunizations. However, the PSE is used in place of an annual comprehensive health evaluation by many teens, which is not consistent with the AMA and AAP guidelines. Establishing mechanisms wherein teens receive annual comprehensive health maintenance visits and PSEs should be a priority. This discussion assumes that the athlete is receiving regular maintenance care in addition to the PSE.

The PSE has evolved over several decades. Thirty years ago it consisted of asking the teen, “Are you okay?,” listening to the heart, and checking for a hema. The second-generation examination included identification of significant past medical problems, a limited examination, and a sport-clearance statement. The next major step came in 1992, when five organizations (the American Academy of Family Physicians, AAP, American Medical Society for Sports Medicine, American Orthopedic Society for Sports Medicine, and American Osteopathic Academy of Sports Medicine) produced a monograph on the preparticipation physical evaluation (Preparticipation Physical Evaluation, 1996). Updated in 1996, it has been used extensively as one model for this examination. In 1996, the American Heart Association (AHA) further developed recommendations specifically concerning cardiovascular screening (Maron et al., 1996).

Objectives

The major objective of the PSE is to identify those musculoskeletal and other medical conditions that could be worsened by sports participation. An additional
objective is to provide liability protection and satisfy insurance regulations for both institutions and sports governing bodies. Specifically, the examination should be
designed to meet the following objectives:

1. To identify medical problems that would preclude some forms of sports participation because of the risk of life-threatening complications during participation
2. To remove unnecessary restrictions on participation in sports for some youth
3. To identify and rehabilitate old injuries
4. To identify and treat medical conditions other than musculoskeletal conditions that could interfere with performance or be complicated by exercise or sports participation
5. To advise athletes with medical conditions which sports or exercises they can or cannot participate in
6. To fulfill legal requirements

A classification of sports based on the risk of collision with participation is provided in Table 19.1; a classification based on the static and dynamic demands of the sport and the increased risk of injury if syncope should occur is provided in Table 19.2. These tables are useful guides in addressing the fifth objective listed above. Table 19.3 is provided as a guide for participation by diagnosis and is discussed later. Figure 19.1 is a sample preparticipation sports evaluation form used at Texas Children’s Hospital. In addition, the PSE form developed by the American Academy of Family Physicians can be downloaded from their Web site (http://www.aafp.org/afp/20000815/765.html).

TABLE 19.1. Classification of sports by contact

<table>
<thead>
<tr>
<th>Contact Level</th>
<th>Example Sports</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>Soccer, Tennis</td>
</tr>
<tr>
<td>Moderate</td>
<td>Football, Basketball</td>
</tr>
<tr>
<td>High</td>
<td>Wrestling, Boxing</td>
</tr>
</tbody>
</table>

TABLE 19.2. Classification of sports based on peak dynamic and static components during competition

<table>
<thead>
<tr>
<th>Dynamic/Static</th>
<th>Example Sports</th>
</tr>
</thead>
<tbody>
<tr>
<td>High Dynamic</td>
<td>Long-distance running, Basketball</td>
</tr>
<tr>
<td>High Static</td>
<td>Swimming, Wrestling</td>
</tr>
<tr>
<td>Low Dynamic</td>
<td>Soccer, Golf</td>
</tr>
<tr>
<td>Low Static</td>
<td>Hiking, Bicycling</td>
</tr>
</tbody>
</table>

TABLE 19.3. Medical conditions and sports participation

Logistical Considerations for the Preparticipation Sports Examination

Ideally the PSE should occur 3 to 4 weeks before preseason practice begins, to allow time for evaluation and treatment of problems. Otherwise, athletes run the risk of presenting with an unrehabilitated injury that will keep them out of play for the first weeks of practice.

Medical History The medical history may be completed by the athlete and/or parents and reviewed by the physician before the examination. Parental input in completing the form is strongly recommended.

Ideally, the histories are reviewed with the team's athletic trainer present. For example, if the PSEs are done at the school, in the training room, the trainer can...
highlight last year's injuries. Alternatively, if the physician served as the team's physician in the previous year, the injury log that should be kept by the team physician and the trainer and the list of last year's injuries can be used for corroboration. Young athletes' recall of injuries during the previous year can be insensitive and nonspecific.

The history should be sports specific, relatively brief, and should assess for the following factors:

1. Past injuries that caused the athlete to miss a game or practice. The clinician may need to ask, for example: Have you ever had a muscle pull? A pinched nerve? A back injury? The clinician may have to ask the same question in different ways: Have you ever fractured a bone? Have you ever broken a bone? Some athletes think very concretely and may not know, for example, that a break and a fracture are different. Other athletes may not volunteer information if they think it will result in exclusion from sports participation.
2. Any loss of consciousness or memory occurring after a head injury
3. Previous exclusion from sports for any reason
4. Past or present conditions or illnesses requiring ongoing physician care
5. Prior surgery and sequelae
6. Allergies, asthma, or exercise-induced bronchospasm
7. Medications and supplements, used currently or in the past 6 months
8. Tetanus immunization
9. The menstrual history in females
10. A history of relatively rapid increase or decrease in body weight and the athlete's perception of current body weight.

In addition, the AHA recommends the following questions for cardiovascular screening (Maron, 1996):

11. Family history of premature death (sudden or otherwise)
12. Family history of heart disease in surviving relatives: significant disability from cardiovascular disease in close relatives younger than 50 years of age; or specific knowledge of the occurrence of certain conditions (hypertrophic cardiomyopathy, long QT syndrome, Marfan syndrome, or clinically important arrhythmias).
13. Personal history of heart murmur.
15. Personal history of excessive fatigability.
16. Personal history of syncope, excessive or progressive shortness of breath, or chest pain or discomfort, particularly with exertion.

Physical Examination

This should be a directed examination emphasizing the identification of medical problems that could worsen the athlete's performance or conditions that might be worsened by athletic participation. The PSE should deemphasize those aspects of the physical examination that would not influence whether an athlete can compete in a particular sport. This PSE philosophy is based on two principles:

1. Most athletes in the adolescent age group are healthy.
2. Most athletes have had previous medical evaluations (as discussed previously).

Many conditions that preclude participation in sports are identified in the preadolescent age group and are not subtle. For example, congenital heart disease and hemophilia have been detected before adolescence. However, subtle presentations of congenital defects or acquired diseases may go undetected. The most commonly detected abnormalities on PSEs are previously undetected or unrehabilitated musculoskeletal injuries. The annual PSE, especially for teenagers, should serve as quality control for the diagnosis and rehabilitation of injuries. With this in mind, the physical examination should include assessment of the following.

1. Height and weight: Used to estimate ideal body weight (IBW). Obesity, by itself, is not a reason for exclusion. However, the increased risk of heart illness and how that risk might be reduced must be mentioned to the athlete, parent, and coach.
2. Blood pressure and pulse: Blood pressure should be taken in the right arm with the athlete sitting. Athletes with hypertension should be evaluated further but not excluded from participation unless the hypertension is severe. Participation in sports for teens with hypertension is discussed later. Pulse can be as low as 25 bpm in highly trained aerobic athletes. A pulse in the 40- to 50-bpm range is routine and does not need evaluation if the athlete is asymptomatic.
3. Visual acuity and pupil equality: Teens with best corrected visual acuity less than 20/40 in one or both eyes should be referred for further evaluation but are not excluded from participation if protective eyewear is worn, in the author's opinion. It is important that anisocoria be noted before any closed head injury occurs.
4. Skin: Infections that are highly contagious (e.g., varicella, impetigo) should be sought. Players with these infections need to be noninfectious before returning to sports in which skin-to-skin contact is possible (Table 19.3).
5. Teeth and mouth: These are examined only if the history suggests an acute problem.
6. Cardiac examination: AHA recommendations for PSE for cardiac examination include the following (Maron, 1996).
   a. Perform precordial auscultation in supine and standing positions to identify heart murmurs consistent with dynamic left ventricular outflow obstruction.
   b. Assess femoral artery or lower extremity pulses to exclude coarctation of the aorta.
   c. Recognize the physical stigmata of Marfan syndrome.
   d. Assess brachial artery blood pressure in the sitting position.
   e. Document the presence of murmurs, clicks, or rubs. Normal or physiological murmurs are characteristically less than 4/6 systolic murmurs that decrease from intensity at rest to 2/6 or less in intensity at rest when the patient moves from the supine to the standing position.
7. Abdomen: Organomegaly is a disqualifying condition for collision/contact or limited contact sports in the author's opinion. A single kidney has traditionally been a contraindication for participation in contact sports.
8. Genitilia: An undescended testicle is not a contraindication to participation in contact sports; however, the player should wear a protective cup to protect the other, descended testis. An evaluation for the unidentified testis is necessary. Genitalia in females do not need examination unless there is a specific complaint.
9. Sexual maturation stage: Tanner stage assessment for sexual maturity is appropriate for male adolescents, but it has no role in deciding whether the teen should play a given sport. Tanner stage assessment is not indicated as part of the PSE in females unless the athlete has a specific complaint.
10. Orthopedic screening: Orthopedic screening should include muscle strength, range-of-motion and joint-stability testing, and evaluation for structural abnormalities of major joints (e.g., ankle, knee, shoulder, elbow, back). Screening examinations have been outlined by many organizations. The screening examination includes the following points (listed in parentheses are diagnoses to consider if the examination is abnormal):
   a. Body symmetry (Fig. 19.2): Observe the adolescent standing with arms at the sides, dressed in shorts and a shirt that allows inspection of the distal quadriiceps muscles and acromio-clavicular joints, respectively. Look for the following.
   - Head tilted or turned to side (consider primary cervical spine injury, primary or secondary trapezius or cervical muscle spasm)
   - Asymmetry of shoulder heights (trapezius spasm, shoulder injury, scoliosis)
   - Enlarged acromioclavicular joint (previous acromioclavicular joint sprain, shoulder separation)
   - Asymmetrical iliac crest heights (scoliosis or leg-length difference, back spasm)
   - Swollen knee; prominent ilial tuberosity (any knee injury, Osgood-Schlatter disease). Ask the athlete to contract ("tighten") the quadriiceps muscles, and look for atrophy of the vastus medialis obliques, a characteristic of any knee or lower extremity injury in which the athlete avoids normal use of that leg.

FIG. 19.2. Body symmetry. (From For the practitioner. Columbus, OH: Ross Products Division, Abbott Laboratories, 1981, with permission, copyright © 1981 Ross Products Division, Abbott Laboratories.)
b. Neck examination (Fig. 19.3): This is especially important in players with a previous history of neck injury and brachial plexopathy (referred to as “stingers” or “burners”).

![Figure 19.3: Neck symmetry.](image)

*FIG. 19.3. Neck symmetry. (From For the practitioner. Columbus, OH: Ross Products Division, Abbott Laboratories, 1981, with permission, copyright © 1981 Ross Products Division, Abbott Laboratories.)*

- Have the athlete do the following maneuvers:
  - Look at the floor (cervical flexion).
  - Look at the ceiling (cervical extension).
  - Look over the left shoulder, then over the right shoulder (left and right rotation, respectively).
  - Put right ear on right shoulder, then left ear on left shoulder (right and left lateral flexion).
- Look for limited or asymmetrical motion with the maneuvers listed (neck injury, congenital cervical abnormalities). *Any athlete with limitation of range of motion (ROM), weakness or pain on neck examination is excluded from contact sports until further evaluation.*

c. Shoulder examination (Fig. 19.4)

![Figure 19.4: Shoulder symmetry.](image)

*FIG. 19.4. Shoulder symmetry. (From For the practitioner. Columbus, OH: Ross Products Division, Abbott Laboratories, 1981, with permission, copyright © 1981 Ross Products Division, Abbott Laboratories.)*

- Have the athlete raise the arms from the side and touch the hands above the head, keeping elbows extended (full abduction). Look for the following:
  - Asymmetrical elevation of shoulder before arms reach 90 degrees (shoulder weakness due to a brachial plexopathy, shoulder instability, impingement syndrome).
  - Inability to raise arms to full abduction position (shoulder weakness due to brachial plexopathy, impingement syndrome, or apprehension from subluxation or dislocation).
- Have the athlete hold the arms in front of the body (forward flexion) and then to the side (90 degrees abduction); examiner pushes hands down. Look for asymmetrical atrophy or fasciculations of anterior and middle deltoid muscles and pain and/or weakness (may be indicative of a variety of shoulder problems).
- Have athlete put hands behind head (maximal external rotation/abduction). Look for the following:
  - Inability to get hand behind head (i.e., lack of external rotation of shoulder).
  - Apprehension or inability to pull the elbows, symmetrically, posterior to the shoulder (anterior subluxation or dislocation).
  - An athlete with limitation of motion should be evaluated further before clearance is granted for further participation.

d. Elbow and hand

- Have athlete extend and flex elbows with arms to the side (90 degrees abduction) (Fig. 19.5). Look for asymmetrical elbow extension or flexion (prior dislocation or fracture, osteochondritis dissecans).

![Figure 19.5: Elbow and hand symmetry.](image)

*FIG. 19.5. Elbow and hand symmetry. (From For the practitioner. Columbus, OH: Ross Products Division, Abbott Laboratories, 1981, with permission, copyright © 1981 Ross Products Division, Abbott Laboratories.)*

- With arms at sides and elbows flexed 90 degrees, have athlete pronate and supinate forearms (Fig. 19.6). Look for asymmetrical loss of motion (residual of forearm fractures, Little League elbow, osteochondritis dissecans of elbow). The cause of a limitation in ROM of the elbow should be established before a young athlete is cleared for participation, especially in throwing sports.

![Figure 19.6: Elbow and hand symmetry, continued.](image)

*FIG. 19.6. Elbow and hand symmetry, continued. (From For the practitioner. Columbus, OH: Ross Products Division, Abbott Laboratories, 1981, with*
In the same position, have athlete spread fingers, then make a fist (Fig. 19.7). Look for lack of finger flexion, swollen joints, finger deformities (residuals of sprains, fractures). Hand injuries should be evaluated and recommendations for sports participation based on the severity of the injury and the specific sport the athlete desires to play. Typically, the athlete is not excluded from participation unless there is a complication of a previous fracture or tendon rupture that needs further assessment.

FIG. 19.7. Elbow and hand symmetry, continued. (From For the practitioner. Columbus, OH: Ross Products Division, Abbott Laboratories, 1981, with permission, copyright © 1981 Ross Products Division, Abbott Laboratories.)

e. Back and leg observation

- Have the patient stand facing away from the examiner (Fig.19.8). Look for the following:
  - Asymmetry of waist (scoliosis, leg-length difference)
  - Elevated shoulder (scoliosis or trapezius spasm from shoulder or neck injury)
  - Depressed shoulder (scoliosis, muscle weakness)
  - Prominent rib cage (scoliosis)
  - Increased lordosis (spondyloysis, tight hip flexors, weak hamstrings)
  - Idiopathic scoliosis is not a contraindication for sports participation in almost all cases, unless the angle is severe (i.e., a Cobb angle greater than 45 degrees). If pain is present or there is a left major thoracic or lumbar scoliosis, then the diagnosis may not be idiopathic scoliosis and the definitive diagnosis should be established. This should include a neurological examination and spine magnetic resonance imaging (MRI).

- Have athlete bend forward at waist/hips (lumbar flexion) to touch toes (Fig.19.9). Look for the following:
  - Twisting or deviating of side (paraspinal muscle spasm)
  - Asymmetrical prominence of rib cage (scoliosis)
  - Inability to reverse the lumbar lordosis (spondyloysis, paraspinous muscle spasm caused by a chronic inflammatory condition such as ankylosing spondylitis)

- Have athlete stand straight and rise onto toes (Fig.19.10). Look for the following:
  - Asymmetry of heel elevation (calf weakness, restricted ankle motion from sprain or fracture)
  - Asymmetry of gastrocnemius (atrophy from incompletely rehabilitated ankle or leg injury)

FIG. 19.8. Back and leg symmetry. (From For the practitioner. Columbus, OH: Ross Products Division, Abbott Laboratories, 1981, with permission, copyright © 1981 Ross Products Division, Abbott Laboratories.)

FIG. 19.9. Back symmetry. (From For the practitioner. Columbus, OH: Ross Products Division, Abbott Laboratories, 1981, with permission, copyright © 1981 Ross Products Division, Abbott Laboratories.)

FIG. 19.10. Leg symmetry. (From For the practitioner. Columbus, OH: Ross Products Division, Abbott Laboratories, 1981, with permission, copyright © 1981 Ross Products Division, Abbott Laboratories.)
Asymmetry of elevation of forefoot or toes (weakness of ankle dorsiflexors, limitation of ankle motion from ankle fracture or sprain)
If asymmetry on toe or heel raising is detected, further evaluation and treatment is indicated before the athlete is cleared for full sports participation.
f. Hip and knee screening: Have athlete slowly assume a painless squatting position (buttocks on heels) (Fig. 19.11). If the athlete cannot do this, then further evaluation is indicated. Ask athlete to take four steps forward in this squatting position (“duck walk”), then turn 180 degrees in this squatting position and take four more steps. Look for the following:

- Asymmetry of heel height off ground (limited ankle motion or Achilles tendon tightness from tendinitis or injury).
- Asymmetrical knee flexion (i.e., difference in heel-to-thigh height from the rear view or inability to get down as far on one side as on the other) (knee effusion, residual limitation of motion from sprain, torn meniscus, quadriceps tightness or weakness, patellofemoral pain, Osgood-Schlatter disease).
- Pain at any point in the range of knee flexion. The cause of the pain should be established and the patient rehabilitated before allowing return to participation without restrictions.
- Ankle screening: Have the athlete hop 5 times as high as possible on each foot. Inability to do so suggests an undiagnosed or unrelievable lower leg, ankle, or foot injury. The ankle should be evaluated and fully rehabilitated before full participation is allowed.

**Laboratory Tests** Blood for hemoglobin and a dipstick of the urine for protein, glucose, and blood have been recommended as screening tests for athletic participation. Although the hemoglobin test may be indicated for teenagers who do not have ongoing general medical care, it is not recommended for teens who are receiving care regularly and are asymptomatic. There is a particular problem diagnosing anemia in highly trained aerobic athletes, who have a reduced hematocrit due to intravascular volume expansion but a normal oxygen carrying capacity. The urine dipstick test is not indicated in the absence of symptoms suggesting genitourinary tract dysfunction (Vehaskari and Rapola, 1982). Screening for iron deficiency in menstruating female athletes, especially those who run long-distance events, has been recommended. However, measurement of serum ferritin is advocated for some experts. However, empirical iron therapy may be the most cost-effective approach to preventing iron deficiency in healthy female athletes (Elliot et al., 1991).

Some centers use isokinetic or isotonic equipment to screen for muscle weakness, especially quadriceps and hamstring weakness or imbalance. This testing may be reasonable if the equipment is available to the athlete at no cost and to evaluate athletes with previous injuries where there is question about their recovery. However, its utility for screening all athletes has not been established. Muscle weakness can be determined through the history and physical examination.

Estimating body composition with the use of anthropometrical measurements (i.e., skin folds) is indicated in wrestling because prediction equations for minimum wrestling weights have been established. Use of skin-fold measurements as screening tests is not indicated for most athletes. Body weight measurement is sufficient for tracking patients who choose to gain or lose weight.

**CLEARANCE OR EXCLUSION FROM SPORT**

After the PSE, the patient should be given one of the following recommendations:

1. Full clearance for participation.
2. Participation with restrictions (give exact restrictions).
3. Clearance withheld pending further evaluation.

If there are restrictions on participation, these should be discussed with the athlete and a parent, coach, or guardian. Otherwise, the message to the athlete may be misinterpreted. If a physician is not going to clear an athlete for participation, the physician should be prepared to discuss the risks associated with continued participation. This requires an understanding of the medical problem and the demands placed on the athlete in that sport. For instance, a football lineman with an ankle sprain would be allowed to return to participation earlier than a ballet dancer. The physician must also consider the importance of this sport compared with another activity; some young athletes may be willing to switch to an activity with a lower risk of reinjury.

In any athlete with an abnormality noted on history or physical examination, the diagnosis accounting for the abnormality should be made and, ideally, successful treatment and/or rehabilitation should be accomplished before full sports participation is allowed. However, each case must be evaluated in the context of the age of the patient, the severity of the injury, the sport, how important the upcoming event is to the athlete (e.g., a state championship game versus a preseason scrimmage), and the sequelae if the athlete is injured further, among other variables. The overriding principle should be that the health of the athlete is always the priority. Parents may argue with medical advice about restrictions until recovery is almost complete, yet that does not change the physician's recommendation regarding return to play.

**Table 19.3** lists disqualifying conditions for sports participation recommended by the AAP. These are guidelines only; they may not apply in specific cases.

**Medical-Legal Issues and Exclusion from Sports Participation**

Athletes may seek to participate in a sport against medical advice, citing section 504(a) of the Rehabilitation Act of 1973, which prohibits discrimination against an athlete who is disabled if that person has the capabilities and skills required to play a competitive sport, or the Americans with Disabilities Act of 1990. Athletes with physical disabilities have successfully argued to retain their right to participate in professional athletics using these legal statues. However, an amateur athlete does not have an absolute right to decide whether to participate in competitive sports. Competition in competitive sports is generally considered a privilege, not a right. The case of Knapp vs. Northwestern University established that “difficult medical decisions involving complex medical problems can be made by responsible physicians exercising prudent judgment (which will be necessarily conservative when definitive scientific evidence is lacking or conflicting) and relying on the recommendations of specialist consultants or guidelines established by a panel of experts” (Maron et al., 1998). Physicians should clear athletes for participation according to generally agreed-on guidelines for participation with known medical conditions. As Table 19.3 indicates, each decision must be made on an individual basis, and there may not be expert panel guidelines for all conditions. Such guidelines do exist in many instances, however, an example being the 26th Bethesda Conference guidelines (see later discussion).

In addition to identifying which sports adolescents with special health care needs can participate in, the physician should assess current physical fitness activities for these youth. If the fitness activities are inadequate, and the youth and family are interested in more sports or fitness opportunities, the physician should either write an exercise prescription for more fitness activities or refer the teen to a physical therapist, physiatrist, exercise physiologist, or sports medicine clinic to design appropriate fitness activities. This should be done in conjunction with the adolescent's subspecialty physician. Youth with special health care needs have limited access to exercise facilities, and physicians should advocate to increase the availability of facilities for these adolescents.

**Management of Cardiac Conditions**

Any athlete complaining of true angina, syncope, presyncope, or palpitations while exercising, independent of the physical examination, should be excluded from...
Mitral valve prolapse (see Chapter 15)

a. Recent studies of mitral valve prolapse in healthy young adults without known cardiac disease report a prevalence of 0.6% to 2.7% (Flack et al., 1999; Gilon et al., 1999).

b. Mitral valve prolapse is generally a benign, asymptomatic condition. Patients can have palpitations, dizziness, supraventricular and ventricular arrhythmias, and chest pain, in which case they should be excluded from sports until fully evaluated. Sudden cardiac death in patients with mitral valve prolapse who die while there is no formal care to the author's knowledge, there have been 12 case reports to date. A mid-systolic click, with or without a late systolic murmur, is the auscultatory hallmark of this condition. However, patient reports of having mitral valve prolapse based on previous physician diagnosis were confirmed definitively on echocardiogram in only 0.45% of cases (Flack et al., 1999). Mitral valve prolapse is a clinical diagnosis not requiring echocardiography unless a murmur is present, in which case an echocardiogram is indicated to assess for mitral insufficiency.

c. Patients with mitral valve prolapse can participate in all competitive sports unless the following exist:

- A history of syncope documented to be arrhythmogenic in origin.
- A family history of sudden death associated with mitral valve prolapse.
- Repetitive forms of supraventricular and ventricular arrhythmias, particularly if exaggerated by exercise.
- Moderate to marked mitral regurgitation.
- Prior embolic event.

d. Athletes with mitral valve prolapse and any of the symptoms just listed may participate only in low-intensity sports (i.e., low static, low dynamic—see Table 19.2, Category I.A.).

2. Asymmetrical septal hypertrophy or hypertrophic cardiomyopathy

a. This is a primary abnormality of the myocardium manifested as an asymmetricaly hypertrophied, nondilated left ventricle in the absence of a cardiac or systemic disease that could cause left ventricular hypertrophy.

b. The mechanism of sudden death is not established, but a factor may be arrhythmia or myocardial ischemia related to myocardial bridging coronary arteries. This suggests a role for angiography in patients with hypertrophic cardiomyopathy (Yellen et al., 1998).

c. In many cases there are no symptoms before the sudden death. When present, the symptoms include exertional dyspnea, angina pectoris, fatigue, and/or syncope.

d. There is increased intensity of murmur from supine to standing.

e. There may be a family history of early sudden death, particularly related to exercise.

The recommendations for sports participation as follows:

- Athletes with hypertrophic cardiomyopathy should be evaluated by a cardiologist before participation.

- Recommendations for participation in sports as follows:

  - Athletes with the unequivocal diagnosis of hypertrophic cardiomyopathy should not participate in most competitive sports, with the possible exception of low-intensity sports (Table 19.2, Category I.A.). This applies to athletes with and without evidence of left ventricular outflow obstruction.

  - The recommendations for sports participation possibly may be more liberal for athletes 30 years of age or older, because the risk for sudden cardiac death may be reduced.

3. Coronary artery anomalies

a. These are rare overall, they should be suspected if the evaluation of syncope or anginal chest pain during exercise is normal.

b. They may lead to sudden death. Identification before death is difficult because many patients are asymptomatic before the sudden death event.

c. The cardiac examination is normal.

d. Cardiac consultation before participation is mandatory if this condition is suspected.

e. If coronary artery anomalies are identified, there is complete exclusion from sports participation.

4. Myocarditis

a. The incidence in young athletes is controversial because of the imprecise criteria for diagnosis.

b. It is a process characterized by an inflammatory infiltrate of the myocardium with necrosis and/or degeneration of myocytes. The disease progresses through active, healing, and healed phases, and arrhythmias may occur at any time.

c. Recommendations regarding sports participation are as follows:

- Athletes without a history of myocarditis should be excluded from all competitive sports for 6 months and then have their ventricular function evaluated at rest and with exercise before being allowed to return to sports.

- Athletes can return to sports when their ventricular function and dimensions are normal and clinically relevant arrhythmias are absent on ambulatory monitoring.

- There is no strong evidence for endomyocardial biopsy as a precondition for returning to sports participation.

- The athlete with an acute febrile illness characterized by fever and myalgia, it seems prudent to withhold that athlete from competition. However, there is no evidence that this precaution protects against sudden death. In athletes diagnosed with sudden death related to myocarditis, there is no clear temporal pattern between the febrile illness and the sudden death.

5. Systemic hypertension

a. Although hypertension is associated with an increased risk for sudden death and complex ventricular arrhythmias, to date it has not been incriminated as a cause of sudden cardiac death in young, competitive athletes.

b. Table 19.4 lists severe hypertension criteria by age group. Athletes with less than severe hypertension in the absence of end-organ damage and heart disease have no restrictions. Those with severe hypertension should be held out of sports, especially high-static sports (Table 19.2, Category III.), until their blood pressure is better controlled.

**Table 19.4. Classification of severe hypertension in adolescents**

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>SBP (mm Hg)</th>
<th>DBP (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10-11</td>
<td>120-129</td>
<td>60-69</td>
</tr>
<tr>
<td>12-13</td>
<td>130-139</td>
<td>70-79</td>
</tr>
<tr>
<td>14-15</td>
<td>140-159</td>
<td>80-89</td>
</tr>
<tr>
<td>16-17</td>
<td>150-169</td>
<td>90-100</td>
</tr>
<tr>
<td>18-19</td>
<td>160-179</td>
<td>100-110</td>
</tr>
</tbody>
</table>

Effectiveness of the Preparticipation Sports Examination

As mentioned, PSEs should not supplant regular comprehensive health examinations. In addition, other issues have been raised regarding these screening examinations.

Pfister et al. (2000) examined 1,110 National Collegiate Athletic Association (NCAA) colleges and universities and found that only 25% had forms that contained at least 9 of the recommended 12 AHA screening guidelines, and 24% contained 4 or fewer of these parameters. Maron (1998) also reviewed this issue and found that 40% of states have no formal screening requirement or approved history and physical examination questionnaires or forms. There is a significant need for national standardization of preparticipation screening that would also include the recommendations of the 26th Bethesda Conference (1994) for disqualification from
For resistance training, perform one set of 10 repetitions at 50% to 75% of the 10-rep max. Then perform a second set of 10 repetitions at 75% of the 10-rep max. Establish a 10-repetition maximum (i.e., the maximum weight that can be lifted 10 times), called the “10-rep max.”

Another issue is whether adult stature can be compromised by excessive sports activities and exercise in the prepubertal and pubertal years. Evidence for reduction in growth potential was reported for a group of adolescent gymnasts with a mean bone age of 12.3 ± 0.2 years who exercised an average of 22 hr/wk, compared with swimmers who exercised a mean of 8 hr/wk (Theintz et al., 1993). A second study suggested a negative impact of gymnastics training (10 to 20 hr/wk) on statural growth (Lindholm et al., 1994). However, the consensus in the literature is that short stature in gymnastics is related to selection bias rather than intense training (Daly et al., 2000; Damsgaard et al., 2000).

Intensity training before prepubertal and pubertal athletes has raised the concern that repetitive microtrauma to epiphyseal plates could affect ultimate adult height. Runners, figure skaters, and ballet dancers may train as hard as gymnasts. As for gymnasts, the consensus is that participation in sports and exercise does not have adverse effects on adult stature, timing of peak height, or rate of growth (Malina, 1994, 1995).

Physical Fitness and Conditioning

The proportion of high school students attaining the Healthy People activity objectives was discussed in the introduction. In addition, nationwide, 48.8% of students were enrolled in a physical education class and 27.4% of students attended such a class daily in 1997 (YRBS, 1998).

Fitness has four principal components:

1. Body composition
2. Cardiovascular fitness—maximum oxygen consumption (VO\textsubscript{2} max) being the gold standard
3. Strength
4. Flexibility

Body Composition

Although a common notion is that the fitness of today’s youth is poor, the only component of fitness that has been documented to have declined in the past three decades is body composition: obesity has increased in both teens and young adults (Gortmaker et al., 1987; National Heart, Lung, and Blood Institute, 1994).

The Healthy People 2010 Objective for overweight and obese children and adolescents is stated in Table 19.5 (DHHS, 2000).

<table>
<thead>
<tr>
<th>Percentage overweight/obese*</th>
<th>Baseline</th>
<th>Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>Objective</td>
<td>1990-1994</td>
<td>2010</td>
</tr>
<tr>
<td>10th</td>
<td>5-10</td>
<td>4-5</td>
</tr>
<tr>
<td>40th</td>
<td>15-25</td>
<td>10-15</td>
</tr>
<tr>
<td>50th</td>
<td>17-30</td>
<td>10-15</td>
</tr>
</tbody>
</table>

*For 10th and 40th perc. cut points used for this analysis, see Table 19.4.

TABLE 19.5. Healthy People 2010 objective 19-3: reduce the proportion of children and adolescents who are overweight or obese

More than one fourth (27.3%) of high school students nationwide thought they were overweight in 1997 (YRBS, 1993). Overall, female students were significantly more likely than male students to consider themselves overweight (33.5% vs. 22.2%, respectively). Overall, 39.7% of high school students were trying to lose weight during the 30 days preceding the YRBS survey. Female students were significantly more likely than male students to be trying to lose weight (59.7% vs. 23.1%, respectively).

With respect to reducing obesity, adolescents need both reduced caloric intake and increased energy expenditure (Hergenroeder and Phillips, 1994). More adolescents choose to diet than to exercise in an attempt to lose weight (YRBS, 1998).

Cardiovascular Fitness

If the goal is to improve cardiovascular fitness, a recommended training program would include aerobic exercise (continuous large muscle contractions that involve maintenance of 50% to 85% of the maximum heart rate) for 20 to 25 minutes, three or four times per week. Almost two thirds (83.8%) of high school students nationwide had participated in activities that made them sweat and breathe hard (i.e., vigorous physical activity) for at least 20 minutes on 3 or more of the preceding 7 days in the YRBS survey (1998).

Recently, emphasis has been placed on the health benefits of adopting a lifestyle approach to increasing activity, rather than a structured exercise program that may appeal least to sedentary adolescents. The Centers for Disease Control and Prevention and the American College of Sports Medicine guidelines recommend moderate-intensity physical activity on most days—either in a single session or in accumulated multiple bouts, each lasting 8 to 10 minutes (Pate et al., 1995). This involves common activities such as climbing stairs (rather than taking the elevator), brisk walking, doing more house and yard work, and engaging in active recreational pursuits.

The objective is to incorporate moderate physical activity into the lifestyle of those who are sedentary. For those who desire more intensive training, an exercise prescription should be tailored to the adolescent’s current level of fitness, desired level of fitness, motivation, and discipline to adhere to a training regime. Examples of aerobic activity are listed in Table 19.2. Categories B. and C. (moderate to high dynamic demands).

Strength

Approximately half (51.4%) of students nationwide had done strengthening exercises (e.g., push-ups, sit-ups, weightlifting) on at least 3 of the 7 days preceding the YRBS survey (YRBS, 1998). Regarding strength training, it is established that pubescent and pubescent subjects, like adults, can increase strength safely by resistance training. The training program should include close adult supervision, a preparticipation examination, and the use of well-maintained equipment (including sturdy shoes). Guidelines for resistance training in teens have been reviewed (Blimpke, 1993). Resistance training is associated with strength gains and neuromuscular adaptation in preadolescents, but it is not associated with muscle hypertrophy. Short-term resistance training has no effect on somatic growth or body composition and is not associated with increased injury rate or recovery or improved sports performance. Muscle hypertrophy will occur with resistance training in pubertal subjects. One standard resistance training program includes the following:

1. Establish a 10-repetition maximum (i.e., the maximum weight that can be lifted 10 times), called the “10-rep max.”
2. For resistance training, perform one set of 10 repetitions at 50% to 75% of the 10-rep max.
3. Then perform a second set of 10 repetitions at 75% of the 10-rep max.
Perform a third set at 100% of the 10-rep max, doing as many repetitions as possible.

Ideally, over 4 to 6 weeks, the exercises should then progress to three to four sets of 10 to 20 repetitions each, with addition of more weight when 20 repetitions are easily performed. One-repetition maximum weight lifting should be avoided because it is a mechanism of injury. The weight should be lifted through the entire ROM of the joint to avoid loss of flexibility. Warm-up and cool-down periods, which could include stretching exercises, should accompany each session. Three sessions per week on alternate days, allowing for a day of rest in between weight training sessions, is adequate. Gains in strength are more resistant to detraining than are gains in aerobic fitness, with up to 50% of the strength capacity retained for 1 year or longer in a person who is no longer training.

Flexibility

Nationally, 51.3% of students had done stretching exercises (e.g., toe touching, knee bending, leg stretching) on 3 or more of the 7 days preceding the 1997 YRBS survey. There is no study demonstrating that stretching in healthy, previously uninjured subjects prevents injuries. However, improving flexibility and strength in previously injured athletes decreases the likelihood of subsequent injuries. A flexibility program for injured joints should include pain-free stretches. If a healthy teen desires a stretching program, the following may be offered. The program should consist of stretching before and after each practice or competition. Each stretch should be held statically for 20 seconds, with three to five repetitions, and with a frequency of 3 to 5 days/wk after each exercise session.

INJURIES

Mobidity and Mortality

Although football has been associated with a high incidence of injuries, the number of injury events resulting in permanent disability or death has been on the decline since the 1970s. However, catastrophic injuries and fatalities still occur in high school and college football and in other sports. A full report is available at the Web site for the National Center for Catastrophic Sports Injury Research, www.unc.edu/depts/nccsi (click on: Annual Reports for 1982 through 2000). At this site the reader can find a breakdown of injuries and fatalities stratified by high school and college and by type of sport. The sports with the highest incidence of fatalities per 100,000 participants were swimming, ice hockey, football, and basketball; the list was similar for injuries. However, for female student-athletes, the leading cause of fatalities and catastrophic injuries between 1982 and 1997 was cheerleading.

Injury Prediction

Factors that may predispose the athlete to injury include

1. Weakness and/or inflexibility related to a previous injury.
2. Accelerated growth.
3. Training errors, including too-rapid increases in pace, distance, repetitions, or weight/resistance. Training errors are the most common factor in overuse injuries.
4. Inappropriate equipment (improper shoes, equipment not sized appropriately).
5. Change in the environment, such as running up hills or on a banked track instead of a flat surface.

Injury Prevention

There are several ways of preventing injuries:

1. Recognize and fully rehabilitate old injuries. The most important function of the PSE may be as a quality control point for injuries and rehabilitation during the past year (Keller et al., 1987).
2. In our opinion, stretching does not prevent injuries unless there is an identified deficit. Pope et al. (2000) confirmed this in a group of military recruits. The stretching methods described in that report are typical of a stretching routine for middle school and high school teams, but they are not ideal stretching exercises because they are done only once for 20 seconds. We recommend stretching of the lower extremities after weight-bearing exercise. This should include gastrocnemius, soleus, hamstrings, and quadriceps stretches, held for 20 seconds each, twice per muscle group.
3. See the discussion of the female athlete, later in this chapter, regarding prevention of acute knee injuries in female athletes.
4. Minimize environmental hazards to injury. Breakaway bases (bases in baseball and softball that are not anchored to the ground) have been associated with fewer and less significant ankle and lower-leg injuries from sliding. The incidence of serious neck injuries decreased after the trampoline was removed from gymnastics competition (National Institutes of Health, 1992).
5. Enforce rules to eliminate behavior that places athletes at high risk for injury. Serious neck injuries in football dropped significantly after spear tackling was made illegal in football (Mueller, 2001).

As mechanisms of injury are elucidated, preventive measures can be planned. This underscores the need for continued research into the causes of sports injuries. Recommendations about injury prevention that are not based on data are not useful. For instance, textbooks and sports medicine experts commonly speak of preseason strengthening and improved flexibility as methods of injury prevention. This has not been demonstrated in athletes except those who have preexisting injuries that require specific rehabilitation.

An excellent review of the approach to the epidemiology of youth sports was published as a result of the Conference on Sports Injuries in Youth (NIH, 1992).

Event Coverage and Sideline Decisions

In general, athletes should not be allowed to return to participation in sports until the following criteria have been satisfied:

1. The injury has been accurately diagnosed.
2. The examiner is reasonably certain that the injury will not significantly worsen with continued play.
3. The examiner is reasonably certain that continued participation (with the injury) will not result in a secondary injury.
4. The athlete has achieved full ROM and strength in the injured joint.
5. The athlete wants to return to play.

The following are examples of injuries or conditions that preclude returning to sports until the criteria just listed have been fulfilled:

1. Unconsciousness, however brief (see section on concussion)
2. Any neurological abnormalities
3. Obvious swelling
4. Limited ROM
5. Pain within the normal ROM
6. Bleeding
7. An injury the examiner does not know how to manage
8. Obvious loss of normal function
9. Athlete's lack of desire to return to play

The criteria and examples given need to be put into context. We have sent players back into football games with ankle sprains and upper-extremity injuries who did not strictly meet these criteria, but in each case the situation was assessed on the sideline with the athlete and a decision was made that the athlete could return to play. Strict adherence to these guidelines is unrealistic because a proportion of athletes would miss a significant part of the season if their injury recovery had to be back to 100% of baseline.

The physician caring for the athlete should be familiar with common injuries and their therapy. A few are discussed in the following section. For further information on specific injuries, see the reference section at the end of this chapter.
Concussion

**Definition** Concussion is a traumatically induced alteration in mental status that is not necessarily associated with loss of consciousness. There are approximately 300,000 sports-related traumatic brain injuries in the United States annually (Sosin et al., 1996).

**Grading and Evaluation** The following grading scale for concussion was proposed by Kelly et al. (1991):

| Grade 1 concussion: | Characterized by confusion without posttraumatic amnesia and without loss of consciousness |
| Grade 2 concussion: | No loss of consciousness but posttraumatic amnesia |
| Grade 3 concussion: | Loss of consciousness or altered mental status at 24 hours. |

The definitions of Kelly et al. are more conservative than those used before 1990 (Cantu, 1988):

- Grade 1: Confusion/amnesia for less than 30 minutes
- Grade 2: Plus or minus loss of consciousness but never greater than 5 minutes; if no loss of consciousness, posttraumatic amnesia lasting for longer than 30 minutes but less than 24 hours
- Grade 3: Loss of consciousness for longer than 5 minutes or altered mental status for longer than 24 hours.

Evaluation of concussion consists of a complete neurological examination, including a mental status examination.

**Second Impact Syndrome** The following guidelines are designed to prevent diffuse cerebral swelling with delayed catastrophic deterioration, a known complication of brain trauma. This has been postulated to occur after repeated concussive brain injury in sports and is known as the second impact syndrome (SIS). The current concussion management guidelines we use are contingent upon this assumption. However, McCrory (1998) reviewed the 17 cases of SIS reported in the literature as of the year 2000, using strict diagnostic criteria, and established that only 5 were probably SIS. He suggested that, because all of the SIS cases have been reported in North America, because player and teammate recall of traumatic brain injury during sports is poor, and because diffuse cerebral edema after initial traumatic brain injury has been described for more than 100 years, SIS may in fact be the cerebral response to the first traumatic brain injury.

All cases of SIS to date have been diagnosed in adolescent boys. Some authors have suggested a different mechanism of cerebral autoregulation in children and adolescents compared with adults (Snoek et al., 1984). It appears most prudent to limit contact sports in adolescent athletes until all postconcussive symptoms have disappeared, regardless of which concussion management protocol is followed.

**Return to Play after Concussion**

**Grade 1 Concussion**

An athlete who has sustained a grade 1 concussion may return to pay if he or she is asymptomatic after 20 minutes—that is, no headaches, no dizziness, oriented, and memory intact at rest and after sprinting and doing a few push-ups. If there are symptoms after the injury, the athlete is out for the duration of the game. The athlete must be asymptomatic for 1 week before being allowed to have contact again. In the meantime, a cardiovascular fitness training program can be followed. If this was the second (grade 1) concussion of the season, the athlete can return in 2 weeks after being asymptomatic for 1 week. If it was the third grade 1 concussion of the season, the athlete must remain out for the rest of the season; he or she may return next season if asymptomatic.

**Grade 2 Concussion**

For the first grade 2 concussion, the athlete is out of the game; he or she may return to participation after 1 week of being asymptomatic. If symptoms are present, consider admission to the hospital, although this is not typical. If there are no symptoms, the athlete can be monitored at home. If the athlete continues to be symptomatic at 7 days, a computed tomography scan is indicated. For a second grade 2 concussion in a season, the athlete is out for a minimum of 1 month, after which he or she may return if asymptomatic for 1 week. For a third grade 2 concussion, the athlete is out for the season. He or she may return next season if asymptomatic for at least 3 to 4 months.

**Grade 3 Concussion**

All players who sustain a grade 3 concussion are sent to the hospital, and computed tomographic scanning should be considered. With the first grade 3 concussion, the athlete can return to play after being asymptomatic for 2 weeks with rest and with exertion. If this was the second grade 3 concussion in a season, the athlete is terminated for the current season and is allowed to play only noncontact sports the next continuous season (e.g., if injured playing football in the fall, the athlete cannot play hockey in the winter but could play a contact sport in the spring). After three grade 3 concussions, advise participation in noncontact sports only.

These guidelines address concussions inflicted in a single season; however, there clearly are sequelae of repeated concussions sustained over years, as discussed in the following paragraphs.

**Sequela of Chronic Head Trauma** There is evidence that traumatic brain injury occurring over an extended period (i.e., months or years) can result in cumulative neurological and cognitive deficits (Gronwall and Wrightson, 1975; Leininger et al., 1990). “Dementia pugilistica” was the description given to the punchy boxer in 1928, and the syndrome also occurs in other sports characterized by repeated head trauma. This syndrome includes

1. Injury in and around the third ventricle, leading to memory deficits, emotion lability, and euphoria
2. Injury to the inferior cerebellar tonsils, manifested as slurred speech and abnormal balance
3. Degeneration of the basal ganglia, leading to Parkinson disease
4. Diffuse neuronal loss, leading to a picture that is similar to Alzheimer disease

Neuropsychiatric abnormalities can persist for up to 6 months after a concussion (not only in sports). This has led to the definition of the postconcussional disorder described in the *Diagnostic and Statistical Manual of Mental Disorders*, 4th ed. (1994).

1. History of head trauma including loss of consciousness, posttraumatic amnesia
2. Evidence of difficulty of attention (concentrating, shifting focus of attention, performing simultaneous cognitive tasks) or memory
3. Three or more of the following occurring shortly after the injury and lasting 3 months or longer
   a. Easily fatigued
   b. Disordered sleep
   c. Headache
   d. Dizziness
   e. Irritability or aggression with little provocation
   f. Anxiety or depression
   g. Change in personality (social or sexual inappropriateness)
   h. Apathy or lack of spontaneity

Dementia (decreased cognition, memory, or any of the above symptoms) resulting from a single head injury is usually not progressive. If the dementia or behavior grows progressively worse, consider another diagnosis, such as hydrocephalus or major depressive disorder.

Collins et al. (1999) evaluated the relationship between concussion and neuropsychological performance in college football players. They found that both a history of
multiple concussions and learning disabilities were associated with reduced cognitive performance. The results of cross-sectional, retrospective studies of head injuries in soccer players have been used to suggest that "heading" of the soccer ball by young athletes should be banned. However, it is not the heading of the ball that appears to be the culprit so much as concussions incurred during the course of play. Masetz et al. (1999) found that concussion in soccer players was associated with impaired performance in memory and planned functions. Concussions in soccer players should be managed using guidelines such as the system discussed previously. Other suggestions we endorse include

1. Adequate on-site medical care for acute brain injuries
2. Full medical evaluation of concussed players
3. Strict rule enforcement
4. Padding of the goal posts
5. Requiring use of mouth guards
6. Teaching proper heading technique (Green, 1998)

**Cervical Spinal Injuries**

The majority of catastrophic sports injuries involve the head and neck. The reader is referred to the Web site for the National Center for Catastrophic Sports Injury Research listed at the end of the chapter. As stated earlier, this center has released data indicating that the rate of catastrophic head and neck injuries is highest in cheerleading.

**General Management**

1. Initially, when a player's head or neck is injured, a spinal cord injury must be assumed to be present. The patient should not be moved until a diagnosis is established that would allow cervical movement. If a cervical spine injury has not been ruled out, the patient's cervical spine should be immobilized and the patient should be placed on a backboard and transported to an emergency room by ambulance.
2. If the patient is unconscious, has neck pain and/or radiating pain to an extremity, or has paraparesis or paraplegia, it should be assumed that a cervical spine injury is present. The patient should be immobilized on a board and transported to an emergency room.
3. If there is no motor or sensory abnormality of the extremities, the patient is conscious, and there is no neck pain, the patient can be allowed to walk off the field for further evaluation. If at any time the patient complains of radiating pain, paresthesia, or neck pain, the physician should consider that a cervical spine fracture is present and initiate appropriate procedures. If a cervical spine injury is suspected, the first priority is to determine that the patient's cardiopulmonary status is normal. The second priority is to do no harm. For a potential unstable cervical spine fracture or dislocation, this means allowing no one to move the athlete, including not taking off the helmet or rolling the patient over, until the appropriate emergency personnel are present. After personnel are present who can prepare the patient for transport, the cervical spine should be stabilized and the patient transported. Physicians who cover football games should be comfortable stabilizing and preparing for transport an athlete with a potential cervical spine fracture. This can be learned only through hands-on training. If the physician is not comfortable with this scenario, then he or she should know what the protocol is for accessing emergency transport services.

**Cervical Muscle Strain**

Cervical muscle strains are common and can be painful. The mechanisms of injury include rapid acceleration of a muscle or muscles as a result of a collision; a quick movement causing the muscle to tear; or repetitive contractions causing muscle fatigue and eventually muscle tearing. There should be no motor or sensory deficits on examination. The athlete will complain of pain typically in the trapezius area. There will be tenderness over the muscle body, limitation of ROM, and pain with resistance. Midline pain and tenderness are consistent with a cervical fracture and should be treated as such in the acute setting. Any player without full ROM and strength is excluded from further contact. Ice, analgesic medication, and physical therapy should be initiated immediately. We rarely use a cervical collar for cervical strains. It may be used, for example, only when the patient is in intractable pain after physical therapy and medication has been started. The physician should reassess the diagnosis if pain is intractable. Once physical therapy has yielded some relief, the player should receive continued physical therapy as needed in the therapist's office, complemented by home exercises. Clearance for return to contact sport requires a normal range of cervical motion and strength.

"Stingers" or "Burners" A "stingers" is a common injury in American football and is the result of trauma to the brachial plexus that occurs when a player hits another opponent on the head or shoulder. The injury is a brachial plexopathy. The player describes a burning pain or weakness, or both, in the distribution of a branch of the brachial plexus. The physician who initially evaluates a stinger should think first about the possibility that the paresthesia is secondary to a spinal cord injury, as discussed previously. Although uncommon in teens, disc herniation occurs often enough that physicians need to be able to recognize it. The diagnosis is made on the basis of radiographic studies, including an oblique view of the lumbar spine, or a bone scan, or both. If the bone scan is abnormal and the plain radiographs are normal, the next step is computed tomography. If the bone scan and plain radiographs are both normal, then computed tomography is indicated to look at all posterior elements, including the facet joints, to determine the cause of the pain.

**Lumbar Spine and Lower Back Injuries**

The common causes of low back pain in adolescents are described here.

**Muscle Strains** An acute lumbar strain is likely to manifest as an acute pain in the lumbar area after an object is lifted from the lumbar flexed position (bent forward). A chronic strain typically has a history of recurrent acute strains that are never rehabilitated and the athlete never returns to 100%, pain-free functioning.

**Muscle Contusions** These occur with direct trauma to the lumbar area; most are limited injuries.

**Spondylolysis** The term spondylolysis refers to a radiographically demonstrable defect at the pars interarticularis, which can occur at any spinal level. It may be the result of a developmental defect or a stress fracture. Lumbar spondylolysis occurs in approximately 6% of the general population, with a tendency for increased prevalence in athletes who participate in sports that involve repetitive lumbar extension loading, such as weight lifting, ballet, gymnastics, basketball, and football (Baltz, 1939; Soler and Calderon, 2000). Many subjects with spondylolysis are asymptomatic, even those who engage in such sports (Semon and Spengler, 1981). If a fracture happens, it may occur after a single traumatic event or, more likely, after repetitive lumbar extension loading. This occurs in many sports, especially ballet and weight lifting. The athlete may have had pain for years before the diagnosis is made.

On physical examination, the hallmark of spondylolysis is reproduction of pain when the patient assumes a lumbar extended position while standing. The diagnosis is made on the basis of radiographic studies, including an oblique view of the lumbar spine, or a bone scan, or both. If the bone scan is abnormal and the plain radiographs are normal, the next step is computed tomography. If the bone scan and plain radiographs are both normal, then computed tomography is indicated to look at all posterior elements, including the facet joints, to determine the cause of the pain.

Treatment includes relative rest, exercises to improve lumbar flexibility, and abdominal and lumbar strengthening exercises. Although it has never been established that a thoracolumbosacral orthosis (i.e., back brace) improves outcome in addition to the treatment already outlined, we often use such a brace for young athletes to reinforce the need for the patient to reduce extension loading of the spine, not just in sports but also in activities of daily living. The patient may miss a few months to 12 months of sports.

If not treated, the spondylolysis can progress to spondylolisthesis, which is characterized by slippage of the vertebral body anterior to the next most distal vertebral body. The risk of slippage may be greatest during the most rapid stages of bony growth, and for this reason, conservative management, e.g., 6 to 12 months of no extension loading activities, in adolescents is critical. However, even with compliance with a good treatment plan, such as the one outlined earlier, spondylolisthesis may occur, especially when spondylolysis occurs at the L4 vertebral level. Six percent to 9% of adults have spondylolysis, and many are asymptomatic (Valkenburg and Haaneen, 1982).

**Disc Herniation** Although uncommon in teens, disc herniation occurs often enough that physicians need to be able to recognize it. The presentation may include the classic sciatica, but it also may manifest as acute or chronic lower back, hip, or leg pain. The straight leg test should be positive, with the sciatic pain being
Morning stiffness

Noninjured structures should be exercised in order to maintain cardiovascular fitness. For instance, patients with a lower-extremity injury could do seated weight lifting or swim with their arms pulling and without leg action. Those with an upper-extremity injury could ride a stationary bike.

Athletes should attend practice sessions so that they are not as likely to withdraw psychologically.

Healing of muscle tendon units manifests as no tenderness or pain with functional testing, full ROM, and progressively less pain with activities of daily living.

Penetrating wound of major joint, muscle, or tendon

Return to exercise or sport free of symptoms

The affected part must be rested and protected. Patients should apply whatever devices are necessary (e.g., wrap, splint, crutches, sling) so that they can limit further injury and control pain and swelling.

Specific exercises should be done within a pain-free ROM. For example, isometric exercises can be started on the first day if there is little pain-free ROM but the subject follows the relative rest principle.

Joint instability perceived by athlete or elicited by physician

Pain ≥ 3 months

Elevation, compression, and ice should be applied as often as possible during waking hours.

Analgesic medication (e.g., acetaminophen, NSAIDs) should be started on running doses, not “as needed.” Physical therapists can apply electrical stimulation to achieve near-normal strength, ROM, endurance, and proprioception of injured structures.

Phase 2: Improve Strength and Range of Motion (ROM) of Injured Structures

Phase 1: Limit Further Injury and Control Pain and Swelling.

1. The affected part must be rested and protected. Patients should apply whatever devices are necessary (e.g., wrap, splint, crutches, sling) so that they can become pain free and protect the site from further injury.

2. Elevation, compression, and ice should be applied as often as possible during waking hours. Icing should be applied continuously for 20 minutes, directly to the skin and three or four times per day for the first few days.

3. Analgesic medication (e.g., acetaminophen, NSAIDs) should be started on running doses, not “as needed.” Physical therapists can apply electrical stimulation to achieve pain relief in the acute setting.

4. Noninjured structures should be exercised in order to maintain cardiovascular fitness. For instance, patients with a lower-extremity injury could do seated weight lifting or swim with their arms pulling and without leg action. Those with an upper-extremity injury could ride a stationary bike.

5. Athletes should attend practice sessions so that they are not as likely to withdraw psychologically.

1. Specific exercises should be done within a pain-free ROM. For example, isometric exercises can be started on the first day if there is little pain-free ROM but the subject can contract muscles isometrically.

2. Relative rest is the cardinal principle, and that means that the patient should do everything possible, so long as it does not cause pain within 24 hours after the activity.

3. Analgesic medication should be continued, not to mask the pain and allow premature return to play, but to interrupt the cycle of pain—muscle spasm—inflexibility, weakness, and decreased endurance. In addition to reducing swelling, ice is a good analgesic modality.

4. General fitness maintenance should continue, as discussed for Phase 1. Other activities, such as water jogging for lower-extremity injuries, may be added.

Phase 3: Achieve Near-normal Strength, Range of Motion, Endurance, and Proprioception of Injured Structures

1. Exercise is progressed so long as the subject follows the relative rest principle.

2. Healing of ligaments treated nonoperatively manifests as minimal laxity with provocative testing, normal ROM, no tenderness along the ligament or pain with stretching, and progressively less pain with activities of daily living.

3. Healing of muscle tendon units manifests as no tenderness or pain with functional testing, full ROM, and progressively less pain with activities of daily living.
Phase 4: Return to Exercise or Sport Free of Symptoms

1. Premature return is likely to result in further injury or another injury.
2. Successful rehabilitation minimizes the risk of re-injury and returns the injured structures to baseline ROM, strength, endurance, and proprioception.
3. Functional rehabilitation should be sport-specific. For example, a baseball pitcher with an upper extremity injury needs to rehabilitate to normal strength and ROM, but, throwing a baseball in a game, he or she should practice throwing gently and work up to full speed over days to weeks, depending on the specific diagnosis and chronicity of the injury.

Knee Injuries

History of the Injury Based on the description of the mechanism of injury, the events after the injury, and the factors that worsen or improve the pain, the physician should be able to prioritize the most likely diagnoses.

1. Knee pain that occurs while running straight, without direct trauma or fall.
   a. Chronic pain: Likely to be patellofemoral dysfunction.
   b. Acute pain: Consider osteochondritis dissecans and pathological fracture. Any teen with knee pain without a history of trauma and with an equivocal examination that does not pinpoint the diagnosis needs to have a radiographic examination of the knee. In addition, if the hip examination is abnormal, radiographs of the hip are needed to rule out slipped capital femoral epiphysis manifested as knee pain. Osgood-Schlatter disease and patellofemoral dysfunction do not require radiographs to establish a diagnosis.
2. Knee injury that occurs during weight bearing, cutting while running, or an unplanned fall: Consider internal derangement including ligamentous and meniscal tears and fracture. A player who injures the knee while cutting, without being hit or having direct trauma, has a torn anterior cruciate ligament tear until proven otherwise.
3. A valgus injury to the knee (i.e., a force delivered to the outside of the knee, directed toward the midline) is likely to tear the medial collateral ligament, possibly the anterior cruciate ligament, and either the medial or lateral meniscus.
4. Chronic anterior knee pain that is worse when going up stairs and/or after sitting for prolonged periods, or after squatting or running, is likely to be patellofemoral dysfunction. In general, if the patient does not give a history of the knee’s giving out or locking, sharp pain, effusion, the sensation of something loose in the knee, or the sensation that something tore with the initial injury, then the injury probably is not significant. If there is hemarthrosis within 24 hours after the injury, then internal derangement is present and a diagnosis must be sought. At the game site or during an evaluation of the patient that takes place within 1 hour or so after the injury, the best indicator of severity of injury of the lower extremity is the ability to bear weight and walk without pain. If the athlete can do this, then he or she has probably not suffered a major injury and does not need to be referred immediately.

Physical Examination The physical examination should include the following:

1. Observation of gait (weight bearing? antalgic gait?)
2. Inspection for swelling and discoloration
3. Observation of vastus medialis obliquis contraction, looking for reduced bulk and tone
4. Peripatellar palpation (tenderness over the tibial tuberosity is diagnostic of Osgood-Schlatter disease; peripatellar pain is characteristic of patellofemoral dysfunction)
5. Quadriceps and hamstring flexibility
6. Evidence of meniscal tears (McMurray and modified McMurray tests)
7. Evidence of ligamentous instability, including valgus and varus testing (for medial collateral and lateral collateral ligaments, respectively)
8. Lachman test and pivot shift test (anterior cruciate ligament); sag sign and posterior drawer test (posterior cruciate ligament)

Radiographic Evaluation of Knee Injuries Meeting any one of the following criteria would be an indication for a radiograph after an acute knee injury:

1. Inability to bear weight
2. Fibular head tenderness
3. Isolated tenderness of the patella
4. Inability to flex the knee beyond 90 degrees
5. Age greater than 55 years

These decision rules, collectively referred to as the Ottawa Knee Rule, had a sensitivity of 100% in detecting knee fractures in adults and could potentially reduce the use of plain radiographs by 28% (Steil et al., 1996a).

Anteroposterior, lateral, and oblique views are standard. The sunrise view details the patellofemoral joint and should be ordered if patellar dislocation is suspected.

MRI evaluation in the acute or chronically injured knee should not be routine (O’Shea et al., 1996). MRI should be reserved for diagnostic dilemmas and for patients who do not respond to conservative management. The most commonly missed diagnoses are chondral fractures, anterior cruciate ligament tears, fibrotic fat pad, and loose bodies (Oberlander et al., 1993). In experienced hands, the MRI added nothing to the diagnosis of knee injuries based on history and physical examination (Oberlander et al., 1993). This emphasizes the financial and clinical importance for primary care and emergency room physicians to have good physical examination skills for diagnosing common musculoskeletal injuries. Deficiencies in physical examination skills have been identified during residency training in all primary care disciplines.

Management of Acute Knee Injuries

1. Establish a working diagnosis.
2. Use the Ottawa Knee Rule.
3. Relative rest: Prescribe use of clutches if the patient cannot bear weight without pain. An elastic wrap is adequate in the initial phase of treatment, or until a definitive diagnosis is made and a treatment regimen planned. Knee immobilizers have a limited role in the management of acute knee injuries because they are bulky and awkward, offer no structural support, and lead to calf strain if the patient tries partial weight bearing with the foot in the plantar-flexed position.
4. Ice: Apply for 20 minutes three or four times per day.
5. Start isometric quadriceps contractions on the first day if possible. If the patient cannot contract the quadriceps and it is anticipated that he or she will be unable to do so for some days, consider an electrical stimulation unit to contract the quadriceps until the patient is able to do so.
6. Maintain elevation of the leg as much as possible.
7. Use a compression wrap.
8. Prescribe analgesic medication.
9. Refer the patient for physical therapy.

Management of Chronic Knee Pain Caused by Patellofemoral Dysfunction

1. The diagnosis is based on a history of knee pain, with peripatellar pain on examination.
2. Refer the patient to a physical therapist for instruction regarding a standard patellofemoral dysfunction home exercise program that includes stretching the quadriceps and hamstring muscles, stretching the iliotibial band if tight, strengthening the vastus medialis muscle, icing the tender areas, and relative rest.
3. Some patients benefit from orthotics if they are pronators and have not responded to the typical treatment within 3 to 4 weeks. Likewise, some patients respond to neoprene knee sleeves.
4. A brief (i.e., 10-day) course of acetaminophen or an NSAID may be useful if there is pain with activities of daily living.
5. Return to sports should be measured and stepwise.

Ankle Injuries
Ankle injuries are the single most common acute injury in adolescent athletes (Hergenroeder, 1990). The diagnosis and treatment of ankle injuries in adolescents is the same as in adults, with the exception that teens may have open growth plates that may be the primary injury site, whereas in an adult the primary injury is likely to be torn ligaments.

**Acute Ankle Injury** The mechanism of acute ankle injury in 85% of the cases is inversion (turning the ankle under or in). Injuries resulting from eversion are generally more severe because of the higher risk of syndesmosis injury and fracture.

**Physical Examination**

1. **Acute injury:** The best time to examine any musculoskeletal injury is immediately after the injury, when the examination can be most informative. However, patients commonly present with diffuse swelling, tenderness, and decreased ROM hours to days after the injury. The physical examination will be limited in terms of diagnosing specific lesions at this point. At a minimum the examination should include the following:
   a. Inspect for gross abnormalities, asymmetry, and vascular integrity.
   b. Palpate for bony tenderness specifically at the medial and lateral malleoli, proximal fibula, anterior joint line, navicular, and base of the fifth metatarsal.
   c. Assess ability to bear weight.
   d. The physical examination may be more informative at 3 to 4 days after injury, when the patient has appropriately used rest, ice, compression, and elevation.

2. **Stretching:** Primarily soleus and gastrocnemius, by doing calf stretches.

3. **NSAIDs:** Use for pain relief and theoretically to control inflammation, but NSAIDs do not effect the outcome

4. **Assess active ROM in six directions:**
   - Plantarflexion; plantarflexion and inversion; plantarflexion and eversion
   - Dorsiflexion; dorsiflexion and inversion; dorsiflexion and eversion
   c. Assess resisted ROM in the same six directions.
   d. Palpate for potential fracture at the sites listed for palpation of bony tenderness.
   e. Attempt passive ROM—plantarflexion and dorsiflexion, talar tilt, anterior drawer test.
   f. Assess for pain-free weight bearing with normal gait and then with heel-and-toe walking.

**Associated Injuries:** Complications Associated with Ankle Sprains

1. Up to 15% of all complete ligament tears have an associated fracture. The most common sites are the talus, fifth metatarsal, fibula, and tibia. If there is bony tenderness in patients with open epiphyses, assume that a fracture is present even if the radiography results are negative. Immobilize without weight bearing for 1 week; if tenderness persists, then cast for 2 weeks. If a fragment is present, it does not always require casting or surgery. If the fragment is small and does not appear to be in the joint space, then treat conservatively and monitor.

2. Tibiofibular syndesmosis injury occurs in 6% of ankle sprains. These are more serious injuries than the typical lateral ligament sprain. On examination there is tenderness proximal to the joint line along the syndesmosis. Pressing the midshaft together and then releasing the pressure may worsen the pain.

3. Talar fractures occur in 7% of ankle sprains. The patient complains of delayed healing, catching, locking, or persistent pain. Initial x-ray results may be negative; repeat radiographs or computed tomography scanning may be required.

4. Peroneal subluxation occurs in 0.5% of ankle sprains. Tenderness is present along the tendon sheath, posterior and superior to the lateral malleolus.

**Radiographical Examination:** Ottawa Ankle Rules

An ankle or foot plain radiograph is indicated if there is bone tenderness at the distal/posterior 6 cm of the tibia or fibula (ankle series) or at the navicular or base of the fifth metatarsal (foot series) or if the patient is unable to take four steps both immediately after the injury and during the examination, regardless of limping (Steill et al., 1996b). The Buffalo Modification of the Ottawa Ankle Rules includes the entire distal 6 cm of the tibia and fibula, not just the posterior portions (Leddy et al., 1998). In our opinion, stress views are not indicated in the evaluation of the acute or chronically injured ankle.

**Treatment:** Acute Phase

1. The goal is to limit disability. Successful treatment is not defined only by the absence of pain but also by return to full ROM, strength, and proprioception.

2. **Relative rest:** As with rehabilitation of all musculoskeletal injuries, advise the athlete to do nothing that hurts.

3. Ice: Used in the same manner as for knee injuries, described earlier.

4. Heat during the first 72 hours has a role only if it is applied by an athletic trainer or physical therapist.

5. Compression: If using an elastic wrap, always wrap distal to proximal, from the base of the toes to midcalf. Advise the patient not to sleep with the elastic wrap in place.

6. Compression and stability can be provided by an air stirrup, which should be used for all acute sprains not complicated by fracture.

7. **Elevation:** For the first 2 to 3 days, elevate the ankle as much as possible.

8. If discussing the injury by telephone, advise the patient not to wait to seek treatment. Athletes should seek treatment immediately.

9. **NSAIDs:** Use for pain relief and theoretically to control inflammation, but NSAIDs do not effect the outcome per se. Acetaminophen is another alternative.

10.** Casting is not indicated for ankle sprains not complicated by fracture** (Brostrom, 1966). Casting should not be routine for ankle sprains because it actually worsens the outcome, specifically the time to return to work. The air stirrup provides stability to inversion and evasion but also allows for active dorsiflexion and plantarflexion, which is key in early rehabilitation.

**Rehabilitation**

Rehabilitation needs to start on the first day of evaluation.

1. **Relative rest:** Progress off crutches as soon as possible; do pain-free exercise.

2. **Stretching:** Primarily soleus and gastrocnemius, by doing calf stretches.

3. **Strengthening:** Band exercises, toe-heel walking, pain free and progressive (can be done with the air stirrup on).

4. **Proprioceptive retraining:** Raising on toes with little support (1 or 2 fingers on a chair) and eyes closed for 5 minutes a day.

5. **Functional progression of exercise:** for instance: toe walking ® walking at a fast pace ® jogging ® jogging and sprinting ® sprinting and jogging on curves ® figure-of-eight running ® back to sports participation.

6. The air stirrup should be worn in competition for 6 months after the injury (Thacker et al., 1999). The air stirrups are most comfortably worn with low-cut or three-quarter height shoes, and they provides excellent stability.

**Chronic Ankle Instability** The leading causes of chronic ankle stability and pain are

1. **Strength deficits**

2. **Loss of flexibility**

3. **Loss of proprioception**

4. **Intraarticular pathology**

All of these need to be considered in the evaluation, and, if deficiencies are found, rehabilitation needs to occur.

**Large Muscle Contusions**

The prototype injury in this category is the quadriceps contusion. This injury occurs from a direct blow to the thigh. It occurs in all sports and is very common in football, even though the players wear thigh pads. The athlete's presentation can range from feeling a mild discomfort or "Charlie horse" after the game to being unable to bear weight immediately after the trauma. The pathophysiology of the injury is bleeding in and around the quadriceps muscle as a result of the contusion. The quadriceps immediately goes into spasm, resulting in pain and disability. If the bleeding is not arrested immediately, bleeding can be substantial.

On examination the physician needs to consider a femoral fracture, which would be characterized by severe pain and the inability to bear weight. A quadriceps
contusion is characterized by more diffuse tenderness over the body of the quadriceps muscle. The athlete typically can bear weight but may not be able to extend the knee actively. With passive flexion of the knee while the athlete is in the prone position, the patient experiences pain as the quadriceps, which is in spasm, is stretched. The injury can be graded according to the degree of passive knee flexion that the patient can permit:

1. Greater than 90 degrees—mild injury. If the injury is treated appropriately, the athlete probably can return to competition within 7 days.
2. Between 60 and 90 degrees—moderate injury. The athlete probably will be able to return to play in 2 to 4 weeks with appropriate treatment.
3. Less than 60 degrees—severe injury. The player may be out for the season.

**Treatmet of Quadriceps Contusions as an Example of Treatment of Large Muscle Contusions**

The key is to stop further bleeding by applying ice for 20 minutes. When not icing, apply a tight compression wrap around the thigh and have the patient elevate the leg. The player should keep the knee in full flexion as much as possible during the first 24 hours after the injury. Cyclooxygenase inhibitors should not be given because they might promote decreased clotting. Acetaminophen can be given for pain.

The patient should start isometric quadriceps contractions as soon as possible. In moderate to severe injuries, treatment by a sports-trained physical therapist is essential. In experienced hands, the use of ultrasound can promote rapid recovery from this injury. Therapy that is too timid or too aggressive can retard recovery. If the bleeding is extensive and the athlete is reinjured before the hematoma is resolved or she is at risk for development of myositis ossificans, which can be career threatening and may require surgical excision if functional ability is compromised.

**Shin Splints and Stress Fractures of the Lower Leg**

Patients with these conditions experience lower-extremity pain that initially appears toward the end of exercise. If the condition is left untreated and the athlete continues in the exercise that caused the injury, the pain will occur earlier in the exercise period and persist longer after the exercise is over. It can occur in any weight-bearing athlete but is most common in runners. A common presentation is medial shin pain. The principal two diagnoses to consider are medial tibial stress syndrome (shin splints) and medial tibial stress fracture, which are discussed here. Other diagnostic possibilities include compartment syndromes and vascular abnormalities, which are not discussed and are less common. If these diagnoses are being considered, referral to a specialist familiar with these conditions is indicated.

On examination, the pain of shin splints should be more diffuse and tenderness should be closer to the muscle, rather than bone, at the muscle-bone interface along the medial tibia. In stress fractures of the medial tibia, the pain should be more pinpoint and over bone, not muscle. There is an injury spectrum from shin splints to stress reaction to stress fracture which can be difficult to distinguish clinically. Further diagnostic studies may be indicated. Stress fractures can occur in any bone and are most common in the tibia and fibula.

Plain radiographs of patients with shin splints will be normal but, unfortunately, so will most of the plain radiographs of patients with tibial stress fractures, at least during the first few weeks after the injury. The most sensitive test to diagnose stress fractures has been the bone scan. This is being challenged, but has not yet been replaced, by the MRI. If the bone scan is normal, then the physician can be more confident that the diagnosis is shin splints due to medial tibial stress syndrome.

A single best treatment protocol for shin splints and stress fractures of the medial tibia has not been established. One treatment protocol includes the following:

1. Relative rest and a functional progressive rehabilitation program. This means doing nothing that hurts within 24 hours of the activity. Alternative activities such as swimming, cycling, and pool running (running in the deep end of a pool supported by a buoyant vest or jacket) can be used to maintain the patient's fitness level while the leg injury is recovering. After 7 to 10 days of pain-free activity, the patient can start on a walking program and progress to a jogging program over 10 to 14 days as long as he or she remains pain free. At any point in this functional rehabilitation progression, if pain reappears, the athlete should have two or three pain-free days before resuming the walk-jog program. After jogging for 7 to 10 days, patients can progress to sprinting and then jumping so long as they remain pain free.
2. Apply ice each day for 20 minutes directly to the site.
3. Provide pronation control if appropriate.
4. Increase shock absorption of the patient's shoes, if appropriate, e.g., they have a rigid foot.
5. Stretch and strengthen the dorsiflexors (anterior tibialis), plantar flexors (posterior tibialis, gastrocnemius, soleus), and everters (peroneal muscles).
6. Analgesic medication or NSAIDs can be used in shin splints for 7 to 10 days but should not be used chronically as it may mask the pain and the athlete may return to activity too soon. Analgesic medications should not be used on a regular basis (i.e., daily) for stress fractures because the number of pain-free days is the criterion for return to activity in the functional rehabilitation progression.

It is difficult to predict when an athlete will recover sufficiently from stress fractures and shin splints to return to exercise or competition. As long as the patient follows a functional rehabilitation program such as the one just outlined, he or she will at least be involved in some rehabilitation toward full activity. Avoid projecting a day on which the athlete will be able to return to competition, to avoid disappointment if the prediction is wrong.

**THE FEMALE ATHLETE**

In general, female athletes have injuries and injury rates similar to those of male athletes in the same sport. The exception to this rule is female athletes in jumping sports, who have a higher rate of anterior cruciate ligament sprains than their male counterparts. The reason for this difference is not established. A reduction in the incidence of acute knee injuries in female athletes after a 6-week neuromuscular training course, compared with a group that did not have this training, has been reported (Hewett et al., 1999). The results of this study and others imply a role for improved neuromuscular control in stabilizing the knee and, potentially, preventing anterior cruciate ligament injuries. It does not establish that neuromuscular control is inadequate in young female compared with young male athletes, because the latter were not studied with a similar intervention program. The issue of overtraining and adult height in female gymnasts was addressed earlier in this chapter.

**Female Athlete Triad**

The effects of excessive exercise on the reproductive system in young females deserves special mention. The so-called female athlete triad—disordered eating, amenorrhea, and osteoporosis—highlights the effects of excessive exercise (Yeager et al., 1993). Female athletes with amenorrhea or oligomenorrhea have lower bone mineral density (BMD) and higher rates of stress fracture than eumenorrheic athletes (Barrow and Saha, 1988; Myburgh et al., 1990; Bennell et al., 1999). A long-term consequence of amenorrhea and osteopenia during the second decade may be increased risk of postmenopausal osteoporosis.

**Evaluation and Treatment**

This section discusses evaluation and treatment of the female athlete triad, including hypothalamic amenorrhea/oligomenorrhea and osteopenia/osteoporosis associated with exercise and inadequate caloric intake.

The first step in addressing primary or secondary amenorrhea is to make a correct diagnosis. Hypothalamic amenorrhea associated with exercise and inadequate caloric intake is a diagnosis of exclusion. The diagnosis is made on the basis of the history (menstrual, diet, and exercise history) and the physical examination.

The menstrual history includes

1. Age at menarche
2. Frequency and duration of menstrual cycle
3. Last menstrual period
4. Longest time period without menstruation
5. Physical signs of ovulation, such as dysmenorrhea
6. Prior hormonal therapy
The conditions that need to be ruled out in the evaluation of amenorrhea are reviewed in Chapter 52.

Assuming the diagnosis of hypothalamic amenorrhea or oligomenorrhea associated with exercise and inadequate caloric intake is made, reductions in training volume and enhanced caloric intake need to occur. Amenorrheic athletes who gain weight through reduced training and improved diet may resume menses spontaneously and increase their BMD (Drinkwater et al., 1986; Lindberg et al., 1987).

If the athlete has a diagnosable eating disorder, then treatment needs to include medical, nutritional, and psychological therapy in a coordinated fashion. In our experience, this condition is approached as a chronic disease, and long term follow-up (years) is anticipated. Weight gain is the mainstay of treatment in trying to restore BMD in a patient with an eating disorder. However, weight gain is not always associated with improved BMD, and, when BMD is improved, it still tends to be below normal (Hotta et al., 1998; Jonnavithula et al., 1993). Therefore, estrogen replacement should be considered (see later discussion).

The lifestyle changes (i.e., improved caloric intake and reduced exercise training) should be made in consultation with a dietician. An example of changing the training volume and dietary intake for a competitive runner who is at least 100% of her estimated IBW would be to reduce running by 1 day/week and to add a beverage containing 360 kcal to the daily diet (Dueck et al., 1996). If the runner athlete weighs 85% to 90% of estimated IBW and is exercising daily, we would recommend more aggressive changes: reduce exercise to 3 days/week and add one or two dietary supplemental drinks or snacks per day. We do not recommend exercise if the body weight is less than 85% of estimated IBW, and until the weight increases to that level, because of the concern that the patient may become oligomenorrheic or amenorrheic. However, as a subgroup these patients (runners with low body weight) appear to have a more robust hypothalamic–pituitary–ovarian axis than other women with anorexia nervosa who resume menses only when their weight is greater than 90% of estimated IBW. If the patient is eumenorrheic, then a BMD measurement might determine whether osteopenia is present. If it is, even in the face of normal menses, increased emphasis would be placed on weight gain.

Exercise may attenuate bone loss in patients with bulimia nervosa compared to those with anorexia nervosa (Sundgot-Borger, 1998). We support exercise in patients with bulimia nervosa if their weight is greater than 90% of the estimated IBW and they are menstruating. Strain on bone (through exercise) and estrogen appear to have additive effects on improving bone strength. The effectiveness of bone modeling through exercise could be limited when estrogen levels are reduced (Damien et al., 1998).

Appropriate Follow-up The athlete should be monitored weekly until weight increases consistently. Then the visits can be reduced to once every 2 weeks assuming the teen’s weight progresses toward 90% of estimated IBW. This assumes the coach is supportive of the plan. We give a written plan to the athlete and encourage her to show it to her coach and ask the coach to call the physician or dietician with any questions.

Osteopenia and Osteoporosis

Measurement of Bone Mineral Density We recommend measurement of the BMD of the lumbar spine and hip by dual-energy x-ray absorptiometry (DXA) if the patient has been amenorrheic for longer than 6 months and refuses treatment with estrogen/progestin. If the athlete is willing to start estrogen/progestin therapy, we do not necessarily order a DXA scan, because the results will not alter the recommendation for hormonal therapy. If the subject has been amenorrheic for longer than 1 year and is malnourished, the DXA scan is more seriously considered. If DXA scanning is done, it should not be repeated at an interval of less than 12 months.

World Health Organization Criteria for Osteopenia and Osteoporosis The World Health Organization (WHO, 1994) has established criteria for the diagnosis of osteopenia and osteoporosis using a T-score. The T-score is the number of standard deviations (SD) above or below the average BMD value for young, healthy women. Osteopenia is defined as a T-score of -2.5 SD or lower; osteoporosis is defined as a T-score between -1 and -2.5 SD. How this designation applies to the risk for subsequent stress fracture, or ultimately to clinical osteoporosis manifested as a fracture, in young athletes with amenorrhea is not known. In addition, the physician should exercise caution in interpreting T-scores and Z-scores (the latter being the number of SDs above or below the age-matched average peak bone mass) in patients with short stature because DXA tends to underestimate BMD in short subjects and overestimate BMD in tall subjects (Leonard et al., 1999).

Hormonal Therapy Does hormonal therapy reduce stress fractures and/or improve BMD?

Oral Contraceptive Pills

It has not been established that estrogen/progestin, in the form of oral contraceptive pills (OCPs), increases BMD more than no such treatment. One longitudinal, randomized study (Hergenroeder et al., 1997) demonstrated improvement in total body and lumbar BMD in young amenorrheic females treated with OCPs, compared with medroxyprogesterone or placebo, for 12 months. A second longitudinal, randomized clinical trial (Gibson et al., 1999) reported no improvement in amenorrheic subjects treated with an estrogen/progestin preparation (Trisequens) containing estradiol (1 to 2 mg) plus estriol (0.5 to 1 mg) every day plus norethisterone (1 mg) for 10 days in a 28-day cycle over 18 months. Two milligrams of estradiol is estimated to be similar to 25 µg of ethinyl estradiol (Fagan, 1998). The ethinyl estradiol dose that would be equivalent to 1 mg of estradiol is not known to us at this time, but the combination of estradiol (2 mg) and estriol (1 mg) appears to be similar to 35 µg of ethinyl estradiol.

It has also not been established that OCPs prevent stress fractures (Bennell, 1999). Two retrospective cohort studies reported lower rates of stress fractures in women who used OCPs (Barrow and Saha, 1988; Myburgh et al., 1990). One prospective study found no relationship between current or past use of OCPs and the rate of stress fractures of the lower extremity, compared with athletes who had never used OCPs (Bennell, 1999).

Other Forms of Estrogen and/or Progestin Replacement

One study demonstrated that conjugated estrogen (Premarin, 0.625 mg taken daily on days 1 through 25 of each month) and medroxyprogesterone (Provera, 5 mg taken daily on days 16 through 25 of each month) for a mean of 1.5 years improved lumbar BMD in females with anorexia nervosa if the patient’s weight at the initiation of therapy was less than 70% of the estimated IBW, compared to a control group (Klibanski et al., 1995). However, the authors did not state that this study was conclusive that weight less than 70% of estimated IBW was the criterion for starting this estrogen/progestin therapy. One report demonstrated an improvement of BMD in adult women taking medroxyprogesterone, 10 mg/day, for 10 days per month, but that study has not been replicated and this is not an accepted treatment protocol for adolescents (Prior et al., 1990).

Other Pharmacologic Treatments to Prevent Osteoporosis

Selective estrogen receptor modulators (SERMs) have been developed to maximize the effect of estrogen on bone while minimizing the effect of estrogen on breast and endometrium.Raloxifene is a SERM that has been approved by the U.S. Food and Drug Administration (FDA) for the prevention and treatment of osteoporosis in
Young women with anorexia nervosa and secondary amenorrhea have mean serum estradiol levels that approximate those of postmenopausal women. Osteopenia/osteoporosis is one of the more serious, long-term consequences of prolonged amenorrhea in adolescent athletes. This is an area that requires further investigation.

In patients with eating disorders there is the concern that treatment with OCPs could interfere with psychological processes. In our experience, patients with eating disorders who are taking OCPs tend to ascribe mood changes and depressed feelings to the OCPs. One randomized study, mentioned earlier, in which anorexia nervosa was treated with conjugated estrogen/medroxyprogesterone versus placebo, reported no difference in overall outcome (Kilbanski et al., 1995). There is a gap in the literature with respect to whether OCPs improve BMD in amenorrheic athletes. A prospective, longitudinal, randomized trial is needed to answer this question. However, the dropout rate in studies of amenorrheic subjects treated with hormonal therapy is 25% to 50%, making longitudinal studies difficult to perform (Gulekli et al., 1994; Hergerroeder et al., 1997; Gibson et al., 1999).

In making the decision to start estrogen/progestin therapy, the physician should consider that the risk of stress fracture is inversely related to the age at menarche (Warren et al., 1986). In the absence of an established standard for the use of estrogen to prevent osteopenia in adolescent and young adult females with secondary or primary amenorrhea related to overtraining and caloric restriction, all of the data presented above should be considered in addition to the following points:

1. Young women with anorexia nervosa and secondary amenorrhea have mean serum estradiol levels that approximate those of postmenopausal women.
2. Osteopenia/osteoporosis is one of the more serious, long-term consequences of prolonged amenorrhea in adolescent athletes.

Clinicians should also be aware that hypoandrogenemia, reduced serum levels of insulin-like growth factor I (IGF-I), and hypercortisolism in anorexia nervosa contribute to BMD loss. These factors improve with weight gain. They may be unaffected by estrogen/progestin therapy, and unless they are improved the effect of estrogen/progestin may be limited.

**Recommendations**

Considering the issues discussed here, we recommend use of combination OCPs to those female athletes who have been amenorrheic for longer than 6 months, especially if they are malnourished, as manifested by weight less than 85% of their estimated BW. If the athlete has been amenorrheic for longer than 12 months, a stronger recommendation is made to commence OCP treatment, in addition to effecting lifestyle changes discussed earlier (Castro et al., 2000).

**Estrogen Therapy in Younger Teens**

Some groups recommend not providing estrogen replacement to patients younger than 16 years of age (AAP, 1989). The dilemma is that delaying estrogen therapy may compromise BMD but premature use of estrogen could compromise adult height. We suggest considering bone age in the decision to prescribe estrogen/progestin to female adolescents with amenorrhea related to excessive exercise and caloric restriction.

A 15-year-old with a bone age of 13 years has achieved 96.4% of her full adult height; with a bone age of 14 years this same teen has achieved 98.3%, and with a bone age of 15 years 99%, of her adult height (Gruehlich and Pyle, 1959). The mean height of females in North America is 163 cm at 19 years of age (Tanner and Davies, 1985). If estrogen therapy completely arrested height gain from the onset of therapy, then the female with a bone age of 15 years and a potential adult height of 163 cm could potentially lose 1.6 cm of height. More likely, height attainment would not be arrested and some additional height would still be achieved. The loss of height could be immeasurable.

On the other hand, bone loss resulting from an eating disorder before menarche could lead to significant arrest of BMD development, compared with bone loss after menarche. The onset of bone loss in relation to bone development is important in that onset of anorexia nervosa before 15 years of age affects bone size and volumetric BMD more than onset after age 15 does (Seeman et al., 2000). Bone fragility is a function of both bone size and volumetric BMD, and these are partly established during pubertal growth. There is a risk to delaying the start of estrogen/progestin therapy until epiphyseal growth is complete.

We recommend prescribing estrogen/progestin replacement for females with amenorrhea at 15 years of age and a bone age of 15 years, and consideration of such therapy for those with a bone age of 14 years, depending on the degree of osteopenia and malnutrition. This is an area that requires further investigation.

**Calcium Intake**

We recommend that amenorrheic athletes have a daily elemental calcium intake of 1,500 mg. However, in a group of healthy adolescents followed longitudinally, changes in BMD were independent of calcium intake, which ranged from 500 to 1,500 mg/day (Lloyd et al., 2000).

**EROGENIC AIDS AND DRUG USE IN ATHLETES**

**Background**

There is current evidence that substance use among high school and college athletes is greater in some cases than in nonathletes, with important differences depending on gender and the specific drug (Anderson and McKaeq, 1989; Wadler and Hainline, 1989). Specifically, in the past several years there is evidence that marijuana and alcohol use are higher in male students who compete in competitive sports than in those not competing in sports; the reverse is true for female athletes (Ewing, 1998; Aaron et al., 1995). Neither marijuana nor alcohol has ergogenic effects on athletic performance. Cigarettes tend to be used less by athletes (Aaron et al., 1995). Anabolic steroids are used more by athletes. Drugs are available starting in junior high school.

The major categories of drugs used to improve performance by athletes include stimulants, pain relievers, and anabolic steroids (Wadler and Hainline, 1989). In addition, over the past decade there has been increased recognition of the use of dietary supplements as ergogenic aids. These supplements include creatine, androstenedione and dehydroepiandrosterone (DHEA), g-hydroxybutyrate, and protein powders. Categories of drugs and ergogenic aids are discussed in the following sections.

For more information about drugs of abuse, contact the National Clearinghouse for Alcohol and Drug Information at 1-800-729-6666 or on-line at [http://www.nida.gov/](http://www.nida.gov/). Therapeutic Drugs

Over-the-counter analgesics, decongestants, antihistamines, laxatives, and antiarrhythmic agents, and weight-loss medications are commonly used by athletes. Athletes should be asked specifically about use of these medications during office or training room visits, because they may not perceive them to be as important as prescription drugs and may not report their use. In addition, these medications have important side effects that can affect performance, and some are banned by sports governing bodies (NCAA and United States Olympic Committee). Physicians are encouraged to use the annual publication, *Athletic Drug Reference,* when...
advising athletes, especially college and elite athletes, about medication and prescription drug use.

Performance-enhancing Drugs

Stimulants Stimulants have been used extensively to combat psychological and muscular fatigue. These substances are banned by the International Olympic Committee (IOC) and can be detected by urine tests.

Amphetamines

Fine motor coordination and performance on tasks requiring prolonged attention have been shown to improve with amphetamine use. Side effects include anxiety, restlessness, tremors, tachycardia, irritability, confusion, and poor judgment, and these effects occur at higher doses.

Cocaine

Regarding the potential ergogenic effects of cocaine, no literature is available to support an ergogenic effect. Effects include increased heart rate, reflexes, and blood pressure, with accompanying euphoria. In the inexperienced user, reflexes are often more rapid but dysynchronous, leading to a decrement in athletic performance. Lethal toxicity can occur unexpectedly, particularly with intravenous use, because the doses of cocaine available on the street vary widely. Symptoms of acute overdose are difficult to treat and include arrhythmias, seizures, hyperthermia, and death. Metabolites can be found in the urine within 24 to 36 hours and up to 4 days after acute ingestion.

Caffeine

Caffeine is probably the most commonly used stimulant. Several studies have documented increased muscle work output for endurance activities. Significant side effects mimic those of other stimulants. A childhood caffeine tic syndrome was described in two first-degree cousins (Davis and Osorio, 1998). Caffeine has a direct diuretic effect, potentially complicating fluid and electrolyte status in prolonged exercise activities. Caffeine is banned by the IOC in amounts greater than 12 µg/ml (approximately equivalent to 4 to 6 cups of coffee or 8 to 16 cups of cola).

Anabolic Steroids

Anabolic steroid use is associated with increased muscle size and strength, especially in athletes who are weight training when the steroid use is initiated and who are consuming a high-calorie diet. It has been demonstrated in the animal models that anabolic steroids result in muscle hypertrophy in nonexercising muscle. There is no evidence that steroid use enhances aerobic power. There is evidence that anabolic steroids may aid in the healing of muscle contusion injury, in contrast to corticosteroids, raising potential ethical issues in the future regarding the use of steroids in muscle healing in response to contusion. FDA-approved uses of anabolic steroids include weight gain in patients with the acquired immunodeficiency syndrome (AIDS), severe anemia, hereditary angioedema, metastatic breast cancer, or male adrenal insufficiency.

Anabolic steroids may be injected or taken orally, and they are often freely available from peers and coaches. Buckley et al. (1988) reported that 6.6% of 12th grade males had used anabolic steroids. About 21% indicated their primary source was a health professional. The lifetime prevalence of illegal steroid use among high school students in the United States in 1999 was 3.7%, unchanged from 1995 and increased from 2.7% in 1991 (YRBS, 2000). In the Monitoring the Future study of 12th graders, the lifetime prevalence rates were 2.3% in 1995, 2.9% in 1999, and 2.5% in 2000 (http://www.monitoringthefuture.org/); in addition, 2.7% of middle school students reported using steroids (Faigenbaum et al., 1998).

Serious side effects of anabolic steroids include the following.

1. Alteration of myocardial textural properties (as detected by ultrasound): These changes are not seen in weight lifters who do not use anabolic steroids but nonetheless experience increased left ventricular mass with weight training. The clinical significance and prognostic significance of these changes is unknown.
2. Altered myocardial function: 17a-Methyl testosterone has been associated with reduced myocardial compliance and reduced myocardial function in rats.
3. Risk of hepatic damage (manifested as elevated liver-specific enzymes): The risk of hepatic neoplasms is unknown, because the reports to date are anecdotal.
4. Decreased high-density lipoprotein (HDL) and increased low-density lipoprotein (LDL) cholesterol levels.
5. Oligospermia and azoospermia with decreased testicular size occurs.
6. Premature epiphyseal closure in pubertal athletes.
7. Acne
8. Masculinization in women: Manifested as deepening of the voice, acne, and hair loss.
9. Feminization in men: Manifested as gynecomastia and a high voice.
10. Adverse psychological effects, including increased aggressiveness and rage in some athletes.
11. Increased use of other illicit drugs.

Injected steroids are detectable in the urine for 6 months or longer. Orally administered anabolic steroids disappear from the urine after days to weeks. More information on anabolic steroids can be obtained at the NIDA Web site on steroid use: http://www.steroidabuse.org/.

Narcotic Analgesics Narcotic analgesics are not perceived as "ergogenic aids" per se because, although they may allow an athlete to perform who is in pain from an injury, they do not enhance athletic performance. In standard doses there does not appear to be a detriment. However, they may be abused as analgesics in an attempt to return to play despite pain. The effects of psychomotor retardation include sedation, dysphoria, and nausea and vomiting.

Dietary Supplements as Ergogenic Aids Common characteristics of dietary supplements are that their long-term effects are not known and that the potency and purity of commercial products are unknown because they are not regulated by the FDA. These are salient points in counseling teens about their use.

Androstenedione

Androstenedione is an androgen produced by the gonads and adrenal glands. It is a precursor to estradiol and testosterone, yet it is marketed as a prohormone or nutritional supplement and not regulated by the FDA. Androstenedione has no beneficial effect on strength compared with controls. It has been associated with increased serum estradiol levels, no change in serum testosterone levels, and an increased LDL/HDL ratio at 12 weeks in healthy adult men (King et al., 1999; Broder et al., 2000).

There is no medically approved use for androstenedione, and its use is banned by the IOC, the NCAA, the National Football League, and other athletic organizations. However, because testing for androstenedione is not possible, its use is likely to continue. We do not advise its use as an ergogenic aid.

Dehydroepiandrosterone

DHEA is an adrenal androgen marketed as a food supplement. It is a precursor of androgens and estradiol. Ergogenic effects have not been demonstrated in athletes. DHEA has been reported to increase IGF. The side effects are androgenic, including hair loss and irreversible deepening of the voice in females. Androgens can hasten the growth of prostatic cancer, and estrogens can similarly affect the growth of breast and endometrial cancer. The effects of DHEA on the growth of these tumors is unknown.

Creatine

Creatine is synthesized in the liver, kidney, and pancreas. Creatine is supplied in the diet in the form of meat and fish. The usual U.S. diet supplies about 1 to 2 g of creatine daily to replenish that which is lost in the urine. Creatine theoretically works as an ergogenic aid by increasing the cellular concentration of high-energy phosphocreatine, the immediate transport entity in the synthesis of adenosine triphosphate (ATP) from adenosine diphosphate (ADP). It has been suggested that those with lower intracellular creatine concentration may benefit most from creatine supplementation, yet there is no method to assay for low intracellular concentration at this time. There may be some benefit for short-duration (i.e., less than 30 seconds), high-intensity exercise, but this effect has been demonstrated in
Recreational Drugs

Smokeless Tobacco

The incidence of smokeless tobacco use among prepertisonal and professional baseball players is estimated to be 30% to 40% (Emst et al., 1990), compared to 4% to 11% for the same age group in the general population. Cigarette smoking is less common among baseball players. Complications of smokeless tobacco include oral cancer, periodontal disease, oral leukoplakia, and mouth and gum irritation. Smokeless tobacco may have a performance-enhancing effect on cognitive tasks. There does not appear to be a demonstrable effect on reaction time, and there is no demonstrable ergogenic effect. The perception of benefit and cultural support for smokeless tobacco use in sports such as baseball, football, and rodeo sustain its use.

Alcohol

Alcohol is the leading drug of abuse among high school and college students, regardless of whether they are involved in sports. Alcohol use in college students has been reported to be better correlated with participation in fraternities and sororities than with participation in athletics. Alcohol has become entrenched in the fabric of sport in America through sponsorship use of athletic events. Beer producers spend large percentages of their advertising budgets on sports. This financial relationship between alcohol and sports appears unlikely to change, and, to the extent that advertising of alcohol influences drinking behaviors, alcohol abuse will remain a problem for adolescents and young adults.

Alcohol use acutely and chronically impairs athletic performance by impairing cognition and visual-motor coordination. However, athletes who significantly abuse alcohol may not have impaired performance until the problem is chronic. Physicians and trainers should attempt to diagnose and refer patients for treatment at the early and middle stages of alcohol abuse and not wait until performance deteriorates.

Testing for Performance-enhancing Drugs

Readers are encouraged to contact the NCAA (telephone 1-913-339-1906) or the U.S. Olympic Committee (1-800-233-0393, Drug Control Hotline). The following five components should be included in a drug testing program at an institution:

1. Written policy: A written policy regarding the purpose of the drug prevention program, the methods of collection, and consequences. In developing this plan, http://acha.org/info_resources/guidelines.cfm Drug testing should be done only when it is accomplished fairly and accurately.

2. Legal counsel: Legal counsel should be involved when a drug testing program is instituted.

3. Testing: Actual testing must take place, preferably at random.

4. Education: An educational component must be prepared and used.

5. Discipline for those who test positive: The mechanism of feedback to the player and coaches must be established. The physician should not be in the role of administering any disciplinary action; rather, he or she should work with the athlete to identify a problem if one exists and to facilitate appropriate care.

The American College of Sports Medicine and the American Academy of Orthopaedic Surgeons have also provided guidelines regarding drug education and testing of student athletes, including the following:

1. The drug education program should reflect the institution's overall commitment to eliminating drug abuse among students, faculty, and staff. The drug education and testing programs should not be restricted to only student athletes.

2. Each institution initiating or evaluating a drug education and testing program should have an advisory committee in place consisting of student athletes and representatives of the athletics department, student health center, counseling center, and student affairs.

3. A single individual should direct and supervise the program.

4. The educational program should target both the athletes and the coaches and staff of the athletic department.

5. Legal counsel should be involved when a drug testing program is instituted.

6. Drug testing should be done only when it is accomplished fairly and accurately.

7. Careful review should be undertaken regarding which athletes will be tested and how often, as well as what sanctions will be imposed.

8. The institution should guarantee that the test results and records will be handled in a strictly confidential manner.

9. It is important that adequate counseling be available for those who test positive.

10. Because alcohol is the most abused drug on campuses, an emphasis on alcohol education should be incorporated into the program.

WEB SITES

For Teenagers and Parents

http://www.sportsmedicine.com/, Site connecting individuals interested in sports medicine.


http://www.sportsmed.org/, Site connecting individuals interested in sports medicine.

For Health Professionals


http://www.ncaats.org/, National Center for Catastrophic Sports Injury Research, data on sports injuries and fatalities.


http://www.physiotherapy.com/, Physician and Sportsmedicine Online.


REFERENCES AND ADDITIONAL READINGS


The Female Athlete/Maturational Issues


Rencken ML, Chesnut CH, Drinkwater BL. Bone density at multiple skeletal sites in amenorrheic athletes. *JAMA* 1996;276:238.


Acne vulgaris, or common acne, is the skin disease most often evaluated by health care practitioners, and it is most prevalent in adolescents. Although 85% of adolescents have acne to some degree, the importance of this disease cannot be measured in numbers alone but must take into account the psychosocial consequences. The impact of acne on self-esteem and body image of the developing teenager can affect social interactions, school performance, and eventual employment.

ETIOLOGY

The pilosebaceous units (well-developed sebaceous glands with miniature hairs) located in highest concentration on the face, upper chest, and upper back are the sites for the development of acne. The key pathogenic factors of acne vulgaris are

1. Androgen-induced increased sebum production
2. Abnormal keratinization of sebaceous and follicular epithelium
3. Proliferation of Propionibacterium acne
4. Inflammation

Androgens and Sebum Production

Acne frequently begins in the prepubertal or early adolescent period with an increase in adrenal androgens leading to an increased production of sebum. With puberty and gonadal development, androgen production increases even further. Androgenic hormones (gonadal and adrenal) stimulate both enlargement and increased activity of sebaceous glands on the face, neck, and upper trunk. The sebaceous glands are androgen-sensitive appendages of hair follicles whose function is the secretion of lipids to lubricate the skin and hair. Serum dehydroepiandrosterone sulfate (DHEA-S) appears to be the earliest marker for the development of acne (Lucky et al., 1991; Stewart et al., 1992). Although testosterone levels are normal in most acne patients, local conversion to the end-organ effector dihydrotestosterone may be increased in acne-bearing skin. Furthermore, androgens may decrease the linoleic acid concentration in the sebum of acne patients, contributing to abnormal keratinization and obstruction of the pilosebaceous ducts. Individuals with acne have higher rates of sebum production, and often the severity of acne is proportional to the amount of sebum production (Federman and Kirsner, 2000).

Abnormal Keratinization

Abnormal keratinization of the sebaceous and follicular ducts results in retention hyperkeratosis and microcomedo formation (comedogenesis). The occluded follicle (the microcomedone) is most likely the initial lesion of both inflammatory and noninflammatory acne. Comedones may be closed (whiteheads) or open (blackheads). The whitehead contains inspissated keratin and lipid debris. Blackheads result from the oxidation of tyrosine to melanin through the open pore.

Propionibacterium acne

The excessive sebum and the anaerobic environment created by the plugged follicle result in colonization and proliferation of the anaerobic diphtheroid, P. acne. This bacteria, although part of normal skin flora, appears to be absent from the skin before puberty. P. acne also seems to be present in higher amounts in those individuals with acne.

Immune and Inflammatory Reaction

P. acne triggers immune and nonimmune inflammatory reactions by the following mechanisms:

1. Lipases are produced that are capable of hydrolyzing the triglycerides of sebum into irritating and comedogenic free fatty acids.
2. Chemotactic factors are released that attract leukocytes. Hydrolytic enzymes released by these neutrophils can produce breaks in the walls of the follicle, leading to disruption of follicular contents, leakage into the dermis, and resultant inflammation.
3. Complement pathways and host response are activated.

EPIDEMIOLOGY

Acne affects 80% of people between the ages of 11 and 30 years. Although it is usually a condition of adolescence, acne vulgaris affects 8% of 25- to 34-year-olds and 3% of the 35- to 44-year-old age group.

CLINICAL DISEASE
Types of lesions include comedones, inflammatory papules, pustules, nodules, true cysts, and scars. Each is discussed in this section.

Comedones

Comedones are the earliest sign of acne. They often appear 1 to 2 years before puberty.

1. Microcomedo: Microcomedos are impactions of keratin, lipids, bacteria, and rudimentary hairs within the sebaceous follicle. They are small and subclinical and are seen only on magnification or on biopsy specimens from acne patients. They are the precursor to all acne lesions.

2. Open comedo (blackhead)
   a. The epithelium-lined sac is filled with keratin and lipids and has a dilated orifice.
   b. The black coloration comes from melanin pigment.
   c. Usually the keratinous material is sloughed, and no inflammation occurs unless traumatized.

3. Closed comedo (Whitehead)
   a. Typically 1 to 3 mm in size, with a microscopic opening preventing the escape of contents.
   b. Active lesions may resolve spontaneously; if the follicular wall ruptures superficially, the lesion becomes an inflamed pustule, and deeper inflammation results in a papule or nodule.

Papules

Papules are inflammatory lesions measuring less than 5 mm in diameter. Superficial papules resolve in 5 to 10 days with little scarring, but they may result in postinflammatory hyperpigmentation, especially in adolescents with dark complexions. Deep papules usually have more intense inflammation. They can take weeks to resolve and may result in scarring.

Pustules

Pustules are lesions with a visible central core of purulent material.

Nodules

Nodules are inflammatory lesions measuring 5 mm or larger that can result as pustules rupture and form abscesses. Nodules commonly occur around the earlobes, neck, and jawline.

True Cysts

True cysts are lined by epithelium and are the rare residual lesions of healed pustules or nodules.

Scars

Types of scarring include

1. Ice pick or depressed scars
2. Perifollicular fibrosis, characterized by a yellow ring around follicle remnants
3. Hypertrophic scars and keloids, which tend to form on the chest, back, jaw line, and ears and are more common in dark-complected individuals

Location

The face is the area most prominently affected. Other affected areas are the back, chest, buttocks, upper arms, and thighs.

Grading

A widely accepted and standardized system for grading acne does not exist, but any classification scheme should take into consideration morphology, distribution, complications, response to therapy, and impact of disease on the individual patient. At present, it is recommended that acne be classified by the predominant type of lesion (e.g., comedonal, papulopustular, nodular) and then graded as mild, moderate, or severe.

Timing

1. Acne may appear as early as 5 to 8 years of age and seems to correlate with pubertal maturation. The prevalence and severity of the acne increases with advancing pubertal development and peaks between the ages of 14 and 17 years in females and 16 and 19 years in males.
2. Acne varies from a short, mild course to a severe disease lasting 10 to 15 years or longer.
3. Many adolescents do not have resolution of their acne by 20 years of age.
4. Males tend to have more severe acne for a shorter time.
5. Females tend to have a milder disease for a longer time.

DIFFERENTIAL DIAGNOSIS

Nonacne Lesions

1. Adenoma sebaceum: The most common cutaneous manifestation of tuberous sclerosis, manifesting as pink to red facial papules that develop in childhood or puberty. The lesions represent angiofibromas.
2. Flat warts: Skin-colored papules that may spread (Koebner phenomenon) with trauma.
3. Perioral dermatitis: Small, 1- to 3-mm erythematous papules or papulopustules of the chin, nasolabial folds, or periorbital areas that may be accompanied by scaling. A granulomatous variant exists. Topical corticosteroids can induce or aggravate this condition, which is related to acne rosacea. It is treated with topical and oral antibiotics. Topical metronidazole is very effective.
4. Hidradenitis suppurativa: Once thought to be a disease of the apocrine apparatus, it appears now to be a disease of the follicle (Webster, 1999). It is manifested by multiheaded comedos and deep, tender nodules and scarring involving primarily the axilla, groin, and buttocks. Treatment is difficult. Isotretinoin may be of some value.

Subtypes of Acne

1. Neonatal acne
   a. It is caused by stimulation of the sebaceous glands by maternal and neonatal androgens derived from the hyperactive neonatal adrenal gland. The lesions are usually closed comedones on the nose, forehead, and cheeks. Spontaneous resolution occurs in 1 to 3 months.
   b. Infantile acne usually manifests between the third and sixth months, and it may be associated with an increased risk of developing acne vulgaris during adolescence (Chew et al., 1990). Males are more commonly affected.
   c. Inflammatory acne lesions may occur.
2. Gram-negative folliculitis
   a. It is usually caused by a secondary colonization with Escherichia coli, Klebsiella, Pseudomonas, Enterobacter, or Proteus spp. during broad-spectrum antibiotic use.
   b. It can produce multiple pustules and nodules with a predilection for the perinasal area.
c. It should be suspected in an adolescent patient with acne who is doing poorly or flaring on antibiotics.
d. Culture results should guide diagnosis and therapy. Isotretinoin (Accutane) is also effective.

3. Occupational acne
a. Certain products can cause obstruction to sebaceous follicles, including mineral oil, crude petroleum, coal tar, and pitch.
b. Halogenated aromatic hydrocarbons can also cause an acneform eruption.

5. cosmetic acne: Less common since the advent of noncomedogenic cosmetics, but comedonal acne may be created by use of occlusive moisturizing creams, cocoa butter, vitamin E oil, flavored lip balms, and pomades.

Occupational acne
a. Drugs that can induce acne include androgens, adrenocorticotropic hormone (ACTH), steroids (oral and topical), barbiturates, cyclosporine A, phenytoin, carbamazepine, isoniazid, rifampin, lithium, ethionamide, bromides, and iodides.
b. These drugs can also exacerbate preexisting acne.
c. Steroid acne is typically a monomorphic eruption of papules or papulopustules that resolves without scarring. It does not produce comedones, nodules, and scars. It may involve areas, such as the extremities, that are not normally affected in acne vulgaris.

6. Acne conglobata
a. Acne conglobata is a severe, suppurative, often chronic form of nodular acne that most often occurs in white males.
b. The back is often severely affected, along with the thighs, buttocks, and upper arms.

7. Acne fulminans: This rare form of nodulolulcerative acne has an abrupt onset and is often accompanied by fever, leukocytosis, anemia, polyarthritis, and, rarely, osteolytic bone lesions (Karvonen, 1993).

8. Acne excoriée des jeunes filles: This is most frequently seen in adolescent girls who excoriate or manipulate the acne lesions; severe scarring and even mutilation may result. It is usually associated with emotional stress.

THERAPY

General

Several considerations are important in treating adolescents with acne.

1. Practitioners must appreciate the significance of this problem to adolescents. The short- and long-term consequences of acne to the adolescent’s emotional well-being should not be underestimated.
2. Most adolescents treat themselves and will often heed peer suggestions more readily than those of a physician. Therefore, practitioners must emphasize the role and necessity of compliance.
3. Practitioners must understand the route, timing, and dose of the drugs administered. Use only a few drugs and know them well.
4. Make sure the adolescent understands how to use the medications.
5. Do not promise instant success. Point out that
   a. Therapy with topical agents often causes acne to look worse in the first 3 to 4 weeks.
   b. Improvement may take months.
6. Explain the side effects of all medications used.
7. Perform a thorough history and physical examination. The female patient should also be examined for the presence of hirsutism, alopecia, and obesity. She should be asked about her menstrual cycle and use of oral contraceptive pills (OCPs).
8. Treat according to severity, as follows
   a. Mild comedonal acne may respond to over-the-counter or prescription acne preparations such as salicylic acid or benzoyl peroxide. Table 20.1 lists common over-the-counter preparations.

   b. Moderate-to-severe comedonal acne may respond to the addition of tretinoin, adapalene or tazarotene, at bedtime.
   c. Mild inflammatory acne may respond to the addition of a topical antibiotic or 3% benzoyl peroxide with 3% erythromycin (Benzamycin) gel.
   d. Unresponsive or moderate-to-severe inflammatory acne requires the addition of a systemic antibiotic.
   e. Nodular or nodulocystic acne that does not respond to oral antibiotics should be treated with isotretinoin (Accutane) by an experienced practitioner.
   f. It is important to remember that combined OCPs in females may be very useful therapy for all of the forms of acne.

9. General measures and misconceptions: It is important to discuss directly with the teen, as well as parents, common misconceptions about acne:
   a. Diet: No evidence exists that foods such as cola, chocolate, nuts, or French fries increase acne severity. Unless a patient notices dramatic differences with certain foods, dietary restrictions are unnecessary.
   b. Hygiene: Uncleanliness does not cause acne. Overemphasis on compulsive scrubbing is unnecessary and may itself cause a dermatitis. Mild soaps or cleansers should be used to wash the face two times a day.
   c. Stress: Stress seems to make acne worse and, in turn, increase the adolescent’s anxiety levels and decrease self-image. Continued support must be given to the affected adolescent.
   d. Neither sexual fantasies or sexual activity causes acne.
   e. Teens should avoid wearing headbands or using grease on the scalp; both can exacerbate acne.
   f. Premenstrual acne flares can occur.

Topical Agents

A list of topical agents available is provided in Table 20.2.

Table 20.1. Over-the-counter products

b. Moderate-to-severe comedonal acne may respond to the addition of tretinoin, adapalene or tazarotene, at bedtime.
   c. Mild inflammatory acne may respond to the addition of a topical antibiotic or 3% benzoyl peroxide with 3% erythromycin (Benzamycin) gel.
   d. Unresponsive or moderate-to-severe inflammatory acne requires the addition of a systemic antibiotic.
   e. Nodular or nodulocystic acne that does not respond to oral antibiotics should be treated with isotretinoin (Accutane) by an experienced practitioner.
   f. It is important to remember that combined OCPs in females may be very useful therapy for all of the forms of acne.

9. General measures and misconceptions: It is important to discuss directly with the teen, as well as parents, common misconceptions about acne:
   a. Diet: No evidence exists that foods such as cola, chocolate, nuts, or French fries increase acne severity. Unless a patient notices dramatic differences with certain foods, dietary restrictions are unnecessary.
   b. Hygiene: Uncleanliness does not cause acne. Overemphasis on compulsive scrubbing is unnecessary and may itself cause a dermatitis. Mild soaps or cleansers should be used to wash the face two times a day.
   c. Stress: Stress seems to make acne worse and, in turn, increase the adolescent’s anxiety levels and decrease self-image. Continued support must be given to the affected adolescent.
   d. Neither sexual fantasies or sexual activity causes acne.
   e. Teens should avoid wearing headbands or using grease on the scalp; both can exacerbate acne.
   f. Premenstrual acne flares can occur.

Topical Agents

A list of topical agents available is provided in Table 20.2.
It is important to remember that the vehicle (cream, gel, lotion, or solution) may be as critical in therapy as the active ingredient of the formulation. The type of vehicle may depend on the patient's skin type. Overall, solutions and gels are drying and nongreasy and therefore are best for those with very oily skin. Creams and lotions are more moisturizing and tend to be preferred by most patients. Creams in particular are appropriate for teens with dry or sensitive skin.

**Benzoyl Peroxide**

1. **Actions**
   a. Bacteriocidal effect on *P. acnes* with low potential for resistance
   b. Mild comedolytic action; decreases free fatty acids

2. **Dose**
   a. Benzoyl peroxide is available in concentrations of 2.5%, 3%, 4%, 5%, 6%, 8%, and 10%.
   b. Benzoyl peroxide comes in gels, lotions, creams, soaps, and washes and is available in both prescription and nonprescription preparations. The aqueous gels are better tolerated thancompounds prepared in an alcohol or acetone vehicle. Benzoyl peroxide in the gel form also appears to have better penetration and higher efficacy than benzoyl peroxide in soaps, washes, or lotions.
   c. Gradually increase concentration as tolerated. The treatment can be started either every other day or once daily and increased to twice daily.

3. **Adverse side effects**
   a. Peeling and irritation
   b. Contact dermatitis (1% to 2%)
   c. Can lead to bleaching of hair and colored fabrics

**Retinoids (Tretinoin, Tazarotene, and Adapalene)** Retinoids are derivatives of vitamin A. They are the most effective comedolytic agent and have been a mainstay of acne therapy for more than 25 years. Newer preparations of retinoids have included adapalene, tazarotene, and less irritating formulations of tretinoin.

1. **Action**: Decreases comedo formation and follicular plugging by reducing hyperkeratosis and decreasing the cohesiveness of follicular epithelial cells, making it very useful in comedonal acne.

2. **Dose and usage**
   a. Tretinoin or Retinoic Acid (Retin-A, Retin-A Micro, Avita, Altinac): Until recent years, tretinoin was the only available topical retinoid. Tretinoin may be effective as monotherapy in teens with noninflammatory or mild inflammatory acne. Because of the potential for significant irritation, close supervision and instruction are required.
      - The following concentrations are available: 0.025%, 0.05%, and 1% cream; 0.01% and 0.025% gel, and Retin-A Micro 0.1% gel.
      - The cream is the least irritating, followed by a microsphere formulation of 0.1% tretinoin gel (Retin-A 0.1% micro gel), which is in a slow-release vehicle. More potent formulations include, in approximate increasing potency, 0.05% cream, 0.025% gel, 0.1% cream, and 0.05% solution.
      - Start with the lower concentrations of cream or Retin-A Micro gel applied every other night 20 to 30 minutes after washing the face; gradually increase to a daily regimen. Tretinoin should be applied in small amounts to clean, dry skin. If this is not effective, increase the concentration as tolerated.
      - Use of benzoyl peroxide in the morning and tretinoin in the evening is considered to be the most effective regimen, but it may cause excessive irritation, particularly in certain climates. Use of tretinoin in the morning is not advised, because the irritation is compounded by sun exposure.
      - After 2 or 3 weeks of therapy, some irritation will occur. If it is severe, therapy can be stopped for a short time. After 3 to 4 weeks, a purulent eruption may occur, indicating the dislodging of microcomedos; treatment should continue. Patients should be warned about this potential flare and that it indicates that the therapy is working.
      - Avoid sun exposure, because tretinoin is not photostable and increases photosensitivity. If used during summer months, a sunscreen rated SPF-15 or higher should be used.
      - Use with caution in black and Asian patients, because tretinoin can cause hyperpigmentation or hypopigmentation.

3. **Adverse side effects**
   a. Peeling, drying, and irritation
   b. Hyperpigmentation or hypopigmentation
   c. Sun sensitivity
   d. There is concern about the potential of teratogenicity, although in at least one study of women exposed to tretinoin in the first trimester of pregnancy there was no increase in the rate of fetal anomalies (Jick et al., 1993).

4. **New tretinoin preparations**
   a. Tretinoin gel microspheres: Tretinoin gel microsphere 0.1% (Retin-A Micro) uses a delivery system designed to improve the tolerability of a topical tretinoin. This system is also used in other cosmetic, sunscreen, and prescription products and consists of macroporous beads approximately 10 to 25 μm in diameter. The active ingredient, tretinoin, is incorporated into the microspheres and gradually released over a sustained period. It is speculated that this enhances delivery to the epidermis and limits irritation.
   b. Tretinoin polymer cream: Tretinoin cream 0.025% (Avita) consists of both tretinoin and a liquid polymer compound called polyolyprepolymer-2 (PP-2). Polyolyprepolymer-2 is composed of large polymer molecules; it enhances delivery to the epidermis and within the pilosebaceous unit, thus limiting irritation. Preclinical and clinical-study results in humans have demonstrated less irritation with this formulation than with traditional tretinoin formulations.
   c. Adapalene (Differin 0.1% Gel, Cream, Pledgets, and Solution) is a derivative of naphthoic acid that behaves like a retinoid but is photostable and causes less irritation. Adapalene appears to possess moderate to potent antiinflammatory activity compared with tretinoin, which has weak or no antiinflammatory activity. Several clinical studies have shown that adapalene 0.1% gel is equally or more effective than 0.025% tretinoin gel (the most potent tretinoin formulation available) in reducing acne lesions. Other studies show equal efficacy in mild-to-moderate acne. Adapalene is applied daily, it may take 8 to 16 weeks to see results.
   d. Tazarotene (Tazorac 0.1% and 0.05% Gel and Cream)
      - Tazarotene is a synthetic acetylenic retinoid that rapidly penetrates skin, where it is converted into its active metabolite, tazarotenic acid. This agent binds to nuclear retinoid acid receptors and appears to influence the cohesion of corneocytes and inflammation.
      - In general, the 0.1% gel is more effective than the 0.05% preparation in reducing the number of acne lesions.
      - The adverse effects are similar to other topical retinoids and include erythema, pruritus, burning, and stinging.
      - It is labeled for use in both psoriasis and mild-to-moderate acne.
      - It is applied overnight or as short contact therapy for 5 minutes and removed with a mild facial cleanser.
      - Its use is not recommended in pregnant women.
      - It is photostable.

**Azelaic Acid**

Azelaic acid (Azaleex) is used to treat mild-to-moderate inflammatory acne. Azelaic acid is a dicarboxylic acid first developed for benign hyperpigmentation disorders. It is structurally unrelated to other acne therapies and possesses bacteriostatic properties against *P. acnes* and other organisms. Azelaic acid does not appear to induce microbial resistance. In addition, azelaic acid appears to normalize keratinization. In some studies, topical azelaic acid was similar in efficacy to topical benzoyl peroxide 5% and 0.05% tretinoin cream. However, it is even more effective when combined with other topical agents. Azelaic acid is available as a 20% cream (Azaleex), which is applied twice daily to clean, dry skin. Side effects are uncommon (less than with tretinoins and benzoyl peroxide) but include pruritus, burning and stinging of the skin, rash, and hypopigmentation. This product should be used cautiously in individuals with dark complexion.

**Topical Antibiotics**

Topical antibiotics appear to reduce the counts of *P. acnes* and also to decrease the percentage of free fatty acids in surface lipids. The most commonly used topical antibiotics are erythromycin, clindamycin, sulfacetamide, and metronidazole. Topical antibiotics allow direct application and have negligible systemic side effects, but resistance is frequently seen. Although they can be effective for mild-to-moderate inflammatory acne, topical antibiotics cannot replace systemic antibiotics in more severe cases. Preparations include:

1. Erythromycin 2% (e.g., A/T/S solution, T-Stat solution, Erygel, Emgel, Acne-mycin): Available in solutions, gels, pads, and ointment; applied twice daily.
2. Clindamycin 1% (Cleocin T solution, C/T/S, Clinda, Clindagel 1%): Available in a solution, lotion, gel, or pledget; applied twice daily. Pseudomembranous colitis has rarely been reported to occur with topical use (Parry and Rha, 1986).
3. Sodium sulfacetamide: This antibacterial agent has been used in antiacne preparations for years, but a new formulation of sodium sulfacetamide without sulfur has recently become available. This lotion (Klaran Lotion) contains 10% sodium sulfacetamide in an aqueous base; it lacks sulfur and alcohol, which may decrease its potential to cause local irritation. Preparations containing sulfur include Sulfacet-R, Novacet, Plexion cleanser, and Vanocin. These agents appear to be more effective for rosacea than for acne. The sulfur-containing products should be avoided in the sulfa-allergic patient.

4. Benzoyl peroxide 5% with 3% erythromycin [Benzamycin gel] and Clindamycin 1%–benzoyl peroxide 5% gel (benzaclin topical gel)—Preparations that combine a topical antibiotic with benzoyl peroxide are favored because bacterial resistance has not been seen.

**Other Agents**

1. Keratolytic washes and lotions: Once the mainstay of acne therapy, keratolytics such as salicylic acid, sulfur, or resorcilon, while available in nonprescription and prescription preparations, have largely been replaced by newer agents. These can act synergistically with benzoyl peroxide or tretinoin, but when used alone they are not as effective as benzoyl peroxide and tretinoin.

2. Cryotherapy with carbon dioxide, acetone slush, or liquid nitrogen: These treatments may increase peeling but usually are not necessary.


**Systemic Therapy**

**Antibiotics**

1. **Actions**
   a. Decreases the population of *P. acnes*
   b. Reduces the amount of free fatty acids
   c. May depress the inflammatory response in the pilosebaceous follicle

2. **Usage**
   a. Doses and advantages and disadvantages of each antibiotic are summarized in Table 20.3.

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Dosage</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tetracycline</td>
<td>500 mg/kg daily</td>
<td>Good penetration into the sebaceous gland</td>
<td>Gastrointestinal upset</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>100 mg/day</td>
<td>Predicted to have lower levels of resistance</td>
<td>Photosensitivity</td>
</tr>
<tr>
<td>Minocycline</td>
<td>50–200 mg daily</td>
<td>Highly lipid-soluble and reaches higher concentrations in the sebaceous gland</td>
<td>Photosensitivity, tooth discoloration</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>500–1000 mg daily</td>
<td>Stronger than tetracycline in the treatment of treatment-resistant acne</td>
<td>Photosensitivity</td>
</tr>
</tbody>
</table>

3. **Side effects**
   a. Tetracycline: Associated with gastrointestinal upset, *Candida* vaginitis, and, rarely, a drug eruption, anemia, neutropenia, or phototoxicity. Tetracycline should not be used in children younger than 8 years of age or in female adolescents who are pregnant. Photosensitivity can occur, as can tooth discoloration in children younger than 13 years of age. Pseudotumor cerebri has also been reported.
   b. Doxycycline: Frequently causes photosensitivity. Other side effects include gastrointestinal upset, vaginal yeast infections, tooth discoloration in children younger than 13 years of age, and pseudotumor cerebri.
   c. Minocycline: Associated with photosensitivity, photosensitivity, and pseudotumor cerebri have been reported. Reports of drug-induced lupus are increasing.
   d. Erythromycin: Side effects include nausea, vomiting, diarrhea, *Candida* vaginitis, and occasionally drug eruptions. Erythromycin can also cause photosensitivity. The gastrointestinal side effects of erythromycin have limited its usefulness in acne therapy.
   e. Routine laboratory monitoring generally is not necessary for healthy adolescents receiving long-term oral antibiotic therapy. However, if a patient has a preexisting condition or develops symptoms, appropriate laboratory tests should be performed.

**TABLE 20.3. Systemic antibiotic therapy**

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Dosage</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tetracycline</td>
<td>500 mg/kg daily</td>
<td>Good penetration into the sebaceous gland</td>
<td>Gastrointestinal upset</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>100 mg/day</td>
<td>Predicted to have lower levels of resistance</td>
<td>Photosensitivity</td>
</tr>
<tr>
<td>Minocycline</td>
<td>50–200 mg daily</td>
<td>Highly lipid-soluble and reaches higher concentrations in the sebaceous gland</td>
<td>Photosensitivity, tooth discoloration</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>500–1000 mg daily</td>
<td>Stronger than tetracycline in the treatment of treatment-resistant acne</td>
<td>Photosensitivity</td>
</tr>
</tbody>
</table>

**13-cis-Retinoic Acid or Isoretinoin (Accutane)** 13-cis-Retinoic acid has dramatically reversed the course of acne in many individuals with severe nodulocystic or recalcitrant disease. Because of significant toxicity, the drug is still reserved for treatment of severe nodular or recalcitrant acne by practitioners who are experienced with its use. Careful laboratory monitoring is also required.

1. **Actions**
   The drug is a synthetic vitamin A derivative that affects keratinization by suppressing sebum production and diminishing the growth of *P. acnes*.

2. **Usage**
   a. Baseline: Complete blood count (CBC), liver function tests, cholesterol, triglycerides, and urinalysis. In females, a serum or urine pregnancy test with a sensitivity of at least 50 mIU/mL should be obtained within 1 week before starting therapy and repeated on the day therapy is started. Female patients should be instructed to start therapy on the second or third day of their normal menstrual period.
   b. Two weeks after beginning therapy: Repeat cholesterol and triglycerides and continue monitoring every 2 weeks if not stable.
   c. At 4 weeks and monthly thereafter: Repeat baseline tests, including serum or urine pregnancy test, but urinalysis is optional.
   d. End of therapy: Repeat CBC, liver function tests, cholesterol, triglycerides, and pregnancy test.
• Other: vaginal dryness, urethritis
b. Musculoskeletal: Arthralgias and myalgias, 16%
c. Hyperostosis: Mainly a problem when drug is used for prolonged periods of time in other dermatological conditions
d. Decreased night vision
e. Headaches, 5%
f. Pseudotumor cerebri, rare
g. Depression: Adolescents with a personal or family history of depression may be at increased risk of developing major depression or suicide.
h. Photosensitivity, 5% to 10%
i. Elevated cholesterol (7%) and triglyceride (25%) concentrations
j. Elevated liver function tests, 15%
k. Renal: Proteinuria and hematuria
l. Hematologic: Elevated erythrocyte sedimentation rate (40%), leukopenia, elevated platelets (10% to 20%)
m. Skin rash: Occasional pyogenic granuloma-like lesions (hypergranulation tissue); Staphylococcus aureus skin colonization and infections
n. Cheilitis and hypertriglyceridemia: Tend to be dose related

Hormones
The major role for hormonal intervention is in individuals who have an endocrine problem such as polycystic ovary syndrome or congenital adrenal hyperplasia.

Combined Oral Contraceptives
Combined OCPs can also be effective in suppressing sebaceous gland activity. By reducing ovarian production of androgens and reducing circulating levels of free testosterone, acne lesions can be reduced. The OCPs of choice would be third-generation OCPs that contain less androgenic progestins, such as desogestrel (Desogen, Ortho-Cept) or norgestimate (Ortho-Cyclen, Ortho Tri-Cyclen). The triphasic combination OCP, norgestimate-ethinyl estradiol (Ortho Tri-Cyclen) is the first low-dose OCP to receive approval by the U.S. Food and Drug Administration for the treatment of acne. For side effects, see the discussion on OCPs in Chapter 43. Estrogens cannot be used in males because of the feminizing side effects.

Corticosteroids
The use of high doses of corticosteroids should be reserved for the treatment of acne conglobata, acne fulminans, and the acute flare of acne precipitated by initiating isotretinoin therapy. Prednisone 5.0 to 7.5 mg or dexamethasone 0.25 to 0.5 mg is effective in reducing adrenal androgen production.

Antandrogens
The agents available are not approved for use in the treatment of acne, and the side effects usually result in poor compliance. However, spironolactone, cyproterone acetate, and finasteride have been used with some success, particularly in female patients with other signs of androgen excess.

Overall
The following drugs and combinations are suggested. In addition, in any of these categories, OCPs may be useful for female patients.

Comedonal Acne
Salicylic acid, tretinoin, benzoyl peroxide, azelaic acid, adapalene, tazarotene, topical antibiotics and OCPs are helpful agents. In general, benzoyl peroxide, topical retinoids, and azelaic acid are the mainstays.

Inflammatory Acne
Tretinoin, benzoyl peroxide, azelaic acid, adapalene, tazarotene, topical antibiotics, OCPs and systemic antibiotics are helpful.

For mixed comedonal and papulopustular conditions, use
1. Retinoid plus topical antibiotic
2. Retinoid plus benzoyl peroxide
3. Retinoid plus benzoyl peroxide plus topical antibiotic
4. Azelaic acid plus benzoyl peroxide
5. Azelaic acid plus topical antibiotic

For papules and pustules, use benzoyl peroxide plus topical antibiotic. Add an oral antibiotic if moderate-to-severe inflammatory acne is present or if results are unsatisfactory.

Nodulocystic Acne
OCPs, systemic antibiotics, and isotretinoin are helpful. In general,
1. Use oral antibiotics and also topical agents if comedonal acne also present.
2. If results are unsatisfactory, consider oral isotretinoin.
3. If results are still unsatisfactory, evaluate for endocrinopathy.

ACNE SURGERY
1. Comedone extraction: Open comedones can be easily removed with a comedo extractor. Closed comedones require puncture with a needle or lancet first. Extensive surgical treatment should be avoided, because manipulation can lead to scarring.
2. Incision and drainage: Do not incise acne pustules and nodules, because of possible resultant scarring.
3. Intralesional corticosteroids: Injection of 0.05 to 0.1 mL per lesion of triamcinolone acetate suspension (1.0 to 2.5 mg/mL) into each papulonodular or cystic lesion can lead to rapid improvement in isolated cystic lesions. Individuals should be cautioned that this treatment can lead to some skin depression at the injection site, which usually resolves in 4 to 6 months but can be permanent.
4. Rehabilitation: After acne lesions have become quiescent, young adults may explore surgical options for scars. At present, alternatives include collagen implants for isolated shallow depressions, punch excision and grafting, chemical peels, dermabrasion, and laser resurfacing. Avoid any cosmetic procedures for at least 6 months to 1 year after discontinuing isotretinoin.

WEB SITES
http://www.healthatoz.com/atoz/HealthUpdate/Alert02182000.asp. Facts about acne from health A to Z.
http://www.m2w3.com/acne. Acne support group.

REFERENCES AND ADDITIONAL READINGS


White GM. Acne therapy. Dis Mon 1999;45:301.


ECZEMATOUS DERMATITIS

Eczematous dermatitis is a superficial inflammatory response of the skin to multiple exogenous and endogenous agents and includes a poorly defined group of problems whose etiology is often either multifactorial or unknown. The two major groups of dermatitis affecting adolescents are contact dermatitis and atopic dermatitis. In a review of the most common dermatological problems seen by internists, dermatitis was the most common diagnosis, making up 15.8% of the dermatological diagnoses (Feldman et al., 1998).

Contact Dermatitis

Clinical Manifestations

1. Distribution: Areas that have been exposed to the inciting agent, often including the hands, eyelids, genitalia, and legs.
2. Lesions: Tendency for confluency, sharp borders, or straight lines. The lesions tend to have vesicles or bullae, coozing, and fissuring.

Types

About 80% of contact dermatitis is irritant and about 20% allergic.

1. Irritant dermatitis: A nonimmunologically mediated dermatitis that occurs in all individuals exposed to the agent in potent enough doses. Prior exposure is not required. Irritants include the following:
   a. Alkalis: Soaps, detergents, bleaches, and cleansers
   b. Acids: Hydrochloric acid, nitric acid, oxal acid, carbolic acid, acetic acid, and salicylic acid
   c. Insecticides
   d. Hydrocarbons: Oils and tars
   e. Fiberglass
2. Allergic contact dermatitis: A cell-mediated reaction (delayed type) that occurs in patients specifically sensitive to the offending agent (usually an environmental chemical). Prior exposure is required for a reaction. Agents commonly include the following:
   a. Rhus (poison ivy, oak, or sumac) dermatitis typically has a linear pattern
   b. Nickel and other metals, particularly mercury and chromium
   c. Rubber compounds
   d. Dichromate: A common cause of shoe dermatitis; also found in metals, paint, cement, and photographic chemicals
   e. Clothing dyes or chemical finishes (e.g., formaldehyde resin)
   f. Adhesives: The rubber component or the glue
   g. Cosmetics: Hair dyes, hair sprays, artificial nails, nail hardeners, lipsticks, eye makeup, preservatives, sunscreens, perfumes, and mouthwashes

Diagnosis

1. Vesicular, erythematous lesions in a well-defined patch or an arrangement, often linear, corresponding to the distribution of contact.
2. History of exposure to an offending agent.
3. Patch testing is helpful in allergic contact dermatitis.
4. Allergic contact versus irritant dermatitis: Clinically, the two may be indistinguishable, but irritant dermatitis usually occurs on the hands. Photoallergic dermatitis usually occurs on sun-exposed areas such as face and neck and is usually in response to photosensitization by ingested drugs.

Treatment

1. Find offending agent and eliminate exposure.
2. In acute reactions, apply cool compresses with Burow solution for 30 minutes several times daily.
3. Apply topical corticosteroid creams.
4. Antihistamines may help decrease the associated pruritus.
5. For widespread, severe contact dermatitis, a course of systemic corticosteroids tapered over 2–3 weeks is indicated. The initial dose can be approximately 40–60 mg/day with decreases of 5 mg/day.

Atopic Dermatitis

Atopic dermatitis is a common, chronic, pruritic dermatitis also known as atopic eczema and allergic eczema, which typically has its onset in childhood and may improve or continue in adolescence. The condition is usually genetically determined. The prevalence decreases with age and is at its most in childhood.

Clinical Manifestations

1. Hereditary predisposition: A positive family history of atopy (asthma, allergic rhinitis, and atopic dermatitis) is present in two thirds of individuals.
2. Association with other atopic conditions: 50% of individuals concurrently have either asthma or allergic rhinitis.
3. Course is chronic and fluctuating.
4. Pruritus: Itching is often severe.
5. Typical morphology and distribution: In adolescence, the morphology resembles the adult pattern of flexural lichenification and involvement of the face, neck, and hands.
6. Skin lesions: Slightly elevated, flat-topped papules that tend to coalesce to form lichenified, scaly plaques. The plaques may become excoriated, exudative, or crusted.
7. Dry skin is a common association.
8. Seasonal variation in disease activity is common.
9. Elevated immunoglobulin E often occurs.
10. Keratosis pilaris: Follicular hyperkeratosis on the lateral upper arms and thighs is commonly associated with atopic dermatitis.
11. Pityriasis alba: Scaly, hypopigmented patches (typically on the face, neck, trunk, and extremities of children and adolescents between the ages of 3 and 16 years) represent a nonspecific dermatitis that may be a variant of atopic dermatitis. The teen is usually asymptomatic, but pruritus may occur.

Complications

1. Infections: Increased susceptibility to herpes simplex virus, Staphylococcus aureus, Trichophyton rubrum, warts, and molluscum contagiosum
2. Eye: Increased prevalence of cataracts, keratoconus, recurrent conjunctivitis, periornital darkening, and retinal detachment
3. Exfoliative dermatitis

Differential Diagnosis

1. Seborrheic dermatitis: Greasy, scally scalp; distribution more likely to include scalp, eyebrows, and ears
2. Contact dermatitis: History of contact with an offending agent and patterned distribution of the eruption
3. Tinea corporis or pedis: Sharp margins; confirmed by positive findings from potassium hydroxide examination
4. Scabies: Distribution usually includes web spaces of hands, groin, buttocks, and axilla; positive skin scraping for mites or eggs
5. Psoriasis: Well-demarcated erythematous plaques with silvery scale; predilection for extensor surfaces; nail pitting common, but not specific

Treatment

1. Avoid hot water.
2. Avoid soaps, detergents, and overheated rooms.
3. Acute weeping lesions: Use tepid, wet dressings with Burow solution (aluminum acetate).
4. Dry skin lesions: Use an emollient such as Aquaphor, Cetaphil, Eucerin, Shepard's, or Lubriderm.
5. Apply topical corticosteroid cream or ointment (see Table 21.1 for classification of topical corticosteroids by potency).

6. Use oral antihistaminic agent.
7. Use oral antistaphylococcal antibiotics if a secondary infection is present.
8. Topical Tacrolimus ointment (Protopic 0.03% and 0.1% ointment) was recently approved to treat atopic dermatitis.

Other Types of Eczematous Dermatitis

1. Lichen simplex chronicus: One or more lichenified plaques probably secondary to repeated local trauma such as rubbing or scratching
2. Dyshidrotic eczema (pompholyx): Recurrent crops of vesicles on palms and soles and sides of fingers and toes; exacerbated by stress and frequent exposure to water
3. Seborrheic dermatitis: Greasy scaling patches on scalp, eyebrows, nasolabial area, intertriginous areas, and chest
4. Nummular dermatitis: Minute vesicles and papules that enlarge to form discrete, erythematous, coin-shaped patches

Pyoderma

Types

1. Acne: See Chapter 20 for discussion.
2. Folliculitis: Infection of a hair follicle is common and usually involves S. aureus or streptococci. The infection is usually superficial and is characterized by tiny pustules near affected hair follicles, surrounded by an area of erythema. Common locations include the scalp, extremities, buttocks, and perioral and perinasal areas. Treatment involves local hygiene with antibacterial soaps or cleansers and a topical antibiotic ointment.

Pseudofolliculitis barbae is a noninfectious, inflammatory condition occurring in men with curly hair, caused by reentry of curved hairs after shaving. Curative therapy includes avoidance of shaving and letting the beard grow. Although this will eliminate the condition, this is not always practical. Steps to improve the condition include the following:

a. Soften facial hair by wetting the beard with warm water; the facial hair should be in contact with water for at least 2 minutes.

b. A soft-bristled toothbrush can be used in a circular motion on the bearded area to dislodge any hair tips that are beginning to pierce the skin. This should be done twice a day, both before shaving and at bedtime.
c. The entire beard area should be covered with a gentle shaving gel that enhances razor gliding motion and minimizes irritation.

d. A special razor should be used to cut the hair at the correct length to reduce the chance that the hair tip will reenter the skin. Examples of special razors include Bump Fighter (American Safety Co.), Fol Guard shaver (American Safety Razor Co.), and PFB razor (Norelco).

e. Shave in the direction of beard growth and never shave against the direction of hair growth or pull the skin taut. Shaving against the direction of hair growth will encourage the tip of the hair to grow under the skin.

f. Aftershave lotion or cologne should be avoided. A moisturizing lotion with a steroid component can be used for a short period. If a steroid component is added, it should be mild and only used for 1–2 weeks. Topical retinoids may also be beneficial.

g. A “collar extender” should be used when wearing neckties to prevent pressure and friction from worsening this condition on the neck and collar area.

h. Impetigo: Although most common in children, impetigo does occur in adolescents. It is characterized by discrete and coalescent lesions that begin as vesicles, quickly become pustular, and then rupture, leaving a thick yellowish crust. The lesions are usually related to group A b-hemolytic streptococci or S. aureus. Localized infection can be treated with topical mupirocin (Bactroban), but more extensive or recurrent disease requires treatment with systemic antibiotics. Resistance to erythromycin and penicillin is being seen with increasing frequency.

i. Pseudomonas folliculitis or hot tub dermatitis: Pruritic papulopustular eruptions typically appear 1–2 days after exposure to a whirlpool, hot tub, or swimming pool, with a predilection for areas covered by a swimsuit, the axillae, and the upper arms. Usually self-limited and resolves in 7–14 days, rarely associated with constitutional symptoms or systemic infection.

5. Furuncles: Staphylococcal abscesses develop around hair follicles. Multiple lesions may coalesce to form a carbuncle. Treatment includes warm compresses, antistaphylococcal antibiotics, and incision and drainage of fluctuant lesions. Recurrent or chronic furunculosis requires eradication of the staphylococcal carrier state.

PAPULOSQUAMOUS ERUPTIONS

Eruptions consisting of scaly patches and plaques that occur with some frequency during adolescence include psoriasis, pityriasis rosea, seborrheic dermatitis, fungal infections, drug eruptions, and secondary syphilis (for a discussion of syphilis, see Chapter 64).

Psoriasis

Psoriasis affects between 1% and 3% of the population, with the age at onset being between 10 and 20 years in nearly 25% of the cases. Psoriasis is a chronic, genetically influenced, and immunologically based inflammatory disease of the skin and joints.

Etiology

Although the cause of psoriasis is unknown, the role of heredity is becoming more apparent as genetic linkage is being identified. Some cases appear to be related to a gene localized to the distal end of chromosome 17q (Linden and Weinstein, 1999) and others appear to be related to chromosomes 3 and 6.

Precipitating Factors

1. Certain infections including streptococcal pharyngitis
2. Trauma
3. Stress
4. Cold weather and low humidity
5. Administration of certain medications

Clinical Manifestations

Psoriasis leads to hyperkeratosis and thickening of the epidermis, as well as increased vascularity and infiltration of the dermis with inflammatory cells. The symptoms of psoriasis are highly variable.

1. Appearance: Round, circumscribed erythematous plaques with a silvery “micaeous” scale. The plaques are usually well demarcated and pinpoint bleeding can occur when a scale is removed. Small teardrop-size or guttate lesions are often associated with streptococcal pharyngitis.

2. Distribution: Scalp, trunk, elbows, and knees are common sites. Usually the condition is mild and affects <20% of the skin. In some individuals, local skin trauma (such as tattoo or burn) will precipitate psoriatic lesions in that area (Köbner phenomenon). Inverse psoriasis is limited to the umbilicus and intertriginous areas.

3. Nails may show pitting, onycholysis, and oil spots in about 10% of individuals with psoriasis.

4. Psoriatic arthritis: A seronegative oligoarthritis that may present as acute monoarticular disease in childhood, and is fortunately uncommon in adolescence.

5. Depression may be present secondary to the significant skin lesions.

Diagnosis

Diagnosis of psoriasis is based on typical appearance, location of lesions, or rarely skin biopsy results.

Treatment

Psoriasis may remit spontaneously or as a result of therapy, but recurrences are almost certain. There is no cure for psoriasis and treatment is oriented to suppress or ameliorate the disease. Treatment depends on the severity, duration, and site of disease, as well as the emotional state and treatment preference of the adolescent. Many individuals will need some continuing maintenance therapy.

1. Evaluation and avoidance of precipitating factors.

2. Topical therapy should be tried first. Topical therapies are convenient and lack serious side effects of systemic therapy. Their efficacy is debatable.

a. Topical corticosteroids: A first choice among most dermatologists. A higher strength preparation is usually used for acute flares and areas with thickened plaques, and medium-potency preparations are used for maintenance. Used alone, topical corticosteroids are most appropriate for lesions limited to isolated small areas of the body. Potent steroids should be avoided in thinner areas of the skin such as face, groin, and genital regions. More potent topical steroid use should be limited to about 2 weeks, at which time a lower potency topical agent should be used. In addition, once the plaques have flattened out, the application can be reduced in frequency (e.g., every 12 hours for three doses, once a week). The practitioner must remember that the topical corticosteroid preparation can vary widely on potency depending on the vehicle. Betamethasone dipropionate at a given concentration can vary from superpotent to midpotent depending on the vehicle (Table 21.1). The concentration can vary widely on potency depending on the vehicle. Betamethasone dipropionate at a given concentration can vary from superpotent to midpotent depending on the vehicle.

b. Calcipotriene (Dovonex) ointment: A synthetic vitamin D3 analogue useful in treating mild to moderate plaque-type psoriasis. The medication can be an effective first- or second-line topical agent for chronic plaque psoriasis. Although not as effective as superpotent topical corticosteroids, it does not have their side effects. In clinical trials, calcipotriene 0.05% ointment was as effective as fluocinonide 0.05% ointment and betamethasone valerate 0.1% ointment in decreasing plaque and disease severity (Linden and Weinstein, 1999). The most common adverse side effect was irritant dermatitis (10%–15% of individuals).

c. Tazarotene (Tazorac) gel or cream: A synthetic retinoid effective for mild to moderate psoriasis, but may cause local irritation including pruritus, burning, and erythema in up to 30% of individuals in a dose-related mechanism. The rate of side effects is higher with the 0.1% concentration, compared with the 0.05% concentration. Efficacy may be increased and irritation reduced when used with a mid- to high-potency topical corticosteroid. Tazarotene is used as a once-daily topical gel or cream.

d. Tar: Not as widely used as in the past because they can be messy and stain clothes. However, they are inexpensive and mostly free of side effects.

 Preparedations such as Eslar gel or Balnetar solution may be more cosmetically pleasing to the adolescent. The most widely used preparation is a tar shampoo for scalp psoriasis.

e. Anthralin: Anthralin inhibits enzymes involved in epidermal proliferation. Anthralin is often used for short periods such as 15–30 min/day. Anthralin also can stain skin and clothing. Healthy skin should be avoided.

f. Keratolytics: Ointments with 2%–10% salicylic acid can help soften plaques and can be used with topical corticosteroids or coal tar to improve penetration.

3. Intrallesional corticosteroids: Useful for localized psoriatic plaques; potential side effects include atrophy and hypopigmentation.

4. Systemic therapy is rarely indicated in adolescents because of the potential long-term side effects. Cases with severe disease should be referred to a specialist and treatment may involve the following:

a. Phototherapy: Two types of phototherapy are available: ultraviolet B (UVB) and psoralen plus ultraviolet A (UVA). UVA combined with oral or topical psoralens is reserved for severe, recalcitrant psoriasis, because of the increased risk of developing skin cancer.

b. Systemic therapy can include methotrexate, acitretin (a systemic retinoid), and cyclosporine A. All should be done under the care of a specialist.
Lesions: Oval, salmon-colored papular and macular, 1- to 2-cm scaly lesions, whose long axes follow the body's lines of cleavage in a "Christmas tree" distribution. The lesions typically have a fine cigarette paper-like scale peripherally.

2. Herald patch: The rash is usually preceded by a large, 2- to 6-cm single lesion known as the "herald or mother patch." The interval between the development of the herald patch and other lesions is usually between 2 and 21 days.

3. Distribution: Symmetrical, occurring mainly on the trunk, upper arms, and lower neck, with occasional involvement of face, scalp, hands, and feet.

4. It is possible for the scalp rash to be severe.

5. Other systemic symptoms: Constitutional symptoms are rare.

**Differential Diagnosis**

1. Tinea corporis
2. Secondary syphilis
3. Seborrheic dermatitis

**Treatment**

1. Reassurance: Condition spontaneously resolves within 6–8 weeks.
2. Antihistamines or topical corticosteroids: Use if pruritus is significant.

**Seborrheic Dermatitis**

Seborrhoeic dermatitis is a chronic inflammatory disease of the skin, limited to areas of excessive sebaceous gland activity.

**Clinical Manifestations**

1. Distribution: Usually involves the scalp, eyebrows, forehead, lips, ears, nasolabial creases, axilla, chest, inframammary folds, umbilicus, and groin.
2. Appearance: Dry, moist, or greasy scales often crusted with yellow patches of various sizes.
3. Pruritus: May or may not be present.
4. Course marked by many remissions and exacerbations.

**Differential Diagnosis**

1. Psoriasis
2. Tinea corporis
3. Pityriasis rosea
4. Atopic and contact dermatitis

**Fungal Infections**

The dermatophytoses are the most common fungal diseases of the skin. The three principal genera responsible are *Trichophyton*, *Microsporum*, and *Epidermophyton*. These are responsible for tinea capitis, tinea corporis, tinea pedis, tinea barbae, tinea cruris, and tinea unguium (onychomycosis). Other common superficial fungal infections in adolescents include tinea or pityriasis versicolor caused by *Pityrosporum orbiculare* and *Candida albicans*, which is the causative agent in many cases of intertrigo, paronychia, vaginitis, and pruritus ani.

**Dermatophytes**

1. Tinea capitis: Tinea capitis is a dermatophyte infection of the scalp and hair follicles, most commonly caused in the United States by *Trichophyton tonsurans*. It usually presents as an enlarging scaly patch of alopecia, often consisting of broken hairs (black dots). A granulomatous mass, a kerion, can develop in response to the infection. Some of these fungi are spread by contact with objects such as combs, brushes, and hats, and others from cats and dogs. The diagnosis can be made by either fluorescence of the infected hairs with a Wood lamp, examination of the hairs with potassium hydroxide, or culture of infected hairs. Some studies show that only one third of individuals will have positive results from examination of a potassium hydroxide specimen, so one cannot necessarily rely on the potassium hydroxide examination alone. If the diagnosis is in question, a culture can be taken. Treatment is with systemic griseofulvin, microscopic 250-500 mg/day or ultramicrosize 330-375 mg/day. Treatment is continued for 6-8 weeks or at least 2 weeks after a negative culture. Itraconazole 100 mg/day (3-5 mg/kg/day) for 2-6 weeks or terbinafine 250 mg/day has been used in resistant cases or in patients who cannot tolerate griseofulvin. In addition, topical selenium sulfide 2.5% or ketoconazole 2% shampoo should be used twice weekly to reduce the shedding of spores.

2. Tinea barbae: A dermatophyte infection of the beard area. This disease is more common in adolescents living in rural areas who work with farm animals. The involvement is mostly one-sided on the neck or face and results in either deep nodular supplicative lesions or superficial, crusted, partially bald patches. Treatment is with griseofulvin (500 mg daily for 4-6 weeks).

3. Tinea corporis. This dermatophyte infection may involve any area of the body except the scalp, beard, face, hands, feet, and groin. It is characterized by a gradually expanding, circular, red ring with a raised margin containing scales and minute vesicles. Pruritus is common. There is a tendency for central healing. The diagnosis is confirmed by a potassium hydroxide examination of a skin scraping or a culture of the fungus. The differential diagnosis includes the other papulosquamous eruptions. The condition is commonly seen in wrestlers. If the lesions are localized, topical therapy can be chosen from various agents (Table 21.2). If the lesions are widespread or resist local therapy, griseofulvin at 500 mg daily for approximately 4 weeks is effective. Systemic fluconazole, itraconazole, and terbinafine are alternative choices but are not approved for the treatment of dermatophytosis. Lesher (1999) reviewed oral therapy of common superficial fungal infections of the skin. Treat sources of infection such as pets, infected family members, or other close contacts, including those that occur during sports such as wrestling.
Tinea cruris: Commonly called "jock itch" or "crotch rot," this is a common dermatophyte infection of the groin in male adolescents. The lesions are usually found on the upper and inner surfaces of the thighs, particularly during summer months. Typical lesions are bilateral or unilateral, crescent shaped, reddish, and scaly, with sharply defined, raised borders. The scrotum is usually unaffected. The diagnosis is generally made on the basis of clinical appearance, negative findings from Wood lamp examination of branches of hyphae on potassium hydroxide wet mount. Cultures of the scales can be performed, if necessary, for diagnosis. Differential diagnoses of common groin eruptions include the following:

- **Tinea cruris**
- **Candidiasis**
  - Eruptions are more inflammatory.
  - The margins are less discrete, with individual satellite papules or pustules outside the confluent area.
  - The scrotum is commonly affected.
- **Erythrasma**: A superficial bacterial skin infection of intertriginous sites caused by Corynebacterium minutissimum (short gram-positive diphteroid).
  - The rash appears as a well-defined pinkish or brownish patch. The rash is smooth or may be covered by a fine scale resembling a cutaneous dermatophytosis.
  - The rash fluoresces a coral red color under a Wood lamp caused by porphyrin production.
- **Potassium hydroxide preparation may show negative results, but Gram stain may show gram-positive filamentous rods (C. minutissimum).**

- **Psoriasis**
  - Often accompanied by psoriatic lesions elsewhere
  - Negative findings from potassium hydroxide preparation and Wood lamp examination
  - Biopsy helpful

- **Psoriasiform eruptions**
  - Red, macerated, foul-smelling skin in inguinal creases
  - Obesity a predisposing factor
  - **Erythematous** eruption with a well-demarcated, nonraised border
  - **Typical** lesions elsewhere
  - Negative findings from potassium hydroxide wet mount and Wood lamp examination

- **Seborrheic dermatitis**
  - **Leathery, lichenified, mottled** eruption with ill-defined borders
  - Negative findings from potassium hydroxide preparation and Wood lamp examination

5. **Topical antifungal drugs and coverage**

   4. **Tinea cruris:**
      - Commonly called "jock itch" or "crotch rot," this is a common dermatophyte infection of the groin in male adolescents. Typical lesions are found on the upper and inner surfaces of the thighs, particularly during summer months. Typical lesions are bilateral or unilateral, crescent shaped, reddish, and scaly, with sharply defined, raised borders. The scrotum is usually unaffected. The diagnosis is generally made on the basis of clinical appearance, negative findings from Wood lamp examination of branches of hyphae on potassium hydroxide wet mount. Cultures of the scales can be performed, if necessary, for diagnosis. Differential diagnoses of common groin eruptions include the following:

     a. **Tinea cruris**
     b. **Candidiasis**
        - Eruptions are more inflammatory.
        - The margins are less discrete, with individual satellite papules or pustules outside the confluent area.
        - The scrotum is commonly affected.
     c. **Erythrasma**: A superficial bacterial skin infection of intertriginous sites caused by Corynebacterium minutissimum (short gram-positive diphteroid).
        - The rash appears as a well-defined pinkish or brownish patch. The rash is smooth or may be covered by a fine scale resembling a cutaneous dermatophytosis.
        - The rash fluoresces a coral red color under a Wood lamp caused by porphyrin production.
     d. **Psoriasis**
        - Often accompanied by psoriatic lesions elsewhere
        - Negative findings from potassium hydroxide preparation and Wood lamp examination
        - Biopsy helpful
     e. **Psoriasiform eruptions**
        - Red, macerated, foul-smelling skin in inguinal creases
        - Obesity a predisposing factor
        - **Erythematous** eruption with a well-demarcated, nonraised border
        - **Typical** lesions elsewhere
        - Negative findings from potassium hydroxide wet mount and Wood lamp examination
     f. **Seborrheic dermatitis**
     g. **Psoriasiform eruptions**
     h. **Irritant dermatitis**
        - History of use of sprays, soaps, detergents, or medication
     i. **Other pruritic groin rashes include scabies, pediculosis pubis, miliaria. Treatment of some of these other common groin eruptions includes:**

         a. **Candidiasis**: Topical nystatin, ketoconazole, or miconazole cream two times a day.
         b. **Erythrasma**: Erythromycin is the treatment of choice and can be used either orally or topically. One gram in divided doses can be given orally for 5–7 days or topical erythromycin twice a day can be used. Alternative therapies have included topical 10%–20% aluminum chloride, 2% clindamycin hydrochloride solution, and miconazole cream. In addition, a single 1-g dose of clarithromycin has been reported to be effective (Wharton et al., 1998).
         c. **Psoriasis**: Low potency topical corticosteroids
         d. **Intertrigo**: Keep affected area dry and use drying powders.
         e. **Seborrheic dermatitis**: Low-potency (class VI–VII) topical corticosteroids, ketoconazole 2% cream.
         f. **Neurodermatitis**: Low-potency topical corticosteroids

5. **Topical antifungal drugs and coverage**

   - **Tinea cruris**
   - **Candidiasis**
   - **Erythrasma**
   - **Psoriasiform eruptions**
   - **Irritant dermatitis**
   - **Other pruritic groin rashes include scabies, pediculosis pubis, miliaria. Treatment of some of these other common groin eruptions includes:**
     - **Candidiasis**: Topical nystatin, ketoconazole, or miconazole cream two times a day.
     - **Erythrasma**: Erythromycin is the treatment of choice and can be used either orally or topically. One gram in divided doses can be given orally for 5–7 days or topical erythromycin twice a day can be used. Alternative therapies have included topical 10%–20% aluminum chloride, 2% clindamycin hydrochloride solution, and miconazole cream. In addition, a single 1-g dose of clarithromycin has been reported to be effective (Wharton et al., 1998).
     - **Psoriasis**: Low potency topical corticosteroids
     - **Intertrigo**: Keep affected area dry and use drying powders.
     - **Seborrheic dermatitis**: Low potency topical corticosteroids
     - **Neurodermatitis**: Low potency topical corticosteroids

6. **Tinea unguum:** Tinea unguum is a dermatophyte infection involving the soles of the feet and the toe webs. Early signs are scaling, maceration, and fissuring of the toe webs. This can extend to scaling, redness, and vesicular eruptions on the soles. Tight-fitting occlusive footwear and warm humid weather predispose the adolescent to infection. This is often transmitted through shared bath and shower facilities. Potassium hydroxide examination will reveal branching hyphae. Tinea pedis can be confused with pitted keratolysis, juvenile plantar dermatosis, dyshidrosis, psoriasis, and contact dermatitis. Treatment for tinea pedis consists of the following:

   - **Employ a regimen of soaks or wet compresses with Burow or Domeboro solution for 15–30 minutes two to four times daily.**
   - **Secondary bacterial infection should be treated with topical or oral antibiotics depending on severity.**
   - **A topical antifungal agent can be helpful, but if infection is severe or unresponsive, a course of griseofulvin microsize 500 mg/day or ultramicrosize 660–750 mg/day for 4–8 weeks may be helpful.**
   - **If there is a severe inflammatory response or an "id" reaction (see item VII), a short 1-week course of topical or systemic steroids is helpful.**
   - **Keep feet dry and well aerated; sandals should be worn if possible or white cotton socks with shoes.**
   - **Use prophylactic program of drying the feet thoroughly after baths, and then use a medicated powder such as Tinactin or Zeasorb-AF, or Lotrimin AF spray once the infection is over.**

6. **Tinea unguum:** Tinea unguum is a dermatophyte infection of the nail plate. Onychomycosis includes all infections of the nail caused by any fungus, including dermatophytes and yeast. The infection begins with a white or yellow discoloration of the distal part of the nail. The nail subsequently becomes thickened, brittle, elevated, and deformed. Identification of the causative organism is essential for therapy. It is important to sample the nail layer near the nail bed for culture. Various nail dystrophies, including psoriasis, may be confused with onychomycosis. The following drugs essentially replaced the use of griseofulvin for this condition. Terbinafine (250 mg/day for 3 months) has been approved to treat toenail infections, but only 6 weeks of treatment is necessary for the fingernails. Itraconazole (100 mg twice daily for 3 months) has been approved or it can be given in a pulsed regimen of 200 mg twice daily for 1 week per month repeated for 3 months to treat toenail involvement. Treatment for fingernails is shorter, with only 6 weeks of daily therapy or 2 months of the pulsed regimen recommended. When prescribing these newer medications, one must consider potential drug interactions, side effects, and appropriate monitoring. The alternatives to systemic therapy include topical ciclopirox 8% topical solution (Penlac nail lacquer) or avulsion of the nail plate followed by topical therapy.

7. **Dermatophytid:** An "id" reaction is a cutaneous or systemic reaction to the fungal antigen borne through the bloodstream from the primary fungal focus to distant sites. This reaction may consist of a widespread follicular scaly eruption or may be limited to a vesiculobullous or scaly eruption of the hands. The former is more commonly associated with tinea capitis and the latter with tinea pedis.

**Tinea (Pityriasis) Versicolor**

1. **Clinical manifestations:** Scaly hypopigmented or hyperpigmented macules or patches typically located over the upper trunk and arms, and occasionally the face and neck caused by P. orbiculare. The lesions are usually asymptomatic.

2. **Predisposing factors:** Humidity, hyperhidrosis, heredity, diabetes, and systemic corticosteroids.

3. **Diagnosis:** Made by observation of hyphae and spores (spaghetti and meatballs) on potassium hydroxide wet mount. Wood light examination is helpful in showing yellowish or brownish fluorescence.

4. **Differential diagnosis:** Pityriasis alba, vitiligo, pityriasis rosea, seborrheic dermatitis, and syphilis.

5. **Treatment:**
   - **Topicals:** Selenium sulfide 2.5% shampoo, ketoconazole 2% shampoo, zinc pyrithione shampoo or soap, sulfosalicylic acid, Tinver lotion (25% sodium thiosulfate, 1% salicylic acid, and 10% alcohol), or Lamisil 1% spray. Usually these agents are used in the shower or overnight as tolerated daily for 2 weeks, then several times a month for maintenance. Topical antifungals of the imidazole class are effective but expensive for large areas of involvement.
   - **Systemic fluconazole and itraconazole:** Fluconazole (400 mg as a single dose) and itraconazole (200 mg for 5–7 days) have been shown to be effective in the treatment of tinea versicolor. These medications are not Food and Drug Administration approved for use in the treatment of tinea versicolor.

**Drug Eruptions**

A skin rash is one of the most common side effects of drug administration. Many drugs can cause skin reactions of various types. The most commonly implicated drugs are sulfamethoxazole, ampicillin, penicillin, gentamicin, cephalosporins, barbiturates, and isoniazid. Other drugs used by adolescents that cause skin eruptions...
less often are diphenhydramine, aspirin, aminophylline, codeine, and tetracycline. The following are various skin eruptions and implicated agents.

**Maculopapular or Morbilliform Rash**

- Ampicillin or amoxicillin: Reaction rate is nearly 90% in patients with infectious mononucleosis.
- Isoniazid
- Barbiturates
- Carbamazepine
- Diazepam and related compounds
- Erythromycin
- Phenytoin
- Tetracycline
- Thiazides

**Urticaria**

<table>
<thead>
<tr>
<th>Nonimmunological</th>
<th>Immunological</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cotuline Aspirin</td>
<td>Barbiturates</td>
</tr>
<tr>
<td>Contrast media</td>
<td>Penicillin</td>
</tr>
<tr>
<td>Opiates</td>
<td>Sulfinpyridine</td>
</tr>
<tr>
<td>Nonsteroidal antinflammatory drugs (NSAIDs)</td>
<td>Tetracyclines</td>
</tr>
</tbody>
</table>

**Erythema Multiforme** Generalized erythematous macules or bullae with targetoid lesions. Mucosae may be involved and fever may accompany more severe reactions.

- Allopurinol
- Hydralazine
- Isoniazid
- Penicillin
- Phenobarbital
- Salicylates
- Sulfonamides
- Tetracycline
- Thiazide diuretics
- Vaccines (measles, polio, diphtheria)

**Erythema Nodosum**

- Bromides
- Oral contraceptives
- Codeine
- Penicillin
- Salicylates
- Sulfonamides

**Exfoliative Dermatitis**

- Allopurinol
- Penicillin
- Quinacrine
- Phenobarbital
- Phenothiazines
- Tetracycline
- Tetrathionate
- Vitamin A

**Acneform Eruptions**

- Adrenocorticotropic hormone
- Androgenic hormones
- Bromides
- Isoniazid
- Lithium
- Oral contraceptives
- Corticosteroids
- Hydantoins
- Iodides
- Phenobarbital
- Vitamin B12

**Photosensitive Eruptions**

- Coal tar
- Disinfectants
- Dyes
- Essential oils
- Griseofulvin
- Methotrexate
- NSAIDs
- Psoralens
- Thiazide diuretics

**Fixed Drug Eruptions** One or few erythematous or hyperpigmented ovoid lesions sometimes containing bullae. They occur in the same location with repeated exposure to the inciting drug.

- Barbiturates
- Erythromycin
- Gold
- Metronidazole
- Penicillin
- Pseudoephedrine
- Trimethoprim
- Quinacrine
- Sulfonamides
- Tetracycline

**Secondary Syphilis** For a discussion, see Chapter 64.

**SKIN GROWTHS**

**Warts: Verrucae**

1. **Etiology:** Human papillomavirus (DNA virus of Papovaviridae family). Numerous human papillomavirus (HPV) types have been identified (more than 70). Although there is some association between HPV type and the clinical type of wart, this is not a 100% correlation. HPV types 1, 2, and 4 are associated with common warts and plantar warts. Flat warts appear more related to types 3 and 10.

2. **Epidemiology**
   a. **Age:** Peak prevalence is between the ages of 10 and 19; thereafter, the prevalence decreases.
   b. **Prevalence:** Seven percent to 10% of the general population.
   c. **Transmission:** Inoculation occurs by direct or indirect contact from one person to another; autoinoculation is common. Local trauma promotes inoculation.
   d. **Incubation:** 1–6 months.

3. **Clinical manifestations:** The clinical classification and appearance of a wart is dependent on the wart's location on the skin.
   a. **Verruca vulgaris**
      - Single or multiple in occurrence
      - Most frequently occurs on hands, fingers, and periangually but can occur anywhere
      - Usually sharply circumscribed, firm hyperkeratotic papules 1–5 mm or larger in diameter when located on hands
      - Flat warts, projecting as threadlike structures often when located on the neck and face
   b. **Verruca plana (flat warts)**

   - **Secondary Syphilis** For a discussion, see Chapter 64.
Verruca plantaris (plantar warts)

- Podophyllin: Condylomata acuminatum can effectively be treated with 20%–25% podophyllin in benzoin, or trichloroacetic acid (80%–90%).
- Autologous skin grafts
- Topical or oral psoralens followed by long wavelength ultraviolet radiation (UVA): Must be used with great caution and administered by a practitioner.
- Acid: Trichloroacetic acid and bichloroacetic acid are particularly useful in plantar warts. The treatment is as follows:
  - Use of a cover-up cosmetic such as Dermablend or Covermark.
  - Pare the wart.
  - Paint the wart with acid and work into wart with needle or toothpick by carefully sticking wart several times.
  - Can dress with salicylic acid pads. May repeat in 1 week.
- Electrodesiccation and curettage: This treatment requires expert skill to avoid unnecessary destruction and scarring.
- Acid: Trichloroacetic acid and bichloroacetic acid are particularly useful in plantar warts. The treatment is as follows:
  - Use of a cover-up cosmetic such as Dermablend or Covermark.
  - Pare the wart.
  - Paint the wart with acid and work into wart with needle or toothpick by carefully sticking wart several times.
  - Can dress with salicylic acid pads. May repeat in 1 week.
  - Podophyllin: Condylomata acuminatum can effectively be treated with 20%–25% podophyllin in benzoin, or trichloroacetic acid (80%–90%).
  - Imiquimod 5% (Aldara) has been approved to treat genital warts.

Molluscum Contagiosum

Molluscum contagiosum is a common, viral-caused growth. For more information, see Chapter 66.

Parasitic Skin Infections


MISCELLANEOUS SKIN CONDITIONS

Vitiligo

Vitiligo is an acquired, disfiguring disease characterized by the loss of melanin, resulting in depigmented areas of the skin. It is associated with ocular abnormalities, autoantibodies, thyroid disease, diabetes mellitus, and leukotrichia (depigmentation of the hair).

Etiology

- The cause is unknown, but autoimmune mechanisms are speculated.

Clinical Manifestations

- Depigmented, well-circumscribed, cutaneous white macules, several millimeters to several centimeters, appear on the skin, usually noticed first during the summer months.
- Any area can be affected, but the face and extremities are most common.
- Usually the distribution is bilateral and symmetrical but may be segmental. Segmental vitiligo is usually not associated with other autoimmune diseases.
- Wood light examination is helpful in identifying early lesions.

Differential Diagnosis

- Morphea (localized scleroderma), pityriasis alba, and tinea versicolor may be confused with vitiligo.

Treatment

- Although treatment is difficult, it is improving.
  - Use of sunscreens for photoprotection and avoidance of sun.
  - Use of a cover-up cosmetic such as Dermablend or Covermark.
  - A 2- to 3-month trial of a low- to mid-potency topical corticosteroid.
  - Topical or oral psoralens followed by long wavelength ultraviolet radiation (UVA): Must be used with great caution and administered by a practitioner experienced in their use.
  - Autologous skin grafts.
  - Spontaneous repigmentation rarely occurs.

Sunburn

Teenagers often spend long days at the beach or are involved in athletic activities without attempting to protect their skin from the sun. Sunburn can be a frequent summer problem. Recommendations to adolescents include the following:

1. Midday exposure: Avoid exposure from 10 a.m. to 3 p.m., when the sun's short ultraviolet rays are at their peak. Adjust 1 hour for daylight savings time.
2. Acclimating: Gradually increase exposure time to sun.
3. Clothing: Wear protective clothing and a hat when possible.
4. Sunscreens: Sunscreens do not prevent a tan, but they do lessen burning. A sun protection factor of 15 or greater with a broad spectrum of coverage should be used regularly (Table 21.3).
Temperature: The cooling effect of water and wind at the beach decreases the ability to detect sunburn; therefore, the adolescent must be educated about the sun’s strong effects.

Medications: Certain medications can increase photosensitivity. These include griseofulvin, NSAIDs, oral contraceptives, diphenhydramine, phenothiazines, thiazides, psoralen, sulfonamides, tetracyclines, and tranquilizers. Phototoxic reactions are uncommon immunologically mediated responses to small amounts of the offending agent. Phototoxic reactions appear as an exaggerated sunburn and occur in nearly all individuals with sufficient exposure to the offending drug.

Treatment of sunburn includes topical corticosteroids and an oral NSAID as indicated.

Urticaria

Appearance Appearance is that of transient, discrete, erythematous wheats, which may coalesce and form large edematous patches with raised borders. Severe pruritis or stinging sensations can occur. Simple urticaria involves only the superficial layers of the skin, whereas angioedema involves edema in the deeper subcutaneous and submucosal tissues, particularly involving the palms of the hands, the soles of the feet, and the head and neck. Angioedema of the throat may cause respiratory obstruction in severe cases. Urticaria has been defined as acute if it lasts less than 6 weeks and chronic if the reaction lasts more than 6 weeks.

Classifications/Triggers The triggers involved in urticaria involve many factors; however, in up to 50% of cases of both acute and chronic urticaria and angioedema, no cause is identified.

1. Type I hypersensitivity
   a. Drug induced: Penicillin and sulfonamides are the most common drugs involved.
   b. Food: Urticaria after eating most commonly involves ingestion of nuts, fish, eggs, fresh berries, shellfish, or food additives. Some of these reactions are immunologically related, whereas others are caused by direct release of histamine.
   c. Insect and arthropod bites and stings

2. Type III hypersensitivity
   a. Infections: Various bacterial, viral, and parasitic infections have been suggested as possible causes of urticaria.
   b. Autoimmune diseases: Systemic lupus, thyroid diseases, and certain malignancies
   c. Drugs: penicillin and sulfonamides

3. Direct mast cell degranulation
   a. Food chemicals such as benzoxates and tartrazine
   b. Drugs such as aspirin, opiates, and NSAIDs
   c. Hyperosmolar radiocontrast media

4. Physical urticarias
   a. Cholinergic urticaria: This reaction can be triggered by heat, exercise, or stress. Cholinergic urticaria is produced by the reaction of acetylcholine on the mast cell. It is characterized by highly pruritic, punctate wheals 1–3 mm in diameter. These wheals are surrounded by large areas of erythema. The palms and soles are always spared. Aquagenic urticaria may be a form of cholinergic urticaria that produces a similar reaction on contact with water. The diagnosis can be confirmed by either soaking a foot in hot water, exercising the adolescent, or using a methacholine (Mecholyl) skin test. These will all reproduce the lesions.
   b. Heat urticaria
   c. Cold urticaria: Localized or generalized hives develop with exposure to cold air or water, rarely accompanied by syncope, hypotension, and drowning. Hereditary and acquired variants exist. The diagnosis may be confirmed in most cases with an ice cube test. Cyproheptadine (Periactin) is helpful, but desensitization may be necessary.
   d. Pressure urticaria: Urticaria in response to slight pressure, such as sitting or clapping
   e. Solar urticaria
   f. Vibratory urticaria
   g. Dermatographism: Characterized by the development of localized wheals and erythema, following stroking of the skin with a blunt instrument

Chronic Urticaria Chronic urticaria can be a serious disabling condition also associated with insomnia and fatigue. Autoimmune diseases such as systemic lupus erythematosus may present with urticaria and should be considered in the differential diagnosis of chronic urticaria.

Evaluation

Acute transient urticarias do not need a further evaluation. Chronic urticarias can be associated with a long list of conditions and further tests should be ordered only after thorough history and physical examination looking for underlying etiologies.

Treatment

1. Avoid the inciting factor, if known. Use of elimination diets may be helpful in determining a specific food involved.
2. Topical therapy: Cold baths or showers may be helpful in relieving some of the itching.
3. Antihistamines are effective, but primarily in acute urticaria. Hydroxyzine (Atarax) (25 mg three times a day) is the drug of choice in cholinergic urticaria and dermatographism.
4. Epinephrine is useful if the urticaria is associated with angioedema.
5. Systemic steroids are beneficial in severe acute reactions, particularly with associated angioedema.

Hereditary Angioedema

Hereditary angioedema is an autosomal-dominant disease resulting in sudden attacks of edema of the soft tissue or mucous membranes of the pharynx and larynx. Gastrointestinal edema can occur, causing nausea, vomiting, and severe abdominal pain. Laryngeal edema can cause death. Often, hereditary angioedema first appears during adolescence and can occur as frequently as every 2 weeks. Attacks can be precipitated by stress or trauma or can occur spontaneously. A low level of C1 esterase inhibitor is found in 85% of patients, whereas in the other 15%, the inhibitor is nonfunctional. The decrease or nonfunctional C1 esterase inhibitor allows for increased activity of the complement system.

Diagnosis The serum C4 level is used as a screening test, as it is reduced even when the patient is asymptomatic. The C2 level is reduced during attacks. If these levels are reduced and the C1 inhibitor protein level is within the reference range, a functional assay should be performed.

<table>
<thead>
<tr>
<th>Chemical</th>
<th>Spectrum</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSA</td>
<td>UV-B</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>UV-B</td>
</tr>
<tr>
<td>Antihistamines</td>
<td>UV-A(1-380)</td>
</tr>
<tr>
<td>Pyrethrin (Mix of pyrethroids)</td>
<td>UV-A</td>
</tr>
<tr>
<td>Pyrethrin</td>
<td>UV-A/UV-B</td>
</tr>
<tr>
<td>Zinc acetate</td>
<td>UV-A/UV-B</td>
</tr>
<tr>
<td>Tinocid doleto</td>
<td>UV-A/UV-B</td>
</tr>
</tbody>
</table>

*PNBA, p-nitroaniline acid; UA, ultraviolet-A; UVB, ultraviolet-B.*

**TABLE 21.3. Sunscreens and protective spectra**
Male pattern baldness: This is produced in genetically susceptible individuals, resulting in a loss of hair secondary to the effects of androgenic hormones.

Scalp disease: Treat underlying condition.

Hair loss secondary to physical factors

Scalp disease: Hair loss can occur secondary to various scalp diseases, including psoriasis, fungal disease, seborrhea, or eczema.

Scarring alopecia: This form of irreversible hair loss is the result of various inflammatory processes or trauma. Some dermatological conditions that may result in

Treatment: Treatment usually includes either glucocorticoids both intralesional and oral; anthralin; topical immunotherapy including dinitrochlorobenzene,

History: An extensive history is indicated, including the onset and duration of hair loss, drug use, skin or scalp disease, and recent stress, surgery, illness, or

Referral to a dermatologist may be necessary for further evaluation and scalp biopsy if diagnosis is in question.

Keloids can form.

Etiology: Autoimmunity is probably the cause in most individuals. Activated CD4 and CD8 lymphocytes have been found around the affected anagen hair

Traction alopecia: Hair loss at the margin of scalp, occurring primarily in African-American females and in women who wear hair tightly braided.

Diagnosis: Clinical presentation of sharply circumscribed patches of alopecia with exclamation point hairs at the periphery of the bald patch

Metabolic disorders: Hair loss can be found with iron deficiency, hypothyroidism, hyperthyroidism, diabetes mellitus, or hypopituitarism.

Anagen effluvium: Anagen effluvium is hair loss occurring during the growing phase. Common causes include antiinflammatory drugs used for chemotherapy,

Unsanitary methods have resulted in bacterial infections, hepatitis, tuberculosis, and syphilis. Concern about transmission of HIV infection exists.

Physical examination: Check particularly for evidence of seborrhea, scalp disease, or an endocrine disorder.

Hair physiology: Scalp hair grows at the rate of 0.35 mm/day. The rate is faster in females and during summer months. The average daily loss is 25–100 hairs, from a
total of about 100,000. Eighty percent to 90% of hair is in the growing, or anagen, phase. Anagen hairs have a heavy external root sheath that looks like a gelatinous
 capsule around the lower third of the hair. Ten percent to 15% of hair is in the resting, or telogen, phase. These hairs have a smooth shaft, ending in a short bulbous
 root. Approximately 5% or less of hair is in a transitional or catagen phase.

Hair Conditions

1. Male pattern baldness: This is produced in genetically susceptible individuals, resulting in a loss of hair secondary to the effects of androgenic hormones.

2. Telogen effluvium: Acute illness, surgery, or other severe stress can stop hair growth and cause hairs to go into the telogen phase. When hair resumes growth

3. Anagen effluvium: Anagen effluvium is hair loss occurring during the growing phase. Common causes include antiinflammatory drugs used for chemotherapy,

4. Alopecia areata: Alopecia areata is characterized by rapid and complete hair loss in patches, usually involving the scalp, beard area, eyebrows, or eyelashes.

5. Hair loss secondary to physical factors

6. Scalp disease: Hair loss can occur secondary to various scalp diseases, including psoriasis, fungal disease, seborrhea, or eczema.

7. Metabolic disorders: Hair loss can be found with iron deficiency, hypo/hyperthyroidism, diabetes mellitus, or hypopituitarism.

8. Systemic diseases: Hair loss can be seen with lupus erythematosus.

9. Scarring alopecia: This form of irreversible hair loss is the result of various inflammatory processes or trauma. Some dermatological conditions that may result in

10. Hair-shaft structural defects: Various defects in hair structure can result in hair loss. These defects are often associated with abnormalities of the skin, teeth,

Evaluation

1. History: An extensive history is indicated, including the onset and duration of hair loss, drug use, skin or scalp disease, and recent stress, surgery, illness, or

dietary changes.

2. Physical examination: Check particularly for evidence of seborrhea, scalp disease, or an endocrine disorder.

3. Pull test: Lightly grasp about 20 hairs and pull gently. Normally one or two telogen hairs will come out. In an adolescent with hair-shaft damage, telogen

4. Examine scalp closely and perform a potassium hydroxide test if indicated. A fungal culture of the hair and scalp may also be productive.

5. A complete blood count, urinalysis, liver function tests, thyroid studies, serum ferritin, and a fasting blood glucose test are ordered as indicated.

6. Referral to a dermatologist may be necessary for further evaluation and scalp biopsy if diagnosis is in question.

Therapy

Therapy depends on the cause.

1. Male pattern baldness: In men, androgenetic alopecia ranges from bitemporal recession of hair to thinning of the frontal area of scalp to complete baldness.

2. Telogen effluvium: Generally reanueuress is all that is needed, because there is usually no significant hair loss. This condition will usually be self-limited.

3. Alopecia areata: See previous discussion.


Tattoos and Body Piercing

Body art, including tattoos and body piercing, have become more fashionable among adolescents and young adults and the prevalence appears to be increasing both
in the adolescent and in the young adult populations. Some body art occurs as a result of either peer pressure or gang participation. However, much occurs as a part
of our culture. Although facial piercing has been practiced in many societies throughout history, piercing of nipples and genitals appears to be a largely modern
Western occurrence. To avoid infections including bacterial, hepatitis, and human immunodeficiency virus (HIV), one must ensure that the piercing is done by a
reliable individual. In most states, minors cannot consent for body piercing and tattoos without parental consent, although this is not always followed.

Complications include the following:

1. Hypersensitivity to the dye

2. Unsatisfactory methods have resulted in bacterial infections, hepatitis, tuberculosis, and syphilis. Concern about transmission of HIV infection exists.

3. Keloids can form.

4. One or more milk ducts may be damaged when piercing a woman's nipple.
Tattoo Removal

The new laser systems can effectively remove most tattoos with minimal scarring or other adverse sequelae. However, not all tattoos can be completely eliminated. Limitations of treatment include the need for multiple treatment sessions, expense, incomplete response of some individuals, and the possibility of pigmented changes.

It is important to discuss the possibility of HIV transmission during tattooing during HIV education sessions. It is also important to promote regulatory control over tattooing establishments and body-piercing establishments to ensure sanitary conditions.

Primary Syphilis and Herpes Simplex

For a discussion of primary syphilis and herpes simplex, see Chapter 64 and Chapter 65, respectively.

Hyperhidrosis

Hyperhidrosis is excessive sweating in response to heat or emotional stimuli. Treatment with topical aluminum chloride preparations such as Certain-Dri, Xerac AC, or Drysol is often beneficial. Systemic anticholinergic agents, glutaraldehyde, and iontophoresis have also been used with varying degrees of success. Referral for botulinum toxin (Botox) injection may be warranted in more severe cases. Rarely should surgical intervention be considered.

Bromhidrosis

Bromhidrosis is malodorous sweating that may be apocrine or eccrine in origin and is caused by bacteria. Good hygiene includes the use of antibacterial soaps, topical antibiotics, antiperspirants, Burow solution or potassium permanganate soaks, and absorbent powders.

Pink Pearly Penile Papules

Pink pearly penile papules are a normal occurrence in about 15% of postpubertal males. The lesions appear as elongated papillae, about 1–3 mm in diameter, on the coronal margin of the penis, particularly in the anterior border. They often appear in one to five rows and are usually of uniform size and shape. The color tends to be pearly white. Microscopically, they have a normal epidermal appearance except for absent pigment in the basal layer. In contrast, condylomata acuminata tend to be less uniform in size and shape, change over time, and are not neatly arranged around the circumference of the penis. No treatment is necessary except reassurance.

Acanthosis Nigricans

Acanthosis nigricans appears as a gray-brown thickening of the skin. It is manifested as symmetrical, velvety, papillomatous plaques, with increased skin-fold markings. The lesions are commonly located on the base of the neck axilla, groin, and antecubital fossa. The lesions may also occur on the dorsum of the hand, elbow, perilumbrial skin, and mucous membranes. It is commonly found during a routine physical examination in an otherwise healthy obese adolescent. Occasionally, a parent is concerned about why the teen does not wash him or herself.

Acanthosis nigricans can be classified into benign and malignant. Most acanthosis nigricans lesions in adolescents are not associated with a malignancy. The common associations in teens are insulin resistance secondary to obesity. Many of these individuals have type 2 diabetes or are at risk for type 2 diabetes and hyperlipidemia.

The condition is difficult to treat. Lactic acid or a-hydroxyacid containing emollients, and tretinoin (Retin-A) have been tried but without any controlled studies demonstrating efficacy.

WEB SITES

For Teenagers and Parents

http://www.mckinley.uiuc.edu/health-info/dis-cond/commdis/condderm.html. Contact dermatitis handout from the University of Illinois student health center.
http://my.webmd.com/content/asset/adam_disease_poison_ivy. WebMD on contact dermatitis.

For Health Professionals

http://tray.dermatology.uiowa.edu/DPT/PathBase.html. Dermatology slides from the University of Iowa.
http://www.emedicine.com/emerg/topic628.html. E-medicine section on urticaria

REFERENCES AND ADDITIONAL READINGS


Odom R. Diagnosis and treatment of common fungal infections. Mod Med 1987a;55:34.


Epilepsy is the most common chronic neurological condition in adolescents. It is defined as recurrent, usually transient, episodes of disturbed central nervous system (CNS) function (seizures), excluding extracerebral causes such as syncope, hypoglycemia, or episodic psychiatric syndromes. Epilepsy has been reported since biblical times and has been seen differently by various cultures. Views have ranged from veneration of epileptics as mystics to imprisoning them or placing them in mental hospitals. As recently as 1965, two states prohibited marriage if a person had epilepsy, and until the early 1970s, immigration into the United States was prohibited for people with epilepsy. Most adolescents with epilepsy have the potential for excellent control with medication and high likelihood of eventual remission of their epilepsy. Recent advances in basic science have contributed to the understanding of mechanisms of epilepsy and seizures. New medications and surgical techniques have improved the outcome of severe, intractable epilepsy. Despite this, fears, prejudices, and social stigma remain common. Epilepsy is thus somewhat more challenging to treat in teens than other chronic illnesses.

Epilepsy is a difficult condition for patients of all ages. However, for the adolescent concurrently undergoing the stresses of peer relationships, independence, and body image, epilepsy can be particularly trying. The goals of management of epilepsy include proper diagnosis, evaluation, treatment of underlying etiologies, appropriate use of anticonvulsant drugs, and recognizing and dealing with the many associated psychosocial problems.

ETIOLOGY

Seizures are caused by an excessive discharge of a population of cortical neurons. The location and pattern of spread of activity determine the clinical expression. Seizures may be due to acute physiological or neurological disturbances or due to epilepsy. Recurrent unprovoked seizures are the hallmark of epilepsy. The diagnosis of epilepsy does not imply a specific etiological factor in the individual. Epilepsy may be genetic, idiopathic, or secondary, due to remote insult to the nervous system. Acutely, infection, trauma, metabolic disturbances, drugs, drug withdrawal, or fever may also provoke seizures.

EPIEDEMOLOGY

1. Prevalence: 1 of 200 in the general population, with a higher prevalence in children.
2. Incidence: Annual incidence is 1:1,000.
3. Onset: Peak periods for the onset of idiopathic and age-related primary epilepsies are during the early school years and during adolescence. The onset of secondary (remote symptomatic) seizures is highest during infancy and in the geriatric age group but may occur at any age.
4. Gender: Epilepsy occurs slightly more often in males than females (relative risk for males, 1.1–2.4 in various studies).
5. Socioeconomic, racial, and ethnic factors: In the United States and Western Europe, epilepsy is slightly more common among lower socioeconomic groups. Epilepsy is more common in Mexico and Central America, and in immigrants from these areas in the United States, at least partially due to the high incidence of cerebral cisticercosis. Epilepsy is more prevalent among African-Americans than whites in the United States.
6. Mental retardation and cerebral palsy are associated with higher rates of epilepsy, as well as lower rates of complete remission of childhood-onset epilepsy.
7. Epilepsy is associated with an increased risk of death, including sudden unexplained death, but the risk in adolescents with epilepsy is low.

CLINICAL MANIFESTATIONS

Table 22.1 lists classifications of seizures, based on international classifications.
SEIZURE COMPONENTS

The progression of a seizure is characterized by several temporal components, variably present:

1. Prodrome: Altered behavior or mood occurring hours to days before the actual seizure; infrequent.
2. Aura: Altered sensation or psychic symptom occurring just before other ictal manifestations. The aura is actually part of the seizure, representing a simple partial seizure, usually with sensory, special sensory, or psychic symptoms.
3. Ictus: The observed seizure event, usually with motor activity.
4. Postictal state: Altered neurological function ranging from coma to mild lethargy, hemiplegia to minimal focal motor dysfunction, lasting minutes to 24 hours.

Grand Mal Seizures (Generalized Tonic-Clonic Seizures)

1. Aura: May have brief, nondescript aura
2. Ictus
   a. Tonic phase: Forceful, postural contractions in flexion or extension. Usually, the early phase, momentary to several minutes, occasionally longer, may include the following:
      • Deviation of head
      • A cry at the onset
      • Loss of consciousness at the start of the seizure
      • Fall to ground
      • Bites tongue or cheeks
   b. Clonic phase: Bilateral, generally symmetrical, brisk jerking movements. Clonic movements have a discernible fast-slow component, as distinguished from other types of movement (withdrawing, sustained posturing, random bilateral nonsynchronous movements), which are less likely a part of a convolution.
   c. After the tonic-clonic phase, the patient usually becomes flaccid, with or without incontinence of urine or stool, as seizure stops.
3. Postictal state
   a. Early: Unconscious state, with decreased tone and reflexes. Patients may have fixed pupils.
   b. Recovery phase: Sleeplike state, but patient is responsive to arousal.
   c. Late phase: Confusion or headache.

Petit Mal and Other Absence Seizures

1. Prodrome: None, but often cluster on arising in the morning.
2. Aura: None; abrupt onset of ictus
3. Ictus: Brief period (few seconds to 30 seconds) of blank staring.
   a. Loss of consciousness, usually without fall
   b. Typical absence: Minor automatisms; may have blinking of eyes; movement of fingers common
   c. Complex absence: Associated with automatisms, myoclonic movements or loss of tone; may be longer than 30 seconds
4. Postictal: No postictal confusion, but amnesia of seizure is usual.
5. One third of absence seizures remit during adolescence (most likely in childhood-onset simple absence; less likely in adolescent-onset absence).
6. The electroencephalogram (EEG) is characteristic, showing 3-Hz spike and wave activity in typical petit mal. Other absence syndromes show generalized polyspike wave discharges, slow spike wave (Lennox-Gastaut syndrome), or 4- to 5-Hz spike wave (juvenile myoclonic epilepsy [JME] of Janz).
7. Specific epileptic syndromes with onset in adolescence combine absence with myoclonic seizures and occasional grand mal seizures, most prominent on arising in the morning. Early morning myoclonus may be viewed as “normal” by the patient and not reported without specific questioning (JME of Janz).
8. Patients with absence or absence plus myoclonic seizures are more likely to be photosensitive than those with other seizure types. “Video-game”-related seizures are generally limited to these patients.

Myoclonic Seizures

1. Myoclonic jerks are brisk and irregular and may involve the trunk or extremities, symmetrically or asymmetrically. Jerks may be of small amplitude or massive, causing the patient to fall.
2. Patients are generally aware of the jerks if they are isolated. They may be unaware if myoclonic jerks are part of absence seizures.
3. Differential diagnosis includes ictus, nonepileptic myoclonus, and other movement disorders.
4. Etiologies
   a. Myoclonic seizures, usually on arising in the morning, with adolescent onset, are a characteristic part of JME. Absence or generalized tonic-clonic seizures often occur in these patients.
   b. Myoclonic seizures may be part of an epileptic encephalopathy, such as Lennox-Gastaut syndrome, beginning in early childhood and continuing in adolescence.
   c. Photomyoclonus may occur with exposure to a strobe or strobe-like conditions in teens with photosensitive epilepsy. They may have other generalized seizures, or this may be their only symptom.
   d. Various degenerative conditions, including progressive myoclonic epilepsies, sialidosis, and subacute sclerosing panencephalitis, may present in the teen years and may be accompanied by myoclonic seizures.
5. There is no prodrome, aura, or postictal period.
6. EEG usually shows bursts of spike wave or polyspike and wave in a generalized distribution. Photosensitivity may be demonstrated on EEG using strobe.

Partial Simple Seizures

1. Benign focal epilepsy of childhood (also known as benign rolandic epilepsy) is the most common cause of focal motor seizures in childhood and early adolescence.
   a. Seizures are partial simple seizures usually involving the face or arm; seizures may secondarily generalize.
   b. Episodes occur during drowsiness or sleep onset, or on awakening.
   c. Seizures resolve by the midteen years.
   d. There is no underlying structural lesion.
2. Partial simple seizures with onset in adolescence or adulthood are more commonly associated with structural pathology (e.g., tumor, arteriovenous malformation, head injury, malformation, and stroke).
3. Sensory phenomena (aura) may be the only manifestation of a brief limited seizure.
4. Ictus: Most partial simple seizures are focal motor.
   a. Consciousness is retained. Speech arrest may occur with dominant hemisphere seizure origin (usually with the seizure involving the right face and left brain in the right-handed person).
   b. Clonic activity may “march” up an extremity or spread from arm to face or arm to leg, and so on (or vice versa).
5. Postictal: Headache, postictal hemiparesis (Todd paralysis).
6. EEG
   a. Benign focal epilepsy of childhood is associated with central-temporal spikes, which are more commonly seen in light sleep. EEG abnormality is commonly bilateral, even if all observed seizures were on same side.
   b. Other partial seizures may be associated with spikes or slowing in a unilateral distribution.
Partial Seizures with Complex Symptomatology

Partial seizures with complex symptomatology are seizures of focal onset with altered consciousness. Older terms include psychomotor seizures and temporal lobe seizures, although not all partial complex seizures originate in the temporal lobe and not all temporal lobe seizures are complex partial (i.e., they may be simple partial).

1. May begin at any age.
2. Structural pathology is more common than in generalized epilepsies or benign focal epilepsy of childhood. Mesial temporal sclerosis may cause seizures of temporal lobe origin with onset in adolescence.
3. Prodrome: Patients may report that "they know a seizure is coming."
   a. May occur hours or days before a seizure.
   b. Includes mood change, headache, and change in appetite.
4. Typical partial complex seizures consist of the following sequence (any of the sequence may be omitted other than the altered state of consciousness):
   a. Aura: Initial sensory, autonomic, or psychic symptoms lasting seconds to minutes; common phenomena include fear, déjà vu, "rising feeling" in abdomen, tingling, and visual, auditory, olfactory, or gustatory hallucination. Flushing or pallor may be observed. Consciousness is generally retained, and patient remembers this part of the seizure.
   b. Blank stare with impairment of responsiveness and consciousness: The patient is motionless and does not remember events clearly during this phase, if at all.
   c. Automatisms: Hand wringing, picking, lip smacking, walking aimlessly, grunting, gagging, or swallowing. Although destructive or injurious behavior may occur, directed deliberate violence does not. Consciousness is impaired or lost during this phase, and the patient does not remember it. Frontal lobe origin complex partial seizures may produce thrashing, agitated movements, bicycling leg movements, or pelvic thrusting, which are difficult to distinguish from hysterical behavior.
   d. Postictal state: Confusion, stupor, headache, and lethargy may last seconds to hours.
5. Precipitants: Sleep deprivation, alcohol, or drug ingestion.
6. EEG: Focal spikes in temporal, frontal, or parietal areas, usually unilateral. EEG findings may be normal. Special procedures such as sleep deprivation, special leads, and prolonged monitoring may be useful for diagnosis.

Features that help to differentiate various seizures reported as "little seizures" or "staring spells" (partial complex, petit mal, and atypical absence) are listed in Table 22.2.

| TABLE 22.2. Features of absence and complex partial seizures |

**DIFFERENTIAL DIAGNOSIS**

**Seizures**

1. Symptomatic seizures (due to acute systemic disturbance or trauma)
   a. Acute metabolic disturbance (e.g., hypoglycemia, hyponatremia, and hypocalcemia)
   b. Acute CNS infection (e.g., encephalitis and meningitis)
   c. Intoxication (e.g., cocaine, alcohol, phencyclidine, phenylpropanolamine, and inhalants)
   d. Drug or alcohol withdrawal (e.g., barbiturates, sedatives, and benzodiazepines after prolonged use)
   e. Acute head trauma (impact seizure and seizure in first few days after significant head trauma)
   f. Syncopal seizure: Brief tonic or clonic seizure occurring after primary syncope
   g. Acute stroke
2. Acquired (symptomatic or secondary) epilepsies due to remote history of CNS insult
   a. Cerebral malformations: Macroscopic or microscopic (cortical dysgenesis)
   b. Intrauterine infections (e.g., cytomegalovirus and toxoplasmosis)
   c. Perinatal insults
   d. Postneonatal infections (e.g., meningitis, encephalitis, and brain abscess)
   e. Posttraumatic epilepsy
   f. Tuberous sclerosis
   g. Brain tumors and other mass lesions
   h. Vascular malformations and infarctions
   i. Cysticercosis
   j. Genetic due to progressive or degenerative conditions
   k. Unknown but presumed symptomatic: Epileptic encephalopathies such as Lennox-Gastaut syndrome and early myoclonic encephalopathy
3. Idiopathic epilepsy (also called age-related epilepsies)
   a. Primary generalized epilepsies
   b. Benign focal epilepsy of childhood

**Other Paroxysmal Events That May Suggest Seizure Activity**

1. Vasovagal syncope
2. Migraine
3. Cardiac disease
   a. Arrhythmias
   b. Low-output states
   c. Mitral valve prolapse
4. Hyperventilation and anxiety states
5. Orthostatic hypotension
6. Sleep disturbances
   a. Narcolepsy: Cataplexy, sleep attacks, sleep paralysis, and hypnagogic hallucinations
   b. Drowsiness or sleep attacks in patients with obstructive sleep apnea or sleep deprivation
   c. Sleepwalking and other parasomnias
   d. Night terrors
   e. Periodic leg movements in sleep
7. Movement disorders
   a. Tics
   b. Paroxysmal kinesigenic choreoathetosis
   c. Still man syndrome and other syndromes of continuous muscle fiber activity
   d. Dystonias (paroxysmal torticollis, activity-related dystonias, dystonia muscularum deformans, and drug related)
   e. Pseudohypoparathyroidism: Teens with hypocalcemic secondary to pseudohypoparathyroidism may present with seizure-like episodes that are primarily dystonic.
   f. Restless leg syndrome
8. Pseudoseizures (hysterical symptoms)
9. Episodic “staring” and inattention
   a. Attention deficit disorder
   b. Disorders of arousal

**DIAGNOSIS**

**History**

Epilepsy is primarily a clinical diagnosis based on the history. An astute observer of the event is more important than any "test."

1. Review the following with the observers of the event:
   a. What was the teen doing before the episode began: Sleeping, quiet, watching television, exercising, reading, anxious?
   b. Where did the event occur?
   c. What time of day?
   d. Relation to sleep state: Did the seizure occur just as the teen was falling asleep, just after awakening, or during deep sleep?
   e. What was the first abnormality noted? Did the teen seem to be aware that something was wrong?
   f. What happened during the seizure?
   g. Could the teen hear or understand people talking during the seizure? Could he or she respond?
   h. Was there incontinence of urine or stool?
   i. What happened after the seizure?
2. Review the following with the patient:
   a. What was the last event he or she remembers before the seizure?
   b. Could the patient hear or understand people talking during the seizure? Could he or she respond?
   c. What happened after the seizure? What is the first thing recalled after the event?
   d. Precipitating events: Sensory stimulation, activity, drugs, meals, medications, sleep pattern, stress, and menses.
   e. Prior seizures or similar events
3. Family history of epilepsy, neurocutaneous syndromes, and other neurological conditions
4. Perinatal history, particularly birth injury, prematurity, and maternal infections
5. History of CNS infections or trauma
6. Drug history, including prescribed, over-the-counter, and “street” drugs and alcohol
7. Any other recent changes in health or function: Any changes in cognition, motor function, or others to suggest onset of neurological disease other than the epilepsy

**Physical Examination**

1. Perform general physical examination for evidence of systemic disease.
2. Skin: Look for signs of a neurocutaneous syndrome such as café au lait spots, depigmented macules, adenoma sebaceum, shagreen patch, and subungual fibromas.
3. Eyes: Perform funduscopic examination for papilledema.
5. Blood pressure: Assess pressure while the teen is lying and standing.
6. Pulse: Check for irregularities, if arrhythmia is suspected.
7. Cardiac examination: Check for evidence of mitral valve prolapse, heart failure, or other abnormalities that might lead to arrhythmias.
8. Hyperventilation: Hyperventilate for 2–3 minutes to induce an episode if absence (petit mal) seizures are suspected or if symptoms are thought to be directly due to hyperventilation.

**Laboratory Tests**

1. Complete blood cell count and routine chemistry panel are indicated before initiating anticonvulsant therapy (as baseline). Platelet count should be included if valproic acid is to be used.
2. In an apparently well teenager without underlying medical problems, electrolytes, phosphorus, or magnesium have a very low yield for finding a cause of seizures. Rarely, an adolescent presenting with seizure-like episodes is found to have very low blood calcium concentration due to pseudohypoparathyroidism, although the condition is congenital and the calcium concentration is low from infancy. Blood sugar measurements may be helpful if hypoglycemia is suspected only if drawn while the patient is symptomatic. These tests are not indicated on a routine basis in most teens with seizures.
3. EEG: Routine study should consist of waking EEG, hyperventilation, and photic stimulation. Hyperventilation is particularly useful if absence (petit mal) seizures are suspected. Photic stimulation is particularly helpful if the patient reports that seizures occur when exposed to video games, television, rapid flashing lights, or in the car. Sleep study (sleep deprived if possible) increases the yield in patients with complex partial seizures, benign focal epilepsy of childhood, and some generalized epilepsies.
4. Neuroimaging: Computed tomography scan or magnetic resonance imaging is indicated for focal seizures (except clear-cut benign focal epilepsy of childhood), seizures associated with neurological abnormalities or papilledema, neurocutaneous stigmata, or suspected degenerative conditions.
5. Lumbar puncture is indicated if infection or hemorrhage is suspected.

**Grand Mal Seizures Versus Syncopeal Episode**

Table 22.3 compares mal seizures with Syncopeal Episode.

<table>
<thead>
<tr>
<th>Component</th>
<th>Grand Mal</th>
<th>Syncopeal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prodromal</td>
<td>Unusual experience, aura</td>
<td>Unusual experience, aura</td>
</tr>
<tr>
<td>Onset</td>
<td>Abrupt-onset tonic-clonic</td>
<td>Abrupt-onset tonic-clonic</td>
</tr>
<tr>
<td>Duration</td>
<td>1–2 minutes</td>
<td>1–2 minutes</td>
</tr>
<tr>
<td>Recovery</td>
<td>Full recovery</td>
<td>Partial recovery</td>
</tr>
<tr>
<td>Agent</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

**TABLE 22.3.** Grand mal seizures versus syncopal episodes
**Hysterical Episodes (Pseudoseizures) Versus Epilepsy**

Table 22.4 compares pseudoseizures with epilepsy.

---

### THERAPY

After the diagnosis of epilepsy is made, two major components of therapy exist: Drug therapy to control the seizures and counseling regarding psychosocial issues.

#### Anticonvulsant Therapy

**General Guidelines**

1. Start with a single anticonvulsant medication. The choice of an anticonvulsant should consider the side effect profile, because this will influence both safety and compliance. For example, sodium valproate, which may be effective in many seizure types, may be associated with some side effects that limit its use by adolescents, particularly female teens. These include an increase in appetite, weight gain, transient hair loss, and menstrual irregularities.

2. Increase the medication slowly by two increments equal to five times the half-life of the drug until seizures are controlled or toxicity occurs, except when control is urgent (frequent seizures or status epilepticus).

3. Use serum levels only as guidelines: Clinical response is more important. Do not overuse levels. At least five half-lives are necessary for medication level to reach steady state before starting or altering the dose.

4. Give medication each day based on half-life: Give a drug more frequently only with refractory seizures, otherwise unmanageable adverse effects, or demonstrated rapid metabolism. Most medications can be given twice a day (b.i.d.), and adherence is better with b.i.d. than three-times-a-day (t.i.d.) schedules.

5. The teen should have close follow-up, including monitoring of seizure frequency, physical examination, and evaluation for drug toxicity. Note that frequent follow-up also allows for early detection of nonmedical effects (social, academic, independence, and vocational).

6. Substitute a second drug only when the first is pushed to tolerance without controlling the seizure, unless allergic or serious idiosyncratic effects are evident. When the second drug is at adequate serum levels, wean the first. Polytherapy is reserved for refractory patients unresponsive to trials of monotherapy with at least two to three different anticonvulsants at maximum tolerated levels.

7. Discontinuation criteria: After some time, the clinician must assess the risks and benefits of continued therapy with anticonvulsants. Medications may be tapered and discontinued after the patient is seizure free for 2–4 years. The estimated risk for recurrence on tapering is 30%–40%, greatest during the period of taper or in the first 6 months after discontinuation of the medication. Risk factors for recurrence are somewhat controversial but include the following in at least some studies:
   
   a. Mental retardation or neurological abnormalities
   b. Long duration of seizures or many seizures before full control with medication
   c. Partial seizures (other than the benign focal epilepsies of childhood such as rolandic epilepsy)
   d. Abnormal EEG findings despite seizure-free period (highest risk: combination of focal slowing and focal epileptiform spikes)
   e. Adolescent-onset seizures less likely to remit than seizures with onset in earlier childhood

Medication should be tapered one drug at a time (generally sedating drugs first), tapering each drug over 6 weeks to 3 months.

#### Drugs for Specific Seizure Types

1. Generalized tonic-clonic seizures (grand mal), either primarily or secondarily generalized:
   
   a. Phenobarbital: Least expensive, can be given once a day
   b. Carbamazepine (Tegretol): Generics are acceptable if same generic is consistently available; avoid switching brands. Two extended-release carbamazepine preparations allow b.i.d. dosing but are expensive (Tegretol-XR and Carbatrol).
   c. Phenytoin (Dilantin): Brand-name capsules can be used once a day. Generic capsules or chewable tablets must be divided b.i.d. or t.i.d.
   d. Valproic acid (Depakene or Depakote): Depakote is preferred
   e. Primidone (Mysoline): Reserve for refractory patients
   f. Lamotrigine (Lamictal): Useful for generalized seizures, including adolescents with JME. Generally reserved for teens intolerant of valproic acid.
   g. Topiramate: Generally reserved for teens who have failed at least one other medication.
   h. Felbamate (Felbatol): This is effective for several seizure types including generalized convulsive (tonic-clonic) and absence seizures. It is only approved for children with Lennox-Gastaut syndrome (mixed generalized epilepsy). An initial alarming incidence of aplastic anemia associated with felbamate has limited the use of this medication in refractory patients able to give informed consent to its risks.

Many practitioners favor either phenobarbital or carbamazepine. Phenytoin is an effective medication but may cause unacceptable side effects (e.g., gum hypertrophy and hirsutism), particularly in children and young adolescents. In patients with mixed generalized seizures (i.e., generalized tonic-clonic plus myoclonic or absence seizures), carbamazepine or phenytoin occasionally may induce or exacerbate myoclonic or drop attacks. Valproic acid, preferably in the long-acting capsules (Depakote), is the drug of choice in mixed generalized epilepsies (grand mal plus myoclonic or absence).

2. Petit mal epilepsy
   
   a. Ethosuximide (Zarontin): Standard therapy usually well tolerated for typical petit mal (3-Hz spike wave EEG pattern).
   b. Valproic acid (Depakote or Depakene): First choice if absence and generalized tonic-clonic seizures coexist, for atypical absence, or for JME.
   c. Clonazepam (Klonopin), other benzodiazepines: Occasionally effective as monotherapy.
   d. Felbamate (Felbatol): This is effective for several seizure types including generalized convulsive (tonic-clonic) and absence seizures. It is approved only for children with Lennox-Gastaut syndrome (mixed generalized epilepsy). An initial alarming incidence of aplastic anemia associated with felbamate has limited the use of this medication to refractory patients able to give informed consent to its risks.
   e. Lamotrigine (Lamictal): Newly released for adults and teens. Effective in JME.
   f. Topiramate (Topamax): Difficult to use, generally reserved for teens who have failed valproic acid and/or ethosuximide.
   g. Zonisamide (Zonegran): Effective in absence seizures in studies done in Japan. This new anticonvulsant is difficult to use due to sedative and behavioral effects.

3. Simple partial seizures (focal motor, focal sensory) and complex partial seizures with or without automatisms
   
   a. Carbamazepine (Tegretol): See previous discussion regarding generic forms and long-acting preparations.
   b. Phenobarbital
c. Phenytoin (Dilantin): See previous discussion regarding generic forms.
d. Primidone (Mysoline): Reserve for refractory patients.
e. Gabapentin (Neurontin): Approved for adjunctive treatment of partial onset seizures. Gabapentin is generally not suitable for monotherapy. This anticonvulsant is not metabolized and does not change metabolism of other medications. Consider in multisystem disease when alteration of drug metabolism of other agents is important.
f. Lamotrigine (Lamictal): See previous discussion. Adjunctive treatment of partial seizures; occasionally effective as monotherapy.
g. Topiramate (Topamax): See previous discussion. Adjunctive treatment of partial seizures. Possibly effective as monotherapy.
h. Tiagabine (Gabitril): Adjunctive treatment of partial seizures.
i. Levetiracetam (Keppra): Adjunctive treatment of partial seizures.
j. Zonisamide (Zonegran): Adjunctive therapy for partial seizures.
k. Oxcarbazepine (Trileptal): An alternative to carbamazepine for patients who had an adverse behavioral reaction to carbamazepine at the therapeutic dose. Patients allergic to carbamazepine may also react to oxcarbazepine. Oxcarbazepine is not metabolized and does not interact with other medications that are affected by cytochrome P-450 system, so oxcarbazepine may be ideal in the teen with multisystem disease needing many other medications (e.g., during chemotherapy or patients with acquired immunodeficiency syndrome).
l. Felbamate (Felbatol): See previous discussion. Reserve for refractory patients.

Note that the use of lamotrigine, topiramate, tiagabine, zonisamide, and felbamate should only be undertaken in direct consultation with a neurologist with expertise in the treatment of epilepsy.

Table 22.5 provides metabolism guidelines for first-line antiepileptic drugs and Table 22.6 shows metabolism of newer anticonvulsant drugs.

**TABLE 22.5. Metabolism and dosing guidelines for first-line antiepileptic drugs used as monotherapy**

<table>
<thead>
<tr>
<th>Antiepileptic Drug</th>
<th>Metabolism and PK Properties</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbamazepine</td>
<td>High affinity for CYP3A4, CYP2C19, CYP2C9, and CYP2D6.</td>
</tr>
<tr>
<td>Oxcarbazepine</td>
<td>Monooxygenation by CYP2C19.</td>
</tr>
<tr>
<td>Lamotrigine</td>
<td>Oxidation by CYP2C19.</td>
</tr>
<tr>
<td>Topiramate</td>
<td>Oxidation by CYP2C19.</td>
</tr>
<tr>
<td>Tiagabine</td>
<td>Oxidation by CYP2C19.</td>
</tr>
<tr>
<td>Levetiracetam</td>
<td>Oxidation by CYP2C19.</td>
</tr>
<tr>
<td>Zonisamide</td>
<td>Oxidation by CYP2C19.</td>
</tr>
<tr>
<td>VPA</td>
<td>Oxidation by CYP2C19.</td>
</tr>
<tr>
<td>Phenobarbazine</td>
<td>Oxidation by CYP2C19.</td>
</tr>
<tr>
<td>Phenytoin</td>
<td>Oxidation by CYP2C19.</td>
</tr>
</tbody>
</table>

**TABLE 22.6. Metabolism and doses of newer anticonvulsant medications**

### Side Effects of Anticonvulsant Drugs

Adverse effects of anticonvulsants can be divided into two major groups: Dose-related reactions and idiosyncratic reactions unrelated to drug level. Mild sedation is common with initiation of any anticonvulsant. This effect generally wanes after a few weeks. Sedation and ataxia with initiation of treatment is more significant with carbamazepine, so treatment is generally started at low doses and increased over several weeks. Potential reproductive effects are also important to consider in teenage girls of childbearing potential.

**Dose-related Effects**

1. Toxic CNS effects are shared among most anticonvulsants.
   a. Excessive levels (or deliberate overdoses) produce ataxia, nystagmus, and sedation progressing to coma, with respiratory and cardiac depression at extremely high doses.
   b. Movement disorders (chorea) may be seen at toxic drug levels, primarily with phenytoin or carbamazepine.
2. Non-CNS dose-related effects are common.
   a. Alterations in vitamin D metabolism produce “chemical rickets,” generally without clinical abnormalities. Clinical rickets is occasionally seen in multihandicapped patients receiving anticonvulsants but having limited sun exposure and lacking vitamin D supplementation. Consider supplementing with oral calcium and vitamin D in teens taking anticonvulsants if dietary intake is low.
   b. Folate metabolism is altered, producing megaloblastic changes, usually without anemia. Female adolescents on anticonvulsants, particularly valproic acid, should be routinely supplemented with a multivitamin containing 400 µg of folic acid.
   c. Thyroid function tests are commonly altered without clinical evidence of hypothyroidism.
3. Drug interactions are also common.
   a. Virtually all anticonvulsants induce hepatic microsomal enzymes, increasing clearance of themselves (autoinduction), each other, and various other medications including steroids, estrogens, anticoagulants, and so forth. Exceptions are the recently introduced anticonvulsants, gabapentin (Neurontin) and oxcarbazepine (Trileptal), which are excreted unchanged in the urine and do not affect other drug metabolism.
   b. Conversely, several drugs significantly inhibit the metabolism of carbamazepine and to a lesser extent phenytoin. The most commonly encountered is erythromycin (and the newer macrolides, clarithromycin and azithromycin). These competitively inhibit carbamazepine metabolism to an extent that previously stable patients may develop significant toxicity less than 24 hours after the addition of the antibiotic. A similar effect is seen with propoxyphene (Darvon). These drugs should be avoided in a patient taking carbamazepine. Grapefruit juice also inhibits the metabolism of carbamazepine and should not be consumed by patients taking carbamazepine.
   c. Isoniazid (INH) inhibits both carbamazepine and phenytoin metabolism. Because it is generally used on a long-term basis, the anticonvulsant drug can be adjusted to account for the decreased clearance.

**Idiosyncratic (Non–dose-related Side Effects)** The following side effects may occur with any anticonvulsant:

1. Allergic reactions: Skin rash, Stevens-Johnson syndrome, lupus-like syndromes, and even death can occur with any anticonvulsant, although most reported
cases are associated with phenobarbital, phenytoin, or carbamazepine.

2. % 2. Bone marrow toxicity, usually reversible, has been reported with several anticonvulsants. Fatal aplastic anemia has been reported with carbamazepine, particularly in older adults. Shortly after its widespread release, an excess incidence of aplastic anemia was found with felbamate (Felbatol), severely limiting its current use.

3. Hepatic toxicity and metabolic abnormalities are seen in patients receiving valproic acid, primarily in infants, but rarely can occur with any anticonvulsant, at any age. These may include hyperammonemia, lactacidosis, and Reye-like syndrome.


5. Hair loss: Moderate hair thinning is relatively common with valproic acid. Frank alopecia does not occur. Other anticonvulsants may produce hair loss as part of allergic reactions.

6. Weight changes: Weight gain is most frequently problematic with valproic acid but has been reported with many anticonvulsants. Weight loss is common with felbamate, particularly at higher doses, and with valproic acid in young children. Topiramate often produces short-term significant anorexia and weight loss.

7. Pancreatitis: Valproic acid can rarely cause serious pancreatitis. In a patient taking valproic acid with abdominal pain or vomiting, serum amylase should be assessed.

Reproductive

1. Facial malformations, particularly cleft palate, microcephaly, congenital heart disease, and minor malformations such as hypoplastic nails have been related to phenytoin, trimethadione (Tridione), and possibly other anticonvulsants. Some authors feel that these nonspecific malformations are more frequent in offsprings of epileptic mothers, regardless of treatment.

2. Open neural tube defects may be more frequent in fetuses exposed to valproic acid. It is prudent to supplement all female patients taking valproic acid with a multivitamin containing 400 µg of folic acid.

3. It is difficult to choose an anticonvulsant that is “completely safe.” Risk of fetal damage must be balanced against the risk of recurrent convulsions if medications are withdrawn.

4. There is no reason to withhold oral contraceptives from a woman receiving anticonvulsants, but higher estrogen doses may be needed due to more rapid metabolism of the component hormones, due to induction of cytochrome P-450 system.

Specific Adverse Effects

Phenytoin (Dilantin)

1. Dose related
   a. CNS: Nystagmus, ataxia, sedation, decreased motor speed, and increased seizures at toxic levels.
   b. Endocrine: Induction of vitamin D metabolism; clinical rickets only with poor intake and decreased sun exposure (e.g., institutionalized individuals not eating dairy products or taking supplements).
   c. Gingival hyperplasia: Particularly a problem with poor hygiene or orthodontic appliances.
   d. Hypertrichosis: Increased facial and body hair may particularly distress young women.
   e. Soft tissue thickening: Particularly orbital ridges, lips, and nose.
   f. Reproductive: Reports of malformations including microcephaly, nail hypoplasia, facial anomalies, cardiac defects, and mental retardation occurring in up to 10% (highest estimate) of fetuses exposed to phenytoin during gestation; risk probably substantially lower.

2. Idiosyncratic
   a. Hematological: Megaloblastic anemia (mild megaloblastic changes are common and dose related), pseudolymphoma (fever, adenopathy, rash, and hepatosplenomegaly)
   b. Allergic or immunological: Lupus syndrome, rash, and Stevens-Johnson syndrome
   c. Hepatitis

Barbiturates (Phenobarbital, Primidone, Mephobarbital [Mebars])

1. Dose related
   a. CNS: Sedation, irritability; overdoses produce coma and respiratory and cardiac depression; worsening symptoms in patients with coexisting attention deficit disorder
   b. Psychiatric: Increased incidence of depression, particularly in patients with family history of a major affective disorder
   c. Reproductive: Unknown risk of malformations; thought to be lower than with phenytoin or valproic acid

2. Idiosyncratic
   a. Allergic or immunological: Lupus syndrome, rash, and Stevens-Johnson syndrome
   b. Hepatitis
   c. Hematological: Megaloblastic anemia

Carbamazepine (Telegrol, Epitol)

1. Dose related
   a. CNS: Dizziness, ataxia, drowsiness, diplopia, and visual symptoms, particularly at beginning of treatment or with high doses
   b. Hematological: Mild depression of white blood cell count is common and reversible
   c. GI: Nausea, vomiting, and anorexia (uncommon)
   d. Reproductive: Unknown risk of fetal malformations; thought to be less teratogenic than with phenytoin, but evidence is poor

2. Idiosyncratic
   a. Hematological: Irreversible aplastic anemia reported but extremely rare in children and young adults
   b. Allergic or immunological: Rash and Stevens-Johnson syndrome
   c. Hepatitis
   d. Hyponatremia, usually asymptomatic

Ethosuximide (Zarontin), Methsuximide (Celontin)

1. Dose related
   a. CNS: Fatigue, lethargy, and dizziness (at high levels)
   b. GI: Nausea, abdominal distress, and vomiting (usually preventable by dividing the dose or giving medication with food)

2. Idiosyncratic
   a. Hematological: Granulocytopenia
   b. Allergic or immune: Skin rash and lupus-like syndrome

Valproic Acid (Depakene, Depakote)

1. Dose related
   a. CNS: Sedation, ataxias at very high doses or in combination with other anticonvulsants are common. Fine tremor may occur at high dose levels.
   b. GI: Nausea, vomiting, and abdominal distress are common (much less common with Depakote, if using Depakene liquid, give with food).
   c. Hematological: All patients taking valproic acid have mildly elevated liver enzymes (serum glutamic-oxaloacetic transaminase, serum glutamic-pyruvic transaminase, and lactate dehydrogenase, generally about two to twice the baseline values). These are not clinically significant.
   d. Metabolic: Serum ammonia is elevated to about two to three times baseline values in patients taking valproic acid. Severe elevations may be associated with idiosyncratic reactions or very high doses. Lactic acidosis may occur at high doses, leading to growth failure. Serum carnitine may be reduced. Supplementation with oral carnitine has been advocated by some to prevent depletion.
   e. Changes in appetite: Approximately 10% of patients experience significant weight gain. Weight loss or failure to thrive occurs with high doses, usually associated with significant anorexia. Look for lactic acidosis, hyperammonemia, or depleted levels of free carnitine in patients with weight loss.
   f. Reproductive: There is an increased risk of open neural tube defects in fetuses exposed to valproate.
2. Idiosyncratic
   a. Hepatotoxicity: Fatal hepatotoxicity resembling Reye syndrome occurs primarily in children younger than 2 years receiving polytherapy. Adolescents on monotherapy have a very low incidence of severe toxicity. Monitoring of liver functions will not always prevent this syndrome, which may occur without warning.
   b. Hematological: A rare but partially dose-related syndrome resembling idiopathic thrombocytopenic purpura may cause profound thrombocytopenia and bleeding. It generally reverses promptly with discontinuation of valproic add. Mild thrombocytopenia commonly occurs with intercurrent viral illness and may reverse spontaneously or with lowered doses.
   c. Pancreatitis: Severe pancreatitis is occasionally associated with valproic acid. Slight elevations of amylase are common and generally not significant in an asymptomatic patient, but in the face of vomiting or abdominal pain, amylase and lipase should be checked.

Benzodiazepines: Clonazepam (Klonopin), Clorazepate (Tranxene), Diazepam (Valium)

1. Dose related
   a. CNS: Sedation, ataxia, and behavioral disturbances are most prominent on initiation of treatment or after dose increases, waning with continued administration.

2. Idiosyncratic
   a. Systemic, allergic, or hematological side effects are rare with benzodiazepines.
   b. Increased salivation may complicate management of the multihandicapped patient or one with severe respiratory disease.

Felbamate (Felbatol)

1. Dose related
   a. CNS: Sedation, ataxia, dizziness, insomnia, and headache are common.
   b. Non-CNS: Appetite decreases, dyspepsia, and nausea are prominent, particularly with high doses in the first few months of therapy. Weight loss can be substantial but is usually regained.

2. Idiosyncratic
   a. Severe aplastic anemia, leading to death in about one third of known cases, has been attributed to this medication. Use should be restricted to patients refractory to other medication, in the hands of experienced epileptologists, and with adequate informed consent.
   b. Death due to liver dysfunction has also been reported. See preceding cautions.
   c. Allergic: Iching, rash, and other allergic symptoms ranging from trivial to Stevens-Johnson syndrome have been reported.
   d. Psychiatric: Agitation, hallucinations, aggressive behavior, and frank psychosis have been reported.

Gabapentin (Neurontin)

1. Dose related
   a. CNS: Sedation, dizziness, ataxia, and diplopia are common.
   b. Non-CNS: Anorexia, dyspepsia, and weight gain are occasionally seen.

2. Idiosyncratic
   a. Rash

3. Other important information: Unlike other anticonvulsants, gabapentin is not metabolized but is excreted unchanged in the urine. Administration of gabapentin does not affect other drug levels. Dose adjustment is necessary for patients with renal impairment, depending on creatinine clearance.

Lamotrigine (Lamictal)

1. Dose related
   a. CNS: Sedation, dizziness, ataxia, and diplopia
   b. Liver dysfunction, including hepatic necrosis (single case report).

2. Idiosyncratic
   a. Rash

Topiramate (Topamax)

1. Dose related
   a. CNS: Drowsiness, dizziness, impaired cognition, word finding difficulty, impaired memory and attention, and paresthesias.
   b. Mild acidosis is expected due to carbonic anhydrase inhibition. Serum HCO$_3$ is lower than normal on routine electrolyte panels. This is not a cause for concern.

2. Idiosyncratic
   a. Anorexia and weight loss
   b. Renal calculi

Tiagabine (Gabitril)

1. Dose related
   a. CNS: Dizziness, headache, somnolence, asthenia, tremor, ataxia, and impaired concentration
   b. Skin rash

Zonisamide (Zonegran)

1. Dose related
   a. CNS: Dizziness, headache, diplopia, ataxia, speech and memory impairment, tremor, and agitation

2. Idiosyncratic
   a. Urolithiasis
   b. Rash: Zonisamide is contraindicated in patients with allergy to sulfonamides.

Levetiracetam (Keppra)

1. Dose related
   a. CNS: Somnolence, coordination difficulty, fatigue, and behavioral changes
   b. Leukopenia

Oxcarbazepine (Trileptal)

1. Dose related
   a. CNS: Somnolence, ataxia, dizziness and nausea
   b. Hypersensitivity disorder characterized by lymphadenopathy, rash, eosinophilia, and arthralgias have been reported.
   c. Hyponatremia, generally asymptomatic
**Other Problems with Anticonvulsant Therapy**

1. Because teenagers in whom epilepsy is well controlled often have no symptoms except for the drug side effects, it is tempting for them to take their medications only intermittently. These and other adherence problems are common (see the suggestions for improving adherence at the end of this chapter).
2. Medications may increase preexisting behavioral problems and occasionally cause depression.
3. Some drugs can increase seizure frequency as their dose is increased.

**Alternative Treatments of Refractory Epilepsy**

**Vagal Nerve Stimulation** Vagal nerve stimulation (VNS) is a newer therapeutic option used as an adjunctive treatment for adolescents and adults with medically refractory epilepsy. The VNS device consists of a programmable battery-operated generator and a silastic-coated lead that is implanted subcutaneously in the chest, with the lead attached to the left vagal nerve. Multicenter trials evaluating the efficacy of the vagal nerve stimulator demonstrated a 50% or more reduction in one third of patients with refractory partial seizures. The common side effects include hoarseness of voice, local pain, paraesthesias, dyspnea, and dysphagia. Uncommon complications include vocal cord paralysis and lower facial muscle weakness.

**The Ketogenic Diet** The ketogenic diet is a tightly controlled, high-fat, low-carbohydrate diet used in the treatment of intractable epilepsy. The diet is designed to place the body in a state simulating starvation, which results in the production of high levels of ketones. Undertaking this diet requires a strong commitment from both the patient and caregivers and a dietician and clinicians expert in the program.

**Epilepsy Surgery** Cortical resection or hemispherectomy may result in cessation or dramatic reduction of seizures for selected adolescents with intractable localization-related epilepsy. Key elements of surgical candidacy include intractable epilepsy; a localized epileptic zone; and a low risk for new postoperative neurological deficits. Surgical options include temporal lobectomy, extratemporal and multilobar resections, and functional hemispherectomy. The potential risk-benefit ratio for surgery must be carefully weighed for each child in light of the many complex age-related issues. Teens with uncontrolled or complicated epilepsy warrant referral to specialized centers with extensive pediatric epilepsy surgery experience.

**Other Important Treatment Issues**

The care of the epileptic teen extends beyond drug therapy. Total care involves dispelling myths and educating, providing for community resources, and providing counseling for the teen's voiced or unvoiced concerns.

**Dispelling Myths and Educating**

Many myths about epilepsy can be eliminated by reassuring the teenager that

1. Epilepsy is not contagious.
2. The seizures may disappear with age.
3. Most seizures can be prevented with medication.
4. Epilepsy does not lower the teenager's intelligence.
5. He or she can participate in almost all activities.
6. Epilepsy is not a “mental illness.”

The parent should also be given these reassurances, in addition to the following:

1. There is no need to feel guilty. It is unlikely that anything the parent did (or did not do) caused the epilepsy.
2. There is no need for special schooling solely due to epilepsy.
3. Neither epilepsy nor anticonvulsants cause learning disabilities or cognitive loss, although the prevalence of learning disabilities is higher in children and adolescents with epilepsy as a group.

The teen and family should be educated about the following:

1. Diagnosis
2. Importance of careful observation and record keeping
3. Avoidance of precipitating factors, if any
4. Side effects of medication
5. Prognosis and follow-up
6. Precautions and restrictions, particularly regarding driving, swimming, and bicycle and motorcycle riding, until seizure control is ensured: State requirements regarding reports to the Department of Motor Vehicles should be explained. Restrictions may need to be imposed regarding use of hazardous equipment such as power tools.
7. For women and adolescent girls of childbearing age, the need for adequate birth control while receiving most anticonvulsant drugs (see recommendations regarding interactions of anticonvulsants and contraceptives)

Family members should be aware of first aid for seizure episodes:

1. Generalized convulsion (tonic, tonic clonic, and clonic)
   a. Help the person into a lying position if there is adequate warning.
   b. Do not try to restrain the person.
   c. Clear the area of dangerous objects.
   d. Remove glasses and loosen tight clothing.
   e. Turn the head to one side (or roll the person onto his or her side) to allow saliva to drain out.
   f. Do not put anything into the person's mouth.
   g. Report what you observe. Try to time the episode with a watch.
   h. Family members should be given specific criteria to call for paramedic help: If the seizure lasts longer than 5–10 minutes, or if seizures cluster without recovery, call for emergency medical help. Specific advice should be individualized, based on the patient's seizure history.
   i. In teens with epilepsy who have clusters of seizures or prolonged breakthrough seizures that require emergency care, family members can be taught to use a rectal dose of diazepam. In the United States, a rectal gel form of diazepam is available in premeasured 5–, 10–, 15–, and 20-mg syringes as Diastat. The dose for teens is 0.2 mg/kg, rounded up to the next available size.

2. Partial seizures (simple and complex)
   a. Do not restrain the person.
   b. Remove harmful objects from the area.

3. Petit mal
   a. No first aid is necessary.
   b. Protect from harm if in dangerous situation until the episode passes.

**Community Resources** Teenagers and parents should be provided with references and should be informed of community resources about epilepsy. Many local epilepsy societies sponsor job search training; some have vocational training and placement programs. Some sponsor teen groups for peer support, camps, and family programs. The Epilepsy Foundation of America has a library of video tapes, pamphlets, and other educational materials for patients and families.
Local chapters can be located through the national offices or are often listed in telephone directories under “Social Service Organizations.”

**Miscellaneous Concerns**

1. Sports and activity: No need for restriction of activities except for swimming alone, scuba diving, mountain climbing, or bicycling in areas with traffic. Contact sports are generally restricted until seizures are controlled.
2. Medical identification: The teen with epilepsy should wear a medical identification bracelet or necklace. This may avoid unnecessary trips to emergency facilities or unneeded testing if a seizure occurs away from home.
3. Driving: Health care professionals should be aware of their state's driving laws regarding epilepsy. These should be explained to the teen, with the reasons for the laws. The wish to be seizure free to receive a license may enhance compliance. Laws regarding mandatory reporting to the state's Department of Motor Vehicles vary among the states.
4. School: The adolescent's school should be informed if seizures are a recurring problem. If the teenager has been seizure free for an extended time, there often is no need to inform the teachers of diagnosis, because this may cause unnecessary restrictions and lowered expectations.
5. Alcohol: Although abstinence is not necessary, more than a couple of drinks of alcohol a day may increase the risk of seizures in teens with epilepsy secondary to lowering of the seizure threshold.
6. Anticipate other concerns: Seizures, because of their unpredictable and abrupt onset, threat of injury, and embarrassment, can have profound effects on the developing adolescent. Try to anticipate and be sensitive to these concerns. Young teens may be concerned about whether their body is normal. Middle teens will have concerns about their peers, driving, and sports restrictions. Older adolescents will be more concerned regarding vocational planning and perhaps future health insurance.
7. Adherence: As stated earlier, adherence can be a significant problem in dealing with an epileptic teenager. Suggestions for improving adherence include the following:
   a. Provide clear explanations of medications used and their expected side effects.
   b. Give adolescent responsibility for taking medications.
   c. Discuss possible consequences of noncompliance with teen, such as recurrent seizures and inability to get or keep a driver's license.
   d. Referral to a teen group sponsored by a local chapter of the Epilepsy Foundation of America may be helpful.
   e. “Day of the week” pillboxes, filled and checked weekly, with parental supervision, may enable a young teen to manage his or her own medications.
   f. Attempt to simplify dosing schedules. Use b.i.d. dosing if possible.
   g. Use medications with acceptable side effects for the involved teen.

**SPECIAL CONSIDERATIONS IN EPILEPSY IN FEMALE PATIENTS**

**Hormonal Influences on Seizures**

Some women with epilepsy experience changes in seizure activity that relate to changes in pubertal status, menstrual cycle, or pregnancy. Morrell (1999) reviews hormonal influence on seizure activity. In general, estrogen increases excitation and reduces inhibition, whereas progesterone has the opposite effect.

**Effect of Puberty on Epilepsy**

Seizures can have their onset or change in frequency during puberty. Both JME and photosensitive seizures often develop during puberty. Childhood absence epilepsy and benign rolandic epilepsy often remit during puberty.

**Effect of Menses on Seizures**

As expected, with the rise of estrogen at ovulation and with the fall in progesterone during menses, seizures are more common during these times.

**Reproductive Dysfunctions**

Fertility in women with epilepsy is about one third that of nonepileptic siblings (Morrell, 1999). This may reflect either a fear of consequences of pregnancy, social pressure not to become a parent, or physiological disruptions to reproductive cycles. Anovulation is more common in women with epilepsy. Women with epilepsy appear to have a higher frequency of reproductive endocrine abnormalities including alterations of daily basal and pulsatile release of luteinizing hormone. Women with epilepsy may also have hormonal abnormalities related to their use of anticonvulsant medications. Valproic acid in particular is associated with a syndrome similar to polycystic ovary syndrome.

**Pregnancy**

As discussed previously, there is an increased risk of abnormal pregnancy outcomes in women with epilepsy regardless of the specific drug treatment.

**Contraception**

Because of the increased metabolism of component hormones, low-dose hormonal contraceptives should be avoided when used with anticonvulsants that induce the cytochrome P-450 system. These would include Norplant and progestin-only pills. Combined oral contraceptives may have a slightly lower rate of efficacy but still could be used. A pill containing at least 50 µg of ethinylestradiol is advised. Depo-Provera efficacy is not reduced with anticonvulsants.

**WEB SITES**

For Teenagers and Parents

http://www.efa.org/. Lots of information from the Epilepsy Foundation of America including driving laws, e-communities, educational information.


http://www.epilepsy.ca/eng/mainset.html. Much information on epilepsy and links elsewhere from Epilepsy, Canada site.

http://137.172.248.46/frequent.htm. Frequently asked questions about epilepsy and links to many other sites.


For Health Professionals


REFERENCES AND ADDITIONAL READINGS


Recurrent headaches are a frequent problem in adolescents and adults, accounting for numerous physician visits and lost days of work and school. By the age of 15 years, at least 75% of people have experienced at least one headache episode. Most recurrent headaches are not associated with severe organic pathology but may be important signs of stress, anxiety, or depression. In contrast, the single severe acute headache, particularly in a patient without prior headache history, may be due to significant central nervous system (CNS) or systemic disease.

PAIN-SENSITIVE AREAS: WHAT HURTS IN THE HEAD

In general, the brain parenchyma and dura are insensitive to pain. Pain-sensitive areas include the following:

1. Intracranial
   a. Cranial nerves (CN) V, IX, and X. (Most intracranial structures are innervated by CN V.)
   b. Dural arteries
   c. Major venous sinuses
   d. Dura at the base of skull
   e. Intracavernous and proximal intracranial portions of the carotid arteries
2. Extracranial
   a. Skin, fascia, muscles, and blood vessels of the scalp
   b. Upper cervical nerve roots
   c. Muscles of the neck
   d. Sinuses and teeth
   e. Eyes and eye muscles
   f. Ears

MECHANISMS OF PAIN

Vascular Dilation

Distention of pain-sensitive cranial arteries causes headaches. The pain is mediated through the trigeminovascular system, which when depolarized, releases neuropeptides that mediate vasodilation and neurogenic inflammation. This mechanism is involved in migraine headaches and in many headaches associated with fever, systemic infection, metabolic disturbances, and vasodilator drugs. Migraine headaches may be associated with vasoactive agents, including serotonin, bradykinin, norepinephrine, prostaglandins, substance P, neuropeptide, calcitonin gene-related peptide, and histamine. The role of these vasoactive substances may be casual or reactive. There is increasing evidence that migraine is neurally initiated, rather than a direct response of the vascular system, with vascular changes being a secondary phenomenon. The “aura” of migraine headaches and the neurological manifestations of complicated migraines are due to vasoconstriction of intracranial arteries, leading to ischemia in affected areas of the brain.

Muscular Contraction

Increased muscular contraction of the head and neck muscles can lead to a headache. This mechanism of headaches is involved in tension and psychogenic headaches but may be a secondary source of pain in migraines. Patients with a migraine commonly have muscle contraction and tenderness as a result of the headache, rather than as a primary event.

Traction

Traction of pain-sensitive structures intracranially may cause a headache. Examples include mass lesions such as a brain tumor, brain abscess, subdural hematoma, and increased intracranial pressure. Brain tumors rarely cause pain directly unless pain-sensitive CNs are involved, intracranial pressure is increased, or there is traction on the meninges.

Inflammation of Pain-sensitive Areas

Examples include meningitis (either aseptic or bacterial), sinusitis, dental disease, orbital inflammation, and vasculitic syndromes involving intracranial or extracranial vessels.

EPIDEMIOLOGY

1. Prevalence
   a. Approximately 40% of children by age 7 years have headaches, 66% by age 12, and 75% of adolescents by age 15 years. Most of these headaches are infrequent and nondisabling.
   b. Migraine headaches: Twenty-five percent of migraineurs first develop symptoms during childhood. There is about a 4% prevalence rate among individuals age 7 years to 15 years. However, migraine is commonly underdiagnosed if mild or infrequent, so the prevalence may be higher.
2. Sex: Headaches occur in about equal prevalence among males and females until around age 12 years. At that time, headaches become more common in females.
3. Types: Acute headaches are usually associated with a systemic disease such as a viral illness or sinusitis. Most recurrent headaches in adolescents and adults
are either vascular headaches (migraines), muscular contraction headaches, or a combination of both. Other causes, such as a brain tumor, are uncommon. Cluster headaches usually start during late adolescence or later but can start as early as 8 years of age and are far more common in males. Depressive headaches may present in the preadolescent or adolescent years, at times with denial of other depressive symptoms.

DIFFERENTIAL DIAGNOSIS AND CHARACTERISTICS

See Table 23.1.

Acute, Nonrecurrent (First or Worst) Headaches

Although this may be the first attack of episodic, recurrent headaches, it is important to rule out serious potentially life-threatening etiologies:

1. Febrile patient
   a. Meningitis: Bacterial, viral, tuberculous (TB), and other aseptic causes
   b. Brain abscess, epidural empyema, or other intracranial infection
   c. Encephalitis
   d. Sinusitis
   e. Nonspecific headache due to fever
   f. Associated with other infections: Headache is a common symptom in strep throat, influenza, mononucleosis, and rubella. Patients with human immunodeficiency virus (HIV) or acquired immunodeficiency syndrome (AIDS) frequently complain of headaches.

2. Afebrile patient
   a. Subarachnoid hemorrhage (arteriovenous malformation [AVM], aneurysm with acute bleed)
   b. Intracerebral hemorrhage (AVM, venous angioma, or trauma)
   c. Other (cysticercosis or acute obstructive hydrocephalus)
   d. Headache after a seizure (postictal)
   e. Variant migraine: 5%–10%
   f. Severe hypertension
   g. Acute dental disease
   h. Eye or orbit: Acute glaucoma or inflammatory disease of orbit

Recurrent Headaches (Episodic, Complete Recovery Between Episodes)

1. Muscle tension headaches: There is now significant doubt in the neurological literature that muscle tension headaches exist, other than in situations of direct neck muscle trauma. Many headache experts consider "tension headaches" to be mostly misdiagnosed vascular headaches.

   a. Bandlike, bilateral, steady pain, occipital more than temporal
   b. Lacking the following: Throbbing, nausea, vomiting, photophobia, and associated neurological symptoms
   c. Often gradual in onset and related to stress or fatigue
   d. May be caused by minor trauma to neck muscles, whiplash, and muscle strain
   e. May be caused by temporomandibular joint dysfunction

2. Migraine (also known as vascular headache)
   a. Classic migraine (newer term is migraine with aura): 10%–15%
      • "Aura" of sensory disturbances: Visual changes, numbness, tingling, dizziness, vertigo, and syncope are common.
      • Throbbing, unilateral, and usually frontal or temporal pain occurs.
      • Anorexia, nausea, and vomiting are often accompanying symptoms.
      • Phonophobia and photophobia are common.
      • Sleep often relieves migraine.
      • Family history is often positive for migraineurs. Although a parent may not describe his or her headaches as migraines, more careful history of family members’ headache patterns often reveals vascular headaches.
      • A childhood history of motion sickness or cyclic vomiting is common.
      • Pattern of headaches varies over time. Exacerbations or onset may be precipitated by puberty, college, or other life stresses.
      • In some subjects, episodes may be precipitated by certain foods, including chocolate, tyramine-containing cheeses, red wines, and foods containing monosodium glutamate (MSG), nitrates, or nitrates.
      • History of relief with ergot compounds or specific serotonin agonists (sumatriptan and ditydroergotamine [DHE]) is supportive of diagnosis.
   b. Common migraine (newer term is migraine without aura): 90%–90%
      • As previous, but lacking aura
      • May be bilateral and variable in pain distribution
   c. Variant migraine: 5%–10%
      • Hemiplegic migraine: Often familial and presents with hemiplegia, aphasia, or speech disturbances, followed by headache and associated symptoms as stated earlier. Headache is generally contralateral to hemiplegia. Headache may be less symptomatic than hemiplegia.
      • Confusional migraine: More common in younger children but may continue into the teen years. A period of confusion and disorientation is usually followed by vomiting, deep sleep, and waking feeling well. Headache may not be reported by child and generally is not prominent.
      • Abdominal migraine: Episodic abdominal pain with nausea or vomiting, followed by or accompanied by a headache. However, the headache may be minimal or absent, and vomiting the most prominent symptom. Aura may precede pain. Relief of episodes by sleep or antimigraine therapies supports diagnosis.
      • Basilar migraine: Dizziness, vertigo, syncope, and dysarthria are common, preceding variable headache and vomiting. Headache may be minimal or even absent. Common in adolescent girls.
      • Ophthalmoplegic migraine: Abnormal eye movements, sometimes with near-complete ophthalmoplegia and diplopia, are followed by more typical migraine symptoms.

3. Cluster headaches: <5% in children and adolescents
   a. Male predominance
   b. Steady burning or pain; usually localized behind one eye: sudden onset; extremely severe but brief
   c. Rhinorrhea, lacrimation, and conjunctival injection on the same side is common.
   d. Horner syndrome ipsilaterally during attack is common.
   e. During clusters, multiple daily episodes, often in early morning hours, awakening patient from sleep.
Differential diagnosis includes occult dental disease, acute glaucoma, and tic douloureux.

Note that several rare metabolic disorders may mimic a migraine, including mitochondrial diseases; mitochondrial myopathy, encephalopathy lactacidosis, and stroke-like episodes syndrome; and several organic acidurias. If metabolic disease is suspected, blood for lactate, pyruvate, and ammonia and urine for organic acids should be collected during the episodes.

**Chronic Headaches (Variable But Essentially Continuous or Increasing Since Onset)**

1. Intracranial mass lesions
   a. Although many patients with brain tumors have headaches, very few patients with headaches have brain tumors.
   b. Headaches due to brain tumors commonly are accompanied by other neurological symptoms such as vomiting, diplopia, gait abnormalities, weakness, neuroendocrine abnormalities, or personality and behavioral changes.
   c. Headaches may be increasing in severity and frequency and may occur nocturnally.
   d. Findings from neurological examination and funduscopic examination are often abnormal.

2. Hydrocephalus (with or without mass)
   a. May be relatively constant, often worse in the morning.
   b. Aqueductal stenosis may present in adolescents, even if congenital.
   c. Head may be large, but this is not universal.
   d. Pain is usually dull, vertex, and not very severe.
   e. Pain may be increased by straining, bowel movements, coughing, or bending.

3. Postlumbar puncture headaches
   a. Headache is positional, often abruptly relieved by recumbency.
   b. Headache, nausea, and vomiting may be severe if the patient is upright.
   c. Primary treatment is 1–2 days of recumbency.
   d. If not relieved in several days and severe, epidural blood patch provides relief in about 90% of cases but may cause some lower back discomfort.
   e. Salt and fluid loading and abdominal binders are of limited efficacy.
   f. Occasionally, spontaneous or posttraumatic occult cerebrospinal fluid leaks may present identically. Opening pressure on a spinal tap is extremely low.

4. Pseudotumor cerebri (also called benign intracranial hypertension): Increased intracranial pressure without mass effect
   a. Papilledema is common. Visual fields may be abnormal, including enlarged blind spot or constricted peripheral fields.
   b. Visual obscuration (transient dimming or loss of vision with straining or position change) may be present. CN palsies, more frequently VI and VII, may be associated.
   c. Pain is usually dull and vertex.
   d. Pseudotumor cerebri is more common in females and obese patients.
   e. May be caused by excessive vitamin A or vitamin D intake, rapid steroid taper, or tetracycline intake.
   f. There is a risk of permanent visual loss if untreated. A patient with headache and papilledema should be treated as an emergency to prevent potential visual loss.
   g. Lumbar puncture (postimaging) may be both diagnostic and therapeutic. Acetazolamide may be useful in some patients provided they tolerate the nausea.
   h. Corticosteroids are often effective but very difficult to wean without recurrent symptoms. Rarely a lumbarperitoneal shunt needs to be placed. Optic nerve sheath fenestration may be necessary to relieve pressure on the optic nerve.

5. "Transformed migraine": Migraine attacks may go from episodic to chronic, essentially continuous pain.
   a. Excessive use (usually about >14 tablets per week) of symptomatic medication (analgesics or ergots) may contribute.
   b. Other migrainous symptoms are usually present but may only be present in retrospect.

6. Depressive headaches
   a. "All day, all the time, every day, no relief."
   b. Other overt depressive symptoms may be absent.
   c. Excessive disability (school absenteeism and social isolation) is common.
   d. Family history is often positive for affective disorders.
   e. Often responsive to antidepressant medications and supportive psychotherapy.

7. Posttraumatic (head trauma)
   a. Headaches usually have mixed migrainous and "tension" quality.
   b. Diminish gradually over time.
   c. Minor head trauma may precipitate episodic migraines.

8. Local extracranial disease
   a. Chronic sinusitis
   b. Dental disease, including temporomandibular joint dysfunction
   c. Glaucoma
   d. Other orbital inflammatory lesions
   e. Vasculitis involving extracranial vessels (rare in adolescents)

9. HIV or AIDS
   a. Chronic or recurrent headaches are common.
   b. May be due to HIV, coexisting other infections (intracranial, sinus, or ear), or treatment, including antiretroviral agents.

10. Pregnancy
    a. Early pregnancy may be associated with headache, nausea, and vomiting.
    b. Pregnancy may exacerbate migraines.

11. Chronic meningitis or other inflammatory conditions
    a. CNS sarcoidosis may present with meningeal or parenchymal involvement.
    b. TB, fungal, or recurrent or chronic "aseptic" meningitis may present with sustained or recurrent headaches.

12. Headaches due to substance or drug abuse
    a. Both drug use and drug withdrawal may cause headaches.
    b. Alcohol causes intense flushing and headaches in genetically prone individuals, usually of Asian origin.
    c. Alcohol withdrawal causes headaches. Be particularly alert for recurrent morning headaches due to daily alcohol consumption.
    d. Cocaine increases blood pressure and may cause headaches.
    e. Excessive (or even therapeutic doses) of over-the-counter (OTC) stimulants such as phenylpropanolamine, pseudoephedrine, or "kava" may cause headaches.
    f. Inhalants may cause prominent headache symptoms.
    g. Amphetamines and withdrawal from amphetamines.

13. Headaches due to obstructive sleep apnea
    a. Headaches are often worst upon awakening.
    b. History of snoring is common.
    c. History of pauses or gasps during sleep is generally elicited only after asking the parent to observe breathing pattern during sleep.
    d. Large tonsils and adenoids and "mouth breathing" are often apparent on physical examination.

14. Headaches due to other medical conditions: Headaches may be intermittent or continuous. Hypoxia, hypercarbia, significant hypertension, severe anemia, uremia, and dialysis all cause intermittent or continuous headaches in some patients. In addition, multiple medications used for other medical conditions, particularly chemotherapy, antiretroviral therapy, and agents used in organ transplant recipients cause headache. This is particularly important in treating adolescents with other chronic conditions such as cystic fibrosis, chronic pulmonary disease, renal failure, sickle cell anemia, cancer, organ transplantations, or cyanotic congenital heart disease. Treatment is generally aimed at the underlying condition and symptomatic relief of pain. Treatment options may be severely limited by the underlying condition for patients with migraine coexisting with other chronic illnesses.

**DIAGNOSIS**

In the evaluation of the patient with headaches, the history is (nearly) everything. The rest is the examination.
(See Table 23.2 and Table 23.3 for International Headache Society [IHS] criteria for migraines.)

TABLE 23.2. International headache society criteria for migraine with aura

1. Onset: Age at first episode; events or illnesses surrounding onset; temporal pattern of headaches (time of day, day of week, and season); frequency
2. Pattern and chronology of pain: Have the patient describe a typical headache episode in detail.
   a. Prodrome
   b. Location
   c. Quality (pounding, dull, sharp, or sticking)
   d. Change in quality or location as headache progresses
   e. Associated autonomic symptoms (sweating, pallor, flushing, and palpitations)
   f. Nausea, vomiting, and anorexia
   g. Duration and diurnal variation
   h. Severity and limitation of activities
   i. Response to medications and sleep
3. Preceding and accompanying symptoms, particularly visual or other neurological symptoms
4. Precipitants of specific episodes or at onset of headaches
   a. Stress: Family, school, and peers
   b. Illnesses
   c. Foods: Nitrate- or nitrite-containing foods, MSG, chocolate, nuts, cheeses, and other specific suspect foods
   d. Medications: Intake of OTC medications (particularly phenylpropanolamine in decongestants or diet pills)
   e. Exertion and orgasm
   f. Caffeine intake or withdrawal
   g. Alcohol intake
   h. Toxic exposures, particularly lead and hydrocarbons
   i. Physical exposures: Bright or flashing lights, temperature changes, and strong odors
5. Other associated illnesses or symptoms, including HIV risks. Changes in menstrual pattern or galactorrhea may suggest pituitary lesion or pregnancy.
6. Medications (prescribed and OTC)
   a. Analgesics
   b. Birth control pills
   c. Other medications used for headaches (acute or prophylactic)
   d. Tetracycline
7. Vitamin consumption, particularly fat-soluble vitamins (e.g., vitamins A, D, and E), unusual diets, and supplements
8. Substance abuse
9. Depression or mood disorders
10. School phobia or school avoidance and other secondary gains
11. Behavior between attacks: Any recent personality change or change in school performance
12. Family history
   a. Migraines or other headaches
   b. Epilepsy
   c. Affective disorders
13. Other criteria for migraines: Raskin (1995) identified additional clinical features that suggest the benign nature of a migraine attack. These exceed the IHS criteria (Table 23.1 and Table 23.2) of migraine and consist of the following factors: (a) precipitation by menstruation, (b) amelioration with sleep, (c) amelioration during pregnancy, (d) appearance after sustained exertion, and (e) triggers such as alcohol, odors, foods, or changes in the weather.

Physical Examination

The physical examination should include a good general physical examination plus a careful neurological examination. If possible, the patient should be examined both during a typical episode and when free of symptoms. Pertinent physical findings include the following:

1. Vital signs: Elevated blood pressure or temperature
2. Eyes, ears, nose, and throat: Sinus tenderness, acute or chronic otitis, poor dentition, and refractive error
3. General physical examination: Café au lait spots, signs of systemic illness, and galactorrhea
4. Neck: Nuchal rigidity, spasm or tenderness of cervical neck muscles, or “trigger points"
5. Funduscopic and visual examination: Papilledema, narrowing of vessels, optic atrophy; visual fields, and visual acuity
6. Neurological examination: Head circumference, mental status, CNs, motor sensory examination, gait, and coordination

Laboratory Tests

In patients with recurrent headaches separated by periods of complete recovery, laboratory and radiological workups are seldom indicated in the presence of normal...
physical examination findings. Laboratory and radiological workups should be guided by the history and physical examination results; that is, sinus films may be indicated if facial tenderness or nasal discharge suggest sinusitis. Neuroimaging (computed tomography or magnetic resonance imaging) is indicated if it is an acute severe headache or if the result from neurological examination, if papilledema is present, or if the head circumference is above the 95th percentile without other explanation. Neuroimaging is not generally needed for low-backstanding recurrent headaches with complete clearing of symptoms between episodes in adolescents. Neuroimaging may be helpful in the evaluation of normal neurological and functional examination results. Other evaluation is guided by physical findings and history. For example, in an adolescent with morning headaches, snoring, and large tonsils, a sleep study to rule out obstructive sleep apnea may be appropriate.

In contrast, an acute severe headache in a patient with no prior headache history must be considered more closely, as underlying systemic or CNS pathology may be life threatening. Neuroimaging and lumbar puncture should be considered to aid in the diagnosis of an acute condition and may be necessary emergently.

THERAPY

Rule 1A: Not having a headache is better than getting rid of it once it occurs. Rule 1B: Not taking pills every day is better than taking pills. Look for precipitants, particularly avoidable ones.

Rule 2: Take the preferred medication at the onset of the headache, the earlier the better.

Rule 3: Do not underestimate the role of reassurance. Adolescents and parents are often more concerned that the headache is caused by a brain tumor than by the discomfort of the headache itself. Once the adolescent is reassured, treatment beyond simple analgesics may be neither necessary nor desired by the patient.

1. Headache diary: The patient should be encouraged to understand causes and precipitants for headaches. Keeping a headache diary can be therapeutic itself, even if no specific precipitants are ever identified. The diary is kept for a variable period, usually until at least three typical headache episodes have occurred or up to 3 months if no attacks occur while keeping the diary. The adolescent (with the help of a parent) records a detailed diary of headaches, medication intake, and results, as well as activities, foods, stresses, sleep pattern, and physical environment. The following items can be important in uncovering the precipitating factors in recurrent headaches:
   a. Foods: Chocolate, nuts, cola, caffeine-containing beverages, and cheeses. (Best to record all food intake in the diary.)
   b. Food additives: MSG, nitrates, and nitrates. Nitrates and nitrates are present in nearly all cured meats such as hot dogs, bacon, sausage, ham, and lunch meats.
   c. MSG is not always clearly listed on food labels. Foods commonly high in MSG include dried soups and noodles, dried flavoring packets for taco or spaghetti sauces, and some snack foods.
   d. Physical stimulants: Exposure to bright lights; rapidly moving or strobe lights (or strobe effect when driving); temperature changes; exercise; and sexual activity.
   e. All medications, including OTC medications and birth control pills, for headache and any other conditions.
   f. Alcohol or other substance intake.
   g. Obvious allergic symptoms (rashes, asthma, and allergic rhinitis).
   h. Stresses: School, tests, and emotional stressors.
   i. Sleep pattern: Deviations from usual pattern, particularly excessive sleep, may precipitate headaches.

2. Treatment of tension headaches
   a. A brief period of relaxation or a nap often brings relief.
   b. Simple physical measures: Massage or stretching exercises of the neck muscles or warm or cold compresses may help, particularly with relaxation.
   c. Biofeedback is occasionally beneficial but is expensive and requires a very motivated patient and family.
   d. Simple analgesics (e.g., acetaminophen, nonsteroidal antiinflammatory drugs [NSAIDs], and aspirin), if not used excessively, are often effective.
   e. Combined analgesic-sedative drugs (butalbital [Fiorinal] or other combinations) should be used sparingly, if at all.
   f. Mixed tension-vascular headaches, if very frequent and disabling, may be treated on a prophylactic basis with low-dose tricyclic antidepressants, usually amitriptyline.

3. Migraine headaches: Things to do on a trial basis for all patients with migraines:
   a. Wear sunglasses, brimmed hat, or visor whenever in bright sun. In many communities, a "doctor's note" is needed to allow a hat or sunglasses to be worn during outdoor activities at school.
   b. Avoid strobes or strobe-like conditions.
   c. Try a diet eliminating MSG and nitrates or nitrates.
   d. Stabilize caffeine intake (same amount every day) or wean off completely.
   e. Try eliminating all alcohol intake.

4. Medications for acute episodic migraine treatment (classic, common, or variant) in patients with relatively infrequent headaches
   a. Simple analgesics, taken as soon as possible at the onset of the episode (e.g., acetaminophen, NSAIDs such as ibuprofen, and naproxen) often abort the migraine, without the need for stronger medications. Caffeine (either as a tablet, combined with analgesic, or as a beverage) may potentiate the effect of the analgesic.
   b. Antiemetic, either orally, rectally, or parenterally: Promethazine (Phenergan), chlorpromazine (Thorazine), or prochlorperazine (Compazine) combined with or followed by an analgesic is very helpful if nausea or vomiting is prominent. Use of a sedating antiemetic will often allow oral analgesics to be tolerated, produce sleep, and relieve nausea and vomiting.
   c. Sedative-analgesic combinations: Small doses of a short-acting sedative such as barbiturate with acetaminophen or aspirin are reasonable if headaches are infrequent and relieved by sleep. Multiple preparations and brands are available (butalbital [Fiorinal], meperidine with aspirin [Equagesic]).
   d. Ergot derivatives work best for common migraines but do work for some common migraines. Ergotamine must be used immediately at the onset of symptoms. Medication should be available to the adolescent at all times, including in school. Sublingual, oral, rectal, or inhaled preparations are available, with multiple brands and combinations. Caffeine and ergotamine may be used with or without aspirin.
   e. Triptans: Several triptans are available, all selective serotonin receptor agonists. They cannot be mixed (i.e., do not use more than one particular triptan in a given 24-hour period). They should also not be mixed with ergot preparations. They are contraindicated in hemiplegic migraines. Generally if one triptan does not work, switching to another may not help. If one type works but has unacceptable side effects, another may be better tolerated.
   f. Sumatriptan, a specific serotonin agonist is administered by subcutaneous injection, nasal spray, or orally. It is not yet labeled for use in children or adolescents, although several published studies have reported on the use in adolescents:
      - Self-injection: The "self-injection" syringes are only available in a 6-mg dose, which may be too high for a smaller adolescent. Fractional doses (2–3 mg) may be used from unit-dose vials using a regular syringe and needle. Because subjective sensory phenomena may be very worrisome to the patient, the first dose should always be given under direct medical supervision. If successful and well tolerated, the adolescent or the parents may be instructed in administration at home, particularly if episodes are infrequent but very severe.
      - Oral: Sumatriptan is available in 25- and 50-mg tablets. The adult dose is 25–50 mg, given once or twice. Onset of action is in about 1 hour, and relief may be long-standing if the event is interrupted.
      - Nasal spray: Sumatriptan nasal spray is particularly effective for those patients with nausea and vomiting and can be used at home or school. The nasal spray is available in 5- and 20-mg single-dose dispensers. Adolescents generally respond to 10–20 mg. The spray generally causes a metallic taste, which lasts for 30–60 minutes. Using the spray with the head tilted forward, then compressing the nostrils for a few minutes may partially prevent this effect, which is quite noxious to some patients.
      - Zolmitriptan, another serotonin agonist that has been used in adults, is particularly useful for cluster headaches. It comes in 2.5- and 5-mg tablets (maximum dose, 10 mg per 24 hours). It also has similar adverse effects such as paresthesias, heaviness, nausea, and tightness.
      - Rizatriptan, 5- and 10-mg oral disintegrating tablets. This form is useful for adolescents who cannot or will not swallow a pill during a migraine.
      - Naratriptan comes as 1- and 2.5-mg tablets. Has not shown significant efficacy for adolescent migraines. It is longer acting and may be useful in adolescents in whom sumatriptan is effective but with recurrent headaches when a dose wears off.
   g. DHE (intravenous or intramuscular injection): DHE-45, given 10–15 minutes after a parenteral dose of diemetic (commonly metoclopramide [Reglan] or chlorpromazine [Thorazine]), may provide rapid relief of migraine symptoms, even several hours after onset. Several small doses may be given under direct supervision in an emergency department or office. Occasionally, the patient or family may be taught to self-administer DHE at home for severe episodes. Do not use for hemiplegic migraines.
   h. Nasal spray is available at home or school and is occasionally effective in adolescents who do not tolerate triptans.
   i. Inhaled high-flow oxygen may relieve cluster headaches rapidly. Patients with cluster headaches often carry a small tank of oxygen with them at all times and become very dependent on the availability of this treatment modality if it is effective at relieving their severe attacks of pain. Warning: If headaches are frequent (i.e., more than twice a week), beware of analgesic or ergot overuse syndromes. This may convert intermittent migraines to chronic "transformed" migraines.
5. Prophylactic treatment: Adolescents with severe recurrent attacks causing significant school absenteeism or functional limitations should be considered for prophylactic treatment. Prophylactic treatment is generally indicated in migraines accompanied by significant neurological deficits (e.g., hemiplegic migraines), even if the episodes are infrequent. Prophylactic treatment may be preferred even in patients responsive to ergotamine, due to the inability to carry medications in school. Continue treatment until the headache pattern has markedly improved for approximately 6 months, then consider a trial of a taper-off medication.

a. b-blockers: Propranolol is effective in approximately 70% of adolescents with severe migraines, although there have been few well-controlled studies. The initial dose is 40–80 mg, divided twice daily (b.i.d.) or three times a day (t.i.d.). Higher doses (up to 240 mg/day) may be used. The effect is not immediate. Usually, a gradual decrease in headache frequency is seen over several weeks to months. Side effects include fatigue, depression, and decreased exercise tolerance, particularly at high doses. Severe asthma, insulin-dependent diabetes, and depression are contraindications. Other b-blockers (e.g., atenolol, nadolol, timolol, and metoprolol) may also be effective.

b. Tricyclic antidepressants (amitriptyline, imipramine, desipramine): Amitriptyline (Elavil) is useful for prophylaxis of migraines or mixed tension-vascular headaches. The initial daily dose is 10–25 mg at bedtime, increased gradually as needed to 75–100 mg/day. Side effects include sedation, dry mouth, arrhythmias, hypotension, and decreased tolerance of warm environments.

c. Low-dose aspirin or NSAIDs (e.g., ibuprofen and naproxen) used in chronic low doses may effectively prevent migraine attacks. NSAIDs may be particularly useful for "transformed migraines," chronic migraines, rebound headache if severe and disabling.

d. Methysergide (Sansert): Significant risks make this a last choice in most circumstances. It should not be used continuously for more than 6 months, because of risk of retinopathy and pericardial fibrosis. Close follow-up is essential. However, this is a very effective modality for patients with refractory, frequent migraines.

e. Calcium channel blockers (e.g., verapamil and nimodipine) have been used with some success for migraine prophylaxis.

f. Lithium carbonate has been reported to be an effective prophylactic medication for chronic cluster headaches.

g. b-blockers: Propranolol is effective in approximately 70% of adolescents with severe migraines, although there have been few well-controlled studies. The initial dose is 40–80 mg, divided twice daily (b.i.d.) or three times a day (t.i.d.). Higher doses (up to 240 mg/day) may be used. The effect is not immediate. Usually, a gradual decrease in headache frequency is seen over several weeks to months. Side effects include fatigue, depression, and decreased exercise tolerance, particularly at high doses. Severe asthma, insulin-dependent diabetes, and depression are contraindications. Other b-blockers (e.g., atenolol, nadolol, timolol, and metoprolol) may also be effective.

PROGNOSIS

Guidetti et al. (1998) studied the evolution of headaches in children and adolescents and found that 34% remitted, 45% improved, 6% worsened, and the condition remained unchanged in 15%. Up to 40% to 50% of childhood-onset migraines may remit during adolescence or young adulthood. Adolescent-onset migraines often continue into adulthood. However, adolescents should be reassured that even people with a strong tendency to have migraines do not have frequent attacks throughout life. Patterns of occurrence are highly variable. The goal is to avoid any offending agents, use effective medication in appropriate doses, and lead a functional lifestyle.

WEB SITES

For Teenagers and Parents

http://www.headaches.org/: Web site of the National Headache Foundation.
http://www.mckinley.uiuc.edu/health-info/dis-cond/headache/headache.html: University of Illinois student health center information sheets on headaches.

For Health Professionals


REFERENCES AND ADDITIONAL READINGS


Bateman DN. Sumatriptan. Lanor 1993;341:221.


SYNCOPE

Syncope implies a brief loss of consciousness, usually lasting several seconds to a minute or so, with loss of postural tone, followed by spontaneous recovery without resuscitation. Although most episodes are neurocardiogenic (vasovagal), any condition that decreases cerebral perfusion, cardiac or noncardiac, as well as metabolic disturbances and psychiatric conditions, may cause syncope. Conversely complicating the evaluation in some instances is the phenomena of syncope "epidemics," particularly in schools or other closed populations.

Up to 30% of healthy teenagers experience some type of syncopal episode during their adolescence. Many terms are used by patients to describe their complaints. Presyncopal symptoms may include lightheadedness, floating feelings, faintness, and spinning sensations. Syncope may also be characterized by a sudden loss of consciousness and may trigger a seizure-like episode. It is important to carefully differentiate complaints of syncopal and near-syncopal episodes, vertigo, and nonspecific dizziness. This differentiation is made primarily by history provided by the patient and observers. Each has separate implications for evaluation and therapy.

SYNCOPE DUE TO DECREASED CEREBRAL PERFUSION PRESSURE

1. Vasodepressor episode, vasovagal syncope, neurocardiogenic syncope, common faint
   a. The most frequent cause of syncope among teenagers and adults, accounting for most syncopal episodes.
   b. Duration: May last for a few seconds to a few minutes.
   c. Onset: Gradual. The patient generally is aware that something is wrong.
   d. Precipitating factors: Acute stress including fear, anxiety, pain, hunger, overcrowding, fatigue, injections, and the sight of blood. Alcohol and exposure to cold or heat can also precipitate an attack. Prolonged standing, particularly without movement, may contribute. Group hysteria may precipitate syncope seizures: In some individuals, a brief tonic or clonic seizure will be precipitated by syncope. It always follows the preceding syncopal symptoms.
   e. Attack description:
      
      - Early phase: The early phase is characterized by an elevated pulse, elevated blood pressure, and increased cardiac output. Symptoms include feelings of apprehension, anxiety, and lightheadedness, as well as a feeling of warmth.
      - Middle phase: Pulse, heart rate, blood pressure, and cardiac output decrease. Symptoms include pallor, nausea, sweating, belching, yawning, mydriasis, weakness, cold hands, and faintness.
      - Faint: If the blood pressure drops to less than 60–70 mm Hg, loss of consciousness will occur. There is gradual loss of muscle tone and a fall to the ground.
      - Syncopal seizures: In some individuals, a brief tonic or clonic seizure will be precipitated by syncope. It always follows the preceding syncopal symptoms.
      - It is more likely if the patient faints while sitting or is kept from assuming the recumbent position on loss of consciousness.
      - Recovery: Consciousness generally returns in <1 minute, often with a brief period of perceived inability to respond despite awareness of the environment. The patient may report fatigue, malaise, weakness, nausea, and headache for up to an hour after fainting.
   f. Position: Episodes generally occur while the patient is in the sitting or standing position. Prolonged standing for hair combing or braiding is a common precipitant in adolescent and preadolescent girls. Assuming a recumbent or head-down position may prevent progression of the episode to full loss of consciousness.
   g. Pathophysiology: The exact pathophysiology is still not completely understood. However, the initial phase is characterized by an increase in catecholamine release. The second phase is characterized by dilation of the vascular bed, with a shift in blood flow to the muscles and a drop in cardiac output. In many patients, there is also an increase in vagal tone, leading to a marked decrease in heart rate.

2. Hyperventilation: Hyperventilation is a frequent cause of dizziness in the adolescent, although syncope less frequently follows. Symptoms of hyperventilation include the following:
   a. Respiratory: Subjective shortness of breath secondary to increased thoracic respiratory efforts; chest pain either secondary to pressure on the diaphragm from gastric distension or related to thoracic muscle strain; and increased thoracic breathing, sighing, and yawning.
   b. Cardiovascular: Palpitations, tachycardia, and precordial pain.
   c. Neurological: Paresthesias in extremities or periorally, lightheadedness, dizziness, disorientation, impaired thinking, tetany, seizures, syncope, and

References and Additional Readings

For Health Professionals

For Teenagers and Parents

Physical Examination

History

Diagnosis

Therapy

Vertigo

Noncardiac Causes

The following problems may also cause dizziness without syncope or “near-syncope.”

Unknown causes

Vasovagal reaction

Psychogenic causes

Hyperventilation

Febrile seizures

Adjustment disorder

One each: Sick sinus syndrome, anxiety, trauma, carotid sinus hypersensitivity, diabetes mellitus, hysterical conversion, migraine, de Morsier syndrome, behavior disorder, myocardial disease, atrioventricular nodal reentry tachycardia, and muscular dystrophy.

REFERENCES AND ADDITIONAL READINGS

Up to 30% of healthy teenagers experience some type of syncopal episode during their adolescence. Many terms are used by patients to describe their complaints. Presyncopal symptoms may include lightheadedness, floating feelings, faintness, and spinning sensations. Syncope may also be characterized by a sudden loss of consciousness and may trigger a seizure-like episode. It is important to carefully differentiate complaints of syncopal and near-syncopal episodes, vertigo, and nonspecific dizziness. This differentiation is made primarily by history provided by the patient and observers. Each has separate implications for evaluation and therapy.

SYNCOPE

Syncope implies a brief loss of consciousness, usually lasting several seconds to a minute or so, with loss of postural tone, followed by spontaneous recovery without resuscitation. Although most episodes are neurocardiogenic (vasovagal), any condition that decreases cerebral perfusion, cardiac or noncardiac, as well as metabolic disturbances and psychiatric conditions, may cause syncope. Conversely complicating the evaluation in some instances is the phenomena of syncope "epidemics," particularly in schools or other closed populations.

Up to 30% of healthy teenagers experience some type of syncopal episode during their adolescence. Many terms are used by patients to describe their complaints. Presyncopal symptoms may include lightheadedness, floating feelings, faintness, and spinning sensations. Syncope may also be characterized by a sudden loss of consciousness and may trigger a seizure-like episode. It is important to carefully differentiate complaints of syncopal and near-syncopal episodes, vertigo, and nonspecific dizziness. This differentiation is made primarily by history provided by the patient and observers. Each has separate implications for evaluation and therapy.
Epigastric pain usually related to aerophagia; dry mouth; belching; bloating; and flatulence.

Spinal cord injury, transverse myelitis, spinal cord tumor, or syringomyelia may cause autonomic dysfunction. Orthostatic hypotension (and positional hypotension, idiopathic hypovolaemia, mitral valve prolapse, vasoregulatory asthenia, and orthostatic anemia. Orthostatic intolerance may be defined as symptoms of inadequate cerebral perfusion when an individual assumes an upright posture, although blood pressure falls <20/10 mm Hg. However, usually a tachycardia, with an increase of >30 beats per minute (bpm), accompanies the upright position. Because of the lack of consistent criteria for this condition, studies are difficult to compare.

a. Epidemiology: Individuals usually range in age from 14 to 45 years. The condition is about five to six times more common in females.

   - Long-standing (>6 months) and disabling orthostatic symptoms
   - Orthostatic tachycardia (>30-bpm increase in heart rate on standing)
   - Absence of an underlying cause (chronic disease, weight loss, bed rest, and medications)
   - Upright norepinephrine level >6 ng/mL

These criteria are mainly for research purposes and not for clinical diagnosis.

c. Treatment: No single therapy has been shown to be successful. Therapies have included the following:
   - Salt and water intake to increase plasma volume, b-blockers to blunt orthostatic tachycardia, phenylpropanolamine or midolmine to blunt venous pooling and increase arterial tone. b-Blockers are probably the most common medication used. A nonpharmacological approach would be to try fitted stockings, although this is unlikely to be well used by adolescents.

4. Orthostatic hypotension: Orthostatic hypotension is uncommon in adolescents. It is considered to be a drop in systolic blood pressure of more than 20 mm Hg and a drop in diastolic pressure of more than 10 mm Hg or an increase in heart rate of more than 20 bpm on attaining an upright position. Reviews of this problem are found in Engstrom and Aminoff (1997), Shannon and Robertson (1997), and Mathias and Kimber (1999). Causes include the following:

a. Inadequate homeostatic mechanisms: Prolonged bed rest, exhaustion after intense exercise, pregnancy, anorexia nervosa, heat exposure, fever, and marijuana use.

b. Reduced effective blood volume: Hemorrhage, dehydration, burns, diabetes insipidus, hemodialysis, adrenal insufficiency, and varicose veins.

4. Medication and street drugs: Antihypertensives, phenothiazines, antidepressants, narcotics, sedatives, calcium channel blockers, and alcohol.

4. Autonomic neuropathies: Pure autonomic neuropathies may be autoimmune or familial (familial dysautonomia). Mixed motor and sensory neuropathies may include autonomic neuropathy and may be genetic or acquired due to autoimmune phenomena (e.g., Guillain-Barré syndrome and chronic immune demyelinating polyneuropathy), diabetes, nutritional or uremic or metabolic causes, heavy metal poisoning, porphyria, pernicious anemia, vincristine toxicity, or chronic hypochromic anemia (deficiency of iron and vitamin B12). The world seems to revolve around the patient or the patient senses that he or she is spinning. In contrast, dizziness is

VERTIGO

Vertigo is a sensation of rotary movement. The world seems to revolve around the patient or the patient senses that he or she is spinning. In contrast, dizziness is

Cardiac Causes

Cardiac causes are uncommon, although not common in the adolescent, occurs with enough frequency that this condition must be considered. Cardiac causes of syncope should be considered in the adolescent with a history of syncope of sudden onset, syncope during vigorous exercise, or syncope occurring in a recumbent position. Several causes can explain cardiac syncope:

1. Mitral valve prolapse: This condition (discussed in Chapter 15) can lead to symptoms of dizziness and syncope. Underlying mechanisms include arrhythmias, a hyperadrenergic state, and orthostatic hypotension.

2. Cardiac arrhythmias and conduction disturbances: Heart block, sinus node dysfunction, paroxysmal atrial tachycardia (PAT), and drug-induced arrhythmias.

a. PAT usually causes weakness or faintness, but not syncope. The onset and end are very abrupt.

b. Cardiac arrhythmias are due to primary cardiac disease or may accompany systemic conditions such as muscular dystrophies, myotonic dystrophy, Friedreich ataxia, or mitochondrial cytopathies, particularly Kearn-Sayre syndrome.

c. Syndrome of prolonged QT interval is familial and predisposes to various arrhythmias, including the potential for sudden death.

3. Left ventricular dysfunction: Cardiomyopathy

4. Obstructive cardiovascular disease

a. Left ventricular outflow obstruction: Aortic stenosis and idiopathic hypertrophic subaortic stenosis (IHSS)

b. Pulmonary outflow obstruction: Pulmonary hypertension, pulmonary embolism, and severe pulmonary stenosis due to congenital heart anomalies

a. Left ventricular inflow obstruction: Mitral stenosis and left atrial myxoma

5. Pericardial tamponade
Peripheral: Most peripheral vertigo is accompanied by tinnitus and/or hearing loss. Vestibular neuritis (acute labyrinthitis): Usually a result of an acute viral or bacterial infection or local trauma. This usually resolves over several days. Vertigo is generally intense, position sensitive, and accompanied by nausea and vomiting.

Central lesions of the brainstem or cerebellar tracts involving vestibular input or vestibuloocular pathways may cause vertigo. Central lesions causing true vertigo are often accompanied by ataxia or other motor signs due to involvement of adjacent structures. Cerebellar or brainstem lesions may be caused by the following:

- Migraine: Basilar migraine may include symptoms of vertigo, although nonspecific dizziness is more common. The history may also be helpful in differentiating peripheral from central vertigo.
- Seizures: Occasionally, vertigo may be the primary or initial symptom of a complex partial seizure (see Chapter 22). Motion sickness
- Vasculitis (lupus, isolated central nervous system [CNS] angiitis).
- Head injury due to head trauma.

2. Central lesions of the brainstem or cerebellar tracts involving vestibular input or vestibuloocular pathways may cause vertigo. Central lesions causing true vertigo are often accompanied by ataxia or other motor signs due to involvement of adjacent structures. Cerebellar or brainstem lesions may be caused by the following:

- Tumors, including of the brainstem and cerebellum.
- Demyelinating diseases (e.g., multiple sclerosis).
- Vascular lesions (i.e., isolated central nervous system [CNS] angiitis).
- Cerebral infarctions (stroke).
- Infections of the nervous system (encephalitis) or postinfectious inflammatory demyelination.
- Migraine: Basilar migraine may include symptoms of vertigo, although nonspecific dizziness is more common.
- Brain injury due to head trauma.

3. Seizures: Occasionally, vertigo may be the primary or initial symptom of a complex partial seizure (see Chapter 22).

DIAGNOSIS

The history is the most crucial part of the evaluation in any of these conditions, because it allows differentiation of syncope from vertigo and seizures. The history is also helpful in identifying the specific etiology of the problem within each of these categories. In most cases, diagnosis is established by history (and negative physical and neurological examination findings). If the diagnosis is not suggested by the history and physical examination, it is unusual to find a cause for syncope as a result of conducting a multitude of tests. Batteries of tests (computed tomography scan, electroencephalogram [EEG], electrocardiogram [ECG], Holter monitor, and blood chemistries) ordered nonselectively rarely determine cause. Tilt-table testing may be useful to demonstrate that syncope is vasovagal and to avoid parental demands for other unnecessary testing.

History

1. Descriptions of the episode and any previous attacks help define the nature of the attack. If the teen cannot describe the attack, it is helpful to get a description from another witness. Description of color changes (initial pallor vs. initial cyanosis or flushing), sweating, and prodromal sensations is critical and may help distinguish syncope from seizure.

2. Circumstances preceding the attack such as a stressful situation or environmental circumstances that might predispose to a common faint or hyperventilation.

3. Precipitating factors: Stress, recent infection (labyrinthitis), fasting (hypoglycemia), exercise, position, and environmental factors such as heat, crowding, and stuffy room. Coincident symptoms in others, particularly peers, may be useful in suspected group hysteria.

4. Allieving factors: Recumbency; food, fresh air, and sudden movements.

5. Suddenness of onset: A common faint is gradual, whereas cardiac syncope and seizures may be sudden in onset.

6. Position during attack: A common faint is always in the sitting or standing position, whereas cardiac syncope or seizures may occur in any position.

7. Duration of the attack and recovery time.

8. Convulsive activity during the attack, urinary incontinence, or tongue biting suggesting epilepsy, although syncope may induce a brief seizure. The order of events is extremely helpful in making this determination.

9. See Table 24.1 for distinguishing features of common faint versus seizure.

10. The history may also be helpful in differentiating peripheral from central vertigo (Table 24.2).

### Table 24.1. Common faint versus seizure

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Common faint</th>
<th>Seizure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>Usually</td>
<td>Rare</td>
</tr>
<tr>
<td>Dizziness</td>
<td>Brief</td>
<td>Frequent</td>
</tr>
<tr>
<td>Location</td>
<td>Usually</td>
<td>Any other</td>
</tr>
<tr>
<td>Color change</td>
<td>Pallor</td>
<td>Cyanosis</td>
</tr>
<tr>
<td>Consciousness</td>
<td>Clear</td>
<td>Confused</td>
</tr>
<tr>
<td>Urticaria</td>
<td>Rare</td>
<td>Common</td>
</tr>
<tr>
<td>Flushing rate</td>
<td>None</td>
<td>Intense</td>
</tr>
</tbody>
</table>

### Table 24.2. Peripheral versus central vertigo

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Peripheral vertigo</th>
<th>Central vertigo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset</td>
<td>Sudden</td>
<td>Abrupt</td>
</tr>
<tr>
<td>Incidence</td>
<td>Sudden</td>
<td>Tonic or clonic</td>
</tr>
<tr>
<td>Duration</td>
<td>Sudden</td>
<td>Tonic or clonic</td>
</tr>
<tr>
<td>Nausea</td>
<td>Rare</td>
<td>Often</td>
</tr>
<tr>
<td>Headache</td>
<td>Rare</td>
<td>Common</td>
</tr>
</tbody>
</table>

Physical Examination
1. General physical examination with special emphasis on the following:
   a. Blood pressure: Both arms (to check for subclavian steal syndrome) and changes with positional maneuvers (orthostatic hypotension)
   b. Skin and mucus membranes for evidence of anemia or dehydration
   c. Cardiac examination
   - Mitral valve prolapse: Mid-systolic click and late systolic murmur
   - IHSS: Bifidalous carotid pulse with brisk upstroke, double apical pulse, precordial thrill, paradoxical split $S_2$, and loud $S_4$
   - Increased intensity of systolic murmur during the strain phase of the Valsalva maneuver
   - Aortic stenosis: Basal systolic ejection murmur
   - Pulmonic stenosis: Loud basal systolic murmur heard best to the left of the sternum
   - Left atrial myxoma: Rare, suspected in the presence of mitral diastolic murmurs or early diastolic sounds
   d. Evidence of cranial nerve deficits, particularly III, IV, VI, VII, and VIII; funduscopic examination

2. Neurological examination, with emphasis on the following:
   a. Evidence of cranial nerve deficits, particularly III, IV, VI, VII, and VIII; funduscopic examination
   b. Focal motor deficits
   c. Tendon reflexes: Loss, asymmetry, and hyperreflexia
   d. Cerebellar function: Truncal or appendicular ataxia
   e. Nystagmus with straight gaze: Horizontal suggests peripheral etiology, whereas a vertical and diagonal nystagmus is more suggestive of central etiology
   f. Sensory abnormalities: Peripheral sensory loss suggesting neuropathy
   g. Skin color, temperature, response to “scratch” to check for evidence of autonomic neuropathy
   h. Epileptic vertigo is rare but generally responds to anticonvulsant drugs (see Chapter 23).
   i. Syncope, dizziness, and vertigo associated with migraine should be treated as migraine (see Chapter 23).
   j. Metabolic: If a metabolic cause is suspected, serum sodium, potassium, magnesium, and creatinine tests should be ordered. More specialized testing, such as for adrenal insufficiency, may be indicated in rare situations.

3. Special examination procedures
   a. Hyperventilation: Have the adolescent hyperventilate for 2–3 minutes. Ask the adolescent to describe the sensations to determine whether they are similar to the presenting symptomatology. This should not be performed if the teen has sickle cell anemia, epilepsy, or cardiac or renal disease.
   b. Vertigo: If vertigo is a symptom, then also have the adolescent perform the following
      - Quick head turn
      - The Valsalva maneuver
      - Sudden turn while walking
      - Nylen–Bárány test: Have the adolescent sit at the edge of a table. Holding on to the adolescent’s head, have the adolescent abruptly lie back as you place his or her head 45 degrees below the table and at a 45-degree angle to one side. Repeat the test with his head at a 45-degree angle to the opposite side. Delayed by a sustained nystagmus is a “positive” test result, suggesting benign positional vertigo.
   c. Laboratory procedures: The history and physical examination suffice to make the diagnosis in most causes of dizziness, vertigo, and syncope. However, certain tests may be beneficial in other circumstances.
      a. Tilt-table testing: Tilt-table testing is helpful to document that syncope and dizziness are vasovagal (neurocardiogenic) if history alone is not adequate. Although tilt-table testing is somewhat time consuming and costly, it may avoid using multiple other tests nonsystematically. In tilt-table testing, the patient’s pulse, blood pressure, and symptoms are monitored first in a supine position, then in a head-up 65-degree tilt for 15 minutes. If tilting does not reproduce the symptoms, graded infusions of isoproterenol are given, first in supine, then in head-up tilt position. Positive test results are defined as reproduction of syncope or presyncope symptoms and either a vasopressor response (mean arterial blood pressure drop of 25 mm Hg or more), a cardiacinhibitor response (heart rate decrease of 45 bpm or more), or both. However, some patients clearly become symptomatic with a drop in diastolic cerebral perfusion velocity without obvious hemodynamic changes. Rechallenge after administration of metoprolol to determine whether b-blockers will inhibit the response may be helpful in assessing whether treatment will prevent syncope.
      b. Cardiac syncope: If cardiac syncope is suspected, then an ECG is necessary. Depending on the underlying mechanism and the disease suspected, an echocardiogram, Holter monitor, and treadmill test may be useful. In some instances, the conduction disturbances are not delineated without intracardiac ECG with and without atrial pacing.
      c. Seizures: If a seizure disorder is suspected, an EEG may be useful. If complex partial seizures are suspected, arrange to have the EEG done after overnight sleep deprivation, with recording of natural sleep, to increase yield.
      d. Hypoglycemia: Hypoglycemia is commonly “diagnosed” by patients and family members without evidence. If hypoglycemia is suspected, temporary provision of a home blood sugar monitoring system for use while the patient is symptomatic may be substantially more useful than several blood sugars drawn when the patient is asymptomatic or prolonged oral glucose tolerance testing. If blood sugar level is found to be low on home testing, further evaluation is necessary.
      e. Referral to an endocrinologist should be considered if symptomatic hypoglycemia is documented and not due to an obvious cause such as skipping meals.
      f. Metabolic: If a metabolic cause is suspected, serum sodium, potassium, magnesium, and creatinine tests should be ordered. More specialized testing, such as for adrenal insufficiency, may be indicated in rare situations.

THERAPY

Therapy is dependent on the specific condition diagnosed. For the vasodepressor syndrome (simple syncope), therapy is reassurance and ensuring that the patient assumes a recumbent or head-down position when symptoms start. If the patient is prone to fainting with prolonged standing, contracting the leg muscles also helps in increasing venous return and cardiac output. If episodes are very frequent and do not respond to simple measures, b-blockers may inhibit the cardiodepressor response in some individuals.

Treatment of hyperventilation includes reassurance, education about the physiology of hyperventilation, and teaching of a strategy to deal with hyperventilation and precipitating stressors. This can include having the patient breathe into a paper bag or teaching diaphragmatic breathing. The teenager should be instructed to place one hand on the abdomen and the other on the chest. The adolescent should then practice breathing so that the lower hand moves while the upper hand is held still.

WEB SITES

For Teenagers and Parents
http://cpmcnet.columbia.edu/dep/syncope/, A comprehensive clinical center for patients who have fainted, who are recurrently lightheaded, or who have related cardiovascular disease. Much information on syncpe.

For Health Professionals
Sleep is one of our basic needs. It helps us think, keeps us alert, and makes us feel better. Lack of sleep makes us sleepy and irritable, decreases short-term memory, and can result in mistakes at work and school as well as sleep-related accidents. Sleep disturbances are common in adolescents, as either a presenting symptom or a positive item on a review of systems (if asked). Sleep disorders include insomnias, hypersomnias (narcolepsy and other causes of excessive daytime sleepiness), parasomnias (nightmares, night terrors, sleepwalking, and nocturnal enuresis), and sleep-disordered breathing (SDB). Sleep disturbances in adolescents may represent a reaction to anxiety or depression, drug use (hallucinogens, alcohol, barbiturates, caffeine, or other stimulants), school or work schedules that call for too little or poor-quality sleep, or a specific sleep disorder (narcolepsy and night terrors). Only 15% of adolescents sleep more than 8.5 hours per night.

SLEEP PHYSIOLOGY

Sleep is divided into rapid eye movement (REM) sleep and nonrapid eye movement (NREM) sleep. Studies of sleep physiology are carried out using polysomnography, which usually includes electroencephalogram (EEG), electrooculogram, electromyogram, and measures of respiratory function such as air flow, oxygen saturation, and end-tidal P\textsubscript{CO\textsubscript{2}} levels.

Rapid Eye Movement Sleep

REM sleep, which occupies 15% to 30% of sleep time, is characterized by a high autonomic arousal state including increased cardiovascular and respiratory activity, very low voluntary musculature tone, and rapid synchronous nonpatterned eye movements. The EEG pattern shows a low-voltage variable frequency resembling the awake state. Most dreams occur during REM sleep.

Nonrapid Eye Movement Sleep

NREM sleep occupies 70% to 85% of sleep time and is divided into four stages:

1. Stage 1: Very light sleep, characterized on EEG by alpha waves similar to the quiet awake state.
2. Stage 2: Medium-deep sleep, characterized on EEG by sleep spindles of 12–16 counts/sec (cps).
3. Stages 3 and 4: Progressively deeper sleep, characterized on EEG by a general slowing of frequency and an increase in amplitude. Muscular and cardiovascular activity are decreased and little dreaming occurs.

SLEEP PATTERN

Normal sleep usually consists of a brief period of stage 1 and stage 2, followed by a lengthier interval of stages 3 and 4. After about 70 to 100 minutes of NREM sleep, a 10- to 25-minute REM period occurs. This cycle is repeated four to six times about every 90 minutes throughout the night. The REM periods usually increase by 5 to 30 minutes each cycle.

Adolescents probably require a minimum of 8.5 to 9.5 hours of sleep per night to awake refreshed and rested. However, the amount of sleep they actually get is usually much less than what they need. On average, on school nights, 10- to 11-year-olds sleep about 9.5 hours, 12- to 13-year-olds about 9 hours, 14- to 15-year-olds about 7.75 hours, 16- to 17-year-olds about 7.5 hours, and 18-year-old college freshmen about 7 hours. The adolescent often tries to make up for the sleep deficit accumulated during the week by sleeping much longer on weekends.

SLEEP HISTORY

Any adolescent with a sleep disturbance should be questioned about the following:

1. Type of sleep disturbances
2. Frequency and duration of disturbances
3. Prior sleep problems
4. Daytime symptoms
5. Family history of sleep disorders
6. Age at onset
7. Bedtime habits: Amount of sleep, what time the adolescent goes to sleep, what time he or she awakens, and what is done before sleep
8. Treatment previously tried
9. Psychosocial history
10. Medications and drug history, including over-the-counter medications, alcohol, coffee, any herbal products, dietary supplements, weight-loss products, performance-enhancing substances, or other stimulants

Having an adolescent keep a 1- to 2-week sleep diary, listing bedtimes, nighttime symptoms, time on awakening, daytime fatigue or sleepiness, and daytime naps, can be a very helpful tool in evaluating a sleep disturbance (Fig. 25.1).
SPECIFIC SLEEP DISORDERS

To treat a sleep problem, one must define the specific disorder. Disorders include the following:

1. Insomnias: Insomnias are frequent sleep disorders in adolescents. They involve either a problem falling asleep, staying asleep, or awakening too early.
   a. Sleep phase delay syndrome: Inability to fall asleep at an appropriate time. This is accompanied by extreme difficulty in arising in the morning. If allowed to fall asleep naturally, the adolescent will fall asleep easily, albeit very late, and will awaken refreshed after 9–10 hours of sleep. If awakened, the adolescent will get up and attend school or work but may, once there, have difficulty staying awake. Sleep phase delay syndromes can be associated with nighttime insomnia and daytime sleepiness.
   b. Motivated sleep delay: Appears similar to sleep phase delay syndrome, but in this case, the adolescent has a conscious desire to stay up late at night and sleep late into the afternoon even if it means being late for school. However, if motivated by something the teen really wants to do, s/he can awake early by him/herself. This is probably a form of school refusal syndrome.

   Insomnia frequently occurs secondary to situational stress, anxiety, or poor sleeping habits. A history of stress and irregular activity is helpful in the diagnosis. Other less common causes of insomnia include any physical illness associated with pain or discomfort and substance abuse or withdrawal (particularly stimulants, alcohol, or sedatives). Other medications may also cause insomnia including SSRI antidepressants, stimulants, prednisone, and two of the newer anticonvulsants, felbamate and lamotrigine.

2. Hypersomnias (excessive daytime sleepiness): The rigorous schedule required of adolescents by school, employment, and extracurricular activities often results in adolescents’ receiving less than the 9–10 hours of sleep they require. This chronic sleep deprivation may cause complaints of fatigue or difficulty staying awake during school or work. It may adversely affect school or work performance and result in stimulant use to stay awake, moodiness, and even automobile accidents related to falling asleep at the wheel. Drowsiness or fatigue is linked to more than 100,000 traffic accidents each year. Insufficient sleep is by far the most common cause of hypersomnia in adolescents. Specific sleep disorders are listed here.

3. Narcolepsy
   a. Onset commonly occurs between the ages of 10 and 25 years.
   b. Characterized by:
      - Sleep attacks: Intuitive and debilitating periods of sleep during the day, which may last a few seconds to 30 minutes, are often precipitated by sedentary, monotonous activity, and are more frequent after meals and later in the day. No amount of sleep can restore the individual to full alertness.
      - Cataplexy: Brief (seconds to 2 minutes), sudden loss of muscle tone while conscious, often in response to emotional or sudden stimulation
      - Sleep paralysis: Temporary loss of muscle tone occurring at the onset of sleep or just before awakening
      - Hypnagogic and hypnopompic hallucinations: False visual or auditory perceptions that occur just before sleep (hypnagogic) or on awakening (hypnopompic)
   c. Frequency of components
      - Sleep attacks: 100%
      - Sleep attacks and cataplexy: 70%
      - Sleep paralysis: 50%
      - Hallucinations: 25%
      - All four: 10%
   d. Evidence of genetic transmission: The exact genetic transmission of narcolepsy is unclear. However, it is strongly associated with human lymphocyte antigen haplotypes DR15,DQ6 (old nomenclature DR2,DQW).
   e. Narcolepsy is diagnosed using both overnight polysomnography and daytime multiple sleep latency test (MSLT). The overnight polysomnography will exclude other sleep disorders, such as sleep apnea. The MSLT is the most specific test for narcolepsy. It will show a shortened time to sleep onset (sleep latency) and early onset of REM sleep.

4. Parasomnias: Undesirable physical events that occur during sleep

   Sleep starts: Jerking motions that occur during the transition from wakefulness to sleep. These are normal events in 60%–80% of people.

   Partial arousals: Somnambulism (sleepwalking) and night terrors (sleep terrors, pavor nocturnus) are both disorders of impaired arousal.

   a. Both conditions occur early at night, about 60–90 minutes after sleep onset, during the rapid transition from deep NREM sleep to a lighter NREM sleep.
   b. Both usually begin in childhood or early adolescence and disappear by older adolescence.
   c. About 40% of 6- to 16-year-old children have at least one episode of sleepwalking, and 1%–3% experience night terrors.
   d. A positive family history can be found in one or both parents in more than 60% of cases.
   e. Associated psychopathology is uncommon if the onset is in childhood but is more common with an onset during adolescence or adulthood.
   f. Characteristics
      - Sleepwalking
         - Usually lasts from 1–30 minutes and emerges 15 minutes–2 hours after sleep onset.
         - The individual usually has a low level of awareness manifested by clumsiness.
         - The individual usually has a blank expression, with indifference to the environment.
         - There is usually no recall of the experience.
      - Night terrors (sleep terrors)
         - Intense anxiety, fear, and sensation of doom that start suddenly
         - Autonomic discharge (tachycardia, tachypnea, and sweating)
         - Vocalizations in the form of screams, moans, or gasps
         - Little recall
         - Usually begin early in the sleep period
   g. Psychological disturbances are suggested as a more likely cause of the night terrors or sleepwalking if the onset is after age 12 years, the condition has persisted for several years, there is a negative family history, and there is maladaptive daytime behavior.
   h. Hypertensive phenomena such as fugue states are suggested by a more alert state, more purposeful movements, and longer duration.

5. Nightmares (dream anxiety attacks)
   a. Affect about 5% of the population.
   b. Onset is usually before age 10 years; more suggestive of psychological cause if onset is after this age.
   c. Often associated with fear of attack, falling, or death.
   d. Drug withdrawal, particularly from barbiturates or alcohol, can lead to nightmares.
   e. Table 25.1 differentiates nightmares from night terrors.
TABLE 25.1. Nightmares versus night terrors

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Night terrors</th>
<th>Nightmares</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration</td>
<td>Intense</td>
<td>Limited</td>
</tr>
<tr>
<td>Autonomic activity</td>
<td>Marked increase</td>
<td>Slight increase</td>
</tr>
<tr>
<td>Ancillary</td>
<td>Difficult</td>
<td>Easy</td>
</tr>
<tr>
<td>Mobility</td>
<td>Marked</td>
<td>Limited</td>
</tr>
<tr>
<td>Recall</td>
<td>Minimal</td>
<td>Yield</td>
</tr>
<tr>
<td>Sleep stage</td>
<td>REM sleep</td>
<td>REM sleep</td>
</tr>
</tbody>
</table>

f. Sleep paralysis, hypnagogic and hypnopompic hallucinations: Although frequently seen in narcolepsy, they can occur in nonnarcoleptics.

6. Nocturnal enuresis (see Chapter 27)
   a. Approximately 1%–5% of adolescents are enuretic.
   b. Enuresis is independent of stage of sleep.
   c. Enuresis may be primary or secondary.
      - Primary: Without a several-month period of dryness since infancy. Primary enuresis may involve a maturational delay and is often associated with a positive family history. There are two prominent theories of its cause:
        - That it is a maturational delay in neuromuscular control of the bladder
        - That it is related to a blunting of the diurnal antidiuretic hormone secretion, resulting in an increased nocturnal urine production that exceeds the functional bladder capacity
      - Secondary: Relapse of enuresis after at least a several-month dry period. Secondary enuresis should prompt further evaluation of an organic cause such as diabetes or infection or a psychological cause such as an acute stressor (death, divorce, new baby in the family, and natural disaster).

7. Sleep-disordered breathing (SDB): Presence of episodes of complete or partial obstruction of the upper airway during sleep associated with the following:
   a. Loud snoring
   b. Daytime sleepiness
   c. Sleep fragmentation
   d. Intermittent hypoxemia, hypercardia
   e. Nocturnal hypertension

Risk factors include obesity, African-American heritage, and other respiratory factors such as chronic cough, occasional and persistent wheezing, sinus problems, and asthma.

Sleep studies looking at SDB evaluate for apnea or hypopneas lasting longer than 10 seconds with an associated greater than or equal to a 2.5% decrease in oxygen saturation. An apnea-hypopnea index (AHI) divides the number of respiratory events by the estimated sleep time. Different thresholds are used with little consensus. An AHI of 10 is a reasonable cutoff for adolescents.

TREATMENT

Insomnia
1. Counseling regarding any existing situational stresses.
2. Regularize bedtime and awakening hours. Try to have the adolescent arise at a similar hour each day. Avoid excessive sleep on weekends. Avoid trying to force sleep when the adolescent is not tired.
3. Teach relaxation techniques.
4. Daily exercise, but not close to bedtime.
5. Curtail alcohol, coffee, tea, cola, or other stimulants.
6. Bedroom environment should be for sleep only (i.e., no television in the bedroom).
7. Keep bedroom dark and as quiet as possible. Morning exposure to bright light also helps.
8. Avoid daytime naps.
9. Severe cases due to sleep phase delays may need chronotherapy (an adjustment of sleep-waking schedule performed by an expert in sleep disorders). This therapy consists of advancing bedtime by 15-minute intervals or by delaying the bedtime by 2–4-hour adjustments and forcing the adolescent to sleep around the clock until reaching an appropriate bedtime with approximately 9 hours of sleep. The motivated sleep delay syndrome is particularly difficult to treat and may need the involvement of a psychologist or psychiatrist.
10. See Seven Sleep Smart Tips for Teens from the National Sleep Foundation (Fig. 25.2).

FIG. 25.2. Seven sleep smart tips for teens (http://www.sleepfoundation.org/pressarchives/seven.html). (From National Sleep Foundation, with permission.)

Somnambulism
1. Protect the patient by removing harmful objects and locking doors.
2. Reassure the patient, if onset is during childhood, that the problem should resolve.

Night Terrors (Sleep Terrors)
1. Reassurance that problem should resolve by itself.
2. Psychological evaluation and treatment are indicated in cases in which psychopathology is present.
3. Benzodiazepines, tricyclic antidepressants, relaxation techniques, or mental imagery may be used to suppress night terrors.
4. Avoid sleep deprivation. Try to regularize sleep-and-wake schedule.

Nightmares (Sleep Anxiety Attacks)
1. Evaluation and treatment of any underlying psychological stresses or fears.
2. Evaluation and treatment of any associated alcohol or other drug abuse problems.

Nocturnal Enuresis

Treatment of nonorganic enuresis can include the following (see Chapter 27, for more detailed information):

1. Drink less fluid in the 2 hours before bedtime.
2. Urinate before going to bed.
3. The adolescent should be responsible for laundering and changing linens. Consider placing a dry towel under the patient to decrease the need for linen changes.
4. Elimination of guilt or blame. Positive rewards and praise for dry nights.
5. Exercises to improve control of urinary stream and to increase bladder capacity.
6. Behavior techniques, particularly the new smaller alarm systems, are the most effective methods for treating enuresis and have the lowest relapse rate.
7. Medications are not as effective in the long term as behavioral techniques, particularly the alarm. However, they have more immediate effects and can be used in conjunction with behavioral techniques. Imipramine (Tofranil) is effective, but relapse is common after stopping the medication. Desmopressin (DDAVP) is also quite effective and has fewer potential side effects than imipramine. It can now be given either as a nasal spray or as an oral tablet.

Narcolepsy

1. Drugs: Methylphenidate (Ritalin) is the drug of choice for sleep attacks.
   a. Administer at least 1 hour after meals to allow for absorption.
   b. Titrate to lowest effective dose.
   c. Avoid late afternoon or evening doses.
2. Imipramine is the drug of choice for cataplexy and sleep paralysis.
   a. Requires only 10–75 mg/day.
   b. Avoid evening dose.
3. Avoid dangerous activities such as driving an automobile or scuba diving.
4. Naps: Short scheduled naps during the day may prevent sleep attacks.

Other Hypersonias

1. Treatment of any underlying disorder.
2. Treatment of sleep phase delay syndrome by chronotherapy if severe (>3–4 hours out of phase).
3. Increase the amount of nighttime sleep with the understanding that teens need 9–10 hours of sleep but often get much less, thus are chronically sleep deprived, resulting in excessive daytime sleepiness.

Sleep-disordered Breathing

The treatment of SDB requires a team effort. Weight loss, tonsillectomy and adenoidecctomy, constant positive airway pressure, and bilevel pressure ventiliation are all modalities used to treat SDB. Consultation is suggested with pulmonology, a sleep laboratory or center, and head and neck surgery. A cardiac echocardiogram, looking for pulmonary artery hypertension or right ventricular hypertrophy, and a lateral x-ray of the soft tissues of the neck are useful studies.

SLEEP DISORDER CLINICS

For severe sleep disorders or diagnostic dilemmas, referral to a sleep disorder clinic can help. Appendix II to this book contains a partial listing of institutions specializing in the treatment of sleep disorders. The National Sleep Foundation keeps an updated list by state of accredited sleep disorder centers (http://www.sleepfoundation.org/). In addition, U.S. clinics accredited by the American Sleep Disorders Association, listed by state, are available at http://www.asda.org/, and Canadian clinics, listed by province, are available at www.css.to/sleep/centers.htm.

RESOURCES

Organizations
American Academy of Sleep Medicine
6301 Bandel Road, Suite 101
Rochester, MN 55901; http://www.asda.org/

National Center on Sleep Disorders Research
National Heart, Lung, and Blood Institute
National Institutes of Health (NIH)
9000 Rockville Pike, Bldg 31
Bethesda, MD 20892; www.nhlbi.nih.gov/about/ncsdr/index/htm

National Sleep Foundation
1522 K Street, NW, Suite 500
Washington, DC 20005; http://www.sleepfoundation.org/

WEB SITES

For Teenagers and Parents
http://www.sleephomepages.org/ Sleep Home Pages.
http://www.nhlbi.nih.gov/about/ncsdr/ NIH site about sleep disorders.
http://www.sleepnet.com/disorder.htm Information about various sleep disorders.

For Health Professionals

REFERENCES AND ADDITIONAL READINGS


Genitourinary tract infections are common in adolescents. Those types most often diagnosed include cystitis, pyelonephritis, urethritis, and asymptomatic bacteriuria.

**CYSTITIS**

**Epidemiology**

1. Over the course of a lifetime, cystitis is likely to occur three to five times more commonly in women than men. For adolescents, this difference is at least 20-fold.

2. Ten percent to 20% of girls have at least one episode of acute cystitis during adolescence or young adulthood. A recent study by Hooton et al. (1996) defined the annual incidence of a lower urinary tract infection (UTI) in female patients as 0.7 infections/person year in a cohort of sexually active female university students. In addition to the risk factors listed here, Foxman (1990) found that 30% of young women had at least one recurrence within 6 months of the first infection, giving evidence that the presence of an infection raises the likelihood of second or third infections.

3. Risk factors for infection
   a. Females: Females are at greater risk than males because of a short urethra, which has close proximity to vaginal and rectal microorganisms. Risk factors for a UTI presumably include the following, although many of these variables have not been substantiated in the literature:
      - Poor perineal hygiene
      - Infrequent cleansing
      - Incorrect “wiping technique”
      - Tight panty hose
      - Coitus and coital behaviors
      - Diaphragm use (relative risk = 5.68 in subjects using a diaphragm five times a week)
      - Coital frequency (relative risk = 4.81 in subjects reporting five coital episodes a week)
      - Use of spermicide-coated condoms (odds ratio = 5.65 for use more than twice weekly) (Fihn et al., 1996)
      - Not voiding soon after intercourse (Strom et al., 1987)
      - Pregnancy
      - Nonsecretor of AB, blood group antigens
      - Insertion of a foreign body into urethra (catheter)
      - Anatomical abnormalities (e.g., urethral stenosis, neurogenic bladder, and nephrolithiasis)
   b. Males
      - Since UTIs in general and cystitis in particular are so much less frequent in males, risk factors and pathophysiology are less understood. In non–sexually active male adolescents, bladder and renal infections may be a result of structural or functional abnormalities of the urinary tract. Additional factors in any male adolescent may include the following:
        - Blood group B or AB nonsecretor
        - P<sub>1</sub> blood group phenotype (epithelial cell receptors facilitate bacterial attachment)
        - Insertive anal intercourse
        - Sexual partner with vaginal colonization by uropathogens
        - Lack of circumcision (possibly by greater colonization of glans)

**Microbiology**

**Females** The most common organism in female adolescents with acute cystitis is *Escherichia coli* (75% to 90%). *Staphylococcus saprophyticus* is probably the second most common cause of UTI in young women (>10%). Other gram-negative organisms cause most of the remainder of the infections. In chronic or recurrent infections, *Klebsiella* species, enterococci, *Pseudomonas aeruginosa*, *Enterobacter* and *Proteus* species, *Staphylococcus aureus*, group B streptococcus, *Streptococcus faecalis*, and *Serratia marcescens* may play a more common role than in acute infections.

**Males** About three fourths of UTIs in male adolescents and young adults are due to gram-negative bacilli, but *E. coli* infections are not nearly as common as in girls. Gram-positive organisms, particularly enterococci and coagulase-negative *staphylococci*, account for about one fifth of infections. *Trichomonas vaginalis* is a rare cause of pyuria in boys, usually involving an infection of the urethra or prostate. *Gardnerella vaginalis* can also occasionally cause infections in boys.

**Symptoms**

**Females**

1. Dysuria
2. Frequency, hesitancy, and urgency
3. Suprapubic pain
4. Pyuria
5. Hematuria
Symptoms caused by infections in the genitourinary tract are difficult to localize. For example, dysuria and dyspareunia in the female patient can be related to infections in either the bladder, the urethra, or the vulva and vaginal tract. However, the location of the dysuria is occasionally helpful. The dysuria associated with cystitis or urethritis is often described as internal pain and is usually worse when a patient initiates micturition. External pain or “terminal pain” (at the end of micturition) is more often associated with other conditions such as a vulvar inflammation, upper genital tract infection, or a herpes simplex infection.

**Males** Aside from the preceding symptoms, male patients may also have symptoms associated with genitourinary infections in the prostate (perineal or rectal pain), epididymitis (tender epididymis), or testicles (testicular pain and swelling).

**Differential Diagnosis of Acute Dysuria**

The most common complaint arousing suspicion of cystitis is dysuria. Dysuria may be a symptom of infection elsewhere in the urinary tract or infection of the genital tract, particularly in adolescents (Demetriou et al., 1982). The following are considerations in the differential diagnosis of cystitis and dysuria:

**Females**

Table 26.1 lists the pathogens, incidence of pyuria and hematuria, urine culture findings, and signs and symptoms of acute dysuria in women.

<table>
<thead>
<tr>
<th>Table 26.1, Differential diagnosis of acute dysuria in women</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1. Acute vaginitis and possible associated Skene glands infection secondary to</strong></td>
</tr>
<tr>
<td><strong>2. Vulvovaginitis due to Candida or Trichomonas.</strong></td>
</tr>
<tr>
<td><strong>3. Local dermatitis. Includes irritations from chemicals and other agents such as soap, contraceptive agents and foams, and feminine hygiene products.</strong></td>
</tr>
<tr>
<td><strong>4. Subclinical pyelonephritis: Some females with only dysuria have an upper UTI. These infections may be more difficult to eradicate. There are no reliable and simple methods to distinguish them from lower UTIs.</strong></td>
</tr>
<tr>
<td><strong>5. Acute urethral syndrome: The presence of frequency and dysuria in women with urine cultures showing between 10^2 and 10^5 colony-forming units (CFU) per milliliter has been termed the acute urethral syndrome or the dysuria-pyuria syndrome. However, studies in the past decade have shown that many women with symptomatic cystitis have fewer than 10^3 CFU/mL. Thus, this lower figure of 10^2 CFU/mL may be the appropriate microbiological criteria for determining the presence of a UTI. Kunin et al. (1993) reevaluated acute urinary symptoms and “low-count” bacteriuria (&gt;10^1 to 10^3 CFU/mL) in women. E. coli and S. saprophyticus were the only microorganisms found in symptomatic and pyuric urine. This revision of bacterial counts has ceased or eliminated the need for the category of acute urethral syndrome or dysuria-pyuria syndrome. The small group of symptomatic women with no growth on urine culture deserves evaluation for urinary or genital tract infections with C. trachomatis, Mycobacterium tuberculosis, herpes simplex virus, Candida, or T. vaginalis.</strong></td>
</tr>
</tbody>
</table>

**Males** In males, the major diseases in the differential diagnosis of cystitis and dysuria include the following:

1. **Urethritis (secondary to sexually transmitted organisms including N. gonorrhoeae, C. trachomatis, T. vaginalis, and others)**
2. **Prostatitis**
3. **Irritation from agents such as spermicidal foam**

**Diagnosis**

1. **History**
   a. In females, are there symptoms suggestive of vulvovaginitis, such as an abnormal vaginal discharge or vaginal itching? With a vaginal infection, symptoms of frequency and urgency are usually less common. In males, is there a history of sexual exposure, past urinary tract problems, or trauma?
   b. Does the patient use any medications or irritants such as douches, feminine hygiene products, strong soaps, bubble bath, or contraceptive products that could cause a local dermatitis? Is there a history of mechanical irritation including frequent masturbation?
   c. Is the teen sexually active? If so, sexually transmitted diseases (STDs), including a cervicitis or urethritis caused by C. trachomatis, N. gonorrhoeae, or T. vaginalis, become a concern.
   d. Are there signs of upper genitourinary tract disease? Fever and flank pain suggest acute pyelonephritis.
   e. Are there factors suggestive of a subclinical pyelonephritis, such as underlying urinary tract disease, diabetes mellitus, urinary infections in childhood, three or more previous UTIs, or acute pyelonephritis in the past?

2. **Physical examination**
   a. In both sexes, an examination of the abdomen and flank for tenderness should be performed. In addition, the genital area should be examined for a local dermatitis.
   b. In girls, a pelvic examination should be performed if the teen is sexually active or if there is history of a vaginal discharge.
   c. In boys, the physical examination should include inspection and palpation of the genitals to check for urethral discharge, meatal erythema, inflammation of the glans penis, penile lesions, an enlarged or tender epididymis or testis, or inguinal lymphadenopathy. A rectal examination is necessary if a diagnosis of prostatitis is under consideration.

3. **Laboratory studies**
   a. Microscopic examination of urine
      - The presence of one or more bacteria per oil immersion field of uncentrifuged urine has an 80% to 95% correlation with bacteriuria in which the bacteria count is 10^5/mL. This examination may also be performed on a Gram-stained specimen of unspun urine.
   - A count of more than ten organisms per oil immersion field on a centrifuged unstained sediment also correlates with positive culture results. Pyuria with five or more leukocytes per high-power field of urine sediment on spun urine has a poorer correlation. Sources of error with the latter include variable volumes of urine, variable time and speed of centrifugation, and inconsistent resuspension volume. However, analysis of unspun urine for leukocytes in a counting chamber does give reproducible results and is significant if the count is more than ten leukocytes per cued millimeter. Urine should be examined within 2 hours of collection. Presence of pyuria is a good indicator that antibiotic therapy will be necessary. Individuals with dysuria but with no recognized pathogen rarely have pyuria and usually do not respond to treatment. A positive finding with a leukocyte esterase dipstick has a sensitivity of about 75% to 86% in detecting pyuria associated with an infection.
   b. Urine culture
      - A bladder or renal infection usually is characterized by a urine culture with a colony count of more than 100,000 CFU/mL of an appropriate urinary pathogen. However, it is now well established that a colony count of more than 100 CFU/mL of a pure culture of an organism indicates an infection in the presence of symptoms and pyuria. A urine culture is not mandatory for the diagnosis and treatment of a female adolescent with signs and symptoms of a UTI, particularly with a first episode. If therapy fails, the infection represents a reoccurrence within the 3 months after an initial infection, or if the patient is a male, a culture is recommended. Cultures are also indicated for female patients with pyuria without bacteriuria. Independent predictors of a positive urine culture result include a history of a prior UTI, back pain, microscopic pyuria, hematuria, and bacteriuria (Wigton et al., 1985).
      - In patients who respond to therapy with the disappearance of symptoms, posttreatment cultures are of limited value. Follow-up cultures are indicated for patients with acute pyelonephritis, a complicated infection, or during pregnancy.
c. Culture alternatives: Several rapid culture kits available for office use are as follows:
- Dipslide: Best studied and most reliable kit culture technique. The test is inexpensive and yields high sensitivity and specificity rates (generally <1% false-positive and false-negative results).
- Filter-paper techniques yield false-negative rates of 3%–20% and false-positive rates of 2%–23%.
- Several other chemical tests use nitrate glucose oxidase or catalase to detect the presence of bacteriuria. These tests are neither highly sensitive nor specific.

4. Other tests

a. Females: In girls, three infections within 1 to 2 years may be an indication for a more complete evaluation of the patient's urinary tract, which may include a renal ultrasound and a voiding cystourethrogram. However, in postpubertal female young adults with uncomplicated cystitis, evaluation after recurrent episodes is unlikely to reveal significant abnormalities that would change either therapy or prognosis. Figure 26.1 is a flow diagram for the evaluation of women with internal dysuria.

b. Males: Although some authorities recommend a full investigation after the first infection, this is probably of greater importance in the young child or infant. In male adolescents, an investigation with more invasive tests is probably not indicated after the first infection, unless there is evidence in the history or physical examination of a possible renal abnormality or there is no response to therapy. This is particularly true for male adolescents who are sexually active. Krieger et al. (1993) evaluated acute UTI in healthy university men. The incidence was 5 per 10,000 men per year. Of this group of men, 92% responded to a single course of antibiotics. None of the men in this study had neurological or anatomical abnormalities, and all the radiographical findings were normal. The major risk factor was a history of sexual activity in the previous month.

Recurrent Infections in Female Adolescents

About 20% of young women will have recurrent infections. Most of these adolescents and young women do not have anatomical or functional abnormalities of the urinary tract. However, recurrent cystitis within 3 months of the original infection should result in a urine culture. Those female patients with a relapse (recurrent infection with original pathogen within 2 weeks after completion of therapy) should also have their urine cultured and in either case should have careful follow-up. Continued infections should result in an evaluation for an occult source of infection or urological abnormality.

PYELONEPHRITIS

Pyelonephritis is an infection of the renal pelvis and medulla. The clinical and laboratory manifestations usually include the following:

1. Symptoms of acute cystitis
2. Fever
3. Costovertebral tenderness
4. Elevated leukocyte count and erythrocyte sedimentation rate
5. Urinalysis revealing leukocytes and bacterial casts
6. Positive urine culture result

The range of symptoms varies from cystitis with mild flank pain to those of septicemia. Most cases of acute pyelonephritis in young women are caused by *E. coli* infection (>80%). Pyuria and gram-negative bacteria are usually present on examination of the urine. Urine culture specimens should always be obtained from these women, and blood culture specimens from those who are hospitalized. If fever and flank pain persist after 72 hours of treatment, then cultures should be repeated and ultrasonography or computed tomography should be considered to evaluate for an abscess. Indications for imaging studies include recurrent pyelonephritis, slow resolution, persistent hematuria, or childhood infection.

Treatment

1. Acute, uncomplicated infections in females (usually caused by organisms such as *E. coli*, *S. saprophyticus*, *Proteus mirabilis*, *Klebsiella pneumoniae*, and others): A growing number of urinary tract pathogens have begun to develop resistance to commonly used antibiotics, particularly *trimethoprim-sulfamethoxazole* and amoxicillin. Local resistance patterns should be consulted before prescribing any antibiotics as first-line treatment of UTIs. Assuming appropriate sensitivity of organisms:
   a. No complicating factors: Use a 3-day oral regimen of one of the following:
      - Trimethoprim-sulfamethoxazole (160/800 mg every 12 hours) or trimethoprim (100 mg every 12 hours)
      - Cefpodoxime (200 mg every 12 hours)
      - Amoxicillin (500 mg every 8 hours)
      - Nitrofurantoin (100 mg every 6 hours)
   b. In older adolescents (older than 16 years), a 3-day regimen of a quinolone would also be appropriate. Appropriate regimens include the following:
      - Norfloxacin (400 mg every 12 hours)
      - Ciprofloxacin (250 mg every 12 hours)
      - Ofloxacin (200 mg every 12 hours)
      - Lomefloxacin (400 mg daily)
      - Enoxacin (400 mg every 12 hours)
   c. Pregnancy: Use a 7-day regimen of:
      - Amoxicillin (500 mg given orally every 8 hours)
      - Nitrofurantoin (100 mg four times a day)
      - Cefpodoxime (200 mg every 12 hours)
      - Trimethoprim-sulfamethoxazole (160/800 mg every 12 hours)

Although there was great interest in the possibility of treating uncomplicated UTIs in women with a single dose of antibiotics, despite a number of studies, a 3-day course of antibiotics appears to ensure greater success than the single-dose antibiotic regimens. The exception to this may be the use of fosfomycin in a single 3-g dose for infections in women older than 18 years (minimum age approved).

2. Acute, uncomplicated pyelonephritis in female patients (*E. coli*, *P. mirabilis*, *K. pneumoniae*, *S. saprophythicus*): Avoid amoxicillin and first-generation cephalosporins because 20%–30% of organisms are resistant to these antibiotics
   a. Mild to moderate illness with no nausea or vomiting: Initial outpatient oral therapy is acceptable in adolescents with a community-acquired infection not associated with severe systemic symptoms or known complications. Oral therapy can include any of the following, with each regimen administered for 10–14 days.

• Trimethoprim-sulfamethoxazole (160/800 mg every 12 hours)
• Cefpodoxime (200 mg every 12 hours)
• Amoxicillin/clavulanate (500 mg every 8 hours)
• Quinolones that can be utilized in older adolescents and young adults:
  a. Norfloxacin (400 mg every 12 hours for 10–14 days)
  b. Ciprofloxacin (500 mg every 12 hours for 10–14 days)
  c. Ofloxacin (200–300 mg every 12 hours for 10–14 days)
• Enoxacin (400 mg every 12 hours for 10–14 days)
b. Severe pyelonephritis or other complicated UTI requiring hospitalization (e.g., patients with diabetes, sickle cell disease, or immunodeficiency): Parenterally administered antibiotics, including one of the following:
  a. Trimethoprim-sulfamethoxazole (160/800 mg every 12 hours)
  b. Ceftriaxone (1–2 g/day)
  c. Ciprofloxacin (200–400 mg every 12 hours)
  d. Gentamicin (1 mg/kg every 12 hours [with or without ampicillin])
• Chlamydia trachomatis
• Trichomonas vaginalis.

Nongonococcal Urethritis (NGU) is an infectious inflammation of the urethra characterized by dysuria and by a mucopurulent penile discharge. As its name implies, it is unassociated with infection by N. gonorrhoeae. Asymptomatic infections are quite common.

Asymptomatic Bacteriuria

The prevalence of asymptomatic bacteriuria (reproducible growth of more than 10² CFU/mL) ranges from about 1% to 7%. There is a tendency toward spontaneous cure. However, women with this condition are at increased risk of an overt UTI (8% in the week after documented bacteria in the urine [Hooton et al., 2000]), and in individuals whose infection begins in childhood, there is a suggestion that their infection can lead to renal impairment. Asymptomatic bacteriuria during pregnancy is a risk factor for the development of acute pyelonephritis, for lower fetal birth weight, and for a higher incidence of prematurity. Treatment is mainly indicated for the following individuals:

1. Those who are pregnant
2. Male patients
3. Female patients with either an underlying renal tract abnormality or an immunocompromising disease

Treatment should be with appropriate antibiotics selected on the basis of culture sensitivities.

Nongonococcal Urethritis

Nongonococcal urethritis (NGU) is an infectious inflammation of the urethra characterized by dysuria and by a mucopurulent penile discharge. As its name implies, it is unassociated with infection by N. gonorrhoeae. Asymptomatic infections are quite common.

Etiology

1. C. trachomatis: There is clear evidence that certain genotypes cause about 40%–50% of the cases of NGU.
2. Ureaplasma urealyticum: Reliable data implicate this organism as a cause of about 20%–30% of additional cases of NGU.
3. In the remainder of cases, the cause is uncertain. Other possibilities include Mycoplasma genitalium, G. vaginalis, herpes simplex virus, S. saprophyticus, E. coli, and T. vaginalis.
Incidence: Extremely common among sexually active men. In England, it is the most frequently recorded STD and this would probably be true in the United States if all jurisdictions required reporting of NGU and chlamydial infection. It is estimated that 3 to 4 million cases occur yearly in the United States.

Clinical Manifestations

1. Discharge: Usually scanty or moderate, watery discharge; some patients have no discharge, whereas others have copious, purulent discharge, which usually starts 8–14 days after contact.
2. Dysuria
3. Rarely, hematuria
4. Complications of untreated infection include epididymitis, prostatitis (rare), and Reiter syndrome (very rare).

Diagnosis

1. Clinical history
2. Gram stain of urethral discharge
   a. More than five polymorphonuclear cells per oil immersion field indicates urethritis.
   b. The lack of intracellular gram-negative diplococci suggests NGU.
3. Urine
   a. A leukocyte count of more than ten cells per high-power dry field of the urine sediment from the first 10–15 mL of a urine stream indicates urethritis.
   b. A leukocyte esterase dipstick test result is positive.
   c. The urine sediment test, although often unnecessary if a discharge is present, is helpful in determining the presence or absence of urethritis.
4. Urethral culture if Gram stain result of the discharge is negative: Culture or nonculture technique for gonorrhea and chlamydial infection

Therapy

1. Recommended regimen
   a. Doxycycline (100 mg orally twice daily for 7 days) OR
   b. Azithromycin (1 g orally in a single dose)
2. Alternative regimens
   a. Erythromycin base (500 mg given orally four times daily for 7 days) OR
   b. Erythromycin ethylsuccinate (800 mg orally four times daily for 7 days)
   c. For a patient who cannot tolerate high-dose erythromycin schedules: Use one of the following regimens:
      - Erythromycin base (250 mg given orally four times a day for 14 days)
      - Erythromycin ethylsuccinate (400 mg orally four times a day for 14 days)

Note that patients with persistent or recurrent objective signs of urethritis after adequate treatment of themselves and their partners warrant further evaluation for less common causes of urethritis. In addition, in some individuals with persistent infections, a longer (14–21 days) course of antibiotics may be effective. Finally, sexual partners must be treated.

PROSTATITIS

Etiology

Prostatitis is an inflammatory reaction confined to the prostate gland. In adolescents, prostatitis is an unusual condition. Acute prostatitis in adolescents is usually associated with infection. The organisms probably reach the prostate as a result of a urethral infection, by reflux of infected urine into the prostatic ducts or by lymphogenous or hematogenic spread. Although it is often assumed that STDs, and particularly infection with N. gonorrhoeae and C. trachomatis, cause a large percentage of the cases of acute prostatitis in adolescents and young adults, proof through adequate studies has not been achieved. Coliform bacteria, S. saprophyticus, Mycoplasma hominis, U. urealyticum, and T. vaginalis, have also been implicated as causative agents. In one study of 409 patients with prostatitis—boys age 19 years and older—the most frequent organism isolated was U. urealyticum (de la Rosette et al., 1993). The cause or causes of noninfectious prostatitis and chronic prostatitis are even more unclear.

Diagnosis

1. In acute bacterial prostatitis, symptoms include the following:
   a. Pain: Perineal, suprapubic, perineal, groin, or back pain or pain that occurs during ejaculation
   b. Bladder symptoms: Frequency, dysuria, and hesitancy
   c. Systemic symptoms: Chills, fever, and malaise
   d. Other symptoms: Hematospermia and hematuria
2. In nonacute prostatitis, the symptoms are less dramatic and may include frequency, urgency, and dysuria.
3. The only method for documenting prostatitis is the segmental culture technique.
   a. Four specimens are collected, including the following:
      - First-voided 10-mL urine
      - Midstream urine
      - Prostatic secretions during prostatic massage
      - First-voided 10 mL after prostatic massage
   b. In individuals with bacterial prostatitis, the third and fourth specimens should grow more colonies than the first two. The presence of more leukocytes in the first specimen suggests urethritis, and growth primarily in the second specimen suggests cystitis. However, because the meaning and interpretation of this test are not standardized and the test is time consuming, expensive, and uncomfortable, it should not be performed routinely in adolescents.

Treatment

In the acutely inflamed prostate gland, antibiotics have good penetration; however in boys with recurrent prostatic infections, treatment is hampered by the lack of good antibiotic penetration. The best antibiotic choices for empirical treatment of prostatic infections include the following:

Trimethoprim-sulfamethoxazole (160/800 mg every 12 hours for 7 days) or
Ofloxacin (300 mg every 12 hours for 7 days) or
Doxycycline (100 mg every 12 hours for 7 days) or
Erythromycin (500 mg every 6 hours for 7 days)

If symptoms persist, more aggressive attempts to obtain specific diagnostic samples need to be undertaken, including the method described previously.

HEMATOSPERMIA

Bloody ejaculate is an unusual condition but can occur in male adolescents. The adolescent may notice a reddish discoloration of his semen either after masturbation or on removing a condom after intercourse. This condition may cause extreme anxiety or feelings of guilt. The teen may be concerned about a malignancy or fear that his behavior has caused the condition. In adolescents, the condition is usually either idiopathic and self-limited or related to an infectious disease such as a


Zhanel GG, Harding GKM, Guay DRP. Asymptomatic bacteriuria: which patients should be treated? Arch Intern Med 1990;150:1389.
Enuresis is defined as the involuntary passage of urine, usually during sleep, occurring more than once a month. Although often considered a childhood problem, enuresis is also found in adolescents, causing major emotional problems and family stress. Current urology literature uses the following terminology regarding enuresis:

- **Primary enuresis**: enuresis without prior periods of consistent dryness
- **Secondary enuresis**: enuresis that develops in patients who have a history of 3–6 months of dryness
- **Nocturnal enuresis**: involuntary passage of urine during sleep
- **Diurnal enuresis**: involuntary or intentional urination into clothing while awake
- **Polysymptomatic nocturnal enuresis**: enuresis associated with severe urgency, severe frequency, or other signs of an unstable bladder
- **Monosymptomatic nocturnal enuresis**: bed-wetting associated with normal daytime urination

**ETIOLOGY**

Most cases of enuresis are related to nonorganic causes. The causes may be multifactorial, with maturational delay an important etiology.

**Organic Causes**

Only 2% to 3% of patients have a true organic cause. Five percent to 10% of enuresis cases are associated with urgency (polysymptomatic enuresis).

1. Neurological lesions
   a. Myelomeningocele, the most common neurological cause of enuresis
   b. Mental retardation
   c. Spinal cord injury
2. Urological abnormalities: Controversy exists over the role and prevalence of urological lesions in enuresis. The prevalence of urological abnormalities in enuretic patients ranges in different studies from 2% to 97%. Described problems include the following:
   a. Recurrent urinary tract infections (UTIs)
   b. Obstructive lesions: Urethral obstruction or posterior urethral valves
   c. Detrusor instability: Khan et al. (1993) found that the mean threshold volume at which detrusor instability was demonstrated was 200 mL in enuretic patients. The mean bladder capacity of age-matched nonenuretic patients was 325 mL.
   d. Incomplete bladder emptying: The common symptom of incomplete bladder emptying is urinary frequency. Common causes of incomplete bladder emptying are lower urinary tract obstruction, neurogenic bladder, and dysfunctional voiding. Adolescents who voluntarily withhold urination during the day and only impartially void at bedtime suffer from dysfunctional voiding. These patients are prone to develop reflux and renal damage.
3. Renal concentrating defects (e.g., sickle cell anemia)
4. Diabetes mellitus and diabetes insipidus: Chronic polyuria is associated with diabetes insipidus and diabetes mellitus. Alcohol, caffeine, and some medications can cause a transient polyuria.

**Genetic Causes**

The evidence for genetic transmission explains the common occurrence of a positive family history in enuretic patients. The prevalence of enuresis in families is as follows:

<table>
<thead>
<tr>
<th>Relatives with Enuresis</th>
<th>Prevalence of Enuresis in Offspring</th>
</tr>
</thead>
<tbody>
<tr>
<td>Both parents</td>
<td>77%</td>
</tr>
<tr>
<td>One parent</td>
<td>44%</td>
</tr>
<tr>
<td>No parents</td>
<td>15%</td>
</tr>
</tbody>
</table>

Prevalence in an identical twin of an enuretic twin is 68%. Prevalence in a fraternal twin of an enuretic twin is 36%. Arnell et al. (1997) found evidence of dominant genetic transmission in 43% of 392 enuretic families studied, as well as evidence of recessive transmission in 9% of the same 392 families. The study also revealed evidence of sex-linked or sex-influenced factors; the ratio of affected males to females was 3:1. Genetic transmission has been linked to both chromosome 12q and chromosome 13q.

**Sleep Disorder**

Enuresis may be associated with incomplete sudden arousal from a deep sleep. In these cases, there is difficulty in arousing the patient. Parents of affected teens often report that their child sleeps too soundly or deeply. Often, the adolescent fails to awaken due to the sensation of a full bladder or even when the bedding becomes wet. However, some studies have demonstrated that enuretic patients are normal sleepers and that enuresis can occur during any stage of sleep.

**Developmental Delay**

It has been postulated that a developmental delay in adequate neuromuscular maturation of the bladder, as well as an immaturity of the central nervous system inhibition of the micturition reflex, is responsible for enuresis. There are differing opinions among experts about the role of these problems in the pathophysiology of enuresis.
Small Functional Bladder Capacity

The current thinking among enuresis experts is that affected teens either produce large nighttime volumes of urine with a normal bladder capacity or produce a large nighttime volume with a small bladder capacity. Symptoms of a small bladder capacity include daytime frequency, wetness every night, occasional wetness several times per night, and the presence of the problem since birth.

Psychological Factors

Most enuretic patients are psychologically normal and psychological stressors do not cause enuresis. It is important to remember that the teen is not deliberately wetting the bed. An increased prevalence of emotional difficulties has been described in affected adolescents. However, this may often be a result of suffering from enuresis, rather than a causative factor.

Vasopressin Levels

Normally, vasopressin levels rise during the night, resulting in a smaller volume of more concentrated urine at night. Therefore, it has been postulated that some adolescents' enuresis is due to an insufficient rise in the concentration of antidiuretic hormone (ADH). However, it has been found that enuretic patients with normal vasopressin levels respond to exogenous desmopressin by reducing urine production. Eggert and Kuhn (1995) studied ADH regulation in primary nocturnal enuretic patients. They found that enuretic children required a markedly increased output of ADH to regulate plasma osmolality, suggesting that there may be a difference between enuretic and nonenuretic children at the ADH-receptor level. No differences were found between enuretic patients and controls regarding urine production, antidiuretic levels at night and during the day, or plasma osmolality.

Another theory postulates that as children approach adolescence, a faulty circadian rhythm of arginine vasopressin (AVP) secretion may be the paramount pathogenic factor.

Epidemiology

1. Prevalence: Decreasing prevalence occurs with increasing age.
   a. Age 4: 30%
   b. Age 5: 14%–20%
   c. Age 6: 10%
   d. Age 10: 5%–10%
   e. Age 12: 3%
   f. Age 15: 2%
   g. Age 18: 1%–2% (according to studies of this group)
   h. Army recruits: 0.1%–2.5% (according to studies of this group)
2. Sex: Male to female ratio is 3:2.
3. Race: More African-American teens are affected than white teens.
4. Timing: Seventy-five percent to 90% of teens have nocturnal enuresis only, whereas 10%–25% of teens have nocturnal and daytime enuresis.

Diagnosis

A thorough history, a focused physical examination, and simple laboratory tests are all that are usually needed to evaluate enuresis, because significant organic lesions are infrequent. The prevalence of organic lesions is higher in adolescents than children. The prevalence of a psychological or organic cause is higher in secondary and daytime enuresis.

History

The history should include the following:
1. Severity of enuresis: How many dry nights per month, most consecutive dry nights, frequency of urination, urgency of urination, evening fluid intake, and whether the bladder is emptied at bedtime.
2. Type of enuresis: Primary or secondary, polsymptomatic or monosymptomatic. If the adolescent suffers from daytime wetness, common etiologies include micturition deferral, UTIs, constipation, vaginal reflux of urine, labial fusion, postvoid dribble syndrome, daytime frequency syndrome, giggle incontinence, stress incontinence, emotional stress, urge syndrome, neurogenic bladder, urethral obstruction, ectopic ureter, diabetes mellitus, and diabetes insipidus.
3. Symptoms of organic disease: Dysuria, intermittent daytime wetness, polydipsia, central nervous system trauma, constipation, or encopresis can indicate an organic disease. Patients with ectopic ureter will complain of constant wetness or dampness. Spinal tumors cause a change in gait, constipation, or encopresis.
4. History of UTIs
5. Toilet-training history
6. Family history of enuresis or small bladders
7. Awakening to use toilet at night: Self-awakens to full bladder, self-awakens to wetness, never awakens spontaneously, awakened by parent, evidence of deep sleep, sleepwalking.
8. Prior therapeutic modalities and results
9. Functional bladder capacity measurement
10. Adolescent's and family's adjustment to the problem
11. Member of the family responsible for changing sheets and laundry
12. History of any sleep disorders, such as night terrors or unusually deep sleep
13. General psychosocial review of family, peers, and school
14. Timing of wetting: Adolescents who suffer from vaginal reflux of urine, labial fusion, or postvoid dribble syndrome wet after voiding. Other etiologies of enuresis cause wetting before voiding.
15. Voiding history: Teens with urethral obstruction need to push to initiate or sustain voiding. The urinary stream is often weak, interrupted, or of narrow caliber. A history of dribbling or hesitancy suggests posterior urethral valves.
16. Urgency of urination: The common causes of urgency of urination are UTIs, bacteria without dysuria (which can irritate bladder mucosa and cause urinary urgency), or constipation. Rare causes include a bladder calculus, a bladder foreign body, and hypercalcuria.

Physical Examination

1. Check blood pressure.
2. Abdomen: Check for masses.
3. Genitourinary tract: Check the urethral meatus for evidence of stenosis. Observe the urinary stream to see whether it is full and forceful or narrow and dribbling.
4. Look for midline defects in the lumbosacral area.
5. Perform a neurological examination.
   a. Gait
   b. Lower extremity: Motor and sensory
   c. Deep tendon reflexes
   d. Perineal sensation
   e. Rectal sphincter tone
   f. Bulbocavernous reflex

Laboratory Tests
1. Urinalysis
Every patient should have a urinalysis. This simple, noninvasive test can screen for UTIs, diabetes mellitus, and diabetes insipidus (a specific gravity of more than 1.015 g or a specific gravity more than 1.025 g after a 14-hour fluid restriction rules out diabetes insipidus). Look for the presence of glucose, protein, or white blood cells, and assess the specific gravity. Urethral obstruction can be associated with hemorrhita.

2. Urine Culture
Obtain a urine culture if the urinalysis suggests a UTI.

3. Uroflowmetry
A noninvasive measure of urine flow rate. It can assist in screening for patients with neurogenic bladder and urethral obstruction. Patients void into a special toilet with a pressure-sensitive rotating disk at the base. A normal uroflow study shows a single bell-shaped curve with a normal peak and average flow velocity for age and size. Patients with urethral obstruction or neurogenic bladder have a prolonged curve or an interrupted series of curves and a low peak urine flow velocity.

4. Bladder Capacity
The teen and his or her family can measure their bladder capacity at home or in the office. The patient drinks 12 ounces of water and then the volume of urine is measured when the patient needs to void. The normal bladder capacity, in ounces, is the age plus two. Normal adult bladder capacity is 50–60 ounces.

5. Imaging Studies
Radiological studies are not needed routinely. If a urethral obstruction or a neurogenic bladder is suspected, then a voiding cystourethrogram is indicated (the neurogenic bladder will appear as a trabeculated “Christmas tree” or “pine cone” configuration). If a neurogenic bladder is suspected and there is no obvious cause, then obtain a spinal magnetic resonance image to look for spinal cord abnormalities. Ultrasonography is indicated for patients with persistent daytime wetness or for patients with failure to empty the bladder (whether due to urge symptoms, urethral obstruction, or neurogenic bladder). A prevoiding and postvoiding bladder ultrasound can be obtained to rule out partial emptying (normal residual bladder volume is less than 10 mL).

**THERAPY**

If a urological lesion is discovered, then referral to a urologist for appropriate management is recommended. As stated, most affected adolescents are without organic lesions. In most teens, the cause of enuresis is generally multifactorial and includes genetic predisposition, small bladder capacity, a sleep disorder, developmental delay, or abnormal secretion of AVP. Therapy includes the following:

1. Motivational Counseling:
Regardless of any other modalities chosen, motivational counseling is helpful. Studies indicate that counseling alone leads to a 25%–70% remission rate. Through motivational counseling, the teen learns to assume responsibility and become an active participant in the management program. In such a program, the practitioner does the following:
   a. Reassures the adolescent and family members that this problem is common to many teens. The parents and the teen should not feel guilty about “causing” the problem.
   b. Gives the adolescent an active role by putting him or her in charge of changing the sheets and placing them in the laundry machines. The parents should be reassured that they do not have to take a backseat position in dealing with the problem.
   c. Reduces secondary friction caused by enuresis.
   d. Gives positive reinforcement for dryness.

Provides initial follow-up with the practitioner.

2. Self-awakening or parent-awakening programs:
These programs work by training adolescents to recognize when their bladder is full, awakening, and walking to the bathroom. It is useful to inform the teens that they do not need to “hold” their urine all night.

   a. Self-awakening programs:
   This method can be taught several ways. One technique is to have the teen lie in bed with eyes closed and pretend it is the middle of the night and his or her full bladder is trying to wake him. The teen then goes to the bathroom and empties her bladder. Another technique has the teen go to bed when he or she has the urge to urinate. The teen then pretends to sleep, “awakens,” and walks to the bathroom to urinate. A third technique has the teen use self-hypnosis by bedtime with the posthypnotic suggestion that the teen will wake up and use the bathroom during the night.

   b. Parent-awakening programs:
   If self-awakening isn’t effective, then parent awakening can be used. The parent awakens the patient, but the teen must locate the bathroom alone. It is recommended that the parent use the minimal prompt necessary to awaken the teen. For example, the parent can start with turning on the bathroom light only. If that is ineffective, the parent can progress to saying the teen’s name, then to touching him or her, and finally to using an alarm clock or smoke detector alarm. If the teen is confused and/or very difficult to awaken, then the parent tries to awaken the patient again in 20 minutes. If the teen becomes angry or yells when awakened, then the parent stops and talks to the teen in the morning. Parents need to awaken their child at the parent’s bedtime each night until the teen awakens quickly to sound for seven consecutive nights. At that point, the patient is either cured or ready for an enuresis alarm.

3. Dry bed training:
This is a more labor-intensive parent-awakening program. The teen needs to be awakened once an hour until 1 a.m. on the first night. When the teen is awake enough to speak coherently, the parent asks him or her if she needs to use the bathroom. The teen is praised if she is dry. If wet, the teen is encouraged to change the pajamas and bedding. At 1 a.m., the teen is instructed to try voiding, even if dry. For the next five nights, the teen is only awakened once. The teen is awakened 3 hours after falling asleep the first night. The second night, the teen is awakened 2.5 hours after falling asleep. By the fifth night, the teen should be awakened 1 hour after falling asleep. On the sixth night, the teen is instructed to self-awaken from then on. If the teen relapses (defined as three consecutive wet nights), then repeat the six nights of awakening. One study found that the cure rate was 92% using this technique and that the relapse rate was 20% (with all patients who relapsed responding to a second trial of training).

4. Alarm systems:
Enuresis alarms have the highest cure rate of any available treatment for enuresis. Several studies have shown comparable cure rates between medications and alarms in the short term. However, these same studies showed persistent effectiveness only with the alarm. The teen has the choice of either wearing an audio alarm or a tactile alarm. The alarms are comfortable, convenient, and inexpensive. The disadvantages to the alarm are that they are time intensive (they need to be used for 2–3 months and are continued until 3 weeks after dryness has been achieved) and the teen and parent must be motivated to use them properly. By learning to awaken as quickly as possible to the alarm, the teen eventually learns to awaken to the internal stimulus of a full bladder.

   a. Types:
   Older alarms required elaborate pad-and-bell systems. Newer alarms are lightweight, easy to use, and relatively inexpensive ($50–$85). The alarms consist of two clips attached to the teen’s underwear and connected to a wrist alarm or pajama-collar alarm. The alarm buzzes if a small amount of wetness occurs on the underwear. Alarms are available from Nyclone ($58) Medical Products, Inc. 2424 South 900 West Salt Lake City, UT 84119 801-973-4090 Wet-stop ($85) Palco Laboratories #038; 8030 Soquel Drive Santa Cruz, CA 95062 800-346-4488

   b. Indications for using alarm:
   The alarm awakens the teen and usually leads to a contraction of the external bladder sphincter. In order for enuresis alarms to be effective, the teen needs to be able to awaken to touch or sound. Therefore, it is worthwhile to see whether the patient can respond to parent awakening or alarm clock awakening. Further, the teen must want to use the alarm. This technique is ineffective for teens indifferent to using the alarm. The alarm should be continued until 3 weeks after dryness has been achieved.

   c. Results:
   Long-term cure rates average 70%. Alarm failure rates range from 20% to 30%. Common reasons for alarm failure include the following:

   • The parents discontinue the alarm too soon.
   • The teen fails to hear the alarm because he or she is such a deep sleeper.
   • The teen refuses to use the alarm.
   • The teen refuses to try any technique (ask the parents to discontinue all reminders of assistance and the teen needs to be responsible for cleanup of the bed and pajamas).

   d. Hypnosis group had maintained a positive response.

   e. (1993) found that 72% of children whose enuresis was treated with hypnosis had a positive response, and at a 9-month follow-up, 68% of patients in the hypnosis group had maintained a positive response.

5. Medications:
No drug exists that is adequately safe and effective for curing enuresis. However, most pediatricians agree that intermittent use of drugs is appropriate for teens when needed for camping trips, school trips, vacations, or overnights. The major drugs available include the following:

   a. Oxybutynin.
   b. Clonidine.
   c. Imipramine.
   d. Methylphenidate.
   e. Propranolol.
a. DDAVP

- **Action:** DDAVP is a synthetic analogue of vasopressin. The mechanism of action of the drug is the reduction of urine production by increasing water retention and concentration in the distal tubules. Treatment of enuresis using desmopressin is based on the hypothesis that ADH secretion at night is insufficient.
- **Dose:** DDAVP is tasteless and odorless and can be administered either intranasally or orally. The medication comes as a nasal spray that delivers 10 µg per spray or as a graduated intranasal tube (Rhinal Tube) that delivers doses of 5, 10, 15, and 20 µg per spray. The usual initial dose is 20 µg, or one spray in each nostril, at bedtime. The dose can be increased by 10 µg weekly to a maximum dose of 40 µg. Some individuals may respond to a dose as low as 5 µg/day. The Rhinal Tube must be used if 5-µg doses are required. If the patient remains completely dry on a particular dose, then a dose of 10 µg less should be tried. The duration of action is 10–12 hours.
- **Results:** DDAVP was approved for the treatment of nocturnal enuresis at the end of 1989. The response to desmopressin improves with increasing age in patients with nocturnal enuresis. Therefore, the best results are seen in patients older than 10 years. A family history of nocturnal enuresis at older than 10 years and a normal bladder capacity are also predictors of a positive response to desmopressin. Seventy percent of patients with nocturnal enuresis who receive desmopressin stop their bed-wetting completely or reduce it significantly. A positive effect of the medication is seen within a few days and is maintained as long as the drug is administered. Most patients relapse after drug withdrawal, particularly if the drug is stopped abruptly. Therefore, the drug should be tapered off slowly. Long-term treatment lasting at least 1 year is becoming more routine. During long-term therapy, treatment-free windows of approximately 3-month intervals are essential to avoid treating a child who has become dry.
- **Side effects:** Side effects are infrequent but can include symptomatic hyponatremia, headache, abdominal discomfort, nausea, nasal congestion, rhinitis, nosebleeds, abdominal cramps, and sore throats. These symptoms usually disappear with a reduction in the dose.
- **Oral desmopressin:** Stenberg and Lackgren (1993) found that oral desmopressin is as effective as intranasal desmopressin and is safe, with similar adverse effects (e.g., headache and abdominal pain). However, at least a tenfold increase in the desmopressin dose is required, compared with the intranasal dose. Effective doses for oral desmopressin have ranged from 200 to 400 µg. Skoog et al. (1997) and Janknegt et al. (1997) found that there is a linear increase in the efficacy of oral desmopressin. Both investigators found that either a 400-µg or a 600 µg dose of oral desmopressin is statistically significant in decreasing the number of wet nights a patient experiences, as compared with placebo.

b. Imipramine (Tofranil)

- **Action:** This drug combines an anticholinergic effect that increases bladder capacity with a noradrenergic effect that decreases bladder detrusor excitability. Imipramine is also thought to increase excretion of ADH from the posterior portion of the pineal gland.
- **Dose:** Imipramine is taken 1 hour before bedtime. The duration of action is 8–12 hours. Start the patient at 25 mg/day and titrate upward by 25 mg every 2 weeks until the patient is dry. The maximum dose is 50 mg/day for patients between 8 and 12 years of age, and 75 mg/day for patients older than 12 years. A sustained-release form of imipramine, Tofranil-PM, is also available.
- **Results:** Response rate is 25%–40%; relapse rate is 40%–60%. The relapse rate is higher when the drug is stopped abruptly or prematurely. The maximal effect of imipramine usually occurs in the first week of therapy. However, one should continue therapy for 1–2 weeks before deciding on efficacy and whether to adjust the dose. The current recommendation is to treat for 3–6 months and then taper the drug by decreasing the dose, frequency, or both for 3–4 weeks. If the patient has a relapse, one can repeat a course of therapy. The drug is most beneficial for occasional use when dyresis is necessary (e.g., trips, vacations, sleepover parties). Imipramine and desmopressin have been found to be equivalent in effectiveness (Glazener and Evans, 2000). An advantage of imipramine is that it is inexpensive ($5 per month for generic formulations).
- **Side effects:** Nervousness, gastrointestinal distress, syncope, and anxiety can occur. Because of imipramine’s lethality when taken in overdose, both parents and teens need to be aware of its toxicity.

c. Oxybutynin ( Ditropan)

- **Action:** Oxybutynin provides an anticholinergic, antispasmodic effect that reduces uninhibited detrusor muscle contractions and increases bladder capacity. Therefore, it may be most beneficial for patients with small capacity bladders who also have daytime frequency or enuresis associated with uninhibited bladder contractions.
- **Dosage:** A sustained-release formulation of oxybutynin is available (10 mg/day), as well as a conventional formulation (5 mg twice daily). Bims et al. (2000) found that the effectiveness and side effect profile are comparable with either formulation.
- **Results:** A success rate of 90% was reported in one study of individuals with daytime enuresis, bladder instability, or both. The drug is rarely helpful in treating patients with only nocturnal enuresis. It is to be used in teens with polysymptomatic enuresis, urge syndrome, or neurogenic bladder. Neveus et al. (1997) found that patients resistant to 400 µg of oral desmopressin were responsive to anticholinergic medication, suggesting nocturnal instability.
- **Side effects:** Dry mouth, flushing, drowsiness, and constipation.
- **Dose:** DDAVP is tasteless and odorless and can be administered either intranasally or orally. The medication comes as a nasal spray that delivers 10 µg per spray or as a graduated intranasal tube (Rhinal Tube) that delivers doses of 5, 10, 15, and 20 µg per spray. The usual initial dose is 20 µg, or one spray in each nostril, at bedtime. The dose can be increased by 10 µg weekly to a maximum dose of 40 µg. Some individuals may respond to a dose as low as 5 µg/day. The Rhinal Tube must be used if 5-µg doses are required. If the patient remains completely dry on a particular dose, then a dose of 10 µg less should be tried. The duration of action is 10–12 hours.
- **Results:** DDAVP was approved for the treatment of nocturnal enuresis at the end of 1989. The response to desmopressin improves with increasing age in patients with nocturnal enuresis. Therefore, the best results are seen in patients older than 10 years. A family history of nocturnal enuresis at older than 10 years and a normal bladder capacity are also predictors of a positive response to desmopressin. Seventy percent of patients with nocturnal enuresis who receive desmopressin stop their bed-wetting completely or reduce it significantly. A positive effect of the medication is seen within a few days and is maintained as long as the drug is administered. Most patients relapse after drug withdrawal, particularly if the drug is stopped abruptly. Therefore, the drug should be tapered off slowly. Long-term treatment lasting at least 1 year is becoming more routine. During long-term therapy, treatment-free windows of approximately 3-month intervals are essential to avoid treating a child who has become dry.
- **Side effects:** Side effects are infrequent but can include symptomatic hyponatremia, headache, abdominal discomfort, nausea, nasal congestion, rhinitis, nosebleeds, abdominal cramps, and sore throats. These symptoms usually disappear with a reduction in the dose.
- **Oral desmopressin:** Stenberg and Lackgren (1993) found that oral desmopressin is as effective as intranasal desmopressin and is safe, with similar adverse effects (e.g., headache and abdominal pain). However, at least a tenfold increase in the desmopressin dose is required, compared with the intranasal dose. Effective doses for oral desmopressin have ranged from 200 to 400 µg. Skoog et al. (1997) and Janknegt et al. (1997) found that there is a linear increase in the efficacy of oral desmopressin. Both investigators found that either a 400-µg or a 600 µg dose of oral desmopressin is statistically significant in decreasing the number of wet nights a patient experiences, as compared with placebo.

**TREATMENT RELAPSES AND FAILURES**

Treatment relapse is defined as the recurrence of enuresis after having been dry for at least 1 month. The remedy is to reinitiate the treatment that was effective previously. Treatment failure occurs when the patient cannot remain dry despite using the alarm or combined therapy. For adolescents, the best approach is to put the teen in charge of solving the problem and emphasize that he or she will become dry once she learns to self-wake.

**PROGNOSIS**

Reported spontaneous cure rates (Forsythe and Redmond, 1974) are as follows:

1. Ages 5–9: 14%/yr
2. Ages 10–14: 16%/yr
3. Ages 15–19: 16%/yr
4. After age 20: 3%/yr

**WEB SITES**

For Teenagers and Parents


http://www.clinicaltrials.gov. This Web site provides good medical information on the diagnosis, etiology, and treatment of enuresis.


http://www.peds.umn.edu/centers/NES/. The Web site for the National Enuresis Society. This site reviews the etiology, diagnosis, and treatment of enuresis. In addition, it provides an 800 phone number for locating a doctor to treat your enuresis, tips for choosing a doctor, and links to other resources on the Internet.

**REFERENCES AND ADDITIONAL READINGS**


Bims J, Lukkari E, Malone-Lea JG, and the Oxybutynin CR Clinical Trial Group. A randomized controlled trial comparing the efficacy of controlled-release oxybutynin tablets (10 mg once daily) with conventional oxybutynin tablets (5 mg twice daily) in patients whose symptoms were stabilized on 5 mg twice daily of oxybutynin. BJU Int 2000;85:793.


Shu SG, Li YP, Chi CS. The efficacy of intranasal DDAVP therapy in children with nocturnal enuresis. Chung-Hua I Hsueh Tsa Chih 1993;52:368.


Asymptomatic Proteinuria and Hematuria

Lawrence S. Neinstein and Lawrence J. D'Angelo

Asymptomatic Proteinuria and Hematuria

Lawrence S. Neinstein and Lawrence J. D'Angelo

Asymptomatic Proteinuria

Etiology

1. Increased glomerular permeability, as in primary or secondary glomerulopathies (e.g., minimal change disease, systemic lupus erythematosus (SLE), membranous nephropathy)
2. Increased production of abnormal proteins (e.g., monoclonal gammopathies)
3. Decreased tubular reabsorption of proteins, as in tubular disease (e.g., Fanconi syndrome, aminoglycoside nephrotoxicity) or chronic interstitial nephritis
4. Miscellaneous—functional proteinuria (e.g., fever, exercise, congestive heart failure) and orthostatic proteinuria

Epidemiology

Up to 10% to 19% of healthy adolescents have protein in their urine on a dipstick test of a random urine sample. This prevalence falls with repeated testing, and a diagnosis of persistent proteinuria should be based on three separate urine tests. The prevalence peaks at about age 16 years.

Clinical Manifestations

Small amounts of protein in the urine are normal, and most individuals excrete 30 to 130 mg of protein per day. Although the maximum "normal" amount for adolescents and adults is 150 mg/day, completely healthy adolescents may excrete up to 300 mg/day without any evidence of clinical or histopathological renal disease. Nonetheless, "isolated asymptomatic proteinuria" refers to excretion of more than 150 mg/day by a person without clinical signs or symptoms. The leading causes of this condition are "benign persistent proteinuria" and orthostatic proteinuria. Orthostatic (postural) proteinuria, which is proteinuria while upright but not while recumbent, is common in adolescents. The etiology is unclear, although functional compromise of the left renal vein has been postulated as a possible cause (Shintaku, 1990). The condition is characterized by

1. An asymptomatic state
2. Age at onset: 10 to 20 years
3. Dipstick urine findings
   a. In the p.m.: 1 to 3+
   b. In the a.m.: Negative finding
   c. Urine sediment: Negative finding
4. Quantitative protein excretion
   a. Supine: 10 to 75 mg in 12 hours
   b. Upright: 150 to 1,200 mg in 12 hours
5. Renal function: Normal

The presence of hypertension, edema, hypoalbuminemia, or hyperlipidemia suggests more profound renal abnormalities.

Differential Diagnosis

1. Mild asymptomatic proteinuria (expected excretion of protein: less than 500 mg/m² in 24 hours)
   a. Benign persistent proteinuria
   b. Orthostatic or postural proteinuria (proved with split 24-hour urine collection)
   c. Pyelonephritis (usually with fever and pyuria)
   d. Renal tubular disorders
   e. Chronic interstitial nephritis
   f. Congenital dysplastic lesions
   g. Other: Exercise, trauma (with hematuria), fever, congestive heart failure (severe)
2. Moderate proteinuria (expected excretion of protein: 500 to 2,000 mg/m² in 24 hours)
   a. Acute poststreptococcal glomerulonephritis (PSGN)
   b. Primary glomerulonephritis
   c. Hereditary chronic nephritis (Alport syndrome)
   d. Systemic diseases: SLE
3. Severe proteinuria (expected excretion of protein: more than 2,000 mg/m² in 24 hours; usually more than 3.5 g), typically associated with edema, hypoalbuminemia, and hypercholesterolemia (nephrotic syndrome)
   a. Idiopathic glomerulonephritis: Minimal change disease, focal sclerosis, membranous or membranoproliferative glomerulonephritis
   b. Systemic disease: SLE; amyloidosis (in setting of chronic inflammatory disease or familial Mediterranean fever)
c. Less common
   - Infections: Bacterial endocarditis, hepatitis, malaria, human immunodeficiency virus
   - Toxins: Mercury, heroin, gold, penicillamine
d. Uncommon
   - Allergens: Bee stings
   - Mechanical: Pericarditis, renal vein thrombosis
   - Cancer: Hodgkin disease, lymphoma
   - Pregnancy
   - Congenital: Fabry disease and Alport syndrome

Diagnosis

The qualitative dipstick test for protein will detect protein levels greater than 10 to 30 mg/dL. An initial positive test result should be confirmed on two more tests, because many individuals have transient proteinuria and then have negative findings on subsequent evaluation. False-positive test results should be considered (Table 28.1). If proteinuria is confirmed, then a more thorough history, physical examination, and laboratory evaluation are indicated to rule out significant disease. A useful screening test is a spot protein/creatinine ratio. A random urine sample is analyzed for protein and creatinine. When both are expressed in milligram amounts, a ratio of less than 0.2 is normal and a ratio greater than 10 signifies nephrotic-range proteinuria. This test is also useful for monitoring the course of proteinuria without performing the more burdensome timed urine collections.

TABLE 28.1. Causes of false-positive test results for proteinuria

<table>
<thead>
<tr>
<th>Cause</th>
<th>False-Positive Reasons</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intoxication</td>
<td>Serum creatinine concentration is increased</td>
</tr>
<tr>
<td>Drug history</td>
<td>Serum creatinine concentration is increased</td>
</tr>
<tr>
<td>Bee stings</td>
<td>Serum creatinine concentration is increased</td>
</tr>
<tr>
<td>Allergic history</td>
<td>Serum creatinine concentration is increased</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>History Inquire about the following:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Recent upper respiratory tract infection or pyoderma</td>
</tr>
<tr>
<td>2. Edema</td>
</tr>
<tr>
<td>3. Skin rashes, arthralgias, or photosensitivity</td>
</tr>
<tr>
<td>4. Flank pain</td>
</tr>
<tr>
<td>5. Diabetes mellitus (10 to 14 years of diabetes is usually required before clinical detection of proteinuria; detection of microalbuminuria is possible at earlier stages of disease)</td>
</tr>
<tr>
<td>6. Intoxications, drug history, bee stings, and other allergic history</td>
</tr>
<tr>
<td>7. Family history of renal disease</td>
</tr>
</tbody>
</table>

Physical Examination Check for the following:

<table>
<thead>
<tr>
<th>Physical Examination</th>
<th>Check for the following:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Blood pressure; height and weight percentiles</td>
<td></td>
</tr>
<tr>
<td>2. Vision and hearing screening, especially if hereditary nephritis is a consideration</td>
<td></td>
</tr>
<tr>
<td>3. Edema</td>
<td></td>
</tr>
<tr>
<td>4. Rash</td>
<td></td>
</tr>
<tr>
<td>5. Abdominal mass</td>
<td></td>
</tr>
<tr>
<td>6. Joint examination</td>
<td></td>
</tr>
<tr>
<td>7. Cardiac examination</td>
<td></td>
</tr>
<tr>
<td>8. Signs of systemic diseases</td>
<td></td>
</tr>
</tbody>
</table>

Laboratory Tests Include the following in the evaluation:

1. Urinalysis
   a. Dipstick tests: Protein, glucose, and blood should be tested. If the dipstick test result is positive for protein, a repeated dipstick test should be performed another one or two times. If protein is still present, a 24-hour quantitative test should be performed.
   b. Microscopic examination for casts and cells: Examination of sediment is crucial because abnormal results suggest an underlying renal problem. Red blood cell (RBC) casts suggest glomerulonephritis; white blood cell casts suggest pyelonephritis or interstitial nephritis.

2. A 24-hour urine specimen for protein: Because a dipstick test provides only a qualitative measurement of urinary protein, a quantitative test is required to determine whether the 24-hour amount is abnormal and to provide a baseline value for monitoring of the patient’s condition and consideration of any potential interventions.
   a. The test should be performed in the following manner to test for orthostatic proteinuria at the same time:
      - At 7 a.m., the patient voids and discards the first morning urine; subsequent urine is then collected in the first bottle (bottle A).
      - At 9 p.m. that evening, the teenager lies in bed for 2 hours and then voids into bottle A at 10 p.m.
      - All urine during the night should go into the second bottle (bottle B).
      - At 7 a.m. the next day, the teenager voids into bottle B, and the collection period has ended.
   b. The sum of the amounts of protein in the urine in the two bottles equals the 24-hour protein content. With orthostatic proteinuria, the total will be greater than 150 mg and usually less than 1 g. The urinary protein collected during the recumbent period should be less than 75 mg. The ratio of protein in bottle A to protein in bottle B can also be used to diagnose orthostatic proteinuria: a ratio of 5:1 or greater is consistent with orthostatic proteinuria. Total urinary creatinine should also be measured during the 24-hour urine collection so that creatinine clearance can be estimated. The serum creatinine concentration is also required to calculate the creatinine clearance. If the 24-hour collection demonstrates postural proteinuria or a 24-hour total of less than 500 mg, then no further diagnostic study is indicated. Follow-up should be done every 6 to 12 months for monitoring increasing proteinuria, a rising serum creatinine concentration, or the development of hemorrhuria or hypertension. Although it is unusual, significant glomerulopathies can begin with orthostatic proteinuria that later becomes persistent.

3. If the protein value is more than 500 mg with no postural proteinuria, then further evaluation is indicated. It should include serum urea nitrogen and creatinine concentrations; complete blood cell count; concentrations of albumin, antinuclear antibody, and cholesterol; hepatitis B screening tests; complement levels (CH50, C3, C4); and an antistreptolysin O titer. Not all tests need be done at once. The clinical history and physical examination should direct the order and amount of testing. Perform the following if signs or symptoms are suggestive of hepatitis, streptococcal infections or SLE:
   b. Recent streptococcal infection: Determine serum complement and antistreptococcal enzyme titers.
   c. SLE: Determine antinuclear antigen and complement levels.

4. Renal ultrasonography: Order if renal function is abnormal or nonpostural proteinuria is present. This test yields useful information, such as the number of kidneys present (1 in every 1,000 people is born with a single kidney, a finding that could influence subsequent evaluation and treatment), the size of the kidneys (small kidney size reflects chronic disease), and echogenicity. Although the test is nonspecific, increased renal echogenicity reflects “medical renal disease” that may require further evaluation.
5. Renal biopsy: Because of the limited number of treatment options for many renal lesions, the frequent use of therapeutic trials, and the ability to diagnose common lesions on the basis of the history and laboratory findings, the indications for a renal biopsy are now more limited than in the past. A biopsy can help define the nature of the renal disease if the history, physical examination, and laboratory tests are not revealing. A biopsy can also define the severity of the lesion and help in determining its prognosis. This information is very important for teens and their families who are confronted with a diagnosis of renal disease.

Refer the patient to a nephrologist for further evaluation and consideration for renal biopsy in the following situations:

a. A 24-hour protein concentration is greater than 1,000 mg.
b. The diagnosis is unclear and significant disease is suspected because of the presence of proteinuria, hematuria, hypertension, or renal insufficiency.
c. The nephrotic syndrome is present and has not responded to a therapeutic trial of corticosteroids for minimal change disease.
d. Renal function is deteriorating.
e. The patient, family, or both express a need for prognostic information.

With a careful history, physical examination, urinalysis, and 24-hour urinary protein test, one should be able to identify those adolescents with significant proteinuria and thus determine which teenagers need follow-up only and which need referral for more expert monitoring or renal biopsy.

Prognosis and Follow-Up

Isolated Proteinuria: In general, the prognosis for asymptomatic orthostatic or persistent proteinuria (excretion of less than 500 mg protein in 24 hours) is good. A study of the 1937 Yale University class revealed a prevalence of proteinuria of 13.8% (Baskin et al., 1972). On 30-year follow-up, the group with proteinuria had a mortality rate similar to that of the rest of the class. Another study of patients observed for 20 years showed only 17% with persistent proteinuria, with the decrease being progressive with time (Springberg et al., 1982). Table 28.2 addresses the risk of chronic renal disease based on the pattern of proteinuria and suggests recommendations for follow-up.

TABLE 28.2. Risk of chronic renal disease and recommended follow-up

Nonisolated Proteinuria: The prognosis depends on the underlying cause of the proteinuria. This is usually indicative of glomerular disease when associated with significant proteinuria. Two more common diagnoses in adolescents (especially after an upper respiratory tract infection) are IgA nephropathy (Berger disease) and PSGN. In the absence of clinical manifestations of a chronic illness, with protein excretion of less than 1 g/day, and with other normal findings on screening tests, follow-up with twice-yearly blood pressure checks, urinalysis, and determination of serum creatinine values is sufficient. IgA nephropathy can be distinguished from acute PSGN by the absence of a period of latency separating the onset of an acute infection from the onset of hematuria. Acute PSGN characteristically has a latency period of 7 to 10 days from the onset of PSGN charangkis to the occurrence of hematuria. Patients with IgA nephropathy often are found to have persistent microscopic hematuria with intermittent, more temporarily immediate episodes of gross hematuria associated with acute, intercurrent illnesses.

Hematuria Associated with Systemic Disease

1. Acute illnesses such as Henoch-Schönlein purpura and PSGN usually carry a good prognosis.
2. Chronic illnesses such as SLE or a vasculitis usually carry a more guarded prognosis that is dependent on the entire disease process and treatment success and not just on the initial severity of the renal involvement.
3. Azotemia or urinary protein excretion greater than 2 g is usually associated with significant underlying renal disease. Evaluation and therapy for proteinuria associated with a chronic systemic disease, for azotemia, or for proteinuria in the nephrotic range should be carried out in consultation with a subspecialist.

HEMATURIA

Hematuria is defined as the excretion of abnormal quantities of RBCs in the urine. Most authorities accept 2 to 4 erythrocytes per high-power field (HPF) on a resuspended centrifuged urine sediment specimen as normal. The orthotoluidine-impregnated paper strips give a positive result with a urine specimen that contains as few as 3 to 5 RBCs/HPF. Hematuria must be differentiated from pigmenteduria caused by myoglobinuria, hemoglobinuria, porphyrinuria, or exogenous pigments.

Epidemiology

Fewer than 3% of healthy individuals excrete more than 3 RBCs/HPF. Several studies have examined the prevalence of hematuria in school-age children and young adults:

1. Vehaskari et al. (1979) examined 8,954 school-age children and found a prevalence of 4.1% in at least one of four urine specimens for 2 days; 1% of children had two or more specimens indicative of hematuria.
2. Dodge et al. (1976) studied 6,070 school-age children and found that 0.5% had hematuria on at least two of three specimens.
3. Froom et al. (1984) examined 1,000 symptom-free Air Force personnel age 18 to 33 years and found that 5.2% had 2 to 4 RBCs/HPF at any one time for a period of 15 years. The cumulative incidence of this finding during the 15 years was 38.7% on at least one occasion, 16.1% on two or more occasions, and 7.9% on three or more occasions. For 3 to 5 RBCs/HPF, the cumulative incidence for at least one, two, or three specimens was 25.7%, 10.7%, and 5.6%, respectively. Only one patient had significant pathological changes. No others had significant renal disease.

Clinical Manifestations

Like proteinuria, hematuria in adolescents is usually asymptomatic. When present, however, the symptoms often suggest a cause. Lower urinary tract infections cause dysuria and frequency, whereas upper tract infections are accompanied by fever and flank pain. Renal stones are often heralded by colicky flank pain, whereas “loin pain hematuria” is characterized by episodic unilateral or bilateral loin pain. Rash and joint pain often accompany SLE, whereas abdominal pain and “palpable purpura” are seen with Henoch-Schönlein disease. Intrinsic renal disease may be accompanied by edema, hypertension, and symptoms of uremia. Decreased hearing or vision may indicate the presence of familial nephritis.

Differential Diagnosis

Although the differential diagnosis of hematuria is extensive, the common conditions in adolescents are much fewer and are listed and discussed here separately. In addition, use of a systematic evaluation will narrow the diagnostic possibilities. The causes of hematuria can be divided into renal parenchymal, urinary tract, and systemic coagulation disturbances. False hematuria must also be considered.
Renal Parenchymal Diseases

1. Glomerular diseases
   a. Primary
      1. IgA nephropathy (Berger disease)
      2. Membranous or membranoproliferative glomerulonephritis
      3. Focal glomerulonephritis or glomerulosclerosis
   b. Secondary
      1. Glomerulonephritis associated with connective tissue diseases, hemolytic uremic syndrome, or Henoch-Schönlein purpura
      2. Glomerulonephritis associated with infections such as streptococcal infection, shunt infections, or infective endocarditis
   c. Hereditary: Alport syndrome, polycystic kidney disease, medullary sponge kidney
   d. Benign familial hematuria: Primary renal hematuria with thin basement membrane

2. Nonglomerular diseases
   a. Vascular diseases
      1. Malignant hypertension
      2. Loin-pain hematuria syndrome
      3. Arteriovenous malformation
      4. Renal arterial emboli
   b. Papillary necrosis: Sickle cell disease, diabetes mellitus, alcoholism, analgesic abuse
   c. Trauma: Usually significant trauma, as from motor vehicle accidents or contusions from contact sports
   d. Acute pyelonephritis
   e. Neoplasms

Urinary Tract Disease

1. Hypercalciuria or renal calculi
2. Inflammatory: Urethritis, cystitis, or prostatitis
3. Neoplasms or arteriovenous malformation within the bladder
4. Vascular diseases
   a. Acute pyelonephritis
   b. Abdomen: Abdominal masses and renal enlargement may suggest polycystic disease.
5. Trauma: Usually significant trauma, as from motor vehicle accidents or contusions from contact sports
6. False hematuria False hematuria can be caused by vaginal bleeding, factitious hematuria, or pigmenturia, including endogenous (porphyrinuria, hemoglobinuria, myoglobinuria) and exogenous (foods and drugs) forms of pigmenturia.

Etiology

The most common causes of microscopic hematuria in adolescents are acute lower or upper tract urinary infections, trauma, overexercise, hypercalciuria and renal stones, benign recurrent hematuria, and hereditary nephritis. The most common causes of gross hematuria are IgA nephropathy, trauma, hypercalciuria, and cystitis.

Diagnosis

The health care practitioner must first differentiate between true hematuria and false hematuria.

1. True hematuria: Positive dipstick finding, RBCs on spun urine, clear spun urine, and clear spun serum (unnecessary unless myoglobinuria or hemoglobinuria is suspected)
2. False hematuria
   a. Hemoglobinuria: Positive dipstick finding, negative result of microscopic examination, red spun urine, and pink spun serum
   b. Myoglobinuria: Positive dipstick finding, negative result of microscopic examination, orange-red or brown spun urine, clear spun serum
   c. Porphyrins or exogenous pigments: Negative dipstick finding, negative result of microscopic examination, red spun urine, clear spun serum
   d. Menstruation: Must be ruled out because menstrual blood can easily contaminate urine specimens

History

1. Pattern of hematuria: Microscopic versus macroscopic. Macroscopic, or gross, hematuria is more likely with severe trauma, severe cystitis, or IgA nephropathy.
2. Family history of renal disease or hematuria: Suggestive of hereditary nephritis, benign familial hematuria, or polycystic kidneys. Family history of vision problems or hearing loss with renal disease may indicate hereditary nephritis.
3. Associated symptoms
   a. Dysuria, frequency: Cystitis, urethritis, or (rarely) hypercalciuria.
   b. Colic: Renal stones.
   c. Weight gain: Nephrotic syndrome.
   d. Fever: Cystitis, pyelonephritis, or a systemic illness.
   e. Joint pain and rashes: SLE or Henoch-Schönlein purpura.
   g. Bleeding tendency: Coagulopathy.
   h. Previous heart murmurs or a history of tooth extractions: Endocarditis.
   i. Loin pain: Loin-pain hematuria syndrome.
4. Drug history: Analgesic abuse; use of warfarin (Coumadin), heparin, or oral contraceptives.
5. Relation to exercise: Short-term hematuria after long-distance running or heavy exercise is suggestive of “athletic hematuria.”

Physical Examination

2. Skin: Rashes may indicate connective tissue disease. Erythema is suggestive of Henoch-Schönlein purpura. Petechiae are suggestive of thrombocytopenia.
3. Corneal and lens abnormalities and hearing loss suggest hereditary nephritis.
4. Abdomen: Abdominal masses and renal enlargement may suggest polycystic disease.

Laboratory Tests As with proteinuria, the occurrence of true hematuria falls with repeated examinations. Therefore, significant hematuria should be confirmed on repeated urinalyses before an extensive evaluation is undertaken. Urine should be examined to determine the presence or absence of RBC casts and proteinuria. RBC casts and greater than 10% dysmorphic RBCs suggest a renal parenchymal origin, usually either glomerulonephritis or interstitial nephritis, and the need for further evaluation. Significant associated proteinuria would also suggest a glomerular cause and the need for further evaluation. Although blood in the urine can cause some proteinuria, even heavy bleeding usually results in less than 1 g/24 hr. If there are no RBC casts or a qualitative proteinuria (greater than 1+), the evaluation will depend on the history and the physical examination findings. Because idiopathic hypercalciuria is now recognized as an important cause of microscopic hematuria, it is useful to obtain a calcium/creatinine ratio on a spot, random urine sample. A ratio of less than 0.2 is normal. If the ratio is greater,
hypercalculia is overwhelmingly likely to be the cause of the hematuria and no further evaluation is required.

1. With signs or symptoms suggestive of infection, obtain a urine specimen for culture.
2. Basic laboratory tests should be ordered, as discussed earlier for proteinuria, and should include a complete blood cell count, platelet estimation, and determinations of blood urea nitrogen, creatinine, and complement levels.
3. If coaguolapathy is suspected, order determinations of the prothrombin time, partial thromboplastin time, platelet count, and bleeding time, as indicated.
4. For African-American patients, order sickle cell screening or hemoglobin electrophoresis to evaluate for sickle cell trait.
5. In adolescents with signs and symptoms suggestive of connective tissue disease or proteinuria and RBC casts, order the following tests: antinuclear antigen (ANA), anti-DNA antibody, third and fourth components of complement (C3 and C4), antistreptolysin O titer (ASO), audiography, serum albumin, cholesterol, quantitative urinary protein, and creatinine clearance.
6. Check urine of first-degree relatives for hematuria. The presence of hematuria in a parent, sibling, or child of an adolescent may indicate either benign familial hematuria (if family members are well) or hereditary nephritis (if family members have renal disease).

Additional Tests If, after evaluation, the diagnosis is unclear and hematuria is persistent or recurrent, then one should obtain a renal sonogram to look for structural causes of hematuria such as cysts or hydronephrosis. If the diagnosis is still unclear, the next step, if the patient has lower tract symptoms of dysuria or urgency and the CBC morphology features are normal, is cystoscopy. In the presence of RBC casts and significant proteinuria, a renal biopsy is indicated, as it is if hypertension accompanies either of these two symptoms. Without this history, almost all individuals will have either normal biopsy findings or changes not indicative of significant pathological changes. If gross hematuria persists without an obvious cause, renal angiography can be considered in looking for vascular causes of the hematuria.

Specific Conditions

Marathon Runner’s (Athlete’s) Hematuria Gross or microscopic hematuria is associated with many forms of exercise, including baseball, track, football, hockey, boxing, cross-country skiing, swimming, crew, lacrosse, rugby, and basic military training. The typical history is one of a normal urine before exercise, with hematuria on the first specimen voided after exercise, lasting up to 24 to 48 hours, possibly in association with dysuria and suprapubic discomfort. The cause is unclear, but the condition seems unrelated to the duration of sustained activity. It may be caused by a decrease in renal plasma flow, local trauma to the bladder, or leakage of blood from spiral vessels in the adventitia of minor calyces. It is less of a problem in children than in older adolescents and adults. The prognosis is excellent unless another renal problem is the underlying cause.

Loin-Pain Hematuria Syndrome This is a cause of hematuria found mainly in young females receiving oral contraceptives. The condition occurs with recurrent bouts of gross or microscopic hematuria with or without dysuria but almost always with unilateral or bilateral loin pain. The blood pressure and renal function are normal. Protein excretion is usually less than 1 g/day. The renal biopsy shows C3 deposits in arterioles by fluorescence microscopy. Treatment has not been satisfactory, although nonsteroidal antiinflammatory agents and calcium channel blockers may be of some use. The use of birth control pills should be discontinued.

Immunoglobulin A Nephropathy (Berger Disease) IgA nephropathy is a relatively common cause of gross hematuria in young adults. It is associated with IgA and IgG deposits in the mesangium. Eighty percent of patients are between 16 and 35 years of age. The male-female ratio is 6:1. Symptoms include recurrent bouts of hematuria (usually gross) after upper respiratory tract infections. The disease may be associated with dysuria and flank pain. The urinary protein excretion is usually more than 1 g/day. Renal function is usually normal, but a moderate percentage of individuals (40%) may progress to renal insufficiency. Poor prognostic signs include hypertension, renal insufficiency, and persistent proteinuria (protein excretion greater than 1 g/day). Serum IgA levels are elevated in 50% of patients. The diagnosis is made by characteristic history or renal biopsy. No treatment is available. Henoch-Schönlein purpura can cause similar renal lesions, but it is associated with nonthrombocytopenic vasculitic purpura, arthralgias, and abdominal pain. These two conditions may represent different parts of a similar pathogenic process.

Hereditary Nephritis (Alport Syndrome) and Polycystic Kidney Disease The adult form of polycystic kidney disease usually manifests in the second or third decade of life with hematuria and hypertension. It is an autosomal dominant disease. Familial nephritis in males often causes an early onset of renal insufficiency. The renal disease is often accompanied by abnormalities of the lens and retina and high-frequency hearing loss.

Benign Familial Hematuria This is a condition characterized by glomerular hematuria (RBC casts), nonprogressive renal disease, and normal renal function in many affected family members. It is often associated with thinning of the glomerular basement membrane. The inheritance is autosomal dominant. The diagnosis is suggested by (a) the presence of hemoglobin or RBC casts in the urine of the adolescent and in that of a parent or sibling, (b) absence of renal insufficiency in the patient, and (c) no history of renal failure or auditory abnormalities in the affected family members. The disease is more common in females.

WEB SITES

Proteinuria

For Teens and Parents

For Clinicians

Hematuria

For Teens and Parents

For Clinicians

REFERENCES AND ADDITIONAL READINGS

Proteinuria
Male Genital Examination

Inspection

1. Inspect pubic hair area. Note sexual maturity rating (Tanner stage) and local pathological conditions such as scabies, crabs, warts, or molluscum contagiosum.
2. Inspect groin and inner aspect of thighs: Note swelling from lymphadenopathy or hernias or the presence or absence of fungal or bacterial infection.
3. Inspect penile meatus: Check for presence of discharge, erythema, warts, or hypospadias.
4. Inspect prepuce: Check for phimosis.
5. Inspect penile glans: Check for redness (Candida infection, balanitis, contact dermatitis) or ulcerations (herpes, syphilis, trauma). It is best to have the patient pull back his own foreskin. It keeps his hands occupied and allows the examiner the use of both hands if needed. Male genital piercing is becoming more prevalent. Observe for signs of infection or contact dermatitis.
6. Inspect corona: Check for pink, pearly penile papules. These are normal small skin appendages located on the corona in as many as 15% of teenagers (Neinstein and Goldenring, 1984).
7. Inspect shaft: Check for ulcers or warts. Warts may be present in many more male adolescents than was originally suspected. Many of these cases can be detected only by close examination or with magnification and acetic acid staining. The warts turn white. However, current recommendations do not call for treatment of these nonexophytic warts.
8. Inspect scrotum: Check for redness, scabies, candidosis, folliculitis, or epidermal inclusion cysts.
9. Inspect testes: Check for gross enlargement (hydrocele, infection, tumor, hernia) or for gross asymmetry suggesting possible atrophy or cryptorchidism on one side.

Palpation

1. Palpate inguinal area: Check for lymphadenopathy or hernia.
2. Palpate testes: Check size, shape, and presence of tenderness or masses. The adult testes are about 4 to 5 cm long and 3 cm wide but vary from one person to another. Examine all parts of the testicle between the thumb and first two fingers. Testicular volume can be quantified with the use of an orchidometer. See Chapter 1 for testicular volumes at different pubertal stages.
3. Palpate epididymis: The epididymis lies on the posterior wall of the testes. It attaches at the upper part of the testicles and runs down the back of the testicles. The epididymis becomes the vas deferens and leaves the testicle as part of the spermatic cord. Tenderness and swelling in this area usually indicate epididymitis.
4. Palpate vas deferens: Check for varicocele. Occasionally a hydrocele of the cord is present.
5. Palpate the external inguinal ring while having the patient cough or strain to check for a hernia.

CRYPTORCHIDISM

Cryptorchidism refers to an undescended testis that cannot be drawn into the scrotum. The normal testicular descent occurs in the eighth month of gestation. If a testis cannot be drawn into the scrotum by the third or fourth month of life, there is little evidence to suggest that it will spontaneously descend later.
Epidemiology

The prevalence of cryptorchidism in newborn infants is 3.4%, decreasing to 0.7% by 9 months of age. This prevalence remains the same throughout childhood and adolescence.

Diagnosis

When a testis is not palpable in the scrotum, gentle massage should be performed along the line of descent from the anterosuperior spine, medially, and downward to the pubic tubercle. If the testis is not truly undescended, it should become palpable in the scrotum. If cryptorchidism is present, the teen should be examined for stigmata of associated disorders (i.e., Noonan, Klinefelter, or Kallmann syndrome or trisomy 13, 18, or 21).

Complications

Infertility Data suggest that potential fertility in the cryptorchid testis may be significantly impaired compared with normal testicular fertility, regardless of patient age at the time of discovery of the undescended testis. The fertility index of the descended mates of unilateral undescended testes may also be somewhat impaired in certain age groups. Fertility is significantly hampered in patients with bilateral cryptorchid testes if the condition is not corrected by 6 years of age.

Malignancy Five to twelve percent of all malignant testicular tumors occur in people with a history of an undescended testis. The relative risk of tumors in such individuals is increased about 10 to 40 times that of a male without cryptorchidism. Moreover, the risk is increased even if the testis is brought down into the scrotum.

In the United Kingdom Testicular Cancer Study (1994), a significant association of testicular cancer with undescended testis (odds ratio, 3.82; 95% confidence interval, 2.24 to 6.52) was found. In this study, the excess risk associated with undescended testis was eliminated in men who had had an orchidopexy before the age of 10 years.

Therapy

Therapy for cryptorchidism in teenagers should be corrective surgery. These teens should be aware of the increased risk of testicular cancer and should be taught testicular self-examination.

SCROTAL SWELLING AND MASSES

Evaluation

This section discusses the general approach to the adolescent with a scrotal mass or a painful scrotum (Fig. 29.1).


History

The adolescent should be questioned regarding the following:

1. Pain: Abrupt onset is suggestive of torsion; lack of pain suggests a tumor or cystic mass.
2. Trauma
3. Recent change in testicular size or scrotum
4. Sexual activity: Epididymitis in adolescence is usually sexually transmitted. However, it can be caused by urinary pathogens in males with or without genitourinary abnormalities.
5. Prior history of pain: Torsion is often preceded by episodes of mild pain.

Physical Examination

1. Inspect testes
   a. In torsion, the affected testis is often higher than on the contralateral side. With infections, the affected testis is often lower.
   b. In torsion, the affected testis and often the contralateral testis lie horizontally instead of in the usual vertical position, secondary to the congenital defect involved.
2. Carefully palpate the testicular surfaces, the epididymis and cord (posterior structures), and the head of the epididymis (lateral structure).
   a. Isolated swelling and tenderness of the epididymis suggests epididymitis.
   b. A tender, pea-sized swelling at the upper pole of the testis suggests torsion of the appendix testis.
   c. Generalized swelling and tenderness of both the testis and the epididymis can be found in either testicular torsion or epididymitis with orchitis.
   d. Presence of a cremasteric reflex makes torsion unlikely. However, it is often present in torsion of the appendix testis.
   e. Prehn sign: Lack of pain relief with elevation of the testis is not a reliable test for torsion.
   f. Nausea or vomiting with testicular pain is usually caused by torsion.
3. If a painless mass is present (Fig. 29.1):
   a. Palpate to assess location:
      • A mass associated with testis is more likely a tumor.
      • A mass unassociated with testis is less likely a tumor.
      • A "bag of worms" on left spermatic cord is probably a varicocele.
      • A mass located near the epididymis is probably a spermatocele or hydrocele.
      • A mass that is separate from the testis/epididymis, intensifies with straining (Valsalva), and is reducible is probably a hernia.
   b. Transilluminate the mass with a light source: clear transillumination suggests a hydrocele or spermatocele. Absence of transillumination suggests a testicular tumor or, if the mass is separate from the testis/epididymis, a hernia.

Laboratory Evaluation

1. Urinalysis: A urine dipstick test that is positive for leukocyte esterase or the presence of leukocytes on microscopy (especially if there are more than 20 white
blood cells per high-power field) is suggestive of epididymitis rather than torsion.

2. Gram stain: In cases of a painful scrotum and a history of urethritis or dysuria, a urethral Gram stain is helpful. Gram-negative diplococci suggest a gonococcal epididymitis. A negative Gram stain suggests either a chlamydial epididymitis, an orchitis, or torsion.

3. Color flow Doppler ultrasound and nuclear scans: In cases of a painful scrotum where torsion is suspected, a Doppler flow study, a nuclear scan, or both can be used in equivocal cases. Color Doppler and scintigraphy perform essentially the same role in demonstrating testicular torsion in males with painful scrotum. However, because of its greater specificity, scintigraphy may help if color Doppler ultrasound shows equivocal flow. In cases of torsion, the scan and Doppler study will show a decreased flow to the affected side.

It should be stressed that torsion is a surgical emergency. In cases of painful swelling of the testis, when the diagnosis of epididymitis is not clear and a nuclear scan or color Doppler study is not readily available, immediate urological consultation and exploratory surgery is indicated.

Differential Diagnosis

1. Painless scrotal mass or swelling (Fig. 29.2)


   a. Hydrocele
   b. Spermatocele
   c. Varicocele
   d. Hernia
   e. Testicular tumor
   f. Idiopathic scrotal edema

2. Painful scrotal mass or swelling
   a. Torsion of spermatic cord
   b. Torsion of appendix testis
   c. Epididymitis
   d. Orchitis
   e. Trauma resulting in hematoma
   f. Hernia—incarcerated
   g. Henoch-Schönlein syndrome
   h. Cellulitis or infected piercing
   i. Hymenoptera sting or insect bite

**TORSION**

**Etiology**

Normally the testes are covered anteriorly with a mesothelial structure, the tunica vaginalis. The posterior surface lies bare. In some males, the tunica vaginalis more completely surrounds the testes. This causes the testis to lie like a “bell clapper” in the scrotal cavity. With this deformity, a testis can twist on the spermatic cord, compromising circulation. Aside from torsion at the spermatic cord, appendages of the testes or of the epididymis can occasionally undergo torsion (Fig. 29.2A).

**Epidemiology**

Peak age prevalence is 12 to 18 years. The additional weight of the testes at puberty leads to increased prevalence at that time. The prevalence is increased tenfold in teens with an undescended testis.

**Clinical Manifestations**

1. Onset is usually abrupt and occasionally starts at night.
2. Fifty percent of teenagers have had brief prior episodes of scrotal pain.
3. Pain may be isolated to the scrotum or radiate to the abdomen.
4. Nausea and/or vomiting may occur.
5. Physical examination shows the following:
   a. The testis is tender and swollen.
   b. The affected side is often higher than the contralateral side because of the elevation from the twisted spermatic cord. The testis that undergoes torsion usually twists so that the anterior portion turns medially. In inflammatory conditions the affected side is often lower.
   c. The epididymis, if palpable, is often out of the usual posterolateral location.
   d. The affected testis and often the contralateral testis lie in a horizontal plane rather than in the normal vertical plane.
   e. The cremasteric reflex is absent.
   f. Fever and scrotal redness are usually absent.

**Diagnosis**

The diagnosis of torsion should be suspected in any adolescent with a painful swelling of the scrotum. As outlined previously, helpful points in diagnosis are acute onset of pain, nausea or vomiting, prior episodes of pain, lack of fever, lack of dysuria or urethral discharge, high-riding testis, horizontal position of testis, and decreased flow on scan or Doppler study (Table 29.1). Generalized swelling of the testes is also more suggestive of torsion, in that it occurs much more frequently in torsion than in epididymitis (77% versus 28%). A urology consultation is an urgent necessity for a teenager whose diagnosis is in question.
TABLE 29.1. Differential diagnosis of torsion

**Therapy**

Therapy involves immediate surgery. Saving testicular function depends on early surgical intervention. If surgery is performed within 6 hours after symptoms begin, recovery is the rule; if surgery is performed between 6 and 12 hours, 70% of patients have recovery of testicular function. If surgery is performed after 12 hours, the success rate falls to 20%.

**EPIDIDYMITIS**

**Etiology**

Epididymitis among sexually active males under 35 years of age is usually caused by *Chlamydia trachomatis* or *Neisseria gonorrhoeae*. Epididymitis by *Escherichia coli* or other bowel flora can be secondary to unprotected insertive anal intercourse. Non-sexually transmitted epididymitis may be secondary to gram-negative urinary tract infection in males older than 35 years of age, or it may be caused by instrumentation, surgery, catheterization, or anatomical abnormalities.

**Epidemiology**

1. Less common in prepubertal males
2. Less common in non-sexually active males and in those without a history of genitourinary tract abnormalities or unprotected insertive anal intercourse

**Diagnosis**

The diagnosis is suggested by the presentation of a sexually active teenager with subacute onset of epididymal swelling and tenderness, urethral discharge, dysuria, possibly fever, and pyuria (*Fig. 29.2B*). Swelling of the epididymis alone is more common with epididymitis than with torsion of the testes (59% versus 15%). The evaluation should include an examination of urine, Gram staining of an endourethral swab specimen, urine ligase chain reaction (LCR) or polymerase chain reaction (PCR) for gonorrhea and *Chlamydia*, and urine culture (as necessary). In the absence of a urethral discharge, leukocytes on a Gram-stained endourethral swab specimen (on microscopy) or urine dip for leukocyte esterase, or pyuria, an urgent urology consultation is called for. If one of the preceding tests shows abnormal findings but the teen has any risk factors suggesting torsion (i.e., prepubertal teen, non-sexually active teen, elevated or rotated testes, history of prior pain episodes, or acute onset with rapid progression), a nuclear scan or a color flow Doppler ultrasound should be performed. Orchitis can cause similar symptoms, but it usually occurs without dysuria or urethral discharge. Mumps infection is the most common cause. Mumps orchitis is usually unilateral and occasionally occurs without a history of parotitis. Other viruses (e.g., adenovirus, Coxsackie virus, ECHO virus, Epstein-Barr virus) may also cause orchitis, but with less frequency.

**Therapy**


1. Scrotal support, bed rest, and analgesics are an adjunct to antimicrobial therapy.
2. Ceftriaxone, 250 mg, is given intramuscularly once, and either doxycycline, 100 mg, is given orally twice a day for 10 days or tetracycline, 500 mg, is given four times a day for 10 days. Alternative regimens include erythromycin base, streptase, or ethylsuccinate in doses listed for uncomplicated chlamydial infections. For patients older than 18 years of age, or if the problem is thought to be caused by enteric organisms or the patient is allergic to ceftriaxone, alternative drugs are ofloxacin, 300 mg twice daily for 10 days, or levofloxacin 500 mg orally once a day for ten days.
3. Failure to improve within 3 days requires reevaluation.
4. Sexual partners should be treated.
5. In HIV/AIDS infection or for other immunocompromised states, therapy is the same except that fungal and mycobacterial infections are more common than in immunocompetent patients.

**TESTICULAR TUMORS**

**Etiology**

Most testicular neoplasias are of germ-cell origin and are malignant. In prepubertal males teratomas are most common, and after puberty seminomas are most common. Other testicular tumors include embryonal cell carcinomas, choriocarcinomas, Sertoli cell tumors, and Leydig cell tumors (*Fig. 29.2C*).

**Epidemiology**

1. Testicular tumors are the most common solid tumor in males age 15 to 35 years.
2. The incidence is 2.3 in 100,000 males.
3. The risk of a testicular tumor is increased 10 to 40 times in a teenager with a history of cryptorchidism.

**Diagnosis**

The diagnosis of tumor should be suspected in any male with a firm, painless mass associated with a testis, especially if the mass proves solid by transillumination or ultrasonography.

**Therapy**

Therapy involves a direct biopsy for confirmative diagnosis and cell type. Definitive therapy is beyond the scope of this book and involves a coordinated effort among the urologist, the primary care specialist, and the oncologist.

**HYDROCELE**

**Etiology**

Hydroceles arise through a defect in the processus vaginalis. The testis descends during the fetal period through a peritoneal sleeve called the processus vaginalis. If
Fig. 29.2D
Varicocele is common in the 10- to 20-year age group, with a prevalence of 5% to 15%. Eighty-five percent of varicoceles occur on the left side, and 15% are bilateral. A difference of more than 2 mL in testicular volume as noted on serial ultrasonic examinations should not be mistaken for an abnormality. The volume of the left testis is at least 3 mL less than that of the right. Testicular self-examination should be performed once a month. The response of either luteinizing hormone or follicle-stimulating hormone to gonadotropin-releasing hormone stimulation is supranormal.

Fig. 29.2E
Small varicocele should be gently rolled between the thumbs and fingers. Bilaterally palpable varicoceles are detected.

Be on the lookout for lumps, irregularities, change in size, or pain in the testicles. Examine each testicle with the fingers of both hands, using the index and middle fingers on the underside of the testicle and the thumbs on the top of the testicle. No therapy is indicated. A spermatocele is a painless, cystic mass containing sperm that is located in the upper portion of the epididymis (Fig. 29.2F). A definite statement about which adolescents need surgery cannot be made.

A varicocele occurs when the valves of the left internal spermatic vein are incompetent, allowing backflow from the testes to the abdomen. Varicoceles are detected in adolescents either on routine examination or secondary to a patient's discovery of more "stuff" filling one hemiscrotum than the other. Occasionally a patient complains of an ache or pain from the varicocele. On examination there is a "bag of worms" appearance above the testes. The distention usually decreases when the patient lies down. If there is no decrease in size of a varicocele in the supine position, an intravenous pyelogram is indicated to eliminate the possibility of intraabdominal disease.

Skoog et al. (1997) recommended surgery for patients with any of the following findings. A large, symptomatic varicocele is present.

1. Varicocele is common in the 10- to 20-year age group, with a prevalence of 5% to 15%.
2. Eighty-five percent of varicoceles occur on the left side, and 15% are bilateral.

Diagnosis
Varicoceles are detected in adolescents either on routine examination or secondary to a patient's discovery of more "stuff" filling one hemiscrotum than the other. Occasionally a patient complains of an ache or pain from the varicocele. On examination there is a "bag of worms" appearance above the testes. The distention usually decreases when the patient lies down. If there is no decrease in size of a varicocele in the supine position, an intravenous pyelogram is indicated to eliminate the possibility of intraabdominal disease.

Therapy
Several recommendations have been suggested as indications for varicocele repair, although this area is still unresolved, particularly as it pertains to fertility. Kass and Reitelman (1995) recommended varicocele repair in adolescents when

1. The results of semen analysis are abnormal.
2. The volume of the left testis is at least 3 mL less than that of the right.
3. The response of either luteinizing hormone or follicle-stimulating hormone to gonadotropin-releasing hormone stimulation is supranormal.
4. Bilaterally palpable varicoceles are detected.
5. A large, symptomatic varicocele is present.

Skoog et al. (1997) recommended surgery for patients with any of the following findings.

1. A difference of more than 2 mL in testicular volume as noted on serial ultrasonic examinations
2. A testicular size that is smaller by two standard deviations when compared with normal testicular growth curves.
3. Scrotal pain

The earlier in life the varicocele appears, the higher the risk of testicular growth arrest; varicocelectomy during adolescence usually results in "catch-up growth" of the involved testis. Left testicular hypertrophy can also occur after surgery. Although varicoceles may cause a progressive loss of fertility during the reproductive years, more than 80% of men with varicoceles are fertile. Although a preponderance of the literature supports a favorable effect of varicocelectomy on fertility, several recent articles have questioned whether there is any such effect. Silber (2000) provided a cogent review of the evidence for and against varicocele repair to increase fertility. A definitive statement about which adolescents need surgery cannot be made.

There are a variety of surgical techniques in addition to nonsurgical embolization and sclerotherapies. A review of the various techniques is beyond the scope of this chapter. However, the bibliography contains several articles addressing this subject.

SPERMATOCELE
A spermatocele is a painless, cystic mass containing sperm that is located in the upper portion of the epididymis (Fig. 29.2F). It is usually felt as a smooth, cystic sac located above and posterior to the testis. No therapy is indicated.

TESTICULAR SELF-EXAMINATION
Although females are commonly taught to self-examine their breasts, males are rarely taught testicular self-examination. In a study of young adult males, only 10% had been taught testicular self-examination (Goldenring and Purfell, 1984). Yet testicular cancer is the most common solid tumor in young adults. The recommendations for self-examination by the American Cancer Society are as follows:

1. Examine the testes during or after a hot bath or shower.
2. Examine each testicle with the fingers of both hands, using the index and middle fingers on the underside of the testicle and the thumbs on the top of the testicle.
3. Gently roll the testicle between the thumbs and fingers.
4. Be on the lookout for lumps, abnormalities, changes in size, or pain in the testicles.
5. The epididymis should not be mistaken for an abnormality.
6. If any abnormality such as a lump is found, it should be reported immediately.
7. Testicular self-examination should be performed once a month.

WEB SITES
For Teenagers and Parents
http://my.webmd.com/content/asset/adam_disease_testicular_torsion. Testicular torsion.
http://my.webmd.com/content/asset/adam_disease_epididymitis. Epididymitis.
INFECTIOUS MONONUCLEOSIS

Infectious mononucleosis (IM) commonly occurs during adolescence or young adulthood. It is usually an acute, self-limited, benign, lymphoproliferative disease caused by Epstein-Barr virus (EBV). Although EBV is responsible for IM in approximately 90% of cases, the syndrome can also be caused by other agents such as cytomegalovirus (CMV), toxoplasmosis, hepatitis A or B, or adenovirus. EBV is usually contracted through saliva and replicates in the lymphoreticular system, where it provokes an intense immunological response frequently involving lymph nodes, spleen, liver, and bone marrow. This immune response results in the clinical symptomatology.

Etiology

In 1968 EBV was identified as the cause of IM. EBV is a member of the herpesvirus family and is ubiquitous in humans. Worldwide, most EBV infections occur in young children and cause no clinical symptoms. When infection occurs in teenagers and young adults, it is more likely to be symptomatic, causing the mononucleosis syndrome. Humans are the only known reservoir for EBV, and transmission requires contact with oropharyngeal secretions. Studies indicate that B cells in the oropharynx may be the site of primary infection. These cells then disseminate the infection throughout the lymphoreticular system. During this time there is a polyclonal B-cell proliferation and a vigorous T-cell response. In reaction to infected and transformed B cells, atypical lymphocytes appear in the peripheral blood. These atypical cells represent primarily an expansion of the T-cell series, mainly cytotoxic or suppressor (CD8) cells. It is the increase in reactive T cells and infected B cells that causes hepatomegaly and splenomegaly. The time from initial acquisition of the virus to the appearance of large numbers of infected B cells in the peripheral circulation and symptoms is usually 30 to 50 days.

The immune response to EBV infection also leads to the formation of non–EBV-specific antibodies (heterophil antibodies) in addition to responses directed at several EBV-specific antigens. However, the major factor in controlling EBV and preventing EBV-induced lymphoproliferative disorders is a strong cellular immune response.

During an acute infection, about 0.001% to 0.01% of circulating B cells are infected. Over 3 to 4 months, this declines to 0.00001%, which persists indefinitely. The EBV persists for life in both the B cells and salivary glands. About 70% to 90% of individuals shed virus until 8 to 24 weeks after resolution of the clinical disease. After this, 60% to 100% of normal asymptomatic EBV seropositive individuals shed virus intermittently.

Epidemiology

More than 90% of all humans are eventually infected with EBV. One study in the United States revealed the incidence to be 45.2 cases per 100,000 population per year, with the highest rate in the 15- to 24-year-old group. Up to 20% of asymptomatic adults in the United States may have EBV present in oropharyngeal secretions.

1. Age
   a. Developing countries: In developing countries, tropical areas, and other areas, including areas of high population density in the United States, infection usually occurs early in life and is usually inapparent. Under these circumstances, most children (more than 90%) seroconvert by the age of 6 years.
   b. Western Europe and the United States: Only 35% to 50% of children are seropositive by 5 years of age. A large group of adolescents and college-aged youth lack immunity. Therefore, infections are quite common among high school and college students. As many as 12% of susceptible college freshman become infected with EBV during their first year of college. The rate in adolescents is approximately 350 cases per 100,000, which is eight times the overall rate in the population. Between 25% and 75% of infected students develop clinical IM. Prevalence in Western Europe and the United States peaks about 2 years earlier in girls (at 16 years of age, compared with 18 years in boys).
2. Gender: The prevalence is equal in girls and boys.
3. Race: EBV-associated mononucleosis syndrome is more prevalent among whites than among blacks in the United States. This is probably a reflection of earlier subclinical infection in blacks related to a higher proportion living in areas of high population density.
4. Season: There is no seasonal variation, except an increase in spring and fall among college students.
5. Contagiousness: Saliva is the main vehicle for transmission of EBV. Transmission requires direct and prolonged contact with infected secretions. Kissing is an important modality of transmission in adolescents and young adults. IM does not occur in epidemics, because EBV has a low contagiousness in young adult populations and requires close personal contact. In families, about 10% to 40% of susceptible members will develop an EBV infection when exposed. EBV has also been found in the genital tracts of men and women. The role of this site in transmission is not yet defined; however, the possibility of sexual transmission exists.

Clinical Manifestations

The majority of EBV infections are either asymptomatic or associated with mild, nonspecific symptoms such as malaise, fever and chills, and anorexia. Even in adolescents, where classic IM is common, a significant proportion of EBV infections are subclinical.

The traditional hallmarks of IM include the triad of...
• Fever, lymph node enlargement, and tonsillopharyngitis (present in more than 50% of cases)
• Lymphocytosis with atypical lymphocytes
• Typical antibody response with presence of heterophil antibodies or EBV-specific antibodies

The incubation period is 30 to 50 days. The prodromal period—3 to 5 days of malaise, headache, anorexia, myalgia, and fatigue—is often followed by more severe symptoms and signs.

**Signs and Symptoms** The common presentation includes fever, which may persist for several weeks. A prominent symptom is sore throat, which can be severe, including an exudative pharyngitis in up to 50% of individuals. Palatal petechiae may also be seen in the throat. Periorbital or facial edema occurs in about 25% of affected teens. Adenopathy is usually significant and is most commonly symmetrical, with posterior cervical nodes more prominent than anterior ones. Palpable splenomegaly may occur by the second week of illness, with hepatomegaly being less common. About 10% of individuals have a rash that may be either erythematous, maculopapular, morbilliform, urticarial, or erythema multiforme in appearance. Approximately 90% of patients receiving ampicillin or amoxicillin develop an erythematous maculopapular rash, which typically does not appear until about 1 week after antibiotic therapy is begun.

### Signs

<table>
<thead>
<tr>
<th>Signs</th>
<th>Prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymphadenopathy</td>
<td>93–100</td>
</tr>
<tr>
<td>Fever</td>
<td>80–100</td>
</tr>
<tr>
<td>Tonsillopharyngitis</td>
<td>69–91</td>
</tr>
<tr>
<td>Palpable splenomegaly</td>
<td>50–60</td>
</tr>
<tr>
<td>Hepatomegaly</td>
<td>15–25</td>
</tr>
<tr>
<td>Palatal petechiae</td>
<td>25–35 (at junction of hard and soft palates)</td>
</tr>
<tr>
<td>Periorbital edema</td>
<td>25–35</td>
</tr>
<tr>
<td>Liver or splenic tenderness</td>
<td>15–30</td>
</tr>
<tr>
<td>Jaundice</td>
<td>5–10</td>
</tr>
<tr>
<td>Rash (usually maculopapular)</td>
<td>3–15 (increased if adolescent receives ampicillin or amoxicillin)</td>
</tr>
<tr>
<td>Pneumonitis</td>
<td>&lt;3</td>
</tr>
</tbody>
</table>

### Symptoms

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sore throat</td>
<td>70–80</td>
</tr>
<tr>
<td>Malaise</td>
<td>50–90</td>
</tr>
<tr>
<td>Anorexia</td>
<td>50–80</td>
</tr>
<tr>
<td>Nausea</td>
<td>50–70</td>
</tr>
<tr>
<td>Headache</td>
<td>40–70</td>
</tr>
<tr>
<td>Myalgia</td>
<td>12–30</td>
</tr>
<tr>
<td>Cough</td>
<td>5–15</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>2–14</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>5–10</td>
</tr>
<tr>
<td>Photophobia</td>
<td>5–10</td>
</tr>
</tbody>
</table>

### Patterns of Presentation

Adolescents and young adults often present with one of three clinical forms:

1. Pharyngeal form (anginose syndrome): The hallmark is an exudative tonsillitis with marked pharyngeal edema. Usually, the tonsillitis has an abrupt onset and is accompanied by a high fever. The resolution in many cases tends to be rapid, within 5 to 7 days. Sometimes these individuals are difficult to differentiate from those infected with group A b-hemolytic streptococcal infections, especially because EBV and streptococcal infections frequently coexist.

2. Glandular form: The adenopathy is prominent and out of proportion to other symptoms, such as pharyngitis and fever, which are generally mild.

3. Febrile, systemic, or typhoidal form: Prolonged fever and malaise without significant pharyngitis predominates. Lymphadenopathy occurs later in the illness. Anorexia, nausea, and vomiting may be severe.

### Recovery

Almost all persons with primary EBV infection recover without problems and develop a significant degree of long-lasting immunity. The symptoms usually begin to subside within 7 days after onset, and they resolve over the following several weeks, although fatigue may persist longer.

### Complications

Sometimes a complication of IM is the prominent clinical manifestation of the disease, and the classical symptoms either never appear or appear later in the course. Overall, the complication rate is about 1% to 2%.

#### Complication

<table>
<thead>
<tr>
<th>Complication</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neuronal</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Seizures</td>
<td></td>
</tr>
<tr>
<td>Facial or peripheral nerve palsies</td>
<td></td>
</tr>
<tr>
<td>Meningoencephalitis</td>
<td></td>
</tr>
<tr>
<td>Aseptic meningitis</td>
<td></td>
</tr>
<tr>
<td>Optic neuropathy</td>
<td></td>
</tr>
<tr>
<td>Reye syndrome</td>
<td></td>
</tr>
<tr>
<td>Coma</td>
<td></td>
</tr>
<tr>
<td>Brachial plexus neuropathy</td>
<td></td>
</tr>
<tr>
<td>Transverse myelitis</td>
<td></td>
</tr>
<tr>
<td>Guillain-Barré syndrome</td>
<td></td>
</tr>
<tr>
<td>Acute psychosis</td>
<td></td>
</tr>
<tr>
<td>Acute cerebellar ataxia</td>
<td></td>
</tr>
<tr>
<td>Hematological</td>
<td></td>
</tr>
<tr>
<td>Autoimmune hemolytic anemia (mild)</td>
<td>0.5–3%</td>
</tr>
<tr>
<td>Thrombocytopenia purpura</td>
<td>Rare</td>
</tr>
<tr>
<td>Coagulopathy</td>
<td>Rare</td>
</tr>
<tr>
<td>Aplastic anemia</td>
<td>Rare</td>
</tr>
<tr>
<td>Hemolytic-uremic syndrome</td>
<td>Rare</td>
</tr>
<tr>
<td>Eosinophilia</td>
<td>Rare</td>
</tr>
<tr>
<td>Profound thrombocytopenia</td>
<td>Rare (mild thrombocytopenia is common)</td>
</tr>
<tr>
<td>Cardiac</td>
<td>1.7–6%</td>
</tr>
<tr>
<td>Pericarditis</td>
<td></td>
</tr>
<tr>
<td>Myocarditis</td>
<td></td>
</tr>
<tr>
<td>Electrocadiogram changes (non-specific ST and T wave abnormalities)</td>
<td></td>
</tr>
<tr>
<td>Splenic rupture</td>
<td>0.5% (90% are male)</td>
</tr>
<tr>
<td>Pulmonary</td>
<td></td>
</tr>
</tbody>
</table>
### Heterophil Antibodies

#### Laboratory Diagnosis

**Hematological Abnormalities** The dramatically distinctive findings with IM are hematological. In general, there is an elevation of the white blood cell count in the range of 10,000 to 20,000/mm³. Lymphocytosis is usually seen, with more than 50% of the leukocytes being lymphocytes. This occurs secondary to the EBV activation of B lymphocytes, which causes a proliferation of T lymphocytes. In addition, at least 10% of the lymphocytes are atypical lymphocytes; they appear similar to large lymphoblasts with a vacuolated basophilic cytoplasm. The atypical lymphocytes are either EBV-transformed B lymphocytes or usually activated suppressor or cytotoxic (CD8) T lymphocytes. These atypical lymphocytes can be seen in other viral infections such as CMV, human immunodeficiency virus (HIV), acute viral hepatitis, rubella, mumps, rubeola, and toxoplasmosis, but they do not comprise more than 10% of the total leukocyte count except with EBV, CMV, and toxoplasmosis.

Other common hematological abnormalities include a mild granulocytopenia and thrombocytopenia (usually in the range of 100,000 to 140,000/mm³). Anemia is unusual. Evidence of a mild hepatitis is present in about 90% of individuals, including elevations in aminotransferases, alkaline phosphatase, and lactate dehydrogenase (LDH; about 2 to 3 times normal). Serum bilirubin is usually only in the range of 1 to 3 mg/dL. Entirely normal findings from liver chemistries may suggest a diagnosis other than primary EBV infection. The frequency of hematological findings includes the following:

<table>
<thead>
<tr>
<th>Test</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymphocytosis</td>
<td>95%</td>
</tr>
<tr>
<td>Atypical lymphocytosis</td>
<td>95%</td>
</tr>
<tr>
<td>Elevated liver function test results</td>
<td>60%–90%</td>
</tr>
<tr>
<td>Hypergammaglobulinemia</td>
<td>80%</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>50%</td>
</tr>
<tr>
<td>Elevated bilirubin levels</td>
<td>40%</td>
</tr>
<tr>
<td>Cold agglutinins</td>
<td>30%–80%</td>
</tr>
</tbody>
</table>

#### Specific Complications

1. **Splenic rupture**

   a. Frequency: About 0.5% of cases

   b. Presentation: Typically there is a sudden pain in the left upper quadrant that radiates to the top of the left shoulder; however, the onset may be insidious. Splenic rupture often occurs between the 4th and 21st day of symptomatic illness, with about 50% of cases occurring during the height of acute illness and the other half in the early convalescent period. On occasion, splenic rupture is the first symptom of IM. Fewer than half of patients with splenic rupture had clinically apparent splenomegaly noted before the rupture. The majority of cases are also unrelated to a history of significant strain or trauma. Because of the frequency of splenomegaly (documented in almost 100% of patients by ultrasonography), caution should be taken when palpating the spleen, and contact sports should be eliminated for a minimum of 4 weeks. Ultrasound may be prudent before the adolescent is allowed to return to sports such as football or hockey. Fatality is rare from this complication.

2. **Airway obstruction**: An uncommon but life-threatening complication of IM related to massive lymphoid hyperplasia and mucosal edema. This tends to be more common in younger teens and typically occurs about 1 week after initial symptoms begin. Corticosteroids have been used in an attempt to reduce the edema and hypertrophy of lymphoid tissue. If needed, tracheostomy or intubation can be performed.

3. **Streptococcal pharyngitis**: Coinfection is relatively common and may occur in approximately 25% of patients.

#### Serological Features

**Heterophil Antibodies**

The classical test for EBV-associated IM is the presence of heterophil antibodies. These tests detect immunoglobulin M (IgM) antibodies induced by EBV infections that cross-react with phylogenetically unrelated antigens (such as horse, sheep, or bovine erythrocytes). Although the presence of heterophil antibody is the hallmark of IM, it can be found in normal human serum in low titer, as well as in higher titer in individuals with malignant disease, serum sickness, or any of several other viral infections. In addition, some patients with IM, especially children, are heterophil negative.

To differentiate heterophil antibodies present during IM from those in normal serum or serum sickness, a preabsorption is performed with either guinea pig kidney or horse RBCs. Heterophil antibodies associate with IM agglutinate sheep and horse RBCs after preabsorption with guinea pig kidney, but not after preabsorption with bovine RBCs. This differential response was used in forming the heterophil screening tests for IM, such as the Monospot and other slide and card tests. The tests are rapid, simple, and inexpensive. Tests such as the Monospot are highly sensitive (96% to 99%) in adolescents and young adults.

Heterophil antibodies are detected during the first week of clinical infection (about 70% of individuals) but are maximal during the second and third weeks (85% to 95%). Delayed appearance may predict a longer convalescence. However, even among adolescents and young adults with EBV infection and classic IM, not all will develop heterophil antibodies, and those that do will not be Monospot negative. This even more commonly occurs in infants and young children. In children younger than 3 years old, the test results are rarely positive; in 3- to 8-year-olds the test results are positive in 50% of cases. Positivity for heterophil antibodies remains for weeks to months after an acute infection. In general, sheep and beef agglutination test results remain positive for about 3 to 6 months, and horse agglutination test results remain positive up to 18 months.
If EBV is suspected and the heterophil test results are negative, EBV-specific antibody tests can be performed.

**Specific Epstein-Barr Virus Antibodies**

Antibody responses to several EBV antigens have been well studied. These include viral capsid antigen (VCA), early antigen (EA), and Epstein-Barr nuclear antigen (EBNA). Currently, these are usually measured by direct immunofluorescence; newer enzyme immunoassay techniques are being evaluated. Enzyme-linked immunosorbent assay (ELISA) techniques may eventually replace the indirect immunofluorescence tests. Figure 30.1 shows the characteristic EBV antibody responses to various EBV antigens. Table 30.1 shows the pattern of serologic results in various EBV stages.

**FIG. 30.1.** The evolution of antibodies to various EBV antigens in patients with infectious mononucleosis is shown above. The titers are geometric mean values expressed as reciprocals of the serum dilution. IgM and IgG antibody responses to EBV capsid antigen develop during the acute phase, as does an IgG response to EBV early antigen in most cases. The IgG response lasts for life, but the IgM response is transient and is shortest in very young children. Antibody response to nuclear antigen lasts for life and is typically quite late in onset. (From Sumaya CV. Epstein-Barr serologic testing: diagnostic indications and interpretations. *Pediatr Infect Dis* 1986;5:337–342.)

**TABLE 30.1.** Patterns of serology

1. Viral capsid antigen: Antibodies against VCA are composed of both IgG and IgM. Antibody levels for both peak at about 3 to 4 weeks after the clinical onset of the disease. IgM declines rapidly and is undetectable by 3 months. IgG declines somewhat with time but persists for life. High persistent levels of IgG antibodies against VCA can indicate any of the following: remote EBV infection, systemic lupus, chronic renal failure, Burkitt lymphoma or nasopharyngeal carcinoma, leukemia, sarcoidosis, cancer, acquired immunodeficiency syndrome (AIDS), Hodgkin lymphoma, lymphoma, rheumatoid arthritis, immunodeficiency state.

2. Early antigen: Antibodies against EA are induced in 70% to 90% of individuals with acute EBV IM. The antibodies are produced very early in the infection and usually persist for 8 to 12 weeks. However, as many as 30% of individuals with past infections have positive titers for EA. These antibodies have been divided into two patterns of staining (diffuse and restricted). Most adolescents and young adults with IM have antibodies against the D (diffuse) component.

3. Nuclear antigen: Antibodies against EBNA develop 2 to 3 months after the onset of infection and tend to persist indefinitely. Positive titers usually indicate an infection at least 1 to 2 months in the past. Absent EBNA titers in patients with an EBV infection are associated with immunodeficiency states and rheumatoid arthritis.

4. Diagnosis: Acute EBV IM syndrome is characterized (Table 30.1) by the presence of both IgM and IgG VCA and EA antibodies. Older and remote infections are characterized by the absence of IgM VCA antibodies and the appearance of IgG EBNA antibodies.

5. EBV serology is best reserved for measurement in adolescents when (a) clinical IM is present and a heterophil test result is negative or (b) clinical syndromes such as thrombocytopenia, pneumonia, or neurological findings are present and the physician wishes to exclude the diagnosis of acute EBV disease.

**Differential Diagnosis**

1. Causes of EBV-negative mononucleosis-like syndrome
   a. CMV
   b. Toxoplasma gondii
   c. Rubella
   d. Adenovirus
   e. Herpes simplex virus 6
   f. Drug side effects
   g. Acute HIV infection: Primary HIV-1 infection can present clinically as the abrupt onset of a febrile illness resembling acute mononucleosis. The symptoms coincide with high titers of culturable plasma viremia and antigenemia (HIV-1 p24 antigen), which rapidly decrease with the emergence of detectable HIV-specific antibody and HIV-specific cytotoxic lymphocytes.

2. Other considerations
   a. Group A b-hemolytic streptococcal pharyngitis
   b. Viral tonsillitis
   c. Mycoplasma pneumoniae
   d. Vincent angina
   e. Diphtheria
   f. Viral hepatitis
   g. Lymphoproliferative disorder or leukemia

**Diagnosis**

The diagnosis is based on the following considerations.

1. Clinical symptoms: IM should be suspected in an adolescent with fatigue, fever, spleno- megaly, adenopathy, and pharyngitis.
2. Abnormal white blood cell count: Patients will usually have the following:
   a. Relative lymphocytosis greater than 50%.
   b. Absolute lymphocytosis greater than 4,000 cells per milliliter.
c. Atypical mononuclear cell counts greater than 10% to 20% of the white blood cell count differential.

3. Positive serology: Almost all adolescents with IM have positive heterophile antibodies. If a patient continues to be symptomatic and heterophile antibodies are negative, titers for EBV (including VCA and EBNA) should be evaluated.

4. A throat culture is indicated in patients with pharyngitis or tonsillitis.

**Chronic Epstein-Barr Virus Infections**

In the vast majority of individuals lifelong significant immunity to EBV develops. There are rare individuals who have very high titers of EBV antibodies and have chronic persistent active EBV infection. This disorder has three features: severe illness lasting longer than 6 months; histological evidence of end-organ disease such as hepatitis, ulcers or pneumonitis; and EBV antigen or DNA in tissue. However, there is little evidence that EBV causes the chronic fatigue syndrome (see Chapter 35). EBV infections can also be associated with specific lymphoproliferative disorders in individuals with underlying abnormal immune responses. These include the virus-associated hemophagocytic syndrome (generalized histiocytic proliferation and hemophagocytosis), lymphomatoid granulomatosis, and the X-linked lymphoproliferative syndrome (XLP), in which affected males die of EBV disease, sometimes in a matter of days. When EBV leaves the latent state and becomes chronically active, it can have a potential to trigger malignancies. Such EBV-associated malignancies include Burkitt lymphoma, central nervous system lymphomas, nasopharyngeal carcinoma, and Hodgkin disease.

Patients with AIDS have a 10- to 20-fold increase in circulatory EBV-infected B cells compared with persons without HIV infection. In patients with AIDS, EBV DNA has been detected in oral hairy leukoplasia, lymphoid interstitial pneumonitis, and non-Hodgkin lymphomas.

**Management**

Only supportive therapy is needed for most patients with IM.

1. Symptomatic care
   a. Rest as needed by the adolescent in the acute phase: Teens and parents should be aware that the acute symptoms usually resolve over 1 to 2 weeks with fatigue lasting 2 to 4 weeks and sometimes longer.
   b. Administer analgesics for fever, arthralgias, and pharyngitis.

2. Antibiotics: In general, antibiotics serve no purpose. If a secondary group A b-hemolytic streptococcal infection or *M. pneumoniae* infection occurs, then appropriate antibiotics are indicated, but amoxicillin or amoxicillin with clavulanic acid specifically should be avoided. Azithromycin does decrease viral shedding, but it has not proved effective in shortening the length or severity of illness.

3. Athletic activity
   a. Teens uninvolved in contact or strenuous sports: Light, nonimpact activities can be resumed after 21 days of illness if the teen feels ready. Full participation can be resumed about 1 month after onset of symptoms.
   b. Teens involved in strenuous training or contact sports: Easy training can be performed early as energy level dictates, but full participation in contact sports should be delayed at least 4 to 6 weeks. If there is a question of continued splenic enlargement, ultrasound could be used to assess and monitor splenomegaly in these athletes.

4. Steroids: Steroids may be needed if hemolysis, cardiac involvement, thrombocytopenia, airway obstruction, or neurological sequelae are life-threatening. Steroids may also be considered for massive splenomegaly.

**MYCOPLASMA PNEUMONIA**

*M. pneumoniae* is a common cause of upper respiratory infections and pneumonias in adolescents.

**Etiology**

Mycoplasma are the smallest free-living microorganisms; they are approximately the same size as large viruses (100 nm). More than 50 species have been identified, including 10 in humans, of which 3 have proved to be pathogenic: *M. pneumoniae*, Mycoplasma hominis, and Ureaplasma urealyticum. These organisms have no cell walls and therefore are resistant to b-lactam antimicrobials. The recent sequencing of the entire *M. pneumoniae* genome helps support the hypothesis that mycoplasmas evolved from gram-positive bacteria.

**Epidemiology**

1. *M. pneumoniae* infections are responsible for 20% to 50% of pneumonias in teenagers and young adults.
2. Spread is by direct interpersonal contact or by inhalation of large aerosolized secretions.
3. Epidemics tend to occur in fall and winter and frequently in 4- to 5-year cycles.
4. Epidemic spread is common among families, recruits in army bases, fraternities, and others in close surroundings.
5. The incubation period is 1 to 3 weeks.
6. Risk of infection in other family members if one member is infected is about 65%.

**Pathophysiology**

By means of attachment proteins, *M. pneumoniae* adheres to ciliated respiratory epithelium, causing cellular damage to the trachea, bronchi, and bronchioles. The organism also causes ciliostasis, which may lead to prolonged cough. A variety of mechanisms have been suggested to explain the extrapulmonary complications, including metastatic infection, autoantibodies and immune complexes, toxin production, hypercoagulability, and altered host immunity.

**Clinical Manifestations**

*M. pneumoniae* causes an influenza-like respiratory illness with malaise, fever, and headache and usually causes upper respiratory tract and pulmonary infections. Symptoms are often of gradual onset and progressive from upper to lower respiratory tract. The majority of *M. pneumoniae* infections involve the upper respiratory tract. These can vary from mild infections with or without pharyngitis to severe bronchitis. Rarely is there associated rhinorrhea or otitis media. The progression from early symptoms to pneumonia takes 6 to 10 days. Postinfectious bronchitis may last many weeks. Nonetheless, the infection is usually mild and lasts between 2 and 4 weeks without treatment. Antibiotics can shorten disease length. Asthma and cigarette smoking may be predisposing risk factors.

1. Symptoms
   a. General: Malaise, fever, chills, and headache occur early in the course.
   b. Respiratory
      • A cough develops 3 to 5 days after the onset. It usually starts as a nonproductive cough and may lead to the production of frothy white sputum. Sputum production is not as copious as in more typical bacterial pneumonias. The cough may become paroxysmal. Occasionally, chest pain and hemoptysis occur.
      • Coryza is unusual.
      • It may lead to reactive airway disease in susceptible individuals, who also may be more prone to pneumonia.
      • Bilateral bullous myringitis is highly suggestive but is rare.
      • Dyspnea.
   c. Gastrointestinal: Nausea, vomiting, and diarrhea may occur.

2. Signs
   a. Pharyngitis: 75%.
   b. Conjunctivitis: 50%.
   c. Lymphadenopathy: 25% to 50%.
   d. Chest: Lung findings are often minimal. If pneumonia is present, there may be isolated crackles or areas of wheezing over one or both of the lower lobes.
Complications
Nonrespiratory infections and complications usually occur 1 to 21 days after initial symptoms. One must use caution in the diagnosis of an *M. pneumoniae* infection in individuals with extrapulmonary manifestations and no respiratory tract symptoms.

1. Musculoskeletal: Arthralgias, myalgias, arthritis, rhabdomyolysis. The arthritis is usually monoarticular or migratory and polyarticular.
2. Gastrointestinal: Gastroenteritis, hepatitis, pancreatitis
3. Dermatological: Most common are erythematous maculopapular lesions or vesicular exanthemas. Other rashes include vesicular-pustular, petechial, and urticarial. Stevens-Johnson syndrome can occur.
4. Hematological: Hemolytic anemia, splenomegaly, thrombocytopenia, disseminated intravascular coagulopathy
5. Cardiovascular: Myocarditis, pericarditis, heart block, congestive heart failure, acute myocardial infarction
6. Central nervous system: Meningitis, Guillain-Barré syndrome, cranial nerve involvement, sensorineural hearing loss, transverse myelitis, focal encephalitis, cerebellar involvement, psychosis
7. Renal: Acute glomerulonephritis, interstitial nephritis
8. Ophthalmologic: conjunctivitis, anterior uveitis, optic neuritis, rarely optic neuropathy

Laboratory Evaluation
1. White blood cell count: Occasionally, leukocytosis is present. If the count is very elevated, consider superinfection.
2. Chest x-ray examination: Variable, may show a lobar or segmental infiltrate (lower lobes in 90% of patients). A reticular or interstitial infiltrate is often present, and occasionally a pleural effusion occurs. Major consolidation is rare. The radiographic findings often appear worse than the clinical findings.
3. Sputum Gram stain: Polymorphonuclear cells without dominant bacterial morphotypes
4. Cold agglutinins: Cold agglutinins are elevated to a titer of greater than 1:32 in 75% of cases. This test is nonspecific, and cold agglutinins may be elevated in patients with viral infections or some noninfectious diseases such as hemolytic anemias. For patients younger than 12 years, cold agglutinins are insensitive and nonspecific.
5. Antibody titers: Both complement fixation titers and enzyme immunoassay (EIA) tests are available. A fourfold increase in titer is highly suggestive of a recent infection. Acute and convalescent serum will capture most cases, but acute serum alone will miss most cases.
6. Cultures: Cultures require about 3 weeks and therefore are too slow to be of clinical use.
7. Polymerase chain reaction (PCR)-based assay for *M. pneumoniae*, where available, is fast, sensitive, and specific.

Differential Diagnosis
1. Streptococcus pneumoniae
2. Viral pneumonia, including adenovirus, parainfluenza, and influenza
3. Chlamydia pneumoniae: Another relatively common, more recently discovered cause of pneumonia in adolescents and young adults. Seroprevalence studies in adult populations around the world suggest that more than 40% of adults have been previously infected. Clinical symptoms usually start with hoarseness and fever; respiratory tract symptoms may not appear for days. Infection with *C. pneumoniae* can trigger acute episodes of wheezing in children with asthma.
4. Legionella pneumonia: Accounts for about 1% to 3% of community-acquired pneumonias and up to one fourth of “atypical” community-acquired pneumonias.
5. Pneumococcal pneumonia: Diagnosis is based on serologic testing, but specific testing for *C. pneumoniae* is hard to obtain and requires acute and convalescent sera. Culture is more difficult than for *C. trachomatis*, and direct detection does not appear to work well. Treatment is with erythromycin, tetracycline, doxycycline, or azithromycin. Some authorities prefer doxycycline or tetracycline if *C. pneumoniae* is the suspected cause of a pneumonia.
6. Mycoplasma pneumoniae: Accounts for about 1% to 3% of community-acquired pneumonias and up to one fourth of “atypical” community-acquired pneumonias. Mycoplasmic illness usually begins abruptly with malaise, headache, myalgia, and weakness. About 24 hours later, a high fever develops in more than half of infected individuals. Nonproductive cough is most common. Other symptoms include pleuritic chest pain, dyspnea, diarrhea, nausea, vomiting, and abdominal pain. Physical findings are mild compared with the radiographical findings. Complications may include lung abscess, hypotension, rhabdomyolysis, disseminated intravascular coagulation, thrombotic thrombocytopenic purpura, and renal failure. Other extrapulmonary infections related to bacteremia include pericarditis, myocarditis, pyelonephritis, pancreatitis, sinusitis, and abscesses.

Diagnosis
The diagnosis of *Mycoplasma* infection involves a compatible symptom complex and a suspicion of the organism. Cold agglutinin test results are positive in 72% to 92% of patients with pneumonia after the first 1 to 2 weeks. The test is nonspecific but can be performed quickly, even at the teen’s bedside. To perform the rapid test, add about 0.3 to 0.4 mL of blood to a standard laboratory collection tube containing 3.8% sodium citrate (blue-stoppered Protime [PT] tube). Place the tube in ice water for 15 to 30 minutes. Tilt on one side and examine for agglutination. The presence of coarse, floccular agglutination is a positive test sign that correlates with a cold agglutinin titer of more than 1:64. About 66% to 85% of patients with a positive cold agglutinin test result have *M. pneumoniae* infection. Complement fixation titers are more specific but require demonstration of a fourfold rise or fall in titer. ELISA techniques are becoming more commonly available to detect IgG and IgM antibodies. Direct tests for the bacterial genome are becoming available with the use of PCR techniques. PCR will probably become the diagnostic test of choice once it becomes more widely available.

Therapy
1. Antibiotics: Tetracycline 500 mg four times a day or erythromycin 500 mg four times a day; use either drug for 10 days. Azithromycin, clarithromycin, and doxycycline are also effective. b-Lactam antibiotics are not effective.
2. Rest, decreased strenuous activity, fluids.

WEB SITES
For Teenagers and Parents

For Health Professionals
http://www.postgradmed.com/issues/200005/05/pedshalt.htm. Postgraduate Medicine Continuing Medical Education article on mononucleosis.

REFERENCES AND ADDITIONAL READINGS


Tobi M, Straus SE. Chronic Epstein-Barr virus disease: a workshop held by the National Institute of Allergy and Infectious Diseases. Ann Intern Med 1985;103:951.


ETIOLOGY

Hepatitis may be caused by viral agents such as hepatitis A virus, hepatitis B virus, hepatitis C virus, delta virus, hepatitis E virus, Epstein-Barr virus, cytomegalovirus, or noninfectious causes such as hepatotoxins. In addition, there are at least two additional viruses, hepatitis G virus (a parenterally transmitted agent) and TT virus (fecal-orally transmitted) that are possible causes of hepatitis but have not yet been causally associated with clinical hepatitis. This chapter discusses primarily hepatitis A, hepatitis B, and hepatitis C.

1. Hepatitis A virus (HAV): Hepatitis A is caused by a 27- to 28-nm, nonenveloped, single-stranded RNA virus. The outer capsid is formed from three to four polypeptides that surround the inner RNA genome.

2. Hepatitis B virus (HBV): Hepatitis B is caused by a 42-nm-diameter virus, with an outer lipid envelope surrounding the inner core containing the DNA genome (Fig. 31.1). Several components of this virus can be detected by electron microscopy.

3. Hepatitis C virus (HCV): HCV is a positive-stranded RNA virus of the Flaviviridae family. It has great genetic heterogeneity, with at least six major genotypes, more than 80 subtypes, and numerous minor variants called quasispecies. There appears to be a genotype-dependent differential response to therapy.

4. Delta virus (HDV): This is an HBsAg-coated 35- to 37-nm diameter particle that is a defective pathogen because it is dependent on the presence of hepatitis B to cause an infection.

5. Hepatitis E (HEV): HEV is a small, nonenveloped, spherical, positive-stranded RNA virus that causes enterically transmitted hepatitis in developing countries. It was recently removed from the Calicivirus family and placed in an unassigned genus of “hepatitis E–like viruses.”

EPIDEMIOLOGY

Table 31.1 outlines the epidemiology for hepatitis viruses. A more detailed discussion follows.
Acute hepatitis caused by a combination of both HDV and HBV (coinfection)

Splenomegaly (10% of cases)

Acute hepatitis with HDV acquisition in a chronic carrier of HBV (superinfection)

14–182 days, average 49 days

Icteric sclera

Arthritis

15–50 days, average 28 days

Tender liver or spleen

15–60 days, average 40 days

42–168 days, average 112 days

The rash accompanying hepatitis B occurs in up to 50% of patients and is usually urticarial in nature but may be maculopapular or petechial.

Hepatitis B

HBV has been documented in almost all bodily secretions, including tears, stools, saliva, blood, bile, breast milk, vaginal secretions, urine, sneeze droplets, and semen. Transmission occurs via percutaneous or per mucosal routes, by infective blood or body fluids, through sexual contact, by contaminated needles, or perinatally from mother to infant. Infection can also occur in settings of continuous close personal contact (such as institutions for persons with developmental disabilities or in households), presumably via inapparent or unnoticed contact of infective secretions with skin lesions or mucosal surfaces.

The Centers for Disease Control and Prevention (CDC) in Atlanta estimates that there are approximately 300,000 new infections caused by HBV each year. The prevalence increases with age, with the majority of cases occurring in adolescence and early adulthood, coincident with the onset of sexual activity and parenteral drug use. However, 25% of infected individuals have no known risk factor for their infection. One quarter of infected individuals develop clinical hepatitis, more than 10,000 patients per year require hospitalization, and an average of 250 per year die of fulminant disease. About 5% to 10% of infected individuals become chronic carriers, and 25% of these carriers develop chronic active hepatitis. There is an estimated pool of 1 million chronic carriers in the U.S. population. The annual number of acute cases of hepatitis B reported in the U.S. decreased by more than 50% between 1990 and 1998, from 21,102 to 10,258, probably as a result of a national strategy of immunization of infants and children.

Hepatitis C

Although HCV infection is the most common chronic bloodborne infection in the United States, the annual incidence of acute hepatitis C infection has decreased dramatically since the 1980s. Between 1989 and 1997, the incidence rate fell more than 80%, to approximately 38,000 new cases per year, owing to a reduction in the number of transfusion-related cases, a reduction in injecting drug use, and, possibly, the introduction of safer needle practices among parenteral drug users. Screening of organ and tissue donors for HCV has essentially eliminated the risk of transmission in transplantation. Through the use of donor testing, the risk of infection from transfused blood has fallen to 0.001% per unit transfused. Likewise, inactivation procedures introduced in the manufacture of clotting factor concentrates have virtually eliminated the risk of infection in the hemophilic population.

Injection drug use currently is responsible for the majority of HCV transmission in the United States. Rates of infection with HCV in users after the initiation of injecting-drug use reach 40% within 3 months and 80% by the first year of injecting. Presently, 60% of HCV transmission in the United States is attributable to injecting-drug use, 20% is associated with sexual exposure, other exposures (e.g., occupational, household, hemodialysis, perinatal) account for 10%, and 10% of transmissions have no known source. Approximately 5% of infants born to infected mothers become infected.

Delta Hepatitis

HDV can cause disease only if HBV is present. At least three clinical pictures can occur:

1. Acute hepatitis caused by a combination of both HDV and HBV (coinfection)
2. Acute hepatitis with HDV acquisition in a chronic carrier of HBV (superinfection)
3. Chronic infection with both HDV and HBV, leading to a more rapid progression in liver disease and a higher mortality rate

The transmission of the virus is usually similar to that of HBV (i.e., blood or body fluids). Risk groups include intravenous drug users, male homosexuals, hemodialysis workers and patients, and recipients of blood products.

Hepatitis E

Hepatitis E is an enterically transmitted form of viral hepatitis seen primarily in developing countries in central Asia and in Pakistan, Africa, and Mexico. It has a variable presentation but is somewhat more severe than hepatitis A, with fulminant hepatitis occurring in 2% to 5% of patients overall but in 20% of pregnant women. Although reported cases of hepatitis E have been identified in the United States, endemic transmission is rare here. Therefore HEV will not be discussed further in this chapter. There is no evidence that U.S.-manufactured immune globulin will prevent enterically transmitted hepatitis E.

CLINICAL MANIFESTATIONS

Symptoms

It is not possible to distinguish among the types of hepatitis based on clinical manifestations. If the date of exposure is known, incubation periods may be helpful in diagnosis:

- Hepatitis A: 15–50 days, average 28 days
- Hepatitis B: 42–188 days, average 112 days
- Hepatitis C: 14–182 days, average 49 days
- Hepatitis E: 15–60 days, average 40 days

Common early symptoms of viral hepatitis include fatigue, lassitude, anorexia, nausea, dark urine, drowsiness, low-grade fever, right upper abdominal discomfort, myalgias, and arthralgias. In hepatitis A approximately 20% of individuals have a history of diarrhea. In viral hepatitis B, immune complexes can lead to arthralgias, arthritis, and a rash. Much less commonly, extrapathetic manifestations such as skin rash and arthralgias have been present with hepatitis A.

The arthritis of hepatitis B may precede the jaundice. The arthritis is usually a symmetrical polyarthritis affecting small joints. Larger joints may be affected, but the feet usually are spared.

The rash accompanying hepatitis B occurs in up to 50% of patients and is usually urticarial in nature but may be maculopapular or petechial.

Signs

1. Icteric sclera
2. Tender liver or spleen
3. Splenomegaly (10% of cases)
4. Arthritis
To understand the clinical course and diagnosis of viral hepatitis, one must understand the various antigens and antibodies and their clinical significance.

1. Hepatitis A (Fig. 31.2)


a. Immunoglobulin M anti-hepatitis A viral antibody (IgM anti-HAV): This antibody is detected early in the illness and remains detectable for approximately 2 to 3 months.
b. Immunoglobulin G anti-hepatitis A viral antibody (IgG anti-HAV): This antibody rises more slowly and is persistent for years. It indicates a past infection and the presence of immunity to viral A hepatitis.
c. HAV in stool: This virus is usually present before the onset of clinical symptoms and is of little clinical utility.

2. Hepatitis B (Fig. 31.3)

FIG. 31.3. Course of hepatitis B infection. Pattern of symptoms and serologic tests. ALT, alanine aminotransferase; Anti-HBc, hepatitis B core antibody; Anti-HBe, hepatitis B e antibody; Anti-HBs, hepatitis B surface antibody; HBeAg, hepatitis B e antigen; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; Ig, immunoglobulin. (From Hollinger FB. Hepatitis markers: guide to test selection. Diagnosis 1986; Aug:58.)

a. HBV: HBV is the etiologic agent of hepatitis B and is also known as Dane particle.
b. HBsAg: This surface antigen becomes positive during the incubation period and disappears in most patients during the course of the clinical disease. However, in over 10% of patients, this antigen may remain positive for life. A positive test result for HBsAg indicates either an acute hepatitis B infection or a chronic carrier state. It signifies that the patient is capable of transmitting HBV.
c. Anti-HBc: Surface antigen (anti-HBs): This antibody becomes positive usually months after the onset of the clinical disease. A positive blood test result can be confirmed by a confirmatory test for HBsAg and indicates past immunization or immunity from immunization. If acute hepatitis is present, the patient probably has hepatitis of another etiology.
d. HBeAg: This core antigen is not routinely assayed for in peripheral blood.
e. Anti-HBc: Core antigen (anti-HBc): This is the only serological marker derived from core virus. It appears as HBsAg is falling and before anti-HBs appears. Anti-HBc can be fractionated into IgM and IgG components. This test is extremely helpful in differentiating between acute and past infections. Anti-HBc (IgM) rises during clinical hepatitis, persists for 2 to 8 months, and then declines, whereas anti-HBc (IgG) rises at the same time to a much higher level and persists for a long time. The detection of anti-HBc (IgM) indicates an acute infection, whereas if only anti-HBc (IgG) is present, the illness must be of at least 6 months' standing. Anti-HBc may be the only test that is positive in some individuals during the window period after HBsAg has fallen and before anti-HBs has become positive.
f. Hepatitis B e antigen (HBeAg): HBeAg is closely associated with the nucleocapsid of HBV. However, its presence, which usually comes during the incubation phase, correlates with increased DNA polymerase activity and increased Dane particles. Persistence of HBeAg beyond 10 to 12 weeks is probably indicative of progression to a chronic carrier state. Persistent presence of HBeAg indicates
   • Active viral replication is present.
   • Development of chronic active hepatitis.
   • The patient is highly infectious. The risk of infectivity in an individual who is positive for HBeAg and HBsAg may be as high as 30,000 times the risk in an individual with only HBsAg positivity. About 10% to 15% of chronic carriers who are HBeAg positive convert each year to negative with the development of anti-HBe titers. These individuals are generally less contagious and have less active liver disease. Conversely, an individual can have reactivation of the disease, especially with immunosuppression, so that anti-HBe titers become negative and HBsAg becomes positive.
g. Anti-HBe: Anti-HBe (anti-HBeAg): This antibody appears with the disappearance of HBeAg and suggests resolving or reduced viral replication. It usually indicates a lower state of infectivity.

3. Hepatitis C
a. Serologic tests for hepatitis C include antibody screening tests and confirmatory tests that measure antibodies with greater sensitivity and specificity for HCV.
b. Enzyme immunoassay (EIA) detects antibodies against antigens from the viral core region (nucleocapsid) and nonspherical and structural proteins. The third-generation ELISA test (ELISA 3) has enhanced sensitivity (99% in immunocompetent patients; 60% to 90% in immunocompromised hosts) and a specificity of 99% in patient populations at high risk for hepatitis C. In populations with low prevalence for HCV infection (less than 10%), the positive predictive value is less and confirmatory testing should be done.
c. Recombinant immunoblot assay (RIBA) is used as a confirmatory test for hepatitis C. The third-generation assay, RIBA 3, has a sensitivity of 99.5% in patients with positive virological tests for HCV.
d. Direct measurement of viral nucleic acid in serum remains the “gold standard” in the diagnosis of HCV infection. Two methods are available: identification of HCV RNA by polymerase chain reaction (PCR) and branched DNA amplification (bDNA). Both are expensive, and false-negative results may occur as a result.
of sample contamination. They should be used as confirmatory tests only, especially in immunocompromised individuals, who may not produce measurable antibody levels.

4. Delta hepatitis
   a. Delta virus (HDV): Etiologic agent of delta hepatitis; it can cause infection only in the presence of hepatitis B.
   b. Delta antigen: Detectable in early acute delta infection.
   c. Delta antibody (anti-delta): Indicates past or present infection with HDV. Current EIA or radioimmunoassay (RIA) tests measure primarily IgG but also detect some IgM. Specific IgG and IgM tests are not clinically available for routine testing at this time. The “gold standard” for diagnosis is liver biopsy with staining for hepatitis D antigen.

Course

1. Viral hepatitis A: The clinical course is summarized in Fig. 31.2.
   a. Most patients are asymptomatic.
   b. Ninety-five percent of patients have a 4- to 6-week course.
   c. Stool isolates for HAV are the first positive finding.
   d. As IgM antibodies and liver enzymes rise, clinical symptoms appear.
   e. As clinical symptoms disappear and IgM antibodies fall, IgG antibodies rise.
   f. In rare instances, individuals can have a relapsing course lasting up to 1 year, which can cause confusion with other causes of chronic liver disease such as HBV.

2. Viral hepatitis B: The clinical course of a typical case is summarized in Fig. 31.3.
   a. HBsAg and HBeAg titters rise 4 to 8 weeks after exposure and 4 to 8 weeks before clinical symptoms appear.
   b. Liver transaminases rise, and clinical symptoms appear.
   c. HBsAg may peak and fall in uncomplicated cases or remain positive in chronic carriers.
   d. Anti-HBc titters rise as HBsAg titters fall.
   e. Anti-HBs appear weeks to months after HBsAg disappears.
   f. A “window phase” may exist in which HBsAg is negative before anti-HBs appears. During this phase, anti-HBc will be positive.
   g. Chronic phase
      • Ninety percent of patients with hepatitis B recover without sequelae.
      • Less than 1% develop fulminant hepatitis and die.
      • About 10% develop chronic liver disease: Seven percent of patients develop benign persistent hepatitis manifested mainly by elevated transaminases. These patients usually heal without sequelae. Three percent of patients develop chronic active hepatitis shown by abnormal transaminases and liver biopsy specimen. These patients may either heal or develop cirrhosis and liver failure.

3. Hepatitis C
   a. The clinical course varies from asymptomatic infection (up to 70%) to icteric hepatitis (25%) to fulminant failure (rare).
   b. Chronic disease develops in about 60% of patients, unrelated to mode of transmission or clinical presentation.
   c. Ten to twenty-five percent of patients with chronic disease develop cirrhosis.
   d. HCV infection is strongly associated with the development of hepatocellular carcinoma.
   e. Serologic test results remain negative for several weeks after onset of disease.

4. Delta hepatitis
   a. Acute infection with both HDV and HBV usually has a sequential expression with dual aminotransferase spikes. The interval between the first illness and the second is usually between 1.5 and 4 weeks (average, 2 weeks).
   b. Acute superinfection with HDV in a chronic carrier of HBV may be asymptomatic and detected only by an increase in transaminases and elevation of anti-delta antibody (IgM), or it may cause acute or chronic liver disease.

CONSIDERATIONS DURING PREGNANCY

1. Hepatitis A
   a. There is no maternal-fetal transmission.
   b. Transmission can occur during delivery.
   c. Positive IgM antibodies in the infant indicate acute infection.

2. Hepatitis B: Transmission of HBV from mother to infant during the perinatal period is one of the most efficient modes of hepatitis B infection. This often leads to severe long-term sequelae. The transmission rate to infants of mothers who are positive for both HBsAg and HBeAg is 70% to 90%, and 85% to 90% of infected infants become chronic hepatitis B carriers. Infants born to mothers who are HBsAg positive and HBeAg negative have 10% risk of acquiring perinatal infection. An estimated 18,000 births occur to HBsAg-positive women each year, resulting in about 4,000 infants who become chronic carriers. Prenatal screening of all pregnant women identifies those who are HBsAg positive and allows treatment of their newborns with hepatitis B immune globulin (HBIG) and hepatitis B vaccine, which prevents development of the chronic carrier state in 85% to 95% of these infants. The Advisory Committee on Immunization Practices (CDC, 1991) advises the following:
   a. All pregnant women should be routinely tested for HBsAg during an early prenatal visit in each pregnancy. If the mother has a particularly high-risk behavior, an additional HBsAg test can be ordered later in the pregnancy. No other serological hepatitis tests are necessary for maternal screening.
   b. If the woman was not screened prenatally, HBsAg testing should be done at the time of admission for delivery. If the mother is identified as HBsAg positive 1 month or more after giving birth, the infant should be tested for HBsAg. If the results are negative, the infant should be given HBIG and hepatitis B vaccine.
   c. After any initial test that is positive for HBsAg, a second test should be performed on the same specimen, followed by a confirmatory test using a neutralization assay. However, if the initial test was done during the hospitalization for delivery, initiation of treatment of the infant should not be delayed more than 24 hours waiting for a second or confirmatory test.
   d. Infants born to HBsAg-positive mothers should receive HBIG (0.5 mL) intramuscularly once they are physiologically stable, preferably within 12 hours after birth. Hepatitis B vaccine should be administered intramuscularly at the appropriate infant dose. The first dose should be given concurrently with HBIG but at a different site. Subsequent doses should be given as recommended for the specific vaccine (Table 31.2). Testing of infants for HBsAg and anti-HBs is recommended when they are 12 to 15 months of age to monitor the success or failure of therapy. If HBsAg is not detectable and anti-HBs is present, the child can be considered protected. HBIG and hepatitis B vaccination do not interfere with routine childhood vaccinations.

   TABLE 31.2. Recommended doses of currently licensed hepatitis B vaccines

<table>
<thead>
<tr>
<th>Age</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-6 months</td>
<td>0.5 mL</td>
</tr>
</tbody>
</table>

   e. Household members and sexual partners of HBV carriers should be tested, and, if susceptible, should receive hepatitis B vaccine.
   f. Obstetrical and pediatric staff should be notified directly about HBsAg-positive mothers so that the neonates can receive therapy without delay after birth.

DIFFERENTIAL DIAGNOSIS

1. Drug-induced hepatitis
2. Alcoholic hepatitis
3. Toxic hepatitis
4. Viral hepatitis
   a. Hepatitis A virus
   b. Hepatitis B virus (with or without delta coinfection or superinfection)
   c. Hepatitis C virus
   d. Hepatitis E virus
   e. Herpes simplex virus
   f. Cytomegalovirus
   g. Epstein-Barr virus
   h. Varicella virus
   i. Enteroviruses—Coxsackie B and ECHO virus
   j. Rubella virus
   k. Adenovirus

**DIAGNOSIS**

1. What causes acute hepatitis?
   a. Clinical history may suggest toxin, drug, or exposure to a source of hepatitis A, B, or C.
   b. Order IgM anti-HAV, HBsAg, anti-HBc, hepatitis C ELISA-3, and a mononucleosis spot test. Table 31.3 provides an interpretation of results from the first three of these tests. Follow-up tests for hepatitis C are necessary because of the long lag phase to seroconversion.

   **TABLE 31.3. Interpretation of hepatitis antibody test results**

2. Acute hepatitis B: What is the infectivity of the patient? Table 31.4 summarizes the infectivity risk of hepatitis B virus.

   **TABLE 31.4. Infectivity for acute hepatitis B virus**

**PREVENTION**

**Disinfection**

1. Heat sterilization
   a. Boiling in water at 100°C for 10 minutes
   b. Steam autoclaving at 121°C and 15 pounds/cubic inch for 15 minutes
   c. Dry heat of 160°C for 2 hours
2. Other presumed effective modalities
   a. Sodium hypochlorite 2.5% for 30 minutes
   b. Formalin 40% for 12 hours
   c. Glutaraldehyde 2% for 10 hours

**Prophylaxis**

*Hepatitis A* The following information is provided by the CDC Advisory Committee on Immunization Practice (ACIP) (CDC, 1999) and is available on the CDC Web site: [http://www.cdc.gov/mmwr/preview/mmwrhtml/rr4812a1.htm](http://www.cdc.gov/mmwr/preview/mmwrhtml/rr4812a1.htm).

**Hepatitis A Preexposure Prophylaxis**

1. Agents: Agents available for preexposure prophylaxis for hepatitis A include human immune serum globulin (HISG) and hepatitis A vaccine.
   a. HISG: This was the traditional and only preexposure prophylaxis for hepatitis A until recent years. The major group for whom preexposure prophylaxis with HISG is indicated consists of international travelers to endemic areas. Risk of infection in developing countries increases with duration of travel and is highest for those who live in or visit rural areas, trek in back country, or frequently eat or drink in settings of poor sanitation.
   b. Hepatitis A vaccine: The scope of prophylaxis changed with the introduction of a hepatitis A vaccine, which offers active immunization and therefore longer and more effective protection than that provided by HISG. Two vaccines are available: Havrix (SmithKline Beecham Biologicals, Research Triangle, NC) and Vaqta (Merck, Inc., White Station, NJ). The vaccines are both inactivated and come in adult and pediatric formulations, with different dosages and administration schedules. Immunogenicity studies indicate that almost 100% of children, adolescents, and adults develop protective levels of antibody to HAV after completing the vaccine series. Recipients of the vaccine have been monitored for up to 6 years and still have protective levels of anti-HAV. Estimates suggest that protective levels can last at least 20 years. The vaccine can be administered simultaneously with other vaccines and toxoids, including hepatitis B, diphtheria, tetanus, oral typhoid, cholera, Japanese encephalitis, rabies, and yellow fever; without altering immunogenicity or adverse effects. However, if other vaccines are given simultaneously, they should be given at separate injection sites. If HISG is given at the same time as the first dose of vaccine, a lower antibody concentration is attained, but this is not thought to be clinically relevant. In addition to the vaccines above, Twinrix, is also available which includes both hepatitis A inactivated and hepatitis B (recombiant) vaccines in one. Using three doses of Twinrix produces similar seroprotection for hepatitis A and B as using vaccines for A and B separately. Recommended dosing is at 0, 1, and 6 months.
2. Recommended dosing schedules are as follows:
Dose (ELISA units)

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>Dose (ELISA units)</th>
<th>Volume (mL)</th>
<th>No. Doses</th>
<th>Schedule (mo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2–18</td>
<td>720</td>
<td>0.5</td>
<td>2</td>
<td>0, 6–12</td>
</tr>
<tr>
<td>&lt;18</td>
<td>1,440</td>
<td>1.0</td>
<td>2</td>
<td>0, 6–12</td>
</tr>
</tbody>
</table>

VAQTA

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>Dose (units)</th>
<th>Volume (mL)</th>
<th>No. Doses</th>
<th>Schedule (mo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2–17</td>
<td>25</td>
<td>0.5</td>
<td>2</td>
<td>0, 6–18</td>
</tr>
<tr>
<td>&lt;17</td>
<td>50</td>
<td>1.0</td>
<td>2</td>
<td>0, 6</td>
</tr>
</tbody>
</table>

After receiving the initial dose of hepatitis A vaccine, persons are considered to be protected by 4 weeks after the initial dose. For long-term protection, a second dose is needed 6 to 12 months later. For persons who will travel to high-risk areas less than 4 weeks after the initial vaccine dose, IG (0.02 mL per kg of body weight) should be administered simultaneously with the first dose of vaccine but at a different injection site.

Persons who are allergic to a vaccine component or otherwise elect not to receive vaccine should receive a single dose of IG (0.02 mL per kg of body weight), which provides effective protection against hepatitis A for up to 3 months. IG should be administered at a dose of 0.06 mL per kg of body weight and must be repeated if travel is for longer than 5 months.

Who: The following recommendations for the use of inactivated hepatitis A vaccine are given by the CDC ACIP (CDC, 1999) and are available at http://www.cdc.gov/mmwr/preview/mmwrhtml/rr4812a1.htm.

a. The following children should be routinely vaccinated: Those who live in states, counties, or communities where the average annual rate of hepatitis A during 1987–1997 was more than 20 cases per 100,000 (i.e., about twice the national average).

b. Vaccination should be considered for the following children: Those who live in states, counties, or communities where the average annual rate of hepatitis A in 1987–1997 was more than 10 but less than 20 cases per 100,000 population (i.e., above the national average but less than twice the national average).

c. All susceptible persons traveling to or working in countries with intermediate or high hepatitis A endemicity (i.e., countries other than Australia, Canada, Japan, New Zealand, and countries in western Europe and Scandinavia) should be vaccinated with hepatitis A vaccine or receive immunoglobulin (IG) before departure. Hepatitis A vaccine at the age-appropriate dose is preferred for persons who plan to travel repeatedly to or reside for long periods in these high-risk areas. IG is recommended for travelers younger than 2 years of age.

d. Other potential target populations:
   - Men who have sex with men.
   - Illegal-drug users, both injecting and noninjecting.
   - Persons with an occupational risk (e.g., research laboratory workers).
   - Persons with clotting factor disorders.
   - Persons with chronic liver disease, including those with other forms of chronic viral hepatitis.
   - Military personnel
   - Day care attendees

Hepatitis A Postexposure Prophylaxis

1. Agent: HISG
2. Who: A serological confirmation test for hepatitis A in the index case is recommended before consideration of prophylaxis in contacts. Serological screening of contacts before giving HISG is not warranted because of cost and time considerations. Considerations for prophylaxis include the following:
   a. Close personal contacts, including household and sexual contacts of persons with hepatitis A, should receive HISG.
   b. Day care centers: For day care centers or homes with children in diapers, HISG should be administered to all staff and attendees if one or more hepatitis A cases is recognized among children or employees, or if cases are recognized in two or more households of center attendees. In centers not enrolling children with diapers, only classroom contacts of an index case need be treated.
   c. Schools: Routine administration of HISG is not indicated for pupils and teachers in contact with a patient. However, if an outbreak clearly exists, HISG may be given to those with close personal contact.
   d. Institutions for custodial care: Because of crowded living conditions, during an outbreak of hepatitis, prophylaxis of residents and staff with close contact with patients is warranted.
   e. Hospitals: Routine HISG prophylaxis for hospital personnel is not indicated. Education should be stressed regarding sound hygienic practices and precautions regarding direct contact with potentially infective material. In outbreaks, prophylaxis of persons exposed to feces of infected patients may be indicated.
   f. Offices and factories: Prophylaxis is not indicated under usual office or factory conditions for persons exposed to a fellow worker with hepatitis A.
   g. Common source exposure: Prophylaxis might be effective in preventing foodborne or waterborne hepatitis if exposure is recognized in time. However, HISG is not recommended for persons exposed to a common source after cases have begun to appear in those exposed, because the 2-week period during which HISG is effective will have passed.
3. When: As soon as possible after exposure; HISG is helpful until about 6 days before onset of symptoms.
4. Effectiveness: HISG decreases clinical disease in 80% to 95% of patients. Anicteric hepatitis is not prevented.
5. Dose: 0.02 mL/kg

Hepatitis B

Hepatitis B Preexposure Prophylaxis

1. Agents: Two types of products are available for prophylaxis against hepatitis B. Hepatitis B vaccines provide active immunization against hepatitis B infection and are recommended for both preexposure and postexposure prophylaxis. HBIG provides temporary, passive protection and is indicated only in certain preexposure settings.
   a. HBIG: HBIG is prepared from plasma preselected to contain a high titer of anti-HBs. In the United States, HBIG has a titer greater than 1:100,000. The plasma used has been both screened for human immunodeficiency virus (HIV) antibodies and treated to inactivate and eliminate HIV from the final product. HBIG has not been shown to transmit HIV.
   b. Hepatitis B vaccine: There are now two recombinant hepatitis B vaccines licensed in the United States: Recombivax-HB (Merck, Inc.) and Engerix-B (SmithKline Beecham). These two vaccines are produced by introducing a plasmid containing the gene for HBsAg into baker’s yeast. HBsAg is harvested, purified, and sterilized. These two vaccines have replaced plasma-derived vaccine.
2. Indications: Previously, the strategy to prevent hepatitis B transmission in the United States rested on identification of mothers who were HBsAg carriers and prophylaxis of their newborn infants at birth, together with vaccination of persons who were in major risk groups for acquiring the infection. These efforts met with limited success because of an inability to identify all those at risk, lack of motivation on the part of certain at-risk individuals (e.g., intravenous drug users), and failure to vaccinate susceptible household and sexual contacts. Therefore, a comprehensive strategy to eliminate transmission of HBV during infancy and childhood, as well as during adolescence and adulthood, was devised. This included the following steps:
   a. Prenatal testing of pregnant women for HBsAg and immunophrophylaxis of their newborns and household contacts.
   b. Universal immunization of all infants born to HBsAg-negative mothers. Recommended schedules for immunophrophylaxis to prevent perinatal transmission of hepatitis B and for vaccination of newborns are listed in Table 31.5 and Table 31.6.

Additional information about hepatitis A vaccine is available from the CDC’s Hepatitis Branch, Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases, telephone 1-404-371-5910 or 1-404-371-5460.
“Catch-up” immunization of all children and adolescents who have not been immunized with hepatitis B vaccine, which may begin at any visit to a physician during childhood. Adolescents are at higher risk of infection because of risk-taking sexual and drug-seeking behaviors that tend to occur during this developmental period. Because adolescents and young adults are not easily identified with regard to high-risk behavior, universal immunization of all preadolescents, adolescents, and young adults—and in particular those living in areas where high-risk behavior is prevalent—is recommended. The appropriate dose for age should be used (Table 31.2) and the schedule of vaccination at 0, 1, and 6 months is preferred.

d. Persons with occupational risk: The risk for health care workers varies depending on exposure to blood or blood products. Individuals at higher risk include those in training, medical technologists, operating room staff, phlebotomists, intravenous therapy nurses, surgeons, pathologists, oncologists, and hemodialysis staff. Other at-risk individuals include dental professionals, laboratory and blood bank technicians, emergency medical technicians, and morticians.

e. Persons with lifestyle risk
   - Heterosexuals with multiple partners (more than one partner in preceding 6 months) or any sexually transmitted disease.
   - Clients and staff of institutions for mentally retarded individuals.
   - Men who have sex with men.
   - Injecting drug users.

f. Special patient groups
   - Hemodialysis patients.
   - Recipients of clotting factor concentrates.

g. Environmental risk factors
   - Household and sexual contacts of carriers.
   - Adoptees from countries of high hepatitis B endemicity. These children should be screened for HBsAg; if they are HBsAg positive, family members should be vaccinated.
   - Populations with high endemicity of hepatitis B infection. In the United States, certain populations including Alaskan Natives, Pacific Islanders, and refugees from endemic areas are at high risk for infection during childhood. In these groups, universal hepatitis B vaccination of infants is recommended to prevent disease transmission during childhood. Immigrants and refugees from endemic areas should be screened for hepatitis B. If a carrier is identified, all susceptible household contacts should be vaccinated.

   - Inmates of long-term correctional facilities.

   - International travelers: Vaccination should be considered for those who plan to reside for longer than 6 months in an area with a high level of endemic hepatitis B infection and those who will have close contact with the local population.

   - Other contacts of hepatitis B carriers: Persons in casual contact with carriers in settings such as schools and offices are at minimal risk of hepatitis B infection, and vaccine is not routinely recommended.

3. Immunogenicity and efficacy
   a. When given in a three-dose series, recombinant vaccines induce protective antibodies (anti-HBs) in more than 90% of healthy adults and more than 95% of infants, children, and adolescents from birth through 19 years of age. The deltoid (arm) muscle is the recommended site for the vaccination in adults and adolescents, because immunogenicity of the vaccine for adults is substantially lower when injections are given in the buttocks. Hemodialysis patients and other immunocompromised persons in general develop a poorer response to the vaccines than healthy individuals do, and they require a larger vaccine dose. The vaccine has been shown to be 80% to 95% effective in preventing infection or hepatitis among susceptible persons.

   b. Although protection during the first years is excellent, there is evidence that by 7 years 30% to 50% of individuals develop low levels of antibodies, and 10% to 15% have undetectable antibodies. However, protection against viremic infection and clinical disease appears to persist. Persons younger than 20 years of age seem to have a higher peak response and longer persistence of detectable levels of antibodies. Vaccination of carriers and immune individuals produces neither therapeutic nor adverse effects.

4. Vaccine dosage and safety
   a. Adults and older children (Table 31.2): Primary vaccination includes three intramuscular doses of vaccine, with the second and third doses given 1 and 6 months after the first. Adults and adolescents should receive a full dose; children younger than 11 years of age should receive half of the full dose. An alternative schedule of four doses of vaccine given at 0, 1, 2, and 12 months has been approved for one vaccine for postexposure prophylaxis or for more rapid induction of immunity. For patients undergoing hemodialysis and for other immunosuppressed patients, higher vaccine doses or an increased number of doses is required. The vaccine should be stored at 2° to 8°C but not frozen. In addition, as noted previously, Twinrix, is also available which includes both hepatitis A inactivated and hepatitis B (recombinant) vaccines in one. Using three doses of Twinrix produces similar seroprotection for hepatitis A and B as using vaccines for A and B separately. Recommended dosing is at 0, 1, and 6 months.

   b. Data are not available on the safety of hepatitis vaccines for the developing fetus. However, because the vaccines contain only noninfectious HBsAg particles, there should be no risk to the fetus. Because hepatitis B may result in severe disease for the mother and chronic infection in the newborn, pregnancy or lactation should not be considered a contraindication to the use of the vaccine.

   c. Side effects: Seventeen percent of individuals experience soreness at site. Fifteen percent experience mild systemic symptoms including fever, headache, fatigue, and nausea. No potentially transmissible diseases, including HIV, have been reported.

5. Prevacuation serologic screening: Screening for past infection is probably cost-effective in groups with a prior high risk of infection (more than 20%), unless the cost of testing is extremely high. For groups with a low expected prevalence, such as health professionals in their training years, screening is not cost-effective. For routine screening, either anti-HBs or anti-HBc should be used. Anti-HBc screening identifies those previously infected, except carriers. Anti-HBc screening identifies all previously infected persons, both carriers and noncarriers. Kwan-Gett et al. (1994) evaluated prevaccination testing in preadolescents and adolescents. They showed that no testing was the most cost-effective strategy. Prevacuation testing increased costs by $2.9 million for every 190,000 patients and also lowered the rate of complete vaccination by 22%, compared with vaccination without testing. Prevacuation testing was only cost-effective when the seroprevalence of anti-HBs was greater than 40%.

6. Postvaccination serology and revaccination
   a. Testing for immunity is not recommended routinely but is advised for individuals who are expected to have a suboptimal response, such as those who

---

**TABLE 31.5.** Recommended schedule of hepatitis B immunoprophylaxis to prevent perinatal transmission of hepatitis B virus infection

<table>
<thead>
<tr>
<th>Age at which vaccine is given</th>
<th>Recommended schedule of hepatitis B immunoprophylaxis to prevent perinatal transmission of hepatitis B virus infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth hospital discharge</td>
<td>Two doses of hepatitis B vaccine (0.5 mL) given intramuscularly at 1 and 2 months of age.</td>
</tr>
<tr>
<td>1 month</td>
<td>Second dose.</td>
</tr>
<tr>
<td>6 months</td>
<td>Third dose.</td>
</tr>
</tbody>
</table>

---

**TABLE 31.6.** Recommended schedules of hepatitis B vaccination for infants born to HBsAg-negative mothers

<table>
<thead>
<tr>
<th>Risk Group</th>
<th>Recommended Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy infants, children, and adolescents</td>
<td>Two doses of hepatitis B vaccine (0.5 mL) given intramuscularly at 1 and 2 months of age.</td>
</tr>
<tr>
<td>Adults and older children</td>
<td>Three doses of vaccine given at 0, 1, and 6 months.</td>
</tr>
</tbody>
</table>
received the vaccine in the buttock, persons older than 50 years of age, persons known to have HIV infection, and individuals whose subsequent management depends on knowing their immune status, such as dialysis patients and staff. When necessary, the testing should be done between 1 and 6 months after completion of the vaccine series.

b. Testing of infants born to HBsAg-positive mothers who received immunoprophylaxis should be performed 3 to 9 months after completion of the vaccination series.

c. Revaccination in nonresponders produces adequate antibody in 15% to 25% after one additional dose and in 30% to 50% after three additional doses when the primary vaccination was given in the deltoid. If the primary vaccine was given in the buttock, revaccination in the arm induces adequate antibody in more than 75%. Revaccination should be considered for nonresponders who received the vaccine in the deltoid muscle, and it is recommended for nonresponders who received the primary vaccine in the buttock.

d. Long-term studies of children and adults suggest that immunological memory lasts for at least 10 years and protects against chronic HBV infection even though antibody levels against HBsAg may become undetectable.

Hepatitis B Postexposure Prophylaxis

Prophylactic treatment to prevent hepatitis B infection after exposure should be considered in the following situations:

1. Perinatal exposure of an infant born to an HBsAg-positive mother: (See earlier discussion of Considerations During Pregnancy.) A regimen that combines one dose of HBIG at birth with the hepatitis B vaccine series started soon after birth is 85% to 95% effective. Regimens involving either multiple doses of HBIG alone or the vaccine series alone have 70% to 85% efficacy.

2. Persons with acute exposure to blood: Decision for prophylaxis depends on whether the source of the blood is available, the hepatitis status of the exposed person, and the status of the source. After such an exposure, a blood sample should be obtained from the person who was the source of the exposure and tested for HBsAg. For greatest effectiveness, passive prophylaxis with HBIG, when indicated, should be given as soon as possible after exposure (the value beyond 7 days after exposure is unclear). A summary of recommendations is given in Table 31.7. Updated U.S. Public Health Service Guidelines for the Management of Occupational Exposures to HBV, HCV, and HIV and Recommendations for Postexposure Prophylaxis can also be obtained at: http://www.cdc.gov/mmwr/PDF/rrr6011.pdf.

3. Sexual contacts of HBsAg-positive persons: These individuals are at increased risk of infection, and HBIG is 75% effective in preventing such infections. Screening of sexual partners for hepatitis antibodies (anti-HBc or anti-HBs) before treatment is recommended but should not delay treatment beyond 14 days after last exposure. Treatment consists of HBIG (0.06 mL/kg), followed by the hepatitis vaccine series, which may be started at the same time if exposure continues.

4. Household contacts of persons with acute infection: Prophylaxis is not indicated unless there is exposure to blood of the index case (e.g., sharing of toothbrushes or razors). If indicated, treatment is with both HBIG and vaccine. If the index patient becomes a carrier, all household contacts should receive hepatitis B vaccine. Treatment with HBIG and hepatitis B vaccine is also indicated for infants younger than 12 months of age whose primary caregivers have an acute hepatitis B infection.

Delta Hepatitis Because HDV is dependent on HBV for replication, prevention of HBV infection suffices to prevent delta hepatitis. Exposures of individuals with known positivity for both HDV and HBV should be treated exactly as such exposures to HBV alone.

Hepatitis C Immune globulin is not recommended for postexposure prophylaxis of hepatitis C.

Hygiene

1. No sharing of razors, toothbrushes, food utensils, or towels.

2. Careful personal hygiene; hand washing after patient contact.

3. Careful handling of secretions of the hepatitis B patient, including saliva, blood, and urine, with needle precautions.

4. Hepatitis A: Isolate the patient until jaundice peaks; use stool precautions.

THERAPY

General Measures

1. Teenagers with acute viral hepatitis should decrease their physical activity level until they are feeling better.

2. Diet: There is no evidence that any special diet affects the course of the disease. Patients may eat as much as is tolerated.

3. Adolescents should avoid alcoholic beverages until transaminases return to normal.

4. Adolescents should avoid oral contraceptives, steroids, and all liver-toxic drugs.

5. Acetylcysteine is useful in acetaminophen-induced hepatitis.

6. Severe disease is indicated by the following findings:
   a. Total bilirubin greater than 25 mg/dL
   b. Elevated prothrombin time
   c. Albumin less than 2.5 g/dL
   d. Evidence of ascites, edema, or encephalopathy
   e. Transaminase levels greater than 2,000 units/mL

7. Most cases of hepatitis in adolescents can be managed at home. If hydration cannot be maintained in the outpatient because of nausea and vomiting, hospitalization should be considered. If the home environment is not supportive or the disease activity is particularly severe (see previous discussion), hospitalization is indicated.

8. The concentrations of serum bilirubin and transaminases should be monitored weekly during the acute illness, then every 2 to 3 weeks as the teen improves and enzymes fall. Monitoring can be stopped when liver enzymes return to normal. In patients with chronic hepatitis B, enzymes should be continuously monitored but at less frequent intervals.

Chronic Hepatitis

Treatment of chronic hepatitis B is beyond the scope of this book. Therapy should be conducted by a specialist who is experienced in the treatment of chronic hepatitis.

1. Agents for treatment of chronic hepatitis B
   a. Interferon-α (IFN-α): Indicated for patients with persistently high aminotransferases; detectable HBsAg, HBeAg, and HBV DNA in serum; chronic hepatitis on liver biopsy; or compensated liver disease. Treatment with IFN-α results in long-term remission in 25% to 40%.
b. Lamivudine: Recently approved by the U.S. Food and Drug Administration (FDA) for treatment of chronic hepatitis B with active viral replication. It reduces inflammation in one half to two thirds of patients and results in seroconversion from HBeAg to anti-HBe in about 20% of patients. Viral resistance has been reported.

2. Agents for therapy of chronic hepatitis C
   a. IFN-a monotherapy: Most patients treated with IFN-a realize decreased aminotransferase levels, with normalization of levels in 40% to 50%. About 50% of patients relapse, however.
   b. IFN-a and ribavirin combination therapy (Rebetron): Now recommended as front line therapy by the FDA, dual therapy results in sustained responses in 40% of patients.

COMPLICATIONS

1. Acute hepatitis
   a. Pancreatitis
   b. Myocarditis
c. Atyypical pneumonia
d. Aplastic anemia
e. Transverse myelitis
f. Glomerulonephritis
g. Arthritis

2. Fulminant hepatitis

3. Chronic carrier state (HBsAg positive for longer than 6 months)

4. Chronic hepatitis
   a. Chronic, persistent, benign hepatitis
   b. Chronic active hepatitis
      • Symptoms longer than 10 weeks
      • Sustained serum aspartate transaminase (AST) at ten times the normal value, or at five times normal with serum globulins two times normal
      • Piecemeal necrosis and other abnormalities on liver biopsy

WEB SITES

For Teenagers and Parents


For Health Professionals


REFERENCES AND ADDITIONAL READINGS


Wright TL, Lau JY. Clinical aspects of hepatitis B virus infection. Lancet 1993;342:1340.

Acquired immunodeficiency syndrome (AIDS) is one of the largest pandemics to hit modern society and the focal point of intense national and international debate. The last 5 years have seen a dramatic reduction in the mortality from AIDS in developed countries. When taken correctly, combinations of antiretroviral medications called Highly Active Antiretroviral Therapy (HAART) enable most infected patients to live healthy lives for prolonged periods. The greatest challenges for care providers of adolescents with human immunodeficiency virus (HIV) infection involve identifying infected youth, engaging them in care, and assisting them with long-term adherence with these medications. In only a fraction of the estimated 20,000 annual new cases of HIV infection in 13- to 25-year-olds in United States does the patient access care while still an adolescent or young adult. Internationally, the problem is even worse, with an estimated 50% of new HIV infections occurring in youth. Developing countries have almost no access to the life-saving medications now routinely available in the United States.

Special issues are important to consider in relation to the adolescent population and infection with HIV, including a host of legal and ethical dilemmas regarding testing, disclosure of information, and consent for treatment in research protocols. For HIV-infected adolescents there is also the problem of availability of age-appropriate services.

Adolescents are in danger of contracting HIV because of their risky sexual behaviors, drug use, or both. Because a large group of adolescents are not yet infected but may be involved in high-risk behaviors, teens are a high-priority target group for preventive measures.

Information about HIV infection is developing rapidly. Several thousand articles are published yearly with information that often quickly becomes outdated. The treatment of HIV has become so complex in recent years that all HIV-infected persons should be treated by physicians with expertise in HIV medications, their side effects and interactions, as well the psychosocial interventions required to maintain adherence. This chapter includes an overview of HIV and AIDS, with a focus on considerations that are important in the adolescent. It is essential for the practicing physician to keep up to date through the literature or continuing medical education courses on the many aspects of HIV infections, including legal issues, diagnosis, evaluation, and treatment.

ETIOLOGY, PATHOGENESIS, AND NATURAL HISTORY

The causative agent of AIDS is HIV, a single-stranded RNA retrovirus. This virus was isolated at the Pasteur Institute in Paris in 1983. HIV-1 is the cause of most cases of AIDS in the world. HIV-2, another retrovirus related to HIV-1, is found primarily in Central Africa. HIV-2 generally has a much slower progression (20 years, versus 5 to 10 years with HIV-1) but a similar spectrum of disease.

HIV-1 infects and leads to the destruction of CD4-positive T lymphocytes. A flu-like illness occurs in most patients 2 to 6 weeks after infection. The illness typically lasts 1 to 2 weeks and typically causes fever, fatigue, myalgias, lymphadenopathy, and sore throat (Table 32.1). The phase of illness after the acute infection was once characterized as one of latency, but it is now clear that viral production is steady at an estimated 10 billion virions daily. T-cell production and destruction remain precariously balanced. A slow but steady depletion of CD4+ T cells occurs in all but a small percentage of patients, who are called long-term nonprogressors. Most patients develop AIDS (severe immune deficiency), without treatment, over a median of 10 years. The level of HIV in the blood, called the viral load, correlates well with the rapidity of CD4+ T-cell depletion.
Recent studies indicate that HAART can suppress the viral load in most patients to undetectable levels. Viral suppression is associated with a steady immune reconstitution in most patients. Even patients with severe depletion of their immune systems can often return to excellent health after months to years of successful treatment. Preliminary studies of adolescents indicate that their “thymic reserve” may allow for even better immune restoration than in adults.

Unfortunately, even when the best therapy is strictly adhered to for several years, patients have been unable to eliminate HIV from their body (i.e., a cure is not currently possible). Reservoirs of latent virus are effectively hidden from the effects of the potent antiretrovirals. Patients who go off HAART after several years usually develop viremia within a couple weeks. Current research is focused on whether some type of immune modulation with medication or vaccines can nullify the inevitable rebound in HIV viremia.

Although the natural history of HIV has changed from a lethal illness to that of a chronic disease, it is unclear whether lifelong viral suppression is feasible. Many adolescents are unable to adhere to or tolerate complex medication regimens. Some patients develop resistance to medications due to nonadherence, and some patients are being infected with HIV that has extensive resistance to many medications. These patients can eventually have immune depletion and succumb to the opportunistic infections and neoplasms that were so prevalent before the advent of HAART.

**EPIDEMIOLOGY**

As of June 2000, more than 753,907 cases of AIDS have been reported to the Centers for Disease Control and Prevention (CDC). Although only 3,865 cases were in teens age 13 to 19 years, approximately 17% of all cases are in 20- to 29-year-olds. With a median incubation period of 7 to 10 years from HIV infection to AIDS, most of these cases in young adults were acquired as adolescents. Persons of color are dramatically overrepresented, making up 57% of all cases in youth age 13 to 24 years. Table 32.2 shows AIDS cases in adolescents and adults under age 25 by sex and exposure category. Table 32.4 shows AIDS cases in adolescents and adults under age 25 by sex and exposure category.
(13%), men having sex with men and injection drug use (5%), and heterosexual contact (15%). For men age 20 to 24 years, 65% of new AIDS cases in 1999 were attributable to men having sex with men, 15% to injection drug use, 5% to men having sex with men and injection drug use, and 14% to heterosexual contact (Table 32.5).

TABLE 32.5. Estimated AIDS incidence in adolescents and adults under age 25, by sex and exposure category, diagnosed in 1999, and cumulative totals through 1999, United States

<table>
<thead>
<tr>
<th>Exposure Category</th>
<th>Females</th>
<th>Males</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heterosexual Contact</td>
<td>66%</td>
<td>77%</td>
</tr>
<tr>
<td>Injection Drug Use</td>
<td>18%</td>
<td>21%</td>
</tr>
<tr>
<td>Total</td>
<td>84%</td>
<td>98%</td>
</tr>
</tbody>
</table>

HIV Staging

In 1993, the CDC expanded their AIDS definition criteria and changed their staging system (Table 32.6). The system uses the lowest-ever CD4+ T-cell count (rows 1 through 3 in Table 32.6) in combination with clinical staging (columns A through C in Table 32.6) based on symptoms. The problem with this current system is that it reflects the most advanced stage a patient has reached but not the patient's current condition. A patient who once had advanced AIDS with life-threatening infections but then successfully started HAART and now is asymptomatic with a CD4+ T-count higher than 500 cells/µL will still be staged as a 3C (the mostly severely ill stage).

TABLE 32.6. 1993 Revised classification system for HIV infection and expanded AIDS surveillance case definition for adolescents and adults

Transmission

HIV can be transmitted only by the exchange of body fluids. Blood, semen, vaginal secretions, and breast milk are the only fluids documented to be associated with HIV infection. Although HIV is found in saliva, tears, urine, and sweat, no case has been documented that implicates these fluids as agents of infection.

HIV is easily transmitted by the sharing of needles. The CDC has provided guidelines for the cleaning of needles with bleach. Because of the unreliability and frequent unacceptance of needle bleaching and unacceptance or inaccessibility of drug treatment, almost all public health organizations support needle exchange. Here injection drug users can turn in dirty needles for clean ones while at the same time gaining access to condoms, bleach, and referral resources. Programs in San Francisco, California, and New Haven, Connecticut, as well as others in the United States and Europe, have shown that injection drug use does not increase in the community or in an individual user when exchanges are available. Also, HIV and other bloodborne disease transmission is markedly reduced with needle exchange.

Sexual transmission of HIV is thought to have a hierarchy of relative risk. Receptive anal intercourse without condoms is riskiest, followed by insertive anal intercourse and vaginal intercourse. Oral sex is less risky but has been shown to transmit HIV. Studies have shown that the proper and consistent use of latex condoms or dental dams can markedly reduce the risk for HIV transmission during sex.

The risk to health professionals of infection caused by needle sticks from HIV-infected patients is estimated to be 1 in 200 to 1 in 500. Injuries involving injection of blood are much riskier than simple pricks. Double-gloving while using needles probably reduces the risk of transmission if a needle stick occurs on the covered hands. The role of antiretroviral medications after needle sticks is unclear, although most hospitals offer it. However, in a preliminary study from the CDC (1995b), zidovudine (AZT) was found to be possibly helpful in reducing the risk of HIV infection to health care workers after accidental needle stick with needles contaminated with an infected patient's blood. For the health care workers in this study, the use of AZT decreased the risk 79%. Current recommendations include consideration of rapid treatment within hours, with multiple medications, after the occurrence of a needle stick from a known HIV-infected patient. Other considerations include whether the patient has been receiving effective HIV therapy and whether there is any known drug-resistant virus in the patient involved. The availability of clinicians with expertise in HIV transmission is essential to assist health care personnel exposed to a needle-stick injury to make complicated decisions regarding the risks and benefits of treatment. Information on occupational exposures and postexposure prophylaxis is available from many CDC and other Web sites included at the end of this chapter.

DEVELOPMENTAL ISSUES RELATED TO HIV INFECTIONS IN ADOLESCENTS

Although most youth do not undergo extreme turmoil and distress in their teenage years, adolescence still provides many opportunities for risk for the teen with regard to HIV infection.

Cognitive and Emotional Development

Cognitive and emotional development factors that put teens at increased risk for AIDS include

1. Greater experimentation and greater degree of influence by peer behaviors
2. Naïveté and lack of good judgment
3. Feelings of immortality and invulnerability
4. Ignorance of modes of AIDS transmission and prevention
5. Denial of personal risk
6. Identification with moral codes (i.e., those of peers) other than those of their parents

Social, Behavioral, and Physiological Development

Adolescent behaviors that increase teens' risk for HIV infection include the following:

1. Sexual activity: A high percentage of adolescents engage in sexual intercourse, often without a barrier contraceptive or any contraceptive. In 1999, 50% of high school students reported that they had had sexual intercourse (CDC, 2000). Teens in urban areas, and particularly inner-city teens and those in group homes and detention centers, seem to have the earliest onset of sexual activity. Many adolescent males (17% to 37%) report having had at least one same-sex experience. A recent survey of urban young men (age 16 to 22) who have had sex with men reported that 41% had engaged in unprotected anal sex in the preceding 6 months (7% were HIV infected). Only 56% of high school students reported using condoms at last sexual intercourse in the 1999 Youth Risk Behavior Survey (CDC, 2000).

2. Sexually transmitted diseases (STDs): The high prevalence of STDs in adolescents is an indicator both of high-risk behavior among teenagers and the lack of condom use. One in four sexually experienced teens contracts an STD annually.

3. Illicit drug use: Although there are no adequate national statistics on injection drug use among teenagers, estimates are that 1 in 50 high school juniors and seniors have injected drugs. Teens who have dropped out of school are more likely to use intravenously. Teens may also be sharing needles in other ways, such as piercing ears, tattooing, or using steroids (i.e., athletes). Crack cocaine users appear to have an especially high rate of HIV infection. In addition, any drug use impairs a youth's ability to make good decisions concerning sexuality.

4. Runaway behavior: About 1 million teenagers run away each year, and many of these are involved in high-risk behaviors, including injection drug use and survival sex (sex for money, food, or a place to stay). AIDS-related risks are high but are often ignored in the context of the immediate crises of survival.

5. Physiological factors: Adolescent girls may be at increased risk of HIV infection because of several physiological features, including:
   a. Differences in the cervix of adolescents (more columnar epithelium)
   b. Alterations of the vaginal pH as compared with adults
   c. Differences in menstrual patterns (less ovulation, less progesterone, and therefore less thick cervical mucus).

Family Relationships

Unresolved issues can lead to powerful conflicts between parents and adolescents. Sometimes the dysfunctional nature of the teen's family significantly increases the chances of the teen's involvement in high-risk behavior.

Levels of Risk

Not all adolescents present with the same risk profile. Hein (1989a) described several levels of risk among adolescents:

1. Not at risk: Many adolescents are not at risk because they are either not involved in risk behaviors (i.e., sexual activity or injection drug use) or they are in a location without HIV infections.

2. Sexually active teens not yet exposed: This group may become at higher risk as the prevalence of HIV infection in adolescents increases.

3. High-risk teenagers: This group includes adolescents exposed to HIV-infected individuals, including same-sex contacts, injection drug users, and partners of either of these groups. Hein et al. (1995) examined the behavioral risk factors in HIV-infected adolescents compared with HIV-negative youth. HIV-positive adolescents were significantly more likely to be sexually abused, to engage in anal sex and survival sex, to have unprotected sex with casual partners, to have sex under the influence of drugs, to have a STD, to use multiple drugs, and to engage in multiple problem behaviors. HIV-positive females reported more oral or anal intercourse (or both) compared to HIV-negative females. HIV-positive males reported significantly higher rates of both insertive and receptive oral and anal intercourse than did HIV-negative males.

HIV TESTING

Most laboratories offer enzyme immunosorbent assay (EIA) screening with a confirmatory Western blot analysis for any blood specimen with two consecutive positive EIA test results. A positive EIA test result should never be reported to a patient as a positive test result for HIV. A positive Western blot has almost 100% specificity. Western blot tests can be indeterminate. This is common for patients in the window phase between acute infection and seroconversion. However, many patients with indeterminate tests will later test HIV negative by EIA or Western blot. It is recommended that testing be repeated until a definitive positive or negative test occurs.

This can be performed after 1, 3, and 6 months for an indeterminate Western blot. The time delay from HIV infection to positive Western blot averages 21 days with newer test reagents. Rare cases of prolonged seroconversion (6 months or longer) have been reported. False-positive serology results may occur in 1 of 200,000 cases. Factitious reporting of HIV infection has also been reported as well. In confusing cases, including indeterminate results, false reporting, and patients who are potentially in the window period, HIV DNA or RNA determination by polymerase chain reaction (PCR) may be helpful in clarifying serostatus.

The technology for HIV testing has expanded greatly. In addition to blood tests, tests of oral secretions and urine are approved by the U.S. Food and Drug Administration (FDA) and have similar sensitivity and specificity (99.5%). Rapid testing of blood can be performed in 10 to 15 minutes and is frequently used in emergency rooms and during labor and delivery. It is recommended that positive tests be confirmed by standard serological testing. Newer, rapid tests that can be read by a clinical provider are expected within the next year and can probably be performed on oral secretions and urine. Little is currently known about the impact of rapid testing on counseling and testing guidelines for adolescents.

Consent and Confidentiality

Health care practitioners must balance the protection of adolescents' rights against the amount of information needed to deliver proper care.

1. Individuals older than 18 years of age who are competent: These individuals must make an informed consent for HIV testing, which involves a dialogue concerning the risks and benefits of the test, the implications of the test, and alternatives to the test.

2. Individuals between 12 and 17 years of age: The laws vary widely from state to state. In most states, the adolescent can and must give his or her own consent; however, as with any informed consent, the individual must be considered by the practitioner as competent to give an informed consent.

3. Individuals younger than 12 years of age and incompetent adolescents: For these individuals, a third party (parent or guardian) authorizes the testing. However, this authorization may be restricted by state laws.

An increasing number of states have statutes governing HIV testing. Without such a statute, general laws regarding minors apply. In most states, adolescents can give their own consent for diagnosis and treatment of STDs or contagious diseases. It is not clear whether HIV testing would fall under this category in states that do not declare AIDS to be an STD. In some states adolescents are authorized and must give their own consent. Generally, those adolescents who are judged to have the right to consent are considered to have also the right to refuse testing and the right of confidentiality.

The physician should be aware of the current local laws regarding the following:

1. Consent for testing: Who can consent? What is the required informed consent? Are pretest and posttest counseling available?
2. Who can get the results of these tests?
3. Where can the test results be recorded?
4. Can results be disclosed to other involved individuals and under what circumstances?
5. What can be written in the chart regarding testing and test results?
Teens whose behaviors put them at risk for HIV should be offered testing. Certain groups of youth are at very high risk:

1. Men who have sex with other men (youth in this group may not self-identify as gay or bisexual)
2. Youth who share needles (including tattooing, ear piercing, steroid injection, and recreational drugs)
3. Youth with partners from the above two groups
4. Youth who have had intercourse or shared needles with HIV-infected persons
5. Youth with STDs
6. Pregnant or parenting youth
7. Sexually active youth from inner-city or economically disadvantaged areas or areas of known high seroprevalence
8. Youth with multiple sexual partners
9. Recipients of blood transfusion before April 1985 in the United States (in some countries blood transfusions remain a risk factor)

Other groups of youth who may benefit from testing:

1. Any sexually active youth
2. Any youth with a history of sexual abuse
3. Any youth who is at no apparent risk but is seeking testing (the adolescent may not be able to confide risky behaviors or past sexual abuse)

Who Should Have HIV Testing Deferred?

1. Suicidal teens and those who seriously state they would be suicidal if HIV positive
2. Intoxicated and drug-withdrawing youth
3. Severely mentally ill youth who cannot provide consent for testing

When Should Testing Be Repeated for Youth with Positive Confirmatory HIV Test Results?

Testing should be repeated for

1. Any youth who desires a second test
2. Any youth who is claiming to be HIV positive but has unreliable documentation (adolescents have falsely reported being HIV positive)
3. Youth who are at extremely low risk and have a single positive test
4. Youth with normal CD4+ T cells and undetectable viral load who are not taking antiretroviral medications and have had only a single positive test in the past

Methods for HIV Testing

1. Anonymous testing: Patients are not identified by name but are given a number. Many teens prefer this method because of confidentiality issues, but it may lower the rate of return for posttest counseling or the rate of follow-up for medical care if the adolescent is found to be HIV positive.
2. Confidential testing: Pretest and posttest counseling are done, and the results are part of the medical record. Normal laws regarding patient confidentiality still protect clients. Because the counselor or physician probably knows the patient's name and address, testers can follow up with positive clients to ensure they receive adequate care.
3. Youth-specific testing: Many testing sites now have counselors (including peers) who are specifically trained to work with adolescents. The testing sites may be perceived as youth-friendly. The counselors may have more time for complete evaluations of risky behaviors and have knowledge of how to help youth change unhealthy behaviors. Often these sites are located where other services or activities are available for teens (e.g., homeless shelters, free clinics, schools, recreational centers). Youth-specific testing should be recommended whenever possible, because it can be an effective component of prevention education.

HIV COUNSELING AND TESTING

The primary goals of HIV testing include identifying patients who are infected with HIV and assisting them with accessing health care. In addition, the CDC includes HIV prevention as a primary goal during counseling and testing. Before the development of HAART (when treatment was much less effective), HIV prevention during counseling and testing of youth was considered a critical function. Many providers now believe that, although it is still important, HIV prevention counseling during the testing process is not critical. Because HIV counseling and testing based on the CDC model requires about 20 minutes for both the pretest and the posttest counseling sessions, it may serve as an impediment to physicians' even offering HIV testing. Clinicians must weigh the needs for HIV testing and HIV prevention counseling for patients. HIV testing with brief informed consent and referral for prevention education when needed may be a reasonable alternative that can increase HIV testing and case finding and still fulfill the needs of most youth for HIV prevention education.

Pretest Counseling

Before testing, the adolescent should receive counseling regarding the nature of the test and the implications of both a negative and a positive test result. The teen must also give voluntary consent for the test, and must be provided with any information on state or local laws that may affect disclosure of the test results. Pretest counseling could be assisted by means of videotapes, printed material, or group lectures.

Good counseling skills are important to the success of the HIV antibody testing process. This includes establishment of rapport with the teen and genuine, nonjudgmental concerns and positive regard for the teen. The practitioner should allow the adolescent time to express feelings and reactions. Additional counseling or referral to specialized services should be done when necessary.

1. Ask why the individual believes he or she should be tested.
2. Explain that AIDS is caused by a virus called HIV (human immunodeficiency virus) and that the virus infects the body and slowly damages the immune system.
3. Explain the modes of transmission:
   a. The virus is spread through the exchange of blood, semen, and vaginal secretions during sexual intercourse.
   b. HIV is spread through injection of blood when syringes and injection drug needles are shared.
   c. Before 1985, when blood screening began, the virus was spread through blood transfusions. This risk has been minimal since 1985.
   d. Infected pregnant women can pass the virus to their unborn children (perinatally, perinatally, or through breast feeding).
4. Explain that the test determines the presence or absence of antibodies to the virus. The estimated time between exposure and a positive test result (i.e., detectable antibodies) is 3 to 12 weeks but may be longer. It is usually recommended that testing be conducted 1 to 6 months after presumed exposure. If a test is done immediately in anxious individuals, it should be repeated in 1 to 6 months.
5. Discuss the meaning of both a positive and a negative test result. A positive test result means that the individual has been infected. Explaining that HIV is no longer a "death sentence" but a very manageable chronic illness is critical to preparing an adolescent for a positive test. Test counselors are often challenged by the desire to not make HIV sound too easily treated for fear that patients will disregard prevention messages. At the same time, trying to scare youth into avoiding risky behaviors is unlikely to be effective and can lead to self-destructive behaviors if the youth turns out to be HIV positive. Although there are no studies on what is the best approach, an honest, factual discussion is the best compromise. A negative test result probably means no current infection but does not suggest future immunity. It is even possible that the individual has been infected but has not yet produced any antibodies.
6. Discuss the possibilities of false-positive and indeterminate results. An indeterminate result is a nondiagnostic band pattern on the Western blot confirmatory test. If this is the case, an alternative confirmatory test may be employed or testing may be repeated in 4 to 12 weeks.
7. Discuss sexual behavior and drug history or other risk behaviors (risk assessment). The practitioner should have taken a psychosocial history (e.g., a HEADSS inventory, see Chapter 3), that focuses on sexual behaviors, as well as a drug history. The physician should use frank, nonjudgmental questions and avoid technical jargon. The teen should be aware of why these questions are being asked. An introductory statement, such as, "To give you the best care I can, I need to ask some specific questions about your lifestyle and behaviors that relate to your health" is a good approach. This history should include:
   a. Prior history of STDs
   b. Current sexual practices and number of steady or nonsteady partners
c. Past sexual practices
d. Regular sexual partners, including any sex with male or female prostitutes, injection drug users, bisexual or homosexual males, or suspected or confirmed HIV infected individuals
e. Regular sexual practices, including
   - Penile-vaginal activity (use of condoms)
   - Oral-genital activity (receptive, insertive, use of condoms)
   - Anal-genital activity (receptive, insertive, ejaculation, use of lubricants, use of condoms)
   - Oral-anal activity (receptive, insertive)
   - Mutual masturbation
f. Use and frequency of drugs, including alcohol, marijuana, barbiturates, amphetamines and other stimulants, hallucinogens, cocaine, and heroin and other injected drugs
8. Discuss risk reduction techniques and safer sex:
   a. Unprotected sex with partners who have AIDS or HIV who engage in high-risk behaviors is dangerous and should be avoided.
   b. The more sexual partners one has, the greater the risk of exposure. The following measures lower the risk:
      - Abstinence or mutual monogamy among partners known to be uninfected provides the surest protection against sexual transmission.
      - The proper use of a latex condom during intercourse provides protection. Ideally a condom demonstration should be given.
      - Sexual activities that could cause cuts or tears in the lining of the rectum, penis, or vagina should be avoided.
      - Sex with male or female prostitutes should be avoided.
      - Sharing needles or syringes with anyone should be avoided.
9. The CDC guidelines refer to client-centered counseling: The counselor avoids a preconceived set of points to be made. The focus is on developing prevention goals and strategies that the client deems realistic and incorporating the risk behaviors a patient has—for example, a patient may not be willing to eliminate anal intercourse but may be willing to use a condom; another patient may not be ready to quit injection drug use but might be willing to clean needles or use a needle exchange program.
10. Discuss the difference between confidential and anonymous testing. Under certain conditions, confidentiality may be broken and information released with confidential testing. In anonymous testing, no identifying patient information is collected. Because laws differ from state to state and change rapidly, the practitioner must become familiar with current local regulations governing reporting and confidentiality. Laws may be particularly ambiguous as to how they pertain to adolescents.
11. Discuss possible stress between the time of testing and the teen's finding out the results.
12. Discuss potential negative social consequences of being tested seropositive. These could include effects on employment, housing, insurance, and personal relationships.
13. Obtain written consent for voluntary testing.
14. Make a follow-up appointment to discuss the results.

Posttest Counseling
Posttest counseling should be given in person and should include the following:
1. Provide the results of the test. This should be done in a direct manner at the beginning of the posttest session.
2. Allow the adolescent time to express feelings and reactions. If the test result is positive, it is important to give the adolescent hope by reiterating the advances in medical treatment discussed during the pretest session.
3. Assess the adolescent's understanding of the result. This is best assessed by asking the teen directly what the test result means to him or her. If negative, the teen should understand how to prevent future infection. If positive, the teen should understand how to avoid infecting others. The teen should also understand that although the virus is probably present for life, a positive antibody test does not mean one has AIDS. Antibody-positive adolescents should be advised as follows:
   a. Do not donate blood, semen, or body organs.
   b. Employ safer sex practices.
   c. Inform physicians and dentists of HIV status.
   d. Encourage sexual partners, children, and needle contacts to seek evaluation and testing (many counties have anonymous partner notification programs).
   e. No evidence exists that HIV is transmitted to family household members or to close contacts by routes other than sexual intercourse, exposure to infected blood, and perinatal transmission.
   f. Household items may be shared by HIV-infected individuals and household members. Dishes and eating utensils should be routinely washed in hot water and a detergent. Personal hygiene items (i.e., razors and toothbrushes) should not be shared.
   g. The HIV-seropositive individual's blood and other body fluids should be handled with care. Soiled clothes or linen should be washed with a detergent or bleach.
   h. Bathroom facilities may be used by all household members.
4. Review routes of transmission.
5. Assess the teen's emotional status and arrange for counseling follow-up when appropriate.
6. Assess risk behavior and work with the teen to promote a commitment to alter high-risk behaviors.
7. Recommend medical follow-up and other support services when appropriate.
8. Refer the patient to an HIV specialist who is experienced with adolescents. Ideally the clinic will have a multidisciplinary team of physician, social worker, nurse, and other caregivers to assist the patient with treatment and with coping with the illness.

MANAGEMENT OF HIV-INFECTION IN ADOLESCENTS

Initial Assessment

History and Physical Examination The history and physical examination should stress the following:
1. Prior exposure to diseases that are likely to reactivate in individuals with HIV, including tuberculosis (TB), syphilis, herpes genitalis, herpes zoster, and cytomegalovirus (CMV)
2. Number of children, their ages, and their health status
3. Injection drug use history and history of alcohol and other drug use
4. Travel history to find out about possible exposure to fungal infections that are endemic in certain areas, such as histoplasmosis, coccidioidomycosis, or blastomycosis
5. Sexual history, including sexually transmitted infections
6. Prior immunizations
7. A review of systems, focusing particularly on the following:
   a. Systemic: Anorexia, weight loss, fevers, night sweats
   b. Skin: Pruritus, rashes, pigmented lesions
   c. Lymphatics: Increased size of lymph nodes
   d. Head, eyes, ears, nose, and throat: Headache, change in vision, sinus congestion
   e. Cardiopulmonary: Cough, dyspnea
   f. Gastrointestinal: Dysphagia, abdominal pain, and diarrhea
   g. Musculoskeletal: Myalgias, arthralgias
   h. Neurological: Memory loss, neuralgias, motor weakness, depression, and headache
   i. Genitourinary: Bumps, ulcers, burning or discharge
8. Careful measurement of weight at each visit
9. Careful examination particularly focusing on the following:
   a. Skin: Seborrhea, folliculitis, Kaposi sarcoma (KS) lesions, psoriasis, tinea, herpetic lesions, and molluscum contagiosum
   b. Eye: Visual acuity and fields, cotton-wool and hemorrhagic exudates on funduscopic examination
   c. Mouth: Periodontal disease (gingivitis), oral hairy leukoplakia (white plaques along lateral aspect of tongue), thrush, oral ulcers, KS lesions
   d. Lymphatics: Asymmetrical, tender, enlarged nodes, particularly posterior cervical, axillary, and epitrochlear nodes
e. Cardiopulmonary: Rales, murmurs (in injection drug users)
f. Gastrointestinal: Hepatosplenomegaly
g. Genitourinary: Herpetic lesions, warts, and penile discharge in males; cervical or vaginal discharge in females
h. Rectal: Perianal herpes, condyloma, fissures, and proctitis
i. Neurological: Focal findings, altered mental status

**Laboratory Evaluation**
Initial assessment should include the following:

1. Complete blood count, looking for anemia, leukopenia, or pancytopenia
2. Platelet count
3. Chemistry panel, looking for hypergammaglobulinemia, hypoalbuminemia, hypocholesterolemia, increased liver enzymes, or decreased renal function
4. Urinalysis
5. CD4+ T-cell count and percentage
6. Viral load (HIV RNA by PCR)
7. Consider HIV resistance testing (genotyping is less expensive than phenotyping) in patients with acute or recent seroconversion.
8. Purified protein derivative of tuberculin (PPD) skin test
9. Serology, for syphilis, and for hepatitis A, B, and C
10. Chest radiograph
11. Tests for gonorrhea and chlamydia infections if sexually experienced
12. Papanicolaou test (Pap smear) in women

**Vaccinations**

1. Influenza: Should be offered annually in October or November to all HIV-infected individuals. In patients not receiving HAART, the viral load may increase transiently after vaccination, but it returns to baseline in approximately 1 month.
2. Pneumococcal: Should be given once to previously unimmunized individuals.
3. Hepatitis A: Recommended for all at-risk individuals.
4. Hepatitis B: Recommended for all patients without evidence of hepatitis B immunity or chronic infection. Retrospective studies demonstrate that many youth with HIV do not develop antibodies to hepatitis B after three immunizations. Physicians can consider a fourth immunization or repeating the series after the patient begins HAART.
5. Measles-Mumps-Rubella (MMR): All patients should have received two MMR vaccinations in their lifetime. MMR is considered safe in patients with HIV.
6. Tetanus-Diphtheria: Same as if uninfected.
7. Polio: Patients requiring primary or booster immunizations should receive the inactivated form, inactivated poliovirus (IPV), not the oral poliovirus vaccine (OPV).
8. Chickenpox (varicella): This vaccine is not advised for use in those with acquired or primary immunodeficiencies.

**Follow-Up**

Patients should have their medical and social needs assessed at least every 3 months. Most patients on HAART should be seen monthly, because adherence issues frequently arise. These appointments should focus on signs and symptoms of disease progression, coping skills, and secondary prevention education. Antiretroviral management is reviewed later in this chapter. Secondary prevention focuses on preventing the spread of HIV to others but also in preventing unplanned pregnancy and STDs that are commonly seen in youth. Follow-up should include the following:

1. Complete blood count with platelet count and CD4+ T-cell count every 3 months
2. HIV RNA by PCR every 3 months
3. PPD yearly
4. Venereal Disease Research Laboratory (VDRL) or rapid plasma reagin (RPR) test for syphilis yearly
5. Pap smear annually in sexually experienced women
6. Regular discussion of safer sex and family planning
7. Discussion of partner notification as needed
8. Discussion of nutrition, exercise, disease progression, medication options, potential clinical trials
9. Regular evaluation of emotional status
10. Focused interval history and physical examination, concentrating on illnesses common for the patient's stage of HIV disease

**Early Manifestations of HIV Infection**

Early manifestations of HIV disease may include the following:

- Chronic lymphadenopathy
- Unexplained weight loss
- Xerosis
- Severe molluscum contagiosum
- Seborrheic dermatitis
- Isolated thrombocytopenia
- Pruritic papular eruptions
- Oral hairy leukoplakia
- Frequent lina
- Leukopenia
- Exacerbations of psoriasis
- Fatigue and malaise

Opportunistic diseases, including infections and neoplasms, typically occur after immune suppression reaches a certain level. Table 32.7 lists some common diseases and the corresponding CD4+ T-cell count associated with these illnesses.

**Table 32.7. Opportunistic diseases**

<table>
<thead>
<tr>
<th>Disease</th>
<th>CD4+ T-cell Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic lymphadenopathy</td>
<td>Low CD4+ T-cell</td>
</tr>
<tr>
<td>Unexplained weight loss</td>
<td>Low CD4+ T-cell</td>
</tr>
<tr>
<td>Xerosis</td>
<td>Low CD4+ T-cell</td>
</tr>
<tr>
<td>Severe molluscum contagiosum</td>
<td>Low CD4+ T-cell</td>
</tr>
<tr>
<td>Seborrheic dermatitis</td>
<td>Low CD4+ T-cell</td>
</tr>
<tr>
<td>Isolated thrombocytopenia</td>
<td>Low CD4+ T-cell</td>
</tr>
<tr>
<td>Pruritic papular eruptions</td>
<td>Low CD4+ T-cell</td>
</tr>
<tr>
<td>Oral hairy leukoplakia</td>
<td>Low CD4+ T-cell</td>
</tr>
<tr>
<td>Frequent lina</td>
<td>Low CD4+ T-cell</td>
</tr>
<tr>
<td>Leukopenia</td>
<td>Low CD4+ T-cell</td>
</tr>
<tr>
<td>Exacerbations of psoriasis</td>
<td>Low CD4+ T-cell</td>
</tr>
<tr>
<td>Fatigue and malaise</td>
<td>Low CD4+ T-cell</td>
</tr>
</tbody>
</table>

The management of conditions associated with HIV is beyond the scope of this chapter, changes frequently, and is frequently left to HIV specialists. Updated treatment information is available on the Web sites listed at the end of this chapter.

**Management of Sexually Transmitted Infections**

1. Uncomplicated chlamydia, gonorrhea, trichomonas, and syphilis are generally treated in the same manner as in adolescents without HIV.
2. Pelvic inflammatory disease can be more difficult to treat in women with HIV, especially if immune dysfunction is pronounced (low CD4+ T-cell count). In general
the CDC treatment guidelines are followed, but the threshold for hospitalization for administration of intravenous antibiotics is reduced.

3. Cervical dysplasia has been shown to be very prevalent in women with HIV. High-risk serotypes such as human papillomavirus 16 (HPV 16) seem to be more common, and spontaneous regression appears to be less common. Still, annual screening and referral for colposcopy for both low-grade and high-grade squamous intraepithelial lesions or recurrent atypical results on Pap smears are recommended. Treatment and follow-up recommendations for abnormal colposcopic biopsies are generally the same as in women not infected with HIV. Whenever possible, refer adolescents with HIV and abnormal Pap smear results to providers with HIV experience.

Management of Family Planning

With the marked improvements in prevention of maternal-child transmission of HIV, family planning has changed. Many youth now acknowledge their interest in having children despite having HIV. Physicians should be honest about the risks of maternal-child transmission. The risk is about 23% without antiretroviral treatment. It was about 8% when HIV-infected mothers were started on AZT and the infants were treated after birth. However, the current standard of care is to treat infected women who desire pregnancy with HAART (minimum of three antiretrovirals). The risk of transmission has been shown to be less than 4% for women taking HAART, and it is probably less than 1% when a patient conceives while following an effective HAART regimen (i.e., viral load is undetectable) and maintains the program during pregnancy.

Although the prevention of maternal-fetal transmission of HIV is no longer the primary reason for birth control, the typical issues of adolescence and being prepared for parenting are still critical. Unplanned pregnancies can disrupt an already complex situation for youth infected with HIV. Providing contraceptive counseling in these youth is complicated by the competing desires to prevent transmission of HIV to sexual partners by using condoms and to prevent unplanned pregnancy (usually with a more effective hormonal method). Studies of adult women with HIV have shown that patients using hormonal methods of contraception were less likely to use condoms. However those using condoms frequently reported using them irregularly. Data from a cohort of HIV-infected adolescents indicated that the majority of adolescents reported condoms as their main method of contraception (Belzer et al., 2001). Unfortunately, the rate of conception was greater than 20% during the first year in the study, and it was high in those reporting contraception use as well. Contraception needs to be addressed frequently and adherence to the method of choice discussed. Oral contraceptive pills may be less effective in patients using protease inhibitors (which increase estrogen metabolism), and their use adds to the pill burden for patients taking other medications. Methods that require less attention (and are more difficult to discontinue), such as depo-medroxyprogesterone or levonorgestrel implants, may be better for pregnancy prevention, but the risks of HIV transmission due to lack of condom use must be factored in.

Common Psychosocial Problems

Common psychosocial problems in HIV-infected adolescents include the following:

1. Depression and suicidal ideation
2. Substance abuse
3. Self-blame
4. Social isolation, including family and peers
5. Unsafe sex
6. Sexual identity
7. Homelessness
8. Survival sex
9. Denial
10. Unplanned pregnancy

The cornerstone to good care is the availability of a strong health care team, including physician, nurse, social worker, psychologist or psychiatrist, nutritionist, substance abuse counselor, and medical subspecialists as needed. Coordinating the team to focus on the patient’s identified needs improves compliance and facilitates normal adolescent development.

Travel

Visiting regions outside one’s normal community can expose an individual to many pathogens. In developing countries, opportunities for exposure to enteric pathogens, including Cryptosporidium and Isospora, increase. Risk for certain respiratory infections such as coccidioidomycosis, histoplasmosis, and TB also increases in many developing countries and in certain geographic regions of the United States. The CDC offers an international travelers’ hotline (telephone 1-404-332-4555). Patients planning significant travel should discuss preventive strategies with their physician.

1. Avoid contaminated food and drink (i.e., tap water).
2. Receive appropriate immunizations.
3. Extended travel should be accompanied by appropriate medications and telephone numbers for emergency care.
4. Seek medical attention promptly if fever, diarrhea, or other illness occurs during or after travel.

Sports Participation

When Ervin “Magic” Johnson announced that he was infected with HIV, many questions surrounding the advisability of vigorous exercise occurred. To date there have been no studies documenting a positive or negative impact of exercise on HIV. Currently, we recommend using common sense in guiding infected youth on sports participation.

There have been no documented cases of HIV transmission during athletic participation. We would not withhold a youth from competitive sports (even full-contact sports like wrestling or football) solely on the basis of HIV-positive status. The principal risks athletes have for acquiring HIV are related to off-the-field settings (Mast et al., 1995). However, all participants (whether infected with HIV or uninfected) should not compete with open wounds, and universal precautions should always be followed when bleeding occurs.

Evaluation of Specific Syndromes

Pulmonary (Cough or Shortness of Breath)

1. If the CD4+ T-cell count is 200 cells/mL or less or the percentage of CD4+ T cells percent is 20% or less, the patient requires the following:
   a. Chest radiographic examination: Look for interstitial or other infiltrates
   b. Pulse oxymetry or arterial blood gas determination for hypoxemia
   c. Consider induced sputum for Pneumocystis carinii pneumonia (PCP)
   d. Consider gallium scan or bronchoscopy for PCP evaluation
2. In patients with a CD4+ count higher than 200 cells/mL and a percentage higher than 20%, it is unlikely to be PCP:
   a. Consider evaluation for bronchitis, sinusitis, TB, and bacterial pneumonia
   b. Chest radiographic examination or sinus films
   c. Subsequent PPD
   d. Sputum for culture and sensitivity, acid-fast bacillus

Fever Evaluation in patients who have severe immunosuppression (CD4+ T-cell count less than 200 cells/mL) but lack of specific organ system signs or symptoms should include the following:

1. Chest radiographic examination: Intersitial infiltrates are consistent with PCP, infection with Mycobacterium avium complex (MAC) or CMV; focal infiltrates are consistent with TB or bacterial pneumonia
2. Complete blood count: Anemia is common in MAC
3. Chemistry panel: Elevated lactate dehydrogenase is common in PCP, elevated alkaline phosphatase is common in MAC
Blood cultures for bacteria, virus (CMV), fungus, and acid-fast bacillus
5. Serum cryptococcal antigen

If fever persists and above tests are inconclusive, consider the following:

1. Lumbar puncture: May pick up cryptococcal infection
2. Bone marrow biopsy: May pick up disseminated MAC, CMV, or fungus
3. Ophthalmology consultation: Looking for CMV
4. Body computed tomography (CT): Looking for lymphoma
5. Sinus films

In patients with mild immunosuppression (CD4+ T-cell count 200 to 500 cells/mL), look for common illnesses (viral or bacterial) and consider looking for TB, sinusitis, and pneumonia.

In patients with minimal immune suppression (CD4+ T-cell count greater than 500 cells/mL), avoid costly workups unless conservative evaluation fails.

**Diarrhea**

In patients with severe immunodeficiency (CD4+ T-cell count less than 200 cells/mL):

1. If diarrhea is mild, consider empiric treatment with diphenoxylate (Lomotil) or loperamide (Imodium).
2. If diarrhea is severe, check stool for ova and parasites, culture and sensitivity. Cryptosporidium or Isospora infection.
3. If these tests are inconclusive, consider colonoscopy looking for CMV, MAC, Microsporidia, and Isospora.

In patients without severe immunodeficiency:

1. Diarrhea is usually self-limited, and costly evaluations should be avoided.
2. Consider stool ova and parasites, bacterial culture and sensitivity if the patient is sexually active, is homeless, or has had recent foreign travel.

**Neurological (New Headaches, Seizures, Focal Neurological Signs)**

In patients with severe immunodeficiency (CD4+ T-cell count less than 200 cells/mL):

1. Emergency CT or magnetic resonance imaging (MRI) of head: Multiple enhancing ring lesions are usually indicative of toxoplasmosis; primary central nervous system lymphoma is also common.
2. Lumbar puncture for cell count, protein, cryptococcal antigen, Gram stain, routine acid-fast bacillus and fungal cultures, and VDRL.

**Dysphagia**

In patients with severe immunodeficiency (CD4+ T-cell count less than 200 cells/mL):

1. If oral thrush is present, consider empiric treatment for Candida organisms with fluconazole or ketoconazole.
2. If there is no oral thrush or empiric treatment fails, try endoscopy with evaluations for fungus, CMV, and herpes simplex virus.

**Prophylaxis**

Prophylaxis is one of the most important ways that patients with severe immunosuppression can maintain their health. Patients who have severe immune suppression but are not ready for HAART should still be encouraged to use prophylaxis.

**Primary Prophylaxis**

The CDC frequently publishes updated guidelines for primary prophylaxis and can be found on their Web site.

1. Pneumocystis: Initiate when the CD4+ T-cell count is 200 cells/mL or less. Patients who start HAART and in whom the CD4+ T-cell count rises above 200 cells/mL for 3 to 6 months may safely discontinue prophylaxis.
   a. Drug of choice: Trimethoprim-sulfamethoxazole double-strength tablet, daily or three times weekly (patients with allergies to sulfonamides are desensitized).
   b. Alternatives: Dapsone 100 mg orally per day (check for glucose-6-phosphate dehydrogenase [G6PD] deficiency before using); nebulized pentamidine 300 mg every 4 weeks using Respigen or Nebulizer (may be the method of choice in noncompliant youth). Altevaquone 750 mg orally twice a day with meals.
2. Tuberculosis: Initiate in teens who are PPD positive (greater than 5 mm), have recent TB exposure, or have a history of inadequately treated TB that healed.
   a. Drug of choice: Isoniazid 300 mg plus pyridoxine 50 mg daily for 9 to 12 months.
   b. Alternative: Rifampin 600 mg plus pyrazinamide 20 mg/kg daily for 60 doses (rifampin is contraindicated in patients taking protease inhibitors).
3. Mycobacterium avium complex (MAC): Initiate when the CD4+ T-cell count is 50 cells/mL or less. Prophylaxis can probably be discontinued if the count rises above 100 cells/mL for 3 to 6 months after initiation of HAART.
   a. Drug of choice: Clarithromycin 500 mg twice daily or azithromycin 1,200 mg orally once per week.
   b. Alternative: Rifabutin 300 mg orally once per day.
4. Toxoplasma gondii risk: Initiate when the CD4+ T-cell count is less than 100 cells/mL and serology results are positive for T. gondii immunoglobulin G.
   a. Drug of choice: Trimethoprim-sulfamethoxazole, one double-strength tablet per day.
   b. Alternative: Dapsone 50 mg orally once a day plus pyrimethamine 50 mg/wk plus leucovorin 25 mg/wk.

**Antiretroviral Therapy**

The CDC regularly updates guidelines on the use of antiretrovirals for adolescents and adults and should be consulted with the assistance of an HIV specialist in determining whether a patient should be treated with HAART. In addition, the Health Resources and Service Administration has published a report titled, Helping Adolescents with HIV Adhere to HAART (available through the National AIDS Clearinghouse). Although a full discussion of the use of antiretrovirals is beyond the scope of this chapter, some basic principles pertaining to youth are important.

**Initiating Highly Active Antiretroviral Therapy (HAART)**

Although the United States Department of Health Services publishes guidelines for the initiation of HAART with adolescents and adults that are based primarily on a patient's immune status (CD4+ T-cell count) and risk for disease progression (viral load, HIV RNA), there has been considerable attention to the issue of a patient's ability to adhere strictly to a regimen for many years and perhaps for the rest of the patient's life. Decisions to initiate therapy must be made jointly by a well-informed patient and his or her health care providers. Empowering patients through education on their ability to control HIV through the proper use of medications, while at the same time helping them to develop a realistic time frame and plan for initiating therapy, is key to eventual adherence and reaching mutual agreement on treatment.

There are currently 15 FDA-approved antiretroviral drugs that belong to one of three classes based on their mode of preventing HIV replication. New medications in each class are currently in development, and new classes are also being researched.

**1. Nucleoside reverse transcriptase inhibitors**
   a. Zidovudine (Retrovir or AZT)
   b. Didanosine (Videx or DDI)
   c. Stavudine (Zerit or D4T)
   d. Lamivudine (Epivir or 3TC)
   e. Abacavir (Ziagen)
   f. Zalcitabine (Hivid or DDC)
   g. Combivir, a combination pill with both zidovudine and lamivudine
   h. Trizivir, a combination of zidovudine, lamivudine, and abacavir

**2. Nonnucleoside reverse transcriptase inhibitors**
   a. Nevirapine (Viramune)
   b. Efavirenz (Sustiva)
   c. Delavirdine (Rescriptor)
   d. Protease inhibitors
The general principles of HAART therapy are listed in **Table 32.8**. The primary aim is to initiate a regimen (frequently described to patients as a cocktail) containing a minimum of three antiretroviral medications with the goal of reducing the patient's viral load to an undetectable level on a highly sensitive assay for HIV RNA. Incomplete suppression, through either inadequate medication or nonadherence, can lead to the development of HIV strains that are resistant to the antiretrovirals. Because of potential cross-resistance, second- and third-line treatment is often more complex, more toxic, and less effective.

**TABLE 32.8. Summary of the principles of therapy of HIV infection**

The patient's need for HAART must be balanced with the ability to adhere to the drug regimen. Research has indicated that physicians are notoriously poor at predicting how likely a patient is to take his or her medication. **Table 32.9** reviews some factors that may influence patients' decisions to start taking medication. **Table 32.10** reviews some basic concepts about adolescents and adherence to HAART. Predictors of poor adherence include psychosocial problems such as poor support, mental health problems (depression was shown to be a predictor of nonadherence in adolescents with HIV in one study), substance abuse, and homelessness. In addition, factors such as patients' trust in their health care providers or concerns that taking medication might inadvertently disclose their HIV status to family, friends, roommates, or coworkers must be considered. Also critical are medication-inherent factors such as the number of pills, the frequency of dosing, the size or taste of pills, potential side effects (many youth fear rashes because they might disclose their HIV status), and food and timing requirements. In general, one would try to keep regimens as simple as possible. Regimens as simple as one pill twice daily are available, and once-daily regimens are currently being investigated and may work well for some youth. Because studies have demonstrated that adolescent adherence to antiretroviral therapy is often poor (less than 40% at 3 months), it is important to chose regimens such that, if resistance develops, options can still be maintained for the future. Close monitoring for nonadherence and giving out small supplies of medications may prevent prolonged, improper taking of medications.

**TABLE 32.9. Medication adherence assessment**

**TABLE 32.10. Barriers to adherence**

As stated earlier, helping patients to prepare for HAART and to maintain it once begun is a challenging task and one that should be reserved as much as possible for physicians with expertise in HIV and adolescent care. Many adolescent HIV specialists have adapted the stages of change model developed by James O. Prochaska and C. C. DiClemente. **Table 32.11** reviews the stages from precontemplation through maintenance and provides goals for health practitioners and key objectives for each stage.
TABLE 32.11. Stages of behavioral change

In summary, the need for HAART in HIV-infected adolescents must be balanced against the potential for benefit from the medications and the potential for harm from the development of resistance due to nonadherence. It is not unreasonable to initiate a short trial (perhaps as short as 1 week); if the patient cannot take the medication regularly or even follow-through with the next appointment, the medications can be discontinued until further efforts have been made. It is very reasonable to hold off on HAART, even for patients with highly advanced AIDS, if the patient and physician conclude that adherence is unlikely. Medication has been demonstrated in many cases to produce immune reconstitution in even the most damaged immune systems as long as the virus is sensitive to the medication and the patient has not developed a terminal or untreatable complication.

Prevention

Until a vaccine is found, health education and counseling are the main tools to reduce the risk of infection. Appropriate educational interventional goals for adolescents include the following:

1. Reducing misinformation and prejudice against HIV-infected persons
2. Helping to reduce high-risk behavior, including recommendations to decrease sexual activity, numbers of sexual partners, and experimentation with drugs
3. Increasing the use of condoms in adolescents who are having intercourse
4. Encouraging adolescents in sexual relationships to get HIV tested with their partners and to maintain monogamy.

HIV/AIDS education needs to be conducted at schools, religious organizations, youth organizations, medical facilities, and meetings with parents. Media (television, radio, magazines) are powerful methods to impart information that may change adolescents' attitudes. Meeting youth, where they congregate, with outreach workers can be an especially effective method of reaching high-risk populations such as homeless youth, gang youth, or out-of-school youth. Topics for HIV prevention include

1. Epidemiology of HIV/AIDS and myths about AIDS
2. Sexual transmission and prevention, including abstinence, safer sex, and condom use
3. Transmission through needles, drug use prevention
4. HIV and pregnancy
5. Testing and counseling
7. Medical aspects of HIV/AIDS
8. Peer pressure and dating skills
9. Community resources

It is important to offer HIV/AIDS education in language that the adolescent can understand. The information must be simple, accurate, and direct. In recent years, the federal government has put a lot of resources into abstinence-only prevention education. Unfortunately there has never been any research documenting benefit from abstinence-only prevention education. Abstinence-based education, which also provides information on how to reduce risk if sexually active, has been shown to delay the onset of sexual activity in some studies. The CDC posts information on their Web site including "Programs that Work" and a “Compendium of Effective Interventions to Reduce HIV.” They include only strategies that have documented in the peer-reviewed literature to be effective.

Kirby et al. (1994) reviewed the characteristics of school-based sexuality education programs. Effective programs were those that

1. Used social learning theory as a foundation for program development.
2. Included a narrow focus on reducing sexual risk-taking behaviors that may lead to HIV, STDs, or pregnancy.
3. Provided basic, accurate information about the risks of unprotected intercourse and methods of avoiding unprotected intercourse through experiential activities designed to personalize this information.
4. Included activities that address social or media influences on sexual behavior.
5. Reinforced clear and appropriate values to strengthen individual values and group norms against unprotected sex.
6. Provided modeling and practice in communication and negotiation skills.

Many youths are not at school and therefore are not reachable through school programs. Street youth service workers who have regular contact with these teens may be effective AIDS educators. Involving peers in the education process can also be helpful.

A recent trend in the prevention of many adolescent high-risk behaviors is called “Youth Development.” These programs

1. Build competencies and self-efficacy (the belief that trying will result in success).
2. Help families and communities send consistent messages about standards for positive behavior.
3. Expand opportunities and recognition for youth who engage in positive behavior and activities.
4. Provide structure and consistency in program activities.
5. Last a minimum of 9 months.

Recommendations for Primary Care Physicians

Primary care practitioners should:

1. Obtain a sexual history and perform counseling on safer sexual behaviors.
2. Be able to perform pretest and posttest HIV antibody counseling.
3. Be able to comanage individuals with HIV infections with HIV specialists (especially if the HIV care provider is not familiar with youth issues).
4. Know how to initiate the evaluation of common AIDS-related symptoms such as fever, lymphadenopathy, headache, and diarrhea.
5. Be familiar with community resources for adolescents in need of more intensive HIV prevention interventions.

Controlling Transmission

Blood and body fluid precautions should be consistently used for all patients, because medical history and examination cannot reliably identify all patients who are infected with HIV.

WEB SITES

General Resources

http://www.cdc.gov/hiv/dhap.htm, CDC site on surveillance, testing, treatment.


Consumer-oriented Treatment Information

http://www.projinf.org/pub/pip_index.html, Project Inform, with numerous articles on many aspects of HIV and AIDS.
Occupational Exposure Issues

Information on Prevention of HIV and Other Occupational Needle-Stick Exposures


Information on HIV and Other Bloodborne Pathogens in Health Care Workers


Postexposure Prophylaxis


Selected National HIV Resources

National Pediatric and Family HIV Resource Center, 30 Bergen Street, ADNC #4, Newark, NJ 07103, telephone 973-972 0410 or 1-800-362-0071, fax 1-973-972-0399.

Magic Johnson Foundation, 6167 Bristol Parkway, Suite 450, Culver City, CA 90230, telephone 1-310-338-8110, fax 1-310-338-8563.

Peer Education Program of Los Angeles (PEP-LA), 5410 Wilshire Boulevard, Suite 203, Los Angeles, CA 90036, telephone 1-310-338-8563.

AIDS Project Los Angeles, 1313 North Vine Street, Los Angeles, CA 90028, telephone 1-323-993-1600, fax 1-323-993-1598.

AIDS Alliance for Children, Youth and Families, 910 17th Street, NW, Suite 422, Washington, DC 20006, telephone 1-800-334-7342.

Adocets for Youth—Media Project, 10999 Riverside Drive, Suite 300, North Hollywood, CA 91602, telephone 1-818-762-9658, fax 1-818-762-9769.


AIDS Hotline, United States Public Health Service, telephone 1-800-342-2437 or 1-800-344-7432 in Spanish or 1-800-243-7889 for hearing-impaired persons.

HIV Information Network—Fax Newsletter, University of Alabama School of Medicine, fax 1-212-481-8534.

National Center for Youth Law—Adolescent Health Care Project, 405 14th Street, Suite 1500, Oakland, CA 94612, telephone 1-510-835-8098, fax 1-510-835-8099.

National AIDS Information Clearinghouse, telephone 1-800-458-5231.


Western AIDS Education—Training Center: For help with a clinical HIV problem, telephone 1-800-933-3413.


Gay and Lesbian Community Services Center—Youth Services, telephone 1-323-993-7400.

Peer Education Program of Los Angeles (PEP-LA), 5410 Wilshire Boulevard, Suite 203, Los Angeles, CA 90036, telephone 1-800-334-7342.

Mag Johnson Foundation, 6167 Bristol Parkway, Suite 450, Culver City, CA 90230, telephone 1-310-338-8110, fax 1-310-338-8563.

Peer Education Program of Los Angeles (PEP-LA), 5410 Wilshire Boulevard, Suite 203, Los Angeles, CA 90036, telephone 1-310-338-8563.

AIDS Project Los Angeles, 1313 North Vine Street, Los Angeles, CA 90028, telephone 1-323-993-1600, fax 1-323-993-1598.

AIDS Alliance for Children, Youth and Families, 910 17th Street, NW, Suite 422, Washington, DC 20006, telephone 1-800-334-7342.

Adocets for Youth—Media Project, 10999 Riverside Drive, Suite 300, North Hollywood, CA 91602, telephone 1-818-762-9658, fax 1-818-762-9769.


AIDS Hotline, United States Public Health Service, telephone 1-800-342-2437 or 1-800-344-7432 in Spanish or 1-800-243-7889 for hearing-impaired persons.

HIV Information Network—Fax Newsletter, University of Alabama School of Medicine, fax 1-212-481-8534.

National Center for Youth Law—Adolescent Health Care Project, 405 14th Street, Suite 1500, Oakland, CA 94612, telephone 1-510-835-8098, fax 1-510-835-8099.

National AIDS Information Clearinghouse, telephone 1-800-458-5231.


Western AIDS Education—Training Center: For help with a clinical HIV problem, telephone 1-800-933-3413.


Gay and Lesbian Community Services Center—Youth Services, telephone 1-323-993-7400.

Educational Resources


Project SNAPP—Skills and Knowledge for AIDS and Pregnancy Prevention: An 8-session curriculum and video for middle school students. From Division of Adolescent Medicine, Children's Hospital Los Angeles; published by ETR Associates, telephone 1-800-321-4407.

CDC National AIDS Clearinghouse: Has lists of HIV or AIDS materials. Telephone 1-800-458-5231.

At Risk Resources: Telephone 1-800-99-Youth.

Advocates for Youth: Has fact sheets on youth sexuality including HIV or AIDS and many educational materials. Telephone 1-202-347-5700.


Really Check: Video for Youth by Youth.

Health Initiatives for Youth—Project AHEAD: Telephone 1-415-487-5777.


San Francisco Study Center (video): Between Friends. Telephone 1-415-626-1650.

REFERENCES AND ADDITIONAL READINGS


Obesity is a serious medical problem that is increasing in prevalence in the adolescent and adult population and affects almost 100 million Americans. About 50% of Americans are overweight, and 25% are obese. The average American gains 20 to 30 pounds in the 20 years after high school, and others gain far more.

Obesity is a common problem among adolescents. The prevalence of obesity and overweight in American teenagers ranges from 16% to 22%, depending primarily on sex, race, family history, and physical activity. It is a disorder in which the psychobiological cues for eating are discordant with energy requirements. Both genetic and environmental factors contribute to obesity and overweight problems. Studies on fraternal twins raised apart suggest a strong genetic influence on body mass index (BMI). Genetic mutations, such as those in the genes encoding leptin, the leptin receptor, propriomelanocortin, and the adipocyte differentiation factor peroxisome-proliferator-activated receptor-g2, have been identified in rodents and humans. Endocrine and metabolic causes such as hypothyroidism, hypercortisolism, and Prader-Willi syndrome are unusual in adolescents.

DEFINITION

Overweight and obesity are defined as either body weight or excess body fat above an arbitrary standard, often defined in relation to height. However, both of these conditions are difficult to define in the developing adolescent because of the difficulty in establishing norms of body fat in relation to a variable height with age. Table 33.1 reviews various definitions of childhood and adolescent obesity.

### TABLE 33.1. Definitions of obesity and severe obesity

<table>
<thead>
<tr>
<th>Definition</th>
<th>Body Mass Index</th>
</tr>
</thead>
</table>
| Adolescents | The Expert Committee on Clinical Guidelines for Overweight in Adolescent Preventive Services (Himes and Dietz, 1994) recommended screening adolescents by using the BMI. The BMI is equal to the weight in kilograms divided by the square of the height in meters: \[ BMI = \frac{W}{H^2} \] It is an easy index to calculate and has a correlation of 0.7 to 0.8 with body fat content in adults. It also correlates well with body fat content in children and adolescents. A BMI exceeding the 85th percentile for age and gender has been suggested as one definition for overweight or for those at risk of being overweight in the adolescent age group. BMI values in adolescents are listed in Fig. 1.20 and Fig. 1.21 in Chapter 1. Figure 4.8 and Figure 4.9 in Chapter 4 also show height, weight, and BMI by age and sex. BMI-for-age charts may also be obtained from the Centers for Disease Control (CDC) on their Web site: www.cdc.gov/growthcharts/.
| Young Adults and Adults | The standards for defining obesity in adults were changed in 1998, following the changes in the World Health Organization (WHO) definitions in 1992. This has increased the number of adults identified in the United States as being overweight or obese. The definitions moved the BMI lower limit for overweight from 27.8 kg/m² in adult men and 27.3 kg/m² in women down to 25 kg/m². |
Body fat measurements: Although total body fat can be measured indirectly by a variety of techniques, its use is limited to the research laboratory or clinical settings, particularly in the context of obesity assessment.

Menstrual irregularities: Aromatization of androgens to estrogen occurs in adipose tissue in the female and is a significant source of extragonadal estrogen. This process can influence menstrual cycle regularity and fertility.

Stunkard et al. (1990) found a high correlation of BMI between twins, even when reared apart. This indicates a significant genetic component in body mass index (BMI).

Stunkard et al. (1986) also demonstrated that there was a strong relationship between the weight class of adoptees and the BMI of their biological parents. This suggests a strong genetic influence on body weight.

18.5–24.9 BMI Range (kg/m²): The BMI classification ranges from underweight to obesity, with the following definitions:

- **Underweight**: BMI <18.5
- **Normal**: 18.5–24.9
- **Overweight (preobese)**: 25–29.9
- **Obesity (obese) class 1**: 30–34.9
- **Obesity (obese) class 2**: 35–39.9
- **Obesity (obese) class 3**: ≥40

Other Methods of Measuring Obesity: Other methods of measuring obesity have included the following:

1. **Weight (W)** for height (H) percentiles: Obesity is defined as weight above the 90th percentile for height, based on data collected in the third National Health and Nutrition Examination Survey (NHANES III) in 1994. Charts are available from the National Center for Health Statistics.

2. **The ponderal index (HW⁴/³)**: This value overestimates obesity when compared with measures of body fat.

3. **Body fat measurements**: Although total body fat can be measured indirectly by a variety of techniques, its use is limited to the research laboratory or clinical studies. However, a related, clinically useful method is the measurement of either triceps and calf skin fold thickness or triceps and subscapular skin fold thickness. Slaughter et al. (1986) advocated use of the following equations to estimate percent body fat:

   **Males**: % body fat = 0.735 (triceps + calf) + 1.0
   **Females**: % body fat = 0.610 (triceps + calf) + 5.1

4. None of the measures listed takes into account the regional distribution of body fat, which in adults has been correlated with future obesity-related health risk. Potentially useful measurements in young adults and adults are the waist circumference and the waist-hip ratio. Many studies have demonstrated that the distribution of body fat is an independent risk factor for cardiovascular disease. Visceral abdominal fat is more likely to contribute to elevated blood cholesterol and other lipid abnormalities, glucose intolerance, and hypertension.

Summary: In summary, methods that use just height and weight are cheap and easy but do not reflect regional body fat distribution. Skin fold measurements are also cheap and easy but can be inaccurate due to inter-observer error. Simple portable office ultrasound instruments help to overcome this problem, but they are expensive for the nonspecialist professional. Updated weight-for-height percentile charts are easy to use and integrate into clinical records. The developmentally based BMI percentile curves that are now available overcome many of the difficulties of the past charts but still do not reflect what may be important regional distribution characteristics.

**PUBERTAL CHANGES**

Effects of Puberty on Body Composition: During adolescence, lean body mass increases in both sexes. The increase is greater in males because of their greater increase in skeletal muscle. The maximum increase in muscle mass occurs at about the time of peak height velocity (PHV) in both sexes, whereas the maximum fat deposition occurs 2 years before PHV. However, in females fat deposition continues throughout puberty, and female adults ultimately have more body fat than males.

Effects of Obesity on Puberty: Obesity may influence puberty, and there is some evidence that obesity can delay puberty. The factors that contribute to this are not fully understood, but they may include hormonal changes and changes in body composition.

**ETIOLOGY**

Many theories have been advanced, but the cause of obesity is still unclear. Obesity is a chronic disease with multiple factors contributing to its etiology. Genetic, cultural, socioeconomic, behavioral, and situational factors all play a role in establishing dietary habits and thus weight control. Clearly a number of subtypes of obesity exist. Recent evidence points to a significant genetic component with certain subtypes. At some future time obesity may be divided into different disease classifications, with therapies tailored to match the underlying cause. At present, only 5% of obese children and adolescents have an underlying specific cause identified. This includes about 3% with endocrine problems (hypothyroidism, Cushing syndrome, hypogonadism) and 2% with rare syndromes (Prader-Willi, Laurence-Moon-Biedl, Fröhlich, Alström, Kallmann).

**INFLUENCING FACTORS**

Familial or Genetic: Many reports have shown a familial pattern of obesity, with a strong correlation between parents and their children. This suggests a hereditary component in the development of obesity.

1. There is an increased incidence of obesity among people with obese parents. In one study of Swedish twins, if one parent was obese, there was a 30% risk for the child to be obese; if both parents, a 70% risk. Despite the genetic implications, these findings may also be partially environmentally influenced.

2. Stunkard et al. (1990) found a high correlation of BMI between twins, even when reared apart.

3. Stunkard et al. (1986) also demonstrated that there was a strong relationship between the weight class of adoptees and the BMI of their biological parents. There was no relationship between the weight class of the adoptees and the BMI of their adoptive parents.

4. West et al. (1994) linked dietary obesity in mice to specific chromosomal loci.

Fat Cell Theory: Fat cells multiply at three stages of life: gestation, first year of life, and adolescence. The fat cell theory suggests that fat cells gained early in life and during pubcy increase the number of fat cells and thus is critical to the development of obesity. Adolescents who have a propensity to obesity have been shown to have an increased number of fat cells compared with normal-weight adolescents.

Activity and Energy Expenditure: There are conflicting reports regarding energy expenditure in obese individuals. Obese individuals filmed in time-lapse photography seem to move less than normal-weight individuals. Although some studies show no evidence to implicate a decrease in energy utilization in those who are overweight, Ravussin et al. (1988) found that the rates of energy expenditure were lower in obese individuals and that these rates of expenditure seem to cluster in families. Dietz (1993), drawing from longitudinal data collected in the NHANES study, stated that the most powerful predictor of the development of obesity in adolescence was the time that a child 6 to 11 years of age spends viewing television, even after controlling for other known variables associated with childhood obesity. However, DuRant et al. (1994) could not
find a relationship between television watching and body composition, and Robinson et al. (1993) only found a weak relationship between television and obesity.

Leibel et al. (1995) demonstrated that maintenance of reduction in body weight of 10% or more was associated with a mean reduction in total energy expenditure in both obese and nonobese individuals. In addition, maintenance of body weight at 10% or more above the usual weight was associated with an increase in total body energy expenditure in both obese and nonobese individuals.

Calories
Caloric intake is variably elevated in obese adolescents and is dependent on where they eat. In one study, obese adolescent boys ingested more calories at school than at home, compared with their lean counterparts. Retrospective diet histories tend to underreport caloric intake in both obese and nonobese adolescents, but more so in the obese.

Behavior
Obese patients often exhibit the following behaviors:
1. Eating fast
2. Skipping breakfast and lunch and ingesting the majority of their calories at night
3. Eating when not hungry but when food is available or when their appetite is stimulated by environmental cues
4. Eating when depressed or anxious
5. Eating in association with other activities, such as watching television
6. Underestimating the total number of calories ingested
7. Overindulging in “fast foods”

Central Regulation Theory
The central regulation theory suggests that the hunger or satiety center in the hypothalamus in obese individuals may not function properly in suppressing appetite. The energy-regulating system, operating at a high set point, gives rise to a predetermined body weight.

Psychological Theory
Psychological theories of obesity contend that obese individuals are depressed or anxious and use eating as a means to alter their mood.

Body Image Theory
The body image theory holds that some obese adolescents have a distorted and fat body image. According to this theory, one cannot achieve weight change until one has visualized and become comfortable with a smaller body image.

Hormonal Theory
A hormone named leptin has recently been discovered that appears to play a role in obesity in some instances. This protein hormone is encoded by the obese gene, is produced by adipose tissue, and appears to signal satiety and alter eating behaviors. This hormone has induced significant weight reduction, decrease in appetite, and increase in activity in mice. The hormone has not been well studied in humans. Leptin appears to play a role in monitoring and controlling body fat and energy balance. In mice, there appears to be a defective gene that does not allow for proper feedback in regard to leptin production. Leptin levels and body fat are highly correlated, and body fat accounts for 50% to 60% of the variation in serum leptin concentrations among humans.

To varying degrees, probably all of these factors play a role in adolescent obesity. The extent to which each plays a role is unique to each adolescent.

EPIDEMIOLOGY

1. Data from the NHANES III showed that a substantial proportion of children, adolescents, and adults in the United States were overweight (Table 33.2). Approximately 14% of children and 12% of adolescents were overweight. Among adults, approximately 33% of men and 36% of women were overweight. This percentage was even higher when the revised BMI criteria for overweight were used.

2. Trends: Comparison to prior surveys indicated that the prevalence of overweight had increased from 1976–1980 to 1988–1991 (from 7.6% to 10.9% for children, 5.7% to 10.8% for adolescents, and 25.4% to 33.3% for adults) and that the prevalence of overweight was higher among blacks than among whites. In the NHANES III study, 20% of boys and 22% of girls age 12 to 19 years were overweight based on measures of BMI. This compared to 15% for both boys and girls in the NHANES II (1976–1980) survey. It appears that the increase in the prevalence of overweight resulted from a positive shift in energy balance such that intake from food exceeds energy expenditure in physical activity. Comparison of the skin fold data from the 1963–1965 National Health Examination Survey (NHES I) with the data collected from 1976 to 1980 revealed a 54% increase in the prevalence of obesity among children 11 years of age and a 39% increase among children age 12 to 17 years (Gortmaker et al., 1987). There was even a greater increase in the prevalence of superobesity (skin fold 95th percentile) among 6- to 11-year-olds (98%) and 12- to 17-year-olds (84%).

3. Adults: Data are available for adults age 20 through 74 years examined in each of the four national surveys undertaken during 1960–1962 (NHES I), 1971–1974 (NHANES I), 1976–1980 (NHANES II), and 1988–1991 (NHANES III phase 1). In the period 1988–1991, 33.4% of U.S. adults 20 years of age or older were estimated to be overweight. There was a dramatic increase from prior studies in all race and sex groups. Prevalence of overweight increased 8% between the 1976–1980 and 1988–1991 surveys. In addition, during this period the mean BMI increased from 25.3 to 26.3 and the mean body weight increased 3.6 kg.

4. Sixty to seventy percent of obese adolescents are female.

5. Eighty to eighty-five percent of obese adolescents will be obese adults. Odds for attaining ideal body weight (IBW) are that if a child is obese at age 12, the odds are 4:1 against attaining IBW; if obese after adolescence, the odds are 28:1 against attaining IBW.

6. Weight loss practices among U.S. adolescents: In a national study, Serdula et al. (1993) found that 44% of female students and 15% of male students reported that they were trying to lose weight. Students had used the following weight control methods in the 7 days preceding the survey: exercise (51% of female students and 30% of male students), skipping meals (49% and 18%), taking diet pills (4% and 2%), and vomiting (3% and 1%).
INFLUENCE OF OBESITY ON HEALTH

Future medical problems are usually not a concern of the obese adolescent, who is more preoccupied with the psychosocial consequences. The obese adolescent who becomes an obese adult will have more severe obesity than those adults whose obesity began in adulthood. A 50-year follow-up study of obese adolescents showed that their rates of mortality and morbidity from cardiovascular disease was significantly increased over those of their lean counterparts (Must et al., 1992). Moreover, the influence of adolescent obesity on adult morbidity and mortality was independent of the effects of adolescent obesity on adult weight. Excess weight is associated with an increased incidence of cardiovascular disease, type 2 diabetes mellitus, hypertension, stroke, dyslipidemia, sleep apnea, osteoarthritis, and some cancers (Must, 1999). However, more than 80% of the mortality related to complications of obesity occurs in individuals with a BMI greater than 30 kg/m\(^2\).

1. **Hypertension** Obesity is associated in some adolescents with elevated blood pressure, although most do not become hypertensive. The NHANES study showed a 2.9 times higher prevalence of hypertension in overweight as opposed to nonoverweight adults (NIH Consensus Development Panel, 1985). The Framingham study (Kannel et al., 1967) demonstrated a tenfold increase in hypertension in people who were 20% or more overweight.

2. **Cerebrovascular Disease** A positive relationship exists between obesity and cerebrovascular disease in adults, as demonstrated in the Evans County Prospective Study (Heyden et al., 1971). Males who were overweight by age 20 years and gained 30 pounds or more thereafter had three times more cerebrovascular disease than thin males who did not gain any weight.

3. **Cardiovascular Disease** Adult males who have more than 25% body fat and females with more than 30% body fat have an increased risk for cardiovascular disease. In the Harvard Growth Study, overweight during adolescence was a stronger predictor than overweight in adults for mortality due to cardiovascular disease. Similarly, a cohort study in Great Britain showed that mortality from cerebrovascular disease was directly related to a greater BMI during childhood. The Framingham study demonstrated obesity to be independent of other risk factors, and Salet et al. (1974) showed that the most prevalent risk factor in young patients with coronary artery disease was obesity. Other studies indicated that the distribution of fat deposits may be a better predictor of coronary artery disease than the degree of obesity (i.e., excess abdominal fat, or android obesity, is more related to disease than are fat deposits in the thigh or gluteal areas). Increased central body fat correlates with other risk factors of hypertension and dyslipoproteinemia that are related to precursor atherosclerotic plaques in children and adolescents. Obesity can also result in alteration of cardiac structure and function, even in the absence of systemic hypertension and underlying organic heart disease. Increased total blood volume can create a high cardiac output state, leading to ventricular dilation and hypertrophy of the left and sometimes of the right ventricle.

4. **Skeletal Deformity and Arthritis** Hyperplasia of trabecular and trilipids are related to weight in a linear fashion. In addition, the more one weights, the lower is the level of protective high-density lipoproteins (HDL). NHANES demonstrated that the incidence of hypercholesterolemia in a young overweight group was 2.1 times that of the nonoverweight group (Denke et al., 1994; NIH Consensus Development Panel, 1985).

5. **Diabetes Mellitus** There is a positive correlation between obesity and an increased risk of noninsulin-dependent (type 2) diabetes mellitus, a condition much more commonly diagnosed in the adolescent than in the past. The increases in type 2 diabetes mellitus are primarily seen in African- and Mexican-American teens. Obesity also increases the insulin needs of insulin-dependent diabetics.

6. **Polycystic Ovary Syndrome** Patients with polycystic ovary syndrome are often but not invariably obese. Seventy-five percent of those who are obese have insulin resistance, compared with 30% of the lean patients with polycystic ovary disease. The obese group also show an increased incidence of type 2 diabetes, hypertension, and dyslipidemias.

7. **Cancer** Obese males have higher mortality rates from colon, rectal, and prostate cancer than do nonobese males. Obese females have higher mortality rates from cancer of the gallbladder, biliary passages, breast, uterus, and ovaries.

8. **Gallbladder Disease** Increased cholesterol production and resultant biliary excretion increases the risk of gallstone disease. In one study, obese women between 20 and 30 years of age had a sixfold increase in the risk of developing gallbladder disease.

9. **Skeletal Deformity and Arthritis** Late-onset tibia vara, characterized by inhibited growth of the medial portion of the proximal tibial growth plate, has been well documented in obese African-American adolescents. The clinical presentation is one of a progressive asymptomatic bowleg deformity that is often masked by the obesity itself. Slipped capital-femoral epiphysis and Blount disease (tibial osteochondrosis) are found predominantly in obese adolescents. The incidence of gout and osteoarthritis in weight-bearing joints in adults is associated with overweight during adolescence and young adulthood.

10. **Mental Health Issues** Adolescents are less likely to be affected by or concerned with the medical complications of obesity than with the psychosocial issues. Psychosocial problems of obesity include the following.

    a. Poor body image: This is especially important during adolescent years and can be significantly altered by obesity. Significant gender differences exist, with girls being more sensitive than boys. Body image also positively correlates with parents’ weight-for-height status.

    b. Social isolation: Obesity may give rise to fears of rejection and nonacceptance by peers of the same or opposite sex. Gotlmaker et al. (1993), in a 7-year follow-up study of 16- to 24-year-olds, found that obese women completed fewer years of school, were less likely to be married, had lower household incomes, and had higher rates of household poverty than women who had not been overweight. Men who had been overweight were less likely to be married, but there was no impact on earnings. Sargent and Blanchflower (1994) also examined the relationship between obesity and wage earnings as an adult and found an inverse relationship for obese women (i.e., obese women tended to earn less than their nonobese counterparts). This relationship was not found in obese men.

    c. Low self-esteem: Living in a world in which “who you are” is so much determined by “how you look,” obese adolescents may feel like failures. They may have a tendency to self-deprecate. Their sense of failure is often reinforced by their inability to lose weight. However, in a prospective study examining the relationship between BMI and self-esteem, Rumpel and Harris (1994) found no relationship.

    d. Depression: The preceding three factors may be interrelated in a downward spiral of feelings of rejection, isolation, and depression, leading to more inactivity and more eating.

**Overall Risk**

In adults, disease risk has been correlated to degree of obesity as well as waist circumference (Must et al, 1999) (Table 33.3).

**TABLE 33.3.**

**MEDICAL EVALUATION**

Medical evaluation includes evaluation of factors that contribute to weight gain or inhibit losing weight, comorbid factors that exist and can benefit from weight loss, and the method of weight loss that is most likely method to succeed.

1. **Contributing factors**

   a. History
   - Family history of obesity
   - Past weight loss efforts
   - Onset of obesity
   - Triggers for weight gain (e.g., illness or injury, medication use)
   - Diet history
• Exercise history
• Abnormal eating habits (e.g., binge eating, purging)
• History of potential secondary causes (e.g., thyroid disease, Cushing disease)

b. Physical examination
• Weight, height, and BMI calculation
• Weight circumference may be helpful in young adults
• Physical findings suggestive of hypothyroidism or cortisol excess

c. Laboratory tests
• Thyroid-stimulating hormone, thyroxine, fasting blood glucose, and lipid profile
• If cushingoid, then 24-hour urine free cortisol and overnight dexamethasone suppression
• If obstructive sleep apnea, overnight oximetry or sleep study

2. Consider medical conditions that may benefit from weight loss. This includes problems such as type 2 diabetes mellitus, impaired fasting hyperglycemia, dyslipidemia, hypertension, arthropathies, obstructive sleep apnea, and gallbladder disease.

3. Explore the best potential intervention for weight reduction, as discussed in the next section.

THERAPY

Therapy for obesity is a challenge for both the health care provider and the patient of any age. Young adolescents are often more difficult to treat than older adolescents because of the lack of motivation. In general, treatment focuses on control rather than cure, as is so often the case with chronic medical conditions. When is it appropriate to strongly recommend weight reduction? Certainly, adolescents with morbid obesity (those with twice normal weight, BMI >40, or greater than 100 pounds overweight) are at significant risk and need to be encouraged to lose weight.

Without other risk factors, obesity becomes clinically complicated at approximately 20% to 30% over ideal weight for sex and height, or BMI >30. In adolescents with medically complicated obesity (i.e., obesity associated with type 2 diabetes mellitus, polycystic ovary syndrome, hypertension, or hypercholesterolemia), weight loss needs to be recommended in even lesser degrees of obesity. It must be kept in mind that severe caloric restriction during the growth spurt can have undesirable effects on growth. No medical therapy promises the majority of individuals long-term significant weight reduction.

Critical areas to assess in the teen include the following:

1. Motivation. Motivation is critical for success. Is the teen motivated, or is the desire for weight loss someone else's idea?
2. Is there a supportive social and family framework for weight reduction?
3. Is there a willingness to increase physical activity?
4. Are there realistic goals for weight reduction? A reasonable goal would be a reduction of approximately 10% to 15% of body weight over a 6- to 12-month period in someone who has completed most of their growth. Weight stabilization might be more realistic in a teen who is in his or her growth spurt.

Diet

An energy deficit is needed for active weight loss and is a critical part of management. However, a diet alone is rarely successful in achieving permanent weight loss. Predicting weight loss for an individual teenager based on caloric intake is difficult and can vary widely. In general, the heavier the adolescent, the faster will be the rate of weight loss. For older adolescents and young adults, a deficit of 250 to 500 kcal/day is associated with a loss of approximately 0.5 to 1 lb/wk. Greater caloric restrictions are very difficult to maintain.

The type of caloric restriction should be well planned and should take into account present food types, eating habits, situation-dependent eating, and family and cultural preferences. In as much as growth and development is often at its peak, there must always be good nutritional balance among the food groups.

Approximate daily energy needs in the postpubertal adolescent can be calculated from the weight in kilograms (W) as follows:

\[
\text{Males} = [800 + (7 \times W)] \times \text{activity factor}
\]
\[
\text{Females} = [600 + (7 \times W)] \times \text{activity factor}
\]

where the activity factor is 1.2 for a low activity level, 1.4 for a moderate activity level, or 1.6 for a high activity level.

The energy requirement to maintain each extra kilogram of body weight is approximately 22 kcal. Therefore, an adolescent who weighs 20 kg more than another needs an additional 440 kcal to maintain that weight. Various nutritional approaches to weight loss and their complications include the following.

1. Ketogenic diets: A ketogenic diet may be useful in treating highly motivated, morbidly obese adolescents who have completed their growth spurt. An initial rapid weight loss can be attained with the use of a high-protein diet that contains 80 to 100 g protein, 25 g fat, and 25 g carbohydrate and totals about 700 cal per day. Abnormalities of serum cholesterol may also be alleviated, while lean body mass is preserved.

2. Very-low-calorie diets: When first introduced, these diets often contained less than 400 kcal/day and used low-quality protein supplements, resulting in deaths usually due to cardiac arrhythmias. More recent examples of very-low-calorie diets usually contain 400 to 800 kcal/day and include high-quality protein as well as carbohydrate and adequate quantities of potassium, magnesium, vitamins, and minerals. These have not been associated with significant arrhythmias.

Wadden (1993) reviewed studies of the treatment of obesity with moderate and severe caloric restriction. Patients treated in randomized trials using a conventional 1,200 kcal/day reducing diet, combined with behavior modification, lost approximately 8.5 kg in 20 weeks. One year later, they had regained approximately two thirds of this weight loss. Patients treated under medical supervision using a very-low-calorie diet (400 to 800 kcal/day) lost approximately 20 kg in 12 to 16 weeks. About one half to two thirds of this loss was maintained in the following year. Both dietary interventions were associated with increasing weight regain over time. The National Task Force on the Prevention and Treatment of Obesity (1993) also reviewed studies from 1966 through 1992 on very-low-calorie diets. In these studies, weight loss averaged 1.5 to 2.5 kg/wk, with a total loss after 12 to 16 weeks averaging 20 kg. These diets averaged 800 kcal/day, compared with standard low-calorie diets of 1,200 kcal/day, which led to weight losses of 0.4 to 0.5 kg/week. There is little evidence that intakes of less than 800 kcal/day result in better weight losses. Intake of at least 1 g/kg of IBW per day of protein of high biologic value appears to be important in helping to preserve lean body mass.

Serious complications of modern very-low-calorie diets are unusual. Long-term maintenance of weight lost with these diets is not very satisfactory and is no better than with other forms of obesity treatment. Incorporation of behavioral therapy and physical activity seems to improve maintenance. The very-low-calorie diets are contraindicated in pregnant women, lactating women, and adolescents who are still growing. They should be limited to individuals older than 18 years of age who are moderately obese (60% to 99% overweight) or morbidly obese (100% or more overweight).

3. Glycemic index: A novel approach to adolescent obesity has been the use of the glycemic index (GI). This index relates to the degree the serum glucose rises after a meal. Starchy and sugary foods tend to have a high GI value, where fruits and vegetables have low ones. A few hours after a high GI meal, blood glucose and fatty acids decrease to relatively low levels, with a compensatory rise in epinephrine. Hunger reappears, causing the individual to eat once again. Subjects on a high GI medical food plan tended to eat 80% more-calories than those on a low GI plan. By helping decrease hunger, a low GI meal plan may help promote weight loss.

4. Prolonged fasting: Fasting is defined as an intake of less than 200 kcal/day. Starvation diets are associated with significant metabolic abnormalities and a high recurrence of weight gain after termination of the diet. Fasting is not a recommended therapy.

5. Special food combinations, such as steak and grapefruit: These diets tend to be monotonous, unbalanced, or expensive and in follow-up studies have found them to be no more efficacious that a calorie-restricted, balanced diet.

6. Balanced diet: A balanced weight reduction diet should contain the following:
   a. Foods from all five food groups (milk, meat, bread, fruits, and vegetables)
   b. Instructions to eat at least three meals per day
   c. Instructions to eat less food or calories than previously
   d. Instructions on ways of preparing low-calorie foods and of substituting foods with fewer calories for high-calorie foods.
Physical Activity

Every weight reduction program should include an increase in physical activity. This can include the following:

1. Changes in regular activity, such as walking instead of using the bus, using stairs instead of elevators, walking to the television set instead of using a remote control (even minor increases in activity can make a difference overall).
2. An exercise prescription.
3. Participation in a regular physical exercise program. The best exercise program is one that the teen will follow through with for 30 minutes or more of moderate-intensity exercise on at least 4 days of the week.

Cognitive Behavioral Therapy or Behavior Modification Techniques

These can be effective when used in combination with diet and medical therapies. This approach has been reviewed by Penich et al. (1971), Stunkard et al. (1970), and Foreyt and Kondo (1984). These programs usually contain several components:

1. A contract and reward system for weight loss
2. An initial food diary that contains items such as time spent eating, place, hunger rating, mood, other activity done while eating, food consumed, and amount
3. Change current behavior through eating awareness and a food diary.
   a. Eat three regular meals instead of gorging at dinner and evening.
   b. At mealtimes, eat favorite dish first.
   c. "Just eat the icing off the cake." For calorie-dense foods, just eat that part that is liked the most (e.g., eat only the chocolate chips rather than the whole cookie).
   d. Eat defensively—avoid the junk.
   e. Eat more slowly; allow the body to signal when it is full.
   f. Do not keep "weakness" foods available or easily accessible.
   g. Eat only where eating is meant to occur (e.g., at the dinner table, in restaurants).
   h. Do not watch television while eating.
   i. Do not eat on the go; sit down to eat
   j. Learn to differentiate between appetite and hunger.
   k. Eat only when hungry and not just when food is available.
   l. Have a breakout activity when out of control or when eating is related to depression, anxiety, or unhappiness.
   m. Be honest about lapses in control.

Groups

Group participation as part of the weight loss program is often beneficial. A group supplies the following:

1. Encouragement and support
2. Opportunity for release of feelings
3. Opportunity for peer contacts and acceptance

Group participation can be in the form of a diet group, such as Take Off Pounds Sensibly (TOPS), Overeaters Anonymous (OA), Weight Watchers, or a group that is part of a more comprehensive weight reduction program, such as that described in the book, Shapedown, by Laurel Mellin (available from Balboa Publishing, 583 Tenth Avenue, San Francisco, CA 94118). However, the practitioner must keep in mind that groups have very high attrition rates (40%–70%).

Some group resources are listed here:

1. Noncommercial support groups
   TOPS Club, Inc. (Take Off Pounds Sensibly): A nonprofit, noncommercial organization with local chapters run by members and elected volunteer leaders providing a supportive environment for the diet and exercise changes recommended by a personal physician. Telephone 800-832-8677. Web site: http://www.tops.org/.
   2. Commercial weight-loss programs
   Diet Workshop: Telephone 800-488-3438.

Anorexigenic Drugs (Sympathomimetic Drugs, Diuretics, or Hormones)

There are at present no excellent studies that show the efficacy and safety of using pharmacological agents in the management of obesity in adolescents. d-Fenfluramine has been removed from the market due to its association with cardiac valvular problems and the risk for pulmonary hypertension. Two new drugs—sibutramine, a serotonin and norepinephrine reuptake inhibitor, and orlistat, a pancreatic lipase blocker—have shown promise in adults. As with all regimens, long-term maintenance is a problem. However, interest in drug therapy remains high and requests even higher.

Appetite Suppressants

Noradrenergic Agents

Phenylpropanolamine (Dexatrim). Phenylpropanolamine is a sympathomimetic drug that was available over-the-counter as either an appetite suppressant or decongestant. It was removed from marketplace in November 2000 because of reports of increased risk of stroke in women.

Phentermine (Ionamin). This medication is similar to amphetamines and modulates noradrenergic neurotransmission to decrease appetite. It was used previously with fenfluramine (now withdrawn) because as a single agent the stimulatory effect was too high. It is currently available only as a single weight loss agent.

As a single agent in adults, combined with caloric restriction, Ionamin was associated with a weight loss of 10.2 kg over 24 weeks, compared with 4.4 kg for placebo. Adverse effects include headache, insomnia, nervousness, irritability, palpitations, tachycardia, and increased blood pressure. The medication should be avoided in individuals with hyperthyroidism, glaucoma, agitated states, cardiovascular disease, hypertension, or history of drug abuse.
Serotonergic Agents

Selective serotonin reuptake inhibitors (SSRIs). These medications are not approved for the treatment of obesity but have been studied in individuals with binge eating disorders. Fluoxetine at 60 mg/day was found to be effective in decreasing the frequency of bingeing episodes but has not been found to significantly reduce weight when compared with placebo.

Adrenergic/Serotonergic Agents

Sibutramine (Meridia). Sibutramine is one of the newer medications used for obesity. Its mechanism of action is to act as a reuptake inhibitor of both serotonin and noradrenaline. It may also stimulate thermogenesis by activating the beta3-adrenoceptors in brown adipose tissue. It differs from fenfluramine which increases serotonin release. The starting dose is 10 mg once daily, which may be increased after 4 weeks to 15 mg once daily.

Daily dosages of 10 and 15 mg have been associated with a weight loss of 10.6 lb and 13.4 lb, compared with 4 lb for placebo. Individuals are more likely to lose weight if weight loss is demonstrated in the first 4 weeks. Adverse effects include headache, dry mouth, constipation, insomnia, and increases in blood pressure. There is no evidence of an association with cardiac valve abnormalities. The medication does not appear to have a high abuse potential. Contraindications include anorexia nervosa, hypersensitivity to drug, therapy with monoamine oxidase inhibitors or other serotonergic drugs, coronary heart disease, congestive heart failure, stroke, arrhythmia, uncontrolled hypertension, severe hepatic or renal disease, pregnancy, and lactation. Caution is advised in individuals younger than 18 years of age and in those with a history of seizures. This medication is not indicated for mildly or moderately overweight individuals in the absence of medical complications.

DASH, the Dietary Approaches to Stop Hypertension.

Thermogenic Agents

The combination of ephedrine and caffeine possesses anorexigenic and thermogenic properties with only mild, transient side effects. It does not appear to lead to significant long-term weight reduction.

Digestive Inhibitors

Orlistat. Orlistat is another newer weight reduction medication. It acts as a lipase inhibitor, blocking the absorption of dietary fat by inhibiting gastrointestinal lipases. The medication has no effect on the absorption of carbohydrates, proteins, or phospholipids. It increases fecal fat from 5% to 30%.

In one study in adults, orlistat, 120 mg three times a day, was associated with loss of 8.8% to 10.2% of body weight after 1 year, compared with 5.8% to 6.1% for placebo (Davidson et al., 1999). The incidence of adverse effects is similar to that of placebo with the exception of more frequent gastrointestinal complaints. There are no reports of vitamin deficiencies. However, individuals should take daily multivitamin 2 hours before or after orlistat. Contraindications include malabsorption syndromes, cholestasis, known hypersensitivity, pregnancy, and lactation.

Gastrointestinal Procedures: Bariatric Surgery

Gastrointestinal procedures are rarely indicated in adolescents or young adults; they are reserved for those who are superobese or have significant medical complications of their obesity (e.g., Pickwickian syndrome, skeletal deformity, arthritis). Success depends on the experience of the medical-surgical team and the avoidance of metabolic complications. Rand and Macgregor (1994) reviewed 34 adolescents age 11 to 19 years who underwent surgery for obesity. Although weight loss and psychosocial adjustment were significant, the patients reported poor compliance with exercise and dietary instructions and also did not follow through with the intake of vitamin B12, multivitamin supplements, and calcium as directed. Procedures available include the following:

1. Roux-en-Y gastric bypass: This separates the stomach into a small-volume upper pouch, limiting oral intake, and connects the stomach to a limb of jejunum. Approximately 85% of individuals lose at least 50% of their excess weight at 4 years.
2. Gastric balloon.
3. Vertical banded gastroplasty.

Individuals undergoing bariatric surgery must be significantly overweight for at least 5 years; must have at least two comorbid medical conditions; must have a BMI greater than 40 kg/m2 or 35 kg/m2 with two comorbid medical conditions; must have failed nonsurgical interventions; must have the absence of significant psychopathology; must have full understanding of the risks, benefits, and uncertainties of the procedure; and must be willing to comply with the postoperative evaluation.

Diet, exercise, behavior modifications, and support are still the mainstay of treatment for obesity in adolescents and young adults. The role of medications is still to be defined and evaluated in this age group.

PREVENTION

1. During pregnancy
   a. Maintain a moderate weight gain in last trimester.
   b. During infancy and childhood
      • Breastfeed in first year of life.
      • Delay cereals until 3 to 4 months of age.
      • Be sensitive to the deceleration of growth at 18 months of age as not to exceed the child's decreased demands.
   c. During puberty and adolescence
      • Encourage healthy nutritional practices in early puberty, when there is programmed propensity to increase fat cells.
      • Encourage a lifestyle of activity and participation, rather than one of inactivity and observation, through role modeling. Discourage television viewing and other sedantary pastimes. Reducing television, videotape, and video game use may be a promising population-based approach to prevention of childhood obesity.

The following reading material may be useful for patients:


Girl Power in the Mirror: A Book about Girls, Their Bodies and Themselves, by H. Cordes (Lerner Publishing Group, 1999)

Safe Dieting for Teens, by Linda Ojeda and Lisa Lee (Hunter House Inc., 1992)

WEB SITES

For Teenagers and Parents
http://www.niddk.nih.gov/health/nuitt/pub/choose.htm, Choosing a safe weight reduction program from NIH.
REFERENCES AND ADDITIONAL READINGS


ANOREXIA NERVOSA

Anorexia nervosa is an eating disorder that primarily affects young women and that requires a comprehensive and integrated approach to intervention. This disorder is a classic psychophysiological syndrome because the psychological and physiological functions are intertwined. It is characterized by a self-induced weight loss; various psychological disturbances including distorted body image, denial of the seriousness of weight loss, fear of obesity, active pursuit of thinness, and a loss of recognition of a number of body enteroceptive sensations; and secondary physiological abnormalities. Anorexia nervosa is now subdivided into a restrictive type and a binge eating and purging type. Few patients arouse as much compassion, confusion, and frustration as those with anorexia nervosa. However, with a good treatment program, reported success rates appear to be improving (full recovery rates as high as 76% and partial recovery rates of 86%). Anorexia nervosa must be distinguished from the following:

- **Weight preoccupied**: Individuals who are constantly aware of body weight, often driven by employment or internal self-concept. There is not a loss of control or lack of enteroceptive awareness. However, these young people are at high risk for a DSM-IV-classifiable eating disorder.
- **Food fadism**: Individuals become preoccupied with the type of food, rather than the amount. Food fadism often may be an associated characteristic or early sign of a restrictive eating disorder.
- **Fat phobia**: With the increased awareness of food content through labeling of food products, young people often avoid and restrict fat content for health reasons. If done without nutritional guidance, deficiencies and malnutrition may develop. Fat phobia may be an early indicator of a restrictive eating disorder.
- **Finicky eater**: An individual eats only a small amount of food or certain types of food but in adequate quantities to maintain a body weight usually less than the 10th percentile. There is no pursuit of thinness and no distorted body image, and the individual is usually well adjusted.

**Etiology**

The exact cause of anorexia nervosa is unknown. In the 18th and 19th centuries, anorexia nervosa was described as “nervous consumption.” In the early 20th century, the disease was ascribed to pituitary failure. In the 1930s and 1940s, the disease was distinguished from organic pituitary disease, and from the 1940s to the 1960s, psychoanalytical theory provided the stimulus for research on the condition. Theorists attributed anorexia nervosa to unconscious fantasies regarding oral impregnation. It was speculated that the weight loss alleviated the young woman’s fear of sexual development and responsibility. The 1960s and 1970s focused on the perceptual disturbances of individuals with anorexia nervosa, family dynamics, and hypothalamic disturbances. Most authorities currently attribute many of the behaviors, physical signs, and symptoms to the state of malnutrition, rather than to intrinsic psychopathology. In the 1990s, there was an increase amount of research on both genetics and neurotransmitters. It is evidenced that starvation, bingeing, and excessive exercising can lead to changes in neurotransmitters, and conversely, there is evidence that such changes can lead to these behaviors. One example is serotonin, a neurotransmitter that appears to be reduced in anorexia nervosa. At the same time, selective serotonin reuptake inhibitors (SSRIs) may have some symptom improvement in individuals with bulimia nervosa and help prevent relapse in some individuals with anorexia nervosa.

Genetics also appears to play a role, as noted in various family and twin studies. These studies have shown a higher rate of eating disorders among identical twins than fraternal twins. Relatives of individuals with an eating disorder are at higher risk of developing an eating disorder. Although some of these effects are difficult to sort out from environmental factors, a genetic predisposition is a strong possibility.

No doubt a combination of biological, psychological, and social factors underlies the cause of anorexia nervosa. A good model is provided by Lucas (1981) and is diagrammed in Fig. 34.1. The figure demonstrates how biological vulnerability, family problems, and emotional problems can combine in a given social climate to cause the typical dieting of an individual with anorexia nervosa. This weight loss, in turn, leads to malnutrition, which contributes to the physical and emotional changes of the patient with anorexia nervosa and perpetuates a vicious cycle.

**Fig. 34.1.** Biopsychosocial model for anorexia nervosa. (From Lucas AR. Toward the understanding of anorexia nervosa as a disease entity. Mayo Clin Proc 1981;56:254, with permission.)

This chapter focuses on eating disorders including anorexia nervosa (anorexia nervosa) and bulimia nervosa (bulimia nervosa). Also mentioned are other disorders that are not in the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV), such as binge eating disorder (BED) or nonspecific eating disorders.
Incidence: The exact incidence is difficult because different studies have such different methods of sampling and assessment. However, the worldwide incidence of anorexia nervosa is approximately 1 per 100,000; whereas the incidence among white, pubertal females in Western countries may be as high as 1 per 200, with a significant increase occurring in the past two decades and also occurring in an increasing diversity and also occurring in ethnic and socioeconomic groups. In the youth risk behavioral survey, about 48% of high school girls dieted, 64% exercised, and 7.6% purged to lose weight. These percentages for males are 16%, 39%, and 2.2%, respectively. Among college women in the 1995 Centers for Disease Control and Prevention study, 42% dieted and 4.2% purged to lose weight. Seven percent of college women in the 2000 National College Health Assessment used diet pills in the past year to lose weight. Combining estimates of anorexia nervosa, bulimia nervosa, and atypical eating disorders, it is possible that 5% to 10% of junior and senior high school and college female population in Western countries have some form of eating disorder.

Risk factors: Katz (1985) identified cultural, familial, and individual risk factors that predispose an individual to anorexia nervosa. These include the following:

- Cultural risk factors
  - Equating thinness with both beauty and happiness, with an emphasis on self and body
  - Capability of disseminating these values and styles through visual media
  - Acculturation to Western values in immigrants
- Family risk factors
  - Achievement oriented
  - Intrusive, enmeshed, overprotective, rigid, and unable to resolve conflicts
  - Frugal with support, nurturance, and encouragement
  - Overinvested in food, maternal preoccupation with diet, weight, appearance, or physical fitness
  - Other family members with a history of an eating disorder or an affective disorder
  - Sexual abuse: Controversy has existed over the relationship between eating disorders and sexual abuse. Several researchers have reported an increased prevalence of past sexual abuse in childhood or adolescence and this might be an additional risk factor.
- Individual risk factors
  - Female gender
  - Adolescence
  - Slightly overweight, having a pear-shaped body
  - Feelings of low self-esteem or ineffectiveness
  - Teasing by peers
  - Conflicts and doubts about sense of personal identity and autonomy
  - Perceptual disturbances regarding body: Girls feeling most negative about their bodies at puberty are at highest risk.
  - Sense of personal competitiveness with peers or family members.
  - Obsessional style.

Clinical Manifestations

Typical Presentation

1. Often anorexia nervosa can be pinpointed to a precise time when the patient decided to diet to lose weight. This is often in response either to the patient feeling too fat or to a critical comment on his or her figure by family members, a teacher, a coach, or peers. The onset of anorexia often precedes or follows changes in the patient’s or family’s life, such as recent growth and development, menarche, parental divorce, or a death in the family.

2. Relentless pursuit of thinness: Weight loss is achieved easily, because the patient is often reinforced by initial positive comments from parents and peers who admire the patient’s willpower and sense of control. In addition, the behavior is reinforced by physiological adaptations within the central nervous system (CNS), and the patient loses control over eating. Weight loss continues due to the difficulty the individual has in overcoming these physiological adaptations and the accompanying distortions of body and body cues that accompany the starving state.

3. Food faddism and rituals: Eating behaviors change. Rituals appear that may take the form of breaking food into smaller and smaller portions, hiding food, secretly throwing food away or hiding it as if it were ingested, or eating the low-calorie foods (e.g., salad with vinegar and no oil, diet frozen foods, and diet soft drinks). These rituals are largely due to a starving brain and are reversed with improved nutrition.

4. Interest in para-eating behaviors: Although eating less, the typical individual with anorexia will often develop or maintain an interest in food by cooking and preparing food for others, collecting recipes, and setting the dinner table.

5. Increased physical activity: Although the individual with anorexia loses weight, the activity level often increases. Young people with anorexia nervosa will often jog, run up and down stairs, or do floor exercises or calisthenics in an effort to expend energy and control body configuration.

6. Purge behaviors: Some patients with anorexia discover that purge behaviors facilitate and expedite weight loss. Purge may take the form of emesis, catharsis, or diuresis.

7. Family characteristics: Families are generally white and middle to upper class, and they are described as “perfect families” in the communities. Families with less characteristic family patterns have become more common. Parenting style tends to encourage enmeshment, to be overprotective and inflexible, and to fail to resolve conflicts.

8. Disagreements and conflict: There is a strong sense of “right and wrong” often to the point of not accepting individual differences.

9. School behavior: Young people with anorexia nervosa usually have average to above-average intelligence and are described as excellent students and overachievers.

10. Peer contacts: Young people with anorexia nervosa usually withdraw from their classmates and friends. This may reflect an attempt to minimize contact with criticizing or teasing peers. It is also a manifestation of their low self-esteem and somewhat constricted social skills.

11. Lack of concern: Despite continued weight loss, there is often a lack of concern for their increasingly emaciated appearance.

12. Food as a battleground: As the weight loss persists, food becomes the central topic of discussion and arguments in the family. This situation worsens as the parents become more concerned and frustrated with their child’s weight loss, and the patient becomes more stubborn and set in his or her behavior. Patients with anorexia nervosa often present wearing bulky pants and sweaters in an attempt to conceal their weight.

Presenting Symptoms

1. Weight loss: A body mass index (BMI) of 14–17
2. Amenorrhea: Almost 100% prevalence. In 25% of anorectic patients, the amenorrhea precedes the weight loss; in about 50%, the amenorrhea occurs at about the same time as the weight loss; and in about 25%, the amenorrhea occurs after substantial weight loss. An increasing number of patients are being seen with premenarchal onset of the disorder. Persistence of amenorrhea despite effective weight gain usually signifies persistence of psychological or social factors that contributed to the problem initially.
3. Hyperactivity
4. Constipation: This is secondary to dietary factors, decreased fluid intake, and a lack of response to the usual enteroceptive cues to defecation.
5. Early satiety
6. Easy bruising
7. Postural dizziness and fainting
8. Apathy
9. Yellow skin
10. Dry skin
11. Blue hands and feet
12. Preoccupation with food
13. Abdominal bloating, discomfort, and pain
14. Cold intolerance
15. Epigastric pain, nausea, and vomiting
16. Fatigue, muscle weakness, and cramps
17. Frequent fractures
18. Common emotional symptoms and issues
   a. Low self-esteem and self-worth
   b. Quest for perfection
   c. Need to control and power
   d. Desire for admiration
   e. Belief in thinness myth
   f. Black or white thinking
   g. Lack of coping skills
   h. Lack of trust in self and others
   i. Social isolation and/or depression

**Presenting Physical Signs** Most of the signs of anorexia nervosa are related to the weight loss and have been reported in starvation and other states of malnutrition.

1. Decreased weight and cachexia: BMI of 14–17
2. Decreased temperature: May be as low as 35°C
3. Bradycardia: No increase with exercise
4. Hypotension often with significant postural changes
5. Acrocyanosis
6. Edema, usually dependent
7. Dry skin with hyperkeratotic areas (dirty skin)
8. Cold extremities
9. Yellowish discoloration of the skin (carotenemia)
10. Nail changes: Pitting and ridging
11. Increased lanugo hair
12. Scalp hair loss
13. Superior mesenteric artery syndrome
14. Systolic murmur sometimes associated with mitral valve prolapse
15. Short stature: Nussbaum et al. (1985a) noted that 76% of their adolescents with anorexia nervosa were below the 50th percentile in height.

**Presentation in Young Adolescents and Children** Atkins and Silber (1993) reviewed cases of anorexia nervosa in children aged 7 to 12 years. Their findings showed that the youngest ones had a diagnostic delay, a high severity of illness, and a positive response to intensive treatment, and there was a high incidence of family psychiatric history. Some of these children also presented with a personality disorder, and another group with features of the “vulnerable child syndrome.”

**Presentation in Males** Olivardia et al. (1995) reviewed eating disorders in males. Although less common in males than in females, males with eating disorders closely resemble the pattern of females with eating disorders. Siegel et al. (1995) suggested that there may be a higher proportion of male adolescents with anorexia nervosa with medical abnormalities due to difficulties in establishing the diagnosis and the delay in seeking medical treatment. In addition, it appears that the cases of boys with anorexia nervosa and bulimia nervosa have been increasing. Although males with all types of sexual orientations develop eating disorders, it appears that there is an increase in males who have sexual orientation issues.

**Coexisting Diagnoses** Anorexia nervosa may coexist with other conditions. Other conditions that have been explored in particular include affective disorders, obsessive-compulsive disorders, and substance abuse disorders.

**Laboratory Features** Laboratory findings in anorectic patients can include the following:

1. **Endocrine:** The hormonal changes in the anorectic patient are most likely related to the weight loss and are partially beneficial in conserving energy expenditure.
   a. Thyroid
      - Thyrotropin (TSH): Within the reference range
      - Thyroxine (T4): Within the reference range or slightly low
      - 3,5,3'-Triiodothyronine (T3) Usually low, probably representing increased conversion of T4 to reverse T3
      - The thyroid changes represent adaptation to starvation and will reverse with weight gain.
   b. Growth hormone: Within the reference range or high levels
      - Decreased somatomedin
e. Prolactin: Reference range levels
d. Gonadotropins
   - Basal levels of luteinizing hormone (LH) and follicle-stimulating hormone (FSH): Usually low or low reference range levels
   - Twenty-four-hour LH pattern: Usually similar to prepuberty or early adolescence, with constant low levels and no spikes or occasional nocturnal spikes
   - FSH and LH response to gonadotropin-releasing hormone (GnRH): Often a severely blunted response to GnRH, particularly if weight loss is severe
   e. Sex steroids
      - Estradiol: Low in females
      - Testosterone: Low in males
f. Cortisol: Normal secretion on stimulation. Basal levels are within the reference range or occasionally slightly high. A decreased response of adrenocorticotropic hormone (ACTH) to corticotropin-releasing hormone has been noted (Gold et al., 1986). This resolves by 6 months after weight gain has occurred. This abnormality of ACTH response is not found in individuals with bulimia and normal weight.
   g. Other hypothalamic disturbances: Hypothermia and partial diabetes insipidus in some patients with anorexia.
   2. **Chemistry**
   a. Increased blood urea nitrogen (BUN) concentration
   b. Mildly increased serum glutamic-oxaloacetic transaminase and serum glutamic-pyruvic transaminase levels
   c. Hypophosphatemia
d. Depressed serum magnesium and calcium concentrations
e. Increased cholesterol
f. Increased serum carotene level in 15%–40% of patients
g. Decreased vitamin A level
h. Decreased serum zinc and copper levels

3. **Hematological**
   a. Leukopenia: May be relative lymphocytosis
   b. Anemia: A late finding
c. Thrombocytopenia
d. Decreased serum complement C3 levels (but reference range levels of C4) and granulocyte killing defect; no evidence for increased susceptibility to bacterial infection
   e. Decreased erythrocyte sedimentation rate (ESR < 4 mm/hr)

4. **Cardiac**
   a. Electrocardiogram (ECG): Bradycardia, low-voltage changes, T-wave inversions, and occasional ST-segment depression
   b. Decreased cardiac size and left ventricular wall thickness
   c. Increased prevalence of mitral valve prolapse (Johnson et al., 1986)

5. **Gastrointestinal (GI)**
   a. Upper GI tract series: Usually normal findings, with occasional hypomotility
   b. Barium enema: Normal findings
   c. Fecal fat: Normal results

6. **Renal and metabolic**
   a. Decreased glomerular filtration rate
   b. Elevated BUN concentration
The patient with anorexia nervosa can be characterized by several psychological, behavioral, and perceptual features, including the following:

1. Psychological
   a. May or may not have personality disorder
   b. Lowered self-esteem or self-worth
   c. Features of depression, anxiety, and obsessional thoughts
   d. Perfectionistic attitude
   e. Social anxiety and withdrawal
   f. Overachieving
2. Perceptual
   a. Distorted body image: Overestimation, particularly of face and body sizes
   b. Misperception of physical sensations: Distorted hunger awareness and denial of fatigue
   c. Sense of ineffectiveness: Feelings of being controlled by, rather than controlling, the environment
3. Behavioral
   a. Preoccupation with food
   b. Hyperactivity
   c. Willful weight loss
   d. Vomiting and laxative abuse
   e. Decreased sexual interest
4. Family: The families of patients with anorexia nervosa generally enjoy academic, social, and economic success and lack obvious problems. Many of the families stress intellectual and physical appearances, rather than emotional concerns. Often, there has been a lack of communication among family members, other than factual information. Although appearing calm on the surface, the families often have problems of
   a. Rigidity
   b. Conflict resolution
   c. Overprotectiveness
   d. Lack of privacy within the family
   e. Development of overly strong ties within certain segments of the family

In individuals with anorexia nervosa, disordered eating and eating rituals help these individuals to adapt to their problems in other areas such as control, perfectionism, self-esteem, and others. These food rituals have often replaced more appropriate mechanisms of relating to people to achieve a sense of "self" or calmness.

Diagnosis and Assessment

The diagnosis of anorexia nervosa should be suspected in any adolescent with unexplained weight loss, hyperactivity, and food avoidance. Other possible causes such as Crohn disease, early pregnancy, hyperthyroidism, tuberculosis, collagen-vascular disease, brain tumors, Addison disease, and depression should be explored.

Diagnostic and Statistical Manual of Mental Disorders Criteria
The diagnosis of anorexia is based not only on the absence of a defined organic cause but also on the presence of certain characteristics. The American Psychiatric Association's DSM-IV criteria for anorexia nervosa include the following:

1. Refusal to maintain body weight more than a minimal normal weight for age and height (e.g., weight loss leading to maintenance of body weight <85% of that expected or failure to make expected weight gain during period of growth, leading to body weight <85% of that expected)
2. Intense fear of gaining weight or becoming fat, even though underweight
3. Disturbance in the way in which one's body weight, size, or shape is experienced, undue influence of body weight or shape on self-evaluation, or denial of the seriousness of the current low body weight
4. In postmenarchal females, absence of at least three consecutive menstrual cycles when otherwise expected to occur (primary or secondary amenorrhea)

Two types of anorexia nervosa are defined:

1. Restrictive type: During the current episode, the person has not regularly engaged in binge eating or purging behavior.
2. Binge eating or purging type: During the current episode, the person has regularly engaged in binge eating or purging behavior.

Evaluation
The evaluation of the anorectic patient should include a comprehensive history and physical examination. Questions regarding eating, weight control behavior, and other issues that may be helpful include the following:

1. How does the teen handle weight control?
2. What was the most and least the teen has weighed and when was that?
3. How much does the teen want to weigh? What are his or her personal goals?
4. What methods has the teen used to control his or her weight?
5. How often does the teen weigh himself or herself?
6. Exercise history: Is the teen a compulsive exerciser?
7. Purging: Is there any purging behavior such as vomiting, laxative abuse, diuretic use, ipecac use, or use of diet pills?
8. What has the teen eaten in the past 24 hours?
9. What is the teen's self-image (fat or thin), and is there any area that is seen as particularly ugly such as buttocks or thighs?
10. How much does the disordered eating or other behaviors interfere with the teen’s life? How much time does he or she spend preparing food, exercising, and weighing himself or herself?
11. Why is the teen and/or the family seeking help?
12. Family information including eating problems, their perceptions of the problem, and how have they dealt with the eating disorder?
13. Support systems: Where does the teen get help? With whom does he or she share information?
14. Psychiatric history: Are there other mental disorders that have been diagnosed in the teen?
15. Substance abuse: Any history of substance abuse?
16. Sexual abuse: Any prior or current history of sexual abuse?
17. Medical history and physical examination focused on the signs and symptoms described previously.

Several instruments have been developed to aid in the diagnosis of eating disorders and the differentiation of anorexia from bulimia nervosa. These include the following:

1. Eating Attitudes Test: A rating scale that attempts to distinguish patients with anorexia nervosa from weight-preoccupied and otherwise normal college-age females. The 26-item questionnaire has three subscales including dieting, bulimia, and food preoccupation, as well as oral control. See Chapter 8 for a review of four questions that have been suggested as useful for screening for disordered eating in young adults. Eat-26 is available online at either http://www.stuaff.niu.edu/csdc/eat26.htm and http://www.river-centre.org/cgi-bin/test.cfm.
2. Eating Disorders Inventory: Used to predict the emergence of an eating disorder in a high-risk group.
3. Bulimia Investigation Test (BIT): Used to measure the symptoms and severity of bulimia.

In addition, an effort should be made to look for behavioral, perceptual, and family changes as outlined in previous sections of this chapter. The laboratory evaluation...
should include the following:

1. Complete blood cell (CBC) count and platelet count
2. ESR
3. BUN and serum creatinine
4. Urinalysis
5. Serum electrolytes and liver function tests: Results are often normal but hypokalemia with an increased serum bicarbonate level may indicate frequent vomiting or use of diuretics, whereas nonanion gap acidosis is common with laxative abuse. Hypokalemia is not seen usually with only restrictive eating patterns. Hyponatremia is common and may be secondary to excess water intake.
6. Serum calcium and phosphate and magnesium concentrations
7. Serum albumin level
8. Carotene level
9. T₄ and thyroid-stimulating hormone level
10. Prothrombin time and partial thromboplastin time if easy bruising is a problem
11. ECG
12. Chest x-ray
13. Bone mineral density (BMD) test (dual-energy x-ray absorptiometry scan) should be measured in females with anorexia nervosa and who have been amenorrheic for more than 1 year.

Optional

1. Stools for occult blood and fat
2. Upper GI tract series and small bowel series
3. Barium enema
4. Computed tomography or magnetic resonance imaging of the head
5. Serum estradiol level

Nutritional Assessment

The nutritional assessment should include weight and skinfold measures. Monitoring the percentage of body fat may be helpful in the ongoing evaluation of adolescents with anorexia. The percentage of body fat can be calculated from skin-fold thickness measurements or approximated from the following formulas:

- Total body water = –10.313 + [0.252 × (weight in kg)] + [0.154 × (height in cm)]
- Lean body mass = total body water + 0.72
- Body fat = body weight – lean body mass
- %body fat = (body fat + body weight) × 100

Most menarchal females have at least 17% of body weight as fat, and most ovulatory females have at least 22% of body weight as fat. The BMI may be another useful measure to follow and normal graphs are available in Chapter 1.

Treatment

Many therapies have been attempted in patients with anorexia nervosa, including individual psychotherapy, cognitive behavioral therapy, drug therapy, hyperalimentation, and family therapy. The important issues in intervention are correction of malnutrition and the associated psychological symptoms of starvation. Concomitantly, work should begin on the resolution of the psychological dysfunction in the patient and the family. Failure to address these issues on both a short-term and a long-term basis will lead to failure of the therapy. The intervention should be divided into several stages:

1. Diagnosis: The first critical step is to make a correct diagnosis and inform the patient and the family of the problem and the plan for treatment.
2. Repletion of nutritional stores: Many of the patient’s physical and emotional problems may center around malnutrition. If the teen is in no immediate physical danger, then nutritional interventions can be performed on an outpatient basis. Indications for hospitalization include the following:
   - a. Significant hypovolemia and hypotension
   - b. Severe malnutrition such as body weight <75% of ideal weight
   - c. Cardiac dysfunction and arrhythmias, prolonged QT interval
   - d. Bradycardia <45 beats per minute
   - e. Significant electrolyte abnormalities such as potassium concentration <2 mg/L or fasting blood glucose level <50 mg/100 mL
   - f. Rapid progressive weight loss despite competent therapeutic interventions
   - g. Intractable multiple bingeing and purging episodes per day with no or little reduction with outpatient therapy
   - h. Suicidal thoughts or gestures
   - i. High dysfunctional or abusive family
   - j. Failure of outpatient therapy such as no weight gain or reduction in binge-purge behaviors or failure to keep outpatient visits

The goals for this hospitalization should be weight gain and institution of a cognitive approach to psychotherapy. Attempts should be made to achieve weight gain through the oral route, if possible. Behavioral contracts have been helpful (Fig. 34.2, Fig. 34.3 and Fig. 34.4 are examples of contracts), but these should only be used in conjunction with the ongoing cognitive work. If cardiac arrhythmias occur without electrolyte disturbances, if the patient is listless, or if oral therapy fails, nutrition should be repleted by the safest method available. This can be done by nasogastric tube or intravenous hyperalimentation.

FIG. 34.2. Sample contract for inpatient with anorexia nervosa. A weight for each step should be negotiated between the teenager and practitioner.
3. Long-term therapy: After discharge from the hospital or after initial evaluation and diagnosis, the patient should begin long-term therapy. This is best achieved through both individual and family sessions. Goals should be to encourage self-control through self-definition and to elevate self-esteem. A contract may also be of value for outpatients. An example of such a contract is given in Fig. 34.4. Particularly in those teens with anorexia nervosa with a significant depression, antidepressants may be of value. An excellent discussion of the classic family dynamics involved in these sessions is found in Minuchin et al. (1978). Additional information and referral sources can be obtained from the National Association of Anorexia Nervosa and Associated Disorders (P.O. Box 271, Highland Park, IL 60035). Another good overview with excellent suggestions for health professionals and families is provided by Costin (1999).

Both individual and family therapy of individuals with eating disorders is beyond the scope of this book. Over the years, psychodynamic, cognitive, behavioral, and disease addiction models have been used individually or combined. A skilled therapist knowledgeable in the treatment of eating disorders should be involved.

4. Team approach: Many individuals with eating disorders whether anorexia nervosa or bulimia nervosa will need the involvement of a skilled team. This may include a physician, therapist, and dietitian with experience in patients with eating disorders. Therapy may include individual, family, and group therapy. The team may also include a psychiatrist and the use of medications. It is critical that there is excellent communication among the members of the team and that information is shared as appropriate.

5. Medications: Psychotropic medications may have a role in individuals with anorexia nervosa or bulimia nervosa but are not a cure. Uses include treating coexisting psychiatric conditions, helping in weight restoration, normalizing mood, reducing anxiety and stress, and preventing relapses. The role of psychotropics and SSRIs in particular is still being defined in anorexia nervosa. In general, medications should be used only after nutritional repletion has begun, the medical evaluation is complete, and therapy has begun. Psychotropics do not appear effective in treating the primary symptoms of anorexia nervosa but may help stabilize recovery in patients who have attained 85% of their expected body weight. The most common medications used have included the SSRIs such as: fluoxetine, sertraline, paroxetine, fluvoxamine, and citalopram.

6. Advice for parents or other caretakers: Several suggestions may be helpful in advising parents on working with their teen with an eating disorder. These include the following:
   a. Patience: Eating disorders may have a prolonged recovery, so expectations of a quick cure should be reduced.
   b. Avoid blaming: It is helpful for family members to avoid blaming someone for the cause of the disorder.
   c. Avoid power struggles particularly over food and let the health professional deal with issues of control over food.
   d. Avoid comments about weight and appearance.
   e. Avoid unreasonable preparations to purchase or prepare special foods.

Complications

1. Cardiovascular
   a. Adaptations to starvation: Sinus bradycardia, sinus arrhythmia, and hypotension
   b. Ventricular dysrhythmias
   c. Reduced myocardial contractility
   d. Sudden death, secondary to arrhythmias
   e. Heart muscle damage secondary to ipecac abuse
   f. Mitral valve prolapse
   g. Sinus bradycardia
   h. ECG abnormalities including low voltage, prolonged QT interval, and prominent U waves
   i. Acrocyanosis
2. Renal
   a. Increased BUN
   b. Decreased glomerular filtration rate
   c. Renal calculi
   d. Edema
   e. Renal concentrating defect
3. GI
   a. Delayed gastric emptying
   b. Superior mesenteric artery syndrome
   c. Constipation
   d. Elevated liver enzyme levels and serum amylase levels
   e. Gastric dilation and rupture
   f. Necrotizing colitis
   g. Rectal prolapse
4. With purging behaviors
   a. Pancreatitis
   b. Parotid gland enlargement
   c. Esophagitis
   d. Mallory-Weiss lesions
   e. Hypokalemia secondary to laxative abuse
   f. Paralytic ileus secondary to laxative abuse
g. Cathartic colon

5. Hematological
   a. Anemia
   b. Leukopenia
   c. Neutropenia
   d. Thrombocytopenia

6. Endocrine or metabolic
   a. Hypokalemia
   b. Hypernatremia
   c. Hypomagnesemia
   d. Hyperphosphatemia
   e. Hypoglycemia
   f. Hypothermia
   g. Euthyroid sick syndrome
   h. Hypercortisolism
   i. Low serum estradiol level
   j. Decreased serum testosterone level
   k. Elevated cholesterol level
   l. Amenorrhea

m. Osteoporosis: Females with anorexia nervosa have been found to have lower BMDs than menstruating females with normal body weights. In addition, nontraumatic pathological fractures have been reported in individuals with anorexia nervosa (Rigotti et al., 1984). In young females with amenorrhea associated with weight loss, BMD loss will occur soon after the amenorrhea develops. The BMD in adolescents with anorexia nervosa can increase as the individual recovers from anorexia nervosa and may start to increase even before menses returns. Females who recover from anorexia nervosa at a young age (younger than 15 years) can have normal total body BMD, but regional (lumbar spine and femoral neck) BMD may remain low (Hergenroeder, 1995). The longer the anorexia nervosa persists, the less likely it is that the BMD will return to reference range values. Hormonal supplementation for females with anorexia nervosa has not been well documented to significantly increase bone density. Seeman et al. (1992) found that the risk of a lower BMD was greatest in women with anorexia nervosa and primary amenorrhea. This study also suggested that women with anorexia nervosa who had received oral contraceptives had BMDs that were greater than those of women receiving no contraceptives but lower than those of a control population. It appears that a chronically low weight condition and malnutrition makes individuals with anorexia nervosa less sensitive to calcium and hormonal supplementation. The treatment protocols are still undergoing study to establish when treatment should be started and what is the best treatment. Although there are areas that need further research, it is still important to discuss the importance of any osteopenia with the teens and their families and the importance of weight gain and normal menstruation in helping to prevent long-term sequelae.

n. Short stature and arrested growth
o. Partial diabetes insipidus
p. Hypercarotenemia
q. Decreased magnesium concentration with resultant muscle cramps, weakness, and restlessness

7. Neuromuscular
   a. Generalized muscle weakness
   b. Seizures secondary to metabolic abnormalities
   c. Peripheral neuropathies
d. Myopathy secondary to ipecac abuse
e. Syncope in absence of orthostatic hypotension
f. Movement disorders
g. Ventricular enlargement
h. Reversible cortical atrophy

8. Correlates of sudden death
   a. Prolonged QT interval
   b. Decreased serum phosphate concentration
c. Ipecac myopathy
d. Weight loss >35% of ideal body weight
e. Suicide

9. Dental
   a. Complications of vomiting
      • Dental and enamel erosions
      • Caries and periodontal disease
   b. Recommendations for dental care in adolescents with a history of vomiting
      • Topical fluoride therapy daily
      • Alkaline mouth rinse after vomiting
      • No tooth brushing after vomiting, because this increases the risk of dental damage
      • Vigorous oral hygiene measures maintained

10. Pulmonary
    a. Aspiration pneumonia secondary to vomiting
    b. Pneumomediastinum secondary to vomiting

Prognosis

Studies regarding the prognosis of anorexia nervosa are often marred by lack of proper diagnosis criteria, failure of adequate follow-up, or inadequate information at follow-up. Hsu (1980) reviewed 16 studies of the outcome of anorexia nervosa between 1954 and 1980, and Herzog et al. (1988) reviewed 33 studies up to 1986. Other recent studies of prognosis include Gilbert et al. (1994), Steinhausen and Seidel (1993), and Strober et al. (1997).

It should be stressed that individuals with eating disorders such as anorexia nervosa and bulimia nervosa can fully recover. The time to recover may be many years and the pathway may be difficult. The following are some of the findings:

1. Mortality: The mortality rate ranged from 0% to 22%, with most of the studies having mortality rates <4%.
2. Nutritional: At follow-up, 22%–79% were within normal limits for weight, 15%–43% were 11%–21% below normal, 2%–10% were overweight.
3. Menses: Thirty-eight percent to 95% of patients with anorexia nervosa were menstruating at follow-up.
4. Eating difficulties: Fifteen percent to 82% were eating normally at follow-up, 23%–67% had restricted food intake, 11%–50% were still vomiting or abusing laxatives.
5. Psychological disturbances: Psychiatric disturbances were common in follow-up studies. Depressive symptoms were common: 24%–45% had anxiety in meeting people; 13%–44% had obsessive-compulsive features; and many also had a definite or probable affective disorder. Estimates of good or satisfactory psychosocial functioning ranged from 22% to 73%. Twenty-five percent to 55% of patients with anorexia nervosa go on to become bulimic.
6. Psychosocial disturbances: Twenty percent of anorectic patients had abnormal attitudes and behavior. Fear of pregnancy was not uncommon.
7. Psychosocial: Most anorectic patients were engaged in full-time employment, with good work attendance. Social anxiety was common, and many had problems with their families.

Certain factors seem to relate to a good prognosis or poor prognosis, whereas other factors have no effect.

1. Good prognosis
   a. Early intervention
   b. Less comorbid psychological diagnoses
   c. Infrequent or no purging behavior
d. High educational achievement
e. Early age at onset
Anorexia nervosa appears to have lower recovery rates than bulimia.

Strober et al. (1997) followed 95 individuals age 12 to 17 every 6 months for 5 years and then annually for 10 to 15 years more. There was full recovery in 75.8%, partial recovery in an additional 10.5%, and chronically no recovery in 13.7%. The relapse rate for those who left the program before full recovery was 30%. The time to full recovery ranged from 57 to 79 months. This particular study, in contrast to others, found no correlation between poor outcome and longer duration of illness, lower body weight, binge eating, vomiting, or prior treatment failures. However, the correlation with dysfunctional family relationships was significant. Other predictors associated with lack of recovery were compulsive exercising when leaving the program and asocial behavior before the eating disorder.

In conclusion, the weight of the patient with anorexia seems to respond best to therapy; menstrual function responds less well to therapy; and psychological readjustment has a poorer prognosis. However, with early and appropriate interventions, a partial or full recovery can occur.

**BULIMIA NERVOSA**

Bulimia nervosa is an eating disorder characterized by binge eating coupled with behavior intended to promote weight loss such as self-induced vomiting, laxative abuse, excessive exercise, or prolonged fasting. The term bulimia derives from the Latin meaning “hunger of an ox.” Some feel that both bulimia and anorexia nervosa are on a continuum. Differentiation is a mute point theoretically, but for the physician, the behavior governs the treatment. With bulimia, the profound emaciation associated with anorexia is not present, and most individuals have a normal weight. The individual with bulimia is usually quite aware that the eating pattern is abnormal. Although many patients with a subtype of anorexia nervosa have binging or purging behaviors, bulimia is classified as a unique disease in the DSM (American Psychiatric Association, 1994).

**Epidemiology**

1. Onset: Onset is usually during late adolescence or early adulthood, although the age range may be from 13 to 58 years.
2. Sex: Ninety percent to 95% are females, although recently a reported increased prevalence in males, particularly those who must weight qualify for interscholastic events (e.g., wrestlers).
3. Prevalence: Estimates are that approximately 1%–3% of young females in Western industrialized countries have bulimia. In a recent survey by Schotte and Stunkard (1987) of college students, 1.3% of females and 0.1% of males were classified as bulimic, based on the DSM-III or DSM-III-R (the revision of DSM-III) classifications. Their conclusion was that bulimic behavior is common, but that clinically significant bulimia is not as common as many people fear. Zuckerman et al. (1986), using DSM-III criteria, found a 4% prevalence of bulimia in college women and 0.4% in college men. Bingeing and purging behaviors were found to be more common than this. For example, 23% of the women and 14% of the men reported binges at least once each week, and 23% of the females and 9% of the males used one of the following methods of weight control: dieting, vomiting, laxatives, or diuretics.
4. Alcohol and substance abuse: This type of problem is not an uncommon association in individuals with bulimia, particularly obese binge eaters. It usually occurs later in the course of the disease.
5. There is an increased prevalence of a major affective disorder in individuals with bulimia.

**Clinical Manifestations**

The DSM-IV diagnostic criteria for bulimia are as follows:

1. Recurrent episodes of binge eating. An episode of binge eating is characterized by both of the following:
   a. Eating, in a discrete period of time (e.g., within any 2-hour period), an amount of food that is definitely larger than most people would eat during a similar period of time and under similar circumstances
   b. A sense of lack of control over eating during the episode (e.g., a feeling that one cannot stop eating or control what or how much one is eating)
2. Recurrent inappropriate compensatory behavioral behavior to prevent weight gain, such as self-induced vomiting; misuse of laxatives, diuretics, enemas, or other medications; fasting; or excessive exercise.
3. The binge eating and inappropriate compensatory behaviors both occur, on average, at least twice a week for 3 months.
4. Self-evaluation is unduly influenced by body shape and weight.
5. The disturbance does not occur exclusively during episodes of anorexia nervosa.

Two types have been identified:

1. Purging type: During the current episode of bulimia nervosa, the person has regularly engaged in self-induced vomiting or the misuse of laxatives, diuretics, or enemas.
2. Nonpurging type: During the current episode of bulimia nervosa, the person has used other inappropriate compensatory behaviors, such as fasting or excessive exercise, but has not regularly engaged in self-induced vomiting or the misuse of laxatives, diuretics, or enemas.

**Binge Episodes**

The most important clinical feature is the binge episode, with the self-perceived loss of control over eating. This results in a panic over gaining weight with subsequent purge behavior. The bulimic episodes often start after a period of pressure to lose weight. This might occur when the adolescent is involved in an activity such as ballet, cheerleading, gymnastics, or running. Any weight loss that occurs is often accompanied by feelings of inadequacy, depression, or low self-esteem. This sense of psychological emptiness leads to binge eating episodes, usually when the adolescent is alone. The binge leads to increased feelings of bloating, loss of control, shame, and fear. The teen may try to resolve these feelings by purging. The purging may initially have a calming effect and relieve guilt over a bingeing episode. This may then lead to a recurrent cycle of bingeing and purging in an attempt to manage feelings of depression and anxiety.

Initially, the binge-purge activity may be infrequent, but with time, it increases to daily or even several times a day. In addition, as the condition progresses, some individuals with bulimia will purge even after ingesting normal or small amounts of any food that might be considered fattening. The binge often occurs after a short period of starvation, typically in the afternoon after having skipped breakfast or lunch. It may begin with an after-school snack. Binges can become enormously large in caloric content. Thus, over time, what began as a diet or weight control measure turns into a means of mood regulation with the bulimic and purging behavior becoming very addictive as a source of coping. Characteristics of the binge eating include the following:

1. Food is eaten fast and frantically, often swallowed without chewing.
2. The quantity of food eaten is large, easily ingested, and usually of high caloric value.
3. The individual often experiences guilt, loss of control and pleasure over the eating episodes.
4. The binge episodes often occur alone and secretly.
5. The binge may have a frenzied quality, with consumption of food occurring in an anxious manner.

**Signs and Symptoms** Signs and symptoms may be minimal but can include the following:

1. **Symptoms**
   a. Swelling of hands and feet
   b. Weakness and fatigue
   c. Headaches
   d. Abdominal fullness
   e. Nausea
   f. Irregular menses
   g. Muscle cramps
   h. Chest pain and heartburn
   i. Easy bruising (from hypokalemia/platelet dysfunction)
   j. Bloody diarrhea (in laxative abusers)

2. **Signs**
   a. Skin changes: Primarily on the dorsum of the fingers related to self-induced vomiting; may include elongated superficial ulceration to hyperpigmentation, calluses, or scarring
   b. Enlargement of the salivary glands, particularly the parotid glands; usually bilateral and painless
   c. Dental enamel erosion (perimolysis): Usually occurs in the lingual, palatal, and posterior occlusal surfaces of the teeth

| Table 34.1 contrasts anorexia nervosa with bulimia. | TABLE 34.1. Anorexia nervosa versus bulimia nervosa: similar and contrasting features |

**Evaluation**

Evaluation includes complete history and physical examination. Laboratory screening includes CBC count; electrolytes; BUN and creatinine levels; glucose, calcium, calcium phosphate, and serum amylase (to confirm vomiting) concentrations; ECG with rhythm strip; and possibly urine samples to detect laxative or diuretic abuse.

**Treatment**

The treatment principles include the following:

1. Do not emphasize purging as the primary target symptom; the focus should be on decreasing the bulimic eating. With a decrease in bulimic eating, a decrease in the need to purge will follow. Eating three normal meals a day should be encouraged.
2. Encourage the adolescent to avoid those foods that trigger a binge such as ice cream or baked goods.
3. Treat the depression that often accompanies bulimia.
4. Have the adolescent participate in individual psychotherapy with or without family therapy, depending on the adolescent's urge and current involvement with the family.
5. Encourage the adolescent to exercise in moderation. Moderate exercise can be used as a modality for weight control rather than purging.
6. Antidepressants: Some studies have demonstrated a positive effect of use of antidepressants for controlling bulimia. Usually, the more stimulant, appetite-suppressant antidepressants, such as the SSRIs or tricyclics, are recommended in higher than usual doses. The use of psychotropic agents appears to be more successful in treating individuals with bulimia nervosa than in those with anorexia nervosa.
7. Groups and self-help organizations may be of benefit to some individuals.
8. If the individual has used diuretics, a low-salt diet may be of benefit, because there may be some fluid retention rebound when use of diuretics is discontinued.
9. If the individual has abused laxatives, bran may help the resultant constipation.
10. Referral for dental consultation for those teens with dental damage secondary to vomiting.

**Complications**

The complications of bulimia are the same as those related to purging behaviors listed earlier in this chapter for anorexia nervosa.

**Prognosis**

Herzog et al. (1999) reviewed seven studies on the outcome of bulimia. Results included the following:

1. Mortality: None.
2. Weight: Most studies reported normal body weights at follow-up.
3. Menses: No data available.
4. Eating behavior: Twenty-nine percent to 87% were having binge eating behaviors; 28%–77% reported at least one induced vomiting episode; 3%–13% reported laxative abuse.
5. Psychological state: Fifteen percent to 36% reported depression.

Herzog et al. (1999) also reviewed the prognosis of anorexia nervosa and bulimia nervosa in a prospective longitudinal study with a median of 90 months of follow-up in 246 women. The full recovery rate of women with bulimia nervosa was significantly higher than that of women with anorexia nervosa, with 74% of those with bulimia nervosa and 33% of those with anorexia nervosa achieving full recovery by a median of 90 months of follow-up. No predictors of recovery emerged among bulimic subjects. Eighty-three percent of women with anorexia nervosa and 95% of those with bulimia nervosa achieved partial recovery. Approximately one third of both women with anorexia nervosa and women with bulimia nervosa relapsed after full recovery. No predictors of relapse emerged. Bulimia nervosa was characterized by higher rates of both partial and full recovery.

In another study by Fichter and Quadfling (1997), 1.1% of individuals with bulimia nervosa shifted to binge eating disorder during follow-up, 3.7% to anorexia nervosa, and 1.6% to an eating disorder not otherwise specified (EDNOS).

**Binge Eating Disorder**
Binge eating disorder was introduced at the International Eating Disorders Conference in 1992 to describe individuals who binge eat but who do not use compensatory mechanisms (fasting or purging) to lose weight. This type of eating pattern can lead to significant weight problems and obesity. Some of these individuals start these behaviors after a period of weight-loss diets and restrictive eating, whereas others use the binge as a calming mechanism unrelated to prior dietary restrictions. It may be that up to 20% of individuals who present with treatment for obesity meet the criteria for binge eating disorder. Although binge eating disorder is not an official diagnosis in DSM-IV, it is listed as a category for proposed diagnoses and further research. The DSM-IV-proposed criteria include the following:

1. Recurrent episodes of binge eating. An episode of binge eating is characterized by both of the following:
   a. Eating, in a discrete period of time (e.g., within any 2-hour period), an amount of food that is definitely larger than what most people would eat during a similar period and under similar circumstances
   b. A sense of lack of control over eating during the episode (e.g., a feeling that one cannot stop eating or control what or how much one is eating)

2. The binge eating episodes are associated with three or more of the following:
   a. Eating more rapidly than normal
   b. Eating until feeling uncomfortably full
   c. Eating large amounts of food when not physically hungry
   d. Eating alone because of embarrassment
   e. Feeling disgusted with self and depressed

3. Marked distress regarding binge eating is present.

4. The binge eating occurs, on average, at least 2 days a week for 6 months.

5. The binge eating is not associated with the regular use of inappropriate compensatory behaviors (e.g., purging, fasting, and excessive exercise) and does not occur exclusively during the course of anorexia nervosa or bulimia nervosa.

In contrast to anorexia nervosa and bulimia nervosa, binge eating disorder affects a more diverse population including more male and nonwhite individuals. Treatment of this condition should focus on controlling binge eating and the inability to control food intake, as well as alternative coping strategies for anxiety or other issues rather than bingeing. Strict weight-loss diets are unlikely to be successful without dealing with the binge behavior and the underlying reasons for the binge behavior.

EATING DISORDERS NOT OTHERWISE SPECIFIED

There are some individuals who have problems with eating or have disordered eating in need of treatment but who do not meet the DSM-IV criteria for anorexia nervosa or bulimia nervosa. The DSM-IV has a category called eating disorders not otherwise specified. These individuals usually fall short of some essential feature of anorexia nervosa or bulimia nervosa. Examples of individuals with EDNOS are as follows:

- Teens with what appears to be anorexia nervosa but who have menses
- Individuals who appear to have anorexia nervosa and despite significant weight loss are still in a normal weight range
- Individuals who purge but never binge
- Individuals who appear to have bulimia nervosa but do not meet the criteria for frequency and duration of symptoms
- Individuals who consume a lot of food but who chew and spit out the food

These individuals are also in need of help in dealing with their disordered eating habits and issues behind the development of these habits.

ACTIVITY DISORDER OR COMPULSIVE EXERCISING

Although there is no DSM-IV diagnosis or criteria for this disorder, there has been an increase in the number of individuals with compulsive exercise behaviors to control or alter their weight, self-esteem, and mood. These individuals have continued to exercise to the point at which they are no longer choosing to exercise but have become addicted to exercise despite adverse consequences. The major feature of this disorder is excessive physical exercise that is carried beyond usual training regimens and goes to the point of being a detriment rather than a help to a person’s health. Individuals with compulsive exercising also often have obsessive concerns about being fat, binge eating, and dissatisfaction with their body. Although this disorder is often a component of anorexia nervosa or bulimia nervosa, it can occur as a separate condition. Features of this condition include the following:

- High level of activity and feelings of discomfort with states of rest
- Dependence on activity for mood stabilization
- Intense, driven quality to the activity that is resistant to change
- Lack of any consistent coexisting personality disorder, although these individuals are often achievement oriented, perfectionistic, and persistent, and often have high academic and vocational accomplishments

The treatment for these individuals is often similar to treatment for teens with anorexia nervosa. Medical issues must be handled, in addition to therapy to handle the underlying issues that have led to the activity disorder.

WEB SITES

For Teenagers and Parents


http://www.anad.org/ The National Association of Anorexia Nervosa and Associated Disorders operates an international network of support groups for sufferers and families and offers referrals to health care professionals who treat eating disorders across the United States and in 15 other countries.


http://childrenshospitalden.org/KidSource/eating/facts_anorexia.html. Information from the Children's Hospital, Denver, Colorado.


For Health Care Professionals


http://www.iaddc.com/. International Association of Eating Disorder Professionals mission is to promote a high level of professionalism among practitioners who treat those suffering from eating disorders by emphasizing ethical and professional standards.


http://www.aapf.org/afp/980600a/ip/mcgililey.html. The American Academy of Family Practice article on bulimia nervosa.

REFERENCES AND ADDITIONAL READINGS


http://www.aafp.org/afp/980600ap/mcgililey.html

http://www.mentalhealth.com/dx/fdx-et02.html

http://www.mentalhealth.com/dx/ft/fs-eat2.html


http://www.edreferral.com/anorexia_nervosa.htm

http://www.aacap.org/about/glossary/anorexia.htm

http://childrenshospitalden.org/KidSource/eating/facts_anorexia.html


http://www.aapf.org/afp/980600a/ip/mcgililey.html

http://www.anad.org/

http://www.cswd.org/

http://www.aedweb.org/


For Adolescents, Parents, and Teachers


Adolescents have abundant energy, so a complaint of fatigue must be taken seriously, particularly if the complaint originates with the adolescent and not his or her parents. Parents commonly complain of their tired or fatigued teen. Such complaints may reflect overly high expectations by the parents, adolescent-parent conflicts, or organic illness. Most fatigue in adolescents is nonorganic in origin, representing a reaction to stress, anxiety, conflict, or depression. However, most adolescents complaining of tiredness are asking for help, either in the form of “I think something’s wrong with me—tell me about it” or “I’m scared or anxious—help me.” This chapter reviews the evaluation of both fatigue and chronic fatigue syndrome (CFS).

CAUSES OF FATIGUE

Psychological Causes

In adolescents, psychological causes are responsible for 80% to 90% or more of fatigue that is unrelated to too much activity and too little sleep. Such fatigue may stem from the following:

1. Depression
2. Anxiety
3. Stressful situations

Physiological Causes

Physiological causes, another common factor in fatigue, may relate to the following:

1. Inadequate sleep
2. Dieting
3. Too much activity
4. Pregnancy

Organic Causes

Organic causes of fatigue are infrequent during adolescence. Such fatigue may result from the following:

1. Drugs: Antihistamines, sedatives, tetracycline, alcohol, anticonvulsants, oral contraceptives, and steroids
2. Infections
   a. Infectious mononucleosis
   b. Viral hepatitis
   c. Influenza
   d. Mycoplasma pneumoniae
   e. Human immunodeficiency virus (HIV) infections and acquired immunodeficiency syndrome
   f. Tuberculosis
   g. Brucellosis
   h. Parasitic infections
   i. Bacterial endocarditis
   j. Lyme disease
3. Allergies
4. Anemia
5. Neoplasm
6. Renal failure
7. Connective-tissue disease
   a. Fibromyalgia
   b. Polymyositis
   c. Systemic lupus
8. Inflammatory bowel disease
9. Congenital heart disease
10. Endocrine-related causes
    a. Hypothyroidism and hyperthyroidism
    b. Hypoglycemia
    c. Addison disease
    d. Diabetes mellitus
    e. Hyperparathyroidism
    f. Hypopituitarism
    g. Cushing syndrome
11. Liver failure
12. Heavy-metal intoxication
13. CFS
EVALUATION

History

1. Careful review of systems, with evaluation for medical conditions causing fatigue
2. Medical history: Evidence of organic disease
3. Thorough history of peer relationships, school attitude and performance, and family situation; history of depression or other psychiatric disorders
4. Diet and sleep history
5. Alcohol and substance abuse history
6. Medical history: History of use of over-the-counter medications
7. History of daily activities
8. History suggestive of emotional fatigue
   a. Fatigue that is present on arising and stays the same or lessens throughout the day
   b. Fatigue that is unchanged despite adequate sleep
   c. Frequent changes in level of fatigue throughout the day
   d. Fatigue that is worse at home or in certain situations
   e. History of conflict with parents, peer problems, sex problems, boredom, or anxiety
   f. Other signs of depression: Acting-out behavior, insomnia, apathy, and social withdrawal
   g. Other signs of anxiety: Headache, abdominal pain, palpitations, and chest pains
   h. Fatigue unassociated with other symptoms
9. History suggestive of organic cause
   a. Fatigue that increases during the day
   b. Fatigue that decreases with rest
   c. History of fever, weight loss, night sweats, lymphadenopathy, change in bowel movements, drug use, arthritis, skin changes, or any symptoms consistent with endocrinopathy, infection, or a neoplastic problem

Physical Examination

Fatigue associated with nonorganic causes is usually accompanied by normal physical examination results. Important areas to examine include the following:

1. General appearance: Evidence of chronic illness
2. Height and weight
3. Lymph nodes: Evidence of adenopathy
4. Thyroid gland: Presence of goiter
5. Cardiac: Evidence of abnormal heart murmur
6. Abdomen: Hepatosplenomegaly
7. Extremities: Evidence of arthritis
8. Sexual maturity rating: Puberty advancement normal or not
9. Mental status examination to identify abnormalities in mood, intellectual function, memory, and personality—in particular, signs of depression or anxiety

Laboratory Tests

Screening Evaluation

Many adolescents will not require any laboratory tests; the diagnosis of psychological fatigue will be evident after taking a history and performing a physical examination. If there is a question over the diagnosis, screening evaluation should include the following:

1. Urinalysis
2. Complete blood cell (CBC) count with differential cell count
3. Mononucleosis test
4. Erythrocyte sedimentation rate (ESR)

Additional Tests

A more extensive evaluation for the teen with severe, prolonged fatigue would also include the following:

1. Thyrotropin and adjusted thyroxine determinations
2. Chest x-ray examination
3. Tuberculin skin test
4. Fasting blood sugar test
5. Electrocardiography
6. Serum electrolytes
7. Creatinine and blood urea nitrogen values
8. Calcium and phosphorus concentrations
9. Total bilirubin concentration; alkaline phosphatase and liver aminotransferase activity
10. Creatine kinase activity
11. Antinuclear antibody measurement
12. HIV antibody measurement

No other additional tests, including neuroimaging studies, have been shown to be helpful in investigating chronic fatigue unless the history, physical examination, or initial laboratory findings suggest a specific disorder.

CHRONIC FATIGUE SYNDROME

CFS is a clinically defined syndrome for adults (see the case definition from the Centers for Disease Control and Prevention [CDC] [1990]) (Table 35.1) that is characterized by new onset, severe disabling fatigue, and a combination of symptoms highlighted by self-reported

| TABLE 35.1. Current centers for disease control and prevention adult definition of chronic fatigue syndrome |
impairments in concentration and short-term memory, musculoskeletal or joint pains, sleep disturbances, headaches, sore throat, tender lymph nodes, and postexertional malaise. The diagnosis excludes uncontrolled chronic illness, past or current mental illnesses such as depression, bipolar affective disorder, or anorexia nervosa. There are no accepted criteria for CFS in adolescents. Adolescents tend to present in a very similar manner to adults. Table 35.2 lists the most common symptoms reported in pediatric CFS cases. There are no specific signs or diagnostic tests for this condition.

Etiology

Clinicians frequently have strong opinions regarding the organic versus the psychological causes of CFS. Although originally linked to Epstein-Barr virus (EBV) and later to other viruses such as human herpesvirus 6, cytomegalovirus, coxsackievirus, and human T-cell lymphotropic viruses (non-HIV type 1), CFS has not been consistently linked to any single virus. More recent studies have focused on immunological abnormalities in patients with CFS including chronic immune system activation and T-lymphocyte dysfunction, with abnormalities of natural killer cell function, mitogen stimulation, and lymphocyte phenotype. In addition, abnormalities in the central nervous system have been theorized as causes of the fatigue symptoms. These changes have included abnormalities in cerebral perfusion, hypothalamic function, and neurotransmitter regulation. The pathogenesis of symptoms remains a mystery.

Bates et al. (1995) studied laboratory abnormalities in 597 patients who met the CDC or the Australian case definition of CFS. The major abnormalities found were immunological; however, each laboratory test lacked sufficient sensitivity to be diagnostic and none had proven specificity in evaluating other organic and psychiatric conditions that can produce fatigue. The most notable abnormalities in the study by Bates et al. (1995) were elevated immune complexes or elevated immunoglobulin G (IgG) levels in 48% of cases who underwent both tests, compared with only 6% in control subjects.

It is unlikely that skeletal muscle defects account for any CFS symptoms. Studies on adult patients with CFS have demonstrated reference range Vo2 maximum values on exercise testing. Studies have not demonstrated muscle weakness, although some have shown reduced endurance. Muscle biopsies occasionally reveal mitochondrial abnormalities. Deconditioning may explain many of the muscle function changes found in patients with CFS.

Autonomic Dysfunction

Recent studies indicate that some of the symptoms of CFS may be related to neurally mediated hypotension, which can be elicited during head-up tilt (HUT) testing. Stewart et al. (1999) compared 26 adolescents with CFS to those with neurally mediated syncope and healthy controls. They found that 25 of the patients with CFS had abnormal test results. The most common findings were orthostatic tachycardia (with or without hypotension) and acral findings (purpurial discoloration of the feet and ankles with livedo reticularis). It is unclear whether this autonomic dysfunction is primary to CFS or secondary to deconditioning.

Epidemiology

The prevalence of CFS in adolescents is not known. Generally CFS appears to be more common in female adolescents than their male counterparts. Although most practitioners note an increased prevalence in higher socioeconomic groups, this may be a result of more use of or access to health care. Lloyd et al. (1990) reported a prevalence of 47.9 of 100,000 10- to 19-year-olds in an Australian community using a less stringent definition of CFS. A 1993 CDC study based on the more stringent 1988 case definition of CFS found a prevalence of only 2.7 of 100,000 12- to 17-year-olds from several U.S. communities. A more recent CDC study in San Francisco using random digit dialing and the current CDC case definition found a prevalence of 116.4 of 100,000 adolescents age 12 to 17 years. The lack of consistency in these studies suggests more work is needed to understand how CFS affects adolescents.

Evaluation of Patients

The evaluation of the patient with fatigue has been presented earlier in this chapter. In general, patients require a thorough history and physical examination with particular attention to excluding physiological fatigue, mental illness, and substance abuse. If the history and physical examination findings are consistent with the CDC definition of CFS, then a laboratory workup would include a CBC count, ESR, chemistry panel (including liver function tests), thyrotropic-stimulating hormone level, purified protein derivative of tuberculin, and urinalysis. Complex patients may require other tests as indicated by the signs and symptoms they present with, but generally this is not needed. There is no known use for viral titers, including EBV antibodies (patients with recent-onset fatigue require a Monospot test). Although most patients with CFS would have an abnormal HUT test result and many would have abnormal sleep study results, these findings are not specific for CFS and generally do not add to the diagnosis or treatment recommendations. Complex patients, those in whom the exclusion of a primary psychiatric disorder is needed, require a referral to a psychologist or psychiatrist familiar with CFS. Psychological testing is often helpful in excluding psychiatric illness when a CFS-experienced provider is not available.

Treatment

1. Reassurance: Adolescents need to know that they do not have a life-threatening illness. Although CFS typically has a prolonged course (2–5 years), most cases will eventually lessen in severity or resolve. Parents also need reassurance and guidance. Frustration with this illness frequently leads to “physician shopping,” expensive evaluations, and the use of unproved and potentially dangerous treatments. Parents should be strongly advised to help their child continue in school and to avoid home study programs. Attending school reduces deconditioning and social isolation.

2. Medications: Trials of low-dose therapy with antidepressants such as fluoxetine (Prozac) at 10–20 mg, sertraline (Zoloft) at 25–50 mg, and doxepin (Sinequan) have been anecdotally reported to improve patients’ sense of well-being. Many patients report that they do not tolerate even small doses of antidepressants. Patients with sleep difficulty may benefit from trazodone or a low-dose tricyclic antidepressant. Monoamine oxidase inhibitors have been reported to be helpful in some adults. None of these medicines have been documented in clinical trials with adolescents, and care must be taken not to worsen the youth’s condition during treatment. A diagnosis of a major depression requires psychiatric evaluation and may require the use of full-dose antidepressant therapy. Adolescents with pain caused by headaches, arthralgias, or myalgias may benefit from nonsteroidal antiinflammatory agents. The use of narcotic analgesics is inadvisable in the treatment of chronic pain. Patients with symptoms of neurally mediated hypotension or positive HUT test results may benefit from fludrocortisone, b-blockers, disopyramide, or oral salt loading.

3. Psychotherapy: Adolescents with CFS frequently have a reactive depression and need support in dealing with the frustrations of a prolonged illness. Patients will typically have trouble coping with typical adolescent issues such as separation and individuation, peer relationships, body image, and school performance, as well as with chronic pain and fatigue.

4. Physical Therapy: With the typical exacerbation of symptoms seen with exercise, many adolescents become severely deconditioned. A program of gentle exercise with gradual increases is critical to the care of adolescents with CFS. Because excessive exercise will exacerbate symptoms, care must be taken to avoid an overly ambitious exercise program. Physical therapy consultation and monitoring aids in developing appropriate goals and reduces nonadherence to recommendations. Severely affected teens who are bedridden may benefit from an inpatient rehabilitation program. Case reports from Great Britain and Canada focus on a joint psychiatric and rehabilitative approach and report success.

| TABLE 35.2. Frequently reported symptoms in pediatric chronic fatigue syndrome |

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Average reported (percentage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>98%</td>
</tr>
<tr>
<td>Headaches</td>
<td>70</td>
</tr>
<tr>
<td>Arthralgias/arthritides</td>
<td>43</td>
</tr>
<tr>
<td>Pruritis</td>
<td>30</td>
</tr>
<tr>
<td>Hypersensitive to sound</td>
<td>19</td>
</tr>
<tr>
<td>Night sweats</td>
<td>12</td>
</tr>
<tr>
<td>Muscle weakness</td>
<td>8</td>
</tr>
<tr>
<td>Headache</td>
<td>6</td>
</tr>
<tr>
<td>Mood disturbance</td>
<td>5</td>
</tr>
<tr>
<td>Sleep disturbance</td>
<td>5</td>
</tr>
<tr>
<td>Fatigue at night</td>
<td>4</td>
</tr>
<tr>
<td>Weakness</td>
<td>4</td>
</tr>
<tr>
<td>Dizziness</td>
<td>3</td>
</tr>
<tr>
<td>Temperature dysregulation</td>
<td>1</td>
</tr>
<tr>
<td>Rash</td>
<td>1</td>
</tr>
</tbody>
</table>

Reassurance: Adolescents need to know that they do not have a life-threatening illness. Although CFS typically has a prolonged course (2–5 years), most cases would have an abnormal HUT test result and many would have abnormal sleep study results, these findings are not specific for CFS and generally do not add to the diagnosis or treatment recommendations. Complex patients, those in whom the exclusion of a primary psychiatric disorder is needed, require a referral to a psychologist or psychiatrist familiar with CFS. Psychological testing is often helpful in excluding psychiatric illness when a CFS-experienced provider is not available.
Clinical Evidence for Treatment of CFS

Reid et al. (2000) reviewed randomized clinical trials (RCTs) involving different therapies and found the following:

- Antidepressants: Few data are available from RCTs providing insufficient evidence to support the use of antidepressants in people with CFS. However, research evidence suggests that antidepressants may be useful in treating associated depression, insomnia, or myalgia.
- Exercise: Two RCTs found that a graded exercise program can substantially improve measures of fatigue and physical functioning for people with CFS.
- Prolonged rest: There is no evidence showing that prolonged rest is effective in the treatment of CFS; however, there is considerable indirect evidence suggesting that prolonged rest may be harmful.
- Dietary supplements: One small RCT found limited evidence of benefit from magnesium injections. Two small RCTs of oral doses of evening primrose oil found mixed results.
- Immunotherapy: Four small RCTs of IgG in people with CFS found only limited benefit and considerable adverse effects. RCTs of other types of immunotherapy have found no evidence of a benefit.
- Cognitive behavioral therapy: A systematic review of RCTs has found that cognitive behavioral therapy administered by highly skilled therapists in specialized settings can be an effective intervention.

Overall, the conclusions were as follows:

Beneficial: Exercise and cognitive behavioral therapy
Unknown effectiveness: Antidepressants and dietary supplements
Unlikely to be beneficial: Immunotherapy
Likely to be ineffective or harmful: Prolonged rest

Prognosis

The natural course of CFS in adolescents remains to be clarified. In a chart review study, Krilov et al. (1998) reported that 95% of their patients were cured or improved at 1 to 4 years of follow-up. The study further indicated that improvement is not necessarily linear. Stressful situations may result in setbacks. Smith et al. (1991) studied 15 adolescents thought to have CFS and reported that at telephone follow-up 13 to 32 months after evaluation, 4 were completely well, 4 markedly improved, and 7 unimproved or worse. Studies of adults suggest that some individuals improve with time, but most remain functionally impaired for several years (Wilson et al., 1994). Table 35.3 reviews prognosis of CFS in children and adolescents.

TABLE 35.3. Prognosis of chronic fatigue syndrome in children and adolescents

WEB SITES

For Teenagers and Parents
http://www.cdc.gov/ncidod/diseases/cfs/index.htm. The CDC Web site for CFS. The CDC also has a 24-hour hot line number (888-232-3228) for information on CFS.
http://www.cfids.org/. Chronic Fatigue and Immune Dysfunction Syndrome Association of America has information for patients and families. To receive information, call 800-442-3437 toll free, call its resource line at 704-365-2343, or send e-mail at info@cfids.org.

For Health Professionals

REFERENCES AND ADDITIONAL READINGS

Cotton P. Treatment proposed for chronic fatigue syndrome: research continues to compile data on disorder. JAMA 1991;266:2667.


Melnick A. When an adolescent is tired all the time.  Consultant 1981;July:150.


Chronic, recurrent abdominal pain (RAP) is a frequent complaint of teenagers and young adults, and treatment efforts can lead to intense frustration among both patients and health care practitioners. The condition is usually defined as three or more separate episodes of pain for 3 months. It often interferes with normal daily activities or performance. No specific organic abnormality is found in most cases (approximately 95%) of RAP occurring in adolescents.

**Epidemiology**

In a study by Oster (1972) of patients age 6 to 19 years, the prevalence of RAP was as follows:

1. Males: 12.1%.
2. Females: 16.7%.
3. Peak prevalence occurred at age 9 years (21% male, 30% female).
4. Prevalence by age 16–17 years was approximately 5% of all adolescents.

**Differential Diagnosis and Clinical Manifestations**

The following sections are provided in approximate order of occurrence during adolescence.

**Functional Pain**

Most RAP in adolescents is functional and related to everyday stresses, eating westernized diets including fried and fast foods, and drinking carbonated beverages.

1. Pain character: Nonspecific periumbilical, crampy, or dull pain. It often occurs two to four times a week. There is usually no radiation. In about 75% of patients, the pain lasts <3 hours. The pain is most often unrelated to physical activity, and does not awaken the patient from sleep. Stool retention with or without symptoms of constipation is the most frequent associated abnormality on examination or abdominal radiographs. Severe, episodic, crampy abdominal pain is common in adolescents with stool retention.
2. Family history of abdominal pain is common. RAP is more frequent in girls.
3. Relationship exists between pain and periods of stress. School and family problems are commonly associated stress factors.
4. Associated symptoms are frequent.
   a. Nausea: Up to 50%
   b. Vomiting: 19%–66%
   c. Headaches: 4%–50%
   d. Fatigue: 45%
   e. Dizziness: 25%
   f. Diarrhea: 4%–24%
   g. Loose stools: 10%–20% (either because of overflow when obstipated or overlapping with cases of irritable bowel syndrome)

**Irritable Bowel Syndrome**

1. Onset is usually during late adolescence or young adulthood.
2. Prevalence in girls is two times more common than in boys.
3. Relationship exists between pain and periods of stress. School and family problems are commonly associated stress factors.
4. Associated symptoms are frequent.
5. Symptoms increase with stress.
6. The cause probably relates to a dysfunctional colon with increased dysfunctional muscular contractions.
7. Considered a variant of functional chronic abdominal pain or RAP.

**Lactose Intolerance**

Lactose intolerance is associated with crampy abdominal pain, diarrhea, flatulence, and belching. It is common in African-American, Asian, Hispanic, and Jewish persons.

**Gynecological Conditions**

1. Pelvic inflammatory disease
2. Ectopic pregnancy
3. Mittelschmerz
4. Endometriosis
Torsion or ruptured ovarian cyst

Musculoskeletal Pain

Costochondritis, myositis, or abdominal wall muscle strain may be the cause of abdominal pain. Abdominal wall pain and tenderness are not uncommon in teens who are in athletic training.

Capsular Distention or Inflammation

1. Hepatitis, hepatomegaly, Fitz-Hugh-Curtis syndrome
2. Splenomegaly

Gastrointestinal Infections

Giardiasis, in particular, may mimic cases of RAP. Individuals with giardiasis may complain of subacute or chronic abdominal pain with bloating, as well as flatulence with or without diarrhea.

Referred Pain

Referred pain may be a result of involvement of the lower lobes of the lung (e.g., pneumonia). An uncommon source of referred pain is from spinal cord tumors (Neinstein, 1989).

Dyspepsia

1. Peptic ulcer disease: The typical pain of this disease is midepigastric burning pain occurring 1–3 hours after meals or at night. Pain decreases with the ingestion of food or antacids. The younger the patient, the more atypical the pain; approximately 50% of adolescents will have the classic pain pattern. Peptic ulcers are usually associated with Helicobacter pylori gastritis.
2. Inflammatory bowel disease: This disease is manifested by the following:
   a. Poor growth
   b. Anemia and elevated erythrocyte sedimentation rate (ESR)
   c. Bloody stools
   d. Systemic symptoms: Arthritis, iritis, hepatitis, and erythema nodosum
   e. Abnormal findings on radiographical contrast studies

Obstructed Viscus

1. Bowel obstruction, caused by adhesions or volvulus, may be present.
2. Biliary tract obstruction can result in recurrent episodes of epigastric and right-upper-quadrant abdominal pain, often with nausea and tenderness of the right upper quadrant of the abdomen. Most adolescents with gallbladder stones have one of the following risk factors: use of oral contraceptives, recent pregnancy, family history, or obesity. In adolescents, gallstones are seldom found to be associated with hemolysis, diabetes mellitus, or congenital biliary tract defects (Adye and Ryan, 1983). Another risk group for gallstones in this age group includes teens receiving parenteral nutrition. A common complication in children and adolescents with gallstones is pancreatitis (8%) (Reif et al., 1991).
3. Ureter obstruction, caused by kidney stones, results in colicky pain, often radiating to the groin.

Systemic Conditions

1. Diabetic ketoacidosis
2. Sickle cell crisis
3. Hereditary angioneurotic edema
4. Polyarteritis
5. Hemolytic-uremic syndrome
6. Lead intoxication
7. Porphyria

Pancreatitis

Pancreatitis is typified by midepigastric pain radiating to the back and associated with nausea and vomiting.

DIAGNOSIS

The organic nature of abdominal pain is usually suggested by the history, physical examination findings, and results of simple screening laboratory tests.

History

1. Pain description: Location, intensity, character, chronology, aggravating and alleviating factors, and associated signs and symptoms. The diagnosis of functional pain should not be made on the basis of exclusion alone but should be made in association with a history of stress, anxiety, depression, or other findings suggestive of stool retention.
   a. Characteristics of functional pain (or RAP)
      - Poorly described periumbilical discomfort
      - Variable location
      - Does not awaken teen from sleep
      - Often exacerbated by stress
      - May have been present for months or years before the teen sought medical assistance
      - Rarely associated with significant weight loss
      - May have other associated systemic symptoms, but they are usually not consistent with disease process
      - Retained stool on examination or abdominal radiographs
      - Local colonic tenderness to palpation on examination
   b. Characteristics of specific nonfunctional abdominal pain
      - Well localized pain
      - Location that usually remains constant
      - May awaken teen from sleep
      - May be precipitated by certain foods
      - Jaundice
      - Rash
      - Onset usually relatively acute
      - Bloody stools
      - Bilious emesis
      - Recurrent or chronic oral “canker sores”
      - May be associated with weight loss or other systemic symptoms that are more consistent with disease process such as arthritis or arthralgias and recurrent fevers
2. Family history: Relevant features of the family history
   a. History of abdominal pain
   b. History of metabolic or hematological problems: Porphyria, diabetes, or sickle cell anemia
   c. Family function and stress

3. Current stresses and relationship to pain: Common stressors for precipitating RAP symptoms
   a. Home
      i. Parental arguments, separation, or divorce
      ii. Illness or abdominal pain in family member
      iii. Loss of family member
      iv. Move to another location
   b. Peers
      i. Loss of friends
      ii. Teasing by friends
      iii. Pressure by friends
   c. School
      i. Change of school
      ii. School failure
      iii. Pressure in school
      iv. Teacher-pupil problems

4. Pain diary: It is usually helpful to have the teen keep a diary of the pain pattern for 1–3 weeks, including timing, severity, and precipitating factors.

5. Dietary diary: Review for the inclusion of fast foods and fried foods and relationship with drinking carbonated beverages

**Physical Examination**

Functional abdominal pain (or RAP) is usually associated with normal findings on physical examination or mild midepigastric tenderness without rebound. Mild lower left colon or rectosigmoid tenderness can be found on abdominal examination. Signs of nonfunctional, specific disease include the following:

1. Lack of growth: Evidence of weight loss, short stature, decreased growth, or delayed puberty—often early signs of organic disease
2. Hepatosplenomegaly
3. Abdominal masses
4. Perianal area: Fistulas or abscesses
5. Pelvic examination: Ovarian masses, adnexal tenderness
6. Arthritis
7. Oral aphthoid lesions
8. Skin rash

**Laboratory Tests**

1. Primary screening tests
   a. Complete blood cell count
   b. ESR
   c. Urinalysis with or without culture
   d. Chemistry profile with liver function tests
   e. Stool samples obtained for evidence of occult blood, ova and parasites, and stool Giardia antigen screening test
   f. Stool a-antitrypsin test (screening test for protein-losing enteropathy and chronic inflammatory bowel disease) (Thomas et al., 1983)
   g. Plain film of the abdomen
   h. H. pylori antibody titer
2. Secondary tests performed if history indicates need
   a. Colonoscopy and biopsy: If evidence of bleeding, abnormal gastrointestinal (GI) tract films, or elevated ESR.
   b. Barium enema.
   c. Upper GI tract x-ray series and small-bowel follow-through.
   d. Endoscopy of the upper GI tract if dyspepsia is present.
   e. Renal ultrasonography if renal or urinary abnormalities are detected.
   f. Serum amylase and lipase if dyspepsia is present.
   g. Abdominal ultrasonography if dyspepsia is present with right-upper-quadrant pain or tenderness.
   h. Pelvic ultrasonograph for appropriate gynecological complaints or findings.
   i. Technetium-99m iminodiacetic acid scan is useful in diagnosing acute cholecystitis.
   j. Sickle cell screening for African-American patients.
   k. Urine porphyrins if unusual, recurrent, severe abdominal pain exists, particularly in association with an abnormal mental status.
   l. Lactose tolerance test.

The diagnosis of functional abdominal pain or RAP depends on symptoms related to stress or life events, diet, a history that is not suggestive of specific organic disease, and normal findings on physical examination and screening laboratory tests. A family history of functional abdominal problems such as irritable bowel syndrome, or “spastic colitis,” is supportive evidence.

**Approach to Evaluation**

After a careful history and physical examination have revealed no obvious specific organic source, the practitioner should explain to the teen that the evaluation seems to indicate a functional disorder called chronic RAP. This is a good time to explain that real symptoms, including pain, can result from feelings. A good example is blushing—a physiological response to the feeling of embarrassment. At this point, the teen should be asked to keep a pain diary, screening laboratory tests may be performed, and a follow-up appointment should be scheduled in 1 to 3 weeks.

**THERAPY**

Therapy for functional RAP includes counseling and dietary changes.

**Counseling**

Counseling consists of reassuring the adolescent and his or her family that functional pain is real, but that no other specific disease exists. Reassurance is given that the adolescent is physically healthy and can continue with all activities. The practitioner should stress that the pain is not “in the adolescent’s head” but is a real manifestation of stress and diet. If the teen is missing school, the family and school nurse should help to keep the teen in school. If the pain becomes severe, the teen should report to the nursing office and be referred to the practitioner’s office for an examination. The relationship of stress and GI distress should be reexplained. Stress-reduction techniques can be offered. If significant depression, anxiety, or family problems are uncovered, the teen and family can be referred for further counseling in severe cases. Significant changes in or atypical characteristics of the pain should prompt reevaluation.

Silverberg (1991) examined chronic abdominal pain in adolescents and found that response to treatment was better in boys who had signs and symptoms for less than 6 months and was relatively poor in adolescents with complaints for 2 years.
Fiber Diet

If constipation, diarrhea, or irritable colon is suspected, a high-fiber diet is essential. Foods high in fiber are listed in Table 36.1.

<table>
<thead>
<tr>
<th>Food</th>
<th>Amount</th>
<th>Fiber fiber (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bran cereal</td>
<td>1/2 cup</td>
<td>33.1</td>
</tr>
<tr>
<td>Pecan</td>
<td>3 cups</td>
<td>15.5</td>
</tr>
<tr>
<td>Wheat cereal</td>
<td>1/2 cup</td>
<td>13.1</td>
</tr>
<tr>
<td>Cornflakes</td>
<td>1/2 cup</td>
<td>11.0</td>
</tr>
<tr>
<td>Rye bread</td>
<td>1 slice</td>
<td>10.0</td>
</tr>
<tr>
<td>Graham crackers</td>
<td>2 crackers</td>
<td>10.1</td>
</tr>
<tr>
<td>Fruits</td>
<td>1/2 cup</td>
<td>10.0</td>
</tr>
<tr>
<td>Peas</td>
<td>1/2 cup</td>
<td>7.5</td>
</tr>
</tbody>
</table>

**TABLE 36.1. Examples of high-fiber foods**

If such foods are unsuccessful, one teaspoon of psyllium seed (Metamucil or Citrucel) in orange juice, one to three times a day, can be used. In some individuals, if gas or flatulence is a significant complaint, particularly in Asian, African-American, and Jewish teenagers, a trial of a lactose-free diet may be indicated. Fast foods and fried foods, as well as carbonated beverages, are to be avoided. A stool softener, such as magnesium hydroxide, is frequently very helpful if there is stool retention. Administration for at least 12 weeks is usually necessary in such cases.

**WEB SITES**

**For Teenagers and Parents**


http://www.informedparent.com/articles/7.lead.abdominalpain.html. RAP review.

**For Health Professionals**


**REFERENCES AND ADDITIONAL READINGS**


Apley J, Naish N. Recurrent abdominal pains: a field survey of 1,000 schoolchildren. *Arch Dis Child* 1958;33:165.


Chest pain is reported by as many as 5% of patients attending clinics for adolescents and accounts for approximately 650,000 physician visits annually from patients age 10 to 21 years. In contrast to adults, acute chest pain of cardiac origin is uncommon among adolescents. Yet 44% of adolescents with complaints of chest pain fear heart attack, 12% fear heart disease, and 12% fear cancer.

**DIFFERENTIAL DIAGNOSIS**

The underlying cause of chest pain in adolescents includes several diverse etiologies. The following sections provide a broad classification, in order of frequency, based on several studies.

**Musculoskeletal (31%)**

In general, musculoskeletal pain is a well-localized, sharp, nagging pain. The onset is often insidious. Movement and breathing may increase the intensity of the pain.

1. Precordial catch/“stitch”: A common cause of chest pain, manifested by a fleeting 30-second to several-minute jabbing or stabbing pain, usually localized to the left sternal border or cardiac apex. The pain varies in frequency and has a sudden onset. The pain often occurs at rest and is increased with deep breathing and by bending over or slouching. The cause is attributed to irritation of the parietal pleura or intercostal nerves.
2. Muscle strain/overuse: Strain of the chest wall, upper back, or shoulder muscles after exercise or lifting can result in chest pain. Localized tenderness is frequently present. Movement of the arms and chest often increases the pain. Prolonged coughing can also lead to muscle strain.
3. Costochondritis (8%): Costochondral pain is usually a well-localized pain with focal tenderness, usually anywhere from the second through the sixth ribs of the anterior chest wall. The pain is more often unilateral and in multiple locations. The pain may radiate to the back or abdomen. Actual swelling is not characteristic. Deep breathing may increase the pain. The clue to the diagnosis is tenderness over the involved articulations at the costochondral junction. Costochondritis may be preceded by an upper respiratory tract infection or by exercise.
4. Tietze syndrome: This rare cause of costochondral pain is associated with a tender solitary swelling or nodule, usually located at the second or third costal cartilage. The swelling is typically unilateral, with either a sudden or a gradual onset. The pain may persist for days to months or longer. The pain is often increased with breathing and movement.
5. Slipping rib syndrome: An unusual cause of lower chest pain. This syndrome is caused by slipping of the eighth, ninth, or tenth rib on the immediately superior rib. These three ribs do not attach to the sternum. A tear in the connecting fibrous tissue between these two ribs can allow for this slippage. The pain is sharp, stabbing, and located in the upper quadrant of the abdomen or at the inferior costal margin. It is usually insidious in onset and unilateral. Occasionally a click is heard with movement.
6. Primary fibromyalgia syndrome: Chronic, persistent pain associated with aching, fatigue, and morning stiffness.
7. Thoracic outlet obstruction: Brachial plexus compression may be due to a cervical rib.
8. Idiopathic/Psychogenic (25%)

**Idiopathic/Psychogenic (25%)**

1. Stress or anxiety: Adolescents under stress may describe a tightness or heaviness in the chest, with or without hyperventilation. Anxiety may also induce intermittent sharp, knifelike pains or persistent precordial aching unrelated to effort.
2. Hyperventilation: Hyperventilation syndrome may cause chest pain associated with lightheadedness, shortness of breath, paresthesias, and syncope. May be more common in female adolescents.
3. Depression: Chest pain may occur among multiple somatic complaints.
4. Bulimia nervosa: Esophagitis or Mallory-Weiss tear from frequent emesis.
5. Pulmonary (21%)

Most pulmonary causes of chest pain in adolescents are associated with other symptoms such as cough, fever, pain on inspiration, and fatigue. The pain associated with pleural and pulmonary causes is usually more diffuse and difficult for the adolescent to describe.

1. Cough (10%): Persistent cough is a frequent cause of chest pain.
2. Asthma (4%): Asthma is another relatively common cause of chest pain.
3. Pneumonia/bronchitis (7%): Pulmonary infection, particularly when the infection involves the pleura, can give rise to pleuritic chest pain.
4. Pleural effusion: Seen in 10% of Mycoplasma lower respiratory tract infections; may be a presenting sign of pulmonary tuberculosis.
5. Pneumonitis: Infections with Mycoplasma pneumoniae often lead to paroxysmal pain in the intercostal muscles. The onset follows a typical viral prodrome.
6. Spontaneous pneumothorax/pneumomediastinum: Symptoms include an acute onset of pleuritic chest pain and dyspnea. Individuals with cystic fibrosis, asthma, or Marfan syndrome are at increased risk of this complication. Cocaine inhalation can also induce a pneumothorax or pneumomediastinum.
7. Acute chest syndrome in sickle cell disease: May be difficult to distinguish from pulmonary infection, infarction, and embolization.
8. Pulmonary embolism/thrombus: A pulmonary embolism can give rise to the acute onset of dyspnea, hemoptysis, and chest pain. This is an uncommon problem in teenagers, unless predisposing factors exist, such as obesity, immobilization, coagulopathy, pregnancy, or use of oral contraceptive pills, particularly with disorders of coagulation.

**Gastrointestinal (7%)**

Numerous gastrointestinal (GI) disorders can cause chest pain. However, the conditions are relatively uncommon among adolescents. Included in this group are...
Reflux esophagitis
Characterization of the pain
Anomalous coronary arteries.
Severity: Does the pain restrict the patient's usual activities?
Severe pulmonic stenosis.
Quality: A localized sharp or aching pain suggests a chest wall etiology, whereas a deep, gnawing pain suggests a visceral cause.
Onset: Patients with acute onset of chest pain are more likely to have organic disease.
Cholecystitis
Nonulcer dyspepsia
Previous treatment: What treatment has worked in the past?
Precipitating and alleviating factors: Substernal pain increasing when lying down suggests reflux and esophagitis. Pain decreasing with antacids suggests
Breast mass.
Fears and concerns: Interview patients alone to determine what they are worried about conditions such as heart disease or cancer.
Gastritis, including alcoholic gastritis
Mastitis.
Sternal contusion or separation
Herpes zoster (shingles)
Coronary arteritis in Kawasaki disease.
Fibrocystic breast changes.
Timing and duration: Brief pain may have a musculoskeletal or chest wall origin. Deep, long-lasting pain suggests a visceral origin. Is the pain related to
Mitral valve prolapse: This condition may be associated with either exertional or nonexertional chest pain.
Dysrhythmias: Supraventricular tachycardia, prolonged QT interval, atrioventricular block, sick sinus syndrome, and ventricular ectopy can cause palpitations and chest pain.
Pericarditis: Infections, particularly viral infections, can cause pericarditis leading to chest pain. Pericardial pain is usually sharp and aggravated by respiratory motion, yawning, or swelling. Sitting up and leaning forward often menos the pain. Distant heart sounds, a friction rub, tachycardia, and a recent viral infection suggest pericarditis.
Myocarditis or cardiomyopathy: May progress to congestive heart failure.
Aortic outlet obstruction: Severe aortic stenosis or hypertrophic obstructive cardiomyopathy can cause chest pain. Both conditions have been associated with sudden death in athletes.
Severe pulmonary stenosis.
Ischemic heart disease: Ischemic heart pain is almost nonexistent in the adolescent age group. Ischemic heart disease in unlikely unless there are predisposing factors such as a strong family history, severe hyperlipidemia, prolonged hypertension, or local arteritis.
Coronary arteritis in Kawasaki disease.
Dissecting aortic aneurysm: Dissecting aortic aneurysm is an extremely rare problem during adolescence, except with a predisposing connective tissue disorder such as Marfan syndrome or Ehlers-Danlos syndrome.
Coarctation of the aorta.
11. Anomalous coronary arteries.
12. Pulmonary artery hypertension.
Miscellaneous (2%)
Mediastinitis
Mediastinal mass
Herpes zoster (shingles)
Cigarette smoking
Carbon monoxide poisoning
DIAGNOSIS
History
A careful history is the most effective means of determining the cause of chest pain in adolescents. The history should include questions regarding the following:

1. Characterization of the pain
   a. Quality: A localized sharp or aching pain suggests a chest wall etiology, whereas a deep, gnawing pain suggests a visceral cause.
   b. Onset: Patients with acute onset of chest pain are more likely to have organic disease.
   c. Severity: Does the pain restrict the patient's usual activities?
   d. Location: Pain in the T1 to T4 dermatome distribution is often referred from the myocardium, pericardium, aorta, or esophagus. Pain in the T5 to T8 distribution may arise from the diaphragm, gallbladder, liver, pancreas, duodenum, or stomach. This pain may also be referred to the back and right scapula.
   e. Is the pain positional?
   f. Timing and duration: Brief pain may have a musculoskeletal or chest wall origin. Deep, long-lasting pain suggests a visceral origin. Is the pain related to meals?
   g. Precipitating and alleviating factors: Substernal pain increasing when lying down suggests reflux and esophagitis. Pain decreasing with antacids suggests peptic ulcer disease. Pain increasing with breathing, cough, or movement suggests pleural or chest wall pain. Pain increasing with stress suggests anxiety with or without hyperventilation. Pain that increases at night or awakens the adolescent suggests an organic cause.
   h. Recent activity: This includes activity that could cause chest wall strain, such as lifting weights, exercising, athletic competition, or performing household chores.
   i. Recent trauma: Has the adolescent sustained an injury?
   j. Recent infections or systemic illness: Are there any systemic illnesses such as asthma or sickle cell disease that could contribute to the chest pain? Has there been persistent cough or vomiting?
   k. Medications or drugs. Are there any medications that could account for the chest pain? Is the patient using cocaine or other stimulants such as “ecstasy” or sympathomimetic herbal preparations containing ephedrine? Any tobacco or alcohol use?
   l. Associated symptoms: Is there lightheadedness, paresthesias, or tingling in the extremities, suggesting hyperventilation syndrome?
   m. Previous treatment: What treatment has worked in the past?
   n. Family history: Known cardiovascular disease? Lipid disorder? Sudden deaths?
   o. Recent stress: A thorough psychosocial evaluation is important, including questions about functioning at home, at school, and with peers. Any history of abuse?
   p. Fears and concerns: Interview patients alone to determine what they are worried about conditions such as heart disease or cancer.

Physical Examination

2. Vital signs: Evidence of tachycardia, tachypnea, or fever? Hypertension?

3. Chest wall palpation: Examine the adolescent for localized tenderness or swelling along the ribs and intercostal spaces. Check for evidence of trauma, such as swelling or ecchymoses. Individual sternocostal and costochondral junctions should be palpated. Is there asymmetry or scoliosis? Check for supraclavicular crepitus, a sign of subcutaneous air. Perform the hooking maneuver to check for "slipping" rib. Pain can be reproduced by hooking the examiner's fingers under the ribs and pulling anteriorly. In males, examine the areolae for palpable breast tissue.

4. Cardiopulmonary examination for the following
   a. Heaves or thrills
   b. Asymmetrical breath sounds: Pneumothorax, pleural effusion, and empyema
   c. Rales: Pneumonia and pulmonary embolism
   d. Pleural friction rub: Pleurisy and pulmonary embolism
   e. Cardiac friction rub/distant heart sounds: Pericarditis and effusion
   f. Mid-systolic click, late-systolic murmur: Mitral valve prolapse
   g. Other structural cardiac lesions: Aortic stenosis, for example
   h. Cardiac dysrhythmia

5. Breast examination

6. Abdominal examination

Laboratory Testing

Most adolescents require no evaluation other than a detailed history and physical examination. Unless these findings are suggestive of a specific organic cause, the laboratory is usually not helpful in diagnosing chest pain. An electrocardiogram and chest radiograph almost always show no abnormalities in this situation. Indications for further evaluation include acute chest pain that is precipitated by exercise, interferes with sleep, or is associated with dyspnea, palpitations, dizziness, or syncope. Adolescents with a history of cardiac disease, asthma, sickle cell disease, or Marfan syndrome may also require diagnostic studies, as will those patients with specific abnormal physical findings. Studies to consider include the following:

- Chest radiograph
- Electrocardiogram
- Echocardiography
- 24-hour Holter monitoring
- Exercise stress testing
- Urine drug screening
- Abdominal ultrasonography
- Upper GI tract endoscopy

THERAPY

Chest pain is rarely life threatening in adolescents and rarely necessitates emergent intervention. Because the diagnosis is usually based on the history and physical examination findings, adolescents rarely need referral to a subspecialist. In most instances, the adolescent needs reassurance that he or she does not have a significant cardiac problem and, in addition, that spontaneous resolution of the chest pain is likely. Consider advising the patient to keep a pain diary for further evaluation if the chest pain is chronic or recurrent. Therapy depends on the specific diagnosis.

1. Musculoskeletal pain
   a. Education and reassurance
   b. Analgesics: Nonsteroidal antiinflammatory drugs (NSAIDs)

2. Psychogenic
   a. Education and reassurance
   b. Stress-reduction techniques
   c. Referral for counseling
   d. Consider prescribing sertraline if symptoms are chronic

3. Pulmonary
   a. Pleurodynia: Analgesics
   b. Pneumothorax
      - Evaluate for Marfan syndrome or other connective tissue disorder.
   c. Pneumonia: Appropriate antibiotics
   d. Pulmonary embolism: Hospitalization and anticoagulation

4. GI
   a. Esophagitis and gastritis: Antacids, histamine H₂ antagonists, gastric acid pump inhibitors
   b. Dietary modification

5. Trauma
   a. Analgesics: NSAIDs
   b. Binder or sling as needed

6. Breast
   a. Education and reassurance

7. Cardiac
   a. Mitral valve prolapse
      - Education and reassurance
   b. Endocarditis prophylaxis in the presence of significant mitral insufficiency
   c. Severe chest pain or chest pain associated with dysrhythmias: May benefit from a β-blocker

WEB SITES

For Teenagers and Parents


For Health Professionals


REFERENCES AND ADDITIONAL READINGS


Muscle and joint complaints are a relatively common problem among adolescents and young adults. The two musculoskeletal pain conditions discussed in this chapter (fibromyalgia and reflex sympathetic dystrophy [RSD]) may occur during the adolescent or young adult period and have been particularly frustrating for practitioners to diagnose and treat.

**FIBROMYALGIA**

The fibromyalgia syndrome (FMS), formerly termed fibrositis, is a disorder characterized by diffuse musculoskeletal pain and the presence of characteristic tender points. Although a common disorder in adults, affecting as many as three to six million Americans, the syndrome is underdiagnosed in children and adolescents. Nevertheless, 28% of adults with FMS reported pain symptoms beginning in childhood, particularly during the teen years. FMS comprises 2.4% of the diagnoses made at pediatric rheumatology clinics in the Pediatric Rheumatology Disease Registry, a higher proportion than either systemic lupus or any of the vasculitides. Due to possible underreporting, the true frequency may be even higher. Although few studies address FMS in the adolescent population, available data suggest that musculoskeletal and nonmusculoskeletal symptoms, as well as the psychological characteristics of these patients, are similar to those found in older populations. FMS is usually found in otherwise healthy patients (primary fibromyalgia), but it may occur in association with underlying musculoskeletal diseases, such as juvenile rheumatoid arthritis (JRA) and systemic lupus erythematosus (SLE) (secondary fibromyalgia). Children and adolescents with FMS are often referred to a pediatric rheumatologist to rule out collagen-vascular diseases such as JRA or SLE, sometimes because of a falsely positive antinuclear antibody test result.

Fibromyalgia, chronic fatigue syndrome, and irritable bowel disease have a number of features in common and may overlap in some individuals. In comparison to adults, however, teens with these diseases have a better long-term outlook.

The cause of fibromyalgia is unknown. Infections have been suspected as triggers (Epstein-Barr virus, Lyme disease), but none have been definitely demonstrated to be causative. There is evidence that emotional factors may play a role in many childhood and adolescent cases. Concomitant medical and psychiatric disorders, such as migraine, irritable bowel syndrome, chronic fatigue syndrome, mood disorders, and panic disorder, are frequently present. Although these teens with FMS are often quite stressed, there is rarely evidence that major depression or other severe psychiatric disorders requiring psychiatric care are present. Although the cause is unknown, various physiological alterations have been observed by some researchers in patients with fibromyalgia. There may be a neurotransmitter abnormality that may play a role. Although there are also abnormalities in sleep patterns and abnormalities in muscle metabolism and structure, it is unclear whether these are a cause or a result of fibromyalgia (Leventhal, 1999).

**Diagnosis**

The diagnosis of FMS requires a history of widespread pain (i.e., pain on both the left and the right side of the body and above and below the waist) that is present for at least 3 months and the presence of tenderness at 11 or more of 18 specific tender points (Fig. 38.1) (American College of Rheumatology 1990 criteria). However, experience suggests that the requirement of 11 or more tender points to satisfy the diagnosis may be too stringent in teens and that it may be possible to make a reliable diagnosis with fewer. The 18 identified tender points are generally in areas where muscles attach to ligaments or bone. When testing for pain at these sites, the practitioner should apply just enough pressure—about 4 kg—to blanch his or her thumbnail.

**FIG. 38.1. Locations of tender points in fibromyalgia.**

In addition to the criteria noted, many patients have comitant symptoms:

1. Sleep disturbance: A detailed sleep history is an important part of the history taking. The teen will often complain of difficulty falling asleep. He or she may also note a problem with waking up in the middle of the night and having trouble falling back asleep again. Most striking, however, is the failure to feel refreshed by sleep on awakening in the morning. There is evidence that patients with fibromyalgia may have an abnormal electroencephalographic sleep pattern with alpha-wave intrusion into nonrapid eye movement sleep (delta-wave sleep cycle). A chronic period of sleep deprivation is not unusual.
2. Severe fatigue.
3. Subjective swelling, numbness, or tingling of extremities.
4. Morning stiffness.
5. Many of these teens also suffer from chronic headaches, irritable bowel syndrome, and temporomandibular joint syndrome.

In contrast to RSD, objective physical changes are not seen. The pain component is substantial, although physical findings are limited. A social history is extremely important in evaluating the teen with suspected fibromyalgia. When seen initially, both the teen and the family are often in crisis. Although the teen is in severe pain, all medical test and study results have been negative. In some cases, medical professionals have told the teen that nothing is wrong, and in other cases, it may even
have been suggested that he or she is malingering. Family members may also doubt the validity of the complaints. Furthermore, the family and the school are often at odds regarding such things as participation in physical education.

Management

Comprehensive and effective treatment of teens with FMS needs to begin with a search for any underlying disease (secondary fibromyalgia). No program for secondary FMS will be successful until the underlying disease is properly diagnosed and treated. The second step is to help the teen and family in crisis. This can best be accomplished by providing a firm diagnosis and a thorough explanation of the best outpatient treatment program, as well as by relaying the message that the prognosis in teens with FMS is a good one.

The treatment program should address both the emotional and the physical aspects of the condition by combining the efforts of physician, nurse, physical and occupational therapists (OTs), and social worker and by enlistling family involvement. Emphasis should be placed on restoring function, rather than on simply relieving the pain.

Team Involvement

The teen should be assessed by the appropriate team members, which optimally might include a nurse, social worker or psychologist, physical therapist, and OT. The nurse can help educate the teen and family about FMS. The social worker can evaluate the teen and the family to assess possible psychological factors or disorders. The social worker can also provide teen and family support or counseling and can arrange for community mental health referral if indicated. Both nurse and social worker can emphasize the importance of participation in usual activities and advise the parents on how to avoid situations in which secondary gain may result from the patient's complaints of pain. Teens with FMS may also need to learn to pace themselves better, limit overtension, and avoid stressful situations and schedules.

Exercise

A supervised, systematic exercise program is a critical component of the treatment program for fibromyalgia. Deconditioning because of physical inactivity is the usual finding in FMS. Therefore, the physical therapist develops a graduated reconditioning exercise program for daily use at home. Strengthening and flexibility exercises are prescribed. The exercise program stresses postural awareness and correction of poor posture, as well as activities aimed at improving endurance. Individuals with fibromyalgia should probably avoid impact-loading exercises (e.g., jogging, basketball, or other activities that involve jumping up and down). Better exercises include walking, riding a stationary cycle, walking on a treadmill, or swimming.

Occupational Therapist

The OT assesses the impact of FMS on the teen's daily life. The use of body mechanics during typical activities is evaluated and modified if necessary. The patient is instructed on the use of relaxation techniques. Myofascial release may be used to relieve trigger points, and patients (and parents) are taught to use these releases at home so they can have an active role in the treatment and reduce dependence on the medical team. With these modalities, muscle stress and pain can be decreased, and overall functioning and sense of well-being improved. Most important, the patient will begin to develop a sense of having some control over the condition.

Schooling

The team should encourage the teen to return to regular school classes as soon as possible. If necessary, a home tutoring program can be arranged for a short period as the teen gradually becomes able to attend more classes without excessive fatigue and distracting pain. The medical team should help the parents educate the school about fibromyalgia. If necessary, the parent may have to seek a special school program under special education procedures, including an individualized educational plan.

Medications

1. Antidepressants and related drugs: Antidepressants such as amitriptyline (Elavil) are often useful in low doses (10–25 mg at bedtime) to treat the sleep disturbance. The drug may cause dryness of the mouth and other mucous membranes, as well as excessive drowsiness. However, these small doses—much lower than those used to treat depression—are usually well tolerated. An alternative is cyclobenzaprine (Flexeril 5 mg h.s.). Fluoxetine (Prozac 10–20 mg in the morning) can help decrease morning fatigue. The combination of amitriptyline and fluoxetine may alleviate fibromyalgic symptoms significantly more than either agent alone (Golenberg et al., 1996).
2. Nonsteroidal antiinflammatory drugs: May be helpful for periods of acute severe pain but generally are not very helpful for the chronic pain of fibromyalgia.
3. Corticosteroids: Have not been shown to be effective and in general should be avoided.
4. Support groups: Sometimes having teens or their parents link up with support groups can be helpful.
5. Other therapies: Various practitioners have used biofeedback, massage therapy, electroacupuncture, hypnotherapy, and cardiovascular fitness training.

Sources of information, education, and support related to fibromyalgia include the following:

Fibromyalgia Network, PO Box 31750, Tucson, AZ 85751-1750; 800-653-2921; [http://www.fmnetsnews.com](http://www.fmnetsnews.com).
American Fibromyalgia Syndrome Association, PO Box 9699, Bakersfield, CA 93389; 605-663-1137; [http://www.afsfa.org](http://www.afsfa.org).
Arthritis Foundation, PO Box 19000, Atlanta, GA 30326; 800-283-7800; [http://www.arthritis.org/](http://www.arthritis.org/).

REFLEX SYMPATHETIC DYSTROPHY

RSD (or reflex neurovascular dystrophy) is a noninflammatory musculoskeletal pain syndrome that includes a syndrome of pain, hyperesthesia, vasomotor disturbances, and potentially dystrophic changes. The pathophysiologic of the disorder is not well understood but is thought to be related to abnormal activity in the sympathetic nervous system. Underrecognized in the pediatric age groups, RSD is most common in adolescent girls but can occur in younger children and in either sex. Although the outlook is better in adolescents than in adults, RSD can produce long-term disability and eventually trophic changes, resulting in permanent damage to the extremity.

Predisposing Factors

1. Personality factors: Certain personality factors seem to predispose individuals to this syndrome. Characteristically, adolescents with RSD are overachievers. These are "perfect children from perfect families." Secondary gain (perhaps a respite from responsibilities) is usually present.
2. Trauma: The classic case of RSD in adults follows a history of trauma or medical illness affecting the involved area. In contrast, RSD in children and adolescents is associated with such an insult in fewer than 50% of cases. Although trauma may be of any type (burn, contusion, fracture, laceration, and nerve injury), it is often minor, such as a sprain, strain, or bruise. Furthermore, the trauma may antedate RSD symptoms by long periods.
3. Neurological factors: These factors include multiple sclerosis, peripheral neuropathy, tumors, and cerebrovascular accidents, but only in few adolescents with RSD.
4. Other precipitating factors: Local cold injury or revascularization of an ischemic injury or postoperative wound.

In summary, the precipitating factor in RSD is frequently trivial and the pain response is out of proportion to the injury.

Clinical Manifestations

Patients with RSD complain of severe extremity pain and inability to use the extremity. Most characteristic of the syndrome is exquisite tenderness to the lightest touch. Many of these patients cannot tolerate so much pain as the weight of a bed sheet on the involved area. Objective changes, caused by vasomotor instability, include swelling, blotchiness or bluish discoloration, reduced skin temperature, and decreased pulsations. Perspiration may be either decreased or increased in the involved area. Pain is present in 98% of cases, decreased motion in 75%, and vasomotor changes in 67%. Early symptoms include burning or aching pain, swelling, and hyperthermia or hypothermia. Diffuse osteoporosis due to disuse is common.

Laboratory Findings

1. Bone scan: A bone scan may reveal reduced blood flow. A normal scan, however, does not rule out RSD and is not required to diagnose RSD.
2. X-ray studies: In long-standing cases, there may be radiologic signs of a macular osteoporosis (Sudeck atrophy), with patchy demineralization of the
epiphyseal and the short bones of the hands and feet.

**Differential Diagnosis**

1. Chronic arterial insufficiency: Pulses are chronically diminished or absent (variable in RSD).
2. Raynaud disease: Episodic diaphoresis in distal extremity, aggravated by cold (RSD is aggravated by exercise).
3. Phlebothrombosis: No associated hyperesthesia or vasomotor changes.
4. Rheumatic disorders such as lupus erythematosus (RSD usually associated with normal laboratory test results, including normal erythrocyte sedimentation rate and a lack of significant elevation in autoantibody antibodies).
5. Localized infections (no fever or leukocytosis in RSD).

**Management**

Treatment outcome is improved if initiated early. Treatment should be aimed at improving function, rather than primarily at controlling the pain. In RSD, pain generally is not amenable to direct therapeutic intervention. Furthermore, experience has demonstrated that as function improves, pain tends to diminish. When the teen complains of pain, the practitioner should listen and then move on to deal with other issues. The basic therapeutic approach, therefore, is to treat with a combination of physical therapy and psychological counseling. We feel that this approach is safe and effective for use in adolescents with RSD. Physical therapy and psychological counseling are aimed at helping the adolescent deal with underlying feelings and conflicts in more appropriate ways. It should be emphasized to teens that the more they use the involved extremity, the quicker the extremity is going to get better; conversely, disuse will worsen the condition.

**Discussion of Disease and Prognosis**

Treatment begins with discussing the diagnosis and its implications with the patient and parents in a clear, straightforward manner. As soon as the diagnosis is established, they should be so informed in definite terms. The important role that emotional factors may play in disease etiology should be explained. The fact that the prognosis is good with treatment should be emphasized. This is the time to set the stage for ongoing psychotherapy. In our experience, helping the family deal with the emotional aspects of the disease is crucial to the achievement of an excellent outcome. Although the prognosis for short-term improvement with physical therapy alone is good, without psychological intervention, it is likely that RSD will recur or another pain amplification syndrome will develop.

**Medications**

1. Steroids and sympathetic blockers: The literature on adults with RSD reports that some patients benefit from corticosteroids, ganglionic blocking agents, and chemical sympathetic blockers. Our experience is that these modes of treatment generally produce short-lived or no benefit and may be associated with adverse effects. Furthermore, they divert the adolescent from dealing with underlying psychological issues. Except for the rare case in which emotional factors are not implicated, these forms of therapy should be avoided.
2. Nonsteroidal antiinflammatory drugs: These drugs usually have little effect on relieving the pain of RSD. The major emphasis should be on improving function. If normal functioning can be achieved, the pain will usually resolve.
3. Phenoxymethylamine: This adrenergic (α-receptor) blocker has been helpful in some of the more classic cases of RSD in adults caused by obvious trauma. This is not an agent used in our practice.

**Hospitalization**

In mild cases and even moderately severe cases, outpatient management may suffice. In some centers, an outpatient program that provides 6 hours of exercises a day has produced good results. With severe and long-standing symptoms or failure of outpatient treatment, admission to an inpatient rehabilitation center may be necessary.

**Admission**

On admission, the diagnosis and its implications, both emotional and physical, must be explained to the patient and family. This is the time to be very clear about the emotional factors involved in most adolescents with RSD. This is also the time that the discharge goal is established. A typical example of a “discharge goal” for the adolescent with lower extremity involvement might be to walk for a reasonable distance, wearing shoes and socks, with no more than a minimal limp. Prosthetic devices and aids, such as wheelchairs, crutches, and braces, are quickly withdrawn. Patients are permitted to receive mild analgesics, such as acetaminophen, if requested, but they are advised that drugs are not likely to provide major pain relief.

**Weekly Conferences**

A weekly conference of multidisciplinary team members is held to review the patient’s progress and to set a series of objectives for the week. These objectives, usually exercises consisting of use of the involved extremity, must be quantifiable and sufficiently challenging so the teen will have to work diligently to accomplish them by the end of the week. At the same time, the objectives must be realistic and attainable. We tell the teen and family that the week begins on Monday and ends on Sunday. If the weekly objective is achieved earlier than the end of the week (e.g., on Friday), the teen may have a weekend pass. If not, we say to the teen: “That’s okay! But, of course, the work must continue until the objective is met”; thus, no pass is given. In this way we attempt to avoid having the teen interpret not receiving a pass as punishment.

**Role of the Therapeutic Team Members**

1. **Physician.** The physician sets the overall direction of the patient’s management, determines the discharge goal, conducts team meetings, regularly examines the patient, and communicates with the patient and his or her parents. The physician may need to play the role of “bad guy” when appropriate.
2. **Nurse.** The registered nurse plays a central role in the day-to-day coordination of the patient’s care. These tasks include scheduling weekly team meetings, presenting and explaining weekly objectives to the teen, and checking on the teen’s progress in meeting these objectives and his or her eligibility for weekend passes. The nurse is responsible for reporting 24-hour daily nursing observations of patient actions and interactions to the team members. Most important, the nurse has a special role to fulfill in fostering a trusting patient-physician relationship with the patient. This includes providing emotional support by encouraging the teenager to talk about feelings and express anger in appropriate ways, listening to the teen’s complaints of pain, and providing support to the family.
3. **Physical Therapist.** The physical therapist provides weight-bearing exercises for the involved extremity. Desensitization techniques, such as vigorous toweling or immersion in contrast baths, are used. Atrophied muscles are strengthened and endurance is improved. Throughout this process, choices are permitted within limits (i.e., a win-win situation is set up in such a way that the teen attains his or her objectives while being allowed a certain amount of control over the treatment regimen). For example, the teen may be given the choice of vigorously toweling the involved extremity for a longer period or having the therapist do so for a shorter period. This fosters assertiveness, a trait frequently lacking in these adolescents. Throughout the process, the therapist uses a firm but nonpunitive approach.
4. **Occupational Therapist.** In adolescents with RSD, upper extremity involvement is less common than lower extremity involvement. When the former is present, however, the OT provides tasks requiring hand and arm use in much the same way as the physical therapist does for the lower extremities. Adolescents with RSD are often overachievers. Clearly, being an overachiever carries with it a psychological “price.” Therefore, the OT evaluates the teen’s capabilities and the psychological costs involved in reaching his or her or the family’s expectations. If these expectations are not appropriate, they need to be modified. The OT’s role extends to facilitating age-appropriate activities and interactions. Occupational therapy provides opportunities for the teen to make choices and exercise age-appropriate independence, as well as to interact with other teens in a nonthreatening milieu.
5. **The Parents.** The parents form a vital component of the therapeutic team. Without their active participation, recovery tends to be slower and relapses are more common. Both mother and father should be enlisted as full members of the team. We encourage both parents to participate with their teenager in the exercise program. We instruct the parents to “cheer the patient on” but to avoid negative statements about the activity. For example, when the teen is working out on the stationary bicycle, the parent might do the same on another bicycle.

**Social Worker or Psychologist.** The role of this team member is crucial in terms of the long-term outlook. His or her first task is to evaluate patient and family psychosocial dynamics. The experience of this therapeutic team member in dealing with many RSD cases has proved to be an extremely valuable asset; patients with
RSD, when previously evaluated elsewhere, may have been informed they had no psychological problems. Our studies, in contrast, have established a high frequency of subtle family conflict, difficulty in expressing anger, and enmeshment with the mother. The father, on the other hand, is frequently viewed by teen and mother as powerful, but remote. Although the patient may be the family member with symptoms, RSD can usually be seen as a family disorder, and family therapy is highly desirable.

The treatment program outlined earlier in this chapter has evolved in our institution over many years. It has proved to be highly effective in returning most patients to normal functioning, with a very low rate of disease recurrence.

Sources of information, education, and support related to RSD include the following:

- [RSD Association of America](http://www.rsds.org/)
- [American College of Rheumatology](http://www.arthritis.org/conditions/diseasecenter/rsds.asp)
- [NIDR](http://www.ninds.nih.gov/health_and_medical/pubs/rsds_fact_sheet.htm)
- [AFSA](http://www.afsa.org/)
- [FMNET](http://www.fmnetnews.com/)

WEB SITES

For Teenagers and Parents

- [Photo gallery of RSD patients](http://www.rsds.org/gallery_page_1.htm)
- [Teen site on RSD](http://www.angelfire.com/wi/rsdhopeteens/)
- [NIDR article on fibromyalgia](http://www.niddk.nih.gov/health_info/fibrofs.htm)
- [NIH factsheet on fibromyalgia](http://www.ninds.nih.gov/health_and_medical/pubs/rsds_fact_sheet.htm)
- [Patient handout from AAFP on fibromyalgia](http://www.rsds.org/conditions/diseasecenter/rsds.asp)

For Health Professionals

- [University of Washington Web site](http://www.rsds.org/)

REFERENCES AND ADDITIONAL READINGS

**Fibromyalgia**

Ballinger SH, Bowyer SL. Fibromyalgia: the latest “great imitator.” Contemp Pediatr 1997;14:140.


**Reflex Sympathetic Dystrophy**


Adolescents are sexual beings, a reality that parents, doctors, and adolescents themselves are not always comfortable addressing. A practitioner who approaches the topic of teenage sexuality by focusing solely on possible outcomes related to vaginal sexual intercourse—such as pregnancy, human immunodeficiency virus (HIV), acquired immunodeficiency syndrome (AIDS), and other sexually transmitted diseases (STDs)—ignores the reality that (a) all teenagers are sexual beings whether or not they are sexually active, and (b) teens engage in sexual activities other than vaginal intercourse. In fact, sexual behavior does not start during adolescence or adulthood, but with childhood sexual curiosity. During adolescence, there is a sudden upsurge of curiosity and interest in one's own body and the bodies of one's peers. Even very young adolescents are interested in "how things work" and are exposed to a wide range of sexual topics through friends, school, and the media. Although problems do arise during adolescence from lack of information, more confusion and difficulties stem from inexperience with sexuality and lack of decision-making skills. It is essential for health care providers caring for adolescents to understand sexuality during the teenage period and to be familiar with ways to deal with teenagers' questions, feelings, and problems. This chapter provides an overview of heterosexual adolescent sexuality and methods by which the professional can better deal with adolescent sexuality. (Please see Chapter 40 for an in-depth look at issues relevant to gay, lesbian, bisexual, and transgender youth.)

ADOLESCENT SEXUAL DEVELOPMENT

Preadolescence

During the preadolescent period, biological sex based on chromosomes, gonads, and hormones is determined. In addition, gender identity or sense of masculinity and femininity is established. Characteristics of preadolescent sexual development include the following:

1. A low physical and mental investment in sexuality exists.
2. Collecting information and myths about sexuality from friends, school, and family is common.
3. Physical appearance is prepubertal.

Early Adolescence

Characteristics of sexual development in early adolescence include the following:

1. Physical maturation starts.
2. Extreme concern and curiosity exists about one's own body and that of one's peers.
3. Sexual fantasies are common and may serve as a source of guilt.
4. Masturbation begins during this period and may be accompanied by guilt.
5. Sexual activities are usually nonphysical. Early adolescents are often highly content with nonsexual interactions such as telephone calls to peers.

Middle Adolescence

Sexual development in middle adolescence is characterized by the following:

1. Full physical maturation is attained and menstruation begins in females.
2. Sexual energy is at a high level, with more emphasis on physical contact.
3. Sexual behavior is of an exploratory and exploitative nature.
4. Dating and making out (petting) are common, and casual relationships with both noncoital and coital contacts are prevalent.
5. Denial of consequences of sexual behavior is typical.

Late Adolescence

Sexual development in late adolescence is characterized by:

1. Full physical maturation.
2. Sexual behavior becomes more expressive and less exploitative.
3. Intimate sharing relationships may develop.

As already outlined here, adolescent sexuality is an important developmental process and cannot be reduced merely to outcomes such as pregnancy and intercourse. Adolescents are struggling with their identity and issues such as the following:

1. How do I know I'm ready for sex?
2. What is important in a relationship?
3. How do I say no? Do I want to?
4. How do I deal with anger, rejection, and loneliness?
5. What is safe sex?
6. Am I gay or straight?

Adolescents are involved with sexual activity because of peer pressure, to experience affection, to feel grown up, to experience closeness, for experimentation, and because it feels good.

SEXUAL BEHAVIOR

In 1998, approximately 38.6 million 10- to 19-year-olds lived in the United States. Although we have relatively good data on rates of vaginal intercourse and its sequelae such as pregnancy and STDs, we have little information on other genital and nongenital sexual activities of this population. Two recent studies help to fill
this gap: (a) the National Survey of Adolescent Males (NSAM) (Gates and Sonenstein, 2000) and (b) the study by Schuster et al. (1996a) on sexual practices of adolescent virgins.

The data from these two studies are summarized in Table 39.1, Table 39.2, Table 39.3, and Table 39.4.

**Table 39.1.** The percentage of 15–19-year-olds never married males who have ever engaged in various sexual behaviors by their experience with vaginal intercourse and by age and race/ethnicity in 1995

**Table 39.2.** The percentage of never married males age 15–19 years who report ever having engaged in various sexual activities, by year, according to experience with vaginal intercourse and to age and race or ethnicity, 1988 and 1995

**Table 39.3.** Percentage of high school virgins in each demographic group who engaged in each heterosexual genital sexual activity during the prior year

**Table 39.4.** Percentage of high school students who used illicit substances and engaged in other problem behaviors during the prior year, by category of sexual experience

Table 39.1 shows sexual behaviors of 15- to 19-year-old never married males by age and race in 1995. Twenty-two percent of males not having had vaginal sex (virgins) have been masturbated by a female and 15% have received oral sex from a female. Only 0.9% report having had insertive anal intercourse.

Table 39.2 describes trends of sexual behaviors between 1988 and 1995. There has been recent media attention regarding the rate of oral sex and the impression that it is of epidemic proportions (Remez, 2000). However, when comparing percentages between 1988 and 1995 of male “virgins” and “nonvirgins,” it is clear that although there is an increase over this time period, it is not significant.

Table 39.3 describes the heterosexual genital sexual activities of high school virgins. Schuster et al. (1996a) studied male and female virgins attending an urban high school. They found that approximately 30% of both males and females have masturbated or have been masturbated by a partner. Eleven percent of male virgins and 8% of female virgins have experienced fellatio with ejaculation, whereas 9% of male and 12% of female virgins have participated in cunnilingus.

Table 39.4 compares rates of other risk-taking behaviors of sexually active virgins compared with nonsexually active virgins. In the study of high school virgins, Schuster et al. (1996a) also found that virgins who engaged in sexual activities had problem behaviors similar to those of nonvirgins when compared with virgins who were not engaged in other sexual behaviors.

Another source of information about teen dating and sexual behaviors is from the Kaiser Family Foundation in a joint project with the magazine YM. They explored teen dating and intimacy in teens age 13 to 18 years in a report entitled National Survey of Teens: Teens Talk About Dating, Intimacy, and Their Sexual Experiences
Overall, the report found that teens as young as 13 and 14 years struggle with complex sexual situations involving pressure, drinking and drug use, and relationships that the teens are feeling are moving too fast. About one third felt they did something sexual or felt pressure to do something sexual that they did not feel ready to do. In this survey, intimacy appeared to play a significant role in teens’ relationships, and deciding to wait to become sexually involved was viewed positively by the teens.

Some major findings included the following:

- Dating was a part of most teens’ social lives as early as age 13 years, but the level of both physical intimacy and “serious” relationships increased with age. Nine (89%) of ten teens age 13–18 years say they have had some romantic involvement with a member of the opposite sex.
- Teens age 13–14 years: For example, among teens age 13–14 years most say it’s typical for couples their age to kiss (72% say this usually happens), but that other forms of physical intimacy are not the norm. Only 45% say French kissing is expected, and far fewer reported that petting (15%) or intercourse (4%) is typical.
- Teens age 15–16 years: These percentages increased for teens 15 and 16 years of age who stated that dating couples their age typically kiss (93%) and French kiss (71%), and just less than half (48%) say they also engage in petting. Only 28% say sexual intercourse is typical for dating couples their age. Most teens age 15 and 16 years say couples their age go out on dates (79%) and spend a lot of their free time together (56%). This age group also stated that they are often in love with each other (63%).
- Teens age 17–18 years: The sexual involvement increases with this age group. More than half of teens this age say it’s typical for couples they know to engage in petting (57%) and about half (52%) say couples typically have intercourse.
- Although dating was common, it was viewed as very acceptable to be unattached. Very few of the teens stated that most of their friends currently have a boyfriend or a girlfriend. Most stated that in their social circle, dating is not very important.
- Teen girls and boys did not agree about what’s going on in teen boys’ minds. Teen girls, particularly older girls, think teen boys attach much greater importance to sex in a relationship than teen boys think their male peers do. Teen girls also think teen boys aren’t as concerned about pregnancy, STDs, and HIV as teen boys say their male peers are.
- A significant percentage of teen girls think they are less experienced than their friends and less experienced than their sexual partners.

There still remains much to learn about the full range of noncoital sexual behaviors of adolescents. Even less well understood is how these noncoital behaviors are perceived by teens. Is oral sex really sex or a form of abstinence (Remez, 2000)?

**Sexual Intercourse**

There are several sources for data on the rates of sexual intercourse in U.S. adolescents. The four major surveys currently available are the following (see the Web sites for full data):

- **National Survey of Adolescent Males (NSAM),** http://www.agi-usa.org/pubs/journals/3229500.html
- **Youth Risk Behavior Survey (YRBS),** and http://www.cdc.gov/mmwr/preview/mmwrhtml/ss4905a1.htm
- **National Longitudinal Study of Adolescent Health (Add Health).** http://www.nichd.nih.gov/about/cpr/dbs/res_add.htm

Data on sexual behaviors in college students are reported in Chapter 85 from surveys collected by the Centers for Disease Control and Prevention (CDC) in 1995 and in 2000 by the American College Health Association. Although all four surveys in adolescents collect information about sexual behavior, they differ in purpose, design, and implementation. The following figures and tables present data from these surveys.

**Youth Risk Behavioral Survey Data on Sexual Intercourse and Number of Partners** Figure 39.1 from the 1999 YRBS details information on the percentage of high school students who had sexual intercourse, by gender and grade. Roughly two thirds of 12th grade boys and girls have had sex.

![FIG. 39.1. Percentage of high school students who had sexual intercourse, by sex and grade, 1999. (From the Youth Risk Behavior Surveillance–United States, 1999. MMWR 2000;49(SS05):1–96, with permission.)](image)

**Figure 39.2 from the 1999 YRBS details the percentage of high school students who are currently abstinent from sex, by gender and grade. Twenty percent of female and 25% of male high school seniors were currently abstinent.**

![FIG. 39.2. Percentage of high school students who are currently abstinent, by sex and grade, 1999. (From the Youth Risk Behavior Surveillance–United States, 1999. MMWR 2000;49(SS05):1–96, with permission.)](image)
Figure 39.3 from the YRBS gives the percentage of high school students who engaged in their first intercourse before the age of 13 years, by gender and grade. About 5% of female and 12% of male high school students engaged in their first sexual intercourse before age 13 years.

Figure 39.4 examines the number of high school students with four or more sexual partners during their lifetime, by gender and grade. Twenty percent of female and male high school seniors have had four or more sex partners during their lifetime.

Pregnancy Figure 39.5 shows the percentage of high school students who have been pregnant or who have gotten someone pregnant, by gender and grade (from the YRBS). Almost 8% of female and 5% of male high school seniors have been pregnant or have gotten someone pregnant.

Sexual Behavior Data from Students at Alternative Schools YRBS data were also collected from alternative schools in 1998. These schools serve approximately 280,000 students who are at high risk for failing or dropping out or who have been excluded from regular schools due to drug and/or alcohol use, behavioral problems, or illegal activities. Similar data are presented in the next figures to those presented for the 1999 YRBS (Web site: www.cdc.gov/mmwr/preview/mmwrhtml/ss4807a1.htm).

Figure 39.6 shows data from the YRBS for alternative schools on the percentage of high school students who had sexual intercourse or who are currently sexually active, by gender and grade (YRBS, 1998). The rates of sexual activity in alternative high schools are much higher than those in traditional high schools. Approximately 90% of alternative high school senior females and males had ever had sexual intercourse, compared with two thirds of traditional high school senior males and females.
Figure 39.7 includes data from the YRBS alternative schools detailing the percentage of students who had their first sexual intercourse before the age of 13 years, by gender and grade (YRBS, 1998). Nineteen percent of 9th-grade females and 32% of 9th-grade males had first had sex before age 13 years.

![Figure 39.7](image_url)


Figure 39.8 examines the number of alternative high school students with four or more sexual partners during their lifetime, by gender and grade (YRBS, 1998). Fifty percent or more of male and female alternative high school seniors have had four or more lifetime sexual partners. This is more than twice the rate for traditional high school male and female seniors.

![Figure 39.8](image_url)


Figure 39.9 examines the percentage of students at alternative high schools who used alcohol or drugs at last intercourse, by sex and grade, in 1998. Drug and/or alcohol use was commonly associated with their last sexual intercourse for alternative high school seniors, with almost 29% of females and 50% of males using alcohol or drugs at their last intercourse.

![Figure 39.9](image_url)


Trends in Sexual Intercourse To put adolescents’ current sexual behavior into perspective, one must look at trends over time. In fact, rates for sexual intercourse and its sequelae have recently been decreasing. Santelli et al. (2000) compared the YRBS, NSFG, Add Health, and NSAM for 15- to 17-year-olds over time. The following tables present data from that article. It is important to note that each survey has different rates for sexual intercourse due to the different sampling methods and populations surveyed. They include in the comparison only in-school youth. Table 39.5 demonstrates the trends in high school students who have had sexual intercourse according to these surveys. Although all the surveys differ in their methodology, the general trend is decreasing rates of sexual intercourse from 1991 to 1995. Table 39.6 reports on the trends of oral contraceptive use, condom use, and numbers of partners according to these surveys. Although oral contraceptive use appears to have decreased, condom use has increased. Table 39.7 reports on the trends on the number of adolescents with four or more lifetime partners according to these surveys. The YRBS shows no significant change in percentage of 15- to 17-year-old females who have had four or more partners in their lifetime from 1991 to 1995, although there was a significant decrease for males as a whole, and specifically for white males. Table 39.8 lists the major protective factors associated with whether a youth had sexual intercourse, some of which were as follows: (a) “made a virginity pledge” was protective for black and Hispanic males and white and black females; (b) perceived personal and social costs to sex; and (c) perceived knowledge of birth control.
TABLE 39.5. Percentage (and standard error) of high school adolescents age 15–17 years who reported ever having had sexual intercourse, by gender and survey, according to race and ethnicity

TABLE 39.6. Percentage (and standard error) of sexually active high school adolescents age 15–17 years who reported using oral contraceptives at last intercourse, who reported using condoms at last intercourse, or who had two or more sexual partners in the past 3 months, by survey, according to gender

TABLE 39.7. Percentage (and standard error) of sexually experienced high school adolescents age 15–17 years who reported having had four or more sexual partners in their lifetime, by gender and survey, according to race and ethnicity

TABLE 39.8. Factors associated with whether youth had sexual intercourse

Protective and Risk-promoting Factors Another important question asks about the reasons why adolescents are having sex and what are the protective and risk-promoting factors. The Henry J. Kaiser Family Foundation and Seventeen magazine formed a public information partnership to provide young people with information and resources on sexual health issues. They report that 86% of teens say young people face pressure when it comes to sex and relationships, 38% said they face some pressure, and 48% said they faced a lot. The following figures describe the major reasons teens say they have decided to wait to have sex or decided to have sex the first time.

Figure 39.10 reviews why teens who have not had sex wait to have sex, with the number one reason being that they were worried about pregnancy (83%).

FIG. 39.10. To have sex or not? Among 15- to 17-year-olds who have not had sex, the percentage who say each was a “major reason” for their decision to wait have sex. (Sex smarts: decision making about sex, the Henry J. Kaiser Family Foundation and Seventeen, Sept 2000. www.kff.org/content/2000/20001011a/SexSmart.pdf)

Figure 39.11 reviews the major reasons why teens who have been sexually active chose to have sex, with the number one reason being that they met the right person.
Factors Associated with Sexual Activity  Blum et al. (2000a) analyzed the Add Health data, looking at several factors associated with having or not having sexual intercourse. In general, the survey showed that sexual intercourse increases from 16% among 7th to 8th graders to 60% among 11th to 12th graders. Factors associated with sexual activity include the following:

- Race: Black youths were more likely to have had intercourse than white or Hispanic youths.
- Socioeconomic status: Teens from wealthier families were less likely to have had intercourse than those from lower income families.
- Single-parent families: Youths in single-parent families were more likely to have had intercourse than youths in two-parent families.
- Gender: Among 7th and 8th graders, females were less likely to have had intercourse than males.

However, the factors of race/ethnicity, income, and family structure explained only 9.7% of the difference between younger teens who have or have not had sexual intercourse and 2.9% for older teens.

To better understand the factors involved, several additional factors were evaluated (Table 39.8 lists these factors). Considered jointly, these factors explain 25% to 34% of the difference between males who have and males who have not had sexual intercourse and 35% to 49% of the difference for females.

Do Physicians Address Issues of Adolescent Sexuality and Do Teens Wish Them to do So?  Schuster et al. (1996b) looked at communications between adolescents and physicians about sexual behavior. Table 39.9 reports on the percentage of adolescents who reported having discussions with physicians, and Table 39.10 reports on the percentage of adolescents who reported that they would find these discussions helpful. Thirty-nine percent of students in 1989 reported having a conversation with a physician about AIDS prevention and 37% about condom use for vaginal intercourse, but only 13% had discussions on how to use condoms or how to say "no." Discussions about sexual orientation only occurred in 8%. Discussions about these topics were more likely with their regular physician and if they were not virgins.

When asked about the value of discussing these issues with a physician, more than 50% found discussions about how to avoid getting AIDS from sex, avoid getting STDs, and avoid pregnancy, and information about condoms and other forms of birth control to be very helpful.

In a recent CDC news release (Marchione M, CDC, 2000), it was found that in a survey of 15,000 high school students from the United States, only 43% of teenage females and 26% of teenage males discuss pregnancy or sexually transmitted infections with their physicians during routine examinations.

The Commonwealth Fund (Schoen et al.) published a survey of health of adolescent girls in 1997. This survey also included information about boys. The survey identified a gap between what boys and girls believe doctors should discuss and what doctors have discussed. Between 35% and 65% of boys thought doctors should discuss issues of physical or sexual abuse, pregnancy prevention, STD prevention, drinking, and drugs, whereas less than one third of doctors actually discussed these issues (Fig. 39.12 and Fig. 39.13). Parents and doctors should be encouraged to communicate about sex with their children and teens. Several studies have demonstrated a salutary effect on sexual behavior secondary to parent-teen discussions (Dilorio et al., 1999; Whitaker et al., 1999).


Age Difference Between Sexual Partners
Several states have enacted or started enforcing statutory rape law because of a concern about adult men fathering babies with female teens (Darroch et al., 1999; Donovan, 1997; Males and Chew, 1996). An analysis of the 1995 NSFG examines the difference between women and their sexual partners. Table 39.11 and Table 39.12 describe the data for 15- to 19-year-old females. Table 39.11 shows that of 3,274 unmarried women between age 15 and 17 years, 0.7% had male sexual partners 3 or more years younger than themselves, 64% were 0 to 2 years younger or older, 26.9% were 3 to 5 years older, and 8.3% were 6 or more years older. In Table 39.12, of the 447,100 pregnancies to women age 15 to 17 years, 50% had a partner less than 2 years younger or older, 30.8% had a partner 3 to 5 years older, and 19.2% had a partner 6 or more years older.

<table>
<thead>
<tr>
<th>TABLE 39.11. Percentage distribution of U.S. female adolescents who had sex in the previous 3 months, by the difference between their age and that of their partner, according to the female’s age and marital status, National Survey of Family Growth, 1995</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>TABLE 39.12. Percentage distribution of pregnancies, births, and abortions to women age 15–17 years by age of partner</th>
</tr>
</thead>
</table>

Unwanted Sexual Experiences

1. The percentage of students in grades 8–11 reporting unwanted sexual comments or actions is shown in Table 39.13. More than 80% of females in grades 8–11 and more than two thirds of males experienced unwanted sexual comments or actions in 1993.

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>Female</th>
<th>Male</th>
</tr>
</thead>
<tbody>
<tr>
<td>Black</td>
<td>64</td>
<td>81</td>
</tr>
<tr>
<td>Hispanic</td>
<td>62</td>
<td>69</td>
</tr>
<tr>
<td>White</td>
<td>67</td>
<td>79</td>
</tr>
</tbody>
</table>

From Alan Guttmacher Institute, Sex and America’s teenagers, New York: Alan Guttmacher Institute, 1994, with permission.
Six of ten students in grades 8–11 reported that they have subjected someone else at school to unwanted sexual comments or actions (Alan Guttmacher Institute, 1994).

Nonvoluntary sexual intercourse: Sexual intercourse in young adolescents in particular may not be voluntary. Data presented by the Alan Guttmacher Institute (1994) indicate that about 74% of women who had intercourse before age 14 years and 60% of those who had sex before age 15 years report having had sex involuntarily (Table 39.14). In 1987, 7% of sexually experienced young people age 18–22 years reported that they had been forced to have sex against their will at least once.

### Table 39.14. Percentage of sexually experienced U.S. females age 19 years and younger with history of involuntary intercourse

<table>
<thead>
<tr>
<th>Year</th>
<th>Percentage of Unwanted Sex</th>
</tr>
</thead>
<tbody>
<tr>
<td>1987</td>
<td>7%</td>
</tr>
<tr>
<td>1993</td>
<td>8%</td>
</tr>
</tbody>
</table>

WHY IS ADOLESCENT SEXUALITY A CONCERN

Assuming adolescent sexuality is part of natural development, why is it a focus of so much attention and concern? The following are some explanations for this dichotomy:

1. Opposing views of sexuality: Inherent in the problem of adolescent sexuality are the differing attitudes about sexuality expressed by adolescents and the community. Predominant views among adolescents are that sex is justified as physical pleasure or as new experience; that it is an index of maturity; that it reflects peer-group conformity; that it represents a challenge to parents or to society; and that it offers an escape from pressures. The adolescent's parents or the community, on the other hand, often views sex among teenagers as a crime, a sin, or a sickness.

2. Body-mind gap: Although the age of physical maturity has progressively declined over the past 200 years, the age of economic independence and marriage has risen. This widening gap of perhaps 1–15 years or more must be filled with some form of developing sexuality for the adolescent. The enlarging time period of adolescent sexuality and society's inability to deal with the issue compound the problems of teenagers' sexuality.

3. Lack of communication: Numerous studies reveal that about two-thirds or more of adolescents cannot communicate with their parents about sex. Many parents assume that their teenagers do not want to talk about sex, although in fact many adolescents wish they could talk with their parents about sex. This miscommunication furthers misunderstanding and lack of trust.

4. Media: The media, including radio, movies, and television, promotes an unrealistic image of sexual behavior, one based primarily on violence rather than love.

5. Peer pressure: Adolescents find increasing pressures from their peers to be sexual, a pressure that represents a formidable struggle for many adolescents.

6. Developmental stage: A typical characteristic of early and middle adolescent development (as discussed in Chapter 2) is a sense of immortality, with resultant risk-taking behavior. Adolescents thus often react without a full sense of the potential consequences of their actions. Caught between peer values, parental values, the image of sex portrayed by the media, and their own developing values, adolescents frequently act impulsively, engaging in sexual intercourse without being prepared mentally for it and thus avoiding “premeditated” sex. The resultant guilt that many adolescents feel can become a barrier to the development of healthy attitudes about sex.

7. Sex education: Many sex education courses, if available, stress reproductive function and menstruation, and many now focus only on abstinence. Although it is important for teenagers to be informed in these areas, adolescents also need help in decision-making skills and in dealing with their feelings, fears, and relationships.

**RECOMMENDATIONS**

Several suggestions to help adolescents better deal with their sexuality include the following:

1. Parental or counselor skills
   a. Trying to understand adolescent attitudes about sex can be frustrating, leading to feelings of anger on the part of the parent or counselor. Communication is enhanced if the parent or counselor tempers his or her own response and tries to listen to and appreciate the adolescent's feelings and concerns regarding sexuality. Parents must be made aware that although adolescents have control over their own sexual behavior, parents can exert a strong positive influence, not through moralizing, lecturing, or invasion of privacy, but through helping the adolescent in his or her decision-making process.
   b. Timing: Because sexuality begins in childhood, it is important to treat sexuality as a natural part of life from birth onward. Given this perspective, it is much less awkward to have discussions about sexuality when children grow up.
   c. Education: Adolescents should be informed and knowledgeable— with the aid of parents, school, or community resources in the following areas:
      - Basic reproductive anatomy and physiology
      - Basic sexual functioning, including common sexual myths and alternatives to intercourse
      - The health consequences of sexual intercourse
      - The relationship between having sex, using birth control, getting pregnant, and being a parent
      - The similarities and differences between male and female roles
      - The range of human relationships
      - The components of decision making
      - The importance of self-esteem and respecting one's choices
      - Available resources to use to answer concerns, ask questions, or address problems
      - Parents need education in the following areas
        - The similarities and differences between parent and adolescent roles
        - The role of sexuality in adolescent growth and development
        - Basic sexual functioning
        - How differences in values affect decision making
        - The similarities and differences in male and female roles during adolescence
        - The role of self-esteem in parent-adolescent relationships
   d. Do not joke: Adolescents are uncomfortable about sexuality, and joking about the subject only heightens their discomfort.
   e. Admit personal discomfort: Adolescents respect honesty, and this approach will often allow for additional trust between the adolescent and the parent or counselor.
   f. Resources: Be informed about available books, pamphlets, and other resources regarding adolescent sexuality. Some valuable references and organizations are listed at the end of the chapter and in Appendix II to this book.
   g. Privacy: Respect the adolescent's privacy. Although allowing the adolescent to feel comfortable about discussing sexuality, it is important not to pry into details.

2. Community resources
a. Sex education: Schools need to incorporate a curriculum on sex education that, in addition to including facts, stresses concepts of sexual responsibility and sexual decision making.

b. Family-planning clinics: Increased availability of family-planning clinics that serve adolescents is essential.

c. Professional education: It is crucial that physicians and other professionals continue to be educated regarding adolescent sexuality, resultant problems, and helpful resources.

3. Contraceptive technology: Development of a safe, effective, easy-to-use contraception that would complement the adolescent's active lifestyle is needed.

WEB SITES

For Teenagers and Parents


http://www.goasaki.columbia.edu/: Go Ask Alice is a source of general health and sex information maintained by Columbia University health educators. Most questions answered are submitted by high school and college-age people.

http://www.itsyourselfilife.com/: It's Your (Sex) Life is sponsored by the Kaiser Family Foundation. Provides sexual health information to young adults.

http://www.ipswaknow.org/: This Web page is specifically designed for teenagers to find answers to their questions about their bodies, sex, and sexual feelings, and to provide them with "responsible educational information in a relaxed, safe, and fun environment."

http://healthfinder.gov/justforyou/: Just for You: Teens. HealthfinderKIDS. HealthFinder Teens Page has multiple links to government-sponsored information for teens and parents.


http://sxsec.org/: Sex. etc. is a teen-oriented newsletter from Rutgers University's Network for Family Life Education, produced by a teen editorial board with professional supervision. Topics include dating, relationships, sexuality, communication, and sexual health.

www.chebucto.ns.ca/HealthTeenHealth/: Teen Health, Dalhousie University. This site provides information to teens on a wide variety of reproductive health topics including healthy sexuality, sexual orientation, STDS, pregnancy, women's health, men's health, and sexual assault.

www.advocatesforyouth.org/CORNER.HTML/: Teen Scene. Advocates for Youth. Provides a place for youth, particularly those involved in educating others about adolescent reproductive health issues, to connect with each other, share information, and describe experiences.


http://www.familyplanning.org/pages/familyteen.htm/: Teen Talk. The Family Planning Council site includes a newsletter, "Keepin' It Real," which discusses adolescent self-esteem and how it influences sexual behavior. Also has a directory of youth-serving clinics and bibliography of relevant articles on adolescent reproductive health.


For Providers and Professionals


http://www.nutrition.uio.no/ARHNe/: Adolescent Reproductive Health Network is a research network including several ongoing research projects and programs. It consists of 18 partner institutions in southern and eastern Africa, as well as in Europe involved in research and/or implementation of programs that target adolescent reproductive health and risk behaviors.

http://www.rho.org/html/adol_links.htm/: Adolescent Reproductive Health Outlook. The reproductive health Web site produced by the Program for Appropriate Technology in Health is designed for reproductive health program managers and decision makers working in developing countries and low-resource settings.


http://www.advocatesforyouth.org/: Advocates for Youth provides information, training, and advocacy to youth-serving organizations. Advocates for Youth creates programs and promotes policies to help young people make informed and responsible decisions about their sexual and reproductive health.


http://www.engenderhealth.org/: Engender Health works to improve reproductive health services worldwide.

http://www.ceda.org/: Center for Development and Population Activities includes the following programs:


2. http://www.ceda.org/trainprog/popgov.htm/: Partnership Projects for Girls and Young Women, which focuses on community projects conducted by Egyptian nongovernmental organizations to help girls in upper Egypt gain vocational and literacy skills and increase understanding of family life issues.

3. http://www.ceda.org/trainprog/jagah/jagah.html/: Adolescent and Gender Project in sub-Saharan Africa. A multicountry initiative to protect and promote the rights of adolescents to reproductive health information and services, with shared responsibility among young women and young men.

http://www.positive.org/: Coalition for Positive Sexuality.

http://www.socio.com/data_arc/dapgp_0.htm/: The Data Archive on Adolescent Pregnancy and Pregnancy Prevention of the U.S. Office of Population Affairs is a repository for data on teenage sexual behavior including pregnancy, contraception, behavioral factors, and STDS. Data sets from more than 130 studies published since the late 1970s (many of them longitudinal) were selected as being among the best in the field by a national panel of experts. These data sets are briefly described and may be ordered on-line in several different formats.

http://ec.princeton.edu/: Emergency Contraception Web site, a site maintained by the Office of Population Research at Princeton University, provides accurate information based on the medical literature about emergency contraception.

http://www.etr.org/: ETR Associates develops health promotion products and services that emphasize sexuality and health education. They also now have an adolescent pregnancy prevention Web site, called the Resource Center for Adolescent Pregnancy Prevention.

http://www.etr.org/recapp/: Designed to provide health educators and program coordinators with practical tools and research on reducing sexual risk-taking behaviors among teens.

http://www.europeeur.lu.net/: Europeeur: AIDS Peer Education is a collaborative effort of the department of community medicine, Lund University, Sweden and policy makers, professionals, and youth in 14 European Union countries, focused on peer education. The site provides knowledge and guidance about the use of AIDS peer education with young people.

http://www.familycareinr.org/: Family Care International is dedicated to improving women's sexual and reproductive health and rights in developing countries. Site includes publications and working papers, including case studies on adolescent reproductive health in eastern and southern Africa, and information on how to purchase video and text resources.

http://www.jisi.com/irit/seats/: Family Planning Service Expansion and Technical Support Project is a program developing and expanding high quality, client-centered, sustainable family planning and reproductive health services in developing countries and enhancing access to these services. SEATS' Youth Initiative information (www.jisi.com/irit/seats/youth/YOUTH.html) includes descriptions of eastern European and African programs.

http://www.pathfind.org/focus.htm/: FOCUS on Young Adults. FOCUS is a Pathfinder International program in partnership with the Futures Groups International and Tulane University School of Public Health and Tropical Medicine. Its goal is to improve the health and well-being of young adults in developing countries.

http://www.itis.avisosonline.de/indexeng.html/: German Foundation for World Population works in developing countries to address the needs of adolescents by providing reproductive health information and services.


http://www.itsyoursexlife.com/: International Planned Parenthood Federation links family planning associations in more than 150 countries worldwide and provides information to a number of other sites.
REFERENCES AND ADDITIONAL READINGS


Homosexuality is an emotionally charged issue. It is a difficult topic to deal with, not only for the adolescent, but also for his or her family and physician. The health care provider should be equipped to address the concerns of adolescents with a clear homosexual orientation and the fears of others who are questioning their feelings. Practitioners also must be prepared to counsel worried parents as they attempt to understand their child. If the health care provider is unable to accept homosexuality as healthy and normal, he or she should be prepared to refer the adolescent to an appropriate resource. This chapter discusses homosexuality in the context of adolescent health. Important features of counseling homosexual teens and their parents are outlined.

**GENERAL CONSIDERATIONS**

Although there is no absolute definition, homosexuality usually connotes the following:

1. “A persistent pattern of homosexual arousal accompanied by a persistent pattern of absent or weak heterosexual arousal” (Spitzer, 1981).

2. Usually this arousal is experienced in sexual relationships with a person of the same gender.

A bisexual person is attracted to both men and women. Youth may also use the term polyamorous to identify bisexuality. Bisexual people should not be presumed to have concurrent male and female partners or multiple partners.

Sexual orientation refers to a person's attraction to either sex or both sexes. The phrase sexual preference implies choice and should not be used in reference to sexual orientation. Sexual orientation should not be confused with gender identity, which is an individual's innate sense of maleness or femaleness. A transsexual person believes that his or her body does not match the gender with which he or she identifies. A transsexual person identifies as a person of the opposite anatomical sex and sexual orientation is usually heterosexual in relation to that gender. Different from transsexuals, transvestites accept their anatomical sex but derive pleasure (sometimes, but not always erotic) by dressing in the clothing of the opposite sex. Usually, transvestites and transsexuals are heterosexual.

Although coined quite a bit earlier, the word gay has been widely used in reference to homosexual people since the gay rights movement of the 1960s. Today, the term gay usually is applied to male homosexuals but also may include lesbian females and bisexual and transgendered individuals. The abbreviation GLBT (gay, lesbian, bisexual, transgendered) is also used to refer to these populations collectively. Gay always refers to males. Youths who engage in sex with the persons of the same gender usually identify as homosexual or bisexual, but sometimes as heterosexual, curious, or questioning. Some male or female adolescents call themselves queer, and some lesbians use the term dyke, in defiance of the terms' pejorative connotations.

The following tenets can help one understand an adolescent's sexual orientation.

1. The broad spectrum of human sexual orientations has been described as a continuum between absolute heterosexuality and absolute homosexuality. Kinsey et al. (1948a, b) developed a seven-point scale to rate sexual orientation by attractions, psychological reactions, and sexual behavior.

2. Many children and adolescents engage in sexual play with their same-gender friends. This is not necessarily predictive of an adolescent's sexual orientation.

3. Although sexual orientation is thought to be determined before adolescence, its expression may be postponed until early adulthood or indefinitely, making it difficult to determine the actual prevalence of homosexuality during adolescence. Teens may engage in sex with male and female partners as a way of testing their own sexual feelings.

4. Some adolescents who have had involuntary or coercive same-gender sex may experience confusion about their sexual orientation.

5. Some adolescents have sex with the opposite sex to hide their homosexual attractions. In one midwestern school-based survey (Saewyc et al., 1999), bisexual or lesbian girls had a significantly higher rate of reported pregnancy than heterosexual or unsure girls.

**PREVALENCE**

Seen in most mammalian species, homosexuality is thought to be a biologically based, natural phenomenon. However, the organization of homosexual subcultures and the visibility of homosexuality vary among different human societies and change over time.

**Males**

1. Kinsey et al. (1948b) found that 37% of males have had some homosexual experience resulting in orgasm between adolescence and old age. Eight percent of males are more or less exclusively homosexual for at least 3 years between the ages of 16 and 55 years, and 4% of males are exclusively homosexual throughout their lives.

2. Sorenson (1973) found that 17% of 16- to 19-year-old men reported some homosexual activity.

3. The 1970 Kinsey National Opinion Research Center (NORC) survey (Fay et al., 1989) found that at least 20.3% of adult men had sexual contact to orgasm with another male at some time. Roughly 90% of these contacts began before age 19 years.

4. The prevalence of homosexual attractions and behavioral intentions among Minnesota students was found to be 6.4% by 18 years of age, although homosexual
In a recent review of various U.S. studies, Seidman and Rieder (1994) estimated that 2% of men are exclusively homosexual and 3% are bisexual.

Females
1. Older studies of women revealed rates of homosexuality that were about half of comparable figures for males. More recent population-based surveys have found a similar prevalence of homosexual orientation in young men and women. Remafedi et al. (1992) noted that homosexual identification was more common among men, but more women reported homosexual attractions and fantasies.
2. Sell et al. (1995) estimated the prevalence of homosexuality in U.S. females to be 17.8% when behaviors and attractions were combined, similar to estimates in men.

ETIOLOGY AND ACQUISITION OF HOMOSEXUAL IDENTITY

The removal of homosexuality from the American Psychiatric Association's (APA) Diagnostic and Statistical Manual of Mental Disorders (DSM) in 1973 signaled a change in our understanding and counseling of homosexual teens and their parents. There are no data from scientific studies to justify the unequal treatment of homosexual people or their exclusion from any group.

The need for health care provider involvement was stated by the 1983 and 1993 committees of the American Academy of Pediatrics (AAP). The AAP recognizes the physician's responsibility to provide health care for homosexual adolescents and for those young people struggling with issues of sexual expression. In an era in which sexually transmitted diseases (STDs) are among the most significant risks to adolescent morbidity and mortality, it is incumbent on the health care provider to become familiar with issues surrounding the care of homosexual youth. There is a rapidly expanding body of information that should be familiar to adolescent health care providers.

The following sections are brief summaries of the major theories of the development of a homosexual identity.

Genetic Theory
Homosexual behavior at some level of frequency exists in many, if not all, cultures but may not be universally well documented because of cultural taboos (Ford and Beach, 1951). The aggregation of homosexuality within family pedigrees has been consistently noted in studies of twin and nontwin siblings, providing evidence of the etiological role of inherited biological factors. Hamer et al. (1993) found possible evidence of a gene on the X chromosome that is associated with homosexuality in males. Thirty-three of 40 homosexual pairs of siblings were concordant for five markers in the distal region of the X chromosome. The remaining seven were discordant at one or more of these loci. These findings are yet to be replicated.

Hormonal Theory
Theorists have proposed that biological determinants are mediated by hormones that affect central nervous system development. Kolodny et al. (1971, 1972) were leading proponents of the theory that sex hormones determine sexual orientation. Controversy continues regarding the influence of sex steroids and gonadotropins on sexual dimorphism and resultant behavioral sequelae.

Psychoanalytical Theory—Social Factors
Evidence of the biological basis of orientation does not preclude the possibility of environmental influences on its expression. For example, social intolerance can deter individuals from experiencing and expressing feelings toward persons of the same sex.

Combination Biopsychosocial Theories
Understanding of the etiology and acquisition of homosexual identity remains incomplete despite a growing body of scientific research. A number of studies have provided compelling evidence of biological differences between heterosexual and homosexual individuals. What is less well understood is how these biological differences interact with an individual's environment to influence the expression of sexual orientation. Biopsychosocial theory offers a unifying explanation of sexual orientation development. It maintains that sexual orientation is controlled by genes whose effects are mediated by prenatal levels of sex steroids that influence the developing brain and the expression of sexual orientation. Environmental factors may also play a role in shaping the expression of the genetic potential at each stage of development.

Stages of Acquisition of Homosexual Identity
Troiden (1979, 1988) outlined the following four stages in the acquisition of homosexual identity:
1. Stage I: Sensitization. In stage I, the child feels a sense of being different, without understanding the reason for these feelings. This stage usually occurs before puberty. By early adolescence, there may be awareness of a different sexual orientation, including feelings and behaviors that would be considered homosexual.
2. Stage II: Identity confusion. In stage II, the adolescent begins to identify behaviors and feelings that could be considered homosexual. The idea of homosexuality may conflict with the adolescent's previously held self-identity. Perceived social condemnation contributes to this identity confusion. The adolescent may use various defenses, such as denying that the feelings exist or avoiding social situations that could confirm them. Some adolescents seek counseling to repair or “cure” the feelings they are having. Adolescents may experience intense social isolation or feel that there is no one else like them.
3. Stage III: Identity assimilation. In stage III, the homosexual identity is shared with others. This is a part of the process known as “coming out.” Adolescents may reach stage III as teenagers, young adults, or in some cases, not at all. Self-definition may be triggered by media images of homosexuality or romantic fantasies.
4. Stage IV: Commitment. In stage IV, the individual experiences satisfaction, self-acceptance, and an unwillingness to alter sexual identity. A homosexual orientation becomes a part of self-concept, rather than a description of behavior.

During the 1990s, gay and lesbian adolescents generally reported first awareness of same-sex attractions by 10 or 11 years of age, self-identification as homosexual at age 15 to 16 years, and first same-sex experiences near the time of self-identification. There is some evidence that young people are becoming aware of homosexual feelings at progressively younger ages. Girls appear to “come out” later, in the context of a relationship, whereas boys appear to come out at a younger age, in the context of sexual encounters (Remafedi, 1994; D’Augelli, 2000).

Self-identification (median age, 16 years) usually precedes sexual debut with either male or female partners (Remafedi, 1994). Some adolescents, however, may use sexual activity as a means to confirm their attractions. It is important to recognize this risk and counsel adolescents appropriately.

Paroski (1987) evaluated 121 male and female homosexual adolescents regarding their acquisition of homosexual identity. An approximate 18-month process was described:
1. Realization of same-sex desire
2. Guilt and shame for these feelings
3. Attempts to change to heterosexual orientation through altering behavior and fantasy
4. Failure to alter sexual orientation, with the subsequent development of poor self-esteem
5. Investigation into homosexual lifestyle through various methods including sexual activity
6. Acceptance and development of positive homosexual identity
There is strong evidence that gay young men are more likely than heterosexual young men to attempt suicide. Reasons for

Establish a “need to know”: Explain that you will ask personal questions and that an honest response will help you give the best possible care.

Some young people your age have started to have sex. Have you ever had sex before?

Men who have sex with other men (MSM) continue to be at great risk for

During the 1970s and 1980s, there was an epidemic of STDs among homosexual men fueled by unprotected anal sex with multiple partners. Considerable progress

Sexually Transmitted Diseases in Gay Youth

al., 1995). Human papillomavirus (HPV) and

nonuse of screening services. This is an area of ongoing research.

Breast Cancer

The hepatitides, too, are a risk for gay youth. Despite the availability of an effective vaccine against hepatitis B, only 3% of young MSM surveyed in San Francisco

and 50% of new HIV infections among teenage youth (Centers for Disease Control and Prevention [CDC], 1999). Adolescents of color were disproportionately

HIV and Other Sexually Transmitted Diseases and Infections Including the Hepatitides

Men who have sex with other men (MSM) continue to be at great risk for human immunodeficiency virus (HIV) infection. From July 1998 to June 1999, MSM accounted for 39% of cases of acquired immunodeficiency syndrome (AIDS) cases

The hepatitides, too, are a risk for gay youth. Despite the availability of an effective vaccine against hepatitis B, only 3% of young MSM surveyed in San Francisco and Berkeley during 1992–1993 were adequately vaccinated against hepatitis B. Despite having received medical services from one or more health care providers, most of the susceptible individuals (86%) had not been vaccinated (CDC, 1996).

Eating Disorders Gay males reported a significantly higher prevalence of poor body image, frequent dieting, binge eating, or purging than heterosexual males in a population-based survey of Minnesota schools (French et al., 1996).

Health Issues of Special Concern to Men Who Have Sex with Men

HIV and Other Sexually Transmitted Diseases and Infections Including the Hepatitides

Men who have sex with other men (MSM) continue to be at great risk for human immunodeficiency virus (HIV) infection. From July 1998 to June 1999, MSM accounted for 39% of cases of acquired immunodeficiency syndrome (AIDS) cases

The hepatitides, too, are a risk for gay youth. Despite the availability of an effective vaccine against hepatitis B, only 3% of young MSM surveyed in San Francisco and Berkeley during 1992–1993 were adequately vaccinated against hepatitis B. Despite having received medical services from one or more health care providers, most of the susceptible individuals (86%) had not been vaccinated (CDC, 1996).

Eating Disorders Gay males reported a significantly higher prevalence of poor body image, frequent dieting, binge eating, or purging than heterosexual males in a population-based survey of Minnesota schools (French et al., 1996).

Health Issues of Special Concern to Women Who Have Sex with Women

Pregnancy and Parenthood The 1987 Minnesota Adolescent Health Survey revealed that lesbian or bisexual women were equally likely to have had intercourse with men but are more likely than their heterosexual peers to report a pregnancy (12% vs. 5%) (Saewyc et al., 1999). Among sexually experienced adolescents, lesbian or bisexual women also were more likely to have engaged in prostitution during the previous year (9.7% vs. 1.9%).

Breast Cancer The risk of breast cancer and its complications among lesbians may be heightened by nulliparity, delayed pregnancy, alcohol use, obesity, and

nonuse of screening services. This is an area of ongoing research.

Sexually Transmitted Infections Concordance between female sexual partners suggests that bacterial vaginosis is sexually transmitted among lesbians (Berger et al., 1995). Human papillomavirus (HPV) and Trichomonas infections may also be transmitted between women.

Sexually Transmitted Diseases in Gay Youth

During the 1970s and 1980s, there was an epidemic of STDs among homosexual men fueled by unprotected anal sex with multiple partners. Considerable progress has since been made in promoting condom use among adults. However, the adolescent population, particularly youth of color, has not responded to the same degree.

History In evaluating men who have sex with men for medical problems, the practitioner first must elicit correct information about sexual practices. The following approach is recommended:

1. Establish confidentiality: Begin by assuring the adolescent that all information will be kept in confidence (unless the adolescent poses a danger to himself or others).
2. Establish a “need to know”: Explain that you will ask personal questions and that an honest response will help you give the best possible care.
3. Ask questions in a nonjudgmental fashion that maximizes the likelihood of an honest response. Sample questions include the following:
   a. Some young people your age have started to have sex. Have you ever had sex before?
   b. How many sexual partners have you had in your lifetime?
   c. Are these partners men, women, or both?

Recognizing that an adolescent who identifies as homosexual may have sex with partners of the opposite gender, it is important to discuss pregnancy and STD
4. Inquiring about specific sexual practices will help determine the adolescent's risk for STDs and will direct laboratory studies. It also provides an opportunity to provide education regarding prevention of STDs. Specific questions should be directed toward the following:

a. Type of intercourse
   - Penile vaginal
   - Oral anal (receptive or insertive)
   - Anal or vaginal
b. Number of sexual partners
   - Lifetime
   - Last 3 months
c. Multiple sexual partners

d. Use of barrier methods
   - Latex or polyurethane condoms
   - Plastic wrap

e. Prior history of STDs
   - HIV status of adolescent and his or her partners (if known)
g. Symptoms suggestive of STDs

**Documentation**

Documentation of information must be handled carefully. Access to the adolescent's chart by health professionals, allied health care workers, insurance companies, the courts, and parents carries certain legal and ethical ramifications. The health care provider should be a patient advocate, protecting confidentiality. The practitioner also must be aware of state laws governing documentation. With the increasing prevalence of HIV in adolescents and the possible devastating social consequences, practitioners must be very careful when documenting HIV status and HIV risk factors (such as anal sex) in an accessible part of the patient's chart. This issue is discussed more completely in *Chapter 32*.

**Sexually Transmitted Disease Screening**

Not all homosexual adolescents need a full STD evaluation. If the history indicates that the teen either is not sexually active or scrupulously avoids risk, a simple physical examination may suffice. The reliability of the teen's history should be considered. It is important to create a safe environment in which the adolescent feels comfortable disclosing personal information. If a question of veracity exists, it may be wise to offer more frequent follow-up appointments to establish a rapport and create an honest dialogue. The importance of careful history taking cannot be overemphasized. Practitioners might routinely offer STD and HIV testing to high-risk populations such as incarcerated youth, youth in the sex industry, and institutionalized and homeless youth.

Appropriate screening of the sexually active homosexual adolescent with risk factors identified during the sexual history might include the following physical examination and laboratory studies.

**Physical Examination**

Because HIV and STDs are a special concern, focus attention on the examination of skin, lymph nodes, genitourinary (GU), and gastrointestinal (GI) tracts.

**Laboratory Studies**

Recommended for persons engaging in unprotected oral, anal, or vaginal sex.

1. Gonorrhea testing: DNA probe, direct fluorescent antibody (DFA) assay, or culture at the potential site of infection
2. Chlamydia testing: DFA probe, DFA assay, or culture at the potential site of infection
3. Syphilis serology
4. Hepatitis B surface antigen and antibody, if the adolescent has not been previously vaccinated
5. Trichomonas testing: Microscopic examination of centrifuged urine in boys if a screening leukocyte esterase test result is positive. Microscopic examination of a vaginal wet prep diluted with saline in females
6. HPV: Papanicolaou (Pap) smear of the cervix in women. Anal Pap smears in patients who have had penile-anal intercourse have been recommended to detect early cytological changes of rectal carcinoma.
7. HIV counseling and testing: HIV testing should be routinely offered to people who have engaged in unprotected intercourse or used injection drugs. Ask specific, rather than global, questions about risk factors and offer risk-reduction counseling, whether or not the adolescent accepts testing.

**Specific Sexually Transmitted Diseases, Infections, or Conditions**

Gay adolescents are at risk of contracting the same STDs as their heterosexual counterparts. A few specific conditions related to sexual practices that are more common among gay adolescents, such as rectal HPV from penile-anal intercourse or pharyngeal gonorrhea from oral-genital intercourse, are elaborated later in this chapter. Refer to the following chapters for specific information on diagnosis and treatment of STDs:

<table>
<thead>
<tr>
<th>Chapter</th>
<th>Sexually Transmitted Infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>31</td>
<td>Hepatitis</td>
</tr>
<tr>
<td>32</td>
<td>HIV</td>
</tr>
<tr>
<td>61</td>
<td>Gonorrhea</td>
</tr>
<tr>
<td>62</td>
<td>Chlamydia trachomatis</td>
</tr>
<tr>
<td>64</td>
<td>Syphilis</td>
</tr>
<tr>
<td>65</td>
<td>Herpes</td>
</tr>
<tr>
<td>55</td>
<td>Trichomonas</td>
</tr>
</tbody>
</table>

**Anal Disease**

Male or female adolescents who engage in anal intercourse may experience the following:

1. Pain with defecation or rectal bleeding from anal fissures.
2. Proctitis or perianal inflammation from contact dermatitis caused by allergies to latex or the ingredients of lubricants.
3. Pruritus ani caused by the use of oil-based lubricants with blockage of anal pores.
4. Anal papules or ulcers caused by a sexually transmitted infection. Anal warts caused by HPV may be found on the inside and outside of the anus. Painful crops of shallow ulcers may be herpes simplex. A single, painless ulcer may be a manifestation of syphilis.
5. Mucopurulent discharge may be caused by bacterial STDs such as gonorrhea or chlamydia.

Offer testing to all sexually active teens who report intercourse without using condoms consistently. Persistent GI symptoms in adolescents who engage in anal intercourse should prompt a comprehensive history and physical. Diagnostic evaluation may include stool cultures for invasive bacteria and microscopic evaluation for ova and parasites. Cultures for gonorrhea, chlamydia, and herpes should be obtained when proctitis is suggested by rectal discharge, tenesmus, or pain. Also consider anoscopy, anal Pap smear, syphilis, and HIV serologies.

**Anorectal Gonorrhea**

1. Clinical manifestations: In a study of gay men presenting at a Los Angeles clinic for STD evaluation, 66% of infected men were asymptomatic; 2%–5% had clinical proctitis, and 30% had nonspecific symptoms of acute proctitis such as rectal burning, tenesmus, or mucopurulent anal discharge (Holmes, 1980).
2. Differential diagnosis: Inflammatory bowel disease; amebiasis; chlamydial proctitis; contact dermatitis or proctitis (allergic proctitis); giardiasis; lymphogranuloma venereum; syphilis; and chancre.
3. Complications: Abscess formation, strictures, fistulas, and chronic fissures.

Treatment for gonorrhea is outlined in *Chapter 61*. 
Pharyngeal Gonorrhea

1. Prevalence: 3%–5% asymptomatic carrier rate.
2. Clinical manifestations: These range from asymptomatic state with normal-appearing pharynx to exudative pharyngitis.

Treatment for gonorrhea is outlined in Chapter 61.

Syphilis

Before the AIDS era, MSM accounted for approximately 50% of syphilis cases among men. With increased condom use among homosexual men, the proportion of total syphilis cases attributable to heterosexual men has grown. Detecting the primary lesion at the anus, where it may not be seen or felt, can be difficult. Although generally painless, rectal syphilis can cause discomfort or may appear as an atypical lesion with shaggy borders, resembling carcinoma. Routine syphilis screening is recommended for adolescents with multiple sex partners. There is evidence that coinfection with HIV may alter the course of syphilis. Syphilis in HIV-positive individuals might not respond to traditional therapy or might have an accelerated course. Evaluation and treatment for syphilis is outlined in Chapter 64.

Hepatitis

Historically, there has been a higher prevalence of hepatitis B in the gay male community than in the general population. The AAP recommends routine hepatitis B vaccination for all children. Hepatitis A can be transmitted by the fecal-oral route during oral-genital and oral-anal sex. Because of this and potential morbidity among infected adults, the hepatitis A vaccine series is recommended for all MSM. Hepatitis is discussed in more detail in Chapter 31.

Cytomegalovirus

As many as 80% of homosexual males who engage in sex with multiple partners will acquire cytomegalovirus within a year (Mintz et al., 1983). This infection is largely asymptomatic but may lead to a severe mononucleosis-like illness, particularly in the immunosuppressed HIV-positive teen.

Enteric Infections

Teens who engage in unprotected oral or anal sex run a higher risk of contracting various enteric pathogens. Pathogens include but are not limited to Entamoeba histolytica, Giardia lamblia, Shigella, Neisseria gonorrhoeae, Treponema pallidum (syphilis), C. trachomatis, HPV (warts), and herpes simplex virus.

Human Papillomavirus

Condyloma acuminate (venereal warts) can be found on the penis, vagina, or rectal area. Management of internal warts is complicated and should be carried out in consultation with an expert. Treatment for condyloma is outlined in Chapter 66. HPV is the cause of cervical dysplasia, which can be a risk factor for cervical cancer. All sexually active female patients, whether they identify as heterosexual, bisexual, or lesbian, should be screened annually with a Pap smear. Anal Pap smears can also be used to screen for anal condyloma. The benefit of screening for anal carcinoma is an area of ongoing research.

Herpes Simplex

Herpes simplex infections of the penis or rectum can occur. Rectal lesions have a typical appearance of multiple shaggy-bordered erythematous punched-out ulcers that are painful to the touch and may cause a nonspecific proctitis. Lesions on the penis may appear in their early forms as multiple crops of blisters, which then ulcerate and are identical to the rectal lesions. Findings associated with herpes simplex proctitis include fever, difficulty with urination or defecation, sacral paresthesias, inguinal adenopathy, severe anorectal pain, tenesmus, constipation, perianal ulcerations, and the presence of diffuse ulcerations or vesicular or pustular lesions in the distal 5 cm of the rectum. Treatment of herpes simplex is outlined in Chapter 65.

Acquired Immunodeficiency Syndrome

AIDS is discussed in Chapter 32. Although all teens need to be informed about AIDS, it is particularly true of men who have sex with other men. Practitioners should be comfortable with this issue and aware of the ramifications of HIV testing within their geopolitical setting. All sexually active teens should use a barrier method of protection. Practitioners should discuss safer sexual practices with the adolescent, including the following:

1. Abstinence from sex or risky sexual practices such as anal intercourse.
2. Use of condoms or barriers consistently during insertive and receptive oral, anal, and vaginal sex.
3. Importance of latex—not natural lambskin—condoms, because the latter have been shown to be potentially porous. Polyurethane condoms are an acceptable, albeit more expensive, alternative for teens with a sensitivity to latex.
4. Lubricants should be water-based products, rather than oil-based ones that can deteriorate condoms and contribute to pruritus ani.
5. Awareness of the danger of sharing needles: If needles must be used, they should be clean, fresh from a sealed pack, or flushed with household bleach and then water.

Counseling Issues

Given the opportunity to grow up in a supportive environment, most gay and lesbian adolescents are no more likely to experience serious mental health problems than the general adolescent population (Gonsiorek, 1988). Homophobia engenders guilt, shame, and psychological problems.

Counseling the Concerned Questioning Teen

1. The health care provider must first create an open environment in which the teen feels comfortable discussing issues of sexuality. This includes an assurance of confidentiality. Acceptance sets the tone for developing an atmosphere of trust. It is important that health care providers examine their own reactions to homosexuality before interacting with clients. Adolescents’ own internalized homophobia may give rise to a fear that others, including their health care provider, will reject them because of their sexual orientation. Health care providers have an obligation to help questioning teens prevent anxiety and depression and build self-esteem.
2. The teen should be assured that homosexuality is a normal variation of sexual orientation, and that sexual orientation is biologically driven. Discussing this may serve to alleviate guilt. The teen should understand that homosexuality is not about making a wrong “choice,” because choosing one’s orientation is rarely, if ever, an option.
3. Adolescents should be cautioned about individuals and groups who falsely claim to change sexual orientation. Data on the long-term effects of “conversion therapy” are sparse. In a review of outcomes, Haldeman (1991) found that attempts to replace homosexual fantasies with heterosexual ones were unsuccessful among men who had not experienced sexual attraction to women. Such attempts may contribute to guilt, low self-esteem, and psychological problems. The APA removed homosexuality as a behavioral disorder from the DSM in 1973. The position of the APA is that conversion therapy is not useful and may be damaging.
4. Discussing homosexuality with teens will not minimize the adolescent’s concerns regarding sexual orientation. Stating that it’s just a phase may actually intensify the teen’s confusion.
5. Discussing homosexuality with teens will not make them homosexual, in much the same way as discussing suicide will not make them suicidal. As with suicide, discussion of concerns regarding sexual orientation may actually alleviate anxiety.
6. There is no need to have teens define their sexual orientation quickly. Sexual orientation unfolds during adolescence. Assuring them that questions about their sexual orientation will resolve over time may take some of the urgency out of the issue of “am I, or am I not?”
7. Whether or not clients have resolved uncertainty about sexual orientation, helping them prevent the spread of HIV/AIDS infection is of paramount importance. This may be the single most important reason today to inquire about a teen’s sexual practices.

Counseling the Unconcerned Gay, Lesbian, and Bisexual Teens

Not all homosexual teens experience difficulties with their orientation. As with other healthy adolescents, well-adjusted homosexual individuals need sensitive and informed health care services. Some individuals will appreciate the opportunity to discuss their unique experiences or concerns as GLBT youth. Whether or not the adolescent presents specific concerns, pregnancy and STD/HIV prevention should be discussed routinely.

Counseling Concerned Parents

In a study of homosexual adolescents, Telljohann and Price (1993) found that 42% of the females and 30% of the males indicated that their families responded negatively to their sexual orientation. Only about one fourth of the students were able to talk with school counselors about the issue. Fewer than one of five students could identify someone who was supportive. The following are some suggestions for helping families:

1. The health care provider should help parents explore and address their feelings. “Coming out” to parents may elicit a wide range of reactions, including anger, fear, shame, guilt, or grief.
Parents need correct information about homosexuality. The points outlined in the section on counseling the questioning teen may be equally useful in counseling his or her parents. Parents may feel that they did something to cause their child’s homosexuality. Mothers may worry about events that occurred while they were pregnant or they may be concerned about being overbearing or raising, in the case of a male, a “momma’s boy.” Fathers whose boys are questioning their sexual orientation may feel that they did not provide adequate role modeling. The converse is true of parents of lesbian teens. These fears should be put to rest. As this chapter has illustrated, the origins of homosexuality are far from that simple.

Parents should be told that not every emotional problem manifested by a teen is a result of his or her homosexuality. Homosexual teens have the same problems as those of the general adolescent population.

Parents should be encouraged to question society's dichotomous belief that homosexuality is bad and that heterosexuality is good.

Religious beliefs should be explored and appropriate counseling sought if possible. Affirming groups exist in most religions and religious denominations.

AIDS should be discussed with parents, particularly if the teen is a boy. Some parents make automatic connections between homosexuality and AIDS.

Counseling of parents can be supplemented by referring them to parent support groups such as Parents and Friends of Lesbians and Gays (PFLAG). Another useful resource is the National Youth Advocacy Coalition (NYAC), which maintains a directory of local resources. The addresses of both organizations can be found in the “Resources” section of this chapter.

Finally, the most important point to emphasize to concerned parents is that the adolescent who just “came out” is the same teen who sat before them before the disclosure. This adolescent’s main need has been, is, and will always be love and acceptance.

RESOURCES

Federation of Parents and Friends of Lesbians and Gays (PFLAG)
1101 14th Street NW Suite 1030
Washington, DC 20005
202-638-4200
Fax 202-638-0243
http://www.pflag.com/

A national organization of parent support groups organized in local chapters. A good resource of information and reading lists for parents. PFLAG’s focus is advocacy, support, and education.

National Gay and Lesbian Task Force (NGLTF)
2320 17th Street NW
Washington, DC 20009
202-332-0207
http://www.ngltf.org/

An international advocacy group creating programs to help youth make responsible decisions about their sexual health. The Web site is youth oriented and has information forums on school, disabilities, HIV-positive youth, and youth of color.

National Latino/a Lesbian, Gay, Bisexual, and Transgender Organization (LLEG0)
1612 K Street, Suite 500
Washington, DC 20006
http://www.llego.org/

A national organization working for the civil rights of GLBT people. It has an extensive library of public policy summaries available on its Web site.

Bisexual Resource Center (BRC)
P.O. Box 639
Cambridge, MA 02140
617-424-9595
http://www.biresource.org/

An organization providing information, programming, speakers, and a historical archive on bisexuality. The Web site has many links to bisexual resources across the Internet.

Gay and Lesbian National Hotline (GLNH)
888-843-4564
http://www.glhn.org/

An organization providing nationwide toll-free peer-counseling, information, and referrals. The Web site includes a collection of resources arranged by region.

National Youth Advocacy Coalition (NYAC)
1638 R Street NW, Suite 300
Washington, DC 20009
202-319-7596
http://www.nyacyouth.org/

A national network and clearinghouse whose focus is advocacy in public policy. A good contact for up to date information on local resources and support. The Web site has a resource directory organized by region.

BOOKS FOR TEENS, PARENTS, AND HEALTH CARE PROVIDERS

Age 6–12 Years

Harris RH. It's perfectly normal. Cambridge, MA: Candlewick, 1994. (Book about sexuality and growing up with nonjudgmental section on homosexuality. Includes same-sex couples in its illustrations.)


Salat C. Living in secret. New York: Bantam, 1993. (Eleven-year-old Amelia runs away with her mother and her mother’s lover when her father will not let them be together.)

Willhoite M. Daddy's roommate. Boston: Alyson, 1990. (A young boy describes his father's relationship with his roommate, Frank, and his healthy, affectionate relationship with these two men.)

Age 12 Years and Older


Teenage Pregnancy

Lawrence S. Neinstein and Mychelle Farmer

EPIDEMIOLOGY OF ADOLESCENT PREGNANCY

1. Teenage pregnancies: Currently each year in the United States, between 800,000 and 900,000 teens younger than 20 years become pregnant. In 1997 this number was 840,000. The overwhelming majority (about 78%) are unintentional. Among all 15- to 19-year-olds in the United States, about 10% become pregnant each year, and among those who have had intercourse, about 19% become pregnant. Of all births in the United States, about 13% are to adolescents and about 31% of all nonmarital births are to teens (a reduction from 50% in 1970). (Fig. 41.1).

2. Birthrates: After rising 24% from 1987 to 1991, the birthrate for teens age 15–19 years declined for the eighth straight year in 1999, from a high of 62.1 per 1,000 teens in 1991 to a low of 49.6 per 1,000 in 1999 (Moore KA et al., 2001). This is a 20% reduction during this last decade. The level in 1991 was the highest since 1971. The previous peak for teen birthrates was in 1957, at 96.3 births per 1,000 (Table 41.1). During the 1960s and 1970s, however, there was a consistent downward trend in births to teenage girls. The largest decline in the birthrate since 1970 was in women age 18–19 years (28%), compared with 19% of adolescents age 15–17 years. However, the birthrates for all age groups fell.

3. Trends in pregnancy rates: Pregnancy rate data are not as current as information on livebirths, because pregnancy rates are calculated from the rates of livebirths, induced abortions, and fetal losses. The estimated pregnancy rate in 1996 was 98.7 per 1,000 girls age 15–19 years. This is down 15% from the high point of 116.5 per 1,000 girls in 1991. Pregnancy rates for teens have been available since 1976, and the 1996 rate is lower than the rate for any year since 1976 (Ventura et al., 2000).

4. Unintended pregnancies: Approximately 80% of teen pregnancies are unplanned, accounting for about one fourth of all accidental pregnancies annually. One fourth of teenage mothers have a second child within 2 years of their first (Kalmuss and Namerow, 1994).

FIG. 41.1. Teenage pregnancy rates, birthrates, and abortion rates. (From Darroch JE, Singh S. Why is teenage pregnancy declining? The roles of abstinence, sexual activity, and contraceptive use [Occasional report]. New York: Alan Guttmacher Institute, 1999-1, with permission.)

TABLE 41.1. Pregnancies, births, and elective abortions, by year for female adolescent, age 15–19 years and young adults age 20–24 years
5. Abortion rates: About 30% of teen pregnancies end in abortion. In 1996, 274,000 abortions were performed on teenagers. Since 1980, the abortion rates among sexually experienced teens has declined because fewer teens become pregnant and fewer teens choose to have an abortion (AGI, 1999) (Fig. 41.1).  

6. Outcomes: Of teenage pregnancies, approximately 56% end in a livebirth (about two thirds of those are unplanned), 30% in abortion, and 14% in a miscarriage.  

7. The United States continues to have one of the highest rates for teenage pregnancy, abortion, and childbirth among industrialized countries. U.S. teen pregnancy rates are about twice as high as those for England and Wales or Canada, and nine times as high as those for the Netherlands or Japan.  

8. Demographics of teen pregnancy  
   a. Age: Birthrates for teenagers in all age groups have fallen. The birthrate for the youngest teenagers, age 10–14 years, fell to 1.0 per 1,000 in 1998, the lowest level since 1969. The number of births also fell 27%. The birthrate for teens age 15–17 years declined 5% from 1997 to 1998 to 30.4 per 1,000, a record low for this age group (a 21% decrease from 1991 to 1998). The number of births in this age group also dropped to the lowest number since 1987. The birthrate for teens age 18–19 years declined 2% in 1998 to 82.0 per 1,000 (a 13% drop from 1992 to 1998). The number of actual births increased 3%, reflecting the 5% increase in the number of female teens age 18–19 years.  
   b. Ethnicity: Birthrates vary considerably based on the race and ethnicity of the adolescent mother. Birthrates are highest for female Latin adolescents, for whom the 1997 birthrate was 97.4 per 1,000 girls age 15–19 years. This trend was first noted in 1994, when the birthrate for female Latin adolescents began to exceed that of African-American adolescents. Nearly 10% of Latin adolescent girls living in the United States delivered an infant in 1997, whereas 8.8% of African-American adolescents became parents. Only 2.4% of Asian teens and 3.6% of white teens had babies in the same time frame. During 1997, the birthrate for African-American teens was 88 per 1,000 women. Birthrates have dropped sharply for all ethnicities since 1991. Rates in black teenagers have dropped 26%, whereas rates in Hispanic teens have dropped 13% from 1994 to 1998. However, birthrates in both of these groups remain much higher than those in white and Asian female adolescents (Table 41.2).

9. Physical and sexual abuse: Abusive relationships are common features in the lives of adolescent mothers. Nearly half of teen mothers have reported previous sexual abuse or previous coercive sexual experiences (Bayer and Fine, 1992). Another study indicates that 25% of pregnant adolescents give a positive history of abuse in the year before the pregnancy, and 50% of that group will continue to experience abuse during the pregnancy (Kenney et al., 1997; Parker et al., 1994). The high rates of sexual abuse among adolescents who get pregnant suggest that sexual victimization may increase the risk of pregnancy.  

10. Economic concerns: Adolescents who live in poverty face many obstacles that may increase their risk of an unintended pregnancy. In many respects, it is part of

---

**TABLE 41.2. Number of births to women younger than 20 years by age and race, 1998 and birth rates 1991–1998 and percent change 1991–1998**

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>65.4</td>
<td>61.5</td>
<td>-5.3%</td>
</tr>
<tr>
<td>Black</td>
<td>72.7</td>
<td>63.7</td>
<td>-11.6%</td>
</tr>
<tr>
<td>Hispanic</td>
<td>59.1</td>
<td>56.7</td>
<td>-4.0%</td>
</tr>
<tr>
<td>Asian</td>
<td>64.6</td>
<td>59.1</td>
<td>-8.5%</td>
</tr>
</tbody>
</table>

---

**TABLE 41.3. Reported sexual activity by age and race**

Although 58% of sexually active adolescents report that a condom was used during their last intercourse, a significant number of adolescents are at high risk for pregnancy. Female students in the 9th grade are more likely to use condoms than female students in the 12th grade (63.1% and 41.1%, respectively). Thirty-one percent of 12th-grade females report using birth control pills, compared with 12.8% of those in the 9th grade (Kann et al., 2000). This suggests that the most effective pregnancy prevention strategies are implemented by older adolescents. Nevertheless, consistency of contraceptive use is required to truly reduce one’s risk of an unintended pregnancy.

2. Physical and sexual abuse: Abusive relationships are common features in the lives of adolescent mothers. Nearly half of teen mothers have reported previous sexual abuse or previous coercive sexual experiences (Bayer and Fine, 1992). Another study indicates that 25% of pregnant adolescents give a positive history of abuse in the year before the pregnancy, and 50% of that group will continue to experience abuse during the pregnancy (Kenney et al., 1997; Parker et al., 1994). The high rates of sexual abuse among adolescents who get pregnant suggest that sexual victimization may increase the risk of pregnancy.

3. Economic concerns: Adolescents who live in poverty face many obstacles that may increase their risk of an unintended pregnancy. In many respects, it is part of

---

**FACTORS CONTRIBUTING TO ADOLESCENT PREGNANCY**

Although many factors are associated with adolescent pregnancy, those that clearly contribute to adolescent pregnancy are as follows:

- High rates of sexual activity
- Abuse, either sexual or physical, and violence in the home
- Living in poverty
- Cultural values that favor parenting during adolescence
- Psychological and behavioral factors

1. High rates of sexual activity: One half of all adolescents attending U.S. high schools have had sex. One third of high school students had sex in the last 3 months, which suggests that a significant proportion of teens are currently having intercourse. Data from the youth risk behavioral surveys indicate that 8.3% of teens initiate sex before their 13th birthday. African-American teens have the highest rates of early sexual activity, followed by Latin and white teens (Table 41.4).
a cycle in which the heads of these households have few job skills, little education, and decreased access to medical services. Adolescents raised in poor families may have poor academic achievement and low self-esteem. In this setting, they are more likely to have unprotected sex and conceive (Manlove et al., 2000).

4. Cultural values: Early initiation of sexual activity is not unusual if other family members have a prior history of becoming pregnant during adolescence (Furstenberg et al., 1987a,b). In this regard, many adolescents live in communities familiar with adolescent parenthood, so they are less likely to view sexual intercourse as a risky behavior. Adolescents who live in families with little parental support, little restriction of risky behaviors, and poorly defined goals are more likely to become sexually active and are more likely to become adolescent parents. Other cultural factors that may play a role in an adolescent's decision to become pregnant include peer pressure, early dating, and lack of religious affiliation.

5. Although psychological factors, such as depression, may have some influence on an adolescent's decision to become pregnant, the role of psychological and behavioral antecedents is unclear. Other risky behaviors may be associated with sexual activity. In fact, the youth risk behavioral survey (YRBS) revealed that overall 24.5% of adolescents used alcohol or drugs when having sex.

Other factors that have contributed to teenage pregnancy include the following:

1. Early puberty: Since the turn of the century, the average age at onset of menarche has decreased approximately 3 months per decade (Stevens-Simon, 1992), from about 16–17 years in the late 19th century to 12.4 years at present (Jaskiewicz and McAnarney, 1994). This earlier physiological maturation has widened the gap between reproductive capacity and cognitive and emotional maturation and has increased the risk of unintended pregnancy in this age group.

2. Developmental issues: Many developmental characteristics of adolescents, particularly of younger teens, interfere with decision making regarding sexual activity and the successful use of contraceptives. These include a limited ability to plan for the future or to foresee the consequences of their actions and a sense of personal invulnerability.

3. Barriers to contraceptive use: Many environmental, social, and psychological barriers interfere with decision making regarding sexual activity and contraception among teens. Significant obstacles to successful contraception include the following:
   a. Inaccurate information: Many teens have misinformation regarding conception and reproduction. Among other myths, many mistakenly believe that they are too young to become pregnant or that pregnancy cannot occur the first time they have intercourse.
   b. Accessibility: Many young people want to prevent pregnancy but may have difficulty obtaining contraceptives. They may lack information regarding available methods. They may not know where to obtain contraceptives. They may have concerns regarding confidentiality. They may have concerns regarding cost. Services are often not offered at times that meet the needs of young people. They may lack transportation to services.
   c. Contraceptive acceptability: Teens may seek out contraceptive services but are often fearful of specific methods and perceived side effects (particularly the possibility of cancer and weight gain) they assume to be connected with oral contraceptives.
   d. Provider issues: Many young people are interested in contraception but are often unable to discuss contraception with their partners or their partners refuse to use available methods.
   e. Intended pregnancy: Some young women do not protect themselves from pregnancy because of a desire to have a baby. This desire may emerge from a need to:
      a. Solidify their relationship with their partner or please their partner
      b. Have someone to love and take care of
      c. Change their status in their family or assert their independence
      d. Rebel against their family
      e. Escape from an abusive home environment by cementing a relationship with another family or by creating their own new family
      f. Establish their fertility

4. Provider problems: Acquiring contraceptive services can be difficult for young people because
   a. Physicians may not address sexuality and contraceptive use with their adolescent patients, who may be too embarrassed to initiate the discussion themselves.
   b. Some providers are unwilling to prescribe contraceptives for their patients without parental knowledge or consent.
   c. Some providers are overtly judgmental about sexual activity among their young patients, which discourages disclosure and discussion of sexual involvement and prohibits the dispensing of appropriate education and birth control methods.

EVALUATION AND MANAGEMENT OF THE PREGNANT ADOLESCENT

When an adolescent presents to a health care facility for reproductive health services or advice, it is important to provide an environment that is welcoming and comfortable. The providers in such facilities must be comfortable with adolescents, and they should be familiar with the common presentations and the initial management of adolescent pregnancy.

Role of the Practitioner

Pregnancy in an adolescent can be a crisis for the teen and her family. The provider is in a unique position to offer guidance and support during this time. This health issue requires the provider to give balanced attention to the pregnant adolescent's medical matters and her counseling needs. In addition, the adolescent's family and her health-care team will need to be considered as a plan is formulated to manage the pregnancy. Opportunities for intervention include the following:

1. Diagnosis of pregnancy and facilitated decision making
2. Open, nonjudgmental service planning
3. Management of pregnancy, if the teen chooses to continue the pregnancy
4. Preparation for parenthood, if the teen chooses to raise the child
5. Referrals for subspecialty services, as needed
6. Family planning and safe-sex education

Open, nonjudgmental service planning is critical as the adolescent and her family begin to address their many needs. Despite a provider's personal preferences, the provider needs to be able to counsel the adolescent about her options. Appropriate referrals should be made for adolescents needing services that are not available within the provider's own health program. Timely referrals are important, because some of the choices are only available during the early weeks of the pregnancy.

Common Presentations of Pregnancy in Adolescents

Adolescents may present with various complaints that may suggest early pregnancy. The most frequent objective concern is a missed or an abnormal menstrual period. Others may report abdominal pain, fatigue, breast tenderness, or appetite changes. Adolescents presenting with such concerns should be questioned about sexual activity, contraceptive use, and desire for a pregnancy test. Adolescents may need additional time to discuss their concerns and any fears that they may have about a possible pregnancy. An open and flexible environment help let them make good decisions during this early phase of assessment.

Pregnancy Tests

The development of very sensitive and specific pregnancy tests has significantly facilitated the diagnosis of early pregnancy. Pregnancy tests measure levels of human chorionic gonadotropin (HCG), a glycoprotein that is secreted by the trophoblast after implantation. The most sensitive pregnancy test is a radioimmunoassay (RIA) that detects serum levels of the beta subunit of hCG as low as 7 mIU/mL. Most urine pregnancy tests will detect HCG when levels exceed 25 mIU/mL, thus giving a positive test result during the first week after fertilization. The ease of use, low cost, and high degree of accuracy make the urine pregnancy test an essential...
1. hCG levels during pregnancy: It is important for the practitioner to remember that hCG levels change significantly during the course of pregnancy and that the results must be interpreted based on the particular test used (sensitivity and specificity). hCG can be detected in a woman’s serum at low levels as early as 7–9 days after ovulation/conception, very soon after implantation. During the first 3–4 weeks after fertilization, hCG levels in a normal intrauterine pregnancy double about every 2 days, so levels should reach 50–250 mIU/mL by the time of the first missed menstrual cycle. The peak is reached about 60–70 days after fertilization, and then the levels dramatically decrease until about 20 weeks, at which time they level off.
   a. Abnormally elevated levels can indicate either a multiple-gestation pregnancy or a molar pregnancy.
   b. Abnormally low levels can indicate a spontaneous abortion or ectopic pregnancy. Low levels may also indicate that the woman is earlier in her pregnancy than thought.

2. hCG levels after pregnancy: Levels gradually decrease after a delivery or abortion and the initial decrease is quite rapid. After 2 weeks, the hCG level should be <1% of the level when the pregnancy was terminated.
   a. Term delivery: Levels should drop to <50 mIU/mL by 2 weeks—undetectable by 3–4 weeks.
   b. First-trimester abortion: Initial hCG levels are much higher, so if the abortion is at 8–10 weeks and initial hCG levels are more than 150,000 mIU, then levels at 2 weeks can be 1,500 mIU/mL and detectable for 8–9 weeks.

3. Types of pregnancy kits
   a. Immunometric tests: These tests are based on enzyme-linked immunosorbent assay (ELISA) techniques and are based on identifying two different antibodies for hCG, so these tests are specific for the beta subunit of hCG. There is no cross-reactivity with other hormones. The kits usually provide accurate quantitative response, with hCG levels as low as 5–50 mIU/mL. This can provide positive test results as soon as 3–4 days after implantation (10 days after fertilization). These tests will give a positive result during the first week after implantation in 98% of pregnant women (Hatcher, 1998). These are the most common tests used in most family planning, teen clinics, and women’s health clinics. Examples of such tests include Clinistrip, Combo card, Double-Check, OSM hCG, Icon II hCG Hybritech, QuickVue, Signify, SureStep hCG, and Testpack plus hCG.
   b. Agglutination inhibition slide tests: These inexpensive tests have been used for the past 20 years and are based on the binding of hCG with an anti-hCG antibody in the test solution. However, because the antibodies used in these tests are not specific for the beta subunit of hCG, cross-reactivity is possible, so the test sensitivity is set higher to avoid more false-positive results. These test results are more likely positive after the 6th week of gestation. Immunometric tests are preferred to make the diagnosis, particularly in early pregnancies or with potentially abnormal pregnancies.
   c. Home pregnancy testing: Home pregnancy tests are popular because they are convenient, quick, and very confidential. Seventeen percent of college women report that they have used a home test at least once. The actual accuracy of home tests is not ideal. Several studies have found that as many as 10% of samples may not agree with standard laboratory testing. Problems with technique and following instructions may cause inaccurate results. A common error is to perform the home test too early. It is best not to base clinical decisions on the result of a home pregnancy test.
   d. Quantitative b-hCG RAI: This is a highly sensitive test for specific levels of hCG. However, it has no advantage over the immunometric urine tests for the regular clinical setting. The test is expensive. The major use is in helping to identify an abnormal pregnancy by checking either the doubling time of hCG or the disappearance over time.

4. False-positive and false-negative results
   a. False-negative results are rare with immunometric tests but can occur if the test is performed incorrectly, improperly labeled, reported in error, or in the case of a color change, if the reader has red-green color blindness. Occasionally elevated lipids, immunoglobulin levels, and low serum protein levels can interfere with the test. False-negative results are much more common with agglutination inhibition tests.
   b. False-positive test results with immunometric tests are very rare but can also occur with laboratory error. Agglutination inhibition tests can lead to false-positive results because of protein or blood in a urine specimen. Very rarely, pregnancy test results are positive from hCG production from a nonpregnancy source such as tumors of the ovaries, breast, and pancreas. For this reason, clinical correlation with the laboratory finding is essential. Should the laboratory result be inconsistent with the clinical presentation, it is imperative that the provider repeat the pregnancy test, using the more sensitive tests available, to verify the pregnancy test result.

Physical Examination
The physical examination is also an essential element of the evaluation of the pregnant adolescent. Although the pregnancy test will determine whether the adolescent is pregnant, the pelvic examination will help determine the gestational age of the fetus, and it will identify any problems that may require immediate attention.

1. Uterine enlargement: Uterine enlargement usually indicates the following
   a. 8 weeks of gestation: Uterine enlargement detected
   b. 12 weeks of gestation: Uterus palpated at symphysis pubis
   c. 20 weeks of gestation: Fundal height at umbilicus. At this point in the pregnancy, fetal movements should be detected, and fetal heart sounds should be audible by Doppler study.

2. Other signs
   a. Softening of the cervix
   b. Discoloration of the cervix (it may appear purple or hyperemic)
   c. Uterine softness

Should vaginal bleeding be present or abdominal pain be elicited, it suggests pregnancy complications, such as a threatened abortion or an ectopic pregnancy.

Ascertaining the Gestational Age
Most adolescents will be curious about the pregnancy, and they will want to know the gestational age of the fetus. Providers should be careful to determine the last normal menstrual period (LMP). This can be accomplished by asking careful questions of the adolescent regarding their cycles. Those having regular cycles lasting approximately 28 days are best able to predict the gestational age, which is calculated by counting the weeks since the LMP.

The expected date of delivery (also called the expected date of confinement) is estimated using the Naegle rule. The formula requires one to add 7 days to the first day of the LMP, subtract 3 months from the month of the LMP, and add 1 year to the calculated date. Physical findings can also be used to estimate gestational age as indicated earlier. An ultrasound will also predict gestational age, although this test has a margin of error of 1 week.

If the uterus is smaller than expected by menstrual dates, considerations include the following: Error in pregnancy test

If the uterus is larger than expected, considerations include the following:

Twins
Uterine fibroids
Uterine anomaly
Hydaldiform mole
Fertilization occurred earlier than dates suggested

ALTERNATIVES FOR PREGNANT ADOLESCENTS AND PREGNANCY COUNSELING

Counseling the pregnant adolescent about her pregnancy options is perhaps the most important aspect of early pregnancy management. Adolescents need information regarding their options, and they need to be encouraged to seek gynecological or obstetrical care as soon as possible. Providers who offer pregnancy tests should be prepared to provide such counseling. They should also be able to perform a pelvic examination, to confirm gestational age of the fetus and to
Critical elements of counseling the pregnant adolescent can begin while waiting for the results of the pregnancy test. Areas to address include the following:

1. An assessment of the adolescent's expectations and desires regarding the possible pregnancy. It is important to initiate this discussion in a private setting, when the provider is alone with the adolescent patient. Some adolescents are very anxious and emotional, whereas others are calm and have begun to formulate a plan for a possible pregnancy. A preliminary assessment of any stressors will be useful while counseling the adolescent about her test results. A private discussion allows the provider to offer counseling without distractions, and it permits the provider to consider the adolescent independent of others who are involved in the pregnancy (Committee on Adolescence, 1998).

2. Support of the partner or concerned adult. The adolescent may be accompanied by a sex partner or by a concerned adult. In such instances, a provider should offer the patient the choice of including this person in a portion of the pregnancy counseling session. If the pregnancy test result is positive, adolescents should be encouraged to seek the support of elders (e.g., parents, grandparents, or other trusted adult). These adults will likely form a “core of support” for the adolescent, should she elect to carry the pregnancy to term or decide to terminate the pregnancy. The sex partner with whom the adolescent is involved may also share in the decision-making process, unless there is concern that including the sex partner will endanger the safety or well-being of the adolescent.

3. Confidentiality: Adolescents are entitled to confidentiality, although those who accompany the adolescent for this medical visit are probably aware that a pregnancy test will be requested. Adolescents should be reminded that any discussions in a health facility remain confidential, unless the adolescent wishes to inform or include others. This allows the provider to make choices of her own regarding disclosure of the pregnancy. Occasionally, there are mental health concerns, such as the threat of suicide or homicide, or there is a threat of abuse, because an adolescent is pregnant. In such cases, it will be necessary to share information about the pregnancy with other health professionals and with the adolescent's adult caregivers (parents or guardians).

4. Nonjudgmental approach: The provider needs to provide the opportunity for open discussion when counseling an adolescent about a positive pregnancy test result. The provider should allow the adolescent to express her wishes for this pregnancy, without imposing the provider's personal values on the teenager. A provider who is nonjudgmental will enhance the adolescent's ability to identify the pregnancy option that is most appropriate for the adolescent. This provider needs to be able to advocate for the adolescent's choice, and appropriate referrals should be available from the provider that will assist the adolescent in achieving her desired pregnancy outcome.

5. Presenting options: The adolescent needs to consider many options for this pregnancy, which include the following:
   a. Carrying the pregnancy to term and assuming parental responsibility
   b. Family-centered care for the adolescent and her new baby, thereby sharing child-care responsibility among the baby's extended family
   c. Placing the baby with adoptive parents after the baby is born
   d. Terminating the pregnancy (e.g., induced abortion)

Adolescents Assuming Parental Responsibility

This is the most common outcome for pregnant adolescents, yet it is, in many respects, the most difficult commitment to fulfill, because it requires the adolescent to assume long-term responsibility for a baby. A comprehensive care program that is designed to address the health and social needs of pregnant adolescents will offer the adolescent the best opportunity for a good outcome. Essential elements for adolescent-focused prenatal programs include a complement of medical, psychological, social, and educational services; staff knowledgeable in adolescent health; services that are culturally sensitive; continuity of care through the postpartum period; and linkages to mother- and infant-care programs.

Family-centered Care for the Adolescent and the Newborn

Because adolescents are rarely able to assume independence after the birth of a baby, the adolescent's family (or community) will usually offer support to the young mother and her child. This allows the adolescent more flexibility and more options for personal development; however, it requires that she abdicate a significant amount of parental responsibility to other family members. Arrangements are unpredictable but may provide (financial and social) stability for the adolescent and the baby. Providers who care for the adolescent parents will need to be linked to community-based services for extended families. Specialized adolescent health services are an essential component of these health programs that reach out to adolescent parents. Such programs offer counseling, health awareness, and parenting classes, in addition to medical care and family planning.

Adoption after Delivery

Most adolescents who continue their pregnancy intend to raise their baby, although few will express an interest in placing their child in a home with adoptive parents. Few adolescents consider this option at the time that the pregnancy test is obtained, although it is important that the pregnant adolescent be counseled about this option. In most states and the District of Columbia, mothers who are minors may legally place their child for adoption without parental involvement. From 2% to 3% of teen pregnancies that end in delivery involve the mother making an adoption plan. Less than 10% of the babies born to unmarried teens are placed in adoptive homes. Correlations with unmarried teen mothers who place their children for adoption are more likely to be white, have higher socioeconomic status and educational aspirations, and be from suburban residences (Mosher and Bachrach, 1996).

Terminating the Pregnancy

Adolescents who are pregnant often indicate that the pregnancy is unintended. Sexual exploration and intercourse are commonplace in adolescence, yet a pregnancy and its long-term consequences are rarely anticipated. Data from the National Institute of Family Growth reveal that about 5% of first trimester abortions are having the baby planned. The number of abortions in 15- to 19-year-olds fell from 351,000 in 1990 to 264,000 in 1996. Nearly 80% of the 806,000 adolescent pregnancies are unintended. Approximately 43% of these unintended pregnancies were terminated by an abortion (Henshaw, 1998). This represents a 24% decline in the abortion rate for 15- to 19-year-olds.

All adolescents who are pregnant should be aware that pregnancy is an option that is available to them. There are many possible explanations for this trend, such as a decline in the availability and accessibility of abortions nationwide. Although abortions are commonly performed in the United States, it is a service that is frequently offered in free-standing clinics that are separate from the more traditional, primary health care programs. Thus, a referral to another facility is generally required for this procedure. Some adolescents lack the skills to negotiate health services in a health facility that is new to them. This may result in a delay in obtaining an abortion, or the adolescent may fail to get the abortion because she is not timely with her preparations (Cates et al., 2000). Such experiences can be very stressful for the adolescent.

Providers of patients who seek an abortion should be aware that careful follow-up and psychological support is needed while the adolescent explores this option. Providers need to be open minded and respectful of the adolescent's wishes in such circumstances. Adolescents will also need the support of loved ones who are familiar with the adolescent, such as a parent, an older sibling, or other adult relative. Sixty-one percent of minors who have abortions do so with at least one parent having knowledge of the abortion. Forty-five percent of parents are notified by their daughter. Most parents appear to support their daughter's decision to have an abortion (Henshaw and Kost, 1992).

Health care providers should be aware of their state's laws governing adolescents who seek abortion services. Many states require that parents of adolescents play an active role in abortion decisions. Careful attention to the legal considerations, including the rights of parents, will be important as the provider advocates for the adolescent. Any financial barriers that may interfere with the adolescent's ability to obtain the abortion should also be reviewed. If possible, the provider may need to refer the patient to an additional source for financial assistance (Committee on Adolescence, 1998).

Adolescents who are certain about their decision to terminate the pregnancy should be encouraged to do so in the early stages of the pregnancy. This will minimize both the complications and the costs of the procedure. Most induced abortions are performed within eight weeks of conception, although some adolescents delay these procedures until the second trimester. These delays will increase the cost, both financial and psychological, for the adolescent and her family.

After a teen has decided to end her pregnancy, she may need help in selecting the best method. There are more options for those who have earlier terminations. Methods in the first 12 weeks include vacuum aspiration, curettage, and medical terminations with either methotrexitate-misoprostol or mifepristone-misoprostol. Between 12 and 24 weeks, methods include dilation and evacuation, misoprostol, amniocinusion, and uterotonici/hypertonic techniques. Most teens have a first-trimester abortion and decide between a medical or surgical method.
Choice of Medical versus Surgical Early Abortion Methods

Medical Method

Advantages to using the medical method are that it avoids surgery and anesthesia, is less painful, may be easier emotionally, provides the girl with more control and involvement, is a more private process, and has less risk of infection.

Disadvantages include bleeding, cramping and nausea, more waiting and uncertainty, extra clinic visit, can only be used for pregnancies up to 7 to 9 weeks, and methotrexate can cause birth defects if abortion is incomplete.

Surgical Method

Advantages to using the surgical method are as follows: quicker (one visit); more certain; teen can be less involved; can be done under general anesthesia; and continuation of pregnancy is rare.

Disadvantages include invasiveness (need for local or general anesthesia) and small risk of uterine or cervical injury or infection.

Types of Surgical Methods In the United States, surgical methods are the most common method of termination of pregnancy.

1. Vacuum aspiration
   a. The most widely used and standard first-trimester surgical abortion method
   b. Relatively simple technique requiring small cervical dilation
   c. May be performed with local anesthesia
   d. Can be done in an office through 14 weeks’ gestation.
2. Dilation and evacuation
   a. Most common second-trimester method of abortion.
   b. Requires more dilation than the aspiration method. Laminaria or other osmotic dilators are often inserted before the procedure to gradually dilate the cervix. This may be a 1- to 2-day procedure.
   c. Is commonly used for procedures between 13 and 16 weeks, although many clinicians use this procedure up through 20-plus weeks.
   d. Paracervical or general anesthesia is used before evacuating the uterus.

Types of Medical Methods In the past several years, new medical methods have been developed for early abortions.

First Trimester

Two new methods in United States include (a) mifepristone (RU-486) with misoprostol or (b) methotrexate with misoprostol.

1. Mifepristone-misoprostol: Mifepristone is a progesterone antagonist that is an effective abortifacient. The efficacy increases with the addition of a prostaglandin analogue such as misoprostol. The earlier in pregnancy that these are used, the higher the efficacy. In women with pregnancies <7 weeks, about 95% have a complete abortion. This decreases to about 80% in the ninth week. Bleeding and cramping are common with the method, because the drugs’ actions are to induce uterine cramping and bleeding. The technique involves at least three visits.
   First visit: Mifepristone 600 mg
   Two days later: Misoprostol dose. Some abortions are complete before this visit. If not, two 200-µg tablets are given orally. In those who have not aborted, two thirds occur within 4 hours of the prostaglandin administration.
   2. Two weeks later: Checkup to ensure completed abortion.

   Complications include incomplete abortion and heavy bleeding.

2. Methotrexate and misoprostol methotrexate is a cytotoxic drug that is lethal to trophoblastic tissue and is an abortive agent. When used with misoprostol, the combination is about 95% successful in terminating early pregnancies. These regimens involve off-label use of the drug. Several protocols have been developed and all involve at least two clinic visits. Similar to the mifepristone technique, the first visit involves administration of methotrexate. The misoprostol is sometimes given for self-administration at home or at a return visit. There is then a follow-up visit to confirm the termination of pregnancy. Complications include incomplete abortion and heavy bleeding.

   Any clinic or clinician contemplating medical terminations of pregnancy must have availability of both ultrasound dating of pregnancies and surgical backup for incomplete abortions.

Second Trimester

Medical techniques for second-trimester abortions include the following:

- Hypertonic saline instillation
- Hypertonic urea instillation
- Prostaglandin E2 suppository

These techniques combined account for less than 1% of all abortions in the United States. Most have been replaced by dilation and evacuation procedures, which are faster, safer, and less expensive.

Abortion Risks and Complications

Short-term

1. Infection (up to 3%): This can be minimized by preprocedure diagnosis and treatment of gonorrhea, chlamydia, and cervicitis, as well as by the use of prophylactic antibiotics. Infection due to retained products of conception requires antibiotic treatment and an additional procedure.
2. Intracervical blood clots (<1%).
3. Cervical or uterine trauma: Women younger than 17 years have an increased risk of cervical injury. Use of laminaria and skillful technique lowers the risk considerably.
4. Bleeding (0.03%–1%).
5. Failed abortion (0.5%–1%).

The mortality rate is less than 1 per 100,000 abortions.

Long-term Postabortion Complications

Medical Data relating to long-term complications of abortion do not show major risks from the most common methods. First-trimester abortion with vacuum aspiration does not appear to affect fertility rates or cause future spontaneous abortions.
MEDICAL MANAGEMENT OF THE PREGNANT ADOLESCENT

Providers will need to review the adolescent's medical history, if the adolescent is not well known to the provider. Many adolescents have underlying medical problems that may affect the outcome of the pregnancy. Other problems may not affect the pregnancy but they may adversely affect the adolescent's ability to parent a newborn infant. These issues should be identified as quickly as possible, even if they do not have to be discussed at length during the pregnancy counseling session (Committee on Adolescence, 1998).

Pregnant adolescents, because of increased maternal and fetal risks, require special prenatal management. Practitioners should note that young women are at risk for inadequate care, so they should make special efforts to ensure early linkages with prenatal providers. Pregnant teenagers are twice as likely, when compared with all pregnant women, to receive no prenatal care or care initiated only at the third trimester. Approximately 4% of teenagers receive either no care or only third-trimester care. Following is a brief guide for the practitioner in important areas of prenatal care for the adolescent patient.

1. Initial evaluation: Should include a thorough history, including both a family history of chronic illness and a personal medical history. A drug history, particularly for tobacco, alcohol, and illicit substances, is important. A thorough and sensitive discussion regarding the pregnant teen's and her partner's risk for human immunodeficiency virus (HIV) infection should be initiated. Due to young people's reluctance to disclose sensitive information during an initial visit, practitioners should continue to assess a teen's risk status throughout her pregnancy. A complete physical examination and pelvic examination should be performed.

   Laboratory evaluation should include the following:
   a. Complete blood cell count
   b. Urinalysis
   c. Blood type and group
   d. Screening syphilis serology (Venereal Disease Research Laboratories test)
   e. Sickle cell test in black patients
   f. Test for Tay-Sachs disease for patients of Mediterranean or Jewish heritage
   g. Rubella titer
   h. Pap smear
   i. Gonococcal culture
   j. Chlamydia test
   k. Hepatitis B serology
   l. HIV antibody counseling and testing

2. Topics to be covered on successive visits
   a. Physiology of pregnancy
   b. Maternal nutrition
   c. Substance abuse
   d. STDs and HIV infection
   e. Discussion and referral to a prepared childbirth class
   f. Childbirth
   g. Breast feeding and infant nutrition
   h. Infant care and infant development
   i. Contraception and sexuality
   j. Postdelivery care needs

3. Nutrition
   a. Ideal weight gain should be 25–40 pounds.
   b. See Chapter 6 for specific changes in daily requirements for pregnancy.
   c. The teen should be advised against dieting during pregnancy.
   d. A prenatal vitamin supplement should be prescribed.
   e. Additional iron is required if iron deficiency is diagnosed.

4. Prenatal visits: Pregnant adolescents should have routine visits every 2–4 weeks, through the 7th month. Visits are every 2 weeks in the 3rd month, and weekly thereafter.

5. Psychological aspects: It is essential to consider that the pregnant teenager's acceptance of the pregnancy and her relationship with her parents or the father of the child may change during the course of the pregnancy. It is important to monitor the teen's psychological needs and to intervene appropriately.

6. Substance abuse: Due to the serious consequences of substance use for both mother and infant, a thorough assessment of drug use history and current practices is necessary at pregnancy diagnosis and throughout the prenatal period. Although pregnancy substance use is high in adolescents, particularly among minority youth, one large epidemiological study found that adolescents were more likely than adult women to stop alcohol and drug use once pregnancy was confirmed. Studies suggest that adolescents also decrease substance use postpartum (Hall et al., 1993; Richardson, 1999). The following is a list of common substances and their effects during pregnancy.
   a. Alcohol: Fetal alcohol syndrome including prenatal and postnatal growth retardation; facial dysmorphogenesis (microcephaly, short palpebral fissures, cleft palate, and micrognathia); abnormalities of the central nervous system (CNS) including mental retardation; and increased risk of cardiac defects, joint abnormalities, hepatic fibrosis, and learning difficulties
   b. Amphetamines: May cause malformations
   c. Cocaine: Increased risk of spontaneous abortion and premature delivery; neurobehavioral deficits in the newborn; increased prevalence of abruptio placentae; increased risk of genitourinary tract defects including prune belly syndrome, hypospadias, and hydrenephrosis; increased reports of other congenital defects
   d. Heroin: Intrauterine growth retardation; neonatal abstinence syndrome; increased risk of hepatitis, HIV, and other infections in the mother
   e. Lysergic acid diethylamide: Increased risk of congenital abnormalities including hydrocephalus, spina bifida, and myelomeningocele
   f. Marijuana: Potentially mutagenic; questionable increased risk of birth defects
   g. Nicotine: Impaired growth; increased risk of spontaneous abortion

7. Medications and pregnancy: Medication should be avoided when possible during pregnancy. The following is a list of commonly used drugs and their effects during pregnancy.
   a. Adrenocortical steroids: Low incidence of cleft palate suspected
   b. Amphetamines: May cause malformations
   c. Angiotensin-converting enzyme inhibitors: Prolonged renal failure in neonates, decreased skull ossification, renal tubular dysgenesis
   d. Anticholinergic drugs: Neonatal meconium ileus
   e. Antacids: May cause malformations; avoid in early pregnancy
   f. Antibiotics
      • Acyclovir: Safety not established; use only under strong indications
      • Aminoglycosides: Possible eighth nerve toxicity in fetus
      • Cephalosporins: Probably safe
      • Clindamycin: None known; caution advised
      • Erythromycin: Considered safe
      • Erythromycin estolate: Risk of cholestatic hepatitis in mother; avoid during pregnancy
      • Isoniazid: Embryotoxic in animals; caution advised
      • Metronidazole: May affect chromosomes; avoid during pregnancy if possible, particularly in first trimester
      • Penicillins: Considered safe
      • Spectinomycin: Probably safe
- Sulfonamides: Hemolysis in newborns with glucose-6-phosphate dehydrogenase deficiency and increased risk of kernicterus in newborns; avoid at term
- Tetracycline: Congenital limb abnormalities, cataracts, inhibition of bone growth in fetus, discoloration of fetal teeth; avoid during pregnancy
- Trimethoprim: Folate antagonism in fetus; potentially teratogenic; avoid during pregnancy

g. Anticonvulsants
- Carbamazepine (Tegretol): Neural tube defects, questionable association with facial dysmorphism, hypoplasia of fingers or toenails, bifid and congenital heart disease
- Diazepam (Valium): Possible risk of cleft lip without cleft palate
- Ethosuximide (Zarontin): Low teratogenic potential
- Phenobarbital: Possible increase in learning difficulties
- Phenytoin (Dilantin): Developmental disturbances appear lower than previously reported and anomalies may be genetically linked to epilepsy; hypertelorism and digital hypoplasia reported in higher frequency with use of phenytoin; other problems more questionable, including intrauterine growth retardation, mental retardation, and developmental delay; craniofacial abnormalities including clefted nasal bridge, plosis, inner epicanthal folds, and ocular hypertelorism; limb abnormalities (digital and limb hypoplasia); cardiac defects; and hernias
- Valproic acid: Teratogenic in rodents; increased risk of spina bifida if used in first trimester

h. Antidepressants: Conflicting reports
i. Antihistamines
- Diphenhydramine: Suspicious of higher rate of cleft palate
j. Antithyroid drugs: Fetal and neonatal goiter and hypothyroidism, aplasia cutis (with methimazole)
- Aspirin: Association with hydrocephalus, congenital heart disease, and hip dislocation; conflicting reports
- Bromochloridrines
- Aminophylline: No current evidence of abnormalities
m. Danazol/androgenic drugs: Masculinization of female fetuses
n. Hypoglycemic drugs: Neonatal hypoglycemia
- Lithium: Ebstein anomaly
p. Misoprostol: Moebius sequence
q. Nonsteroidal inflammatory drugs: Constriction of the ductus arteriosus, necrotizing enterocolitis
r. Phenothiazines: Cleft palate, hypoplasia, microcephaly, syndactyly, cardiac malformations, club foot
s. Retinoic acid: Severe teratogenic effects causing craniofacial, cardiac, and thymic malformations

8. The chronically ill adolescent: Pregnancy in chronically ill adolescents presents specific challenges and requires coordination with their specialty care providers. Each illness is associated with specific risks. For an overview of the relationship between chronic illness and pregnancy, see Neinstein (1994).

9. HIV disease: Practitioners should offer HIV counseling and testing to all pregnant teens. Education regarding the risks of perinatal transmission should also be provided. Pregnant women infected with HIV should be referred for appropriate treatment and supportive services. Some women found to be infected may choose to terminate their pregnancy once their HIV status is known. Others will want access to specialized care designed to manage their infection and reduce their risk of perinatal transmission. Due to the risks of HIV transmission through breast milk, breast feeding is not recommended for HIV-infected mothers.

10. Battering: Battering often starts or becomes worse during pregnancy. Studies suggest that 8% of all pregnant women are battered (Helton, 1990). Prenatal risk assessment should include specific questions regarding family and partner violence. Practitioners must be knowledgeable about domestic violence-reporting laws in their state and should be familiar with community resources.

MEDICAL COMPLICATIONS OF PREGNANCY IN ADOLESCENCE

Adolescents, as a group, are not significantly at a higher risk of developing complications during early pregnancy.

1. Spontaneous abortion: As with adults, a spontaneous abortion may occur in 20% of pregnancies. A spontaneous abortion occurring in the first 20 weeks of pregnancy usually results from abnormal chromosomal development in the fetus or abnormalities of the pelvic structure within the adolescent. Occasionally, an infection or a chronic underlying disorder (such as endocrinopathy) may cause the fetus to abort.

Abdominal cramping and vaginal bleeding characterize the early stages of a miscarriage, or a spontaneous abortion. The term threatened abortion refers to pregnancies complicated by bleeding and cramping, but the cervix remains long and closed. Should the condition progress, the pregnancy becomes nonviable, and an abortion is considered “inevitable.” Physical changes include a widening of the cervical os and an increase in the bleeding and cramping. When products of conception have passed, it is considered a “complete abortion.” A sonogram will confirm the absence of the fetus, and physical examination will show that the cervical os is closed. If the miscarriage is considered an incomplete abortion, a dilation and evacuation procedure will be necessary to prevent blood loss and infection. (A sensitive urine pregnancy test will confirm the pregnancy, even in the patient with a threatened abortion.)

2. Ectopic pregnancy: Abdominal cramping and bleeding also suggest an ectopic, or extrauterine, pregnancy. An ectopic pregnancy occurs in only 2% of all pregnancies (see Chapter 26).

3. Hydatidiform mole, or gestational trophoblastic disease, may occur in 1 of 1,000 pregnancies each year. Although adolescents commonly experience vaginal bleeding and abdominal cramping with a problem pregnancy, those with a hydatidiform mole usually have severe and profuse bleeding. The uterus is larger than expected given the estimated gestational age of the fetus, and the hCG levels are very high. The hCG levels are often >100,000 mIU/mL. Ultrasound of the uterus demonstrates the characteristic appearance of the mass.

An immediate procedure is needed to terminate a molar pregnancy. Treatment with dilation and suction is the treatment of choice, although the procedure is complicated because it places the patient at increased risk for severe hemorrhage. Close follow-up of the hCG level is required to ensure that the tumor has been adequately removed. The hCG level should remain <2 mIU/mL for 1 year. If the hCG level remains elevated, it suggests that the tumor has not been sufficiently removed; if the hCG level rises, it suggests the tumor has recurred. To follow the patient for persistent or recurrent disease, she should use a reliable method of contraception for the year after the diagnosis of trophoblastic disease.

OTHER CONSEQUENCES OF ADOLESCENT PREGNANCY

Growth and Development

No data suggest that adolescent pregnancy adversely affects psychosocial growth and development. Young adolescents (e.g., those younger than 15 years) may not fully understand the long-term implications of childbirth, particularly in the early stages of the pregnancy.

General Health Risks

For adolescents receiving adequate prenatal care, there are no significantly increased health risks during the pregnancy. Controversy exists regarding the adolescent's risk of pregnancy-induced hypertension, cephalopelvic disproportion, and prematurity.

Education

Fifty percent of adolescent mothers complete high school by 18 years of age, compared with 97% of adolescents who do not get pregnant before finishing high school. By age 35–39 years though, 70% of adolescent mothers have high school degrees. This finding still indicates that educational attainment of adolescent mothers lags behind that of women who delay parenthood.

Socioeconomic Issues

Teen parenthood is associated with socioeconomic disadvantage. An estimated 53% of funds of the Aid to Families with Dependent Children (AFDC) budget was expended on families in which the mother was a teenager when her first child was born. As teenage mothers get older however, many move off public assistance. A recent follow-up study of teenage mothers found that a substantial majority finished high school, found regular employment, and achieved economic independence. Although many adolescent mothers are employed, they generally have a lower family income.
Subsequent Childbirth
The rate of second births to adolescent mothers has declined over the past decade. In 1991, second births approached 220 births per 1,000 teenage women who already have one child. By 1997, this rate decreased to 174.

MALE ADOLESCENTS AS FATHERS
Young fathers rarely get the same degree of attention and support that is offered to adolescent mothers. Fathers may not be included in decisions regarding pregnancy options, they may not participate in prenatal or childbirth classes, and they may not establish a long-term supportive relationship with the mother of the child.

Whenever possible, the provider should attempt to discuss reproductive health issues with their male patients who are sexually active. This is easily done during health maintenance visits, but it should also be done during acute visits for STD evaluation. Asking the male patient about whether he has fathered a child is reasonable when he indicates that he is sexually active. Supportive counseling should be available to male adolescents who are actively involved with babies they have fathered and to male adolescents who have pregnant girlfriends.

WEB SITES
For Teenagers and Parents

For Health Care Professionals

REFERENCES AND ADDITIONAL READINGS


Boyer D, Fine D. Sexual abuse as a factor in adolescent pregnancy and child maltreatment. Fam Plann Perspect 1992;24:44.


Adolescent sexual activity rates have increased steadily over the last century, reflecting earlier onset of menarche as well as changing social conditions, although in more recent years those rates appear to have plateaued. In 1995, it was reported that 51% of women age 15 to 19 years had ever had sexual intercourse since menarche (Singh and Darroch, 1999) and that by 19 years of age 94% of African-American, 87% of Hispanic, and 83% of white male adolescents had had sex (Moore et al., 1998). The Centers for Disease Control and Prevention (CDC) reported that 39% of ninth graders had had sexual intercourse in 1999 (CDC, 2000a). In the 1999 CDC Youth Behavior Risk Survey, more than one third (36.5%) of students nationwide said that they had had sexual intercourse during the preceding 3 months.

The forces underlying these trends are outlined in Chapter 40 and the impacts of teenage pregnancy are detailed in Chapter 42. Adolescent contraception prevented an estimated 1.65 million pregnancies among U.S. women 15 to 19 years of age in 1995 (Kahn et al., 1999). In the 1999 CDC Youth Behavior Risk Survey, more than one third (36.5%) of students nationwide said that they had had sexual intercourse during the preceding 3 months.

The sexual activity of American adolescents mirrors the activities of teenagers in many developed countries, but the pregnancy rates of teens in those countries differ significantly. The unintended pregnancy rates in developed European countries are 50% to 85% lower than in the United States, in part because of the lack of societal consensus in the United States about birth control, especially for adolescents. U.S. teen pregnancy rates have been decreasing; between 1990 and 1996, they dropped 16%. However, in 1996, 10% of U.S. women age 15 to 19 years became pregnant, and 35% of those pregnancies ended in abortion. In 1997, 863,700 teen girls became pregnant (CDC, 2000b), and the rate of live births was 52.3 per 1,000. Eighty-five percent of all adolescent pregnancies were unplanned, unintended, or mistimed (Institute of Medicine, 1995). Most of the recent reduction in U.S. teen pregnancies has resulted from a decline in birth rate for adolescents who already had at least one child (Neinstein, 1994; Kaufmann et al., 1998), which has been attributed to the use of long-term progestin contraceptive methods. However, one fourth of the decrease is attributed to a delay in age at sexual debut (as a result of improved sex education and parent-teen communication) (Manlove et al., 2000).

Contraceptive use by adolescents has increased dramatically since the mid-1980s in response to concerns about sexually transmitted diseases (STDs). The vast majority of adolescents now report using some form of birth control at the time of first intercourse; 76% of teenage girls and 72% of teenage boys used a condom with first coitus (Kahn et al., 1999), and 58% had used a condom at last intercourse (CDC, 2000a). However, condom use at last intercourse declined from 66.6% in 9th graders to 47.9% in 12th graders (and to 37.7% among 18- to 24-year-old college students). There are still significant delays in obtaining contraception by prescription. Most young women are sexually active for months before they seek medical attention; only 40% seek medical contraceptive services within 12 months after they begin intercourse. In this setting, adolescent women with negative pregnancy tests would seem to be an important group to target with information about contraception. However, the opportunity may not be utilized effectively; Zabin et al. (1996), found that 60% of pregnant teens had presented for pregnancy testing after they began intercourse. In this critical situation, adolescent women with negative pregnancy tests would seem to be an important group to target with information about contraception. However, the opportunity may not be utilized effectively; Zabin et al. (1996), found that 60% of pregnant teens had presented for pregnancy testing before becoming pregnant. Shew et al. (2000) raised the concern that home pregnancy testing may eliminate clinicians’ ability to intervene with contraceptive counseling in this critical situation.

Most sexually active adolescents today in the United States are using contraceptives on an ongoing basis. The 1995 National Survey of Family Growth showed that 72% of 15- to 17-year-olds reported uninterrupted use of contraception (23% were using effective methods); 20.5% were using contraception methods sporadically, and only 7.5% never used contraception. Among the 18- to 19-year-olds, only 4.8% never used contraception (Table 42.1). Adolescent contraception prevented an estimated 1.65 million pregnancies among U.S. women 15 to 19 years of age in 1995 (Kahn et al., 1999).

### Table 42.1. Percentage distributions (and standard errors) of women who are at risk for unintended pregnancy, by contraceptive use pattern during past year, according to age group, 1995 National Survey of Family Growth

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Unprotected</th>
<th>Contraceptive Use</th>
<th>% of Women at Risk for Unintended Pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>15-16</td>
<td>10.6</td>
<td>0.5</td>
<td>0.1</td>
</tr>
<tr>
<td>17-18</td>
<td>14.6</td>
<td>3.2</td>
<td>0.3</td>
</tr>
<tr>
<td>19-20</td>
<td>18.6</td>
<td>5.6</td>
<td>0.5</td>
</tr>
</tbody>
</table>

The ideal contraceptive method for adolescents would be one that is safe, effective, reversible, inexpensive, convenient, and private and has few side effects. In the following chapters, each of the major methods of birth control is analyzed using this list as a yardstick. Overall, however, several important generalizations must be recognized:

1. Every method of contraception for adolescents is safer than pregnancy.
2. There is no ideal contraceptive method. Every decision about birth control is a compromise.
3. In the absence of an ideal contraceptive, the goal of health care providers is to have a rich array of contraceptive choices available to meet the individual needs of patients, respecting their religious and cultural beliefs and medical conditions.
4. Sexually active adolescents who face two risks (STDs and unintended pregnancy) are candidates for two interventions: one method for STD risk reduction (condoms, safer sex practices) and another to effectively reduce the pregnancy risk (usually hormonal contraception).

5. Compliance with contraception depends on motivation, which in turn depends on patient education and understanding. Age-appropriate counseling and patient education is crucial.

6. Adolescents with chronic medical problems have more complex decisions to make when determining a balance between risk and benefits.

To effectively reduce the rate of unintended pregnancy, health providers must be familiar with each of the methods of birth control and should closely analyze their practices to ensure teens' effective access to those methods. This chapter provides an overview of the efficacy and safety of reversible contraceptives, a discussion of the key elements needed to ensure access and to integrate family planning services into comprehensive adolescent health care, and a summary highlighting the special contraceptive needs of adolescents with chronic medical problems. Subsequent chapters discuss specific contraceptive options in detail.

CONTRACEPTIVE EFFICACY

The measure of the effectiveness of a method of contraception is its failure rate. The clinically appropriate estimate of efficacy is the typical-use failure rate, because that number best reflects the pregnancy rate in conditions of actual use by the average patient. The failure rate with correct and consistent use (formerly called the “perfect use” or “method” failure rate) may provide motivation to encourage patient compliance, but it should not be routinely quoted as a realistic prediction of any individual patient’s experience. Although precise estimates of efficacy vary, the following tables are provided as a basis for patient counseling and insight into factors that affect outcome. Table 42.2 summarizes for each birth control method the typical use failure rate and the failure rate with correct and consistent use. These rates are based on use by all women of reproductive age. Table 42.3 estimates the range of failure rates for adolescents compared with the average for all users where data are available.

![Table 42.2: First year failure rates by contraceptive method](image)

**TABLE 42.2.** First year failure rates by contraceptive method

![Table 42.3: Estimates of highest and lowest age-specific failure rates (ages 15–44 and 15–19)](image)

**TABLE 42.3.** Estimates of highest and lowest age-specific failure rates (ages 15–44 and 15–19)

CONTRACEPTIVE SAFETY

All methods of birth control are safer for a young woman’s health than pregnancy. Only abstinence is truly safe. Table 42.4 provides estimates by age of the risk of mortality per 100,000 women using various methods of contraception. Although at first glance it may seem inconceivable that there could be any mortality associated with the use of condoms, it should be noted that most of the “risk” associated with each of the reversible methods arises from method failure (i.e., maternal mortality).

![Table 42.4: Risk of death by contraceptive method and age](image)

**TABLE 42.4.** Risk of death by contraceptive method and age

Despite the proven safety of contraception, surveys show that patients grossly overestimate contraceptive risks. The wide discrepancy between observed clinical safety of contraceptives and public perception is in part fostered by the techniques used to report contraceptive efficacy for Food and Drug Administration (FDA) package inserts. The default option to contraception is always assumed to be abstinence, not unprotected intercourse. Therefore, the contraceptive benefits of prevention of maternal morbidity and mortality are often overlooked. On the other hand, the “side effects” associated with, but not necessarily attributable to, the method are tallied and stand alone with no benefits to counterbalance them in the patient's eyes.

Adolescents are particularly vulnerable to misinformation. Often they count on peer group members for advice. But even when teens consult adult authorities, those experts may not be well informed. Surveys of school sex education teachers have demonstrated serious lack of information (Davis, 1994). When true-false questions were administered to more than 1,300 sex education teachers, only 72% answered correctly that having a baby was a greater risk for a teenager than taking the pill; only 30% knew that the statement, “Pill use by teenagers may have a detrimental effect on later fertility,” was false; and only 23% correctly said that the statement, “Pill use should be stopped periodically to give the body a rest,” was false.
ACCESS TO CONTRACEPTIVE SERVICES AS PART OF COMPREHENSIVE HEALTH CARE

Adolescent patients are confronted with several challenges in accessing contraceptive services. They can be classified into the following groups of concerns:

Access to Low-cost, Appropriate Medical Services

Adolescents often have limited financial resources. Even low-cost medical services can be prohibitively expensive for them. Lack of familiarity with large managed care systems can functionally limit access. Once in a system, teens must find providers to address their issues. Adolescents often wish to discuss issues of sexuality and contraception with their providers but are reluctant to introduce the subjects themselves. This reluctance, together with the provider's hesitancy, results in a wide discrepancy between what teens want to discuss and what they do discuss with their primary health care physicians (Table 42.5).

| TABLE 42.5. Adolescents' desires to discuss sexuality issues versus actual discussion with physicians |
|---|---|
| Desires to Discuss | Actual Discussion |
| Sexuality issues | % |
| Contraception | 67 |
| Reproductive use | 59 |
| STDs | 10 |
| Pregnancy | 47 |
| Other issues | 54 |
| | |
| Access to Confidential Services

Ford et al. (1997) concluded from a randomized, controlled trial that teens are more willing to communicate with and seek health care from physicians who ensure confidentiality. Health care providers, for their part, strive to maintain patient confidentiality but are faced with several special challenges in regard to adolescent patients. The wishes of the patients and those of their parents may conflict, and this may create an impossible situation, especially when the parents are paying for the patient's care. Any failure to disclose information to the parents can result in loss of the patient from the practice. As adults and parents themselves, providers may feel sympathetic to the patient's desire to have complete access to information about their children. Finally, even if the provider were immune to all these pressures personally, the insurance billing system often discloses facts about services provided to the teen that can seriously compromise patient confidentiality. The bill for pregnancy testing destroys confidentiality for the teen who had not told her parents she was sexually active. Providers trapped in such situations may prefer to refer their patients to settings where confidentiality can be better preserved, such as low-cost family planning clinics.

Access to Age-appropriate Services

Modern media have profoundly affected adolescents' attitudes toward sex as well as their communication and learning styles. Estimates are that the average teen witnesses 14,000 instances of sexual behavior on television each year, and that in only 9% of those sexual encounters is there any mention of contraception or STDs. These exposures may not increase the accuracy of teens' database on sexuality and its risks, but they increase their curiosity and expectations and significantly influence behavior.

Television and videos have also transformed adolescent learning styles. Attention spans have been constricted to the 40-second sound bite. In the age of MTV, written handouts may have very limited educational benefit. If written materials are used, they must be corrected for age-appropriate literacy and for short reader attention spans. Furthermore, because many adolescents may not have confided to their parents that they are sexually active, written materials found in their possession might be incriminating. Videotapes played in the office before the patient-provider interaction are quite helpful, as are individual counseling sessions with nursing staff trained in dealing with teens. Peer counselors are also effective adjuncts in outreach programs and in practice settings.

In providing contraceptive services to adolescents, it is crucial to remember that adolescents are not just younger versions of adults. They are in transition to adulthood, and they progress through different developmental stages with different thought processes over time. Although adolescents progress through the various stages at different rates, there are some generalizations that are helpful in providing counseling:

1. Adolescents aged 12 to 14 years are in early adolescence. Traditionally, they struggle for autonomy, identify with same-sex peer groups, and are preoccupied with body image. They are very concrete thinkers and somewhat self-centered. Effective communication tools for those teens must be very specific (rather than abstract), written in pictographic style (rather than tables or graphs), and focused on issues that most concern these patients (e.g., weight gain, acne).
2. Adolescents aged 15 to 17 years are strongly attached to their peer groups and have concerns with appeal to the opposite sex. Often they are risk takers and view themselves as invincible. They have a strong urge to prove their autonomy. A health care system that is perceived by teens as an authority figure trying to control them runs the risk of inciting rebellious behavior in adolescents of this age. It is crucial to have the teenager (and possibly his or her peers) identify with the health care message to ensure compliance and success. Peer counseling, if carefully selected, can be effective with this age group.
3. Older adolescents aged 18 to 19 years often have achieved a more adult level of abstract reasoning and respond well to more traditional counseling approaches, although chronological age by itself is no guarantee of mental maturity.

Access to Teen-friendly Services

Most adolescents do not get out of school until late in the afternoon, and they may have difficulty keeping appointments during usual office hours. This may be particularly true if they have limited access to transportation and are trying to maintain privacy. Late afternoon or early evening office hours or weekend availability can enhance adolescent access to services. Privacy needs may also limit the times and ways in which the teen can interact with a health care provider. The adolescent who calls from a pay phone or cell phone to ask about a contraceptive side effect during lunch break cannot be put on hold and cannot be called back later when the provider is between patients. One successful arrangement is to identify someone on the staff to answer such calls and then arrange the staff person's lunch hour around the teen's schedule. Because teens may interact with any member of the staff, each staff member should be selected and trained to be responsive to teens and their special needs.

Access to Broader Community-based Programs

Each of the access issues listed previously is relevant at the individual provider level. To make even more impact on adolescent pregnancy rates and teenage sexuality, political, community, educational, and religious institutions will require modification and involvement (Brindis, 1999). Demonstration projects have shown that broader, multicomponent, community-based programs are needed (Paine-Andrews et al., 1999). One project that aimed to increase teen awareness of and accessibility to family planning services was provided in a large metropolitan area in Philadelphia; 2 years after its introduction, there was no detectable change in teen pregnancy rates, contraceptive use, or understanding (Hughes et al., 1995). On the other hand, a comprehensive community-based program in a section of a South Carolina county that involved media, local clergy, and schools emphasized decision making, communication skills, self-esteem enhancement, and human reproduction saw the pregnancy rate for 14- to 17-year-old women fall from 67 to 25 per 1,000 (Koo et al., 1994). After removal of key providers and support elements of that program, the pregnancy rate rose again.

Other programs using peer counseling in schools and nurse practitioner counselors in off-campus sites have also been successful, but a coordinated effort that focuses on the root causes of teen sexuality and other risk-taking behaviors has even more leverage. Often girls have unprotected sex because of a secret desire to keep a boyfriend (by becoming pregnant), to have someone of her own to love, or to act out against a parent (Dodson, 1996). Smith et al. (1999) reported that 74% of
adolescent sexually active women who did not use contraception said that they were not interested in pregnancy, but 64% of the women in that group said they would keep the baby. This may support the conclusion that risk takers do secretly desire to become pregnant or that they are unable to plan for the future. Hacker et al. (2000) found that teens were a diverse group and offered various solutions to the problem of teen pregnancy. In that study, abstainers thought more emphasis on abstinence education would reduce teen pregnancy rates, whereas contraceptive users thought that easier access to contraception would work.

The practitioner must be aware of whether his or her own office or clinic hours and setup are conducive to adolescent health care needs. In addition, the practitioner should become familiar with sources of referral for services such as contraception, STD treatment, and therapeutic abortion. Finally, because virtually all studies show that parent-teenager communication is key to improving contraceptive use (Whitaker et al., 1999), clinicians, particularly pediatricians, can counsel parents of small children about sexuality education to prevent problems in the future as those children enter adolescence.

GENERAL CONSIDERATIONS IN METHOD SELECTION

In counseling adolescent patients, it is crucial to determine their knowledge base, motivations, and personal characteristics and conditions.

1. Knowledge base: Adolescents can be very embarrassed to describe their own understanding of sexual activity and contraception when directly questioned. Even though they may have had family life classes in school, quizzing them about what they know is often unappealingly interpreted by the young adult as yet another test. On the other hand, reflective questions such as, “What would you want to tell a friend who was thinking about having sex?” can be richly revealing about your teen patient's attitudes and understanding.

2. Motivation: Effective counseling of teens to aid them in selecting birth control methods requires that the provider know the following:
   a. What is the teen's sexual history including the possibility of early first sexual activity?
   b. How important is it to the teen to avoid pregnancy, and what is the teen's perception of the risks of pregnancy?
   c. What is the teen's understanding about STD risks?
   d. What is the teen's relationship with her or his partner (or partners), and what does the teen believe the partner’s childbearing plans are? This is particularly important because so many adolescent women (48%) have partners more than 2 years older than they are (Darroch et al., 1999).
   e. What concerns does the teen have about contraception in general and about any of the methods offered?
   f. How much control does the teen have in the relationship over sexual activity and contraceptive use? This is important because nationwide surveys indicate that 1 in 4 young women experience sexual abuse before age 18 years (Butler and Burton, 1990).
   g. How would the teen react to contraceptive side effects?

3. Personal characteristics and conditions: The living conditions and personal characteristics of the teen (particularly the young woman) profoundly influence the selection and use of a contraceptive.
   a. How strong is the teen's self-esteem? Her upward mobility?
   b. Does she have siblings or friends who have been sexually active, used birth control, or become pregnant?
   c. Will it be possible to integrate the method into the teen's lifestyle (e.g., private space for storage of birth control pills, access to condoms)?
   d. What is the frequency of intercourse? Is it anticipatable?
   e. Is the teen able to discuss or negotiate with the partner or partners?
   f. Is the teen comfortable touching his or her genitals?

RECOMMENDED CONTRACEPTIVE METHODS FOR TEENS

The most frequently recommended methods of contraception for adolescents are condoms, oral contraceptives (OCs), and hormonal injections. Several birth control methods are discussed in depth in the subsequent chapters, but a summary is included here.

Regardless of the contraceptive method used, the at-risk teen should use a latex or polyurethane condom with every act of intercourse to reduce the risk of acquiring STDs. Male condoms are also recommended for contraception for first intercourse, for sporadic intercourse, and for young women who cannot tolerate or use hormones. OCs (plus condoms) are useful for adolescents who would like the noncontraceptive benefits of OCs, including regular menstrual cycles; who can remember to take a single pill every day; and who do not inject drugs. Injectable progestins (plus condoms) are useful for teens who want the convenience of not having to remember a daily pill (or who have a contraindication to estrogen) but do not mind having irregular menses or amenorrhea. Once-a-month combination hormonal injections (plus condoms) are well suited for women who seek the convenience of once-a-month administration and good cycle control and who can arrange their schedules to return every 23 to 33 days for reinjection. Emergency (postcoital) contraception (EC) is underutilized by all age groups, but it is particularly important to teens. EC should be more widely available for teens, both by advance prescription and as an after-the-fact intervention to prevent many unwanted pregnancies.

However, it is an urgent intervention that should be followed by a more effective ongoing method of contraception. Teens themselves often use withdrawal as a method of birth control. Withdrawal has a typical failure rate of about 18%, which is comparable to that of many of the female barrier methods. Other sexual practices are followed by adolescents, not only to avoid pregnancy, but to achieve sexual pleasure without formally qualifying as “sexual activity.” In this class would be oral-genital activity, sexual “outercourse,” and rectal intercourse for heterosexual couples. Teens need to understand that these practices, although they may help with contraception and hymenal preservation, still carry STD risks for the participants.

The following methods are not frequently used in adolescents but could be used in highly selected teens: intrauterine devices (IUDs), diaphragms, cervical caps, spermicides, female condoms, and natural family planning (NFP).

CONTRACEPTIVE CONSIDERATIONS IN ADOLESCENTS WITH CHRONIC ILLNESSES OR DISABILITY

As many as 10% to 20% of all children and adolescents experience a chronic illness or disability by age 20 years. Sexuality issues, including the contraceptive needs in this group of patients, are often forgotten by health professionals (Hakim-Ehah, 1991). When contraception is discussed, accurate advice is often difficult to obtain. Most information about the effects of each of the methods of birth control is based on experience with healthy subjects. As a result, theoretical concerns and small-scale studies have an exaggerated impact on “knowledge” about the safety of birth control methods for patients with medical problems. Often lost in this discussion is consideration of the problems that pregnancy would pose. Providers must strike a balance between these two risks.

Outstanding references are now available detailing the impacts of contraceptive methods on a wide array of medical conditions based on comprehensive reviews of the literature (Neinstein, 1994, 1998) or expert consensus conferences (Grimes et al., 1993). In addition, the World Health Organization (WHO) has published an excellent summary of medical eligibility criteria for starting contraceptive methods. Current versions can be obtained in more detail at:

www.reproline.jhu.edu/english/6read/6multi/tgwg/pdf/tgwh_e.pdf

The following sections attempt to summarize the concerns and conclusions of those authors for a selected subset of diseases found in the adolescent population.

Cardiac or Thromboembolic Disease

Hypertension and Thromboembolic Disease

1. Patients with mild or well-controlled hypertension may be considered for low-dose combination oral or injected combination hormonal contraceptives or progestin-only methods (implants, injections, mini-pills), particularly in the absence of other risk factors such as smoking, diabetes, hyperlipidemia, or obesity. Selection of a particular method should also consider the method's impacts on other risk factors for myocardial infarction, such as lipid profile, glucose tolerance, and weight.

2. Despite warnings on package labeling, progestin-only methods (implants, injections, mini-pills) may also be used in patients with histories of unexplained thromboembolic disease or pulmonary embolism. Contraceptives containing estrogen would be contraindicated in patients with any of these thrombotic histories. Patients with histories of venous thromboembolism who are anticoagulated are candidates for estrogen-containing hormonal methods. Patients with histories of venous thromboembolism that does not suggest a coagulopathy (e.g., from trauma, immobilization) may also be candidates, especially if they have experienced hypercoagulopathy states (pregnancy, prior use of oral contraceptives) without cloting and if they do not carry the factor V Leiden mutation.

3. IUDs may be used if the hypertensive or thrombophilic patient is otherwise an IUD candidate.

4. Barrier methods and natural family planning (NFP) approaches are associated with higher failure rates and, if selected, must be fastidiously utilized. Combining them with EC can boost their efficacy.

5. For severely affected patients in whom pregnancy could be life-threatening, sterilization should be offered. Those with progressive disease might consider early
Oral contraceptives (OCs), injections, and potentially vaginal rings and patches provide ovulation suppression and reduce the risk of internal hemorrhage associated with monthly oocyte extrusion in patients with mechanical valves who are anticoagulated. Nonanticoagulated patients with significant valvular disease should not be offered estrogen-containing contraceptives.

2. Progestin-only methods (implants, injections, and misoprostol) must be evaluated for their effects on fluid retention, but they often are quite useful.

3. IUDs are often feasible, but appropriate American Heart Association–approved antibiotic prophylaxis must be used at insertion and removal. The IUD’s effects on menstrual flow should be considered, because anticoagulation itself increases menorrhagia. For this reason, the IUDs that release levonorgestrel are generally preferred over the copper IUDs in anticoagulated women.

4. Barrier methods do not directly affect cardiac disorders but may be associated with unacceptably high failure rates, which could present a health hazard to the adolescent.

**Neurological Disease**

1. OCs do not have a clinical impact on the frequency or intensity of seizures despite the theoretical concern that estrogen lowers seizure threshold and increases spike amplitude. Balancing the estrogen in the pill is the progestin, which has opposite effects. More clinically significant are the known drug-drug interactions between anticonvulsants and estrogen-containing contraceptives (especially oral contraceptives), which have the potential to either increase or decrease the serum concentration of the drug. Therefore, the use of triphasic and ultra-low-dose OC formulations should be avoided in women using these anticonvulsants; the lowest dose that should be used is 35 µg of ethinyl estradiol, and that should be coupled with barrier methods for at least 3 months to assess effectiveness. If breakthrough bleeding persists for more than 3 months with the 35-µg dose, a higher-dose formulation (50-µg ethinyl estradiol) should be considered. Estrogen may speed the metabolism of anticonvulsants, and serum levels of anticonvulsants should be rechecked about 1 month after initiation of OC use. Neither the metabolic clearance rate nor the failure rate of the other estrogen-containing hormonal contraceptive methods (e.g., monthly injections, rings, patches) has been tested, so use of these methods in women taking anticonvulsants may not be prudent.

2. Medroxyprogesterone acetate (DMPA, Depo-Provera) is an outstanding choice for teens with seizure disorders, because progestins themselves are weak anticonvulsants.

3. IUDs are extremely effective for appropriate candidates (parous women in stable, mutually monogamous relationships), but the impact of copper-containing IUDs on neurological systems is generally not candidates for combination hormonal contraceptives. On the other hand, women with menstrual migraines may benefit greatly from continuous use of OCs (see Chapter 43). Other patients with migraines without aura may be candidates for low-dose estrogen-containing hormonal contraceptive methods, but they should be closely monitored to ensure that there is no worsening of the intensity or frequency of the migraines. Progestin-only methods do not pose any medical risk for these women.

All hormonal methods of birth control have been associated with complaints of headaches, although a placebo-controlled study showed no risk of headaches attributable to use of OCs (Redmond et al., 1999). If headaches are severe and are not responsive to over-the-counter therapies, the hormonal contraceptive may need to be discontinued. Implant users who experience new onset or significant worsening of headaches should undergo funduscopic examination to rule out papilledema associated with pseudotumor cerebri. If papilledema is discovered, the implants should be removed.

Copper IUDs, barrier methods, and NFP have no known impacts on headaches.

**Pulmonary Disease**

**Asthma** Some theoretical concern was initially raised about estrogen’s effect on mucus production and progestin’s thickening of it, but clinical studies failed to find any consistent association between use of OC and asthma attacks. Decreased clearance of aminophylline in users of combination OCs may require a reduction in its dose by about 30%, depending on the estrogen-containing contraceptive used. Other methods of birth control have no impact on asthma. However, patients who are using chronic steroid therapies have reduced ability to fight infection and are not candidates for IUDs.

**Cystic Fibrosis** The major potential side effect that exists with OCs in individuals with cystic fibrosis involves the effect of progesterone on mucus. Progesterone causes thick cervical mucus, and this same effect could lead to thick bronchial mucus. A preliminary study (Fitzpatrick et al., 1984) suggested that OCs at 50 µg doses may not exacerbate pulmonary disease. Stead et al. (1987) studied the pharmacokinetics of sex steroids in women with cystic fibrosis using OCs and found that women with cystic fibrosis receive contraceptive protection similar to that achieved by healthy women. However, hormonal contraceptives should be used with extreme caution in teens with cystic fibrosis until further studies indicate that they are safe in such patients. If used, lower dose formulations would be preferred.

**Gastrointestinal Disease**

**Inflammatory Bowel Disease** If disease is active or malabsorption exists, OC pill use is not appropriate. Parenteral hormonal methods (implants, injections, patches, and rings) bypass the enteric absorption problems and can therefore be used. In teens with stable, quiescent inflammatory bowel disease, OCs can be used with caution under close monitoring for possible impact on disease activity. IUDs would be feasible in appropriate candidates unless the patient is immunocompromised by chronic steroid use. Barrier methods and NFP are not contraindicated, but enthusiasm for them is tempered by their higher failure rates.

**Hepatitis** Contraceptive steroids not only alter hepatocellular function but also rely on hepatic metabolism for clearance. Hormonal methods are contraindicated during active liver disease flares or cirrhosis. After a bout of acute hepatitis, liver function test results should be normalizing before use of hormonal contraceptives is considered. IUDs would be feasible in appropriate candidates unless the patient is immunocompromised by chronic steroid use. Barrier methods and NFP are not contraindicated, but enthusiasm for them is tempered by their higher failure rates.

**Endocrine Disease**

**Diabetes Mellitus** There has been a dramatic change in contraceptive practices for women with diabetes in the last decade due to an increased appreciation of the safety of low-dose OCs in women with uncomplicated diabetes women (i.e., those without end-organ damage).

1. Development of Diabetes Mellitus Older studies of patients using OCs reported that the pills caused an increased risk for development of reversible glucose intolerance. However, more recent studies, including one by the Royal College of General Practitioners (Hannaford and Kay, 1989), demonstrated no evidence of an increased risk of glucose intolerance among healthy current users of modern formulations. The Nurses Health Study found no increased risk of type 2 diabetes in current or former OC users (Rimm et al., 1992). Even among women with a history of recent gestational diabetes, Kjos et al. (1990) found no differences in glucose tolerance among those assigned to various low-dose OCs or to nonhormonal contraceptive methods. Conversion to overt diabetes was not accelerated by the use of OCs. Skouby et al. (1984) found a decrease in insulin sensitivity among women with a history of gestational diabetes, but it was not of sufficient magnitude to alter glucose tolerance as measured by serum glucose or insulin levels.
2. Glucose Control in Women with Diabetes Mellitus For women with diabetes, studies have also examined the effect of OCs on glucose control. Skouby et al. (1986) compared the metabolic effects of four OC formulations in insulin-dependent diabetic women. They found no differences in fasting glucose, 24-hour insulin requirements, glycosylated hemoglobin, low-density lipoprotein (LDL) cholesterol, or the ratio of high-density lipoprotein (HDL) cholesterol to total cholesterol. Steel and Duncan (1978) evaluated women with insulin-dependent (type 1) diabetes who were taking a combination low-dose OC. There were few problems with glucose control; 81% of women reported no changes in insulin. Glycemic control does not worsen significantly in insulin-treated diabetic women using combination OCs. Klein et al. (1990) found no association between current or past OC use and the number of years of use and severity of retinopathy, hypertension, or glycosylated hemoglobin. Two studies indicated no change in cardiovascular risk profile (Peter sen et al., 1994) or in renal or retinal complications (Garr, et al., 1994), in diabetic women taking OCs. However, women with complicated diabetes (those with proteini na or other indication of vascular compromise), women with prolonged diabetes (more than 20 years), and women with uncomplicated diabetes who have other significant health problems (e.g., hypertension, heavy smoking) are not good candidates for combination hormonal contraception.

3. Progestin-only Pills Progestin-only pills contain lower doses of progestin and have an even lower impact on glucose tolerance. Steel and Duncan (1978) found no problems in insulin requirements in 45 insulin-dependent women using norethindrone 0.35 mg/day. Kjos et al. (1986) did report a slight increase in deterioration of glucose control among amenorrhoeic, breast-feeding women who used progestin-only methods in their first postpartum year.

4. Other Hormonal Methods The effects of other hormonal methods of birth control on glucose tolerance have not been studied in diabetic women. Implants have been found to have no clinically significant impact on glucose tolerance in normal subjects (Konje et al., 1992). During clinical trials, patients demonstrated no change in fasting blood glucose levels or in 2-hour post-glucose challenge test levels when tested before capsule placement and after 2 years of use; the 1-hour test value of the 2-hour oral challenge test did show slight elevation. DMPA injections had a more profound impact on glucose tolerance test results, affecting both insulin and glucose levels, although all values stayed within normal ranges in nondiabetic subjects. No significant impact on glucose or insulin levels has been detected in normal nondiabetic women with the other combination hormonal methods (injections, patches, rings). However, they have not been directly tested in diabetic women. They would be expected to have less significant metabolic impacts than the OCs or DMPA injections because the circulating hormone levels are significantly lower.

5. Effect on Cardiovascular Disease Another critical issue for diabetics is the impact of contraceptives on cardiovascular disease risk factors. OCs have been thought to affect coronary artery disease via several potentially conflicting mechanisms. Considerable interest has been focused on the impacts of OCs on lipoprotein profiles (Yeshurun et al., 1984). Estrogen is known to increase HDL cholesterol and triglycerides and lower LDL cholesterol. Progesterone (androsten derivatives) in OCs have had an opposite effect, lowering HDL and raising LDL. Some progestins (desogestrel, norgestimate) have been designed to minimize their androgenicity, and others have minimal androgenic effects (norethindrone). Barrier methods and NFP have no deleterious effects. Copper-bearing IUDs tend to induce heavier menstrual bleeding and could aggravate problems of anemia. Barrier methods and NFP have no deleterious effects.
radiation below the diaphragm. Age also is a factor, in that chemotherapy seems to cause less damage in prepubertal individuals than in individuals receiving such treatment after puberty (Quigley et al., 1989). Radiation and chemotherapy have also been reported to cause fetal wastage and malformations. It is recommended that pregnancy be avoided until 1 year after successful chemotherapy.

Effects of Hormones or Pregnancy on Tumor No evidence exists that pregnancy or OCs have an adverse effect on nonhormone-dependent tumors. Adolescents with such tumors should use an effective contraceptive and should time pregnancy based on their therapy schedule, severity of disease, prognosis, and preference. However, women with hormonally sensitive tumors (e.g., melanomas), are not good candidates for estrogen-containing contraceptive methods, at least for the first 2 to 4 years after their effective treatment. Often, delays in conception are recommended to determine whether treatment is successful, and contraceptive efficacy becomes of paramount importance.

Psychiatric Disease and Mental Retardation

Mentally ill adolescents frequently have their family planning needs overlooked. Sometimes, their sexuality is seen as acting out or a manifestation of their underlying disease. Once recognized as having contraceptive needs, these patients may have difficulty in providing informed consent or in effectively using a contraceptive method. Many mentally ill patients, even in adolescence, have dual diagnoses, such as substance abuse and mental illness (often depression) or epilepsy. Barrier methods, even in the non-breast-feeding women, are not contraindicated. Some studies have indicated that OCs may be associated with a relatively higher failure rate.

Connective Tissue Disease

Systemic Lupus Erythematosus Systemic lupus erythematosus (SLE) has been closely related to hormones. The strong bias in the female-to-male ratio and the relative frequency of flares during pregnancy raise concerns for the use of estrogen-containing hormonal contraceptives. Although only small-scale studies (usually without control groups) have been conducted, many authorities caution against the use of combination OCs in patients with SLE or limit their use to women with very mild lupus with no hypertension or vascular involvement. Progestin-only methods appear safe in most women with lupus; in studies to date there have been no significant differences in numbers of episodes of active SLE flares in progestin users versus controls. Care should be taken to minimize infection risk with insertion if implants are selected. Some SLE patients experience depression, and this aspect must also be considered when choosing a hormonal method. IUDs are not recommended if the SLE patient is immunocompromised by her condition or by corticosteroid use. Barrier methods have the least number of associated side effects and offer STD risk reduction; however, they have high failure rates, and pregnancy can pose serious hazards to the woman with SLE. NFP similarly has no direct adverse effects but is associated with a relatively higher failure rate.

Rheumatoid Arthritis Hormonal contraceptive methods are excellent choices for women with rheumatoid arthritis. Some studies have suggested that OCs may reduce the risk of developing this disease, but there is little evidence they reduce the severity of preexisting disease. The IUD may be used by affected women who are able to check monthly for strings, except for those using steroids or other immunosuppressive therapy. Barrier methods are not contraindicated, but female barrier methods may not be appropriate for women with severe disabilities of their hands or hips.

Renal Disease

Emodialysis Most adolescents with chronic renal failure are infertile secondary to hypothalamic-pituitary dysfunction. During dialysis therapy, however, some women resume normal ovulatory function. For those adolescents with menstrual function, contraception is an important issue. The major contraindications to OC use in these adolescents are hypertension and thromboembolic complications. Progestin-only methods are effective alternatives, even for those with prior thromboembolic complications. Some renal transplant patients are treated with high dose steroids, levels of which are capable of causing amenorrhea. IUDs are contraindicated owing to anemia and/or the immunocompromise associated with renal failure. Barrier methods are not contraindicated but may be associated with unacceptably high failure rates. NFP methods are difficult to use in the face of irregular menstruation.

Transplantation Ovulation and fertility often return within 6 months after successful renal transplantation. Information regarding OC use in an adolescent with a renal transplant is very limited. In teens with no significant hypertension, low-dose OCs or the minipill could be used with extreme caution. IUDs would not be feasible because the women are immunosuppressed to prevent graft rejection. Other methods may be used as outlined earlier.

Postpartum and Breastfeeding Teens

Ovulation usually does not return in women who fully breast-feed until the third postpartum month, but non-breast-feeding women may see a return of fertility by 3 to 6 weeks postpartum.

In non–breast-feeding women, combination hormonal methods can be started between the third and fourth postpartum week, after the hypercoagulated conditions induced by pregnancy have resolved. Progestin-only methods may be started immediately postpartum.

In breast-feeding women, combination hormonal contraceptives should be avoided until the infant is receiving supplemental feedings. In general, WHO guidelines discourage the use of estrogen-containing contraceptives in breast-feeding women because of concern that estrogen may diminish breast milk production and because of the prevalence of malnutrition in women worldwide. However, the American Academy of Pediatrics has long maintained that estrogen-containing contraceptives may be used in healthy women once the infant is supplemented in its feedings (extra bottles or solid foods). The progestin-only OC can be started soon after pregnancy. Labeling indicates that the use of Norplant implants and DMPA should be delayed until 4 to 6 weeks postpartum, although most authorities advocate their initiation immediately after delivery. The IUD can be inserted 6 to 8 weeks postpartum, after the uterus has completely involuted. Lubricated condoms may alleviate problems associated with postpartum vaginal dryness.

Human Immunodeficiency Virus Infection Because the rate of human immunodeficiency virus (HIV) infection in women and the rate of heterosexual transmission of HIV infection are increasing, contraceptive concerns of HIV-infected women are becoming increasingly important. Fertility rates are not affected by HIV infection or by acquired immunodeficiency syndrome (AIDS). HIV-infected individuals who choose to continue to be sexually active require maximal protection from pregnancy, from STDs, and from spreading the virus. Hormonal contraceptives appear safe in these individuals along with the use of condoms. Although there has been a theoretical concern that OCs would enhance shedding of virus from infected women, there is currently no evidence to support this concern. The IUD would not be recommended once the patient becomes immunocompromised, but it is not an appropriate choice at all if she is at risk for acquiring other STDs. Male condoms are key to reducing spread of the virus; female condoms also should offer reduction in the risk of horizontal transmission of HIV.
MEDICATION INTERACTIONS

Medication interactions are shown in Table 42.6, Table 42.7, and Table 42.8. For a more complete discussion, see Neinstein's articles (1994, 1998).

TABLE 42.6. Drugs reported to be possibly associated with reduced oral contraceptive efficacy

<table>
<thead>
<tr>
<th>Drug</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

TABLE 42.7. Drugs reported to be possibly associated with enhanced oral efficacy or increased side effects

<table>
<thead>
<tr>
<th>Drug</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

TABLE 42.8. Drugs reported to have altered effects when used with oral contraceptives

WEB SITES

For Teenagers and Parents

http://www.arhp.org/arhpfaqadult.htm, Patient education site from the Association of Reproductive Health Professionals. Includes interactive programs to test your contraceptive IQ and to choose the right birth control method.

http://www.itsyoursexlife.com, Henry J. Kaiser Family Foundation site provides sexual health information for young adults and their parents.

http://www.sxetc.org, This online teen newsletter examines love, sex, relationships, and health.

http://www.taenwire.com, This teen site from the Planned Parenthood Federation of America provides information and news about teen sexuality, sexual health, and relationships.

http://www.youngwomenshealth.org, The Center for Young Women's Health site, sponsored by Children's Hospital in Boston, provides information on health issues that affect teenage girls and young women.

http://www.reproline.jhu.edu/english/1fp/1methods/1methods.htm, Reproductive Health Online: On methods.

http://www.reproline.jhu.edu/english/1fp/1special/1special.htm, Reproductive Health Online: On special circumstances.

For Health Professionals

http://www.acog.org, Information and resources from the American College of Obstetricians and Gynecologists.

http://www.ago-usa.org/index.html, Information and resources from the Alan Guttmacher Institute, a nonprofit organization focused on reproductive health research, policy analysis, and public education.

http://www.arhp.org, Information and resources from the Association of Reproductive Health Professionals, an interdisciplinary organization that fosters research and advocacy to promote reproductive health.


http://www.cochrane.org/cochrane/cochrane/cochrane/ctdr.htm, Access to the Cochrane database of systematic, evidence-based reviews of controlled clinical trials.

http://www.conrad.org, Contraceptive Research and Development Program site provides general information on birth control methods, updates on ongoing research projects, and provides information on contraceptive technology workshops.

http://www.fhi.org, Family Health International's site provides information on AIDS/HIV, STDs, family planning, reproductive health, and women's studies.

http://www.ncbi.nlm.nih.gov/PubMed, National Library of Medicine search service to access the 9 million citations in MEDLINE and other related databases, with links to participating online journals.

http://www.reproline.jhu.edu, The Reproductive Health Online site, which is based at The Johns Hopkins University, provides information on family planning and selected reproductive health issues.

REFERENCES AND ADDITIONAL READINGS


Combination hormonal contraceptives are agents that include both estrogen and progestin. In general, the progestin component provides contraception (primarily by cervical mucus thickening and ovulation suppression), and the estrogen component provides cycle control. Today, several forms of combination hormonal contraception are available in the United States: oral contraceptive (OC) pills, the combination hormonal contraceptive injections, combination hormonal vaginal rings, and combination hormonal contraceptive patches. Progestin-only pills are also discussed in this chapter.

**ORAL CONTRACEPTIVES**

Oral contraceptives (OCs) are the most widely used method of reversible birth control in the United States. With more than 40 years of successful use in this country, considerable professional confidence has developed in the safety and efficacy of OCs, and a growing appreciation is building among health-care providers for the extensive noncontraceptive benefits they offer. However, public understanding of these issues lags considerably. Until recently most Americans could not name a single noncontraceptive benefit of the pill; today many women are at least aware of acne treatment and cycle control. However, many women remain concerned about the safety of the pill. These public (mis)perceptions directly influence patient compliance and continuation rates. Much of the circulating misinformation results from a failure to understand the difference between the effects of earlier pills and those of more modern formulations. A brief review of the history of the pill can be instructive in clarifying these issues.

**History of Oral Contraceptives**

In 1960, the U.S. Food and Drug Administration (FDA) approved the birth control pill for contraception. The first pill approved, Enovid, contained 150 µg of estrogen (mestranol) and 9.8 mg of progesterin (norethynodrel). By the time the pill was approved in this country, physicians in Europe had had several years of experience with virtually unrestricted use of these high-dose pills, and they were soon to gain a few years’ experience with pills with slightly lower doses. By 1967, reports from the Royal College of General Practitioners began to emerge linking pill use with deep venous thrombosis, pulmonary emboli, stroke, and myocardial infarction (MI). Within a very short period, follow-up studies reported that the risk of serious complications was markedly increased in older women and indicated that there was an increase in risk with duration of OC use.

From these studies came the advice that women older than 35 to 40 years of age should be discouraged and that the body should be periodically given a “rest” from sex steroids. It has taken decades to conclusively demonstrate that these conclusions and advice were flawed. Early in the history of OC pills, no restrictions were placed on the patients who were pill candidates. Women with uncontrolled hypertension or histories of MI or thrombotic disorders used these high-dose pills. Because the incidence of many of these disorders increases with age, older women tended to have a higher incidence of serious complications with OC use. The duration-of-use effect that was reported in the early studies is now understood to have been a dose response. English women in 1967 who had used OCs for several years had, perfecr, been taking high-dose pills because lower-dose ones were not introduced overseas until early in the 1960s. Women who had been using pills for shorter periods had been given the newer, lower-dose pills. The problems the “longer users” were having should have been attributed to the higher-dose pills they were using. Today, it is recognized that modern low-dose birth control pills are safe and effective, but there are at-risk women who need to be identified and kept from using pills.

**Current Formulations**

The doses of the sex steroid components of the OC pills have been dramatically reduced over four decades without significantly sacrificing efficacy. All pills with more than 50 µg of estrogen have been removed from the market. The hormones used in birth control pills in the United States include an estrogen component and a progestin component:

1. Estrogen component: All combination OCs contain one of two synthetic estrogens, mestranol or ethinyl estradiol (EE), as diagrammed in Fig. 43.1. These two estrogens differ by only a methyl group at the C-3 site. Mestranol must be hepatically cleaved into EE; 50 µg of mestranol is approximately equivalent biologically to 35 µg of EE. There is no clinical indication for mestranol-containing pills. Most combination pills prescribed today contain 30 to 35 µg of EE, although formulations with 20 µg or 25 µg of EE are increasing in popularity. Formulations with 50 µg of EE are reserved for women with special conditions and those using medications that increase hepatic sex steroid clearance, such as anticonvulsants.
2. Progestin component: All pills in the United States today have one of seven synthetic progestins: norethindrone, norethindrone acetate, ethynodiol diacetate, norgestrel, levonorgestrel, norgestimate, and desogestrel. Each progestin is derived from androgens and produces both progestational and androgenic effects. In many instances the latter can be interpreted as antiestrogenic. Fig. 43.2 diagrams these progestins. One pill contains drospirenone, an antimineralocorticoid derivative of spironolactone.

An extensive array of formulations (Table 43.1) has evolved over the years in an attempt to meet the needs of women with individual sensitivities to particular sex hormone combinations and strengths. U.S. pills are packaged in one of three patterns:

**TABLE 43.1. Oral contraceptive formulations currently available in the United States**

1. Monophasic packets: Each of the 21 active-ingredient pills has the same dose of estrogen and progestin.
2. Multiphasic packets (biphasic or triphasic): The active-ingredient pills vary in strength of the estrogen and progestin components throughout the 21-day (active pill) cycle. In most of these, the progestin progressively increases in dose; however, one formulation holds the dose of progestin constant and increases the estrogen dose over the cycle.
3. Progestin-only or minipill packets: Each pill contains a small dose of a progestin. No estrogen is included in the pills.

In addition to the variation in active pill components, packaging also differs. The combination pills are available in 21-pill packages and in 28-pill packages with 21 active pills and 7 placebo pills (sometimes including iron). One formulation has 21 estrogen/progestin pills, 2 placebo pills, and 5 more pills with 10 µg of EE. The progestin-only pill packages contain no placebo pills; one active pill must be used each day.

Finally, there is variation in the way pills may be taken: 28-day cycles, first day start, multicycling, or continuously (see later discussion).

**Efficacy for Contraception**

The typical-use first-year failure rate for combination OCs is 5%–8% in all age groups, although the failure rate with correct and consistent use is less than 1%. The typical-use failure rate in adolescents is 8%. Progestin-only pills have typical-use failure rates of up to 9%.

**Noncontraceptive Benefits**

**Menstruation-related Benefits** Cyclically administered combination OCs significantly reduce monthly menstrual blood loss, the number of days of bleeding, and dysmenorrhea. Mittelschmerz is markedly reduced because ovulation is inhibited in all but a small proportion of cycles. Women with anovulatory cycles or dysfunctional uterine bleeding—common problems for adolescents—achieve predictable, controlled cycles with the use of OCs (Davis et al., 2000). Women who are taking medications that increase menstrual blood loss (e.g., anticonvulsants, anticoagulants) benefit from OC use. Women who have bleeding diatheses also benefit from suppression of ovulation, which reduces their risk of internal hemorrhage each month.

More creative applications of birth control pills, such as extended use of monophasic active pills (“bicycling,” “tricycling,” or continuous use), can provide important benefits to women who suffer exacerbations of their medical problems during menses. For example, women who have menstruation-related migraine headaches, catamenial seizures, or worsening of asthma with menses can eliminate those problems by eliminating the placebo pills and avoiding hormone withdrawal. Flexibility in pill use can allow women to control when they have their menses. Health care providers have used OCs to avoid onset of menses while a patient is on her honeymoon; these same techniques can prevent menses from overlapping with other important events in young women’s lives. Two monophasic formulations with 84 active pills to provide 3-month cycling are now in clinical trials.

Dysmenorrhea is a particularly important problem faced by adolescent women (see Chapter 50). It is the single greatest reason that women younger than 25 years of age miss days of school and work. This disabling pain inflicts considerable suffering and compromises a woman’s productive potential. With combined continuous OC
Anemia is reduced because menstrual blood loss is diminished by OC use. This can benefit women with sickle cell disease and those with iron deficiency.

Hypothalamic Hypoestrogenism

Many adolescents have eating disorders (e.g., anorexia nervosa, bulimia), excessive exercise programs, and/or stresses that suppress gonadotrophin production and create a hypoestrogenic state. The lack of estrogen in a teen can compromise bone mineral density accumulation and put her at risk for severe osteoporosis and fracture at an early age. Although it is vital important to deal with the underlying problems that cause hypoestrogenism, it is also critical to supply adequate estrogen to preserve bone health. In most circumstances, the physiological replacement doses of estrogen used in postmenopausal women are not adequate to treat an adolescent woman’s need for estrogen to build bone mineral density. Birth control pills are the mainstay of therapy (Hergenroeder et al., 1997). However, because menses are perceived to reduce athletic performance, many coaches oppose OC use unless the pills can be used in continuous fashion to ensure amenorrhea.

Ovarian Carcinoma

OCs are the only reversible contraceptive method for which there is strong epidemiological support demonstrating that its use reduces the risk of developing ovarian cancer later in life. Women who have ever used OCs reduce their risk of developing epithelial ovarian cancer by 40%. Long-term users (more than 10 years) have an 80% reduction in risk. This effect endures for more than 15 years after the last pill. Importantly, ovarian cancer protection is most clearly demonstrated in young women, just as childbearing and breast feeding reduce ovarian cancer risk only if they occur before 30 years of age. A case-controlled study suggested that carriers of the BRCA1 genetic mutation also experience a reduction in ovarian cancer with OC use (Narod et al., 1998). They mechanisms have been postulated to explain this risk reduction: the inhibition of “incessant ovulation” and the increased success of follicular cell apoptosis.

Endometrial Cancer

OC use at any time during the reproductive years significantly reduces a woman’s risk of developing any of the three major histologic forms of endometrial carcinoma by providing progestin. This protection increases with longer duration of use; women who use OCs for 12 years reduce their risk of endometrial carcinoma by 72%. This protection endures 19 years beyond the last pill use (Schlesselman, 1995). Women with anovulatory cycles achieve the greatest risk reduction.

Mechanisms of Action

1. Thickening of cervical mucus: The progestin component produces thick, viscous, scanty mucus that blocks sperm penetration. This is the single most important action of all hormonal methods of contraception.
2. Inhibition of ovulation: The progestin-only pill has such a low dose of progestational activity that ovulation is inhibited in only 40% to 60% of cycles. The combination pill, however, contains higher doses of progestin as well as estrogen, which suppresses ovulation in 95% to 98% of cycles by inhibiting the surge in luteinizing hormone (LH). With the combination pill, levels of follicle-stimulating hormone (FSH) are decreased to 70% of normal; LH levels are only 20% of those found in women who are not taking OCs.
3. Endometrial changes: The presence of a progestin early in the cycle induces a thin endometrium with atrophic glands and minimal glycogen stores, which is not conducive to implantation.
4. Slowed tubal motility: The progestin in the pill slows tubal motility and disrupts the carefully orchestrated sequence of events necessary for successful fertilization and impregnation.

Metabolic Impacts

Metabolic effects of oral contraceptives. Coagulation Factors Factors associated with the extrinsic pathway (fibrinogen and factors I, V, VII, VIII, and X) are uniformly increased by estrogen-containing birth control pills in proportion to their estrogen dose. Balancing this increase in virtually all women is a compensatory increase in fibrinolytic and anticoagulation factors. The clinical significance of these changes is discussed later in the section on thromboembolism. Binding Globulins Estrogen increases hepatic synthesis of carrier proteins such as albumin, SHBG, thyroxine-binding globulin, and corticosteroid-binding globulin, which affects the interpretation of laboratory tests and also has clinical implications. Increased levels of SHBG bind more free testosterone and, with time, reduce androgen-related problems such as hirsutism and acne (see earlier discussion). The effect of the progestin depends on its androgenicity and dose; more androgenic formulations may blunt the increase in hepatic synthesis of SHBG. Angiotensinogen The estrogen component of the combination birth control pill increases hepatic production of renin, which then is serially converted to angiotensin. Angiotensin can cause reversible hypertension in vulnerable patients. However, angiotensin sensitivity is difficult to predict. Women with a history of pregnancy-induced hypertension are not as a group at increased risk for development of increased blood pressure while using OCs. However, women who have
Lipid Metabolism

Estrogen increases total cholesterol, high-density lipoprotein (HDL) cholesterol, and triglycerides while decreasing low-density lipoprotein (LDL) cholesterol. The androgenic component of the progestin has the opposite effect. The net impact on lipids, therefore, depends on the hormonal composition of the pill. The newer progestins, designed to have greater selectivity for progestin receptors, have less of an androgenic impact. In combination with estrogen, they may cause no change in LDL. Triglyceride levels are increased by exogenous estrogen use. Many lipid experts claim that these estrogen-induced so-called “fluffy” triglycerides are not conducive to plaque formation, but they may pose a problem if a patient has baseline elevated triglyceride concentrations near the pancreatic islets range. Older progestins at lower doses also have minimal impacts on lipid metabolism. At higher doses some of the older, more potent progestins have a slightly adverse impact on HDL/LDL ratio. Whether these alterations should cause concerns about increased risks for cardiovascular disease has been questioned by data from experiments showing that dyslipidemia in female monkeys given OCs was not accompanied by any increase in coronary artery plaque size (Clarkson et al., 1990). However, until human data are more firmly established, patients with dyslipidemia should be offered appropriate formulations and should be monitored.

Glucose Metabolism

Both of the sex steroids have been implicated in influencing glucose metabolism: estrogen may suppress insulin response, and progestins can increase peripheral insulin resistance. With higher hormonal doses, older formulations of birth control pills were noted to cause a deterioration in glucose tolerance in a minority of patients. Most studies have found that modern formulations with lower hormonal doses cause no impairment in glucose tolerance in euglycemic women, but some remnant of insulin resistance remains (Godsland and Crook, 1994). In a prospective study of women with a history of gestational diabetes who used low-dose OC pills, Kjos et al. (1998) reported no acceleration in glucose intolerance or overt diabetes compared with similar women using nonhormonal contraceptives. OC use in overt diabetics rarely changes insulin requirements and has been shown not to increase the risk of diabetic nephropathy or retinopathy. OCs do not cause a hyperthyroid or hypothyroid state. Other proteins that bind to hormones (cortisol binding globulins, albumin) also circulate at higher levels and can similarly confuse test interpretation unless unbound hormone levels are tested.

Contraindications (From Labeling)

1. History of cholestatic jaundice or jaundice with prior pill use
2. History of thromboembolism (or thrombophilia)
3. Cerebral vascular or coronary artery disease
4. Known or suspected cancer of the breast or endometrium or other estrogen-sensitive neoplasm
5. Hepatic tumor (benign or malignant)
6. Unexplained abnormal vaginal bleeding
7. Known or suspected pregnancy
8. Exclusive breast feeding
9. Postpartum (less than 3 weeks)

Note: Clinical deviations and clarifications include the following:

1. Women who are currently anticoagulated after deep venous thrombosis, pulmonary embolism, or mechanical cardiac valve placement may be candidates for OC use. OCs should be stopped 1 month before anticoagulation is discontinued.
2. Women with non–estrogen-dependent tumors, such as cervical tumors, may benefit from use of OCs during evaluation and treatment.
3. Once the cause of abnormal vaginal bleeding is established (e.g., fibroids, adenomyosis), OCs can often be used to control the bleeding.

Relative Contraindications

1. Undiagnosed breast nodules or abnormal breast examination
2. Diabetes with evidence of end-organ damage
3. Elevated cholesterol or triglycerides (because triglycerides increase with OC use, women with baseline triglyceride levels near the pancreatic range should probably avoid estrogen-containing OCs)
4. Migraine, mainly migraines with focal neurological symptoms or signs (menstruation-related migraines may be an indication for continuous OC use)
5. Gallbladder, heart, or kidney disease
6. Mental depression (especially if the patient is suffering an acute exacerbation, has suicidal ideation, or is otherwise uncontrolled in her disease)

Drug Interactions

Because estrogen and progestin are hepatically cleared, any drug that induces cytochrome P-450 microsomal enzyme activity reduces circulating hormone levels and can potentially compromise OC efficacy. Drugs in this class include anticonvulsants such as phenobarbital, phenytoin, troperimate, and carbamazepine. Rifampin increases hepatic clearance of sex steroids and can also raise transaminase levels. OCs should be used cautiously with griseofulvin. Preliminary studies suggest that St. John’s wort may halve the circulating levels of sex steroid hormones.

Earlier authors warned that use of antibiotics could reduce OC efficacy by preventing sex steroid absorption from the intestines. However, studies with broad-spectrum antibiotics (ampicillin and tetracycline) demonstrated that these antibiotics do not affect cervical mucus or ovulation suppression (Friedman et al., 1980) and do not decrease serum levels of either estrogen or progestin. The sex steroids do not effect circulating antibiotic levels (Murphy et al., 1991). Routine use of backup methods with antibiotics is not warranted.

Impact on Laboratory Tests

A major alteration in clinical laboratory tests that the clinician should be aware of is related to the increase in thyroxine-binding globulin resulting from exogenous estrogen. This causes a rise in total thyroxine. However, adjusted thyroxine and free thyroxine (T₄) and triiodothyronine (T₃) are normal.

Impact on Thromboembolic Events

The first-year relative risks of serious side effects associated with OC use in the past face at least a 10% risk of recurrence.

Thromboembolism

Estrogen-containing OCs increase hepatic production of extrinsic clotting factors. Some women, such as those with the factor V Leiden mutation, are unable to compensate for this increase in clotting factors and may be subject to an increased risk for thromboembolic events. The overall RR of thrombosis is between 2.6 and 4.0; the absolute incidence of venous thrombosis is 15 to 30 per 10,000 women-years for most of the low-dose formulations. The first-year relative risks of
venous thromboembolism are even higher, but these rates are still lower than the incidence of venous thromboembolism in pregnancy (about 60 per 100,000). Reports in the mid-1990s that third-generation progestins (desogestrel and gestodene) may have had more profound thrombotic impacts (three 1995 articles from the World Health Organization [WHO 1995a, 1995b, 1995c]) were questioned by later analysis, which controlled for selection bias (Lewis, 1999). The fact that venous thromboembolism rates in the United Kingdom increased after the market share of the third-generation OC formulations decreased from 40% to 5% suggests the lack of increased risk with third-generation progestins. Labeling reflects the uncertainty of the data. However, the controversy did highlight the need to identify women at risk of venous thromboembolism when taking OCs, not only on the basis of a personal history of prior clots, but also by inquiring about a possible history of multiple family members with multiple unexplained clots at an early age. Routine laboratory screening of all potential OC candidates for coagulopathies, such as factor V Leiden mutation, is inappropriate because it is clearly not cost-effective and because today’s testing can identify only 60% of at-risk women. The recommendation to stop OC use 1 month before any scheduled surgery has been tempered to reflect modern surgical practices; OC use may not need to be interrupted if a low-risk patient is not expected to require prolonged postoperative bed rest.

Studies with low-dose formulations have detected no overall increased risk of hemorrhagic or ischemic stroke with OC use, but one study did find that women reporting a history of migraine headaches doubled their risk of stroke with OC use (Schwartz et al., 1998). Analysis of the Transnational Research Group study concluded that the attributable risk of occlusive stroke for healthy OC users is very small and is overwhelmed by other risk factors such as hypertension and smoking (Heinemann et al., 1998).

**Cardiovascular Disease** There is no consistent pattern associating the use of low-dose OCs with any increase in the risk of MI for healthy, nonsmoking women. Several-large-scale, controlled studies have demonstrated no increased risk of heart attack or death from MI in OC users younger than 45 years of age compared with controls. For example, in the 6-year Puget Sound study of 10,000 healthy OC users and 30,000 healthy controls age 15 to 44 years (Porter et al., 1987), there were no heart attacks among OC users or only one among the controls. Only 1 OC user and 14 controls had a stroke. The Finnish study of low-dose OC users versus controls (Hirvonen and Itänpää-Heikkilä, 1990) found an 80% reduction in the RR of death from cardiovascular disease in OC users.

Analyses in the mid-1990s found somewhat conflicting results concerning the relationship between OC use and MI. The WHO multicenter study found a fivefold increased risk of acute MI in current OC users, but most affected women had not been screened for risk factors; the odds ratio dipped to 2.6 in women who had had their blood pressure checked before being prescribed OCs (WHO 1995c). On the other hand, the Transnational Study found an odds ratio of 2.35 among current users of second-generation progestin-containing OCs compared with community and hospital control cases, whereas the third-generation progestins were associated with an odds ratio of 0.82 (Lewis et al., 1997). In a population-based, case-control study at two sites in the Kaiser system, Sidney et al. (1996) found that current OC users had an adjusted odds ratio for MI of 0.56 (95% confidence interval [CI], 0.21–1.49) compared with nonusers, and they concluded that low-dose OCs used in appropriate populations were safe with respect to MI. The latest and largest study (448 cases) showed an odds ratio for MI of 1.40 (95% CI, 0.78 to 2.52) for all combination OC users, indicating no statistically significant increased risk. Furthermore, there was no increase in cardiovascular risk with duration of use or by type of progestin (Dunn et al., 1999).

There are clearly identified groups of at-risk women. Smokers at all ages have increased risks for cardiovascular disease when they use OCs. In the study of Dunn et al. (1999), the adjusted odds ratio for MI in OC users who smoked 20 or more cigarettes per day was 12.5 (95% CI, 7.3 to 21.5). Schwingl et al. (1999) estimated that the attributable risk of death from cardiovascular disease resulting from OC use is 0.06 per 100,000 nonsmokers age 15 to 34 years. In smokers, this risk rises to 1.73 per 100,000. However, the absolute risk for death with OC use in smokers is less than the risk of death with pregnancy until women are 35 to 40 years old. Smoking cessation should always be promoted with teens who smoke, but they do not need to avoid pill use while they continue to smoke. Selection of a low-androgenic formulation may be prudent for smokers (Straneva et al., 2000), as would shortening the pill-free interval.

**Hypertension** Up to 3% of OC users experience increased blood pressure while using birth control pills. Estrogen is responsible for this increase via augmented levels of angiotensinogen. Progestin has been peripherally implicated through its impacts on fluid retention. The increases in both diastolic and systolic measures are usually reversible within 3 months. If the hypertension does not spontaneously resolve, then other causes must be considered. The need for initial therapy depends on the severity of the hypertension.

**Liver and Gallbladder Effects** A doubling of the risk of gallstones has been suggested by several prospective and retrospective studies. Although the risk is more impressive with higher-dose pills, it is still apparent with the lower-dose formulations. Cholelithiasis is secondary to increased cholesterol saturation and biliary stasis. The risk appears to be concentrated in a few short-term users who may be prone to gallbladder disease.

Cholestatic jaundice is very rare, but it has been reported as a result of OC pill use. Pruritus similar to that seen in pregnancy may develop with OC use.

**Impact of Oral Contraceptive Use on Neoplasia** The single largest concern women voice about OC use is the risk of cancer. Almost one third of all women believe that OCs cause cancer, but only a small minority is aware that OC use decreases the incidence of ovarian and endometrial cancer. Table 43.3 summarizes the current data about OC use and neoplasia. A few of the more pertinent neoplasms for adolescents are discussed here.

---

**Leiomyoma** Historically, there has been concern that OC use might stimulate growth of leiomyomas (fibroids), because leiomyomas are known to be estrogen-sensitive tumors. Chiaffarino et al. (1999) found in a case-controlled study of 843 women with fibroids that the risk for current users of OCs was lower than for those who had never used OCs (RR, 0.3; 95% CI, 0.2 to 0.6). The risk of uterine fibroids decreases with duration of OC use. Marshall et al. (1998) also reported a reduction in risk of fibroids in current OC users; however, he noted a higher risk (RR, 1.26; 95% CI, 1.05 to 1.51) for development of clinically diagnosed fibroids in nurses who started using OCs at age 13 to 16 years, compared with never-users. This should not deter OC use by adolescents, because this association may reflect an age effect of menarche, which is itself a risk factor for fibroids. Furthermore, the magnitude of the risk in young users is modest. Women who have existing fibroids often are successfully prescribed OCs to reduce their menorrhagia.

**Endometrial Hyperplasia and Cancer** Epidemiological data are very persuasive that use of combination OC pills significantly reduces the risk of endometrial hyperplasia and cancer by preventing unopposed estrogen stimulation. There is a clear duration effect (Schlesselman, 1995). For this reason, it is important to offer teens who have oligomenorrhea progestin-containing hormones to reduce their risk of developing endometrial cancer later in life. OCs with low doses of progestin are quite adequate, especially in women with polycystic ovary syndrome, who also benefit greatly from pharmacological doses of exogenous estrogen.

**Ovarian Epithelial Carcinoma** Epidemiological studies show that the longer a woman uses OCs, the more significant is the reduction in her risk of developing epithelial ovarian cancer; 10 years of use reduces lifetime risk by 80%.

**Cervical Cancer** Early studies that linked OC use with cervical cancer were confounded by design flaws and biases, including inappropriate control groups. It is clear that OC use causes a slight increase in the risk of cervical dysplasia. However, the risk for squamous cell carcinoma does not appear to be affected by OC use. The
risk of adenocarcinoma of the cervix may be increased, although this has not yet been conclusively demonstrated. OC users do not require any more intensive or more frequent Pap smears than their relevant risk factors (e.g., number of sexual partners, exposure to human papillomavirus, smoking) would routinely indicate.

**Breast Cancer** In contrast to the obvious benefits OCs have in reducing the risks of endometrial and ovarian cancer, the impact of OCs on breast cancer has been more controversial. In humans, there is no evidence that either estrogen or progestin can initiate the development of abnormal mitotic figures in normal breast cells. However, breast cancer cells do divide more rapidly in the presence of estrogen.

Epidemiological studies of present and past OC users have presented conflicting results, but virtually all the risk ratios for breast cancer calculated in these studies show either no increased risk or a small, short-lived, and reversible increased risk. One particular exception is the study by Pike et al. (1983), which found an unequivocal increase in breast cancer in a very special subgroup of women younger than 25 years of age who had used OCs with high-dose gestagens (such as those used in the 1960s) for more than 5 years. In that same study, however, no increased risk of developing breast cancer was found in a group of similar women who had lower-dose OCs.

The Cancer and Steroid Hormone (CASH) study of the Centers for Disease Control and Prevention (CDC) found no overall increase in breast cancer with OC use (CDC, 1983), but in young women who used the pill the risk of development of breast cancer by the age 35 years was raised by 2 to 3 cases per 100,000 women (CDC, 1984). Importantly, these researchers investigated several high-risk groups and found that OC use was not associated with an increased incidence of breast cancer in the following important subgroups: (a) women with a family history of breast cancer, (b) women with and without benign breast disease, and (c) women who started using OCs before their first pregnancy.

The Collaborative Group on Hormonal Factors in Breast Cancer meta-analysis of 54 studies from 23 countries (1996) reported that current users and women who had used OCs within the previous 10 years had a slightly increased risk of developing breast cancer (RR, 1.24; 95% CI, 1.15 to 1.33). Women who started OC use before 20 years of age had an even higher increase in risk when they were current or recent users. However, the magnitude of this increased risk was minimal; the estimated excess numbers of cancers diagnosed up to 10 years after stopping use was 0.5 per 10,000 women. The risk was reversible; no group displayed any increased risk 10 years after stopping OCs. No duration of use effect was seen. More importantly, the increase in breast cancer was concentrated in the development of localized disease; in fact, the meta-analysis demonstrated that the risk of metastatic breast cancer with lower-dose pills was not increased among current or recent OC users.

Grabrick et al. (2000) studied 394 first-degree relatives and 3,002 other relatives of women who were diagnosed with breast cancer between 1944 and 1952. Use of pills before 1975 (higher-dose pills) was associated with an increase in breast cancer only among first-degree relatives (RR, 3.3; 95% CI, 1.6 to 6.7). Other relatives had no increased risk with any pill formulation. Importantly, modern, lower-dose pills were not found to have any association with breast cancer risk, either because of lack of risk or because of insufficient follow-up time.

Based on all of these studies, it is not appropriate to deny an adolescent hormonal contraceptive because she has fibrocystic breast changes or a family history of breast cancer, unless the patient has a strong family history of breast cancer, including (at a minimum) one affected first-degree relative. Even that latter setting is, at most, a relative contraindication for the use of modern, low-dose pills.

**Advantages**
1. Safe, effective contraception
2. Relatively easy method (once a day)
3. Taken at a time independent of coitus
4. Rapidly reversible method
5. Many noncontraceptive health benefits (see earlier discussion)

**Disadvantages**
1. Daily administration required
2. Side effects (see later discussion)
3. Counseling on safer sex practices required
4. Post-pill amenorrhea

**Side Effects**
As described earlier, the sex hormones in OCs have various degrees of progestogenic, estrogenic, antiestrogenic, and androgenic activity. These differences are important to understand, especially when responding to a patient's concerns about side effects. The impacts of the relative potencies of different formulations vary from individual to individual.

The prospective, double blinded, placebo-controlled studies that were conducted to evaluate the role of the triphasic, nonoestrogen-containing birth control pills in treating acne provided a unique opportunity to evaluate the incidence of side effects (Redmond et al., 1999). In the 6-month study period, the placebo group had approximately the same incidence of headache, nausea, mastalgia, and other side effects generally attributed to OCs, as the OC group did. Even weight gain was almost identical (2.1 versus 2.2 pounds). This neutrality on weight had earlier been demonstrated by Reubinoff et al. (1995), who also reported that users of low-dose OCs did not change body composition or fat distribution. However, there are women with particular sensitivity to sex steroids. They may experience side effects either as a result of the pharmacological doses of hormone or because of hormonal imbalances. Many side effects are temporally self-limited and resolve spontaneously in the first few cycles, but sometimes women require a change of pill formulation. When these side effects arise, it is important to analyze them by their constituent hormones and to evaluate the incidence of side effects (Table 43.4). Additional changes result from interactions among the constituent hormones. For some problems, there are at least two possible approaches: increase one component or decrease the other.

**Management of Common Side Effects**
1. **Breakthrough bleeding:** Typically, 20%–25% of women experience irregular spotting or bleeding during the first three cycles. The incidence of breakthrough bleeding with the more recent ultra-low-dose (20-µg) formulations containing levonorgestrel or desogestrel is roughly comparable to that of 30- to 35-µg pills, although an earlier 20-µg formulation containing low-dose norethindrone did have higher rates (DelConte et al., 1999; Rosenberg et al., 1999; Sulak et al., 1999). The possibility of other causes of vaginal spotting or bleeding must be entertained for adolescent women. Chlamydiae cervicitis is a common cause of postcoital bleeding. Inconsistent pill use also commonly causes breakthrough bleeding or spotting. Smokers have notably more challenges with breakthrough bleeding. Treatment for persistent spotting due to OCs in the face of appropriate pill use depends on the timing of spotting within the woman's cycle (Table 43.4).
Acne, hirsutism, and noncyclic generalized progressive weight gain: These symptoms may be caused by the relative increase in free androgens. Approaches include the following.

1. Increase the estrogen content, which will increase SHBG and reduce the level of unbound testosterone.
2. Decrease the progestin dose or switch to a formulation with a less androgenic progestin.
3. Chloasma or melasma: These symptoms are caused by estrogen stimulation of melanocytes. In this situation, it would be prudent to decrease (or eliminate) estrogen content and advise the use of sunscreen and hats.

Coping with Missed Pills

Package labeling for all birth control pills offers the following standard advice about how to manage missed pills:

WHAT TO DO IF YOU MISS PILLS

If you MISS 1 “active” pill:
1. Take it as soon as you remember. Take the next pill at your regular time. This means you may take two pills in one day.
2. You do not need to use a backup birth control method if you have sex.

If you MISS 2 “active” pills in a row in WEEK 1 or WEEK 2 of your pack:
1. Take two pills on the day you remember and two pills the next day.
2. Then take one pill a day until you finish the pack.
3. You MAY BECOME PREGNANT if you have sex in the 7 days after you miss pills. You MUST use another birth control method (such as condoms or spermicides) as a backup for those 7 days.

If you MISS 2 “active” pills in a row in the THIRD WEEK:
1. If you are a Day 1 Starter, THROW OUT the rest of the pill pack and start a new pack that same day. If you are a Sunday Starter, keep taking one pill every day until Sunday; on Sunday, THROW OUT the rest of the pack and start a new pack of pills that same day.
2. You may not have your period this month, but this is expected. However, if you miss your period 2 months in a row, call your doctor or clinic because you might be pregnant.
3. You MAY BECOME PREGNANT if you have sex in the 7 days after you miss pills. You MUST use another birth control method (such as condoms or spermicides) as a backup for those 7 days.

If you MISS 3 OR MORE “active” pills in a row (during the first 3 weeks):
1. If you are a Day 1 Starter, THROW OUT the rest of the pill pack and start a new pack that same day. If you are a Sunday Starter, keep taking one pill every day until Sunday; on Sunday, THROW OUT the rest of the pack and start a new pack of pills that same day.
2. You may not have your period this month, but this is expected. However, if you miss your period 2 months in a row, call your doctor or clinic because you might be pregnant.
3. You MAY BECOME PREGNANT if you have sex in the 7 days after you miss pills. You MUST use another birth control method (such as condoms or spermicides) as a backup for those 7 days.

If you forget any of the seven “reminder” pills in WEEK 4:
1. THROW AWAY the pills you missed.
2. Keep taking one pill each day until the pack is empty.
3. You do not need a backup method.

FINALLY, IF YOU ARE STILL NOT SURE WHAT TO DO ABOUT THE PILLS YOU HAVE MISSED:

1. Use a BACKUP METHOD (such as condoms or spermicides) anytime you have sex.
2. KEEP TAKING ONE ACTIVE PILLS EACH DAY until you can reach your doctor or clinic.

Emergency Contraception for Missed Pills

It is also important to remember to offer EC if the woman had unprotected intercourse within the first 3 days before missing one or more pills. The most vulnerable period for pregnancy in this context is when a woman misses pills at the beginning of a cycle. This increase in the pill-free interval permits maturation of the follicle. However, EC can be added at any time pills are missed if the woman is not certain about her pill-taking earlier in the cycle if she is quite concerned about pregnancy. If the woman had unprotected intercourse within 3 days before missing her pill, start her first dose of EC as soon as possible; have her take the second dose of EC 12 hours later, and then resume usual pill-taking with the next day's pill. She can discard her missed pills. Use of a backup method is generally recommended for 7 days after pills are missed, as specified on the package labeling.

Increasing Adolescent Compliance

Adolescent compliance with contraceptive methods is often suboptimal; however, adult compliance is also far from perfect. In one San Francisco study, fewer than 20% of adult women reported that they took pills every day at approximately the same time for 6 months (Oakley et al., 1991). Electronic monitors in pill packs reflected an even greater problem with utilization; in the third cycle, more than half of women missed more than two pills (Potter et al., 1996). This work questions the practice of starting women on a 30-35-µg monophasic formulation for the first 3 months, suggesting that lower-dose formulations should be offered after they have learned to incorporate pill-taking into their daily lives. If a woman is thought to be a candidate for an ultra-low-dose or triphasic formulation, there is no reason why she should not be started on that formulation initially.

Many factors play important roles in compliance. Studies of high-risk teen mothers found a 50% discontinuation rate by 12 months (Berenson and Wiumann, 1995). The desire of teens for independence and seeming invincibility decreases their motivation to use contraception. The unpredictability and frequent disruptions in their relationships cause them to frequently stop contraception. Many adolescents are receiving incorrect information from sex education teachers in American schools (Davis, 1994): this misinformation about OC affects the effectiveness of the method and also reduces compliance.
To enhance compliance, experts have suggested several measures:

1. **Emphasize the noncontraceptive benefits of OCs.** Robinson et al. (1992) found that adolescent women who experienced reduction in dysmenorrhea with OC use were eight times more likely to be consistent OC users.
2. **Demonstrate concretely how to use the pills.**
3. **Have the patient explicitly discuss her concerns about pill use so that they can be addressed.** Widespread myths about the dangers of OCs abound and can magnify the significance of a minor side effect in the mind of a young user.
4. **Help the teen plan for crucial logistics, such as where to store the pills (school lockers don’t work on weekends) and how to remember to take the pills each day (placing them next to makeup or an earing holder may work better in the real world than placing them near the tube of toothpaste).**
5. **Start the pills on the first day of bleeding (no backup method is needed), or consider starting pills immediately if pregnancy can be ruled out, to simplify instructions, and use a barrier method as backup for first cycle.**
6. **Shorten the pill-free interval.** Start each new pack of pills on the first day of menses. Or eliminate the pill-free interval for several packs (“bicycling,” “recycling,” or “combination continuous use”).
7. **If the patient is unable to take daily pills, use a longer-acting product such as the injectable hormonal contraceptive.**

**Special considerations in adolescents:**

1. **When to start:**
   a. **Young users:** Ideally a teen would have at least three to six regular periods after menarche before starting the pill. However, if a young menarchal teen is sexually active, the risks of pregnancy exceed those of taking hormonal contraceptives; there is no evidence that the early use of OCs leads to premature epiphyseal closure or to any disruption in the maturation of the hypothalamic-pituitary-ovarian axis.
   b. **After pregnancy:** A first-trimester therapeutic abortion or miscarriage, the pill should be started immediately to prevent ovulation. After a pregnancy, a 3- to 4-week delay should be allowed before starting OCs, because of the risk of thromboembolism. However, progestin-only methods can be initiated immediately.
2. **If the teen has very irregular cycles,** she should be informed that her cycles are likely to be regular while she is using the pills but will return to their usual, irregular intervals when the pills are stopped, and also that her menses may not return for some time after discontinuation. However, there is no evidence that the teen’s fertility rate will be any lower after she finishes the pills than if she had never used them.
3. **Initial examination:**
   a. **History:** Menstrual history, past history, risk factors for sexually transmitted diseases (STDs), history of problems that suggest any contraindications for use of the pill, and sexual and family histories.
   b. **Physical examination:** The optimal examination would include weight and blood pressure measurements, thyroid examination, breast examination, abdominal examination, and pelvic examination. However, only a blood pressure measurement and perhaps a breast examination are required to start pills. The pelvic examination may be deferred for 3 to 6 months at least (Stewart et al., 2001). This is particularly the case for women who are being prescribed OCs for noncontraceptive benefits and who may not be sexually active.
   c. **Laboratory tests:** A Pap smear and screening for Chlamydia are recommended for every sexually active teen. However, while each of these tests is recommended for well-woman care, they are not required for pill prescription.
   d. **Education:** Counseling is the most critical component of the visit.
4. **Follow-up:**
   a. It is preferable to see the teenager at 1 month and again at 3 months after starting the pill, and then every 6 months. The visit after 1 month is important, especially in younger teens, because more than 10% of women discontinue pill use during the first month because of minor side effects.
   b. **Check blood pressure at 3 months and then as indicated for well-woman care.**
   c. **Perform a breast and pelvic examination every 12 months for routine care.** Annual screening for Chlamydia is required for sexually active women younger than 25 years of age.

### Injectable Combination Hormonal Contraceptives

There is currently one injectable combination hormonal contraceptive available in the United States. **MPA/E** (Lunelle) is a 0.5-mL, once-a-month intramuscular injection containing 25 mg of medroxyprogesterone acetate (MPA) and 5 µg of estradiol cypionate (E₂C₄). The estrogen ester, E₂C₄, is cleaved in the bloodstream and circulates as estradiol, not ethinyl estradiol as used in OCs. The dose of MPA is lower than that found in the depot medroxyprogesterone acetate (DMPA) injectable.

This preparation was specifically designed by the WHO (1993) to close the gap between daily hormonal contraceptive administration and the once-every-3-months injection interval used overseas for almost two decades under names such as Lunella, CycloP, Luna, and Cyclo-Provera. It is more effective than other injectable compounds available overseas, such as Perlatol, Mesigyna, or Chinese Injectable No. 1.

**Usage**

1. **First injection:** The first injection of MPA/E₂C₄ is administered during the first 5 days of the menstrual cycle or within 7 days after a first- or second-trimester abortion, or 21 to 29 days postpartum if not breast feeding.
2. **Reinjection:** Reinjection is given every 28 ± 5 days—no earlier than 23 days and no later than 33 days after the prior injection.

**Method of Action**

The mechanisms of action for the monthly combination hormonal injection are the same as those of OCs. The progestin provides contraception, and the estrogen provides cycle control. Circulating levels of progesterin are high enough to suppress ovulation for up to 44 days. Estrogen levels support the endometrium for 2 to 3 weeks. Withdrawal bleeding is quite predictable; for each individual, bleeding starts at about the same time after each injection. The interval between injections determines the length of each menstrual cycle. Women need counseling to expect the first withdrawal bleed early (it is not breakthrough bleeding) and to time their reinjections by the calendar, not by their menses. Once women determine the interval between their injections and their next menses, they can control when they have their menses by timing their reinjections.

**Efficacy**

In U.S. comparative efficacy trials, none of the 782 users of MPA/E₂C₄ became pregnant, whereas 2 of the 321 users of triphasic norethindrone/ethinyl estradiol OCs became pregnant (Kaunitz et al., 1999). In international studies in Asia, Latin America, and the Middle East involving more than 16,000 women, the failure rate has been in the range zero to 0.2% (Shulman, 2000). Product labeling reports a first-year typical-use failure rate of less than 1%.

**Metabolic Impacts**

In the comparative clinical trials, the metabolic impacts were found to be quite similar to those of OCs. There was no change in hemoglobin, transaminase levels, bilirubin, creatinine, or glucose with either agent. Compared with OCs, MPA/E₂C₄ had less profound impacts on clotting factors; there was no increase in factor X activity, but there was a reduction in plasminogen and factor VIII activity and an increase in tissue plasminogen activator (t-PA) with MPA/E₂C₄ (Cromie et al., 2000). The impact on lipids was also favorable: LDL values were lower with MPA/E₂C₄, as were triglycerides. HDL impacts were variable: in the U.S. trials, HDL decreased (but less than with OCs), but in international studies no change in HDL was seen.

**Contraindications**

Although the intermediate markers of coagulation and lipids may be more favorable for the injectable, clinical experience has been accumulated in only tens of thousands of women. For rare events such as thromboembolism or MI, the impact of these biochemical differences is unknown. Therefore, the labeling for the estrogen-containing injections includes all the same contraindications as for estrogen-containing OCs. In addition, an allergy to any of the components of the
injectable is a contraindication to its use.

**Drug Interactions**

Drugs that increase hepatic enzyme activity may decrease efficacy of the monthly injections. Studies have not been conducted to provide reassurance about the efficacy of the injections with anticonvulsants or rifampin. However, there is no concern about the use of any interaction with broad-spectrum antibiotics.

**Advantages**

1. Safe, effective contraception
2. Convenient, once-a-month injection instead of daily administration
3. Rapidly reversible; return to fertility parallels that with OC use (Rahimy and Ryan, 1999; Bahamondes et al., 1997a).
4. Used at a time independent of coitus
5. Regular, predictable cycles
6. After 6 to 9 months of use, menstrual blood loss decreases
7. Private
8. Eliminates mittelschmerz
9. May be used by women who experience breakthrough bleeding with DMPA and by those who dislike amenorrhea
10. Well accepted by users; in U.S. clinical trials, 90% said they would recommend it to a friend (Shulman et al., 1999)

**Disadvantages**

1. Requires monthly injections
2. Usually available only from professional providers (physicians, pharmacists, clinics)
3. Requires counseling on safer sex practices
4. Side effects (see later discussion)

**Side Effects**

Side effects associated with MPA/E₂/C injections were found to be very similar to those experienced by new-start users of OCs in clinical trials. However, there were a few exceptions. Most women have predictable withdrawal bleeding, with fewer days of breakthrough bleeding and spotting than in OC users. Weight gain was greater in the injectable group, and 5.8% of women discontinued use of the injections for this reason. Although the range of weight change was quite dramatic in the 60-week trial (from a loss of more than 40 pounds to a gain of almost 60 pounds), the median weight gain with MPA/E₂/C was slightly more than 4 pounds the first year. Lighter women gained less weight than heavier women did. Breast tenderness and acne also were more frequently reported with injections than with pills.

**Increasing Compliance**

The clear advantage of injectable combination hormonal contraception is that efficacy is greatly enhanced by elimination of the need for daily administration. A more subtle advantage is that it works for longer than a month, which protects teens who are insured by plans that provide one 28-day pack of pills per month regardless of the number of days in the month.

The challenge will be to streamline office practices to allow rapid reinjection. Clearly, this can be done as a nurse-only visit; practitioner involvement is needed only for women with side effects or complications. In some areas of the country, pilot programs are testing the feasibility of having pharmacists provide reinjections in their stores. Self-injection is possible now in many states with proper training of patients for the intramuscular injection, but it would be much easier with a subcutaneous formulation, which may be developed in the future (Bahamondes et al., 1997b).

**VAGINAL RINGS**

The NuvaRing is a thin, flexible plastic ring, mixed with ethinyl estradiol and etonogestrel (a metabolite of desogestrel), that is placed in the posterior vaginal fornix within the first 5 cycle days and remains in place for 21 days. The ring is removed for 7 days to permit menses, and then a new unit is reinserted. The ring does not need to be removed for coitus, and cleaning is not indicated. Efficacy is at least comparable to that of OCs, and convenience is a clear advantage. Systemic side effects are diminished because serum hormone levels are less than half of those seen with OCs (Timmer and Mulders, 2000). In a comparative trial with a series of different hormonal formulations, rings were found to contribute little to epithelial lesions on colposcopy (Fraser et al., 2000).

**TRANSDERMAL PATCHES**

The Evra patch is a 20 cm² patch containing ethinyl estradiol and 17-diacetyl norgestimate (a metabolite of desogestrel), that is placed on the posterior vaginal fornix within the first 5 cycle days and remains in place for 21 days. The ring is removed for 7 days to permit menses, and then a new unit is reinserted. The ring does not need to be removed for coitus, and cleaning is not indicated. Efficacy is at least comparable to that of OCs, and convenience is a clear advantage. Systemic side effects are diminished because serum hormone levels are less than half of those seen with OCs (Timmer and Mulders, 2000). In a comparative trial with a series of different hormonal formulations, rings were found to contribute little to epithelial lesions on colposcopy (Fraser et al., 2000).

**WEB SITES**

For Teenagers and Parents

- [For Teens from Planned Parenthood](http://www.young womenshealth.org/conthormpills.html)
- [Teenwire from Planned Parenthood](http://www.teenwire.com/index.asp)
- [Sex Education 101](http://www.sex-ed101.com/oral.html)
- [Teen Health from Planned Parenthood](http://www.teenwire.com/index.asp)
- [Fact sheet from the National Institutes of Health](http://www.fhi.org/en/fp/fpfaq/fpfaq8a.html)
- [Frequently Asked Questions sheet on combined OCs from Family Health International](http://www.young womenshealth.org/conthormpills.html)
- [Facts from the National Institutes of Health on OCs](http://www.nlm.nih.gov/medlineplus/ency/disorder contraceptive, reproductive.html)
- [Sex Education 101 Web site on OCs and other contraceptives](http://www.sex-ed101.com/oral.html)
- [For Teenagers and Parents](http://www.young womenshealth.org/conthormpills.html)
- [Association of Reproductive Health Professionals](http://www.arhp.org/arhpframe.html)
- [Family Planning A to Z](http://www.familyplanningaz.org)
- [Family Planning A to Z](http://www.familyplanningaz.org)

**REFERENCES AND ADDITIONAL READINGS**


Creasy R, et al. Compliance with the weekly patch was superior to adherence with OCs for 13 cycles (Creasy et al., 2000).

Fraser et al. Efficacy is at least comparable to that of OCs, and convenience is a clear advantage. Systemic side effects are diminished because serum hormone levels are less than half of those seen with OCs (Timmer and Mulders, 2000). In a comparative trial with a series of different hormonal formulations, rings were found to contribute little to epithelial lesions on colposcopy (Fraser et al., 2000).

Rahimy and Ryan. Efficacy is greatly enhanced by elimination of the need for daily administration. A more subtle advantage is that it works for longer than a month, which protects teens who are insured by plans that provide one 28-day pack of pills per month regardless of the number of days in the month.

Shulman et al. Breast tenderness and acne also were more frequently reported with injections than with pills.

Timmer and Mulders. In a comparative trial with a series of different hormonal formulations, rings were found to contribute little to epithelial lesions on colposcopy (Fraser et al., 2000).

The intrauterine device (IUD) is a safe and effective long-term method of birth control for appropriately selected patients (CDC, 1997). The recommended IUD user is a parous woman who is in a stable, mutually monogamous relationship and has no history of pelvic inflammatory disease (PID). These features are designed to ensure that the potential IUD candidate has no obvious risks for acquiring a sexually transmitted disease (STD). Although many adolescents fail to meet these criteria, there are some teens and young adults for whom the IUD is an ideal method. It is important to note that IUD candidates need not have completed their families; the IUD is an excellent interval method. Even nulliparity is not an absolute contraindication to IUD use, but nulliparous women require careful screening and counseling. The woman needs to understand that her fertility is untested, and she may experience difficulty conceiving after IUD removal that is not related to the IUD. There are two different systems currently available in the United States: the T-380A copper IUD and a levonorgestrel intrauterine contraceptive system (IUS).

Although the primary characteristic of IUD candidates is that they be at low risk for STDs, there are other restrictions to IUD use. Specific IUDs may impose additional restrictions. However, in general the following contraindicate IUD use:

1. Pregnancy or suspicion of pregnancy
2. Abnormalities of the uterus resulting in distortion of the uterine cavity
3. Acute PID (a history of PID is a contraindication only if the patient is still at risk for STDs or if she has not had a subsequent pregnancy)
4. Postpartum endometritis or infected abortion in the past 3 months
5. Known or suspected uterine or cervical malignancy, including unresolved, abnormal results from Pap smear (atypical squamous cell of undetermined significance [ASCUS] is not a contraindication)
6. Unexplained abnormal genital bleeding
7. Untreated acute cervicitis (including genital actinomycosis) or vaginitis (including bacterial vaginosis)
8. Patient or her partner has multiple sexual partners
9. Conditions associated with increased susceptibility to infections with microorganisms. Such conditions include, but are not limited to, leukemia, acquired immunodeficiency syndrome (AIDS), intravenous drug abuse, chemotherapy, and long-term corticosteroid therapy.
10. A previously inserted IUD that has not been removed.

COMMON MISCONCEPTIONS ABOUT INTRAUTERINE DEVICES

IUDs are tremendously underutilized by women of all ages in the United States compared with other developed countries. A great deal of the difference can be traced to the experience with the Dalkon shield and to significant misconceptions about the safety and mechanisms of action of the IUD.

Issues Regarding Pelvic Infection

Studies in the 1970s and 1980s linked Dalkon shield use to an increased risk of PID. Over time, the longer-term consequences of PID, such as ectopic pregnancy, infertility, and pelvic pain were also observed in women who had used the Dalkon shield. Because the Dalkon shield dominated the IUD market in those days, all IUDs were initially implicated. Further analysis, however, revealed that there are three issues involved in IUD-related infections: the IUD design, the IUD user, and the insertion technique. The polyfilament tail of the Dalkon shield allowed pathogens from the vagina to ascend into the upper genital tract by wicking action (Tatum et al., 1975). Modern IUDs, with their monofilament tails, do not facilitate such infection. IUD users who were at risk for STDs were found to be more likely to have upper tract involvement, but monogamous IUD users faced no increase in their long-term risk for PID (Cramer, 1985; Daling, 1985). Finally, it is important to note that there is a transient increase in infection immediately after IUD insertion. The PID risk is generally limited to the first 20 days of use and results from endometrial contamination during IUD insertion (Farley, 1992).

With current patient selection criteria and pretesting, the risk of PID is extremely rare (1 in 1,000) (Skjeldestad, 1996; Walsh et al., 1998). However, this potential does underscore the need to carefully evaluate the woman for possible cervicitis or vaginitis (especially bacterial vaginosis) and to use meticulously sterile insertion techniques. Routine antibiotic prophylaxis for insertion is not warranted (Grimes and Schulz, 1999). Recent Turkish studies comparing IUD users with noncontraceptive users in married women found no difference in gonorrhea, Chlamydia, Trichomonas, or vulvovaginitis incidence rates between the groups, but the IUD users were at higher risk for development of bacterial vaginosis (Hodoglugil et al., 2000).

Issues Regarding Ectopic Pregnancy

The T-380A copper IUD reduces a woman’s risk of ectopic pregnancy compared to the risk faced by a woman using no method of birth control. This protection is so dramatic that women with prior ectopic pregnancies can consider IUDs for this risk. The levonorgestrel IUS has been shown to provide this protection. Therefore, women with a history of an ectopic pregnancy and risk factors for an ectopic pregnancy are advised not to use hormonal IUDs.

Issues Regarding Fertility

All IUDs are rapidly reversible birth control methods and, as such, are excellent contraceptive choices for appropriate candidates to use to space their children. In prospective, controlled studies of IUD users, the fertility of women after IUD removal was shown to be comparable to that in the general population; within 48 months after IUD removal, 91.5% of the nulligravida women and 95.7% of the gravid women had conceived. Wilson found that there was no difference in the first-year rates of fertility, ectopic pregnancy, miscarriage, or preterm delivery for women who asked to have IUDs removed in order to conceive compared with women who had IUDs removed because of complications (Wilson, 1989). The longer-term IUDs, especially the T-380A copper IUD, are also particularly suitable for women who have completed their families. The T-380A copper IUD offers effectiveness and convenience to comparable to sterilization and is considerably more cost-effective.

Estimates are that every T-380A copper IUD used for 5 years saves the health care system $14,122 (Trussell, 1995). Completed their families. The T-380A copper IUD offers effectiveness and convenience to comparable to sterilization and is considerably more cost-effective.
although a “hostile endometrial environment” is often offered as a mechanism of action. This hypothesis has been rejected because intrauterine flushing experiments failed to yield blastocysts. The most compelling direct experimental support for the contraceptive (preferitization) action of IUDs comes from tubal flushing/salpingectomy specimens, which were obtained from dozens of women undergoing sterilization procedures who had timed periovulatory intercourse. In the control group, 50% of the women were found to have normally dividing fertilized ova indicative of successful fertilization. None of the IUD users had any normally dividing ova, which demonstrates the profound contraceptive action of all IUDs (Alvarez, 1988).

TYPES OF INTRAUTERINE DEVICES

Two different designs of IUDs are currently available in this country: the T-380A copper IUD (ParaGard T-380A) and the levonorgestrel IUS (Mirena). Each provides effective and safe birth control, but each has sufficiently different individual characteristics to warrant separate discussion.

ParaGard T-380A Copper Intrauterine Device

Description of Device The T-380A copper IUD is composed of a T-shaped polyethylene frame whose vertical stem is wrapped with a copper wire coil and whose horizontal arms are each encased in a collar of solid copper. The copper surface area totals 380 mm². Monofilament strings are threaded through the bulb at the end of the stem. The stem contains barium sulfate to render it radiopaque. The T-380A copper IUD is approved by the U.S. Food and Drug Administration (FDA) for 10 years of continuous use, but long-term studies show that it is quite effective for 12 years (UN Development Programme et al., 1997). The IUD is traditionally inserted during menses to exclude the possibility of pregnancy; however, it can be inserted at any time in the cycle if the patient is not pregnant. In fact, early expulsion rates can be halved if insertion is delayed until the end of menses (White et al., 1980). Postpartum insertion is best done after uterine involution is complete. A new IUD can be placed immediately after the prior one has been removed if the patient is still an appropriate candidate.

Effectiveness The typical first-year failure rate of the T-380A copper IUD is between 0.7% and 0.8%, and the 10-year cumulative failure rate is 2.7%. This 10-year failure rate is lower than the typical first-year failure rate with oral contraceptives. It also is lower than the 10-year failure rates of many interval sterilization techniques used in young women (Peterson et al., 1996).

Mechanisms of Action The copper released from the IUD interferes with sperm transport and capacitation (Zipper, 1971). Forward motility of sperm is markedly impaired and sperm head-tail disconnection is frequently observed (WHO Scientific Group, 1987). The inflammatory reaction in the endometrium induced by the foreign body is spermicidal (Sagiroglu, 1971). Copper ions that spread into the fallopian tubes also inhibit acrosomal enzyme activation. Without the acrosomal enzymes, the sperm are unable to penetrate the zona pellucida. Ova fertilizability is also reduced due to increased prostaglandin levels probably induced by copper. The best overall description of the mechanism of the T-380A copper IUD is that it is a “functional spermicide.”

Contraindications The T-380A copper IUD should not be inserted if any of the previously listed contraindications exist or if the patient has (a) Wilson disease or known allergy to copper or (b) a uterine cavity less than 6 cm or greater than 9 cm on sounding.

Relative Contraindications

1. Anemia
2. Menorrhagia
3. Severe dysmenorrhea

Advantages

1. Extremely effective form of contraception
2. Decreased risk of ectopic pregnancy
3. Convenient: Requires only monthly string checks to confirm its presence
4. Private: The IUD is not generally detectable by parents and is often unnoticed by partner
5. Rapidly reversible after removal by practitioner

Disadvantages

1. Available only through medical providers: Professional assistance is required for insertion and removal, and trained providers are limited but increasing in number.
3. Provides no protection against STDs and may increase risks for complications of STDs (e.g., PID).
4. Risk of Actinomyces colonization and infection increases with duration of IUD use.
5. Side effects (discussed later).
6. Relatively high initial cost, which may not be covered by insurance.

Side Effects

1. Increased menstrual bleeding and cramping: The T-380A copper IUD typically increases menstrual blood loss by about 35%, and dysmenorrhea can result.
2. Treatment with nonsteroidal antiinflammatory drugs (NSAIDs) readily controls this increase; however, patients must initiate NSAID use at the beginning of the flow to effectively block prostaglandin formation. An isolated episode of increased or untimely bleeding or cramping may indicate partial expulsion or failure and requires prompt medical evaluation.
3. IUD expulsion: First-year expulsion rates range from 2% to 10%, with an average of 6%. Expulsion rates are higher in nulliparous women. Other risk factors for expulsion include young user age, menorrhagia, and severe dysmenorrhea before T-380A copper IUD insertion.
4. Perforation or embedment: The partial or total uterine perforation is a rare event with the T-380A copper IUD (1 in 1,000). Rates are increased in a woman whose uterus is not fully inviolated after delivery, who is lactating, or whose uterus is markedly verted or immobile. The most important predictive variable, however, is the experience of the inserter. Embedment of the T-380A copper IUD in the endometrium or myometrium can make removal difficult. Removal of an adherent IUD generally can be accomplished with alligator forceps in an office setting, but a more deeply embedded IUD may require hysteroscope-guided or surgical removal.

Mirena Intrauterine System (Levonorgestrel IUS)

Description of Device The levonorgestrel IUS is composed of a flexible T-shaped frame with a steroid reservoir surrounding its vertical stem. The reservoir consists of a cylinder made of a mixture of levonorgestrel and polydimethylsiloxane, which releases 20 µg of levonorgestrel per day. The polymer is mixed with barium sulfate, which renders it radiopaque. The unit is also visible ultrasonographically, but its appearance is subtler than that of the T-380A copper IUD. The levonorgestrel IUS has two monofilament tail strings, which are threaded through a bulb at the base of the T. With its arms open, the levonorgestrel IUS measures 32 mm in both the horizontal and vertical directions. The levonorgestrel IUS is approved for 5 years of use. It is recommended that insertion be performed during the first 5 days of menses to ensure that the levonorgestrel IUS will provide adequate first-cycle protection. The insertion technique for the levonorgestrel IUS is quite straightforward, but it differs significantly from that of other such devices and requires formal training. It is recommended that removal be accomplished on menses unless medically indicated otherwise.

Effectiveness The typical first-year failure rate for the levonorgestrel IUS is less than 0.2%. The cumulative 5-year failure rate found in various studies has ranged from 0.5% to 1.1%. Ectopic pregnancy rates are reduced to 0.02% to 0.06% per year, but in clinical trials about 50% of pregnancies were ectopic.

Mechanisms of Action The levonorgestrel IUS prevents pregnancy primarily by exerting a very potent, continuous progestin effect on the cervical mucus to render it impermeable to sperm penetration. The IUS induces inflammatory changes in the endometrium that are spermicidal. The progestin produces a thin, atrophic endometrium and slows tubal motility. The clinical significance of these last two progestin effects is not yet known. Systemic progestin levels are not sufficiently...
**Contraindications** In addition to the general contraindications for IUD use, the levonorgestrel IUS is not intended for use in women who have allergic reactions to any of its ingredients or who have liver disease. The appropriate uterine size for use of the levonorgestrel IUS is 6 to 10 cm. Menorrhagia is not even a relative contraindication to use of the levonorgestrel IUS, because the levonorgestrel IUS significantly reduces monthly menstrual blood loss. In fact, in some European countries, the levonorgestrel IUS is used to treat menorrhagia as a labeled indication (Irvine, 1998).

**Advantages** The advantages are similar to those of the T-380A copper IUD, except that the levonorgestrel IUS reduces menstrual loss (Ronnerdag and Odlind, 1998). One small study found that levonorgestrel IUS users had an 85% lower incidence of Pap smears showing Actinomyces-like organisms, compared with users of a copper IUD (Merki-Feld, 2000).

**Disadvantages** The disadvantages are similar to those of the T-380A Copper IUD.

**Side Effects** The side effects are similar to those of the T-380A copper IUD, except for the following:

1. Vaginal bleeding patterns are different. Initially, most levonorgestrel IUS users experience more unpredictable spotting or bleeding, which usually resolves within 3 to 6 months and is replaced by either complete amenorrhea or significant oligomenorrhea due to endometrial atrophy.
2. Ovarian cysts are seen more frequently with the levonorgestrel IUS because the locally increased progesterin concentration slows follicular atresia. Therefore, physiological cysts may persist longer.
3. Other systemic progestin effects (breast tenderness, acne, headaches) have also been reported initially by levonorgestrel IUS users, although the circulating levels of the progesterin are much lower than with oral contraceptives.

**USE IN ADOLESCENTS**

Diaz et al. (1993) compared the clinical performance of 995 parous adolescents using a T-380A copper IUD with a cohort of paired controls 10 years older of the same parity. Although the rates for pregnancy, expulsion, and removal were higher in adolescents, the ranges were within those reported in the literature for the IUD. Removals due to infection were few, and the rate was not significantly different from that for older women. Overall, the performance was similar or better than other reversible methods in this age group. Therefore, in the appropriate adolescent or young adult (i.e., parous woman in a monogamous relationship), an IUD should be considered along with other methods. Selection of the appropriate device should be tailored to individual needs.

**PREGNANCY WITH AN INTRAUTERINE DEVICE IN PLACE**

Pregnancies in current IUD users are rare. The location of the pregnancy should be determined as early as possible, because 8% of pregnancies that occur with the T-380A copper IUD and 50% of pregnancies with the levonorgestrel IUS are ectopic. It is recommended that the IUD be removed in the first trimester of an intrauterine gestation if the strings are visible in the vagina. Early removal reduces the risk of spontaneous abortion by about 50%. Late in pregnancy, the strings are rarely visible unless the placenta is low-lying, and there is no demonstrated benefit to IUD removal at this time. If the strings are not visible, it is prudent to obtain an ultrasound study, because the most common reason for pregnancy is a previously undetected expulsion. If the IUD is present, there is no reason to attempt to remove it. The risk of birth defects is not increased, but the patient should be alerted to signs and symptoms of preterm labor, because an increased risk of premature birth has been demonstrated. If a teen elects to abort the pregnancy, the IUD can be removed at the time of the procedure.

**GUIDELINES FOR PATIENTS**

The following is a suggested format for informing teens about IUDs.

1. What is an IUD?
   - The IUD (intrauterine device) is a small plastic device that is placed in the uterus (womb).

2. How does the IUD work?
   - The IUD appears to work primarily by preventing fertilization. The copper in the T-380A copper IUD probably has an antispem effect, and the hormones in the medicated IUDs block sperm from entering the womb.

3. Are there different types of IUDs?
   - In the United States today, there are two types of IUDs available. One contains copper, and one contains the potent hormone levonorgestrel. Both are shaped like the letter T and are about 1¼ inches tall. Each IUD has a thread or tail on the end, which allows the woman to check that the IUD is in place and also makes it easier for the provider to remove the IUD. The T-380A copper IUD has copper sleeves on the arms and copper wire coiled around the stem. The T-380A cooper IUD can be left in place for up to 10 years. The levonorgestrel IUS can be used for up to 5 years.

4. How effective are these devices?
   - IUDs are among the most effective forms of birth control. For every 1,000 women using the levonorgestrel IUS, fewer than 2 will become pregnant the first year. With the T-380A copper IUD, only 7 or 8 will become pregnant.

5. Are there side effects?
   - With the T-380A copper IUD, the most common side effects are increased menstrual flow and cramps, which can be reduced by use of an over-the-counter pain medication such as ibuprofen. These side effects lessen after the first few months. With the levonorgestrel IUS, spotting and bleeding are most common in the first 4 to 6 months, but after that a woman's periods decrease dramatically and may stop altogether.

6. Are IUDs safe?
   - IUDs are a safe and effective method of birth control when used in the appropriate individuals. They should be used in women who have had children and who have only one long-term sexual partner. Women at risk for an STD should not select the IUD. This is important because the IUD can increase a woman's risk of developing serious complications (such as a pelvic infection or infertility) if she gets an STD.

7. What are the benefits of an IUD?
   - IUDs are a safe, effective, easy-to-use, and cost-effective form of contraception. There is no need to remember to use the method every day or with every act of sex. However, the IUD must be protected against STDs. If you may be at risk for STDs, you are not a candidate for IUDs. Use a latex or polyurethane condom to help protect yourself against infection.

Remember:

1. Check for the string of the IUD frequently during the first months and at least after each period thereafter. If the strings are longer or shorter than previously, see your provider, because you may be losing your IUD.
2. If you ever have fever, pelvic pain, severe cramping, unusual vaginal bleeding, or a foul-smelling vaginal discharge, contact your clinician immediately. These may be signs of a serious infection or pregnancy or a warning that you are losing your IUD.
3. If you have any symptoms of pregnancy, contact your provider immediately.
4. Do not remove the IUD yourself or pull on the strings.
5. If you have any problems or questions, call your provider.

WEB SITES
REFERENCES AND ADDITIONAL READINGS


Sivin I. IUDs are contraceptives, not abortifacients: a comment on research and belief. Stud Fam Plann 1989;20:355.


Barrier contraceptives are agents that kill sperm or block their movement toward the upper genital tract. Barrier contraceptives are available in a wide variety of designs, including male and female condoms, diaphragms, cervical cap, and vaginal spermicides. In general, barrier methods have higher failure rates but fewer systemic side effects than other modern contraceptive methods. Barrier methods also offer some reduction in the risk of sexually transmitted disease (STD). Many barriers are available over the counter and improve adolescent access to birth control. The high typical-use failure rates of barrier methods could be considerably lowered if they were used more consistently and if they were combined with the use of emergency contraception (see Chapter 46).

MALE CONDOMS

Male condoms (Fig. 45.1) are the oldest and most reliable male method of contraception. They are the second most popular reversible method of birth control in the United States. Surveys in the late 1990s reported that 67% of sexually experienced male adolescents used a condom at last intercourse, which was a 10% increase from 57% in 1988. Consistent condom use was reported by fewer than half (45%) of the sexually experienced adolescent men, and intermittent use was claimed by another 45.5% (Sonenstein et al., 1998; Centers for Disease Control and Prevention [CDC], 1999). The 1995 National Survey of Family Growth also found that condoms were used by greater numbers of adolescents at the time of sexual debut than in earlier iterations of the survey (Abma et al., 1997). Condoms are very cost-effective for episodic intercourse, which is often found among teens. For long-term use, however, the condom’s higher failure rate drives its overall total cost much higher.

FIG. 45.1. The male condom—patient information sheet.

The human immunodeficiency virus (HIV) epidemic has heightened public awareness and acceptance of condoms. A significant degree of STD protection is afforded by latex and polyurethane condoms, which are impermeable to Chlamydia trachomatis, Neisseria gonorrhoeae, herpes simplex virus, cytomegalovirus, hepatitis B virus, and human papillomavirus. Millions of women use condoms in conjunction with other methods (sterilization, birth control pills, foam) to capture this STD risk reduction benefit. Seventeen percent of adolescents combined the male condom with a female method of contraception for STD risk reduction and/or enhanced contraceptive efficacy (Sonenstein et al., 1998).

Uses of Male Condoms
Contraceptive Uses

1. As a primary method of birth control, alone or in conjunction with spermicides or female barrier methods
2. As a backup method of contraception after a late start with a hormonal method (e.g., oral contraceptives, injections) or whenever two or more consecutive pills have been missed
3. As a barrier contraceptive, used as part of the fertility awareness method (FAM) of contraception during vulnerable days of the woman's cycle

Noncontraceptive Uses

1. To reduce transmission of STDs
2. To blunt sensation, to treat premature ejaculation
3. To reduce cervical antisperm antibody titers in women with associated infertility
4. To reduce allergic reaction in women with sensitivity to sperm

Types of Male Condoms

The more than 100 brands of condoms available in the United States provide a wide range of choices in size, shape, thickness, lubricant, and design features to trap the ejaculate. A review of the individual types of condoms and reliability was published in Consumer Reports (Consumer's Union, 1999). Three different materials are used in manufacturing condoms: latex dominates the market (99%), while skin condoms and polyurethane together account for less than 1%. Condoms are available in several colors and sizes. The largest are 175 mm long and 52 mm wide. The thickness ranges from 0.03 to 0.10 mm. Condom shapes vary (straight-sided, baggy, or contoured), as do their textures (smooth or ribbed). Condoms are lubricated internally and externally by a wide range of materials: silicones, spermicides, or water-based surgical gels. Other condom features that are intended to make them more aesthetically appealing include a wide array of colors and scents. Having choices of condoms permits flexibility in selection and is intended to enhance utilization. Some latex condoms are available with spermicidal coating. Spermicides may provide lubrication, but they do not contribute to STD risk reduction or pregnancy protection. On the other hand, spermicides may cause vulvar/penile irritation, and the spermicidal coating drastically reduces the shelf life of latex condoms, from an average of 5 years to 2 years.

The newer polyurethane male condoms are nonbiodegradable and require less faddishing handling before use. They are not susceptible to damage by petroleum-based lubricants, lack the latex allergens, and do not have the unexpected taste occasionally associated with latex condoms during oral-genital contact. Polyurethane itself is a stronger material than latex, but it lacks elasticity. Pregnancy rates in clinical trials were not higher in polyurethane condom users, but the slippage and breakage rates for the polyurethane condoms were four to eight times higher than for a standard latex condom, which may reduce the STD protection afforded by these new, thin condoms (Frezieres et al., 1998). Polyurethane male condoms may best be reserved for couples who cannot tolerate latex products. The natural skin condoms afford almost equal pregnancy protection but do not reduce STD risks.

Mechanism of Action

Condoms are sheaths made of latex (rubber-based), processed collagenous tissue, or polyurethane that fit over the erect penis and block transmission of semen. Condoms with spermicidal agents (e.g., nonoxynol) may also work by killing sperm.

Effectiveness

The male condom is the most effective barrier method available for pregnancy protection. The first-year failure rate for typical use of the latex male condom is 12%, and the failure rate for correct and consistent use is 3%. Adolescent failure rates for typical use average 18%, but certain subgroups have even higher failure rates. The most critical variable in predicting efficacy is consistent use, followed closely by proper technique. Condom quality has improved dramatically in recent years. Research described in Consumer Reports found that 7 of 37 condom models failed routine testing in 1995, but by 1999 only 2 of 30 models failed those tests (Consumer's Union, 1995, 1999). The self-proclaimed "strength" and "contour" of the condom did not influence test scores.

Improving Condom Success

Dozens of excellent studies have been conducted to identify factors that predict consistent use of barrier methods, variables that would predict poor use, and ways to design interventions that might improve barrier use. Most such research has focused on the male condom. Given the vital role that barriers play in slowing the spread of STDs, answers to these questions are desperately needed. Unfortunately, studies show that solutions will not be easy to achieve.

There are profound differences in condom use by gender (Brown et al., 1992; Leland and Barton, 1992; Ku et al., 1994), with adolescent women reporting far less use of condoms than adolescent men. (This reflects not only safer sex practices of gay men, but also the profound role that older men play in adolescent female activity.) A perceived risk of STD or HIV infection is associated with higher condom use and also with intention to use condoms in the future (Brown et al., 1992; Donald et al., 1994; Orr and Langefeld, 1993). However, several studies show that many of those adolescents who are clearly at increased risk for STDs have little appreciation of their vulnerability (Rosenthal et al., 1994; O'Donnell et al., 1995).

A common finding of virtually all studies is that adolescent use is increased when adolescents believe that their peers use condoms and that condoms can prevent STDs; when they can talk to their partner about risks; when they have easy access to a supply of condoms; and when they carry condoms with them (Joffe and Radius, 1993). Condom use is decreased when risky sexual behavior is just one of a cluster of risky health behaviors (e.g., smoking, substance abuse) or other lifestyle risks (e.g., violence). Substantial societal changes apparently will be needed to address these issues. Putting condoms in open containers may be necessary to provide adolescent access to condoms, but it is clearly not sufficient to ensure their condom use.

For individual success in clinical practice, providers should be aware of condom misuse (Wood and Buckle, 1994) and should do the following.

1. Teach the patient how best to use condoms (Fig. 45.1):
   a. Place where to store condoms for ready access, privacy, and condom safety. One convenient location is between two photographs in a wallet. Not only is this discrete, but the photographs protect the condom from puncture injuries.
   b. Incorporate condom placement into the lovemaking process—when the penis is still somewhat flaccid, but certainly before any genital contact. The prepuce may be retracted to allow better access to the glans. Experiences may vary greatly from the opportunity to practice placing condoms on models or even over two fingers during office visits.
   c. Open the packaging carefully. Avoid using sharp objects. Any foil edges shearing across the condom may tear the latex. Between 24% and 65% of latex condom breakages occur before intercourse.
   d. Correctly place the condom. Judge which way the condom will unroll. Allow some slack at the top of condoms that have no reservoir tip; more snugly fit those with ejaculatory reservoirs once erection is complete. Squeeze the air out of the reservoir areas. Completely unroll the full length of the condom.
   e. Change condoms if different body orifices are penetrated. In particular, if a condom is used during anal or oral sex, it must be removed and replaced before vaginal penetration.
   f. Use only water-based lubricants or spermicides to reduce vaginal friction against the latex condom. Lubricant should be applied only to the external surface of the condom or to the vaginal area; lubricant should not be placed on the penis or on the inner surface of the condom, because that practice increases problems with slippage and breakage. Avoid petroleum-based products such as Vaseline, baby oils, and lotions. All vaginal antifungal treatments and some of the vaginal products for treatment of bacterial vaginosis also contain petroleum-based ingredients. Petroleum can react with the latex in seconds and undermine the strength of the condom; within 1 minute, microscopic tears may develop and become large enough to permit the passage of virus.
   g. After ejaculation, firmly grasp the rim of the condom at the base of the penis and carefully withdraw the unit while the penis is still firm. Any delays in removal can result in spillage and loss of protection.
     h. Inspect the condom for signs of breakage or slippage.
     i. Be prepared with fast-acting spermicide should the condom break or spill.
   j. Use emergency contraception as needed (see Chapter 46).
2. Be responsive to patient complaints and apprehension
For the young woman who is unsure that her partner will use condoms, role-play different scenarios with her until she believes she has the ability to discuss the issue with her partner and persuade him to use condoms. The same techniques are helpful to reduce STD risk for the receptive partner when men have sex with men.

b. If the male partner complains of constriction or blunted sensation, recommend one of the following strategies.

- Try a larger condom size.
- Try a different condom style. Condoms with reservoirs at the side are available; these reduce glans pressure and purportedly enhance stimulation.
- Ridged condoms are also designed to increase sensation.
- Advise the couple to place a second, larger condom over the first one after the outer surface of the first condom has been well lubricated. The friction between the condoms may enhance penile sensation. It also reduces the impact of breakage problems.

Advantages

1. Readily available: Condoms may be purchased in drug stores, mail order houses, or vending machines or obtained in family planning or school clinics without prescription.
2. Relatively inexpensive: Sometimes they are even available free from clinics. Male condoms cost $0.30 to $1.50 each. Frequent use raises the direct (out-of-pocket) costs and indirect (pregnancy-related) costs because of their moderately high failure rates.
3. Portable: Condoms can easily be carried in wallet, purse, or other vehicle to be available whenever the need arises.
4. Male participation: Even though women purchase more than half of condoms, the sheaths are still used by men; men definitely benefit from detailed instructions.
5. Visible proof of protection: Couples can get reasonably accurate feedback that protection was offered by observing the ejaculate contained in the condom.
6. Significant reduction in risk of STDs, including HIV infection and cervical dysplasia. Transmission of bacterial STDs, such as chlamydia and gonorrhea, is markedly reduced by effective condom use (Cates and Holmes, 1996; Cates, 1997; d'Oro et al., 1994; Rosenberg et al., 1992). The impact that condom use has on the transmission of viral STDs depends on the site of infection. Studies consistently demonstrate that condoms provide important protection against HIV transmission, although such protection is less than the protection against pregnancy. A metaanalysis of 25 studies of serodiscordant heterosexual couples found that condoms reduced transmission by 87% (range, 60% to 90%). Consistent users had annual HIV seroconversion rates of 0.9%, compared with 6.8% for those who never used condoms (Davis and Weller, 1999). However, the transmission of herpes simplex virus 2 and human papillomavirus may not be as easily prevented, because infections can involve anatomical sites not sheathed by the condom.

Disadvantages

1. Requires placement with each act of intercourse.
2. May interrupt lovemaking.
3. Requires cooperation of male partner: Women cannot enforce male condom use.
4. Carries a higher pregnancy rate than hormonal contraceptive methods or intrauterine devices.
5. May diminish the pleasure of intercourse.
   a. May blunt sensation for man; less “natural.”
   b. May result in less vigorous intercourse due to fear that the condom may slip or break.
   c. Requires prompt withdrawal after ejaculation, which may not permit sexual satisfaction of partner.
   d. May increase vaginal irritation in women, especially those with inadequate or low adequate lubrication.
6. May encourage unsafe sex practices (e.g., multiple sex partners) or selection of at-risk partners by inappropriately decreasing an adolescent’s sense of STD vulnerability.
7. Side effects (see later discussion).

Side Effects of Male Condoms

Latex allergies are becoming more common in the United States; estimates are that latex allergies are found in 2% to 4% of couples using condoms. Among latex-exposed workers, the average may be as high as 18%. This number may be lower in the teen population with less previous exposure to latex. Polyurethane condoms are strongly recommended for latex-allergic couples, because the transition from mild reactions to anaphylaxis can develop rapidly. Some authors have suggested that the unsensitized partner could still use a latex condom if it were covered by a plastic condom. This strategy may reduce topical irritation, but the latex powder is a potent allergen and can induce severe, even life-threatening allergic reactions.

Future Developments

Condoms made of newer, nonlatex plastic materials, such as Tactylon, are in clinical trials and may be able to reduce the slippage and breakage problems associated with polyurethane. Male condoms with new shapes (cap condoms) and smaller sized condoms (snugger fit condoms) are also needed. The Unisex Condom, which can be used by either partner, is available in Canada.

FEMALE CONDOMS

The only female condom currently available in the United States is the Reality female condom (Fig. 45.2). The device is a thin polyurethane sheath measuring 17 cm in length and 7.8 cm in width. It contains two flexible polyurethane rings. The inner ring is loose within the sheath. At the time of insertion, the inner ring is pivoted parallel to the axis of the vagina and is used to introduce the device through the introitus to the vault, just as a diaphragm is placed. After insertion, the inner ring is rotated at the top of the vault to stabilize the device during intercourse. The outer ring, which is fixed to the base of the device, and remains outside the vagina. The female condom provides a barrier along the length of vagina and partially covers the introitus. It is lined internally with a silicone-based “dry” lubricant and may be combined with vaginal spermicides. The female condom should never be used with the latex male condom, because each device can compromise the integrity of the other.

FIG. 45.2. The female condom.

Efficacy

The female condom underwent 6-month clinical efficacy trials, during which time a 12.5% failure rate was observed in typical use in the United States. This rate has been annualized, by adjusting for various factors, to a typical first-year failure rate of 21% to 25%. Perfect-use rates are considerably lower (2.2% to 2.6% failure in 6 months), reflecting perhaps the difficulty users experienced using this method. The efficacy of the female condom in STD protection has not been tested, but is assumed to parallel the pregnancy rates.
Advantages and Disadvantages

The female condom is available over the counter in single-size disposable units (Fig. 45.2); they are considerably more expensive than the male condom. The female condom causes no known adverse physical side effects. The polyurethane is not sensitive to petroleum-based products. However, its use may be challenging; even users who are experienced with diaphragm insertion may find the female condom difficult to insert. The package instructions say that correct placement may be difficult in the first or second attempt due to the device’s lubrication. The female condom may be inserted up to 8 hours before intercourse to permit a relaxed insertion. The consumer is warned not to tear the sheath with fingernails or other sharp objects. During intercourse, the penis should be manually guided into the device. The couple is to remain attentive throughout coitus to the position of the outer ring to ensure that it does not ride up or get pushed into the vagina. The male partner must avoid excessive friction between his penis and the device, which could increase the breakage rate or cause inversion of the device on withdrawal. Additional lubrication applied within the condom can help reduce this risk and also reduces the noise the device may make during intercourse.

The relative complexity of the device, its low typical efficacy rate, and the lack of evidence demonstrating reduction in STD risk make the female condom a second choice after the male latex or polyurethane condom. However, the female condom may make an important contribution for women whose partners refuse to use male condoms. For adolescents, extensive education and hands-on practice may be needed to ensure correct use of the female condom. Emergency contraception should be offered in advance to all female condom users.

Future Developments

A variety of so-called bikini condoms have been developed to provide women more external protection by covering not only the vagina and cervix but also much of the external genitalia with latex or plastic materials. However, none has emerged as a feasible design for phase III testing.

**DIAPHRAGM**

The diaphragm (Fig. 45.3) is a dome-shaped latex device which, when introduced into the vagina, extends from the posterior fornix to the anterior vaginal wall to completely cover the cervix. The semi-rigid outer ring stabilizes the device in the upper vagina, and the dome holds the spermicide directly against the cervix. As a mechanical barrier alone, the diaphragm has an unacceptably high failure rate; it is intended for use with contraceptive gel. The diaphragm must be professionally fitted and is available only by prescription.

**Types of Diaphragm**

Diaphragms are available in sizes ranging from 50 to 105 mm in 5-mm increments and in four styles, which vary primarily by the construction of the rim or the seal.

1. Arcing spring rim: A very sturdy rim that folds for insertion but springs open to stabilize the device’s position within the vagina. It is designed for universal use, but is uniquely good for vaginas with limited muscle tone. There are two versions: one that folds only in one direction and another that is flexible in all directions. This latter design is the most popular style because of its ease of introduction. Most diaphragms used in the United States today are versions of the arcing spring rim.
2. Coil-spring rim: Sturdier rim that folds flat for insertion with no arc. It is suitable for a woman with average muscle tone and pubic arch angle. A plastic diaphragm introducer may be used, if needed.
3. Flat-spring rim: Thin, delicate rim with gentle spring action that is more comfortable for women with firm vaginal wall tone. A plastic diaphragm introducer may be used.
4. Wide seal rim: Has a flexible flange attached to the inner edge of the rim to hold spermicide in place and to maintain a better seal. It has very limited availability and can be obtained only by direct order with arcing spring and coil-spring rims.

**Contraindications to Use**

1. History of toxic shock syndrome
2. Allergy to latex or spermicidal agents
3. Recent pregnancy, before renormalization of anatomy
4. Inability of patient to correctly insert and remove diaphragm

**Effectiveness**

The typical-use failure rate varies between 16% and 18%. The failure use with correct and consistent use is estimated to be 6%. Women who are more successful users of diaphragms usually are older, are comfortable touching their genitals, and are able to anticipate coitus. However, adolescents certainly can be taught to be effective diaphragm users (Fig. 45.3).

**Tips to Improve Success of Method**

1. Correct fitting of device (see later discussion)
2. Detailed, hands-on instruction for patient education (see later discussion)
3. Careful monitoring of diaphragm between uses to identify any defects (see later discussion)
4. Careful selection of patient
   a. Offer only to motivated woman willing to touch her genitals and to use the device with every act of intercourse.
   b. Avoid offering to a woman with a markedly anteverted or retroverted uterus (diaphragm tends to dislodge).
   c. Discourage coital positions that compromise stability of diaphragm, particularly the female superior position.

**Correct Fitting of Diaphragm**

A diaphragm must be fitted properly to be effective. The diagonal length of the vaginal canal from the posterior aspect of the symphysis pubis to the posterior vaginal fornix is measured during the bimanual examination. The second and third fingers are inserted deeply into the vagina until the tip of the middle finger touches the posterior vaginal wall; then the point at which the index finger touches the symphysis pubis is marked with the thumb. The hand is withdrawn and the diaphragm is placed on the tip of the third finger with the opposite rim in front of the thumb to measure the correct size. This is a first approximation, which requires reconfirmation.
through actual fitting. The diaphragm is inserted and checked. Then the next larger size is fitted. The correct size is one size smaller than the first one perceived by the patient. For example, starting at size 60 and increasing the sizes until the patient perceives pressure with a size 70 would suggest that a size 65 would be appropriate for her. This is confirmed by examining the patient with the diaphragm in place. The diaphragm should touch the lateral vaginal walls, cover the cervix, and fit snugly between the posterior vaginal fornix and behind the symphysis pubis. A diaphragm that is too large may buckle and permit sperm to bypass the diaphragm. A diaphragm that is too small may slip out of place. The health care provider should appreciate that the adolescent may be tense during initial fitting, causing the fitting of a smaller diaphragm than would be required if the adolescent were relaxed.

**Patient Education**

Patient education programs should include the following.

1. Demonstration of insertion and removal techniques. After being shown how to place the diaphragm, the teen should insert and remove it at least once in the office and have the placement checked by the provider.
2. Detailed guidance about use of spermicide
   - a. Coat the inner surface of the diaphragm with spermicidal gel. One application is effective for up to 6 hours.
   - b. Add additional spermicide with the applicator if intercourse is delayed beyond 6 hours or if additional acts of coitus are anticipated. Additional doses must be placed into the vagina; the diaphragm should not be removed to add spermicide.
   - c. Apply an extra dose immediately if the diaphragm is dislodged during intercourse, and consider using emergency contraception.
3. Removal instructions
   - a. Wait at least 6 hours after the last episode of coitus to remove the device.
   - b. Remove before 24 hours of use to reduce the risk of toxic shock syndrome.
4. Concrete instructions about cleaning and storage of device: Recommend washing device in soap and water, then soaking it in an alcohol solution (70% isopropanol or 80% ethanol) for at least 20 minutes after each application. Coat the device with cornstarch or another agent to prevent contamination or cracking, and store it in a dry container.
5. Return for refitting of the diaphragm every 1 to 2 years, after every pregnancy, and after any 10% to 20% change in body weight.

**Advantages**

1. The most effective of the female barrier methods available today
2. Reduced risks of cervical and vaginal STDs
3. May be placed in anticipation of coitus.

**Disadvantages**

1. Requires professional sizing and is available only by prescription.
2. Requires motivation and extensive education for proper use.
3. Requires preparation and access to supplies; therefore, it may limit spontaneity and may not meet the impulsive needs of the adolescent.
4. May be considered messy, especially for multiple acts of intercourse.
5. Not an acceptable method if either partner is allergic to spermicide or latex.
6. There is a small risk of toxic shock syndrome associated with poorly timed or prolonged use.
7. As with all female barrier methods, the diaphragm increases the risk of cystitis by increasing the count of enteric organisms within the vagina.

**CERVICAL CAP**

The cervical cap is a thimble-shaped rubber device with a firm round rim. A small amount of spermicide is placed inside the dome of the device. A groove on the inner aspect of the rim helps create and maintain a vacuum seal over the cervix. The cervical cap has a contraceptive protection for multiple acts of intercourse for up to 48 hours without device removal. It can be placed hours before coitus. Its position should be reconfirmed before each coital act. It must be removed 48 hours after placement to reduce problems with odor and the possibility of toxic shock syndrome. The cervical cap comes in four sizes, measured by the internal rim diameter (22, 25, 28, and 31 mm); approximately 80% of women can be fitted.

Contraindications for the cervical cap include all those mentioned for the diaphragm and, in addition, a known or suspected cervical or uterine malignancy, an abnormal result from a Pap smear, and a vaginal or cervical infection. The cervical cap is not intended for use during menses.

**Efficacy**

Typical first-year failure rates for the cervical cap are 18%, virtually the same as for the diaphragm. The perfect-use failure rate in nulliparous women is calculated to be 6%. Younger cervical cap users have lower failure rates than more mature women do. This difference may be explained in part by parity: The parous cervix covered with nabothian cysts and superficial irregularities is more challenging to fit correctly. Typical failure rates in parous women have been estimated at 25% to 35% (Trussell et al., 1994). Pregnancy prevention is enhanced by combining the cervical cap with male condoms and/or emergency contraception.

**Fitting the Cervical Cap**

Formal training is necessary to obtain proficiency with the fitting procedure for cervical caps. In general, the position, size, and contour of the cervix are gauged by bimanual examination. Size and contour are reevaluated by speculum examination. A fitting cap is placed, a seal is created, and the position of the rim on the cervix is verified by palpating the edge of the cap to confirm that there are no gaps between the cap and the cervix. Stability is tested by attempting to dislodge the cap by thrusting against the dome with the examining finger. After the cap has been in place for 1 or 2 minutes, the suction should be tested. When traction is placed on the dome, it should remain collapsed and maintain its position. The final test is to rotate the cap. If the cap resists rotation, it is too small. If it rotates too easily or falls off, it is too large.

**Advantages**

1. A single application is effective for up to 48 hours: additional doses of spermicide are not required for multiple acts of intercourse.
2. The cap may be placed early and usually is not detected by the partner.
3. The cap offers some reduction of STD risk, especially for cervical and upper genital tract infections.

**Disadvantages**

1. It must be professionally fitted by a trained provider and requires a prescription; also, there are few trained fitters.
2. It requires training in placement, removal, cleaning, and storage.
3. It requires application with each series of acts of intercourse.
4. It requires a second Pap smear 3 months after initiation of use. In clinical trials, an increase in dysplasia was noted at 3 months, compared with diaphragm users; the risk of dysplasia at 12 months was the same for both groups.
5. Replacement is necessary every 2 to 3 years, and refitting is needed after each pregnancy.
6. Its use increases enteric organisms in vaginal flora, which may increase the risk of cystitis.

**VAGINAL SPERMICIDES**

Vaginal spermicides are available in a wide array of delivery systems (Table 45.1). Spermicides can be used alone or in combination with barrier methods. They can play an important role in contraception for the adolescent, because they require neither a prescription nor a pelvic examination and are free from systemic side effects. Spermicides have been shown to have bactericidal and viricidal activity in vitro, but clinical data in vivo have failed to demonstrate any significant risk
reduction. Several studies of spermicide use in high-risk women (professional sex workers in Africa) found that spermicides do not protect against HIV infection, but there is no clear evidence that the risk of seroconversion is increased by the use of spermicides.

### Types of Spermicides

The various spermicidal preparations differ in their onset and duration of action and mode of application. Table 45.1 displays the more commonly used types of spermicidal agents. In general, each agent is active for approximately 1 hour unless used with a diaphragm or cap. Foam, which is the most commonly used agent, is instantly effective. Suppositories and film require 10 to 15 minutes to melt and distribute over the cervix. Each type of suppository comes with complete and appropriate patient instructions for use. Encourage patients to choose a spermicidal agent with a use pattern that will work well for them.

### Efficacy

Earlier estimates of typical first-year failure rates for spermicidal agents used alone ranged from 18% to 21%. However, more recent studies using more modern criteria reported a 6-month failure rate of 26%, which corresponds to an annual failure rate of about 40% (Raymond and Dominik, 1999). Correct and consistent use of spermicidal agents is estimated to reduce the pregnancy rate to 6%. When used in conjunction with other methods, such as barriers and emergency contraception, the pregnancy rate drops.

### Mechanism of Action

The components of spermicidal agents include an inert base (foam, cream, or jelly), which holds the spermicidal agent and blocks sperm from entering the cervical os, and a spermicidal chemical to immobilize and kill sperm. The most commonly used agent in the United States is nonoxynol 9. In other countries, agents such as octoxynol and benzalkonium chloride are also available as spermicides. However, benzalkonium has been shown to be irritating to vaginal epithelial cells and to reduce lactobacillus counts (Patton et al., 1999).

### Contraindications

1. Allergy or sensitivity to spermicidal agents or to the ingredients in the base
2. Inability to use due to vaginal abnormalities or inability to master the insertion technique

### Advantages

1. No proven systemic side effects
2. Readily available without prescription
3. A fairly convenient, easy-to-learn method for teenagers
4. May be used by women with or without involvement of partner
5. May provide lubrication
6. May be useful as a backup method for other contraceptives

### Disadvantages

1. Relatively high failure rate
2. Considered messy by some teenagers (some forms)
3. Must be used only a short time before intercourse is started
4. Requires 10 to 15 minutes for activation (some formulations)
5. Requires that woman be comfortable with touching her genitals
6. Unpleasant taste if oral-genital sex is involved
7. May cause a local allergic reaction

### Future Developments

The need for vaginal agents that provide protection against pregnancy as well as antimicrobial protection is increasingly compelling. Much of current research and development activity is centered on developing an agent with these properties. However, Murphy et al. (2000) reported that interest in female-controlled methods may be lowest among women who are at highest risk for HIV infection and other STDs; those who are most interested in vaginal microbicides/spermicides are already using existing methods to protect themselves.

### CONTRACEPTIVE SPONGE

The nonprescription vaginal contraceptive sponge (Today) contains nonoxynol 9. The manufacturer of sponges in the United States discontinued its production in early 1995 because the FDA found possible contamination along the production line, although the product was not compromised. At present, another manufacturer is applying for permission to manufacture and sell this sponge. Other versions, such as the Protect Aid sponge, are available in Canada and may eventually be brought to the United States.
http://www.youngwomenshealth.org/femalebarrier/html#condoms/. Information from Boston Children's Hospital on female condoms.

**Diaphragms**

http://www.ccm.emory.edu/WHSC/MED/FAMPLAN/diaphragm.html. Information sheet from Emory University on diaphragms.


http://www.umass.edu/ums/diaphragm.html. University of Massachusetts Health Services handout on diaphragms.


**Spermicides**


**Contraceptive Sponge**


For Health Professionals

http://www.repronline.jhu.edu/english/1fp/1methods/1condom/condom.htm. Web site with presentation slides on condoms.

REFERENCES AND ADDITIONAL READINGS


Consumer's Union. Condoms get better: tests of 30 models show far fewer failures than in past years. Consumer Reports 1999;84(6):46.


Emergency contraception (EC) has a tremendous potential to reduce the numbers of unplanned pregnancies and to decrease the need for abortion in women of all ages. It has been estimated that proper use of EC could prevent 1.5 million unplanned pregnancies and 0.7 million abortions each year (Trussell et al., 1992; Henry J. Kaiser Foundation, 2000a). Adolescent use of contraception has increased in the last decade (see Chapter 42), but unprotected intercourse occurs at a high rate because of unanticipated intercourse (e.g., impulse, date rape) (Koval, 1989); lack of perceived need for protection; and/or incorrect or inconsistent contraceptive use. In such a setting, the need for after-the-fact postcoital contraception is clear.

### EMERGENCY CONTRACEPTION METHODS

Three types of EC are available in the United States. The first two are hormonal methods that should be started within 72 hours of exposure. The Yuzpe method, which has been available for more than 25 years, calls for two doses of at least 100 µg ethinyl estradiol and 0.5 mg levonorgestrel (or 1.0 mg norgestrel) given 12 hours apart (Yuzpe and Lancee, 1977). The progestin-only method calls for two doses of 0.75 mg levonorgestrel (or 1.5 mg norgestrel) taken 12 hours apart. The third method is insertion of a copper IUD within 5 days of exposure.

The Yuzpe method has been the most commonly used postcoital method of birth control since its introduction in 1974. Table 46.1 lists the birth control pills that can be used and their appropriate doses. In 1998, the FDA approved a dedicated product (PREVEN Emergency Contraceptive Kit) to provide EC using the Yuzpe method. The kit includes clear instructions for EC, a pregnancy test, and two doses of two pills each. An institutional version excluding the pregnancy test is also available.

<table>
<thead>
<tr>
<th>Item</th>
<th>Manufacturer</th>
<th>Tablets per dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Progesterone-estrogen combination</td>
<td>Preco</td>
<td>1 white tablet</td>
</tr>
<tr>
<td></td>
<td>Ovrette</td>
<td>1 ovule</td>
</tr>
<tr>
<td>Progestin-estrogen combination</td>
<td>Plan B</td>
<td>1 white tablet</td>
</tr>
<tr>
<td></td>
<td>Levlen</td>
<td>1 white tablet</td>
</tr>
<tr>
<td></td>
<td>Levora</td>
<td>1 white tablet</td>
</tr>
<tr>
<td></td>
<td>LuGuna</td>
<td>1 white tablet</td>
</tr>
<tr>
<td></td>
<td>Liletta</td>
<td>1 white tablet</td>
</tr>
<tr>
<td></td>
<td>Levlen Ultra</td>
<td>1 white tablet</td>
</tr>
<tr>
<td></td>
<td>Nordette</td>
<td>1 white tablet</td>
</tr>
<tr>
<td></td>
<td>Ovrette</td>
<td>1 white tablet</td>
</tr>
<tr>
<td>Copper IUD</td>
<td>CuT380 A</td>
<td>1 copper IUD</td>
</tr>
<tr>
<td></td>
<td>Cu375</td>
<td>1 copper IUD</td>
</tr>
<tr>
<td></td>
<td>Cu200</td>
<td>1 copper IUD</td>
</tr>
<tr>
<td></td>
<td>Cu200 std</td>
<td>1 copper IUD</td>
</tr>
<tr>
<td></td>
<td>Cu250</td>
<td>1 copper IUD</td>
</tr>
<tr>
<td></td>
<td>Cu250 std</td>
<td>1 copper IUD</td>
</tr>
<tr>
<td></td>
<td>Cu270</td>
<td>1 copper IUD</td>
</tr>
</tbody>
</table>

**TABLE 46.1. Hormonal emergency contraception regimens: two doses 12 hours apart**

The progestin-only method of EC has several advantages over the Yuzpe method (Ho and Kwan, 1993; Task Force, 1998). The efficacy of the progestin-only method is superior to that of the Yuzpe method (Table 46.2); virtually every nonpregnant woman is eligible to use it, and side effects (especially gastrointestinal complaints) occur significantly less often with the progestin-only methods (Table 46.3). Until recently, the only way to provide adequate amounts of progestin was to provide two doses of 20 tablets of Ovrette. This volume of pills was overwhelming to many women. In 1999, however, the U.S. Food and Drug Administration (FDA) approved a dedicated product (Plan B), which includes clear instructions and two single-tablet doses. A progestin-only EC product should be used whenever possible.

<table>
<thead>
<tr>
<th>Item</th>
<th>Content</th>
<th>Progesterone (%)</th>
<th>Copper</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Progesterone-E</td>
<td>1</td>
<td>100</td>
<td>10</td>
</tr>
<tr>
<td>Progesterone-E</td>
<td>1</td>
<td>100</td>
<td>1</td>
</tr>
</tbody>
</table>

**TABLE 46.2. Comparative efficacy of combination emergency contraception (EC) pills versus progestin-only EC pills versus copper intrauterine device (IUD)**
The third type of EC, the T-380A copper IUD, can be inserted up to 5 days after unprotected coitus and provides the best pregnancy protection. Although the copper IUD is more effective than the hormonal options, it can be used only by a select group of carefully screened women (see Chapter 44). It is also very expensive for single use. Therefore, its use in the United States for this indication is expected to be quite limited.

**Efficacy**

The expected pregnancy rate per single act of intercourse is estimated to be 8%. Efficacy for ECs can be expressed in two ways—the observed pregnancy rate or the percent reduction in the expected number of pregnancies (Table 46.2). For example, the single-use failure rate for the Yuzpe method is a little over 2%, which represents a 75% reduction in expected pregnancies. The failure rate for women using the progestin-only method is 1%, which is an 89% reduction in the expected number of pregnancies. The copper IUD is the most effective EC method currently available; its failure rate is 0.1%, which is a 99% reduction in the expected number of pregnancies (Sivin and Schmidt, 1987).

The estimates of overall efficacy for the Yuzpe hormonal method were calculated from a wide range of results observed in different clinical trials. One trial found only a 56% reduction in expect pregnancy rates with the Yuzpe method, while another found 89% (Trussell et al., 1999). In part, this variation may have reflected the impact of women who were already pregnant when they were treated (in studies done before sensitive pregnancy tests were available), but there may be other reasons for this variability. A recent, large-scale World Health Organization (WHO) trial demonstrated that the effectiveness of hormonal EC depends on how soon it is initiated after intercourse (Piaggio et al., 1999; Task Force, 1998) (Table 46.4), although earlier studies did not show such a temporal relationship (Trussell, 1996). In the WHO study, when hormonal EC was started within the first 12 hours, the pregnancy rate was 0.5% (a 94% reduction), but if the first dose was delayed until 60 to 72 hours after the exposure, the pregnancy rate was 4% (a 50% reduction). The 72-hour limit may be expandable, but later use would be associated with diminished protection. The observation that early use is more effective has revolutionized prescribing patterns for EC (see later discussion).

**Mechanisms of Action**

The hormonal methods (Yuzpe or progestin-only) are approved by the FDA as contraceptives. This classification is supported by the observations (a) that most conceptions occur when intercourse precedes ovulation and (b) that EC with oral contraceptives is more effective if administered early.

The primary action of the hormonal methods appears to be to delay or inhibition of ovulation, but new analysis suggests that other mechanisms may be important (Trussell and Raymond, 1999). EC can also alter tubal motility, production of progesterone by the corpus luteum, and the composition of the endometrium to block implantation (van Santen et al., 1988; Glasier, 1997; Ling et al., 1983).

Although it may not be clear in each application of EC with oral contraceptives whether the EC is working as a contraceptive (i.e., blocking fertilization) or as an interceptive (i.e., impeding implantation), it is clear that EC is not working as an abortifacient. EC taken after a pregnancy has been established has no effect; it will not disrupt the pregnancy, and it will not increase the risk of fetal malformations (Raman-Wilms et al., 1995; Bracken, 1990). EC is neither an abortifacient nor a teratogenic (Blumenthal and McIntosh, 1996). EC is contraindicated in pregnancy only because it carries some risk of maternal side effects without offering any offsetting benefits.

The mechanisms of action for the copper IUD as a postcoital method have not been elucidated, but it is doubtful that the copper ions that are so important to the IUD’s ongoing contraceptive effect play any role in this application (Rivera et al., 1989). The insertion process itself, as well as the presence of a foreign body, alters the endometrium and blocks implantation. In this particular setting, the copper IUD functions as an interceptive.

**Contraindications**

Yuzpe Method

The labeling for PREVEN (and, by extension, for all combination oral contraceptives used for EC) includes almost all of the contraindications for combination oral contraceptives taken on a daily basis (see Chapter 43). However, a quarter-century of use has shown that such stringent restrictions for single use are not necessary. A history of previous thrombosis should not be a contraindication to single-dose Yuzpe (Webb and Taberner, 1993), although, if progestin-only pills were available, they would be preferable for medicolegal reasons. The International Planned Parenthood Federation (1994) has stated that there is no absolute contraindication to the use of the Yuzpe method except pregnancy.

Progestin-only Method

There are relatively few contraindications. The labeling for Plan B (and, by extension, for all progestin-only oral contraceptives used for EC) includes the following contraindications:

1. Pregnancy

---

**Table 46.3.** Comparative efficacy (reduction in pregnancy rate) of combination emergency contraceptive (EC) pills versus progestin-only EC pills over various timer periods

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Combination EC pills</th>
<th>Progestin-only EC pills</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-8 h</td>
<td>7%</td>
<td>9%</td>
</tr>
<tr>
<td>24 h</td>
<td>3%</td>
<td>8%</td>
</tr>
<tr>
<td>48 h</td>
<td>3%</td>
<td>8%</td>
</tr>
</tbody>
</table>

**Table 46.4.** Comparative efficacy (reduction in pregnancy rate) of combination emergency contraceptive (EC) pills versus progestin-only EC pills over various timer periods
2. Hypersensitivity to any component of product
3. Undiagnosed abnormal genital bleeding

Note: The progestin-only method is preferred for breast-feeding women.

Copper Intrauterine Device Method

The copper IUD for long-term use has an extensive list of contraindications (see Chapter 44). Because short-term use cannot be ensured, these same contraindications are also applied for short-term use.

SIDE EFFECTS

Side effects are largely hormone related and can last for 2 to 3 days. The most common side effects are gastrointestinal. With the Yuzpe method, 30% and 66% of women report nausea, and 12% to 22%, vomiting. Gastrointestinal complaints can be reduced by delaying the patient 1 hour before the first EC dose with a long-acting antiemetic over-the-counter agent such as meclizine 50 mg. Raymond et al. (2000) reported that antiemetics can halve the risk of nausea and vomiting, but most women experience drowsiness instead (Table 46.3).

The progestin-only method has a lower incidence of gastrointestinal side effects; only 23% of women report nausea, 5.6% vomit, and 5% report diarrhea. It is generally not necessary to offer antiemetics to women who are using progestin-only EC.

Other hormone-related side effects that may affect EC users include breast tenderness, headache, abdominal bloating, fatigue, and dizziness. Depending on the time in the cycle at which EC is used, the timing and flow of the next menses may be significantly altered. However, 98% of women should have withdrawal bleeding within 3 weeks; if an EC user has not started her menses in 21 days, she should return for pregnancy testing to avoid delaying a diagnosis of pregnancy.

MANAGEMENT ISSUES

1. Advance prescription: Until recently, EC was administered primarily after the fact, generally to women who had been sexually assaulted. The other site of extensive use was in student health centers on college campuses. However, the most effective way to provide EC is in advance of need. Not only is EC efficacy greatly enhanced by immediate use, but Glasier and Baird (1998) demonstrated that if patients had EC at home, they were 74% more likely to use it than were women who had to obtain EC on demand at a clinic. Raine et al. (2000) found that those who had EC in advance tripled their use of it. Importantly, women in the study by Glasier and Baird (1998) who were given EC in advance did not reduce their use of their primary birth control method. Therefore, every woman using a potentially failable method (e.g., condoms, diaphragms, Natural Family Planning), as well as women using methods fallibly (e.g., forgetting to take pills, being late for medroxyprogesterone acetate [DMPA] reinjection) should be provided with EC to keep readily available for prompt use in case of need.

2. Education: Even if a woman does not want an advance prescription, EC should be discussed during routine office visits with all sexually active women who are trying to avoid pregnancy, because a woman cannot request or use the method unless she knows of its existence and a source for obtaining it (Grossman and Grossman, 1998).

3. Assessment: A woman who presents after the fact for EC needs only a minimal assessment. It is prudent to record her last menstrual period, the number and timing of any previous acts of intercourse (protected or not) during the cycle, any symptoms of pregnancy, prior experience with EC or birth control pills, and any contraindications to EC that she may have. No physical examination is needed for established patients. No laboratory tests are mandatory, although some providers order a sensitive urine pregnancy test if there is any question about the history. This procedure is so minimal that many practitioners are prescribing an EC for established patients after telephone triage. In some states, pharmacists can provide EC without a prescription.

4. Multiple doses: Women who present with multiple episodes of unprotected intercourse can be provided EC for their last coital exposure if they are not pregnant. In addition, there is no absolute limit to the number of times EC can be used within one cycle if there is need. However, women who are using EC frequently should be advised that other birth control methods are more effective over the long run.

5. Because of variations in menstrual cycle length and the long lifespan of sperm, exposure at any time in the cycle (except the first 3 days) may mandate EC protection (Witcoff et al., 2000).

6. Courts have ruled that EC is a community standard of care for women who have been exposed to potential unwanted pregnancy (especially for sexual assault victims) (Brownfield v. Daniel Freeman Marina Hospital, 1989). Other authorities, such as the American College of Obstetricians and Gynecologists (1997), have reconfirmed that postcoital contraception is standard of care.

7. EC may be combined with other ongoing methods of birth control. Daily use of oral contraceptives can be started 24 hours after the second EC dose. DMPA can be administered the same day if the patient understands and accepts the uncertainty of the impact her contraceptive will have on her next menses, and if she agrees to return for routine pregnancy testing in 21 days. Appropriate backup methods should be provided for the first cycle. Of course, women who have a copper IUD inserted are provided with both EC and ongoing contraceptive protection.

MANAGEMENT OF SIDE EFFECTS

1. Nausea and vomiting
   a. These symptoms can be reduced either by using progesterin-only EC or by taking a long-acting antemiotic 1 hour before starting the Yuzpe method (Raymond et al., 2000).
   b. The nausea and vomiting do not result from gastric irritation but rather from central nervous system stimulation. Therefore, the first dose should be repeated only if the vomiting occurs within 30 to 60 minutes after ingestion of the first dose. Most experts also recommend repeat administration of the second dose if the patient vomits it within 30 minutes, although the importance of the second dose has recently been questioned.

2. Change in menstrual flow: In clinical trials, about 13% of women experienced heavier flow and the same number had lighter flow after EC use. Most have their next menses at the expected time or a few days early or late (Task Force, 1998).

3. Amenorrhea: A woman who does not menstruate within 21 days after starting EC should be tested for pregnancy. If she is pregnant, she should be reassured that the use of EC will not adversely affect her fetus or the pregnancy. If she is not pregnant, watchful waiting for return to normal cycling is appropriate for up to 3 months, but contraception should be provided.

ACCESS ISSUES

EC is remarkably cost-effective. Routine advance prescription of EC to male condom users saves the health system $263 per user in managed care systems and $99 in public sector settings (Trussell et al., 1997). Nevertheless, EC remains underutilized in this country. Studies show that obstetrician-gynecologists, emergency room physicians, and family practitioners are very aware of EC, and most feel comfortable prescribing it. However, the average number of prescriptions written each year by the most actively prescribing doctors is only about 5.5 (Delbanco et al., 1997). Most physicians use EC only for victims of sexual assault. A recent Kaiser survey found that 83% of obstetrician-gynecologists prescribed EC in 1999, but 52% of them had written only one to five prescriptions for it within the last year. Although 37% of family practitioners had prescribed EC in the last year, more than half of them had given it only one to five times. Only 17% of family practitioners and 31% of obstetrician-gynecologists had written six or more prescriptions for EC in the preceding 12 months (Henry J. Kaiser Family Foundation, 2000b). A survey of pediatricians found that knowledge deficits, not attitude-related variables, were associated with low EC use and counseling (Sills et al., 2000).

Gold et al. (1997) reported the results of her survey of adolescent health experts’ attitudes toward EC. 88% said they would prescribe EC to teens, but 12% were concerned that doing so would encourage contraceptive risk taking; 29% believed that repeated EC use could pose a health threat; and 56% would not prescribe EC in advance of need. On the other hand, Rowlands et al. (2000) found in a 4-year study of 14- to 29-year-old women in Britain that about 5% of them received EC each year, and only 4% of them used it more than twice in any year. EC can be an entry into more consistent contraceptive use. More than 70% of those EC users who had no previous record of contraceptive use started to use regular contraception within 1 year after EC use.

Many physicians justify underutilization of EC by noting that women do not ask for it. This should not come as a surprise, because few women know that EC is available. Studies have shown that fewer than 40% of American women are aware that anything can be done after intercourse to prevent pregnancy (Delbanco et al., 1997). Adolescent women were even less informed—only about 25% had ever heard about EC (Delbanco et al., 1998). Public service campaigns and articles in teen and women’s magazines have highlighted the availability of EC. Special episodes of popular television shows (e.g., “ER,” MTV) have featured the use and availability of EC. Each of these efforts has had a measurable but temporary impact on public awareness. A sustained one-on-one approach, especially with adolescents, is needed.
to ensure that every woman is aware of EC and, ideally, has an EC kit readily available if and when the need arises.

Pharmacies in many areas of the country refuse to carry EC because of their confusion about its mechanisms of action (Cohen, 1999). Some states have passed “conscience clauses” that provide a legal basis for this refusal practice. Other pharmacists and pharmacy chains claim that their decisions are based on economic factors—that the demand for EC is too low to justify the cost of the shelf space. The need for advance prescriptions is particularly critical in these settings. It may take a patient quite some time to locate a pharmacy with the available kits—precious hours to lose in the face of an acute need. If a patient presents after the fact for EC and it is known that she may encounter problems filling a prescription for an EC kit, it may be prudent to use one of the standard oral contraceptive formulations (Table 46.1), with prescription instructions to “take as directed,” while you provide the patient with specific instructions.

At the other extreme is the success that some pilot projects have experienced in allowing pharmacists to dispense EC without direct physician contact with the patients. Working under protocols with physicians, pharmacists in Seattle, Washington, have been evaluating patients and prescribing and dispensing EC for over more than two years. Their experience has been very instructive. The greatest demand for EC is on weekends (Hutchings et al., 1998). A similar project is running in Georgia, and a pharmacist EC-prescribing legislation is law in California.

Patients can learn the names and addresses of local providers of EC by accessing the EC Hotline, either by telephone at 1-800-NOT-2-LATE (Trussell et al., 1998) or on the World Wide Web at http://www.NOT-2-LATE.com/. Physicians and clinics can contact these same hotlines to join the network of EC providers.

Endres et al. (2000) reminds us that while improvements in access to EC are necessary, they may not be sufficient to make EC successful. In a survey of 192 women who were given EC packets, only 23% had used it within the 6- to 8-month follow-up period. Women need effective counseling and encouragement to use EC appropriately. Exposure helps. Harvey et al. (1999) found that 81% of 235 women who had received EC experienced one side effect, but 91% were satisfied with EC, and 97% said they would recommend it to friends and family.

OTHER METHODS

Mifepristone

Mifepristone at 10 mg (1/60 of the dose needed for pregnancy termination) given within 72 hours after unprotected intercourse has been shown in clinical trial to prevent 98.8% of pregnancies with few side effects. One international study, which allowed initiation up to 120 hours after exposure, reported a 85% overall effective rate (Task Force, 1999).

High-dose Estrogen

In the past, high-dose estrogen (2.5 mg ethinyl estradiol twice daily for 5 days) was used for EC, and this method is still popular in the Netherlands and other areas in Europe (Haspels, 1994). Pregnancy rates with estrogen-only therapies range between 0.1% and 1.0%, but this treatment is associated with a greater incidence of side effects, especially nausea (70%) and vomiting (33%). Moreover, continuing the method for 5 days may increase the risk of thrombosis, which is not increased by the Yuzpe method.

Androgens

Androgens, especially danazol, are not used for EC because of a higher failure rate and the concern that high-dose androgens may masculinize the fetus if the medications are not successful in preventing pregnancy.

Over-the-counter EC with levonorgestrel is available in some European countries and is being considered in the United States. The American Medical Association voted to support the Yuzpe product being offered over the counter, but the idea has not yet garnered much public support. A survey of EC users in a San Diego Kaiser pilot project found that only 28% believed that EC should be available over the counter, and only 6% thought that EC should be available in vending machines (Harvey et al., 1999). The progestin-only EC formulations may increase American support for the concept of over-the-counter EC.

WEB SITES

For Teenagers and Parents


http://www.plannedparenthood.org/ec/. EC information from the Planned Parenthood Federation of America.

http://healthydevl stuff.duke.edu/info/healthinfo.html. Duke University Student Health Center information site on reproductive health, contraceptives, and other information.

http://www.go2planb.com/. Women’s Capital Corporation Web site for Plan B.


For Health Professionals

http://www.hosppract.com/issues/1998/08/stewart.html. Article from Hospital Practice on EC.

http://www.arhp.org/ec/sldes2.htm. Site to download PowerPoint presentation on EC from Association of Reproductive Health Professionals.

REFERENCES AND ADDITIONAL READINGS


Long-acting progestin contraceptives have been available in two forms in the United States: subdermal progestin implants (Norplant system) and the depot medroxyprogesterone acetate injection (DMPA or Depo-Provera). These progestin-only methods achieve failure rates among the lowest of any reversible method of birth control. They are also remarkably convenient. Because they contain no estrogen, they may be used by women with contraindications to estrogens, such as women with histories of deep venous thrombosis or pulmonary emboli. Newer systems are available overseas, and others are under development.

SUBDERMAL PROGESTIN IMPLANTS (NORPLANT SYSTEM)

Description of System

The Norplant Contraceptive System is composed of a set of six Silastic capsules filled with levonorgestrel powder that are implanted in the subcutaneous tissue in the medial aspect of the patient’s nondominant arm. The capsules steadily release levonorgestrel into the surrounding tissue, from which it is absorbed into the general circulation. Initially, 85 µg of levonorgestrel per day is released, by 48 months, the release rate drops to 35 µg/day. Thereafter, the daily release of levonorgestrel remains relatively steady, reaching a nadir of 30 µg. The changing blood levels alter the system’s mechanism of action and side effect profile over the 5 years of use, but they do not have a noticeable impact on efficacy, except in heavier women. Virtually 100% of the drug is available, because it is not subject to the hepatic first-pass clearance effect. Studies have demonstrated that the system provides effective contraception for 7 years for women weighing less than 70 kg, although U.S. labeling still suggests removal and replacement after 5 years of use (Sivin et al., 2000).

Under local anesthesia, the system is implanted in an office setting through a small incision during the first 7 days of a woman’s menstrual cycle. If the system is implanted later in the cycle, it is prudent to rule out pregnancy before insertion and to provide backup pregnancy protection for 3 days after insertion. Removal is more challenging than insertion but usually can be achieved rather straightforwardly in uncomplicated cases. The time required depends on the removal technique used as well as the quality of the insertion and the experience of the remover. For example, removal time for correctly placed implants using the Norgrasp clamp averages slightly more than 6 minutes, whereas the same system would typically take 19 minutes to remove with the use of the Wyeth technique.

Once the implants are removed, full return to fertility is prompt, and any side effects resolve rapidly because the low circulating hormone levels are cleared from the circulation within days. Several studies have shown that adolescent acceptance of this method and its side effects has been at least as good as its acceptance by older women. Teen continuation rates and satisfaction ratings with Norplant are considerably higher than with oral contraceptives, even though the implants can cause more side effects in the early months after initiation and lack many of the noncontraceptive benefits of birth control pills.

Efficacy

The Norplant system is the most effective method of reversible birth control available. Typical first-year failure rates are reported by the U.S. Food and Drug Administration (FDA) to be 0.09%; the cumulative 5-year failure rate is 1.3% with no pregnancies occurring in women under 79 kg (Sivin et al., 1998b). Failure rates in heavier women (more than 70 kg) diverge from the rates in lighter women only during the fifth year of use.

Mechanism of Action

The implantable progestin-only method has several important contraceptive effects (Fraser et al., 1998), listed here in descending order of significance:

1. Thick cervical mucus: The progestin thickens the cervical mucus, which renders it hostile to sperm penetration. Because the failure rate is constant throughout the years, even after ovulation has returned (see later discussion), it is logical to expect that the cervical mucus effects are the clinically significant ones.
2. Inhibition of ovulation: Ovulation is inhibited in the majority of cycles for the first year or two of use. Ovulation returns for most women in the final years of use.
3. Endometrial atrophy: Progestin causes endometrial atrophy, which could block implantation.
4. Suppression of progesterone production: Should ovulation occur, the pharmacological doses of progestin suppress uterine progesterone production and result in levels typically associated with luteal phase defects.
5. Alteration of tubal motility: Altered sperm or ovum transport can reduce fertilization and implantation rates.

Metabolic Effects

The circulating levels of levonorgestrel are relatively low, (300–400 pg/ml) so metabolic impacts are minimal. No changes in coagulation factors are seen with Norplant. Glucose tolerance is only marginally affected. In trials of normal subjects tested before implant insertion and after 2 years of use, fasting glucose and 2-hour glucose levels were unchanged. One-hour levels were minimally affected. The studies of lipid metabolism have been mixed but, overall, the impact appeared to be minor. Total cholesterol and triglyceride levels fall. High-density lipoprotein (HDL) cholesterol reportedly remains the same or decreases slightly; no consistent
increase in low-density lipoprotein (LDL) cholesterol has been seen.

Contraindications (From Product Labeling)

1. Active thrombophlebitis or thromboembolic disorders
2. Undiagnosed abnormal genital bleeding
3. Known or suspected pregnancy
4. Acute liver disease; benign or malignant liver tumors
5. Known or suspected carcinoma of the breast
6. History of idiopathic intracranial hypertension
7. Hypersensitivity to levonorgestrel or any of the other components of the Norplant system

Other Considerations

Possible relative contraindications that should be evaluated include cholecystitis, coronary artery disease, renal failure, labile hypertension, and complicated diabetes. The absence of estrogen makes Norplant an excellent contraceptive option for women with a history of thrombosis. Similarly, hypertension would not preclude Norplant use. Breast nodules that have been diagnosed as benign (e.g., benign fibrocystic changes, fibroadenoma) are not a contraindication to Norplant use; only abnormalities with carcinoma potential should forestall Norplant implantation. Hypertensive women who are stable enough to tolerate incision are candidates for the levonorgestrel-releasing implants.

Drug-Drug Interactions

Because circulating levels of levonorgestrel are minimal, any drug that activates the hepatic microsomal enzyme system will compromise the efficacy of the Norplant Contraceptive System. In one small series of patients receiving anticonvulsants (e.g., phenytoin, phenobarbital), the first-year failure rate soared to 17%. Similarly, the implantable progestin system should not be used in patients receiving rifampin, griseofulvin, or aminoglutethimide. Although it is often overlooked in drug medication history taking, St. John's wort is thought to increase the hepatic clearance of sex steroids by as much as 50% and could seriously compromise the efficacy of Norplant.

Not Contraindicated

1. Postpartum women: This is an excellent method, particularly for postpartum adolescent women. The only caveat is that involution of the uterus may be slowed by progestin. In several studies, adolescent mothers continued to use the implant at much higher rates than they did oral contraceptives.
2. Breast-feeding women: Implants are an excellent contraceptive choice for breast-feeding women. Studies of babies exclusively breast-fed by Norplant users have shown no adverse impact on any infant growth parameters.
3. Smokers older than 35 years of age

Advantages

1. Extremely effective method of birth control
2. Decreases risk of ectopic pregnancy
3. Constant low dose of hormone: No swings occur throughout the day
4. Long-lasting: One set may be used for at least 5 years.
5. Convenient and low maintenance: A single insertion procedure provides continuous contraception.
6. Discrete (but not invisible)
7. Rapidly reversible: Return to fertility is rapid.
8. Progestin-only, and therefore available to women with contraindications to estrogens.
9. Cost-effective: Amortized over 2 to 5 years of use, the cost of the system is quite competitive. The manufacturer has attempted to lower the initial cost by offering a warranty: The company will replace any set that must be removed within the first 6 months.
10. Decreases total menstrual blood loss; less anemia
11. May be used immediately by postpartum breast-feeding women, even though FDA labeling does not encourage this application.
12. Thick cervical mucus may reduce the risk of against pelvic inflammatory disease.

Disadvantages

1. Progestin-only side effects (see later discussion).
2. Must remind patients to practice safer sex and provide barrier methods to susceptible patients.
3. Has relatively large initial cost.
4. Requires trained provider for insertion and removal.
5. Counseling: Is initially more time-consuming than many other methods.
6. Removal: May be complicated and associated with return visits; rarely, operative removal is required.
7. History of litigation now resolved.
8. Lack of ready access to product. Currently, the company is not distributing any more sets until product consistency can be reverified.

Side Effects

1. Menstrual disturbances: Virtually every user of the implantable progestin system experiences some changes in her menstrual patterns. Initially, these changes include prolonged bleeding (40%), irregular bleeding (38%), intermenstrual spotting (32%), more frequent bleeding (16%), and amenorrhea (12%). However, unlike other progestin-only contraceptives, the cycles of Norplant system users usually normalize after the first year of use. By the fifth year, 62% of women using Norplant have regular cycles, 38% have irregular periods, and amenorrhea is very rare. a. Decreased flow: About 20% of Norplant users notice a slightly decreased flow but continue to have predictable withdrawal bleeding from the time of insertion. No therapy is needed for them. Similarly, as cycles return in women who initially experience amenorrhea (see later discussion), their menstrual flow is usually diminished. b. Amenorrhea: About 10% to 15% of women initially experience amenorrhea or very infrequent menstrual bleeding. If they can be reassured that they are not pregnant and are not expected to have withdrawal bleeding (due to an atrophic endometrium), many teens tend to enjoy this change. Certainly there is no clinical concern of endometrial hyperplasia and cancer that such symptoms do for women with unopposed estrogen exposure. Progestin functionally downregulates the estrogen receptors in the endometrium, which significantly reduces endometrial proliferation and often causes atrophy. Progestins also increase the caliber of the vessels underlying the endometrium, rendering them more fragile. Researchers have found on routine uterine biopsy that amenorrhea usually is associated with endometrial atrophy, whereas women with spotting are more likely to have proliferative endometrium (Hickey et al., 1999). This may reflect intermittent estrogen production from unsustained follicle stimulation. Explicit counseling about these bleeding possibilities is critical to successful long-term use. Reassurance can often persuade a woman to continue her Norplant use at least temporarily. The goal is to wait until the release rate of levonorgestrel from the implants declines and ovarian production of estradiol resumes. However, medical interventions are often needed, especially during the first year. The following therapies have demonstrated varying degrees of efficacy in helping control spotting:
   - Use of nonsteroidal antiinflammatory drugs (NSAIDs), such as oral ibuprofen 800 mg, three times daily for 3–5 days, starting when the menses stop and spotting commences. This therapy is taken only during affected cycles.
   - Progesterone supplementation

(1) Ethinyl estradiol 0.02 to 0.05 mg orally every night, on days 8 through 28 of the cycle, for 1 to 3 months
Conjugated equine estrogens 0.625 to 1.25 mg orally every night, on days 8 through 28 of the cycle, for 1–3 months. Other equivalent 
equivalent replacement preparations are helpful too.

(3) Estrogenic oral contraceptive pills with low progestin content, 1 tablet orally every night, for one to three cycles.

- Pretesting of women with other progestin-only products, such as DMPA or the progestin-only “mini-pill,” predicts neither the type of bleeding pattern a particular patient may develop with the implants nor how she will respond to it. It should also be noted that, in real use, adolescent Norplant users have tended to tolerate the menstrual disorders with at least as much equanimity as their adult counterparts (Damey et al., 1990; Shoupe et al., 1993; Cromer et al., 1994; Cullins et al., 1994; Berenson and Wiemann, 1995).

2. Weight changes: Slightly more than half of Norplant users gain weight, about one third lose weight, and the rest experience no weight change. Some Norplant users note abdominal bloating and more generalized fluid retention. Long-term studies have not found significant weight gain attributable to Norplant use, although individuals may be sensitive to sex steroids.

3. Breast tenderness: Some women complain of mastalgia, which may lessen as levonorgestrel levels fall over time but occasionally may require implant removal.

4. Mood changes: Progestrone has been linked to an increased incidence of depression, but in clinical trials the implants have not significantly worsened the moods of depressed patients. Occasionally, mood changes do force the removal of the implants; because the progestrone is so rapidly cleared, the attributable mood changes are quickly resolved. Some patients complain of anxiety or nervousness and others of fatigue; it is not clear that the Norplant system is responsible for these changes.

5. Local changes at insertion site: Infection occurs in fewer than 1% of cases. Cellulitis may be treated with antibiotics; abscess formation requires incision, drainage, and capsule removal. Superficial thrombophlebitis can occur distal to the implantation site, which responds well to warm compresses and several days of NSAIDs. Expulsion occurs in 0.4% of cases. Norplant can be visible, especially if the system is implanted very superficially. In addition, reversible hyperpigmentation may occur over the capsules. After insertion, some patients describe a temporary internal tugging or pulling sensation with elbow extension, which responds to local massage. Distal neuropathy resulting from nerve injury is extremely rare but requires immediate attention.

6. Ovarian cysts: Norplant does not suppress physiological ovarian cyst formation as effectively as DMPA or higher-dose oral contraceptives do. Low-dose levonorgestrel may even slow the involution of those cysts. Patience is prudent in managing the small, simple ovarian cysts that are incidentally palpated in implant users unless the patient develops symptoms.

7. Headaches: Migraine headaches are not a contraindication to progestin-only methods, but some women do complain of worsening or more frequent tension headaches when using Norplant. If a woman complains of visual changes or of severe headaches not relieved by over-the-counter medications or rest, she should have a funduscopic examination to rule out papilledema, which might indicate the development of pseudotumor cerebri (idiopathic intracranial hypertension). The incidence of pseudotumor cerebri has not been found to be higher in Norplant users than in the general population, but it is recommended that the capsules be removed promptly should the condition develop.

8. Other changes: A wide range of complaints has been reported at low frequency in Norplant users, including acne, hair loss, vaginal discharge, increased varicocities, changes in libido, and nausea.

Access and Implementation Issues

The introduction of an implantable contraceptive system raised concerns in some communities, especially about the use of Norplant in adolescents. In Baltimore, several issues were also brought about the concerns were learned about the constituency of community leaders before launching a program to offer Norplant to teens (Bellinson et al., 1995). Early in the introduction of the implant system, investigators were worried that teens would have low continuation rates, but experience has shown the opposite. In one study of parous teens that compared oral contraceptives and implants, only 33% of teens were still taking birth control pills after an average follow-up period of 15.5 months, compared with a 95% continuation rate among the Norplant users (Polaneczky et al., 1994). Another study in Texas showed no discontinuation of Norplant use over a 6-month period, but there was a 43% dropout rate among oral contraceptive users.

Other crucial concerns were that if adolescents were provided long-term contraception, they would not return for routine health screening appointments and would not use barrier methods to reduce their risks for sexually transmitted diseases (STDs). In comparative trials, appointment compliance was about equal for pill users and implant users (Cromer et al., 1994; Polaneczky et al., 1994). Another study showed that teens were equal to adult users of implants in their failure to comply with follow-up appointments (Cullins et al., 1994). As with any effective contraceptive method, the use of condoms is significantly reduced with Norplant. It is critical to reinforce the need for condom use for STD protection while using Norplant to maximize protection against unwanted pregnancy.

Although the Norplant-6 insertion and removal procedures are straightforward, formal training is needed to ensure low complication rates. The implants are inserted into the subcutaneous layer in a fan-like distribution in the medial aspect of the nondominant upper arm. Optimally placed implants are best removed by the digital extrusion technique (also known as the “pop out” technique), which minimizes trauma and the need for anesthesia. For other placements, the modified-U technique using norfold or Morigrass clamp is the fastest removal approach and the one that is most rapidly mastered. Deeply placed, nonpalpable implants can usually be removed in an office setting under real-time ultrasound guidance.

The use of Norplant soared after its initial introduction: More than 900,000 women had Norplant inserted during the first 18 months after its FDA approval. However, after the initial exuberance, concerns were raised by numerous lawsuits filed on behalf of women claiming unexpected and severe side effects. The courts rejected most of those cases; only a few went to jury trial, and in virtually every one of those the juries found for the manufacturer. Once the medicolegal issues were cleared, it was expected that the proven convenience and efficacy of Norplant would make it an attractive option, especially for adolescent women. However, problems in the production line have shut down U.S. distribution of Norplant for at least the near term. It is hoped that the improvement in the medicolegal environment may encourage other manufacturers to introduce their implant systems.

Future Implants

Several alternative contraceptive implants may become available in the future.

1. Norplant-2 is a two-implant levonorgestrel contraceptive system in that the levonorgestrel is not a powder but a gel, which is mixed in the plastic matrix. The Norplant-2 implants are slightly longer. The contraceptive efficacy of the two systems is comparable; the 3-year and the 5-year rates were both 0.8% (Sivin et al., 1998a).

3. Implanton delivers a single-constant-release etonogestrel (a metabolite of desogestrel) and provides extremely effective pregnancy prevention for 2 to 3 years.

5. Implanon is available in several foreign countries; plans to introduce the system in the United States are being evaluated.

3. Other implantable systems, such as the Uniplant containing nomegestrol acetate, lipid spheres, and biodegradable pellets, have been studied.

DEPO-MEDROXYPROGESTERONE ACETATE INJECTION

DMPA provides features that are critically important to many adolescent women. The first-year failure rate in typical use is 0.3%. The need for only four injections per year, as well as DMPA's enduring effect, greatly enhances effective use. In fact, a significant portion of the decrease in adolescent pregnancies seen in the 1990s has been attributed to widespread use of DMPA and Norplant.

Overall, first-year continuation rates among teens (27% to 61% at 12 months) are somewhat lower than those seen in clinical trials (Matson et al., 1997; Sangi-Haghpeykar et al., 1996). However, adolescent women often follow a “start-stop” pattern of use (Polaneczky and Liblanc, 1998). After one or two injections, they may discontinue use or switch to another method such as oral contraceptives or condoms, although quite frequently they return at a later date for at least another full cycle of DMPA. In part this intermittent pattern of use reflects the dynamics of adolescent sexual activities and relationships. However, in part it reflects the response of these young women to side effects. Two important lessons can be learned from these observations. Anticipation of side effects and counseling of patients about potential interventions before they start using DMPA can enhance longer-term use. One prospective study showed that women who were told about the possibility of amenorrhea were 2.5 times more likely to continue to use DMPA than women who were not so informed (Hubacker et al., 1999). Because irregular bleeding has been found to be the most common reason for discontinuation, this is a significant issue. Secondly, even if a woman has previously abandoned DMPA use, it should be reoffered to her at a future visit, when she may be again interested. Telling women specifically when to return for reinjection enhances continuous use by twofold (Hubacker et al., 1996), but reminder systems (e.g., telephone calls, letters) may not (Kedder et al., 1998; Madlon-Kay, 1996).

Description of Method

DMPA is a crystalline suspension that is available in prefilled syringes containing 1 mL of 150 mg/mL. The suspension should be injected intramuscularly into a large
muscle mass (gluteal or deltoid) within the first 5 days of the menstrual cycle. However, more flexibility in timing is possible (see later discussion). Caution should be exercised to avoid massaging the area directly after injection, because doing so spreads the drug over a larger surface area. When such an increased surface area occurs, drug uptake is more rapid and the effect more short lived. Each dose is effective for 11 to 13 weeks.

Questions have been raised about the use of the less expensive preparation of DMPA used for cancer therapy, with a concentration of 400 mg/mL. There are several problems with this preparation:

1. It is difficult to measure 150/400 or 0.37 mL.
2. This preparation is not approved by the FDA for contraception.
3. The injection of the more concentrated DMPA can be painful.
4. Clinical trials with this preparation tested as a contraceptive had unacceptably high failure rates throughout the treatment period (Hatcher et al., 1994).

Similarly, a generic version of DMPA used in Thailand was found to have a significantly higher failure rate.

**Efficacy**

The typical first-year failure rate for DMPA is 0.3%; the cumulative 5-year failure rate is 0.9%. In postpartum teens, O’Dell et al. (1998) compared DMPA users with users of oral contraceptives and reported a median duration of use of 8.1 versus 5.4 months, respectively, and a repeat pregnancy rates by 15 months of 15% versus 36%, respectively.

**Mechanism of Action**

DMPA is a progestin-only method that thickens the cervical mucus to prevent sperm penetration. DMPA also significantly suppresses gonadotrophin levels, especially at midcycle, to reliably block ovulation. The progestin alters the endometrial lining and tubal motility, affecting both sperm motility and implantation.

**Contraindications**

Contraindications are the same as those for the Norplant system, except that the injection is also contraindicated in patients with known sensitivity to DMPA sterile aqueous suspension.

**Drug-Drug Interactions**

Circulating levels of DMPA are sufficient not to be affected by increased cytochrome P-450 activity induced by drugs such as anticonvulsants. In fact, because progesterone has antiseizure activity itself, DMPA is an excellent choice for teens with convulsive disorders. Aminogluthethimide depresses the availability of DMPA. Rifampin use may decrease contraceptive efficacy.

**Metabolic Impacts**

Because there is no estrogen component, there are no alterations in coagulation factors, angiotensinogen, or hepatic globulin production. Blood pressure measurements are unchanged with DMPA (World Health Organization, 1983). However, the levels of progestin with this injectable are higher and result in a greater impact on glucose tolerance, insulin levels, and lipid profiles than is seen with the implants. For healthy, normal subjects the changes in glucose tolerance are not clinically significant (Liew et al., 1985). Because glucose and insulin levels were increased during DMPA use at all time points of the tolerance test, teens with glucose intolerance or overt diabetes must be monitored closely when using the DMPA injections. DMPA can lower total cholesterol and triglycerides; it has a negligible impact on LDL and HDL cholesterol (Deslypere et al., 1985).

**Advantages**

1. Extremely effective. Pregnancy protection is excellent, although that is not highly prized by teens themselves. Only 15% of those interviewed cited that as a reason for selecting DMPA.
2. Conveniences/Privacy method. With DMPA there is no external evidence of contraceptive use (no pill packs or condoms to hide), but itemized insurance bills or changes in needs for sanitary protection may raise adult suspicions.
3. Convenient and low maintenance. Many studies have found that this feature is “most important” or “likely important” to 89.3% of teens surveyed (Harel et al., 1995). This same survey found that the most important reason teens continued to use DMPA was that “they didn’t have to take the pill every day” (54%), and the second reason was that it was “easier to take” than their previous method (16%). Most teens were not concerned about the need for return to health care providers for reinjection.
4. Cost-effective without high initial cost. Because payment for DMPA is almost “pay as you use it,” DMPA can be more affordable than Norplant.
5. Intermediate-term method with built-in grace period
6. No estrogen contraindications or side effects. May be used by breast-feeding women immediately after delivery. Providing convenient and reliable contraception to teen mothers can make a significant contribution to reducing the rate of recidivism.
7. Thick cervical mucus and amenorrhea: This limits the incidence of pelvic inflammatory disease in patients with cervicitis.

**Disadvantages**

1. Side effects (see later discussion)
2. Must remind patients of the need for safer sex practices and provide a method to reduce the risks of STDs
3. Requires medical intervention
4. Delays return to fertility: Average delay is 10 months after last injection (depending not on the number of injections but on patient weight).
5. Immediate anaphylactic reactions (extremely rare)

**Side Effects**

1. Menstrual changes: Missed menstrual periods and amenorrhea become more common over time with DMPA. After the first year of use, about 50% of DMPA users are amenorrheic, and after 2 years that number rises to 75%. Some women also experience irregular menstrual spotting, and a few have heavy bleeding. The bleeding changes with DMPA are more challenging to manage during the first few injections than during early use of implants, but the same approaches are helpful (see earlier discussion): Early reinjection (at 6 weeks) did not alter the bleeding episodes, onset of bleeding, or total days of bleeding after the second injection, compared with standard timing of reinjection (Harel et al., 1995). Similarly, the practice of giving a 300-mg dose initially is not recommended, because the risk of developing other side effects is proportionately increased.
2. Weight changes: Uncontrolled studies conducted in the late 1960s and in the 1970s showed that women who used DMPA had a mean weight increase of 5 pounds during the first year, 6.1 pounds by 2 years, and 13.8 pounds by 4 years (Schwabie and Assenso, 1974). Subsequently, carefully controlled studies demonstrated that the average weight gain was 1.5 kg (3.6 pounds) per year. Clinic patients tended to gain more weight than private provider patients. Pre-use weight was not predictive of subsequent gain with DMPA use. Moore et al. (1995) monitored women who used oral contraceptives, DMPA, or implants for 1 year and found no significant weight gain in any group; the average weight gain with DMPA use was +0.1 pounds. Cromer et al. (1994) did not note weight gain in teens with DMPA use, but Harel et al. (1996) noted weight gain that persisted for 6 months after discontinuance. Ongoing studies should help provide even better data.
3. Breast tenderness: Progestosterone stimulates ductal activity and fluid retention in the breast. Mastalgia is reported in 15% to 20% of women starting DMPA, but it usually decreases over time.
4. Hypoestrogenic effects: Most users of DMPA maintain adequate estradiol levels in the follicular range. However, in a small percentage of users, ovarian
hormonal production is more profoundly suppressed and estradiol levels can fall into the postmenopausal range. Those rare patients may complain of dry vagina, dyspareunia (Miller et al., 2000), and even hot flashes. Once other causes have been excluded, these symptoms respond well to physiological estrogen replacement.

For this group of hypoestrogenic women, there is also the concern that DMPA might decrease bone mineral density (BMD). This is a critical issue for adolescents, because most bone mineralization occurs between the ages of 14 and 18 years. Controlled cross-sectional studies of older, long-term DMPA users found that, although the BMD of DMPA users was statistically significantly lower than that of controls, their BMD normalized after they stopped using DMPA. The current understanding is that DMPA may create temporary, reversible decreases in bone mineralization, akin to the changes seen during pregnancy and breast-feeding. In younger women, the data are not as reassuring or complete. Cromer et al. (1994) demonstrated not only that DMPA use in younger adolescent women slowed the rate of increase (accumulation) in BMD significantly, but that these women experienced a 1.5% decrease in the calcification they had previously accumulated. It is not known if, when such teens stop taking DMPA, they will reaccumulate BMD to the same level as before they initiated therapy or whether they will accumulate even more BMD and emerge at the level they should be later in life. A phase IV clinical trial is currently underway to answer these questions and also to discover the effects that pregnancy and breast-feeding may have on an adolescent woman's bone function. Pending the results of these trials, it is important to remind adolescent DMPA users (as well as all teens) that calcium supplements and weight-bearing exercises are critical to long-term bone health.

5. Mood disturbances: DMPA has been associated with a wide range of psychological effects, such as nervousness, insomnia, somnolence, fatigue, dizziness, and depression. Many patients with chronic depression tolerate DMPA, but use in those cases must be individualized. Westhoff (1996) reported that community epidemiologic survey depression scores after DMPA did not change compared with baseline scores, but Civic et al. (2000) reported an increased likelihood that DMPA users would report depressive symptoms, compared with nonusers.

6. Headaches: Progestin may increase headaches by increasing fluid retention. No association has been noticed with pseudotumor cerebri.

7. Other changes: Acne, alopecia, hirsutism, fluid retention, changes in libido, changes in cervical secretions, nausea, cholestatic jaundice, and local skin reaction to injection have been reported but seldom have been serious enough to warrant a change in method.

Algorithms for DMPA Use

Package labeling recommends that the initial dose of DMPA be injected during the first 5 days of the cycle. Rejections can be given routinely every 11 to 13 weeks thereafter. Routine pregnancy testing is never indicated, even when amenorrhea develops, as long as the patient returns on time for reinjection and has no signs or symptoms of pregnancy. In actual practice, however, the initial injection can be administered at any time during the menstrual cycle provided the patient is not pregnant. However, if the injection is given later than the first 5 days of the cycle, the patient must use a backup method for the first 7 days (Petta et al., 1998). Similarly, because the average return to fertility is 10 months, a great deal of flexibility can be introduced into the protocols for initial injections and reinjections. One such algorithm, which also recognizes the occasional need for emergency contraception (see Chapter 46), is displayed in Fig. 47.1.


TELEPHONE HOTLINES FOR HEALTH PROVIDERS

1-800-760-9030 Norplant Foundation Supply and Removal Program
1-800-975-2589 Norplant System Provider Support Center
1-800-364-5809 Norplant System Information Line

WEB SITES

For Teenagers and Parents

http://www.depo-provera.com/, Pharmacia Inc. site on Depo-Provera.
http://depts.washington.edu/hhpcweb/women/provera.html, University of Washington Health Services handout on Depo-Provera.
http://www.youngwomensshift.org/femalehormone.html, Boston Children's Hospital Web site on contraception including Depo-Provera.
http://www.cfirc.org/3/teen/3_whats.cfm#Depo-Provera, Teen site with information about many reproductive issues including Depo-Provera and other contraceptive devices.

For Health Professionals


REFERENCES AND ADDITIONAL READINGS

Cromer BA, Harel Z. Prescribing long-acting progestin-only contraceptives to adolescents. Contemp OB/GYN 1997;March:145.
Gynecological Examination of the Adolescent Female
Merrill Weitzel and S. Jean Emans

A gynecological examination is an essential component of the health care of adolescent girls. Most adolescents are apprehensive about the examination of their genitalia, especially during a first examination. A sensitive approach to the adolescent's concerns and needs can aid in creating a positive and instructive experience. This is especially important because the first pelvic examination can influence an adolescent's attitudes about reproductive health care for the rest of her life.

OFFICE SETTING

To create a positive atmosphere a clinician should do the following:

1. Provide an office setting that is a comfortable and friendly environment. Support staff should be welcoming. A special seating area or corner of the waiting area should be reserved for teens with appropriate reading material is optimal. An assessment of office procedures—such as weighing patients in the examination room, not in hallways—is key to meeting the needs of teens for privacy. Teens who wish to contact the office by telephone should have easy access to staff to schedule appointments and ask questions.
2. Special appointment times can be reserved for teens. Late afternoon or evening appointments may be more convenient for teens than morning times.
3. Practices limited to adolescents can have posters and pamphlets directed at the concerns of teens, such as smoking cessation, healthy nutrition, sexual decision-making, "how to say no," birth control, sexually transmitted diseases (STDs), and human immunodeficiency virus (HIV) infection. Practices with a wider age range of patients ages usually opt for neutral decor but can still have pamphlets and materials displayed in areas "especially for teens" within the examination room.
4. Parents of adolescents should be included as much as possible in the history gathering and medical plan. However, the adolescent's need for medical privacy and confidentiality should be respected. An explicit statement (and in some practices a written statement) about confidentiality should be included early in the discussion because it will encourage more open discussion about risk behaviors. The limits of confidentiality (conditions that are life-threatening or that require reporting by law) should also be discussed with the patient and her family.
5. During part of the gynecological assessment, the adolescent should be interviewed privately in a comfortable environment about risk behaviors and health-promoting behaviors. If at all possible, she should be fully clothed and seated eye-to-eye with the examiner for the first visit. Reassure her that what she communicates regarding her reproductive health will be kept confidential. She should be aware that the results of the examination will not be discussed with her parents or others without her permission but that you will encourage her to share her health concerns, medications prescribed, and management plans with her parents.
6. Be aware of the fears and worries of the adolescent about the pelvic examination. These fears may be expressed as anxiety or occasionally as hostility. Ask the patient about her feelings concerning the examination and the worries or questions that she may have regarding her body. Many teens are worried about pain, discomfort, or embarrassment ("It will hurt" or "The doctor will judge me") and need to be reassured about the tempo of the examination. The adolescent needs to feel in control of the tempo of each part of the examination.
7. Listening rather than lecturing the adolescent is essential. The examination can be a critical time for health education and for helping the teen value and protect her body. A virginal teen may be concerned about whether the examination will alter her hymen and should be reassured that the small speculum that is used was designed for girls who have not had intercourse. Girls who have used tampons are generally more comfortable with their bodies and can be particularly reassured as to the ease of the examination. Dispelling myths and respecting cultural feelings about pelvic examinations is important.
8. During each step of the examination, it is important to reassure the teen of her normality, as appropriate. The question, "Am I normal?" may be an underlying reason for any teen's visit. Other concerns may be "Do I have a STD?" or "Are my labia too big?"

INDICATIONS FOR GYNECOLOGIC EXAMINATIONS

The indications for a complete or modified pelvic examination in an adolescent vary with the patient complaint. For example, a 13-year-old girl who is not sexually active and who has a white vaginal discharge may be evaluated by obtaining two saline-moistened cotton-tipped applicator samples of the discharge and examining the samples under the microscope for physiologic leukorrhea or Candida vaginitis. In contrast, a 16-year-old, sexually active girl who has had lower abdominal pain for 2 days and has a vaginal discharge deserves a complete pelvic examination. It is also important for clinicians to assess whether the answer can be obtained by the use of urine-based STD screening for Chlamydia or by pelvic ultrasound. For example, a girl with primary amenorrhea may be willing to allow only an external genital inspection; the internal genital structures can then be assessed by ultrasound.

It is also important for clinicians to distinguish between reproductive care and screening for all sexually active girls (clinical preventive services) and requirements to obtain tests or examinations solely related to the use of a particular contraceptive method. Delaying a first pelvic examination until the adolescent is comfortable with the idea should not prevent the use of effective oral contraceptives or other hormonal methods in the meantime.

Most professional organizations suggest that pelvic examinations be initiated at 18 years of age or whenever the patient becomes sexually active. However, the age of 18 years should be seen as a general guideline, and the wishes and background of the patient should be respected. Most importantly, the first pelvic examination should be an educational and positive experience. Indications for modified or complete pelvic examinations therefore include the following:

1. Ever sexually active (vaginal intercourse)
2. Symptoms of vaginal or uterine infection
3. Menstrual disorders including amenorrhea, dysfunctional uterine bleeding, severe dysmenorrhea, or mild-to-moderate dysmenorrhea unresponsive to therapy
4. Undiagnosed lower abdominal pain
5. Sexual assault (modified to collect the appropriate information and samples)
6. Suspected pelvic mass
7. Request by the adolescent

OBTAINING THE HISTORY

The history should include a gynecological assessment, general health history, review of systems, and information on risk behaviors. The HEADSS framework can be used; it focuses on Home, Education/career plans, Activities, Drugs/alcohol/Tobacco, Depression, Suicidality, Sexuality, and Safety. These questions can be asked through the use of a clinical interview, a written questionnaire, or a computer-aided questionnaire. Most of the visit should be devoted to seeing the teenager alone, because her presenting complaint is often different from her parents' concerns. However, it is essential to understand the concerns and the family history of the patient or parents. Mothers often attribute symptoms of their daughters to diagnoses that they themselves have had, such as ovarian cysts or other gynecological problems within the family. Although some medical conditions (e.g., polycystic ovary syndrome, endometriosis) clearly can occur within families, many other conditions are not related to the complaint that brings the teen to the clinician.

It is essential to know what the parent told the patient about the reason for the visit and whether an examination was explained. If the parent discussed the
examination with the patient, it is important to gather information on how it was explained. Some patients are told, “Don’t worry, you don’t need an examination,” and others are told about the full speculum examination when potentially they only need one or two cotton-tipped applicator samples. It is also important to know what and how the parent has explained to the young adolescent about menstrual periods, sexuality, and other issues.

The younger teen may feel more comfortable if most of the history is obtained with parent or parents in the room. A few moments of privacy are all that is needed to obtain pertinent negatives about risk behaviors. It is often best to begin the interview by asking the adolescent why they have come to the office for an evaluation that day. It is imperative to address the chief complaint and to relate the gynecological examination (modified or complete) to that concern. Reasons for the visit may include pelvic pain, vaginal discharge, a menstrual disorder, or a possible pregnancy. A presenting complaint such as irregular menses may actually lead to a diagnosis of pregnancy; in such cases, the patient may be denying the possibility of pregnancy, or a menstrual complaint may be the only way for her to access medical care. Dysmenorrhea may mask a “hidden agenda” for obtaining oral contraceptives. The sexual history should be part of the structured questioning: “Have you ever had sexual intercourse?” “Have you ever been forced to have sexual intercourse?” “Tell me about your partners.” “Have you ever used condoms?” “If yes, how often?” It is important that these questions be preceded by the comment, “I ask all my patients these questions.”

The history should include the following:

1. Menstrual history
   a. Age at menarche
   b. Duration of menses and interval between periods; intermenstrual staining
   c. Amount of flow and any recent changes in amount of flow (this is often best accomplished by asking whether the patient uses tampons or pads and how often during the day she needs to change)
   d. Date of last menstrual period
   e. Dysmenorrhea—if present, severity and extent of missed school or activities
   f. Premenstrual symptoms

2. History and type of vaginal discharge

3. Sexual history
   a. Relationships, sexual contact, number and age of partners (men, women, or both), age at first sexual intercourse.
   d. Prior pregnancies (number and outcome of each—abortion, term, ectopic, miscarriage), fertility concerns. Trying to get pregnant now?
   e. Has the patient ever had a Pap smear? When was the last Pap performed? Colposcopy?
   f. If the patient is sexually active, ask whether her partner treats her well and whether she has ever been in a situation where she felt unsafe, felt coerced to have sex, or was hit or slapped.

4. Family history
   a. Family gynecological problems (e.g., polycystic ovary syndrome, endometriosis)
   b. Blood clotting disorders

GYNECOLOGICAL EXAMINATION EQUIPMENT

Materials needed for the gynecological examination include the following:

1. Examination table with ankle supports: Oven mittens or other cloth holders placed over the metal supports increase foot comfort.
2. Gowns, sheet
3. Light source (speculum light or lamp)
4. Specula: metal—Pederson or Huffman (also sometimes called a Huffman-Graves speculum)—or plastic (medium and small), with or without self-contained light source
5. Gonorrhea culture medium or other nonculture gonorrhea test
6. Chlamydia screening test: Swabs should be rayon or Dacron (urine tests are an alternative)
7. spatula and cytobrush for Pap smear
8. Cotton swabs and either tubes or slides for wet mounts
9. Ten percent potassium hydroxide (KOH) and saline for wet mounts, pH paper
10. Pap slide containers and fixative, or kits for ThinPrep or other Pap systems
11. Water-soluble lubricating jelly
12. Warm water source
13. Nonsterile gloves
14. Handheld mirror (use is optional and up to the patient)
15. Tissues
16. Tampons and sanitary napkins
17. Rapid pregnancy test kits

PELVIC EXAMINATION

A pelvic examination is generally performed annually for sexually active adolescents. The adolescent should be made to feel that she is in control and can stop the examination at any point to ask questions or, if need be, stop the examination entirely. A handheld mirror to permit viewing of her own genitalia is helpful for some adolescents. The clinician should acknowledge that adolescent girls may feel nervous, particularly with the first examination. Explain that it only takes 2 or 3 minutes to perform the examination. Adolescents should be given the choice of whether to have their mother or another person (e.g., sister, aunt) stay in the room as support. The young adolescent may request that her mother stay with her during the pelvic examination; most older patients prefer that their mothers stay in the waiting room. The patient’s wishes should be respected. Generally, male providers use a female chaperone for pelvic examinations. Women providers in some settings always use chaperones, and in other settings the use is considered optional. Many patients actually prefer to have only the provider in the room.

Before the examination begins, it is helpful to explain to the teen, while she is still fully clothed and seated, the various parts of the examination: general physical examination, inspection of the genitalia, speculum examination, and bimanual examination, indicating the reasons why each part is important for evaluating her medical complaint. It is also a good time both in the early discussion and during the examination to talk about feelings related to the examination and ways to relax and feel in control, such as the use of imagery, deep breathing and other relaxation techniques, a mirror, a step-by-step format, or distraction from a family member. She should also be reassured that adequate drapes will be used. Each step is then explained again as the actual examination is done.

The steps are as follows:

1. Make sure that the patient has emptied her bladder before the examination.
2. Ask the patient to undress completely and put on a gown.
3. Perform a general examination including inspection of the skin (acne, hirsutism, acanthosis nigricans); palpation of the thyroid gland; and examination of the breasts, heart, abdomen, and inguinal area for lymphadenopathy.
4. Have the patient lie supine on the examination table, feet resting either in or on the ankle supports. Instruct the patient to slide her buttocks to the edge of the table. Elevating the head of the table 30 degrees is optional; it can provide the adolescent an increased sense of control and can make sliding down easier. The foot of the examination table should be turned away from a doorway. The drape or sheet should be positioned so that eye contact can be maintained with the patient.
5. Ask the patient to touch her knees to your hands, which are held out to the side. Do not try to pry her legs apart.
6. Inspect the external genitalia (Fig. 48.1).
a. Note pubic hair distribution and sexual maturity rating (Tanner stage).

b. Assess for signs of erythema, inflammation, nevi, warts, or other lesions over the perineum, thighs, mons, labia, and perianal region. After informing the patient that you are about to do so, place the palms of both hands adjacent to the labia majora and gently separate them to examine the external structures. Check the size of the clitoris, which is typically 2 to 4 mm wide; a width of 5 to 10 mm is considered a possible sign of virilization, and more than 10 mm indicates definite virilization.

- Skene glands: These are two small glands located just inside the urethra. They usually are not visible.
- Bartholin glands: These are two small mucus-secreting glands located just outside the hymenial ring at the 5 and 7 o'clock positions. They can become enlarged or infected or both.

c. The hymen should be carefully inspected for estrogen effect (light pink, thickened), for congenital anomalies (septate, imperforate, microperforate), and for transections that might result from consensual or nonconsensual sexual intercourse. For girls who are being evaluated for prior sexual abuse or assault, a saline moistened, cotton-tipped applicator can be used to run the edge of the hymen to look for transections. With gentle retraction, the anterior vagina may be visible and again the estrogen effect can be observed: pink mucosa, white vaginal secretions.

d. Obtaining samples: For patients who need a vaginal smear done to assess estrogenization (amenorrhea) or who need wet mounts obtained to evaluate vaginal discharge, saline-moistened or dry cotton-tipped applicators can be used to obtain samples (see later discussion). This may be all that is needed to assess the particular gynecological complaint.

7. Speculum examination: The correct size of speculum should be selected, and the speculum should be warmed, if possible, before insertion. It should not be lubricated with anything other than water if a Pap smear or culture samples are to be taken (Fig. 48.2). If the hymeneal opening is small, a Huffman (Huffman-Graves) speculum (1/2 × 4 1/2 inches) is used to visualize the cervix. For the sexually active teen, a Pederson speculum (1/2 × 3 1/2 inches) or occasionally a Graves speculum (1/4 × 3 1/2 inches) is appropriate. A plastic speculum with an attached light source is also useful for facilitating the examination. Some examiners believe it is helpful to remove the speculum from its package and show it to the patient. Other experts believe that the value of showing the adolescent the speculum in advance is limited and that the adolescent may become more fearful of the examination. If you choose to show the adolescent the speculum, explain that although the speculum is long it is the exact length of the vagina and allows visualization of the cervix, which is the opening of the uterus located at the end of the vagina. In the virgin teenage a one-finger, gloved (water-moistened) examination demonstrates the size of the hymenal opening and the location of the cervix and allows subsequent easy insertion of the speculum. To avoid surprising the patient during the speculum examination, touch the speculum to the thigh first and tell the patient that you are going to place the cool speculum into the vagina. The speculum should be inserted posteriorly in a downward direction to avoid the urethra (Fig. 48.3). Applying pressure to the inner thigh at the same time the speculum is inserted into the vagina may be helpful.

![Fig. 48.2](https://example.com/fig482.jpg)

**FIG. 48.2.** Types of specula (left to right): infant, Huffman, Pederson, and Graves. (Reproduced from Emans, et al. Pediatric and adolescent gynecology, 4th ed. Philadelphia: Lippincott Williams & Wilkins, 1998, with permission.)

![Fig. 48.3](https://example.com/fig483.jpg)

**FIG. 48.3.** Speculum examination of the cervix. (From Clarke-Pearson D, Dawood M. Green's gynecology: essentials of clinical practice, 4th ed. Boston: Little, Brown, 1990, with permission.)

a. Observe the vaginal walls for signs of estrogenization, inflammation, or lesions.

b. Inspect the cervix. The stratified squamous epithelium of the external os is usually a dull pink color. There is often a more erythematous area of columnar epithelium surrounding the cervical os, called a cervical ectropion. The junction between the two types of mucosa is called the squamocolumnar junction, and it is particularly important that this area be sampled during the Pap smear screening. This ectropion may persist throughout the adolescent years, especially in oral contraceptive users. Mucopurulent discharge from the cervix characterizes cervical, typical of infections with gonorrhea, chlamydia trachomatis, and herpes virus. Small, pinpoint hemorrhagic spots on the cervix, so called “strawberry” cervix, can occur rarely with herpes infection, and a pH greater than 4.5 suggests bacterial vaginosis or Trichomonas infections. The cervix should be examined for any lesions or polyps. Any abnormal growth on the cervix should be referred for further evaluation and colposcopy.

c. To assess signs and symptoms of vaginitis, swabs for wet mounts and pH can be obtained from the vagina and then placed into a one or two drops of saline on one slide (for Trichomonas, white cells, or “clue cells”) and one drop of 10% KOH (for pseudohyphae) on another slide. A swab should also be applied to pH paper; a pH lower than 4.5 suggests normal leukorrhea or Candida infection, and a pH greater than 4.5 suggests bacterial vaginosis or Trichomonas infection.

d. Obtain a Pap smear of the cervix. This should include at least a 360-degree rotation of the spatula in contact with the cervix, with care taken to sample the “transition zone” or squamocolumnar junction. Nylon cytobrushes are also commonly used in addition to the spatula, thus ensuring the collection of cells from the endocervical canal.

e. Endocervical tests for STDs: Use individual tests, such as cultures plated on Thayer-Martin plates for Neisseria gonorrhoeae; DNA probes, cultures, ligase-chain reaction (LCR), or polymerase chain reaction (PCR) tests for Chlamydia; or combined DNA probe kits. For gonorrhea cultures from the
endocervix, a sterile cotton swab should be inserted into the endocervix and left in place for 30 seconds, rotated 180 degrees before being withdrawn, and streaked directly onto the medium. Because Chlamydia is an intracellular organism, cells are best collected by a Dacron swab or brush. Alternatively, urine 

8. Bimanual examination: The bimanual vaginal-abdominal examination involves the insertion of one or two gloved, lubricated fingers into the vagina while the other hand is placed on the abdomen. If this is her first bimanual examination, it is worthwhile to have the patient practice relaxing her abdominal muscles first: “Take a few deeps breaths and blow it out.” Once her abdomen is relaxed, the bimanual examination can begin. Remind the patient that you will be examining her uterus and ovaries and to communicate any feelings of discomfort she may be experiencing during the examination. If it is not comfortable for the patient to tolerate a vaginal-abdominal examination or there are cultural issues, then a rectal-abdominal examination, in the lithotomy position, usually will yield the needed information.

a. Palpation of the vagina and cervix: Check for lesions along the side walls and on the cervix and any tenderness on cervical motion.

b. Palpation of the uterus: Assess the size, the position of the uterus, and any masses or tenderness. Pushing backward on the cervix causes the uterus to move anteriorly, allowing for its palpation with the abdominal hand.

c. Gently explore the posterior fornix and the rectouterine pouch (pouch of Douglas) for masses, fullness, and tenderness.

d. Palpation of the adnexa: Assess for any masses, tenderness, or abnormalities of the ovaries or the adnexal area. To palpate these structures, insert the examining fingers into each lateral fornix, positioning them slightly posteriorly and high. Sweep the abdominal examining hand downward over the internal fingers. Normal ovaries are usually less than 3 cm long and are rubbery.

If there is a history of significant pelvic pain or an adnexal mass is felt, a rectovaginal-abdominal examination can help complete the evaluation of the adnexa or uterus and the rectovaginal fossa and, posterior cul-de-sac. A rectovaginal-abdominal examination is performed with the index finger in the vagina, the middle finger in the rectum, and the other hand on the abdomen. The examination permits evaluation of the uterosacral ligaments and cul-de-sac as well as the mobility of the uterus. It is important to inform the patient that she may experience an urge to defecate (“You may feel like you are having a bowel movement, but you won’t go. Your brain is just giving you a different message”). The rectovaginal septum should be thin and pliable, and the pelvic floor should be free of masses and tenderness. On indication stool retrieved can be tested for occult blood.

9. At the completion of the examination, offer the patient a box of tissues to be used to remove the lubrication from her perineum after you leave the room. Some patients may require assistance in sliding up the table before taking their feet out of the ankle supports. Instruct the patient to dress fully and return to the office for a discussion of your findings and plan. Before the practitioner leaves the room, the patient should be in a sitting position and draped.

During the postexamination discussion, the patient should be congratulated for her cooperation, and the importance of the findings (positive or negative) of the examination in relation to her chief complaint should be discussed. All questions should be answered, and any therapy and further tests should be outlined. This is an important time for discussion of the adolescent’s concerns about normal anatomy and physiology, contraception (including emergency contraception), and sexuality. During this discussion with the adolescent, it is important for the examiner to listen carefully, remembering that teenagers may not communicate all their concerns initially. At the conclusion of the discussion, the parent or partner can be invited to join the health care provider and the teenager. The parent can be informed of the results of the examination and the treatment plan. Any confidential information that is revealed to the parent should have been previously agreed on with the teenager, so as to maintain trust. Parents should be encouraged to ask questions and to voice concerns.

Helping a teen through her first gynecological visit sets the stage for reproductive health care for a lifetime. The gynecological visit provides an ideal opportunity to provide education, listen to concerns, assess medical and psychosocial complaints, and promote a healthy future. The examination also provides the clinician an opportunity to impart to the teenager a positive attitude toward her body and the importance of health maintenance.

WEB SITES

For Teenagers and Parents

http://www.youngwomenshealth.org/pelvicinfo.html. Information about your first pelvic examination from Boston Children’s Hospital.


http://www.goaialice.columbia.edu/0645.html. From Columbia University for college students and older teens. Questions and answers about reproductive health and specifically here about pelvic examination.

http://www.psu.edu/dept/UHS/pelvicexam.html. From Penn State University Health Service, information about pelvic examination and Pap smears.

For Health Professionals


REFERENCES AND ADDITIONAL READINGS


This chapter reviews normal menstrual physiology, and the next several chapters discuss common abnormalities to menstrual function in adolescents.

MENARCHE

Although the exact trigger for puberty is unknown, hypothesized mechanisms for the onset of menarche and puberty include the following:

1. A progressive decrease in the sensitivity of the hypothalamus to gonadal steroids
2. A critical body composition or percentage of body fat
3. An increase in the pulsatile secretion of gonadotropin-releasing hormone (GnRH), both in amplitude and in frequency, leading to an increase in sex steroids

Menarche has been reported to occur at about 17% body fat, with 22% body fat reported to be required to maintain or restore menstruation (Frisch and McArthur, 1974). In the United States, menarche occurs in girls at an average of about 12.7 years, with a range (2 standard deviations) of 11 to 15 years. In about two thirds of girls, menarche occurs at sexual maturity rating (SMR) 4 (Tanner pubertal stage 4). Menarche occurs at SMR 2 in 5% of girls, at SMR 3 in 25%, and not until SMR 5 in 10%. Menarche occurs about 3.3 years after the start of the growth spurt, about 2 years after thelarche, and about 1.1 years after the peak height velocity. Data from a large cross-sectional, observational study of more than 17,000 girls suggest that puberty is beginning at an earlier age than previously reported (Herman-Giddens et al., 1997). For example, among 8- to 9-year-olds, 7.7% of Caucasian and 34.3% of African-American girls had Tanner stage 2 or greater pubic hair, and 5% of Caucasian and 15.4% of African-American girls had Tanner stage 2 or greater breast development. Although the age at menarche was not examined in that study, it may also be declining. Menarche is followed by approximately 5 to 7 years of increasing regularity as the cycles shorten to reach the usual reproductive pattern. The highest incidence of anovulatory cycles occurs before 20 or after 40 years of age.

The development of the menstrual cycle depends on several hypothalamic events that occur during puberty:

1. A rise in luteinizing hormone (LH) secretion: During early puberty these spikes occur only at night, in a pulsatile fashion. In late puberty and adulthood, pulsatile LH secretion occurs throughout the day and night.
2. A decrease in the negative feedback settings of the hypothalamus to estradiol and testosterone, resulting in higher levels of LH and follicle-stimulating hormone (FSH): The rise in LH and FSH may be secondary to changes in GnRH based on a central biological clock and unrelated to feedback sensitivity to gonadal steroid secretion.
3. The development of a positive feedback system, allowing critical levels of estradiol to trigger pulsatile secretion of GnRH and ultimately LH.

Although the gonadotropins act synergistically, FSH primarily affects follicular growth and LH mainly stimulates ovarian steroid biosynthesis.

DEFINITION OF MENSTRUAL CYCLE

A menstrual cycle is defined as that period of time from the beginning of one menstrual flow to the beginning of the next menstrual flow. Based on current understanding, the menstrual cycle may be defined at the levels of the endometrial response (proliferative and secretory phases), the ovarian response (follicular, ovulatory, and luteal phases), and the pituitary response (i.e., FSH and LH levels) (Fig. 49.1).

**Fig. 49.1.** Normal menstrual cycle. (Reproduced from Neinstein LS. Menstrual disorders. *Semin Fam Med* 1981;2:184.)

**Follicular Phase**

The duration of the follicular phase is usually 14 days, but the length is highly variable (range, 7 to 22 days). This phase ends with ovulation. The duration of the follicular phase is the major determinant of menstrual cycle length.

1. During the end of the prior menstrual cycle, corpus luteum involution occurs, with resulting low levels of estradiol and progesterone. Low levels of these hormones stimulate the hypothalamic release of GnRH, which, in turn, increases the pituitary’s release of FSH and LH.
2. FSH stimulates the maturation of ovarian follicles, with usually one follicle predominating.
3. At present, it is believed that LH stimulates theca cells of the ovary to produce androgens, which are then converted to estrogens in the granulosa cells of the ovary under the influence of FSH (Fig. 49.2). Estradiol increases FSH binding to granulosa cell receptors, leading to amplification of the FSH effect.
Under the influence of estrogen, the proliferative phase of the endometrium occurs. The binding of estradiol to its receptor sites on the endometrium results in

Negative feedback:
In response to rising estradiol levels in the middle and late follicular phase, FSH release begins to fall. Unless there is fertilization with subsequent production of human chorionic gonadotropin, the corpus luteum involutes after about 10 to 12 days. This leads to

At this stage there are copious, clear vaginal secretions, with maximum spinnbarkeit and a positive ferning test result.

A preovulatory estradiol surge leads to a midcycle LH surge, which initiates ovulation approximately 10 to 16 hours after the LH surge. An estradiol level of

The decreased levels of estrogen and progesterone lead to increased levels of LH and FSH, with a repetition of the menstrual cycle.

The cervical mucus becomes thick during the luteal phase, owing to the influence of progesterone, and no ferning or spinnbarkeit occurs.

A mature follicle releases an oocyte and becomes a functioning corpus luteum.

The corpus luteum produces large amounts of progesterone, as well as increased levels of estrogen. This results from an invasion of blood vessels into the collapsed follicle, exposing granulosa cells to low-density lipoprotein cholesterol, which acts as a substrate for progesterone synthesis. A progesterone serum level of greater than 3 ng/mL is presumptive evidence of ovulation. Rising levels of estrogen and progesterone lead to falling levels of FSH and LH.

2. Progesterone antagonizes the action of estrogen by reducing estrogen receptor sites and increasing conversion of estradiol to estrone, a less potent estrogen. Progesterone halts the growth of the endometrium and stimulates differentiation into a secretory endometrium. The secretory phase is characterized histologically by increased tortuosity of glands and spiraling of blood vessels. Secretory activity is maximal, and stromal edema occurs. The secretory endometrium is prepared for implantation.

Local progesterone produced by the corpus luteum suppresses follicular development in the ipsilateral ovary so that ovulation the following month usually occurs in the contralateral ovary.

4. The cervical mucus becomes thick during the luteal phase, owing to the influence of progesterone, and no ferning or separation occurs.

5. Unless there is fertilization with subsequent production of human chorionic gonadotropin, the corpus luteum involutes after about 10 to 12 days. This leads to sloughing of the endometrium, secondary to a loss both of estrogen and of supporting progesterone. Local prostaglandins cause vasodilatation and uterine contractions.

6. The decreased levels of estrogen and progesterone lead to increased levels of LH and FSH, with a repetition of the menstrual cycle.

For normal ovulation to occur, both the positive and the negative feedback systems must be functioning.

1. Negative feedback: Estradiol and progesterone suppress LH and FSH. Estradiol predominantly suppresses FSH, while estradiol and progesterone together suppress LH. With low levels of estradiol, LH and FSH are stimulated.

2. Positive feedback: Rising estradiol above 200 pg/mL during preovulation leads to a positive feedback surge of LH, causing ovulation. This positive feedback occurs only after puberty has begun and ovulation occurs.

LH and FSH are secreted in a pulsatile fashion about every 60 minutes during the follicular phase and every 90 minutes during the luteal phase. The pulsatile spikes are higher in amplitude during the luteal phase. The pulsatile secretions of LH and FSH are secondary to the pulsatile secretion of GnRH from the hypothalamus. The GnRH is secreted in a pulsatile fashion about every 90 minutes during the follicular phase and every 60 minutes during the luteal phase. The pulsatile spikes are higher in amplitude during the luteal phase. The pulsatile secretions of LH and FSH are secondary to the pulsatile secretion of GnRH from the hypothalamus. The pulsatile secretion of GnRH can be modulated by estradiol and progesterone feedback but also by other neurotransmitters (i.e., dopamine, norepinephrine).

Endorphins also seem to play a role in modulating GnRH secretion. It is possible that these other compounds, in centers above the hypothalamus, lead to the effects of weight loss, stress, exercise, and drugs on the menstrual cycle.

WEB SITES


REFERENCES AND ADDITIONAL READINGS


Dysmenorrhea and Premenstrual Syndrome
Paula K. Braverman and Lawrence S. Neinstein

More than 50% of female adolescents experience some menstrual dysfunction, including dysfunctional uterine bleeding, amenorrhea, dysmenorrhea, and premenstrual syndrome. Many of the problems associated with dysmenorrhea and minor variations in menses are secondary to organic disease such as endometriosis, outflow tract obstruction, or pelvic inflammatory disease. The term primary dysmenorrhea refers to pain associated with the menstrual flow, with no evidence of organic pelvic disease. Secondary dysmenorrhea refers to pain associated with menses secondary to organic disease such as endometriosis, outflow tract obstruction, or pelvic inflammatory disease.

Etiology

Psychological Factors Probably a small association exists between dysmenorrhea and the power of suggestion and imitation of mother or peers (Widholm and Kantor, 1971).

Myometrial Factors

1. Follicular phase: Uterine contractions occur one to three times per minute and at 10 to 30 mm Hg, with a basal pressure of 0 to 10 mm Hg.
2. Ovulation: Basal pressure is 40 to 60 mm Hg, with low-intensity contractions of 5 to 10 mm Hg every 3 to 5 minutes.
3. Luteal phase: During this phase basal pressure is 10 to 20 mm Hg, with infrequent (less than one per minute) contractions of 40 to 60 mm Hg.
4. Menses: Basal pressure is 0 to 10 mm Hg, with infrequent, labor-like contractions of 100 to 120 mm Hg.
5. Anovulatory cycles: Contraction occurs similar to those in the follicular phase, with no strong contractions or pain.
6. Dysmenorrhea: Four changes occur that contribute to pain—an elevation of myometrial resting tone to greater than 10 mm Hg, an increase in the frequency of contractions, and a dysrhythmia of uterine contractions.

Prostaglandins Prostaglandins seem to be the cause of the changes just noted that lead to dysmenorrhea. Prostaglandins are formed during ovulatory cycles in the secretory endometrium. Locally, prostaglandins cause uterine contractions; but they enter the systemic circulation and cause associated symptoms such as headache, nausea, vomiting, backache, diarrhea, dizziness, and fatigue. Studies have shown that prostaglandin levels in menstrual fluid during ovulatory cycles are higher than in anovulatory cycles. Arachidonic acid, a fatty acid, is the precursor for prostaglandin synthesis. Prostaglandin E2 (PGE2) and PGF2α are the key prostaglandins involved in dysmenorrhea, although PGE2 is considered the most important. They are formed through the cyclooxygenase pathway, which also produces PGD2 thromboxanes, and prostacyclin. PGF2α causes myometrial contractions, vasoconstriction, and ischemia and mediates pain sensation, while prostaglandin E2 causes vasodilation and platelet disaggregation. Their production seems to be enhanced by progesterone. It has been noted that:

1. Exogenous injection of PGE2 and PGF2α produce myometrial contractions and pain similar to dysmenorrhea, although E prostaglandins also inhibit contractions in the nonpregnant uterus.
2. Anovulatory cycles are associated with lower prostaglandin levels and usually no dysmenorrhea. Because many cycles in the first 2 years after menarche are anovulatory, most adolescents do not experience dysmenorrhea from the outset. Rather it occurs more frequently 1 to 3 years after menarche.
3. Patients with dysmenorrhea have higher levels of prostaglandins in the endometrium.
4. Most of the prostaglandins are released in the first 48 hours of menstruation, correlating with the most severe symptoms.
5. Prostaglandin inhibitors decrease dysmenorrhea.

From this evidence it has been presumed that primary dysmenorrhea is related to prostaglandins released during menses, which seems to be increased during ovulatory cycles under the influence of progesterone. It is postulated that women with dysmenorrhea may be more sensitive to prostaglandins. Prostaglandins have also been shown to be locally elevated in cases of secondary dysmenorrhea such as endometriosis (Koike et al., 1992).

Epidemiology
About 45% to 70% of all postpubescent females have some degree of dysmenorrhea; up to 15% of these females describe the pain as severe and are incapacitated for 1 to 3 days per month. Approximately one third to one half of adolescents describe their symptoms as mild. Dysmenorrhea is the greatest single cause of lost work and school hours in females, with more than 140 million hours lost per year. Robinson et al. (1992) found a prevalence of 79.6% for dysmenorrhea in a group of 308 female adolescents. The prevalence rose from 39% of 12-year-old girls to 72% of 17-year-old girls. The prevalence of dysmenorrhea also increased from 38% at SMR 3 to 66% at SMR 5. Similarly, Pedron-Nuevo et al. (1998) found rates of 52.1% for those younger than 15 years of age and 63.8% for those 15 to 19 years old.

**Clinical Manifestations**

Primary dysmenorrhea usually begins 6 to 12 months after menarche and before the age of 20 years, with the establishment of ovulatory cycles. Local symptoms include pain that is spasmodic in nature and is strongest in the lower abdomen, with radiation to the back and anterior aspects of the thighs. About 50% of females have associated systemic symptoms, including:

- Nausea or vomiting: 89%
- Fatigue: 85%
- Nervousness: 67%
- Dizziness: 60%
- Diarrrhea: 60%
- Backache: 60%
- Headache: 45%

It may be useful to grade dysmenorrhea:

1. **Grade I:** Mild dysmenorrhea that does not interfere with the adolescent's participation in everyday activity
2. **Grade II:** Moderate dysmenorrhea that may interfere in the adolescent's participation in some activities; minimal, if any, systemic symptoms
3. **Grade III:** Severe discomfort; adolescent restricted from activities for several days; often associated with systemic symptoms

**Differential Diagnosis**

**Gynecological Causes**

1. Endometriosis: Endometriosis involves endometrial implants in various locations throughout the pelvis. Although not common in adolescents, this condition is probably not so rare in adolescents as previously thought. Endometriosis has been reported in women as young as 10.5 years. Studies show that up to 65% of adolescents with chronic pelvic pain have this condition (Chatman, 1982). The typical symptoms of endometriosis in adolescents include chronic pelvic pain, which may precede menses and continue after menses; abnormal uterine bleeding; abdominal pain; pain on defecation; and dyspareunia. Although usually cyclic, the pain can be acyclic. On examination a tender or nodular cul-de-sac or tender uterosacral ligaments may be found. However, adolescents may not have the classic thickened nodular sacrouterine ligaments. Goldstein et al. (1980) found pelvic tenderness in 76% of adolescents with endometriosis. The more common presentation in this age group is cyclic pain with localized pelvic cul-de-sac tenderness just before menses. Often a combination of antiprostaglandins and oral contraceptive pills relieves the symptoms.

2. Pelvic inflammatory disease
3. Benign uterine tumors: Polyps, fibroids
4. Intrauterine device
5. Anatomic abnormalities: Congenital obstructive müllerian malformations, outflow obstruction. Obstructive müllerian abnormalities predispose the patient to endometriosis.
6. Pelvic adhesions
7. Ovarian cyst or mass

**Nongynecological Causes**

1. Gastrointestinal disorders: Inflammatory bowel disease, irritable bowel syndrome, constipation, lactose intolerance
2. Musculoskeletal pain: Inflammatory process, trauma, tumor
3. Genitourinary abnormalities: Cystitis, ureteral obstruction, calculi
4. Psychogenic disorders: History of abuse, trauma, psychogenic

**Diagnosis**

**History**

1. Menstrual history: Primary dysmenorrhea usually starts 6 to 12 months after menarche, most commonly begins between the ages of 14 and 16 years, and peaks at age 17 or 18 years. It usually decreases during the twenties and thirties. Secondary dysmenorrhea should be considered if the pain starts with the onset of menarche or after the age of 20 years. Adolescents should be asked about the degree of pain and the amount of impairment in school and other activities. Any previous use of therapeutic modalities and their effectiveness should be ascertained.
2. Prior sexually transmitted diseases and sexual history: This information helps to eliminate infection as a cause.
3. Gastrointestinal and genitourinary systems history: This information helps to eliminate gastrointestinal or genitourinary problems (e.g., cystitis, irritable bowel syndrome) as a cause of pain.
4. Musculoskeletal history: This reveals bone or joint problems including trauma or possible tumor.
5. Psychosocial history: This assesses stress, substance abuse, and sexual abuse. Cigarette smoking, especially heavy smoking, has been found to increase the duration of dysmenorrhea (Hornsey et al., 1998).

**Physical Examination**

Examine the pelvis for evidence of endometriosis, endometritis, polyps, fibroids, or uterine or cervical abnormalities. However, if the teen is not sexually active and the history is typical for dysmenorrhea, a pelvic examination is indicated only if the symptoms do not respond to standard medical therapy. The musculoskeletal examination should focus on range of motion of the hips and spine to assess for tenderness and limitation in motion.

**Laboratory Tests**

A complete blood count and a determination of the erythrocyte sedimentation rate should be done if pelvic inflammatory disease or inflammatory bowel disease is suspected. Testing for sexually transmitted diseases and pregnancy should be conducted on sexually active adolescents. A urinalysis and urine culture will help diagnose urinary tract problems. If a müllerian abnormality is suspected, pelvic ultrasound or magnetic resonance imaging will define the anatomy. If evaluation of the genitourinary, gastrointestinal, and musculoskeletal tracts fails to reveal a cause of the pain and the pain is severe and intractable despite treatment with antiprostaglandins and oral contraceptives, then consideration should be made for diagnostic laparoscopy. Among adolescents who do not respond to this therapeutic combination, the rate of endometriosis is as high as 70%.

**Therapy**

The two most effective treatments for primary dysmenorrhea are nonsteroidal antiinflammatory drugs (NSAIDs) and oral contraceptives.

**Education**

The patient should be educated and reassured that the problem is physiological and can be helped.

**Nonsteroidal Antiinflammatory Drugs**

NSAIDs are the primary modality of therapy; 80% of dysmenorrhea can be relieved with these medications. Because much of primary dysmenorrhea is secondary to prostaglandin-mediated uterine hyperactivity, prostaglandin inhibitors can alleviate menstrual cramps and associated systemic symptoms. Many NSAIDs have been found effective in alleviating menstrual cramps. They are divided into two classes: carboxylic acids and enolic acids. Carboxylic acids are more widely used and are divided into four subgroups: salicylic acids (aspirin), acetic acids (indomethacin), and the two most useful subgroups—propionic acids such as ibuprofen (Motrin), naproxen (Naprosyn), and naproxen sodium (Anaprox) and the fenamates such as mefenamic acid (Ponstel) and ketoprofen. Of the
propionic acids, naproxen sodium may have a shorter onset of action because it is more rapidly absorbed. Mefenamic acid has an additional mechanism of action: It competes with prostaglandin binding sites and antagonizes existing prostaglandins in addition to inhibiting prostaglandin synthesis. Some of these drugs and their typical doses are as follows:

<table>
<thead>
<tr>
<th>Drug (Trade Name)</th>
<th>Initial Dose (mg)</th>
<th>Following Dose (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Propionic acids</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ibuprofen (Motrin)</td>
<td>400</td>
<td>400 q4–8h</td>
</tr>
<tr>
<td>Naproxen (Naprosyn)</td>
<td>500</td>
<td>250 q6–8h</td>
</tr>
<tr>
<td>Naproxen sodium (Anaprox)</td>
<td>550</td>
<td>275 q6–8h</td>
</tr>
<tr>
<td>Fenamates</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mefenamic acid (Ponstel)</td>
<td>500</td>
<td>250 q6h</td>
</tr>
</tbody>
</table>

Over-the-counter ibuprofen is available in preparations such as Advil and Nuprin. Naproxen is available as Aleve. Because these over-the-counter medications come in lower doses than the prescription formulations, a larger number of tablets may be needed for effectiveness. The medications should be started either as soon as possible when dysmenorrheic symptoms occur or to coincide with the first sign of menstruation. It is not necessary to start before the onset of menses. Usually these medications are needed for only 1 to 3 days. After one of the NSAIDs is started, it should be tried for three or four menstrual cycles before being judged ineffective. At that time, a trial of a different prostaglandin inhibitor should be performed.

With the outlined doses used for short periods, side effects are usually minimal, but they include the following:

1. More than 1% of patients
   a. Gastrointestinal: Nausea, epigastric pain, vomiting, constipation
   b. Central nervous system (CNS): Dizziness, headache
   c. Skin: Rash
   d. Cardiovascular: Edema, fluid retention
   e. Other: Tinnitus
2. Fewer than 1% of patients
   a. Gastrointestinal: Ulcer, hepatitis
   b. CNS: Depression, confusion
   c. Skin: Stevens-Johnson syndrome, alopecia
   d. Hematological: Pancytopenia, hemolysis
   e. Other: Hearing loss, scotoma, dry eyes

A recent study showed good results in the treatment of primary dysmenorrhea with rofecoxib, a cyclooxygenase-2 inhibitor, which has the advantage of having less gastrointestinal side effects (Morrison et al., 1999).

**Hormonal Therapies** If the patient wishes contraception or the pain is severe and not responsive to NSAIDs, oral contraceptives can be tried. Combined oral contraceptives inhibit ovulation and lead to endometrial hypoplasia, resulting in decreased menstrual flow and prostaglandin release. Oral contraceptives decrease symptoms in more than 90% of patients with primary dysmenorrhea. They are also useful to treat endometriosis, because they decrease endometrial proliferation and thereby decrease total local prostaglandin production. The maximal effect may not become apparent for several months.

**Other Modalities** Transcutaneous nerve stimulation (Dawood and Ramos, 1990); acupuncture (Helms, 1987; National Institutes of Health, 1998); l-lysine clonixinate (Di Girolamo et al., 1999); and calcium channel blockers such as nicardipine, nifedipine, and flunarizine (Earl and Mercola, 1992; Schroeder and Sanfilippo, 1999) have also been used. Calcium channel blockers appear to cause smooth muscle relaxation. However, the side effects can be significant, making them less useful.

**PREMENSTRUAL SYNDROME**

The term *premenstrual syndrome* (PMS) is used to describe an array of predictable physical, cognitive, affective, and behavioral symptoms that occur cyclically during the luteal phase of the menstrual cycle and resolve quickly at or near the onset of menstruation. It is characterized by a broad spectrum of symptoms and until recently had confusing definitions; as a result, some women seeking treatment were excluded from the diagnosis. In the mid 1980s, rigorous criteria were defined, and studies evaluating both the pathophysiology and treatment modalities were designed according to strict scientific standards. Evidence is accumulating that PMS is not a single condition but a set of interrelated symptom complexes, each with its own pathophysiological mechanism. The exact prevalence is unknown, but estimates are that up to 85% of menstruating women have some degree of symptoms before menses and that 5% to 10% are so severely afflicted that daily activities are hindered (Chakmakjian, 1983; Singh et al., 1998; American College of Obstetrics and Gynecology [ACOG], 2000). In one longitudinal study of 384 15-year-old adolescent girls, 69% reported at least one symptom considered severe, and 43% had at least one symptom considered extreme (Fisher et al., 1989). (Chakmakjian, 1983; Singh et al., 1998; American College of Obstetrics and Gynecology [ACOG], 2000). In one longitudinal study of 384 15-year-old adolescent girls, 69% reported at least one symptom considered severe, and 43% had at least one symptom considered extreme (Fisher et al., 1989).

**Risk Factors**

Risk factors for PMS include advancing age (beyond 30 years) and genetic factors. Some studies suggest that women whose mothers report PMS are more likely to develop PMS (70%, versus 37% of daughters of unaffected mothers) (Van der Akker et al., 1987; Dalton, 1987). In addition, concordance rates for PMS are considered moderately severe, 59% reported at least one symptom considered severe, and 43% had at least one symptom considered extreme (Fisher et al., 1989). Others, particularly in the mental health field, have defined this syndrome as premenstrual dysphoric disorder (PMDD). Although the two conditions overlap, in PMDD the focus is more on the problems with mood, the symptoms are more severe, and they lead to a higher level of dysfunction before the onset of menses.

**Pathophysiology**

The exact mechanism is unknown, but theories include the following:

1. Estrogen excess or progesterone deficiency.
2. Alterations in hormones, including prolactin, growth hormone, thyroid hormone, adrenal activity, luteinizing hormone (LH), follicle-stimulating hormone (FSH), antidiuretic hormone, insulin, aldosterone, renin-angiotensin, and cortisol, none of which has been proven. The levels of sex steroids, estrogen, progesterone, and testosterone are normal, but women with PMS may be more vulnerable to normal fluctuations.
3. Vitamin deficiencies—zinc, vitamin A, vitamin E, thiamine, magnesium, and pyridoxine (vitamin B6)—have been implicated but not documented. No significant differences have been found, and the data show inconsistent scientific evidence.
4. Alteration in glucose metabolism.
5. Alterations in neurotransmitters: Endorphins (drop in endogenous opiate levels), monoamines, and serotonin have been implicated. Serotonergic dysregulation is the most plausible theory, although not all women respond to selective serotonin reuptake inhibitors (SSRIs), implying that other factors must be involved.

**Clinical Manifestations**

More than 150 symptoms have been described in literature, ranging from mild symptoms to those severe enough to interfere with normal activities.

1. Emotional symptoms
   a. Irritability
   b. Depression
   c. Fatigue or lethargy
   d. Anger
   e. Insomnia or hypersomnia
f. Mood lability

g. Marked anxiety

h. Poor concentration

i. Tearfulness

j. Social withdrawal

2. Physical symptoms
   a. Headaches
   b. Swelling: Legs or breasts
   c. Increased appetite
   d. Food cravings
   e. Weight gain
   f. Sense of abdominal bloating
   g. Fatigue
   h. Muscle and joint aches and pains

Diagnosis

The diagnosis relies on the history of cyclic symptoms. No specific physical findings or laboratory tests have proved useful. Three important findings are usually needed to diagnosis PMS:

1. Symptoms must occur in the luteal phase and resolve within a few days after onset of menstruation. Symptoms should not be present in the follicular phase.

2. The symptoms must be documented over several menstrual cycles and not caused by other physical or psychological problems.

3. Symptoms must be recurrent and severe enough to disrupt normal activities.

A calendar such as the one shown in Fig. 50.1 can be helpful in the diagnosis and in monitoring teens after the start of any therapy. Other assessment tools include the Self-Assessment Disk (Magos and Studd, 1988), the Premenstrual Assessment Form (Halbreich et al., 1982), Calendar of Premenstrual Experience (COPE) (Mortola et al., 1990), and the Prospective Record of the Impact and Severity of Menstrual Symptoms (PRISM) (Reid, 1987).

![Fig. 50.1. Premenstrual symptom calendar.](image)

The National Institute of Mental Health (NIMH) criteria require a change of 30% in intensity of symptoms, as measured with the use of an instrument, comparing days 5 through 10 of the cycle with the 6 days before menses. These changes must be documented for at least two consecutive cycles (ACOG, 2000).

The Diagnostic and Statistical Manual of Mental Health Disorders, 4th edition (American Psychiatric Association, 2000) lists similar criteria for PMDD (Table 50.1). It is important to remember that the symptoms cannot represent exacerbation of an existing disorder such as major depression, panic, dysthymic disorder, or personality disorder, but they may be superimposed on one of these psychiatric disorders. Many women who have signed up for clinical trials have psychiatric disorders that become exacerbated during menstruation (menstrual magnification). Certain medical disorders can also become worse during menses, including seizures, migraine headaches, irritable bowel syndrome, asthma, and allergies.

<table>
<thead>
<tr>
<th>TABLE 50.1. Diagnosis of premenstrual dysphoric disorder (DSM-IV criteria)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy</td>
</tr>
</tbody>
</table>

No single treatment is universally acceptable as effective. Studies have yielded conflicting results with all therapies, and most trials have not been well controlled. Treatments include the following:

1. Education: The teen should be educated regarding menstrual physiology and the relationship of changing hormones to symptoms.

2. Stress management: The teen can be taught or referred for techniques to manage stress (e.g., biofeedback, self-hypnosis, relaxation exercises).

3. Exercise: Regular aerobic exercise has been reported to help some women with PMS (Steege and Blumenthal, 1993; Prior et al., 1987).

4. Vitamin and mineral supplementation
   a. Pyridoxine (vitamin B₆) has been used extensively in the past, particularly in treating the emotional symptomatology of PMS. However, review of the literature has shown conflicting results, and it is considered to be of limited benefit. The other concern is that peripheral neuropathy can develop with doses higher than 100 mg/day (ACOG, 2000; Wyatt, 1999).
   b. Calcium (1,200 mg/day) was reported to reduce physical and emotional symptoms in a well-designed, multicenter study (Thys-Jacobs, 1998; ACOG, 2000).
   c. Magnesium (200 to 400 mg/day) has been noted to reduce negative mood and to reduce water retention. The mechanism of action is not known, and the usage is not well studied (ACOG, 2000).
   d. Vitamin E (400 IU/day) was found to improve somatic and affective symptoms. However, there is limited evidence of its effectiveness (London et al., 1987; ACOG, 2000).
   e. Carbohydrate supplements: In a small study, mood and carbohydrate food craving improved. Carbohydrates may increase tryptophan, which is a precursor to serotonin (Sayegh et al., 1995).
   f. Primrose oil: This method does not appear to be effective.
5. Suppression of ovulation: Because PMS appears to be a cyclic disorder of menses occurring in the luteal phase, suppression of ovulation has been used as a therapy.
   a. Combination oral contraceptives: These have been tried, and some authorities consider them to be first-line medications. However, their effectiveness is not widely supported by data. Symptoms in some individuals with PMS worsen with use of oral contraceptives, especially the triphasic preparations. The current thinking is that oral contraceptive pills should be considered if the symptoms are primarily physical and not mood related, because they appear to be better for the physical symptoms. Medroxyprogesterone acetate (Depo-Provera) is an alternative contraceptive to suppress ovulation.
   b. Gonadotropin-releasing hormone (GnRH): Most studies have shown benefit from the use of GnRH, but the hypoestrogenic effects with loss of bone density is concerning, especially for adolescents, and would limit use. GnRH can be considered when other modalities have failed (Freeman et al., 1997; ACOG, 2000).
   c. Bilateral salpingo-oophorectomy would not be considered in adolescents.

6. Natural progestogenes: Progestogen suppressors have been reported to help in doses of 200 to 400 mg/day, used from midcycle to menses (days 17 through 25 of cycle). However, double-blind, crossover, placebo-controlled trials of vaginal and rectal suppositories have failed to show any benefit.

7. Medications to suppress symptoms
   a. Prostaglandin inhibitors: NSAIDs have been used to treat PMS particularly for the physical symptoms. These have included naproxen sodium, naproxen or mefenamic acid during the luteal phase. Therapy is stopped after menses begins.
   b. Propranolol, and calcium channel blockers including verapamil. None of these would be recommended for routine use in adolescents, but only for use in selected adolescents with severe symptoms unresponsive to other treatment modalities.
   c. Selective serotonin reuptake inhibitors: SSRI s are the drugs of choice for severe PMS. Studies have shown that they are effective for severe PMS and PMDD.

   Summary: Steps in the Treatment of Symptoms of Premenstrual Syndrome

   The following successive steps were outlined in an ACOG Practice Bulletin (2000):

   Step 1: Supportive therapy with good nutrition, complex carbohydrates, aerobic exercise, calcium supplements, and possibly magnesium, vitamin E, or spironolactone.

   Step 2: SSRI therapy with fluoxetine or sertraline. An anxiolytic can be used for specific symptoms not relieved by the SSRI medication.

   Step 3: Hormonal suppression with oral contraceptive pills or GnRH agonists.

WEB SITES

For Teenagers and Parents

http://www.mckinley.uiuc.edu/health-info/womenhlt/mencramp.html, Education handout on dysmenorrhea from the University of Illinois Student Health Center.

http://www.saonet.ucla.edu/health/healtheed/handouts/cramps.html, University of California at Los Angeles Student Health Center handout on dysmenorrhea.


http://www.med.umich.edu/1libr/adult/crs/dysmen.htm, University of Michigan Health System patient information sheet (Frequently Asked Questions) on dysmenorrhea.

http://www.womens-health.com/gyn_health/gyn_md_dysmen.html, Women’s health site with information on dysmenorrhea.

http://www.aafp.org/afp/990800ap/489.html, American Academy of Family Physicians (AAFP) article on primary dysmenorrhea.

http://www.womenshealthonline/hotline.html, Hotline information site on PMS with 800 phone number available.

http://www.vh.org/Patients/IBF/FamilyPractice/AFP/November/NovThree.html, AAFP information on PMS.

http://www.obgyn.upenn.edu/mudd/PMSarticle.html, Information on PMS from University of Pennsylvania Obstetrics and Gynecology Department.

For Health Professionals


http://www.vh.org/shared/courses/authors/06_author.cfm, Continuing Medical Education course on dysmenorrhea in teens.

REFERENCES AND ADDITIONAL READINGS


Dysfunctional uterine bleeding (DUB) is a common menstrual problem during adolescence. When severe, it can result in life-threatening anemia. Even when mild, it usually is both a concern and a nuisance for the adolescent. By definition, DUB is irregular and/or prolonged vaginal bleeding due to endometrial sloughing in the absence of structural pathology. In adolescents, anovulation secondary to physiological immaturity explains most cases of irregular bleeding. Although structural pathology accounts for less than 10% of abnormal uterine bleeding during adolescence, it must be excluded before the diagnosis of DUB can be established.

**DEFINITIONS**

1. **Normal menstrual cycles** during adolescence are 21–40 days long, with 2–8 days of bleeding and 20–80-ml blood loss per cycle.
2. **Ovulatory cycles** are characterized by a follicular phase ending with ovulation and a luteal phase ending with menstruation. During the follicular phase, rising serum levels of follicle-stimulating hormone (FSH) stimulate ovarian follicular maturation and estrogen production. The rising serum estrogen levels stimulate endometrial proliferation and progressive thickening. A preovulatory surge in estrogen is followed by a surge in luteinizing hormone (LH), which triggers ovulation, or release of an ovocyte from the predominant follicle. During the luteal phase, the residual follicle converts to a corpus luteum that produces increasing levels of progesterone and estrogen. The progesterone stabilizes the thickened endometrium and stops further proliferation. In the absence of fertilization, the corpus luteum involutes, estrogen and progesterone levels fall, and the endometrium sloughs, resulting in menstrual bleeding.
3. **Menorrhagia** is prolonged or heavy uterine bleeding that occurs at regular intervals.
4. **Metrorrhagia** is uterine bleeding that occurs at irregular intervals.
5. **Menometrorrhagia** is prolonged or heavy uterine bleeding that occurs at irregular intervals.
6. **Oligomenorrhea** is uterine bleeding that occurs at prolonged intervals of 41 days to 3 months but is of normal flow, duration, and quantity.

**DIFFERENTIAL DIAGNOSIS**

An estimated 10% of adolescents managed as outpatients for abnormal bleeding, compared with 25% of those requiring hospitalization, have an identifiable structural, infectious, or clotting abnormality. The likelihood of finding an underlying abnormality is four times higher among adolescents hospitalized with hemoglobin levels less than 10 g/dL than for those hospitalized with higher values. Among adolescents hospitalized with hemorrhage at menarche resulting in a hemoglobin level less than 10 g/dL, 50% have a systemic bleeding disorder, 40% have a minor structural abnormality, and 10% have a minor structural abnormality.

The differential diagnosis of abnormal bleeding is quite different in the adolescent than the adult. Uterine fibroids and endometrial dysplasia or malignancy lead the differential diagnosis in the adult but are rare in the adolescent. Conversely, congenital anomalies of the outflow tract may be subclinical until menarche but rarely remain unrecognized until adulthood. Aside from DUB, the differential diagnosis of abnormal bleeding during adolescence includes the following conditions:

1. **Pregnancy-related causes:** Ectopic pregnancy; spontaneous, threatened, or incomplete abortion; placental polyp; hydatidiform mole
2. **Local pathology (vagina, cervix, uterus):** Foreign body in the vagina (e.g., retained tampon) or uterus (e.g., intrauterine device); cervicitis or endometritis due to a sexually transmitted disease (STD) or instrumentation; laceration or other trauma; polyp of the cervix or uterus; congenital anomaly of the outflow tract; premalignant or malignant lesion of the cervix or uterus
3. **Bleeding diathesis:** Idiopathic thrombocytopenic purpura; von Willebrand disease; abnormal platelet function due to drugs (e.g., aspirin) or systemic illness (e.g., renal failure); bone marrow suppression (e.g., chemotherapy) or infiltration (e.g., leukemia); coagulopathy due to inherited clotting factor deficiency, systemic illness (e.g., liver failure), or anticoagulant therapy (e.g., warfarin)
   a. von Willebrand disease: It is important that primary care providers consider the diagnosis and be aware of appropriate management of girls with von Willebrand disease, the most common inherited bleeding disorder. Even though many girls are diagnosed during childhood with typical symptoms of easy bruising, frequent or prolonged nosebleeds, and prolonged bleeding after surgery, injury, or dental work, it is often menorrhagia at menarche that leads families to seek medical attention. There have been significant advances in effective therapy for von Willebrand disease that can be administered at home under medical supervision. In addition, primary care providers should be aware of the existence of the federally supported regional network of Comprehensive Hemophilia Diagnostic and Treatment Centers. Thus, this diagnosis should be considered in teens presenting with excessive menstrual bleeding, and the physician should take the necessary family history and conduct the appropriate coagulation workup in consultation with the hematologist at a local hemophilia treatment center, particularly if the diagnosis is in question.
4. **Hormonal causes:** Anovulatory bleeding

Anovulatory bleeding usually relate to one of three hormonal imbalance conditions:

a. Estrogen breakthrough bleeding: This occurs when excess estrogen stimulates the endometrium to proliferate in an undifferentiated manner. With inadequate progesterone levels to provide support to the endometrium, portions of the lining will slough at irregular intervals. In addition, the vasoconstriction mediated through progesterone and prostaglandin levels does not occur, often resulting in profuse bleeding.

b. Estrogen withdrawal bleeding: This bleeding results from a sudden decrease in estrogen levels. This could occur after stopping exogenous estrogen therapy or just before ovulation in the normal menstrual cycle. This type of withdrawal bleeding is usually self-limited.

c. Progesterone breakthrough bleeding: This occurs when the ratio of progesterone to estrogen is high, such as with progesterone-only contraceptives.

In these individuals, the endometrium becomes atrophic and more prone to frequent, irregular bleeding.

Hormonally mediated DUB therefore tends to be associated with less dysmenorrhea than normal menses following ovulation or abnormal bleeding due to a structural or infectious problem. The most common causes of hormonally mediated DUB (anovulatory bleeding) during adolescence are the following:

1. **Gynecological immaturity:** Immaturity of the hypothalamic-pituitary-ovarian axis is the leading cause of DUB during adolescence. After menarche, anovulation is associated with 50%–80% of bleeding episodes during the first 2 years, 30%–55% during years two to four, and 20% during years four to five. The likelihood of anovulatory bleeding increases with menarcheal age. More than 50% of bleeding episodes are anovulatory for 1 year when menarche occurs before age 12 years, for 3 years when menarche occurs at age 12–13 years, and for 4 years when menarche occurs after age 13 years. Despite these high rates of anovulation, the negative feedback of estrogen on the hypothalamic-pituitary axis protects most adolescents from DUB. Even when ovulation does not occur, gonadotropin levels decrease in response to increasing estrogen levels. Estrogen production then declines before the endometrium becomes excessively complex.
Defective corpus luteum: DUB can occur in an ovulatory cycle with early involution of the corpus luteum and inadequate progesterone production.

Family history: PCOS, bleeding diathesis

Prothrombin time, partial thromboplastin time, and bleeding time: Preliminary screen if a systemic bleeding disorder is suspected. Special tests may be needed if

Pelvic ultrasonography: Transabdominal ultrasonography performed through a full bladder is essential in the virginal patient with possible structural pathology

Hormonal contraception or replacement therapy: The combined oral contraceptive, progesterone-only oral contraceptive, depot medroxyprogesterone acetate (DMPA), subdermal levonorgestrel implant, and emergency contraceptive all block ovulation and therefore may result in anovulatory bleeding. Hormone replacement therapy generally is prescribed because of hypogonadism and anovulation. If a uterus is present, the regimen must include both estrogen and progesterone, administered either cyclically or in fixed daily doses. In either case, breakthrough bleeding occasionally occurs.

Hypothyroidism or hyperthyroidism: Although either condition may cause DUB, hypothyroidism is more commonly associated with amenorrhea than hyperthyroidism.

Polycystic ovary syndrome (PCOS): See Chapter 52.

Late-onset congenital adrenal hyperplasia (e.g., partial 21-hydroxylase deficiency): See Chapter 58.

Stress and excessive exercise: Both can lead to anovulation and either DUB, amenorrhea, or oligomenorrhea.

EVALUATION

The evaluation of any patient with bleeding begins with an assessment of hemodynamic stability. The next objective is to determine the site of the bleeding (e.g., gastrointestinal, urinary, vaginal, cervical, or uterine). Once the bleeding is found to be uterine, the evaluation focuses on determination of its cause.

History

Part of the history should be obtained from the adolescent and, if possible, the parent or guardian. The sexual history should be obtained from the adolescent alone unless she makes it clear that she is comfortable discussing it with the parent present.

1. Menstrual history: Age at menarche, cycle regularity, cycle duration, flow duration, change in cycle or flow, change in number of saturated pads or tampons, dysmenorrhea, pelvic pain between menses, change in pain associated with menses
2. Sexual history: Age at coitarche, use of condoms, contraception, pregnancies, deliveries, miscarriages, abortions, past STDs, past pelvic inflammatory disease (PID), number of partners, recent partner, vaginal discharge, known exposure to a partner with an STD
3. History of systemic illness
4. Endocrine history: Symptoms suggestive of hypothryoidism (e.g., fatigue, weight gain, dry skin), hyperthyroidism (e.g., palpitations, increased appetite, weight loss), or hyperandrogenism (e.g., hirsutism, acne, weight gain); use of hormonal contraception or exogenous hormones
5. Family history: PCOS, bleeding diathesis
6. Review of systems: Fatigue, lightheadedness, rapid heart beat, palpitations, gum bleeding, epistaxis, significant weight changes, stress

Physical Examination

1. Vital signs: Blood pressure and heart rate to rule out any systemic disorder.
2. Sexuality assessment:
3. Skin, hair, and mucousa: Scalp hair thinning or dryness, hirsutism, acanthosis nigricans, acne, petechiae, purpura, ecchymoses, gum bleeding, epistaxis
4. Thyroid Enlargement, tenderness, nodules
5. Breasts: Galactorrhea
6. Lymph nodes: Lymphadenopathy
7. Abdomen: Hepatosplenomegaly, palpable uterus, mass
8. Pelvic examination: Examination in all sexually active adolescents; also indicated if the history suggests structural pathology as the cause of the bleeding; can be deferred in the adolescent with suspected anovulatory DUB who has never had sexual intercourse.

Laboratory Tests: Laboratory testing may not be necessary in the adolescent with mild anovulatory DUB associated with physiological immaturity. Depending on the history and physical examination results, other patients may require the following laboratory evaluation:

1. Pregnancy test: A urine test for b-human chorionic gonadotropin (b-hCG) should be done in all patients if there is any question of past sexual intercourse. If the urine test result is positive, a quantitative serum test for b-hCG should be performed. In these cases of possible ectopic pregnancies, an ultrasound and gynecology referral should strongly be considered.
2. Complete blood cell count: Unless the bleeding is mild and of recent onset, all patients should have a hemoglobin and hematocrit test. If these values are low, red blood cell indices (e.g., mean corpuscular volume) can help differentiate acute from chronic blood loss. A white blood cell count with differential is indicated if PID is suspected. A platelet count is indicated if a systemic clotting abnormality is suspected.
3. STD screening Endocervical tests for gonorrheal and chlamydial infections are indicated for all adolescents who have ever had sexual intercourse.
4. Erythrocyte sedimentation rate: Evaluation of the integrity of the vascular system and the presence of an underlying systemic disorder.
5. Thyroid function tests
6. Prothrombin time, partial thromboplastin time, and bleeding time: Preliminary screen if a systemic bleeding disorder is suspected. Special tests may be needed if von Willebrand disease is suspected, such as von Willebrand factor antigen and ristocetin cofactor activity.
7. Urine hormone tests, blood urea nitrogen, creatinine clearance: Additional screening if there is evidence of abnormal clotting factors or platelet function
8. Antinuclear antibody: Preliminary screen for autoimmune disease
9. LH, FSH, testosterone (total and free), dehydroepiandrosterone sulfate, if PCOS is suspected (see Chapter 52).
10. Pelvic ultrasonography. Transabdominal ultrasonography performed through a full bladder is essential in the virgin girl with possible structural pathology who cannot tolerate a pelvic examination. Transabdominal and transvaginal ultrasonography is indicated if the pregnancy test is positive or if a mass is palpated on pelvic examination.
11. Endometrial aspirate and/or biopsy are rarely indicated in adolescents.

THERAPY

The severity and cause of the bleeding guide its management. Severe bleeding with hemodynamic instability, regardless of cause, requires immediate intervention with intravenous fluids and/or blood transfusion. Adolescents without underlying cardiovascular disease usually respond quickly to intravenous fluids and supplemental iron therapy, without the need for transfusion. Severe anemia that developed over years or months of abnormal bleeding is better tolerated than the same level of anemia that developed over hours or days of acute bleeding. Bleeding secondary to pregnancy, infection, or structural pathology requires prompt treatment of the underlying condition. Bleeding secondary to a systemic problem, such as a clotting abnormality or thyroid dysfunction, may require short-term hormonal therapy identical to that for anovulatory bleeding until the systemic problem is brought under control.

Anovulatory DUB

The approach to anovulatory DUB depends on bleeding severity, hemoglobin and/or hematocrit value, hemodynamic tolerance, and emotional tolerance. It generally can be divided into the following categories:

1. Light to moderate flow, hemoglobin level of at least 12 g/dL: Reassurance, multivitamin with iron, menstrual calendar, reevaluation within 3 months.
2. Moderate flow, hemoglobin level of 10–12 g/dL: Begin a 35- to 40-day combined oral contraceptive pill to be taken every 6–12 hours for 24–48 hours until the bleeding stops, along with an antiepileptic if necessary for nausea and vomiting. Oral supplemental iron therapy should be initiated as early as possible but may not be tolerated during the first 2 weeks of high-dose hormonal therapy. Nonsteroidal antiinflammatory drugs (NSAIDs) can be used as adjunctive therapy, along with the oral contraceptive to decrease both bleeding and, when present, dysmenorrhea. taper the oral contraceptive to one pill daily by day five. Begin a new 28-day pill packet and inform the patient that a withdrawal bleed is likely during the week of placebo pills. Continue the combined oral contraceptive for 3–6 months.
3. Heavy flow, hemoglobin level <10 g/dL: If the patient is hemodynamically stable, reliable, and able to tolerate the oral contraceptive, management is as stated
Persistent bleeding on a 20-µg combined oral contraceptive pill usually stops when a higher-dose estrogen (e.g., 30–35-µg) pill is prescribed. Persistent bleeding on a 30–35-µg pill requires either a 50-µg pill for one cycle or the addition of conjugated estrogen at 0.625-mg daily to the 35-µg pill for one cycle. Persistent bleeding on DMPA or the levonorgestrel implant can be managed with the addition of conjugated estrogen (1.25–2.50 mg daily for 5–7 days) and NSAIDs. Although this will stop the bleeding, the likelihood of subsequent spotting is also increased because of the estrogen-induced endometrial proliferation.

DUB Secondary to Hormonal Contraception

The oral contraceptive, DMPA, and levonorgestrel implant may all cause irregular bleeding.

1. Persistent bleeding on a 20-µg combined oral contraceptive pill usually stops when a higher-dose estrogen (e.g., 30–35-µg) pill is prescribed.
2. Persistent bleeding on a 30–35-µg pill requires either a 50-µg pill for one cycle or the addition of conjugated estrogen at 0.625-mg daily to the 35-µg pill for one cycle.
3. Persistent bleeding on DMPA or the levonorgestrel implant can be managed with the addition of conjugated estrogen (1.25–2.50 mg daily for 5–7 days) and NSAIDs. Although this will stop the bleeding, the likelihood of subsequent spotting is also increased because of the estrogen-induced endometrial proliferation.

Bleeding Diatheses

DUB secondary to systemic bleeding disorders is increasing along with the increasing prevalence of both diseases and treatments that alter bone marrow, platelet function, and clotting factors. Management of the DUB is directed either at decreasing menstrual frequency or inducing endometrial atrophy. Options are as follows:

1. Combined oral contraceptive pill (21-day packet), one pill daily continuously. The pill should be discontinued for 1 week every 3 months to allow a withdrawal bleed and thus prevent excessive endometrial proliferation.
2. DMPA, 150 mg intramuscularly every 12 weeks.
3. Progesterone, 10 mg orally daily for 5–10 days.
4. Gonadotropin-releasing hormone analogue (e.g., leuprolide acetate). Due to its hypoestrogenic side effects, this option should be used for no more than 6 months. It is an excellent choice for conditions associated with short-term thrombocytopenia, such as chemotherapy or bone marrow transplantation.

WEB SITES

For Teenagers and Parents

http://www.mckinley.uiuc.edu/health-info/womenhlt/ir-mense.html. Information handout from University of Illinois student health center on irregular uterine bleeding.

For Health Professionals

http://www.naspag.org/cme/september00.html. North American Society for Pediatric and Adolescent Gynecology (NASPAG), Continuing Medical Education (CME) on DUB.

REFERENCES AND ADDITIONAL READINGS

Amenorrhea
Catherine M. Gordon and Lawrence S. Neinstein

DEFINITION
There are various reported definitions of amenorrhea. However, strict adherence to these criteria can lead to improper management in some cases. Chronological age and developmental age, plus clinical data, must be integrated into the criteria to establish more useful evaluation guidelines. Such guidelines are listed in this chapter (the more criteria present, the stronger the case for evaluation). First, a brief review of normal development.

- For the American adolescent, the average age at menarche is 12.7 years, with a two standard deviation range of 11–15 months.
- Ninety-five percent to 97% of females reach menarche by age 16 years and 98% by 18 years.
- An average of 2 years is between the start of thelarche and the onset of menarche.
- The onset of menarche is fairly constant in adolescent development, with about two thirds of females reaching menarche at a Tanner sexual maturity rating (SMR) of 4. Menarche occurs at SMR 2 in 5% of girls, SMR 3 in 25%, and not until SMR 5 in 10%.
- Ninety-five percent of teens have attained menarche 1 year after attaining SMR 5.

1. Primary amenorrhea
   a. No episodes of spontaneous uterine bleeding by the age of 14–15 years, with secondary sex characteristics absent.
   b. No episodes of spontaneous uterine bleeding by age 16 years regardless of normal secondary sex characteristics (chronological age).
   c. No episodes of spontaneous uterine bleeding, despite having attained SMR 5 for at least 1 year or despite the onset of development (age previously defined): Most teens have menarche within 2–2.5 years after thelarche.
   d. No episodes of spontaneous uterine bleeding in any individual with clinical stigmata of Turner syndrome (clinical correlation).

2. Secondary amenorrhea: After previous uterine bleeding, no subsequent menses for 6 months or a length of time equal to three previous cycles.

ETIOLOGY

1. Primary amenorrhea without secondary sex characteristics (absent breast development) but with normal genitalia (uterus and vagina)
   a. Genetic or enzymatic defects (hypergonadotrophic hypogonadism): About 30% of primary amenorrhea cases are secondary to a genetic cause. The most common disorders are as follows:
      - Turner syndrome (45,X): Stigmata include short stature (height usually <60 inches); streaked gonads; sexual infantilism; and somatic abnormalities (webbed neck, short fourth metacarpal, cubitus valgus, coarctation of the aorta).
      - Structurally abnormal X chromosome: Short- or long-arm abnormal. Phenotype varies. Long-arm deletion commonly causes normal stature, no somatic abnormalities, streaked gonads, and sexual infantilism. Short-arm deletion leads to a phenotype similar to that of Turner syndrome.
      - Mosaicism: XXX. Eighty percent of such individuals are short, 66% have some somatic anomaly, and 20% have spontaneous menarche. The characteristics for XXX and XXX/XXX individuals are similar to those for XXX individuals.
      - Pure gonadal dysgenesis (46,XX with streaked gonads): Stigmata include normal stature, streaked gonads, sexual infantilism, and usually no somatic abnormalities.
      - 17a-hydroxylase deficiency with 46,XX karyotype: These individuals have normal stature, sexual infantilism, hypertension, and hypokalemia. Their laboratory test results show an elevated progesterone (>3 ng/mL), low 17a-hydroxyprogesterone (<0.2 ng/mL), and elevated serum deoxycorticosterone level.
   b. Isolated pituitary gonadotropin insufficiency: Very rare.
   c. Hypothalamic failure secondary to inadequate gonadotropin-releasing hormone (GnRH) release.

2. Primary amenorrhea with normal breast development, but absent uterus
   a. Androgen insensitivity (testicular feminization [complete form]): In these XY-karyotyped individuals, the Wolffian ducts fail to develop and the external genitalia develop as female in absence of a response to testosterone stimulation. The underlying defect is a mutation in the androgen receptor, rendering it insensitive to testosterone's actions. Because müllerian inhibitory factor (MIF) continues to be made by the male gonads, the müllerian ducts regress, and the teen does not form internal female genitalia. Internally, the teen has normal male gonads and fibrous müllerian remnants. The low levels of endogenous gonadal and adrenal androgens, unopposed by androgens, result in breast development. Because of the end-organ insensitivity to androgens, the teen develops sparse or absent pubic and axillary hair. In summary, manifestations include the following:
      - 46,XY karyotype
      - Female phenotype (in the case of complete androgen insensitivity: genital ambiguity often present) in incomplete forms
      - Testes present
      - Lack of axillary and pubic hair
      - Normal breast development
      - Blind vaginal pouch with absence of ovaries, uterus, and fallopian tubes
      - Normal male levels of testosterone
   b. Congenital absence of uterus
      - 46,XX karyotype
      - Ovaries are present: These adolescents may experience cyclic breast and mood changes.
      - Normal secondary sex characteristics.
      - Uterus absent or rudimentary cords.
      - Absent or blind vaginal pouch.
      - Normal female levels of testosterone.
      - May have associated renal, skeletal, and other congenital anomalies.
3. Primary amenorrhea with no breast development and no uterus: This condition is extremely rare. The individual usually has a male karyotype, elevated gonadotropin levels, and testosterone values that are either equal to or less than a normal female level. These individuals produce enough MIF to inhibit development of female internal genital structures but not enough testosterone to develop male internal and external genitalia. The causes include the following:
   a. 17,20-lyase deficiency
   b. Agonadism, including no internal sex organs
c. 17α-hydroxylase deficiency with 46,XY karyotype: Manifestations include sexual infantilism, absent uterus, and hypertension.

4. Primary and secondary amenorrhea with normal secondary sex characteristics (breast development) and normal genitalia (uterus and vagina)
   a. Hypothalamic causes
      - Idiopathic: Usually associated with a normal response of luteinizing hormone (LH) and follicle-stimulating hormone (FSH) to GnRH. The disorder is probably secondary to a subtle defect in GnRH secretion. Unstimulated levels of FSH and LH are typically within the normal range.
      - Medications and drugs: Particularly phenothiazines, oral contraceptives, glucocorticoids, and heroin.
      - Stress: Common in adolescents and may relate to family, school, or peer problems, or the fear of pregnancy.
      - Exercise: Athletes, particularly runners, gymnasts, competitive divers, figure skaters, and ballet dancers, have higher rates of amenorrhea and higher rates of disordered eating (female athlete triad includes a combination of disordered eating, amenorrhea, and decreased bone density). Sports that may place athletes at higher risk for this condition include those that emphasize leanness or those that use weight classification such as martial arts. The prevalence of secondary amenorrhea in adult athletes ranges from 3.4% to 66% depending on the sport studied (American Academy of Pediatrics [AAP], 2000). As many as 18% of female recreational runners, 50% of competitive runners training 80 miles per week, and 47% to 79% of ballet dancers may be amenorrheic (Calabrese et al., 1983; Cumming and Rebar, 1983). The prevalence of secondary amenorrhea in the teen athlete is unknown.
   b. Hypothalamic failure
   c. Lesions: Rare, but can be secondary to craniopharyngioma, tuberculous granuloma, or meningiopapillomatosis
   d. Polycystic ovary syndrome (PCOS): Many researchers believe PCOS to be a primary hypothalamic disorder. More than half of affected individuals have an LH : FSH ratio >3, with an LH level >10 mIU and often >25 mIU (see the section on PCOS).
   e. Idiopathic
      - Lesions: Rare, but can be secondary to craniopharyngioma, tuberculous granuloma, or meningiopapillomatosis
      - Polycystic ovary syndrome (PCOS): Many researchers believe PCOS to be a primary hypothalamic disorder. More than half of affected individuals have an LH : FSH ratio >3, with an LH level >10 mIU and often >25 mIU (see the section on PCOS).

Chapter 34

The evaluation of amenorrhea can be done easily with a thorough history, physical examination, and performance of several laboratory tests in a logical sequence. Too often, adolescents are subjected to an expensive shotgun approach to evaluation. It is essential to rule out the diagnosis of pregnancy before conducting an extensive evaluation.

DIAGNOSIS

The evaluation of amenorrhea can be done easily with a thorough history, physical examination, and performance of several laboratory tests in a logical sequence. Too often, adolescents are subjected to an expensive shotgun approach to evaluation. It is essential to rule out the diagnosis of pregnancy before conducting an extensive evaluation.

History

History should include the following:

1. Systemic diseases: Diseases associated with secondary amenorrhea should include anorexia nervosa, inflammatory bowel disease, diabetes mellitus, and pulmonary adenoma. A history of thyroid dysfunction is particularly important, because even mild thyroid dysfunction can lead to menstrual dysfunction.
2. Family history, including ages of parental growth and development, as well as mother's and sister's ages at onset of menarche: In addition, a family history of any thyroid disease, diabetes mellitus, eating disorders, or menstrual problems.
3. Past medical history including childhood development.
4. Pubertal growth and development, including breast and pubic hair development, and the presence of a growth spurt.
5. Emotional status.
6. Medications: Including illicit drugs (heroin and methadone are strongly correlated with menstrual dysfunction).
7. Nutritional status and recent weight changes.
8. Exercise history, particularly for sports that might predispose to amenorrhea.
10. Menstrual history.
11. History of androgen excess suggesting PCOS, or another ovarian or adrenal abnormality.

Physical Examination

The physical examination should include the following:

1. Check for signs of systemic disease or malnutrition.
2. Evaluate for SMR: This is important for evaluating progress in secondary sex characteristics, because most adolescents are not menarcheal until SMR 4, and 95% are menarcheal by 1 year after SMR 5.
3. Check height and weight.
4. Check for signs of androgen excess.
5. Check for signs of thyroid dysfunction.
6. Check for signs of gonadal dysgenesis: Webbed neck, low-set ears, broad shieldlike chest, short fourth metacarpal, and increased carrying angle of the arms.
7. Test for anosmia in females with primary amenorrhea to evaluate for Kallmann syndrome.
8. Breast examination: Check for galactorrhea.
9. Pelvic examination: Search for a stenotic cervix, vaginal agenesis, imperforate hymen, transverse vaginal septum, absent uterus, or pregnancy. An external genital examination is a critical component of the workup. A full pelvic examination may not be necessary if the teen is not sexually active, and the history or physical examination has revealed the cause of amenorrhea.

Laboratory Evaluation

The laboratory evaluation can be divided into those adolescents with the following:

1. Primary and secondary amenorrhea with normal secondary sex characteristics and normal genitalia
2. Primary amenorrhea and absent secondary sex characteristics or absent uterus or vagina

*Figure 52.1 and Figure 52.2 review the evaluation of primary and secondary amenorrhea.*

**FIG. 52.1.** The evaluation of primary amenorrhea.

**FIG. 52.2.** The evaluation of secondary amenorrhea. CNS, central nervous system; CT, computed axial tomography; TSH, thyroid-stimulating hormone.

1. For primary and secondary amenorrhea with normal secondary sex characteristics
   a. If evidence of galactorrhea or androgen excess is present, the adolescent should be evaluated, as described in Chapter 57 and Chapter 58, respectively.
   b. Pregnancy should always be considered and ruled out.
   c. Diabetes mellitus and hypothyroidism should be considered and if clinically indicated, should be ruled out with fasting blood sugar or thyroid function tests.
   d. Uterine synechiae, or Asherman syndrome, should be considered if there is a history of dilation and curettage or endometritis. This condition may cause partial or total obliteration of the uterine cavity. If this problem is suggested by the history, a gynecological referral for evaluation by hysteroscopy or hysterosalpingography is indicated.

   If the results of the aforementioned evaluation are negative, the workup should proceed as follows (**Fig. 52.2**):

   **Administer progesterone withdrawal test:** A positive response correlates with circulating E2 levels adequate to prime the endometrium. A positive response (ranges from minimal brown staining to normal menstrual flow) indicates a serum E2 level >40 pg/mL.

   - A positive response to progesterone indicates the presence of adequate estrogen levels, as seen with either hypothalamic-pituitary dysfunction or PCOS
   - Prolactin level should be measured, because this is the most sensitive test for pituitary microadenomas. Rarely, a patient who withdraws to progesterone can have a microadenoma. In addition, thyroid-stimulating hormone and T4 should be measured to rule out the possibility of either primary or central hypothyroidism. LH or LH : FSH ratios have been used in the past to evaluate for PCOS. However, these values lack sensitivity and specificity.
   - If there is no response to progesterone, then either hypothalamic-pituitary dysfunction or ovarian failure is likely. A high FSH level indicates ovarian failure, whereas a normal or low FSH level suggests a hypothalamic-pituitary disturbance. If ovarian failure is suspected, a karyotype, antiovarian antibodies, and screening for autoimmune endocrinopathies should be considered. If hypothalamic-pituitary failure is suspected, a magnetic resonance imaging (MRI) scan, visual fields, and pituitary stimulation tests should be considered.
   - Individuals with weight loss, anorexia nervosa, heavy substance abuse, or heavy exercise may or may not withdraw to progesterone. If they do not experience withdrawal bleeding within 10–14 days after discontinuing the progesterone, it is indicative of low E2 levels. If the teen has a normal prolactin level, she would not require an MRI scan unless otherwise indicated on the history and physical examination. However, a prolactin test would be indicated every 6–12 months if there are no spontaneous menses. An MRI should always be considered in a female patient with a history of headaches or visual changes.

2. For primary amenorrhea with either absent uterus or absent secondary sex characteristics (**Fig. 52.1**)
   a. A physical examination will divide the teens into three groups
• Absent uterus, normal breasts; absent breasts, normal uterus; and absent breasts, absent uterus: In general, breast development should be at least at stage SMR 4 to be considered indicative of full normal gonadal function. A breast stage of SMR 2 or SMR 3 may indicate adrenal function alone without gonadal function.

b. If the examination reveals normal breast development, but an absent uterus and blind vaginal pouch, a karyotype and a test for testosterone level are indicated.

XX karyotype plus female level of testosterone: Congenital absence of uterus
XY karyotype plus male level of testosterone: Androgen insensitivity

• A low or normal FSH level suggests a hypothalamic or pituitary abnormality, and a careful neuroendocrine evaluation is in order.

• A high FSH level and a blood pressure within the reference range suggest a genetic disorder or gonadal dysgenesis. A karyotype should be ordered.

• A high FSH level and hypertension suggest 17a-hydroxylyase deficiency. This is confirmed by an elevated progesterone level (>3 ng/mL), low 17a-hydroxyprogesterone level (<0.2 ng/mL), and an elevated serum deoxycorticosterone level.

d. The absence of both breast development and uterus or vagina is very rare. These findings suggest gonadal failure and the presence of MIF secretion from a testis. This could arise from anorchia occurring after MIF activity was present or an enzyme block, such as a 17,20-lyase defect. The evaluation should include LH, FSH, progesterone, and 17-hydroxyprogesterone measurements, and a karyotype.

TREATMENT

Primary Amenorrhea

Hypothalamic Hypogonadotropic Hypogonadism (Hypothalamic Failure) Therapy should begin with estrogen therapy (0.3 mg/day or less if the adolescent is short to avoid premature epiphyseal closure). Patients with normal height can receive 0.625 mg/day of conjugated estrogens (Premarin). High doses of estrogen and premature introduction of progesterone should be avoided early to avoid abnormal breast development manifested by increased subareolar breast development and abnormal contours.

A typical maintenance schedule would be 0.625 to 1.25 mg/day of conjugated estrogens on days 1 through 25 of each month, with 10 mg of medroxyprogesterone acetate (Provera) on days 12 through 25. The progestin is added to induce withdrawal bleeding and thus avoid endometrial hyperplasia. This schedule can be repeated beginning the first of each month. The dose of estrogen can range from 0.625 to 2.5 mg/day, depending on the individual and the estrogen response, but usually does not exceed 1.25 mg/day. GnRH will probably be used for these conditions when a more easily tolerated delivery system is available. If pregnancy is desired, pulsatile GnRH is an option.

Pituitary Defect Hormonal therapy, as outlined earlier in this chapter.

Genetic Abnormalities Leading to Gonadal Defects Hormonal therapy, as already outlined. If a Y chromosome is present in an XX-karyotyped individual, gonadal removal is necessary. If a 46,XX karyotype is present, then the gonadal tissue should be visualized to assess whether more than a streaked gonad is present. It is important to start hormonal replacement therapy in early adolescence. These individuals are universally sterile. However, with an intact uterus, the individual could be able to bear children after donor oocyte implantation and hormonal support.

Enzyme Defects For 17a-hydroxylase deficiency, both glucocorticoid and estrogen-progesterone replacement are needed and removal of gonads if Y chromosome is present. For 17,20-lyase deficiency, prescribe estrogen-progesterone replacement; remove gonads if Y chromosome is present.

Androgen Insensitivity

1. Gonadal removal: All intraabdominal gonads associated with a Y chromosome have a relatively high potential for malignancy. Tumors in patients with androgen insensitivity are rare before the age of 25 years. Because gonadal secretion of sex steroids contributes to the development of secondary sex characteristics, gonadectomy should generally be delayed until the age of 20 years in these patients.

2. After the testes are removed, maintenance estrogen therapy is needed.

3. The adolescent should be informed that she may require vaginoplasty to have normal sexual function.

4. The adolescent should be informed that she cannot become pregnant.

5. Counseling: The adolescent should be informed that she has an abnormal sex chromosome, not that she has male chromosomes. She may require extra reassurance and counseling regarding her identity and concerns about infertility and sexual function.

Congenital Absence of the Uterus Because these adolescents have normal-functioning ovaries, they do not require hormonal replacement therapy. They may require a vaginoplasty for normal sexual function and an MRI or intravenous pyelogram to rule out renal anomalies. These adolescents must be informed that they cannot become pregnant; thus, they may require additional support and counseling regarding their identity and body image.

Primary and Secondary Amenorrhea with Normal Secondary Sex Characteristics

1. PCOS
   a. Medroxyprogesterone acetate (10 mg) should be given for 10 days every 1–2 months to induce withdrawal bleeding, and oral contraceptives with or without a progestin contraceptive should be given.
   b. When pregnancy is desired, referral for use of clomiphene citrate is recommended.

2. Hypothalamic-pituitary dysfunction
   a. Alleviate the precipitating cause if known.
   b. Hormonal therapy with progestins to induce uterine bleeding every 1–2 months is recommended.

3. Hypothalamic-pituitary failure
   a. The cause must be evaluated and corrected if possible.
   b. Replacement therapy with cyclic conjugated estrogens and progestins, as outlined earlier for hypothalamic failure, is recommended.
   c. If the adolescent or young adult desires pregnancy, refer her to an infertility clinic.

4. Ovarian failure
   a. These adolescents also require cyclic estrogen and progestin therapy.
   b. These adolescents are generally sterile and should be counseled regarding this aspect of their problem.

5. Uterine synchiae: This problem requires referral to a gynecologist for possible transhydrosurgical lysis of the adhesions.

Amenorrhea Associated with Weight Loss

In young women with amenorrhea associated with weight loss, bone mineral density (BMD) loss can occur soon after amenorrhea develops. Treatment to prevent BMD loss or promote bone accretion should probably start after 6 months of amenorrhea (Hergenroeder, 1995). The efficacy of estrogen replacement therapy in this setting is uncertain. Estrogen likely has beneficial effects on bone and other tissues, but other supplements such as calcium, vitamin D, and protein may also be warranted (Gordon, 1989). Most adolescents who recover from anorexia nervosa at a young age (younger than 15 years) can have normal total-body BMD, but regional (lumbar spine and femoral neck) BMD may remain low (Hergenroeder, 1995). The longer the duration of anorexia nervosa and/or weight loss, the less likely the BMD will return to normal values.

The Female Athlete Triad

Female children and adolescents who participate regularly in athletics may develop the female athlete triad, which includes disordered eating, menstrual dysfunction (typically amenorrhea), and decreased BMD.

1. Disordered eating: Physically active female adolescents and young adults may develop an energy deficit of calories that may either be unintentional, related to increased demands of training, or intentional in an attempt to lose weight or body fat for enhanced performance or appearance. Disordered eating behaviors may include restricting food intake, bingeing and/or purging by vomiting, laxative use, diuretics, and diet pills. These individuals may also develop compulsive...
exercise behaviors. Disordered eating behaviors may impair athletic performance, increase risk of injury, and increase the risk of menstrual dysfunction and loss of BMD.

2. Menstrual dysfunction: Menstrual dysfunction in athletes may include primary amenorrhea, secondary amenorrhea, oligomenorrhea and luteal phase deficiency. Menstrual dysfunction is more common in athletes than in the general population. Athletes, particularly runners, gymnasts, and dancers, with secondary amenorrhea may fall into either the hypothalamic-pituitary dysfunction or the hypothalamic-pituitary failure category.

3. Decreased BMD: There is evidence to suggest that athletes with amenorrhea have low levels of estrogen and may be at risk for osteoporosis and stress fractures (Cann et al., 1984; Drinkwater et al., 1986; Marcus et al., 1985). Some studies suggest that when amenorrhea persists for 6 months with bone loss, the bone loss may never be regained, whereas other studies indicate a 20% increase in bone mass when weight is gained. Baer (1993) compared reproductive function in ten amenorrheic and eumenorrheic adolescent female runners and seven untrained controls. Amenorrheic subjects were found to run more miles per day and consume fewer calories per day compared with eumenorrheic subjects. Mean levels of fasting plasma E₂, LH, FSH, free Tₐ, and Tₐ were significantly lower in amenorrheic patients compared with eumenorrheic patients and the control subjects. In addition, those who were amenorrheic indicated that they were very concerned about their weight and fearful of gaining fat mass. Other studies have indicated that the change in bone density may also relate to the type of athletics performed, with gymnastic exercises, for example, yielding a stronger bone mass. One recent Scandinavian study demonstrated that most women who exercise regularly at moderate levels are not at significant risk for athletic amenorrhea with its accompanied decrease in BMD. Summary considerations for athletes with amenorrhea include the following (Hergenroeder, 1995):

1. Most bone mineralization in female adolescents occurs by the middle of the second decade of life.
2. Premature bone demineralization occurs in young women with hypothalamic dysfunction that manifests as either amenorrhea and oligomenorrhea in the setting of athletic participation and eating disorders.
3. Regular menses and fertility should return with a decrease in the intensity of activity. An adolescent with significant menstrual dysfunction attributed to exercise should be encouraged to increase her caloric intake and modify excessive exercise activity.
4. Calcium intake should be increased to 1,500 mg/day in these young women.
5. Insulin resistance: Insulin resistance may exist in both obese and lean women with PCOS. Some individuals may develop HAIR-AN syndrome, a combination of hyperandrogenemia, obesity, insulin resistance, and acanthosis nigricans.
6. The practitioner should evaluate these individuals, as outlined previously, to eliminate the possibility of pregnancy, thyroid dysfunction, prolactinoma, or a disorder of androgen excess. It should not just be assumed that amenorrhea is simply secondary to exercise.

POLYCYSTIC OVARY SYNDROME

Definition

PCOS is a disorder of the hypothalamic-pituitary-ovarian system, giving rise to temporary or persistent anovulation and usually androgen excess. The syndrome was originally described in 1935 by Stein and Leventhal as amenorrhea, hirsutism, and obesity associated with enlarged polycystic ovaries. For many years, there was an emphasis on the morphological changes in the ovary. However, enlarged polycystic ovaries may occur with other conditions such as Cushing syndrome and congenital adrenal hyperplasia (CAH), and women with other classic features of PCOS may have ovaries of normal size. The features stressed recently for PCOS include clinical evidence of hyperandrogenism such as facial hair and acne, anovulation, and laboratory evidence of elevated androgen levels. Diagnosis is particularly important because PCOS is now believed to increase metabolic and cardiovascular risks, which is linked to insulin resistance and compounded by obesity. Insulin resistance and its associated risks are also present in nonobese women with PCOS. PCOS is one of the most common endocrine disorders, affecting approximately 5% to 10% of premenopausal women.

Etiology

Endocrine Findings

PCOS is characterized by menstrual irregularities ranging from amenorrhea to oligomenorrhea to dysfunctional uterine bleeding. An androgen-excess state is often present, leading to hirsutism and rarely virilization. The changes in gonadotropins and steroid hormones that cause these manifestations are as follows:

1. Inappropriate gonadotropin secretion (IGS) characterized by:
   a. Elevated serum LH level (>21 mIU/mL)
   b. Reference-range or low FSH level
   c. Exaggerated response of LH, not FSH, to GnRH
   d. LH : FSH ratio often >3
   e. Elevated bioactive LH (generally a research tool, but even more sensitive for PCOS than an elevated immunoreactive LH level)

2. Steroid hormones
   a. Estrone (E₁): Significantly elevated serum levels
   b. E₂: Reference-range level of total E₂, but elevated unbound or free E₂ level
   c. Androstenedione and dehydroepiandrosterone sulfate (DHEAS): Elevated serum levels
   d. Testosterone: Often minimally elevated serum levels seen

3. Source of excess androgens: The source may be secretion from the ovaries, the adrenal gland, or both, although hyperandrogenism is principally ovarian in origin in women with a primary diagnosis of PCOS. Two other sources contribute to androgen excess:
   a. Androstenedione is converted peripherally in adipose tissue to testosterone.
   b. There is a decrease in binding of testosterone to sex hormone-binding globulin (SHBG). Healthy females have approximately 96% of their testosterone bound to SHBG, where it is inactive, whereas patients with PCOS have only 92% of their testosterone bound; thus, there is a larger percentage of free and active testosterone in patients with PCOS.

Pathophysiology

The exact initiating cause of PCOS is a mystery but may be related to the following:

1. Abnormal hypothalamic-pituitary function
2. Abnormal ovarian function
3. Abnormal adrenal androgen metabolism
4. Insulin resistance: Insulin resistance may exist in both obese and lean women with PCOS. Some individuals may develop HAIR-AN syndrome, a combination of hyper androgenism, insulin resistance, and acanthosis nigricans.

Factors leading to the development of PCOS include the following:

1. Insulin increases at the time of puberty, because insulin resistanceselectively affects peripheral glucose metabolism.
2. Insulin and insulin-like growth factor I have mitogenic effects on the ovaries, causing theca cell hyperplasia, which leads to excessive androgen production.
3. The increased ovarian androgen levels cause follicular atresia, impairing E₂ production.
4. The E₂ levels are elevated due to increased conversion of androstenedione to E₁ in adipose cells, which leads to suppression of FSH and tonic stimulation of LH, which further aggravates theca cell stimulation.
5. The combination of theca cell hyperplasia and arrested follicular maturation constitutes the typical histological features of PCOS.
6. Because not all adolescents ultimately develop PCOS, it is thought that there is a genetic factor involved. Genetic studies of family clusters have shown a high incidence of affected relatives (Legro, 1995). A dominant mode of inheritance seems most likely, but the type and degree of expression may vary within the same family. The syndrome may be transmitted through paternal or maternal sides of a family. Both the insulin receptor genes and the LH b-subunit gene have
been mapped to chromosome 19. However, chromosomal studies of patients with PCOS have shown no consistent abnormality.

Guclu et al. (1993) compared adolescent girls with PCOS and adult women with PCOS and found that clinical manifestations and hormonal changes were similar. Valproate can also induce menstrual disturbances, polycystic ovaries, and hyperandrogenism (Isojarvi et al., 1993). In a study of 238 women with epilepsy, Isojarvi et al. (1993) found 43% of the women using valproate had polycystic ovaries. In those women using valproate before reaching age 20 years, 80% had polycystic ovaries or hyperandrogenism.

Clinical Consequences

PCOS can present with many symptoms. Table 52.1 indicates the prevalence of various signs and symptoms associated with PCOS.

### Table 52.1. Prevalence of major clinical features of polycystic ovary syndrome

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anovulation</td>
<td>100%</td>
</tr>
<tr>
<td>Hyperandrogenism</td>
<td>80%-100%</td>
</tr>
<tr>
<td>Obesity</td>
<td>75%-80%</td>
</tr>
<tr>
<td>Insulin resistance</td>
<td>50%</td>
</tr>
<tr>
<td>Hypertrichosis</td>
<td>80%-90%</td>
</tr>
<tr>
<td>Infertility</td>
<td>40%-50%</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>15%</td>
</tr>
<tr>
<td>Elevated Lipoprotein Profile</td>
<td>30%</td>
</tr>
</tbody>
</table>

1. **Anovulation** Anovulation is a key feature. Usually the anovulation in PCOS is chronic and presents as either oligomenorrhea or amenorrhea of perimenarcheal onset. Some women who report normal menses may be anovulatory. A small number of women with PCOS may have ovulatory function.

2. **Polycystic Ovaries** The ovaries in patients with PCOS are usually enlarged, pearly white, splotch with multiple (20 to 100) cystic follicles. Normally, follicles develop to about 19 to 20 mm and then ovulation occurs. In women with PCOS, multiple follicles develop, but only to about 9 to 10 mm in size. Histologically, the ovaries have the same number of primordial follicles, but the number of atretic follicles is doubled. Also, there is an absence of corpora lutea. The polycystic ovary is a sign, not a disease entity on its own. The typical histological changes of the polycystic ovary can be seen in ovaries of any size. A sonographic spectrum exists within patients with PCOS, and polycystic ovaries on ultrasonography are not sufficient alone for diagnosis of PCOS.

3. **Hyperandrogenism/Hirsutism** Hyperandrogenism is another key feature of PCOS. Hyperandrogenism in PCOS is primarily ovarian in origin, although adrenal androgens may contribute. The development of hirsutism depends not only on the concentration of androgens in the blood, but also on the genetic sensitivity of the hair follicles to androgens. Clinical hirsutism may not occur in all women with PCOS, but most women with PCOS have elevated blood androgen levels.

4. **Obesity** Originally, obesity was regarded as a classic feature, but its presence is extremely variable and not mandatory for diagnosis. About 40% to 50% of women with PCOS are obese. Obesity in women with PCOS is usually of the android type, with increased waist-hip ratios. The obesity in PCOS also worsens insulin resistance and increases cardiovascular risks.

5. **Infertility** Although infertility is usually not of concern to the adolescent patient, the risk is significantly elevated due to anovulation.

6. **Cancer Risk** There is an increased risk for cancer of the endometrium due to prolonged unopposed estrogen stimulation of the endometrial lining from chronic anovulation. There may also be an increased risk of breast cancer associated with chronic anovulation during the reproductive years. The risk of endometrial cancer is increased threefold, and there may also be an increased risk of breast cancer in these women.

7. **Elevated Lipoprotein Profile** The abnormalities in women with PCOS include elevated levels of cholesterol, triglycerides, and low-density lipoprotein cholesterol (LDL-C) and lower levels of high-density lipoprotein cholesterol (HDL-C) and apolipoprotein A-I. Although hyperandrogenism plays some role in these changes, hyperinsulinism (insulin resistance) probably has a larger effect.

8. **Insulin Resistance and Hyperinsulinemia** Insulin resistance is associated with obesity, insulin resistance is associated with obesity, it can also be found in normal-weight women with PCOS. The cause-effect relationship between insulin and androgens in PCOS is still controversial and is under investigation. It has also been suggested that anovulation is a major factor associated with insulin resistance in women with PCOS. The exact pathogenesis of insulin resistance is not clear and may be related to excessive serine phosphorylation of the insulin receptor.

9. **Impaired Glucose Tolerance and Diabetes** Women with PCOS are at increased risk for impaired glucose tolerance and overt type 2 diabetes mellitus because of the insulin resistance. One study found that 31% of obese, reproductive-age women with PCOS had impaired glucose tolerance and 7.5% had overt diabetes (Legro et al., 1999). Even in the nonobese women with PCOS, 10.3% had impaired glucose tolerance and 1.5% diabetes, three times the rate in the general population.

10. **Cardiovascular Disease** Although not an immediate issue for adolescents and young adults with PCOS, because of the prevalence of the risk factors listed previously, women with PCOS may be at long-term risk for increased cardiovascular disease. Adult women with PCOS have an estimated sevenfold risk of myocardial infarction (Lobo and Caminha, 2000). In addition, these young women can also have increased levels of plasminogen-activator inhibitor-1 (PAI-1), which inhibits fibrinolysis and is a risk factor for myocardial infarction (Ehrmann et al., 1997).

### Differential Diagnosis

1. Familial hirsutism
2. Androgen-producing ovarian and adrenal tumors
3. Cushing syndrome: Potential influence of Cushing syndrome is usually excluded by history and physical examination, and if needed, an overnight dexamethasone suppression test.
4. CAH: An incomplete 21-hydroxylase deficiency can mimic PCOS. The diagnosis of CAH is based on elevated serum 17-hydroxyprogesterone level, particularly after a single-dose injection of adrenocorticotropic hormone.
5. Stromal hyperthecosis: Stromal hyperthecosis probably represents a disorder related to PCOS. However, in this disorder, the testosterone levels are higher and may be as high as those in patients with androgen-producing tumors. These patients may be not only hirsute but also virilized. The history is one of slow-onset progression of symptoms and signs. Ovarian vein catheterization shows increased, but equal amounts, of testosterone from each ovary.

### Diagnosis

Criteria for the diagnosis of PCOS include the following:

1. Irregular menses: Chronic anovulation with a perimenarcheal onset of menstrual irregularities.
2. Hyperandrogenism with or without skin manifestations: Biochemical or clinical evidence of androgen excess. Serum testosterone level is the best marker for ovarian causes of hyperandrogenism whereas DHEAS is the best marker for adrenal sources.
3. Absence of other androgen disorders (adrenarche, hirsutism, or polycystic ovary).
4. Polycystic ovaries on ultrasonography (not required for diagnosis but extremely prevalent).

The following are not needed for diagnosis but are supportive evidence of the diagnosis:

1. Increased body weight (ponderal index: height [inches] divided by the cubed root of weight [pounds] is <12): Obesity is not absolutely necessary for the diagnosis, if the other criteria are present. However, although all patients may not appear obese, most should have a ponderal index <12.
2. IGS (LH or FSH >3, provided LH level is not <6 mlU/mL). Although LH and FSH have been widely used, the sensitivity and specificity of these hormones are low.
3. Prolactin: Most individuals with PCOS have reference-range levels of prolactin, although 20% have mildly elevated levels (Luciano et al., 1984). Prolactin may augment adrenal androgen secretion in this subset of patients.

Therapy

Infertility Infertility is usually not a concern in the adolescent patient. However, when fertility is desired, clomiphene citrate may be used to stimulate ovulation.

Hirsutism

1. Cosmetic methods, including shaving, waxing, or electrolysis.
2. Oral contraceptives work in 60%-100% of women, but 6–12 months are required before noticeable differences are seen. Combination pills should be used that contain low androgenic progestins such as norethindrone, norgestimate, or desogestrel. Oral contraceptives work by
   a. Suppressing LH production and thus reducing ovarian androgen production
   b. Increasing the binding capacity of SHBG and thus decreasing free testosterone
   c. Decreasing adrenal androgen production
   d. Decreasing 5α-reductase activity

In addition to oral contraceptives, antiandrogens such as spironolactone can be used (see Chapter 58). The combination of low-dose oral contraceptives and spironolactone is very effective.

Menstrual Irregularities

The patient with amenorrhea or oligomenorrhea can receive medroxyprogesterone acetate (Provera) (10 mg daily for 10 days every 6 to 12 weeks) for withdrawal bleeding. However, the monthly use of medroxyprogesterone acetate has no significant effect on androgen production by the ovaries, so it is not helpful if hirsutism is present. Combination oral contraceptives are the most efficacious therapy, because they are directed toward the primary pathophysiologic abnormalities.

Obesity

Obesity may be a major focus of preventive health care for women with PCOS to lower associated cardiovascular risks. However, weight loss is difficult to achieve.

Metabolic Changes

Because of the potential for abnormal glucose tolerance (insulin resistance) and hyperlipidemia, it can be important to measure these in adolescents with PCOS. Women with PCOS should probably have their cholesterol, triglycerides, and both LDL-C and HDL-C measured, although there is no consensus at what age this should occur and how often the tests should be reordered if the results are normal. In addition, these women probably should be checked and followed for impaired glucose tolerance and diabetes. Diagnosis and continued monitoring of these individuals may reduce the risks of metabolic and cardiovascular disease. Reduction in insulin resistance is important, and diet and exercise are critical first-line steps. Insulin-sensitizing medications may prove beneficial, but a consensus regarding guidelines for their usage has not occurred to date for adolescents with PCOS.

WEB SITES

For Teenagers and Parents

http://www.turner-syndrome-us.org/. The Turner's Syndrome Society of the United States. This Web site provides information and allows young women to exchange information.
http://www.medhelp.org/www/atis/. Androgen Insensitivity Syndrome Support Group. This site contains medical information about androgen insensitivity, support group contacts, newsletters, and personal accounts of people with androgen insensitivity syndrome.

PCOS Web Sites

http://www.pcossupport.org/. The PCOS Association's Web site includes facts and figures on PCOS, as well as on-line support.
http://www.obgyn.net/pcos/pcos.asp. The PCO Teenlist home page is dedicated to teenagers with PCOS. Includes a chat room and bulletin board so teens can share their thoughts on the disease.

REFERENCES AND ADDITIONAL READINGS

Pelvic Masses

Anita L. Nelson and Lawrence S. Neinstein

CONGENITAL ANOMALIES

Reproductive tract anomalies are not uncommon, particularly in recently menarchal women. The uterus is formed by fusion of paramesonephric ducts in the midline. If fusion is incomplete, then a uterus didelphys may form with two separate uterine halves (each with its own cervix, corpus-attached fallopian tube and ovary, and possibly vaginal canal). This diagnosis may be suspected when a woman fails to control her menstrual flow with a tampon or has habitual abortions (15% to 25% incidence in this group). On examination, one of the two uteri may be mistaken for an adnexal mass. If uterine fusion is partial, there may be a bicornuate uterus or blind uterine horn, which over time can expand with menstrual blood. If fusion is complete, but the resorption of the midline is incomplete, a septate uterus can result.

The vagina also forms in two parts: The upper three fourths forms from the inferior portion of the paramesonephric duct fusion and the lower quarter from the sinovaginal bulbs. The lowest portion of these bulbs fits with a solid core of tissue called the vaginal plate. If the upper and lower vaginal portions do not fuse, then a transverse vaginal septum forms. Similarly, if the solid core of tissue at the junction of the vaginal plate and the urogenital sinus do not canalize completely, the women can have an imperforate hymen or vaginal agenesis. Both of these anomalies present with hematocolpos, which may be perceived as a "pelvic mass." The phenotypical women with testicular feminization (46,XY) has a blind vaginal pouch, a uterus and bilateral pelvic testes, which could be considered pelvic masses.

Another class of anatomical congenital anomalies that can create pelvic masses arises from remnants of the mesonephric duct system or mesovarium that should have degenerated in utero in the presence of antimüllerian hormone. At least 25% of women have remnants of these systems. These remnants can present in the lateral adnexa as paraovarian cysts or paratubal cysts. Paratubal cysts can also arise spontaneously from the tubal tissue. They are often multiple and can vary in size from less than 1 cm to 20 cm. Along the lateral wall of the vagina or uterus, these remnants present as Gartner duct cysts.

Urachal cysts can be found along the midline above the bladder and be confused with other pelvic masses. A pelvic kidney must also be included in the differential diagnosis, particularly in a young woman who has not had a previous pelvic or renal evaluation. Any other structure in the pelvis, such as a full bladder or hard stool in the bowel, can be confused with a pelvic mass.

PREGNANCY-INDUCED PELVIC MASSES

The possibility of an intrauterine pregnancy enlarging the uterus or an ectopic pregnancy (see Chapter 63) causing an adnexal mass must be considered in the differential diagnosis of every young woman with secondary sexual characteristics. A sensitive urine pregnancy test can very reliably rule out a clinically significant pregnancy. However, in many instances, the test is not ordered because the provider does not consider it likely that the young woman has been sexually active. Today, it is recognized that both sexual abuse and early consensual sexual activity occur at surprisingly high rates. If pregnancy testing is a routine order, then its use in any individual case does not require justification.

INFECTION-INDUCED PELVIC MASSES

As the rates of sexually transmitted diseases (particularly chlamydia) have increased among our adolescent populations, the incidence of upper tract involvement—such as pyelonephritis or pelvic abscess (tuboovarian abscess [TOA])—has increased (see Chapter 63). Sexually active adolescents have the highest rates of pelvic inflammatory disease (PID) of any age at-risk group. Gonococcal PID has a classic collection of signs and symptoms and is relatively easy to diagnose clinically. However, chlamydial PID is more subtle in its presentation. Usually Chlamydia trachomatis elaborates a heat shock protein that silently destroys the cilia lining the fallopian tube with only minimal symptomology; if the tissues become secondarily infected with enteric organisms, a clinically apparent salpingitis can develop. In the acute stage, pelvic infection is often accompanied by fever, cervical discharge, pain, and possibly adnexal masses (pyosalpinges or TOAs). After resolution of the acute infection, the tubes may remain dilated and filled with fluid (hydrosalpinges), particularly if their fimbriae have been sealed. Treated pelvic abscesses may also cause palpable masses from matting or agglutination of bowel, ovary, fallopian tube, and other structures. Other infectious causes of pelvic masses include an appendiceal abscess or diverticulitis or Meckel diverticulum.

A pelvic mass can be identified during a routine screening pelvic examination or it can be discovered during a workup for abdominopelvic pain or abnormal bleeding. The differential diagnosis of a pelvic mass for prepubertal and adolescent women is different than that for older women, although there may be some overlap. For example, an imperforate hymen causing severe cyclic abdominal pain and a large pelvic mass are more likely to present in a 14-year-old girl than in a 34-year-old woman. Similarly, dermoid cysts are more prevalent in adolescents than uterine fibroids. Germ cell tumors of the ovary are more common in teens than epithelial carcinoma. Figure 53.1 reviews management of pelvic masses in asymptomatic women.

FIG. 53.1. Management of pelvic masses in asymptomatic women.
ADNEXAL TORSION

An acute pelvic mass can develop when there is torsion of any adnexal structure. In young women, the most common causes of adnexal torsion are dermoid cysts, parauterine polyp, and other masses that are rotated over their vascular bases by intestinal peristalsis. Once rotated, the venous flow to the mass is obstructed while arterial flow continues, inflating the mass until arterial flow is compressed. Women usually describe a twisting sensation and intermittent bouts of intense pelvic pain (with the torsion) separated by intervals of generalized aching (when the mass untwists). Intriguingly, with interruption of the arterial supply, the symptoms can temporarily abate until either hemorrhage or perforation ensues. Adnexal torsion is a surgical emergency. If diagnosed early, the mass can be untwisted and the ovary can be spared while the cyst is excised. If therapy is delayed, the necrotic fallopian tube and ovary must be extirpated.

UTERINE NEOPLASMS

In adenocarcinoma, uterine neoplasms are quite rare.

Leiomyomas (fibroids) develop within the wall of the uterus (intramural myomas) and later extend toward the endometrium (submucosal myomas) or toward the external surface of the myometrium (subserosal myomas). Although about 20% of women in their 30s have fibroids, most adolescent women have not had sufficient time to develop clinically significant or palpable fibroids.

Adenomyosis—the other common cause of uterine enlargement in older, parous women—is extremely rare in adolescent women. Adenomyosis results from the extrusion of endometrial glands and stroma into the myometrium, usually during parturition. These glands respond to cyclic hormonal stimulation and slough as the corpus luteum regresses each cycle. The sloughed endometrium is trapped in the myometrium and initiates local inflammatory reactions. Over time, the uterus becomes enlarged and somewhat globular and is likely to be tender during menses. Affected women also suffer heavier menstrual bleeding (menorrhagia) and dysmenorrhea.

GENITOURINARY NEOPLASMS

Benign ovarian masses include functional ovarian cysts, endometriomas, and benign ovarian neoplasms.

Physiological (Functional) Ovarian Cysts

The age of a patient and the size of a cyst can be helpful in deciding management. The incidence of functional ovarian cysts is higher in menstruating adolescents than in premenstrual adolescents. Size of a cyst has been correlated to regression. Spontaneous regression occurs in 82.6% of cysts 4 cm or smaller; 63.4% of cysts 4 to 6 cm; and 28.6% of cysts 6 to 8 cm.

1. Follicular cysts: In postpubescent adolescent women, physiological cysts are one of the most frequent causes of adnexal masses. Hospitalization rates for functional ovarian cysts are currently about 500 per 100,000 women years in the United States, which has been reduced from even higher levels by the availability of ultrasonographic evaluation. The most common type of functional ovarian cyst is a follicular cyst. Follicular cysts range in size from 3 cm to 15 cm in diameter but rarely exceed 8 cm. They do not usually cause any symptoms but occasionally torsion (see previous discussion) or rupture occurs, at which time they can cause pain. Follicular cysts usually resolve in 4 to 8 weeks unless the patient is taking progestins (e.g., Mieraus, depot medroxyprogesterone acetate [DMPA]), which can slow follicular atresia and require a longer time for resolution. In general, conservative management of cysts smaller than 8 cm in a premenopausal woman is recommended for up to 8 weeks (Fig. 53.1).

2. Polycystic ovary syndrome: Female patients with polycystic ovary syndrome (now more correctly called chronic anovulation with hyperandrogenemia) (see Chapter 52) often have “polycystic appearing ovaries” (PAOs) with multiple small follicles near the cortex in a single ultrasonographic plane in the “black pearl necklace” pattern. The volume of the ovary is often increased by a factor of two to three, not only by the presence of these follicles, but also by an increase in the ovarian stroma. PAOs can also be seen in many other settings, such as prepubertal women and women on oral contraceptives.

3. Corpus luteum cysts (CLCs): CLCs are a variant of the normal corpus luteum. By definition, CLCs exceed 3 cm in diameter, but they can reach 15 cm and often are associated with delayed menses. CLCs are less common than follicular cysts but clinically are more significant because they are prone to rupture and can cause acute hemoperitoneum. This can be quite hazardous if the patient is anticoagulated. A frequent clinical scenario is rupture during intercourse late in the cycle (days 21 to 26), although rupture can also follow pelvic examination, strenuous exercise, or trauma.

Oral contraceptives reduce the risk of CLCs and at higher doses reduce the risk of follicular cysts (Grimes et al., 1994). DMPA also reduces the risk of functional ovarian cyst formation. Smoking doubles the risk of developing functional ovarian cysts (Holt et al., 1994).

Administration of oral contraceptives, which was used in the past to distinguish between functional and neoplastic ovarian cysts in menstruating patients, is no longer recommended as a diagnostic tool. Administration of oral contraceptives to induce cyst regression is no more effective than an observation period with no hormonal therapy, although it will suppress the development of a second physiological cyst, which could confuse the diagnosis.

Endometriomas and Endometriosis

Until recently, endometriosis was rarely reported in adolescent women, although with the earlier onset of menarche, the prevalence of endometriosis in young women is now more frequently recognized. The presenting symptoms include worsening dysmenorrhea, premenstrual pelvic pain (possible hematuria or hematochezia), and deep thrust dyspareunia. On pelvic examination, findings of diffuse or localized tenderness, diminished uterine motility (a result of adhesion formation particularly between the uterus and the sigmoid), cervical motion tenderness (from adhesions), and possibly an ovarian mass (endometrioma) are suggestive of endometriosis. Rupture of an endometrioma (chocolate cyst) can cause signs and symptoms of an acute abdomen because the fluid from the endometrioma induces a chemical peritonitis. Endometriomas larger than 2 cm require surgical excision.

Benign Ovarian Neoplasms

Benign Germ Cell Tumors

Benign cystic teratomas (dermoid cysts) are the most common benign ovarian neoplasm of adolescent and reproductive years. In one study, 62% of all surgically excised ovarian masses in women younger than 40 years were dermoid cysts (Koonings et al., 1989). Dermoid cysts are composed of all three germ cell layers. They are generally thick-walled cysts, filled with lipid (sebaceous liquid material) and hair, and they contain characteristic firm areas of cartilage and teeth. Dermoid cysts vary from millimeters to 25 cm, but 85% are smaller than 10 cm. On examination, they are unilateral (only 10% are bilateral), very mobile, anteriorly positioned (fat floats), nontender adnexal masses. Benign cystic teratomas are usually (50% to 60%) asymptomatic. Surgical intervention with cystectomy is recommended because the risk of torsion with dermoid cysts is about 15%. Malignant transformation is very rare in young women but can reach 2% in postmenopausal women.

Benign Ovarian Neoplasms

Serous cystadenomas account for 20% of benign ovarian neoplasms in women during their reproductive years. These tumors are multiloculated, fluid-filled cystic masses that can reach very large diameters. Benign mucinous cystadenomas have smooth, lobulated surfaces with multiloculations filled with viscous mucoid material. Even though these tumors are not invasive, leakage of the fluid into the abdominal cavity can cause a critical condition called pseudomyxoma peritonei. Surgical removal of these adenomas is necessary for tissue diagnosis and to prevent torsion.

Sex Cord-stromal Tumors

Overall, these tumors are relatively rare, but they occur with higher prevalence in premenarchal girls. They are hormonally active. Granulosa cell tumors and theca cell tumors produce estrogen while Sertoli-Leydig cell tumors produce androgen with or without estrogen. As a result of this sex-steroid production, sex cord-stromal tumors can cause precocious puberty, endometrial hyperplasia or carcinoma, or hirsutism, acne, and virilization.

MALIGNANT OVARIAN MASSES

Germ Cell Tumors

In women younger than 20 years, almost 70% of all ovarian tumors are of germ cell origin and one third of those tumors are malignant. These germ cell tumors
Dysgerminomas comprise 5% to 10% of ovarian cancers in young women. They represent abnormal proliferations of the basic germ cell. They are usually encapsulated, bosselated masses measuring 5 to 15 cm in diameter and have spongy consistencies. These tumors are particularly frequent in phenotypically female patients with gonadal dysgenesis (e.g., 46,XY streak ovaries). One important feature of the dysgerminoma is bilaterality, which is rare among germ cell tumors.

2. Endodermal sinus tumors ("yolk sac tumors") of the ovary have a median age at detection of 16 to 18 years. Most (70%) patients present with abdominal or pelvic pain. Most of these tumors secrete tumor markers such as a-fetoprotein (AFP) and b-human chorionic gonadotropin (b-hCG). Other germ cell tumors include embryonal carcinoma and choriocarcinoma tumors.

3. Immature teratomas represent 10% to 20% of all ovarian malignancies in women younger than 20 years. About half of all pure immature teratomas occur in adolescent women. Immature teratomas contain elements that resemble tissues derived from the embryo that do not mature. The amount of immature neural tissue is most predictive of lethality.

Epithelial Carcinomas

Although these tumor types are the most common (75%) type of ovarian carcinoma in postmenopausal women, they rarely develop in adolescents. Included in this group of neoplasias are serous cystadenocarcinoma, mucinous cystadenocarcinoma, and endometrial cystadenocarcinoma. They are generally quite advanced when diagnosed.

Other Carcinomas

Carcinoma metastatic to the ovary is not uncommon because the ovary is a well-perfused organ. In young women, the more common metastatic lesions include lymphomas and leukemias. In older women, gastric and breast carcinomas more frequently spread to the ovary.

REFERENCES AND ADDITIONAL READINGS


PREVALENCE

The high-risk sexual behavior of adolescents is reflected by high rates of human papillomavirus (HPV) and abnormal cytology. Several recent large studies have shown that approximately 3% to 14% of women aged younger than 19 years have abnormal cytology (Bjorge et al., 1994; Mount et al., 1999; Sadeghi et al., 1984). However, most of these abnormal cytologies are primarily low-grade squamous intraepithelial lesions (LSILs), which are considered benign changes due to HPV. These rates are consistent with the high rates of HPV reported in this age group, which range from 20% to 57% (Moscicki et al., 1990, 1999; Rosenfeld et al., 1989).

Although the high-grade SILs (HSILs), considered true precancer lesions, are substantially lower than those of LSILs in adolescents, recent studies suggest that these rates are higher than previously reported. In 1991, Sadeghi et al. (1984) performed an analysis of more than 194,000 Papanicolaou (Pap) smears in adolescents age 15 to 19 years. Using the World Health Organization’s cytological classification, they found a combined rate for cervical intraepithelial neoplasia (CIN) grades 1 and 2 of 18 per 1,000 smears, and for carcinoma in situ, 1 per 1,000. In comparison, Mount et al. (1999) examined more than 10,000 Pap smears from young women and found that 14% of the smear results from women age 15 to 19 years were considered abnormal, with 7% having LSIL and 0.7% having HSIL. Interestingly, the rate of HSIL in the 15- to 19-year-old group was similar to that reported in comparable smear tests from women age 20 to 29 years (0.8%) and higher than that for women age 30 to 39 years (0.5%). These rates reported for adolescents are likely underestimates because they reflect women who enter the health care system in a nationwide organized cervical screening program. Bjorge et al. (1995) reported a 2% incidence rate for HSIL among 20,000 smears of adolescents age 15 to 19 years. However, the LSIL rate was highest for this age group. Because of this disproportionate rate between LSIL and HSIL in adolescents, most adolescents with abnormal cytology are unnecessarily referred to colposcopy.

PHYSIOLOGY OF CERVIX

The characteristic histological changes of the cervix associated with HPV infections generally occur within the transformation zone (T-zone). It is useful to review the formation of this zone in understanding abnormal cervical changes.

The müllerian ducts originally form the tubes, uterus, and vagina. These structures in the fetus are lined by immature cuboidal epithelium (which becomes columnar epithelium) from the uterus to the hymenal ring. At 6 to 16 weeks of embryonic life, the urogenital sinus epithelium grows up the vaginal vault and replaces the native epithelium up to the ectocervix with squamous epithelium. This replacement is usually incomplete, creating an abrupt squamocolumnar junction (SCJ) located onto the ectocervix. During the rest of fetal life, the process of squamous metaplasia begins and continues until menopause. Squamous metaplasia is the process during which undifferentiated columnar cells transform themselves into squamous epithelium. However, the process is relatively quiescent until puberty resulting in little changes to the SCJ during childhood. The area of columnar epithelium seen on the ectocervix is referred to as the physiological T-zone.

With puberty, menarche, and raising estrogen levels, several events occur:

1. Connective tissue and elastic fibers of the cervix are rearranged so the lips of the cervix evert and bring more columnar epithelium into the vagina.
2. The pH level of the vagina drops. This is associated with glycogen production by squamous cells induced by rising levels of estrogen. The glycogen provides a source of carbohydrate for the vaginal flora. Vaginal bacteria proliferate, and the lactobacilli convert glycogen to lactic acids, resulting in a lowered pH level.

This new acidic environment most likely contributes to the augmentation of the squamous metaplastic process, resulting in relatively rapid replacement of columnar epithelium by squamous epithelium.

Transformation Zone (T-zone)

Location With conversion of the columnar epithelium to squamous epithelium, a T-zone is created. The T-zone is a relatively fluid area of definition, because it represents the area between the original SCJ and the current SCJ. By a woman’s late 20s and early 30s, most have had substantial replacement of their columnar epithelium, resulting in little to no visible ectopy. Although squamous metaplasia continues, it is now found well inside the endocervical canal.

Native squamous epithelium appears as smooth, pink, and featureless epithelium. In general, it covers the vagina and a portion of ectocervix. Native columnar epithelium is a single-layer, mucus-producing, tall epithelium extending between the endometrium and into the T-zone. This area has an irregular surface with long papillae and deep clefts, often referred to as having a “grapelike” appearance. The physiological T-zone has a combination of columnar and squamous epithelium features, as well as several unique features, which are dependent on the stage of development. In early stages, the zone is predominantly covered with columnar epithelium and discrete patches where the fusion of the villi causes a loss of translucency and the villi assume a ground glass appearance. Later, successive villi are fused and the intervening spaces are filled. Eventually the papillary structures are lost, and the new surface takes on a less translucent, vascular, pearly tongue appearance. Because the conversion of columnar epithelium to squamous epithelium occurs in often disjointed or fragmented segments, the examiner can often see small glands that are predominantly lined with columnar or metaplastic epithelium. When these gland openings become completely closed by squamous epithelium, the mucus-secreting epithelium may continue to produce mucus. If that mucus becomes impregnated, the gland dilates and a nabothian cyst results. Nabothen cysts eventually self-destruct from the pressure of the inappased mucus.

Vulnerability of the T-Zone The T-zone is the area of the cervix most prone to the development of SILs and invasive squamous lesions. The vulnerability of the T-zone is most likely related to the process of squamous metaplasia and its vulnerability to HPV and SIL development (Moscicki et al., 1999). This association reflects the natural life cycle of HPV and its dependence on host cell proliferation and differentiation, both characteristics of squamous metaplasia. Initial HPV infections are thought to occur by invasion of cells of the basal epithelium. Disruption of the epithelium by inflammation or trauma may cause an increased risk for infection. Differentiation of these basal cells to well-differentiated squamous epithelial cells supports HPV replication by allowing expression of certain viral proteins at different layers of differentiation. The expression of these proteins in turn causes histological changes, which include abnormal cell proliferation, cytoskeletal collapse, and abnormal mitotic figures, all of which are features of SIL. Features that are mild in nature and restricted to the basal and parabasal areas are referred to as LSIL. When these features become more extensive and extend into the upper half of the epithelium, the changes are referred to as HSIL. Consequently, SIL is a pathological change due to HPV infection.

CERVICAL DYSPLASIA

Impact of Cofactors

HPV infection, as described, is clearly the causative factor for cervical SIL. However, because rates of HPV are 4 to 10 times more common than SIL and 100 to 700 times more common than invasive cancers, it is assumed that HPV is necessary but not sufficient for the development of these lesions. In the case of cancer,
numerous molecular events most likely are needed. Although HPV infection is clearly one of the first steps, most HPV infections are quickly eliminated by the host immune response. Lack of an adequate immune response results in persistence of HPV infection, and in turn, HPV persistence is a strong risk for the development of HSIL (Ho et al., 1995; Moscicki et al., 1998). HPV persistence is a common problem among persons with immunodeficiencies including human immunodeficiency virus infection (Sun et al., 1997). Other factors associated with HSIL and cancer development include tobacco exposure. Even when adjusted for numbers of sex partners, women who smoke have a higher risk of developing cervical SILs and invasive cancers than nonsmokers. This relationship appears to be dose related, because women who are heavier smokers for a longer time have the highest risk for developing SIL and cancers. Other risk factors implicated include herpes simplex virus infections, multiparity, and prolonged history of oral contraceptive use.

Cervical Screening Tests

Current recommendations for Pap smear testing are that a woman start having Pap smears when she first becomes sexually active or at age 18 years (American College of Obstetricians and Gynecologists [ACOG], 1996; American Family Physician, 1996; American Medical Association, 1997). After a patient has had three consecutive annual tests whose results are read as normal, she may be screened at 3-year intervals. Annual screening is recommended for women who continue to have high-risk sexual behaviors, which include older-age sex partners, high rates of sexually transmitted diseases (STDs), and multiple partners (ACOG, 1995; Guidelines for Adolescent Preventive Services, 1997). Recent thinking addresses the fact that most LSIL in young adolescents will regress and that few cases of HSIL develop within a short period after HPV exposure. Recommendations may include waiting to begin Pap screening until 3 years after the onset of sexual activity. This is in contrast to using chronological age or immediate screening after the onset of sexual activity when the risk of HSIL is low and rates of regression of LSIL are high.

Most cytologists in the United States have adopted the Bethesda reporting system and now will provide more descriptive reports of their findings after screening of the specimen for adequacy and correct preparation. Smear tests that are considered inadequate or are missing endocervical cells should be repeated. A summary of the Bethesda system findings is found in Table 54.1. The follow-up evaluation required for benign Pap smear findings not associated with neoplastic changes is shown in Table 54.1. Current triage practices for abnormal Pap smear changes are outlined here:

Table 54.1 Follow-up evaluation recommendations for abnormal Pap smear findings

1. Atypical squamous cells of undetermined significance (ASCUS)
   a. Less than one fourth of adolescents and young women with ASCUS will have HSIL detected on biopsy. Because most adolescents with abnormal cytology will have LSIL or less, it is currently recommended to repeat the Pap smear within 4–6 months. If the Pap smear results remain ASCUS or worse, the patients should be referred for colposcopy. If the second Pap smear result is normal, another Pap smear should be obtained within 6 months. After two consecutive smears, the patient may return to routine screening.
   b. Triage the patient with other tools, including HPV testing and Polarprobe. HPV testing is best performed in the situation of reflex testing. This currently refers to using a liquid cytological method in which the sample obtained for cytology is also adequate to test for the presence of HPV DNA at a later date. Manos et al. (1998) found that the sensitivity of a positive high-risk HPV test for detecting HSIL in women who had an ASCUS smear result was 89.2% and the specificity was 64.1%. Although the sensitivity of high-risk HPV DNA testing for HSIL was equivalent to that of a repeated Pap test, reflex testing does not require an additional patient visit. This triage works best in women older than 35 years. Currently, Digene Hybrid Capture II HPV Test (Digene Diagnostics, Gaithersburg, MD) is the only FDA-approved commercially available test kit for HPV DNA detection in the United States. Polarprobe (Polarteknich, Sydney, Australia) is a computerized instrument placed directly onto the surface of the cervix. Electric and optical impulses are sent to the surface. The probe relays information on voltage decay and scattering of light to a computer, where mathematical models categorize the results into categories suggesting benign tissues, CIN1, CIN2, or CIN3, or invasive cancer. The sensitivity of Polarprobe for the detection of invasive cancers and HSIL in adult women is between 90% and 99%. The utility and cost-effectiveness of Polarprobe in adolescents is unknown.

2. LSIL. This category includes evidence of HPV infection referred to as koilocytosis and CIN1 lesions merged together to reflect the fact that very few of these lesions have any progressive or oncogenic potential.

The original intent of the developers of the Bethesda system was to permit more conservative management of patients with low-grade lesions. However, as many as 25% to 30% of patients with LSIL on Pap smears actually harbor more advanced disease including HSIL and rarely invasive cancer. This rate is less for adolescents (approximately 17%) (Moscicki et al., 1998). For that reason, many recommend colposcopic evaluation and directed biopsy to fully evaluate the cervix. With compliant adolescents, others use protocols that follow such patients with Pap smears every 4 to 6 months until they develop HSIL or if the LSIL persists past 18–24 months. Adjunctive evaluation tools, such as Polarprobe, might be helpful in triaging these patients. HPV testing is not recommended in the triage of LSIL (Atypical Squamous Cells of Undetermined Significance/low-Grade Squamous Intraepithelial Lesions Triage Study Group, 2000).

3. HSIL. This category includes moderate and severe dysplasia and carcinoma in situ. HSIL unequivocally requires colposcopic evaluation with directed biopsies and endocervical evaluation.

ThinPrep Sample preparation may contribute to the poor sensitivity of the Pap smears; that is, most Pap smears are difficult to read because of obscuring cells, drying artifact, and cell distortion. A relatively new collection system (Preserv cyt, Cytyc Corp., Marlborough, MA) has been devised, into which exfoliated cells are placed immediately into a liquid fixative rather than smeared onto a slide. The fixative solution is transported to the laboratory, where monolayers are prepared using the company’s processor, the ThinPrep processor. The cells are transferred from the filter onto a glass slide for routine Pap staining. An advantage is clearer images of the cells because the samples are depleted of blood and inflammatory cells that can obscure test readings. On the other hand, studies have found that ThinPrep smears were more likely to lack cells representative of the T-zone. Because the agreement rate between conventional smears and ThinPrep smears is more than 90% and the cost of ThinPrep smears is sometimes substantially more than that of conventional smears, the cost-effectiveness of using ThinPrep smears is in question. One advantage may be that the cells preserved in the liquid fixative can be used for ancillary studies such as reflex HPV testing.

Therapy for Cervical Dysplasia

The colposcopically directed biopsy and the endocervical test results determine the extent of the lesion and direct therapy. The principle in developing a treatment plan is that cervical dysplasia, specifically HSIL, is treated to prevent progression to cancer. One practice to be avoided, particularly in adolescents, is to combine the diagnostic and treatment steps by performing colposcopic examination to rule out invasion and excising the T-zone by a loop electrocautery excision procedure (LEEP) without biopsy confirmation. This practice has proven extraordinarily expensive. Nearly 40% to 60% of such referred patients have no dysplasia found on the specimen undergoing an LEEP, and the cost exceeds the benefit for patients without dysplasia in regards to side effects. Preservation of cervical integrity is important to maintain future fertility. As can be seen in Table 54.2, each of the major treatment modalities has minimal adverse impacts when used once. However, because recurrent lesions may develop and require further treatment, the cumulative effects of multiple treatments (particularly LEEP) must be considered. Hildard et al. (1991) reported on another complication of treatment of cervical dysplasia related to cryotherapy in a group of 67 adolescents. Nine percent developed pelvic inflammatory disease (PID) within 1 month of treatment, and two teens developed cervical stenosis and hematometra. In general, screening for STDs before cryotherapy or LEEP is recommended to avoid the complications of PID.

<table>
<thead>
<tr>
<th>TABLE 54.2. Cervical dysplasia treatment regimen response rates</th>
</tr>
</thead>
</table>

In addition, the following is recommended:

1. If the endocervical canal is involved with the dysplastic changes seen on endocervical curettage or by colposcopy, it is recommended that the area of involvement be excised. This can be done by LEEP using a "top hat" loop procedure and repeated applications of acetic acid to ensure that the entire area of apparent involvement within the endocervical canal is removed. This is necessary to rule out carcinoma and will, hopefully, eliminate the dysplasia cells. A cone biopsy using traditional cold-knife procedures is an alternative method for treatment of endocervical canal disease. It is done while the patient receives anesthesia in the operating room. Complications after cone biopsy are common, so cold-knife cone biopsies in adolescents are rarely recommended.

2. If the lesions are confined to the ectocervix, a wide range of treatment options is available (Table 54.2).

3. All women with dysplasia who smoke should be encouraged to stop smoking. Advise them that continued tobacco use increases susceptibility to cancer.

After successful treatment, patients require frequent Pap smear screening (every 3 to 4 months) until three consecutive normal Pap smears are reported. The patient then can return to normal screening, including annual Pap smears for 3 years, then if all results remain normal, every 3 years. Although condoms have not been shown to be protective against HPV infection or SIL development, advice about safer sex practices is recommended because preventing cofactors may be important in the prevention of invasive cancer. It is currently not recommended to screen male partners of women with abnormal Pap smears for HPV infections because few studies have demonstrated HPV disease in this group. Most women also appear to be clear of HPV after treatment as measured by HPV testing. HPV test persistence after treatment is a risk for recurrent SIL (Ho et al., 1995).

WEB SITES

For Teenagers and Parents

http://www.youngwomenshealth.org/abpap.html, Center for Young Women's Health information sheet for teens on abnormal Pap smears.


http://www.saqnet.ucr.edu/health/healthed/handouts/pap.htm, Patient handout on abnormal Pap smear results from the University of California, Los Angeles, student health center.

http://www.nccc-online.org/, National Cervical Cancer Coalition site.

http://www.4woman.gov/faq/pap.htm, National Women's Health information center frequently asked questions sheet.

For Health Professionals


REFERENCES AND ADDITIONAL READINGS


infection.

Sidawy MK, Tabbara SO. Reactive change and atypical squamous cells of undetermined significance in Papanicolaou smears: a cytohistologic correlation.

Shew ML, Fortenberry JD, Miles P. Interval between menarche and first sexual intercourse, related to risk of human papillomavirus infection.

Sherman ME, Kurman RJ. The role of exfoliative cytology and histopathology in screening and triage.

Sadeghi SB, Hsieh EW, Gunn SW. Prevalence of cervical intraepithelial neoplasia in sexually active teenagers and young adults.


Reid R, Greenberg M, Jenson AB, et al. Sexually transmitted papilloma viral infections: the anatomic distribution and pathologic grade of neoplastic lesions associated with different viral types.


Moscicki AB, Shiboski S, Broering J, et al. The natural history of human papillomavirus infection as measured by repeated DNA testing in adolescent and young women.


After menses, there is little secretion, but with increasing estrogen levels, a cloudy, sticky, whitish secretion develops.

Vaginal Secretions

Vaginal flora Before the onset of puberty, the vagina is colonized with various bacterial species ranging from fecal flora to skin flora. This results in a pH environment of more than 4.7 in the prepubescent vagina. After puberty, lactobacilli become the predominant vaginal flora contributing to the lowering of the vaginal pH level to less than 4.5 (Nyırjesy, 1999). This normal flora, composed of more than 95% lactobacilli, appears to protect the individual from colonization by more pathogenic organisms. These organisms are normally associated with the vaginal epithelium in a stable relationship. A change in the environmental conditions provided by the vaginal epithelium can cause a significant change in the bacterial flora of the vagina.

Vaginal secretions are a normal result of the changing hormonal milieu of the menstrual cycle. Six to 12 months before menarche, there may be a physiological increase in vaginal secretions. This may be copious but is not associated with an odor or pruritus. Vaginal secretions may arise from the adnexa, the uterus, or the vaginal epithelium itself.

Changes during the menstrual cycle include the following:

1. After menses, there is little secretion, but with increasing estrogen levels, a cloudy, sticky, whitish secretion develops.
2. Just before ovulation, the cervical secretions become profuse and clear.
3. After ovulation, progesterone stimulates a thick and sticky cervical secretion.
4. Before menses, a watery cervical secretion develops again.

These normal secretions, which are odorless, nonadherent, and nonirritating, are composed of mucus, with occasional squamous cells from the vaginal wall.

Defense Mechanisms of the Vagina

Normal defense mechanisms in the postpubertal teen include the following:

1. Acid pH level of 3.8–4.4: This is a result of lactic acid production from the breakdown of glycogen laid down in vaginal epithelial cells. The low pH level fosters growth of acidophilic lactobacilli. The epithelial cell glycogen is dependent on estrogen secretion. The lack of estrogen-stimulated glycogen production is the major reason for the relatively alkaline vaginal pH level in prepubertal girls and postmenopausal women.
2. Protective thick epithelium
3. Estrogen support
4. Commensal bacterial flora, leading to low pH levels
5. Physiological mucous secretion

Factors Predisposing to Infection

Factors predisposing to infection include the following:

1. Low estrogen levels, particularly in girls before puberty and in postmenopausal women
2. Pregnancy
3. Menstruation, due to menstrual blood acting as a culture media and the loss of a protective mucous plug
4. Multiple sex partners
5. Diabetes mellitus
6. Broad-spectrum antibiotics
7. Immunosuppression
8. Tight clothing
9. Poor hygiene
10. Douching alters the bacterial milieu of the vagina (Merchant et al., 1999).
11. Smoking is weakly associated with changes in vaginal pH level, thus likely affecting the bacterial flora of the vagina (Carr et al., 1998).

Vulvovaginitis in Pubertal Females

Vulvar skin in prepubertal girls is more susceptible to irritation because of the lack of "estrogenization" and the absence of protective labial hair and fat. Most vulvovaginitis in this group is related to either poor hygiene, obesity, tight clothing, or nonabsorbent underpants. Usually, the organisms involved are either normal flora including lactobacilli, diphtheroids, streptococci, and Staphylococcus epidermidis or gram-negative enteric organisms, usually Escherichia coli. The respiratory and enteric pathogens can also play a role in causing vaginal infections in these individuals. Other organisms to be concerned about in prepubertal females are the sexually transmitted organisms. All sexually transmitted organisms can be associated with vaginitis in prepubertal females. The finding of Neisseria gonorrhoeae or Chlamydia trachomatis should be regarded as evidence of sexual contact and lead to an investigation of sexual abuse. Vaginal rather than cervical cultures for these organisms are sufficient, because N. gonorrhoeae or C. trachomatis infect the vagina and not the cervix in prepubertal females.
Vulvovaginitis in Pubertal Females

Prevalence: Approximately 75% of women have vaginitis during their lifetime, with most first episodes occurring during adolescence. In most cases, vaginitis results in a vaginal discharge or vulvar irritation and itching. In addition, a vaginal odor may be present. Trichomoniasis (caused by *Trichomonas vaginalis*), bacterial vaginosis (BV) (caused by a replacement of normal vaginal flora with anaerobic bacteria and *Gardnerella* vaginitis), and candidiasis (usually caused by *Candida albicans*) cause about 97% of nongonococcal infectious vaginitis. Other causes of discharge include birth control pills (estrogen effect), stress (psychophysiological), chemical irritants, tampons left in place, trauma, allergies, and poor hygiene. A vaginal discharge secondary to cervicitis from *N. gonorrhoeae* or *C. trachomatis* can be indistinguishable to the teen from a discharge secondary to vaginitis.

Evaluation

History

The history in a female adolescent with vaginitis should include questions regarding the following:

1. Sexual activity including changes in sex partners, as well as frequency and type of sexual activity.
2. Type, duration, and extent of symptoms
3. Location of the pain: vulva, introitus, or deep vagina; location of any associated pain may help to differentiate urinary tract infection from vaginitis. External pain with urination is usually associated with vaginitis, whereas internal pain may occur with either condition.
4. Contraceptive method and any recent changes in method.
5. Changes in diet, exercise, stress, and medications including antibiotics, steroids, use of spray deodorants, soaps, or douches
6. History of prior sexually transmitted diseases (STDs)
7. Family history of diabetes mellitus
8. Relationship of symptoms to the menstrual cycle

Examination

The physical examination in a teen with vaginitis includes checking the following:

1. Perineum, vulva, vagina, and cervix for erythema, swelling, lesions, atrophy, and signs of trauma
2. Introitus for tenderness
3. Color, texture, origin (vaginal or cervical), adherence, and odor of the vaginal discharge
4. Uterus and adnexa for tenderness or masses
5. Other infections such as a cervicitis, herpes, or syphilis
6. Chronic vulvar changes
7. Close inspection of the vaginal walls
8. Inspection for foreign bodies such as forgotten tampon

Laboratory

The office evaluation should include the following:

1. pH value of vaginal secretions: The normal pH value of the vagina is <4.5 (3.8–4.4). A pH value >5.0 is commonly found with *T. vaginalis* and *G. vaginalis* infections. Candidal infection is usually associated with a pH value in the reference range. The pH should be sampled from the anterior vaginal fornix or lateral side wall; cervical mucus should not be used, because it has a pH value of about 7.0.
2. Amine or "whiff amine test": Fishy, amine odor after addition of potassium hydroxide (KOH) to vaginal discharge
3. Saline wet mount preparation for microscopic evaluation looking for the following:
   a. Presence of white blood cells (WBCs): The normal wet mount should have <5–10 WBCs per high-power field or E1 WBC per epithelial cell.
   b. Motile trichomonads
   c. Type of background bacterial flora: Normal long lactobacilli versus pleomorphic coccobacilli.
   d. "Clue cells": Epithelial cells covered with bacteria and indistinct borders
4. KOH preparation for microscopic evaluation: Checking for the presence of pseudohyphae or budding yeast forms
5. A screening test for *C. trachomatis* and *N. gonorrhoeae*: To rule out cervicitis

Other laboratory tests as needed include the following:

- Gram stain of vaginal or cervical secretions
- Urinalysis
- Pregnancy test

Recent advances include the following:

1. Urine-based nucleic acid amplification tests for *C. trachomatis* and *N. gonorrhoeae*
2. Easy-to-use culture systems (InPouch TV subculture kit) and DNA polymerase chain reaction (PCR) tests (T. vaginalis)
3. Amine/pH test cards to assist in the diagnosis of BV

Vulvovaginal Candidiasis

Vulvovaginal candidiasis is a common form of vaginitis in girls. A major problem in diagnosis is determining true infection from nonpathogenic colonization.

Etiology: Vulvovaginal candidiasis is usually caused by *C. albicans* in about 85% of clinical cases and occasionally by other *Candida*, *Torulopsis* sp., or other yeasts. *C. albicans* has greater affinity and adherence qualities for vaginal epithelium than the other species of *Candida*. This may explain why more disease is seen with the *C. albicans* species.

Epidemiology

1. Prevalence: The overall prevalence of candidal vulvovaginitis is unknown. *Candida* is present in the vagina of 25%–50% of healthy females, with an increased prevalence in oral contraceptive users. *Candida* can be isolated in high concentrations in clinically asymptomatic women, presumably not contributing to disease states but indicating a commensal relationship of the candidal species with other vaginal flora. However, an estimated 75% of women have at least one episode of candidal vulvovaginitis during their lifetime.
2. Transmission: Although candidal vulvovaginitis is usually not sexually acquired or transmitted, evidence exists that sexual contact plays a role in transmitting candidal infections in some patients. About 20% of male partners have asymptomatic penile colonization. Symptomatic male partners might present with balanitis.
3. Predisposing factors: Strong evidence exists that infection, particularly recurrent infections, is the result of certain predisposing factors including the following:
   a. Diabetes mellitus
   b. Pregnancy
   c. Oral contraceptive use, particularly high-dose estrogen-containing preparations. Presumably, estrogen enhances the ability of *Candida* organisms to adhere to vaginal epithelium (Carr et al., 1998).
   d. Steroids
1. Antibiotic therapy: Particularly, broad-spectrum antibiotics such as tetracycline
2. Immunosuppressive therapy
3. Human immunodeficiency virus (HIV) infection
4. Some evidence suggests a selective macrophage defect (Witkin et al., 1986) or an acquired Candida antigen-specific immunological deficiency (Sobel, 1995) in women with recurrent candidiasis.

For adolescents, antibiotics and oral contraceptives are the most frequent predisposing factors.

4. Age: The highest prevalence of infections occurs between the ages of 16 and 30 years.

Clinical Manifestations

1. Candidal infections are usually accompanied by intense burning, pruritus, vulvar pruritus, and erythema, but these symptoms are nonspecific. In a large cross-sectional study using multivariant analysis, certain symptoms of external dysuria, vulvar pruritus, pain, burning, swelling or vulvar erythema, edema, fissures or excoriations, vaginal signs of erythema, and thick curdy discharge were associated with positive candidal cultures. However, no single sign was both sensitive and specific enough for the diagnosis of candida (Eckert et al., 1998).

2. Symptoms may worsen before the onset of menses.

3. Discharge
   a. Onset: May worsen before menses
   b. Amount: Usually described as thick curdy, cottage cheese appearance
   c. Color: Milky white
   d. Odor: Usually no odor

4. Occasional dysuria or dyspareunia

5. May affect the thighs and skin folds, particularly in obese females

6. Often accompanied by a history of risk factors such as pregnancy, antibiotic use, or oral contraceptive use.

7. The examination reveals the following:
   a. Normal or erythematous vulva, fissures, excoriations, satellite lesions
   b. Vulvar edema
   c. Thick, white, cheesy, adherent discharge

Diagnosis

1. A wet mount with saline or KOH shows budding yeast with pseudohyphae. The use of KOH lyses epithelial cells, allowing better visualization of yeast. A KOH preparation has a sensitivity of 40%–80%.

2. The pH range is usually <4.5.

3. Yeast cells appear as gram-positive oval masses, and pseudohyphae appear as long gram-positive tubes. The sensitivity of the Gram stain is about 70%–100%.

4. Rapid in-office tests for Candida antigens in vaginal discharge are commercially available and appear to be more sensitive than the KOH preparation. Their use in the clinical setting has not been well studied.

5. Culture is expensive and time consuming. The culture may be useful in the individual with symptoms consistent with candidal vulvovaginitis and negative results from KOH preparation or in patients with recurrent episodes of vaginal candidiasis.

6. The diagnosis is suggested by vulvar pruritus and erythema. The diagnosis can be made in the presence of signs and symptoms of vaginitis with positive results from wet mount or KOH smear demonstrating yeasts or pseudohyphae. Colonization can be difficult to differentiate from infection. Women who have the presence of Candida but are asymptomatic should not be treated.

Therapy

1. Topical agents: 3- and 7-day regimens are probably superior to single-dose therapy, particularly for more severe infections. Azoles are more effective than the nystatin agents (CDC, 1998, 2001). Azoles have a clinical cure rate of 80%–95%, whereas nystatin agents have a cure rate of 70%–90% (Association of Genitourinary Medicine, 1999a). Relief of symptoms and negative cultures seen in 80%–90% of patients who complete therapy (CDC, 1997). Effective regimens include the following (an asterisk [*] indicates agents that are oil based and may weaken a latex condom or diaphragm. OTC indicates over-the-counter preparations. However, OTC treatments need to be considered very carefully in the adolescent population):
   a. Intravaginal preparations
      - Butoconazole 2% cream (Femstat), 5 g intravaginally for 3 days or Butoconazole 2% cream BSR, single intravaginal application, or
      - Clotrimazole 1% cream (Gyne-Lotrimin, Mycelex-G), 5 g intravaginally for 7–14 days OTC, or
      - Clotrimazole 100-mg vaginal tablet (Gyne-Lotrimin, Mycelex-G) for 7 days, or
      - Clotrimazole 100-mg vaginal tablet (Gyne-Lotrimin, Mycelex-G), two tablets for 3 days,* or
      - Clotrimazole 500-mg vaginal tablet (Mycelex), one tablet single application,* or
      - Micronazole 2% cream (Monistat-7), 5 g intravaginally for 7 days* OTC, or
      - Micronazole 200-mg vaginal suppository (Monistat-3), one suppository for 3 days* OTC, or
      - Micronazole 100-mg vaginal suppository (Monistat), one suppository for 7 days* OTC, or
      - Nystatin 100,000-unit (U) vaginal tablet for 14 days, or
      - Ticlofenazole 6.5% ointment (Vagistat), 5 g intravaginally in a single application* OTC, or
      - Terconazole 0.4% cream (Terazol 7), 5 g intravaginally for 7 days,* or
      - Terconazole 0.8% cream (Terazol 3), 5 g intravaginally for 3 days,* or
      - Terconazole 80-mg suppository (Terazol 3), one suppository for 3 days,* or
   b. Oral Preparation
      - Fluconazole 150-mg oral tablet, one tablet in a single dose
      - Alternative regimens: Oral azole agents including ketoconazole and itraconazole have been shown to be as effective as in some clinical trials as topical azole agents including one study by Sobel et al. (1995). One advantage of the oral medications is their ease of use. In most studies, patients prefer oral therapy over intravaginal therapy. However, because of the potential toxicity, there is still concern about using oral agents as first-line agents. Oral ketoconazole has a risk of mild reversible hepatitis of 5%–10% and a risk of serious, potentially life-threatening hepatitis of 1 in 15,000. Ketoconazole should therefore be reserved only for resistant, recurrent cases of candidal vulvovaginitis. Oral agents also have frequent interactions with other medications the patient may be taking. In summary, the treatment of candidal vaginitis should take into account the severity of disease, the history of recurrent vaginitis, the existence of any immunosuppressive state, and patient preference.
   c. Management of sex partners: Because vaginal candidiasis is not considered a sexually transmitted infection, it is not considered essential to treat partners unless the male partner has symptoms and signs of balanitis.
   d. Cream versus suppository: If symptoms are more consistent with vaginitis than vulvitis, suppositories are superior to creams with increased cure rates (Carr et al., 1998).

2. Duration of therapy is currently being evaluated to classify vaginitis based on various criteria as complicated versus uncomplicated. Uncomplicated infection (i.e., mild or moderate infection that is not recurrent) will respond well to a short topical regimen. More severe local or recurrent candidiasis, particularly in patients with altered immune status such as a diabetic, will require a longer treatment period.

3. Follow-up: Follow-up is not necessary for individuals who become asymptomatic after treatment. If symptoms occur three or more times in a year, an evaluation should be performed for the predisposing conditions listed earlier.

4. Pregnancy: The topical azole medications can be used during pregnancy, but oral agents should be avoided. Seven-day therapy is preferred during pregnancy. Currently, there are several treatments that have been studied and approved for use during pregnancy including topical butoconazole, clotrimazole, miconazole, and terconazole, with a 7-day course recommended.

5. Allergies and side effects to therapy: Topical azole medications do not usually cause systemic side effects, but occasional problems with local irritation or burning can occur. Oral azole agents can cause nausea, abdominal pain, headaches, and an elevation in liver enzymes. Ketoconazole can be associated rarely with severe hepatotoxicity reported in one in 10,000–15,000 cases. Clinically important drug interactions can also occur with ketoconazole use, and a careful history of concurrent medications is necessary to ascertain before prescribing ketoconazole. Some of the interacting drugs include oral hypoglycemics, phenothiazines, and theophylline.

9. HIV infection: Adolescents with HIV infection should usually be treated for candidal vulvovaginitis in a similar fashion to those without HIV infection. However, candidal vulvovaginitis may be more severe in these women, and some experts have employed oral agents more frequently. HIV should be considered in
women with recurrent vaginal candidal infections, because frequently this may complicate HIV infections, although routine screening is not recommended (CDC, 1997).

10. Recurrent vulvovaginal candidiasis (four or more episodes per year) seen in <5% of women (National Guidelines for the Management of Vulvovaginal Candidiasis, 1999):
   a. Eliminate or reduce risk factors
      - Switch to a lower estrogen oral contraceptive agent
      - Discontinue broad-spectrum antibiotics
      - Discontinue or reduce steroids
      - Review control of diabetes
      - Avoid constricting clothing, douching, and vaginal sprays
      - Wear cotton underwear
      - Ingest yogurt with live lactobacilli to re-colonize the intestines
      - Consider relationship with menstruation, stress, and intercourse (Spinillo et al., 1993)
   b. Eliminate any sources of reinfection
      - Dry-clean or wash all undergarments in hot water.
      - Dispose of all diaphragms and obtain new ones.
      - Discontinue oral-genital contact.
      - Oral nystatin (500,000 U two to three times a day for 10 days). The intestines may serve as a source for reinfection. However, Spinillo et al. (1993) could not demonstrate a lower recurrence rate after treatment of candida colonization in the intestinal tract in females with recurrent vaginal candidiasis.
   c. Examine and treat partner if candidal balanitis is present, because there is evidence that identification and treatment of male sex partners’ candida colonization leads to lower recurrence rates in women with recurrent candidal vaginitis (Spinillo et al., 1993).
   d. Consider HIV testing if risk is present.
   e. Treatment with longer course of topical agents or use of oral agents. Recommendations have included:
      - Topical azole for 14–21 days intravaginally
      - Fluconazole (Diflucan), 100–150 mg PO one time
      - Ketoconazole (Nizoral), 200 mg PO b.i.d. for 5–14 days
      - Itraconazole (Sporanox), 200 mg PO q.d. for 3 days
      - Boric acid, 600-mg capsule b.i.d. intravaginally for 14 days (requires special formulation by pharmacist)
      - Chlorotrimazole, one 500-mg vaginal tablet each month
      - Miconazole, 100-mg vaginal tablet twice weekly
      - Fluconazole 150 mg, PO once each month
      - Ketoconazole 200 mg, PO q.d. for 5 days each month or 100 mg PO q.d. for up to 6–12 months (less preferred to fluconazole because of higher toxicity of ketoconazole)
   f. Long-term prophylaxis: Several studies have shown decreased recurrences with long-term prophylaxis. Regimens have included the following:
      - Chlorotrimazole, one 500-mg vaginal tablet each month
      - Miconazole, 100-mg vaginal tablet twice weekly
      - Fluconazole 150 mg, PO once each month
      - Ketoconazole 200 mg, PO q.d. for 5 days each month or 100 mg PO q.d. for up to 6–12 months (less preferred to fluconazole because of higher toxicity of ketoconazole)
   g. Vaginal suppositories with 600-mg boric acid powder in gelatin capsules, one every day for 14 days, then three per week for up to 12 months or longer.
   h. There is little systemic absorption, so these are well tolerated. However, the capsules appear similar to vanilla jelly beans and should be kept out of the way of children. The oral regimens, particularly that of ketoconazole, can be associated with systemic toxicity and are expensive for long-term therapy. The doses and relative effectiveness and toxicity of these regimens still require further study.

Trichomoniasis

**Etiology**

*T. vaginalis* infection is caused by a flagellated protozoa with three to five anterior flagella and one posterior flagellum that infects the vaginal epithelium.

**Epidemiology**

1. Prevalence: *T. vaginalis* is one of the most frequently acquired STDs, with an estimated 2.5–3 million cases annually in the United States and as many as 180 million cases worldwide. The organism is found in 28% of female adolescents in juvenile detention centers.
2. Transmission: The organism is almost always transmitted by sexual intercourse. The organism can survive for about 1.5 hours on a wet sponge. Transmission can possibly occur through sharing of washcloths, communal bathing, or during routine child care.
3. Age: The peak prevalence rates are between the ages of 16 and 35 years. The prepubertal vagina is not hospitable to trichomonal infection.
4. Incubation period: 4–28 days.
5. Sites of colonization: Trichomonads, when present, usually occur at other sites in addition to the vagina, the most common extravaginal sites being the urethra (82.5% of cases) and the periurethral glands (98% of cases).

**Clinical Manifestations**

1. Up to 25%–50% of females may be asymptomatic. Most (90%) males are symptomatic.
2. Symptoms
   a. Pruritus: 60%–75% of cases
   b. Discharge: 50% of cases
      - Onset: Any time during the menstrual cycle
      - Amount: Diffuse discharge, bubbly or frothy
      - Color: Cream colored or greenish
      - Odor: Only 10% of women complain of odorous discharge
   c. Dysuria: 25% of cases
   d. Dyspareunia
   e. Lower abdominal pain: Approximately 5% of cases
   f. Postcoital bleeding
3. Signs
   a. Edema and excoriation of the external genitalia
   b. Frothy, foul-smelling vaginal discharge
   c. Erythematous, edematous, and granular vaginal walls
   d. Cervix: May have erosions or petechiae of the cervix (colpitis macularis, “strawberry spots”) only seen in 2% of cases
   e. Bartholinitis
   f. Urethritis
   g. Rarely, abdominal tenderness producing symptoms that may be consistent with pelvic inflammatory disease (PID)
4. Complications: Trichomoniasis does not cause disseminated disease; however, it has been associated with a higher incidence of postpartum endometritis. It may increase the risk of HIV due to a decrease in the normal vaginal defenses during a trichomonal vaginitis.

**Diagnosis**

1. Wet mount: This is the simplest and most frequently used method for demonstrating the presence of trichomonads. The sensitivity is approximately 60%–80%.
2. Test tube technique: Saline in the amount of 0.5–1.0 mL is placed into a small test tube. A drop of the discharge is collected and mixed into the test tube. Then a drop of suspension is transferred to a slide with a dropper, and a coverslip is applied.
3. Direct slide technique: A drop of saline is placed on a slide and then a drop of the discharge is introduced into the saline and mixed. A coverslip is applied.
4. Postcoital bleeding
5. Appearance: Positive wet mount results reveal a few to a multitude of pear-shaped motile organisms about the size of a polymorphonuclear leukocyte with
2. pH: The pH value is usually >4.5.

3. Stained smears: Smears are more difficult and time consuming to perform than wet mounts and tend to have lower sensitivity.

4. Cultures: Cultures are more time consuming and expensive than wet mounts. However, these can be used in cases of treatment failure or recurrence of symptoms. Diamond medium culture has sensitivities of 91%–100% (Othleneyer, 1998). The InPouch TV subculture kit is a new culture method available to clinicians for culture of T. vaginalis. The technique is useful in diagnosing disease in lower concentrations of organisms than that required for wet mounts. The sensitivity of this culture method is higher than wet mounts, identification of Papanicolaou (Pap) smear, and approaches the sensitivity of Diamond medium cultures. It may become a reasonable cost-effective alternative for clinicians instead of Diamond medium cultures in the future. If treatment failures are seen, the clinician must think of resistance, which has begun to emerge (CDC, 1997).

5. Pap smear: Pap smears are unreliable for the diagnosis of T. vaginalis infection. The sensitivity to detect T. vaginalis by Pap smear is only about 50% when compared against culture. The sensitivity is even lower in populations in which trichomonal infections are <20% (Wiese et al., 2000).

6. Urine sediment: Trichomonads are occasionally seen in the urinary sediment. Microscopic examination of urine sediments in conjunction with wet mounts has been shown to increase sensitivity (Blake et al., 1999). This can be a useful technique in the diagnosis of infections in males (80% sensitivity). Although described as related to “atypia” in older studies, it is most likely that such studies did not control for the presence of human papillomavirus (HPV)—the most likely candidate associated with atypical changes on Pap smear.

7. Immunological testing: This includes the direct monoclonal antibody test, a rapid test with similar sensitivity to a culture. These tests require further evaluation before their use in the primary care setting can be recommended.

8. Advances in DNA PCR have gained much attention. Different collection techniques have been investigated in conjunction with these PCR tests. One such trial involved sample collection via tampon versus urine. Both samples were tested using PCR methods. The tampon samples were more sensitive for disease than the urine samples. This type of technique will become available to clinicians (Tabrizi et al., 1998). Distal vaginal specimens have also been shown to be adequate for detecting T. vaginalis when using the PCR technique (Heine et al., 1997).

Therapy

1. Regimen
   a. Recommended: Metronidazole, 2 g PO in a single dose
   b. Alternative: Metronidazole, 500 mg b.i.d. for 7 days
   c. Both these regimens have a cure rate of about 95%. The single-dose regimen is preferred in adolescents to increase compliance. Systemic therapy with metronidazole is the only therapy well documented to be effective. Treatment of asymptomatic girls is advisable.
   d. Intravaginal metronidazole gel has not been shown to be effective and therefore is not recommended for treatment of T. vaginalis (CDC, 1997).
   e. Side effects of therapy: Nausea and vomiting, a metallic taste, and effects similar to those caused by disulfiram (Antabuse) occur if alcohol is ingested. No alcohol should be used the same day and for 24 hours after the medication is taken.

2. Treatment of sex partners: Treatment of the adolescent’s sex partner is recommended. Patients should avoid sex until both the patient and the partner are cured, that is, assurances that both partners have taken the medication and are asymptomatic.

3. Follow-up: Follow-up is not necessary for individuals who become asymptomatic after treatment. If failure occurs with either regimen, the adolescent should be retreated with metronidazole (500 mg b.i.d. for 7 days). For repeated failures, the teen can be treated with a single 2-g dose of metronidazole daily for 3–5 days.

4. There is an increased prevalence of cellular atypia on Pap smear. However, there have been no studies that have carefully controlled for the presence of HPV to account for the “atypia” that most recently is associated with HPV infection. No association with cervical cancer has been demonstrated.

5. There is some evidence that trichomonads may secrete a sperm mobility-inhibiting factor that may play a role in infertility (Moskowitz and Mellinger, 1992).

6. Allergies to metronidazole: Effective alternative therapies to metronidazole are not currently available. Persons deemed allergic can be treated as a part of a desensitization program.

7. HIV infection: Adolescents with HIV infection should be treated for trichomoniasis in a similar fashion to those without HIV infection.

Complications

1. Usually there is no significant morbidity beyond the discomfort of vaginitis.

2. There may be an increased risk for adverse pregnancy outcomes including premature rupture of the membranes and preterm delivery. There also may be a higher rate of postpartum infections.

3. There is an increased prevalence of cellular atypia on Pap smear. However, there have been no studies that have carefully controlled for the presence of HPV to account for the “atypia” that most recently is associated with HPV infection. No association with cervical cancer has been demonstrated.

4. There is some evidence that trichomonads may secrete a sperm mobility-inhibiting factor that may play a role in infertility (Moskowitz and Mellinger, 1992).

Bacterial Vaginosis (G. vaginalis)

BV has also been known as Gardnerella vaginitis, “clue cell” vaginitis, Haemophilus vaginitis, or Corynecetabacter vaginitis. The current term BV was adopted to reflect the syndrome that is characterized by the presence of diverse bacteria without the signs of vaginal mucosal inflammation. It is the most frequent cause of abnormal vaginal discharge and odor.

Etiology The syndrome results from the replacement of normal lactobacilli in the vagina with anaerobic bacteria (Bacteroides sp., Mobiluncus sp.), G. vaginalis, and Mycoplasma hominis. In most females without BV, the dominant organism is Lactobacillus sp. (>95% of all vaginal organisms), whereas in infected women, lactobacilli are often not found or found in much lower bacterial counts (<100-fold to 1,000-fold decrease).

Lactobacilli help maintain an acid pH level by converting glucose into lactic acid. The normally lower pH level helps to prevent the growth of G. vaginalis and anaerobes such as Mobiluncus sp. With an elevated pH level, there is a loss of lactobacilli and an overgrowth in high concentrations of G. vaginalis; anaerobes such as Bacteroides, Peptostreptococcus, and Mobiluncus sp.; and genital mycoplasmas.

G. vaginalis is present in about 40% of sexually active unmarried females without signs or symptoms of vaginitis. Although considered a commensal in many females, it appears that in combination with other vaginal bacteria, particularly anaerobes, it can be a pathogenic organism. Even in women who meet the clinical criteria for BV, as many as 50% have no symptoms. In only a minority of asymptomatic females with “clue cells” or positive culture results for G. vaginalis do these laboratory findings persist without treatment.

Epidemiology

1. Transmission: The exact mechanism of transmission of BV is unresolved. Sexual transmission is suggested by the age and sexual experience of the infected patients (Shaffer et al., 1985), and the isolation of the organism from the urethras in 70%–90% of male partners. Although rarely isolated from nonsexually active individuals (Shaffer et al., 1985), it is not an exclusive STD. G. vaginalis, Mobiluncus sp., and M. hominis have been isolated from the rectum of females with BV and indicate a potential source of autoinfection (Cattin, 1992).

2. Prevalence: BV is one of the most common infections in females and the most common cause of abnormal vaginal discharge. Because the condition is not required to be reported to local health departments, the exact prevalence is unknown. However, BV has been reported in 10%–41% of women studied, with higher rates noted in women attending STD clinics (McCregor and French, 2000).

Clinical Manifestations

1. Vaginal discharge
   a. Onset: Unrelated to menses
   b. Amount: Slight in 85% of cases and moderate in about 15% of cases
   c. Color: Grayish white
   d. Odor: Often a fishy smell, particularly in the presence of either semen or KOH. The combination of G. vaginalis and anaerobes produces organic acids and several amines that in the presence of an elevated vaginal pH level volatilize to the malodorous compounds of putrescine and cadaverine. Trimethylamine may also be a cause of the fishy odor associated with BV.

2. Pruritus or burning is either absent or mild.
3. Up to 50% of patients with the syndrome of BV are asymptomatic.
4. Physical examination
   a. Thin, frothy, grayish-white discharge, adhering to the vaginal walls
   b. Usually no vulvar or vaginal wall changes
   c. Possibly a pungent 'fishy' odor

**Diagnosis** The CDC suggests the Amsel criteria for the diagnosis of the syndrome of BV, which depends on the presence of three of the following four clinical symptoms and signs (CDC, 1998):

1. The presence of a homogeneous, white, noninflammatory discharge that smoothly coats the vaginal walls.
2. The presence of "clue cells" on microscopic examination (clue cells are epithelial cells that appear granular and stippled with indistinct cell borders due to adherence of bacteria and cellular debris between cells). In general, clue cells should comprise at least 20% of the cells examined.
3. The vaginal pH level is >4.5.
4. The vaginal discharge has a fishy odor before or after the addition of 10% KOH, known as the "whiff test." This may also occur in trichomonal infections.

**Complications** There is growing evidence that BV is linked to serious upper genital tract disease including clinical chorioamnionitis, postabortive or postpartum endometritis/PID, and upper genital tract infections such as chorioamnionitic infection and preterm labor (Krohn et al., 1995; Peipert et al., 1997). However, there is controversy over the effectiveness of preterm diagnosis and treatment of BV as a recent important multicenter study by the National Institute of Child Health and Human Development concluded that treatment of BV during pregnancy did not have an impact on the rate of preterm delivery due to spontaneous labor, spontaneous rupture of membranes, or delivery before 32 weeks (Carey et al., 2000).

**Therapy**

1. Treat symptomatic women: In most instances, only women with vaginal signs or symptoms should be treated without respect to pregnancy status. Prevention of transmission to males is not a goal of therapy, because males are asymptomatic and the treatment of partners has not altered the course in females in regard to relapse or reinfection rates. Although currently not recommended by the CDC, because of the possible risk of invasion of these organisms into the upper genital tract with invasive procedures including uterine curettage and intrauterine device placement, it may be reasonable to treat symptomatic or asymptomatic BV before a surgical abortion procedure. Treatment of BV with metronidazole has been shown to reduce postabortal PID rates. Although controversial, treatment has also been suggested in some women considered as having high-risk pregnancies (National Guidelines for the Management of Bacterial Vaginosis, 1999).

2. **Regimen**
   a. Recommended
      - Metronidazole, 500 mg PO b.i.d. for 7 days, or
      - Clindamycin cream 2%, one full applicator (5 g) intravaginally for 7 days, or
      - Metronidazole gel 0.75%, one full applicator (5 g) intravaginally b.i.d. for 5 days
   b. Alternative
      - Metronidazole, 2 g PO in a single dose or
      - Clindamycin, 300 mg PO b.i.d. for 7 days

The Food and Drug Administration has approved use of Flagyl 750 (metronidazole, 750 mg) orally every day for 7 days. However, no data exist on its efficacy (CDC, 1997).

The single-dose metronidazole regimen has the advantage in adolescents of having a higher compliance rate but a lower efficacy rate compared with a 7-day regimen. In a number of controlled trials, the rate of cure using the intravaginal clindamycin cream 2% or intravaginal metronidazole gel 0.75% were equivalent to the 7-day oral metronidazole regimen, associated with clinical cure rates similar to those obtained with oral metronidazole (CDC, 1997). Individuals should be warned not to use alcohol during treatment and for 24 hours after completion to avoid nausea and vomiting secondary to a disulfiram-like reaction. The mineral oil base in the clindamycin cream may weaken latex; therefore, teens should avoid the use of condoms and contraceptive diaphragms for 72 hours after using the cream.

3. Patients are also advised to avoid douching.
4. Treatment of sex partners: Treatment of contacts is not routinely recommended because it does not alter the response rate or the rate of relapse or recurrences.
5. Follow-up: Follow-up is not necessary if the teen becomes asymptomatic. Adolescents with recurrent or persistent infections should be reevaluated for other infections.
6. Pregnancy
   a. Treat all symptomatic women in any trimester but avoid intravaginal therapy as data does not support the use of intravaginal therapy in pregnant women.
   b. The treatment of asymptomatic BV among pregnant women requires further confirmatory studies before routine screening and treatment during pregnancy can be routinely recommended (CDC, 2001) as the optimal screening and therapy is unclear. If screening and therapy is done, it is recommended that this be performed at the first prenatal visit.
7. **HIV infection:** HIV-infected teens can be treated for BV with the same regimens as those individuals without HIV.

**Other Causes of Vaginal Discharge**

1. Pubertal physiological discharge: A normal increase in vaginal secretions occurs 6–12 months before menarche.
2. Extravaginal disease: Extravaginal lesions may cause staining of the underwear, suggesting a vaginal discharge to the adolescent. These lesions include the following:
   a. Perineal lesions: Herpes, syphilis, intertrigo
   b. Bartholin gland abscess
   c. Proctitis
   d. Bleeding hemorrhoids
3. Physiological discharge: Vaginal and cervical secretions change depending on the hormonal state. High estrogen levels induce a more profuse discharge. At the time of ovulation or just before menses, vaginal secretions are more likely to increase. Progesterone induces a thicker discharge. Physiological discharge is characterized by the following:
   a. Lack of offensive odor
   b. Lack of pruritus or burning
   c. Lack of vulvar, vaginal, or cervical erythema
   d. May leave a brown stain on the underwear
   e. Lack of polymorphonuclear leukocytes on wet mount
4. **Enterobius vermicularis** (pinworms)
5. Irritant vaginitis: Irritations can occur with chemical douches, vaginal deodorants, vaginal sprays, tampons or pads, colored or perfumed toilet paper, bubble bath, laundry detergents, fabric softeners, swimming pools or hot tubs, powders, spermicides, or medications used by the male that remain on the penis.
6. Foreign bodies: Foreign bodies causing a vaginal discharge include forgotten tampons, intrauterine devices (uterine discharge), and objects for masturbation.
7. Vulvodynia or vulvar vestibulitis: Clinical manifestations include pain with penetration during intercourse and small inflamed areas at 5 and 7 o'clock on the perineum that are exquisitely tender to touch. The vaginal examination results, including pH, flora, and wet mount, are normal. A course of topical steroids may be beneficial.
8. Gonorrhea: See Chapter 61. Gonorrhea generally infects the endocervix and not the vaginal walls. Most females are asymptomatic, although approximately 25% experience a foul-smelling discharge.
9. **C. trachomatis** infections are common; because of the cervical discharge, patients may complain of vaginal discharge (see Chapter 62).
Table 55.1 outlines treatment of vaginitis in adolescents.

TABLE 55.1. Vaginal discharge in the adolescent

CERVICITIS

Cervicitis is common in sexually active women. The condition is usually caused by STDs and is a significant problem because it often produces very few, if any, symptoms. Infections of the cervix are a source for transmission of STDs to males and newborns. Cervical infections also precede PID.

Cervicitis represents an infection of the cervix and should not be confused with cervical ectopy. During adolescence and young adulthood, the junction of columnar and squamous epithelium is on the ectocervix. This condition has unfortunately often been mislabeled as cervicitis. With increasing age and after a pregnancy, the squamocolumnar junction recedes into the endocervical canal.

Cervicitis may produce a significant enough discharge to be confused with a vaginal infection.

Etiology

Common causative microorganisms include the following:

1. C. trachomatis
2. N. gonorrhoeae
3. T. vaginalis
4. C. albicans
5. Herpes simplex

Symptoms

1. Vaginal discharge
2. Dyspareunia
3. Postcoital spotting

Signs

Cervicitis is presumed if all the following are found on pelvic examination:

1. Mucopurulent endocervical discharge visible on a white swab
2. Ten or more WBCs per high-power field on a Gram stain specimen from the endocervix that is not contaminated with vaginal secretions (90% of chlamydial cervical infections have this finding)
3. Endocervical friability: Easy bleeding from endocervical tissue after contact with first swab

Diagnostic Tests

1. Wet mount: Examine for evidence of motile trichomonads
2. Gram stain of endocervical specimen
3. Gonorrheal culture or other screening test
4. Chlamydia screening test
5. KOH

Treatment should cover both N. gonorrhoeae and C. trachomatis unless the cervicitis is known to be caused by T. vaginalis or herpes. For a further discussion of gonococcal and chlamydial cervicitis, see Chapter 61 and Chapter 62, respectively.

WEB SITES

For Teenagers and Parents

http://www.saonet.ucla.edu/health/healthed/handouts/vaginosi.htm. University of California, Los Angeles, student health center handout on BV.
http://www.mckinley.uiuc.edu/health-info/womenhlt/monilia.html. Handout on candidal vaginitis from the University of Illinois student health center.

For Health Professionals


REFERENCES AND ADDITIONAL READINGS

Ectopic Pregnancies must be considered in the differential diagnosis of the pregnant adolescent with pelvic pain, particularly early in gestation if such pain is associated with abnormal uterine spotting or bleeding. A useful approach to reproductive-age women with pelvic pain or irregular bleeding is to assume that they are pregnant until proven otherwise and that all pregnancies are ectopic until proven otherwise. The number of ectopic pregnancies increased from 17,800 (4.8/1,000 livebirths) in 1970 to 108,600 (19.7/1,000) in 1992 (Centers for Disease Control and Prevention [CDC], 1995). This rise in ectopic pregnancies has been attributed to early detection (many early ectopic pregnancies that resolved spontaneously would previously have gone undetected); to an increase in salpingitis, tubal damage, and other risk factors; and to the high recurrence rate for ectopic pregnancies treated conservatively. In 1992, ectopic pregnancies accounted for 2% of reported pregnancies and 13% of all pregnancy-related deaths. Ectopic pregnancies are now the second leading cause of maternal mortality in the United States and the leading cause of maternal death during the first half of pregnancy (Atrash et al., 1987). Although the overall death-to-case rates have declined by nearly 90% (from 35.5 per 10,000 ectopic pregnancies in 1970 to 3.8 per 10,000 in 1988), the risk of death from ectopic pregnancy is 50 times greater than the risk of death from legal abortion and 10 times greater than the mortality risk associated with childbirth. Washington and Katz (1993) estimated that the total cost of ectopic pregnancies in the United States in 1990 was $1.1 billion, with hospitalization and other medical treatments contributing to 77% of the total costs. The systematic use of sensitive quantitative tests for pregnancy hormones (the human chorionic gonadotropin [h-HCG]) and transvaginal ultrasound to identify early intrauterine pregnancies has revolutionized the diagnosis of ectopic pregnancy and permitted medical management to replace surgical management in uncomplicated cases. This has reduced complication rates and overall costs for treatment.

ETIOLOGY

The precise cause of ectopic implantation is not clear, but several hypotheses have been suggested (Chavkin, 1982; Corson and Balzer, 1986; Marchbanks et al., 1988).

1. Delayed ovulation and fertilization: Implantation usually occurs 7 days after fertilization. If either ovulation or fertilization is delayed, the blastocyst may not have time to implant in the endometrium but may be swept by menstrual flow back into the tubal lumen. Transmigration has been used to explain ectopic pregnancy on this basis as well; 30 to 50% of ectopic pregnancies occur when the corpus luteum is on the side opposite the tubal pregnancy. However, this evidence is not conclusive, because women with single ovaries on the side opposite their single fallopian tubes are not at increased risk for ectopic pregnancy. Another special risk group is women undergoing in vitro fertilization (IVF), when the hydraulic force used to place the embryo into the endometrium can transport one or more of them through the tubal ostium into the fallopian tube.

2. Slowed tubal motility or damaged fallopian tubes: If the progression of the fertilized ovum is delayed through the tube because of distorted tubal anatomy or slowed tubal flow, the zona pellucida covering the conceptus may have time to shred and permit tubal implantation in the fallopian tube. Previous pelvic inflammatory disease (PID) is the most common cause of abnormal tubal anatomy (see Chapter 63); tubal motility derangement is most frequently caused by hormonal imbalance.

3. Endometrial abnormalities: The lack of appropriate intrauterine implantation sites might block pregnancy establishment inside the uterine cavity, and combined with contractions and menstrual flow, may facilitate ectopic implantation. Polyps, intrauterine septa, and submucous myomas can contribute to this problem.

4. Defects in ovum: The clinical significance of ovum issues is not clear. Some DNA flow cytometry studies have revealed that one third of ectopic human concepti include vaginal douching and smoking (which more than doubles the risk for ectopic pregnancy).

RISK FACTORS FOR ECTOPIC PREGNANCY

1. Tubal abnormalities: The most common risk factor for tubal abnormalities is previous tubal infection (Brenner et al., 1989). Evidence of previous tubal infection has been found in 40–50% of tubal pregnancies (Chavkin, 1982). Most women with gonococcal salpingitis are likely to be aware of their risks because gonococcal pelvic infections provide significant pain and discomfort. However, women with a history of chlamydial infections may not be able to relate this risk factor, because chlamydial salpingitis has a more subtle clinical presentation; the heat shock proteins elaborated by Chlamydia trachomatis can stimulate significant tubal damage while causing only minimal symptomatology. Tubal problems can also be caused by diethylstilbestrol exposure, previous ectopic pregnancy, prior tubal surgery for sterilization or infertility, prior ectopic pregnancy, or tubal adhesions from previous appendicitis or abdominopelvic surgery. Salpingitis isthmica nodosa is an intrinsic tubal defect that also increases ectopic risk and is found ten times more often in patients with tubes with ectopic implantations than in control subjects.

2. Pregnancy after tubal ligation or with IUD or progestin-only contraceptives: The absolute risk of ectopic pregnancy is significantly reduced by each of these methods of birth control compared with women who use no method of contraception. However, if a pregnancy occurs, the risk that the fetus will implant ectopically is increased. For example, 15–50% of pregnancies after tubal ligation are ectopic (this percentage increases with time since surgery), and 5–8% of pregnancies in copper IUD users are ectopic. A history of previous IUD use does not increase a woman’s risk of ectopic pregnancy after the IUD has been removed for at least a month.

3. Unexplained infertility is also a risk factor, particularly in women with normal menstrual cycles.

4. Assisted reproductive technology dramatically increases the risk of ectopic pregnancy. Overall, 5% of IVF pregnancies are ectopic, and at least 1% are heterotropic (i.e., an ectopic pregnancy in conjunction with an intrauterine pregnancy). About 4% of pregnancies resulting from gamete intrafallopian transfer are ectopic.

5. Other risk factors include vaginal douching and smoking (which more than doubles the risk for ectopic pregnancy).

DIFFERENTIAL DIAGNOSIS

The differential diagnosis includes the following (Table 56.1).
Fluids: The patient will require large-bore intravenous lines and hydration. Transfusion may be started if clinically indicated, but surgery should not be delayed if rupture is likely.

Table 56.1, Differential diagnosis of ectopic pregnancy

<table>
<thead>
<tr>
<th>#</th>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>PID</td>
</tr>
<tr>
<td>2</td>
<td>Normal intrauterine pregnancy</td>
</tr>
<tr>
<td>3</td>
<td>Threatened or spontaneous abortion</td>
</tr>
<tr>
<td>4</td>
<td>Appendicitis</td>
</tr>
<tr>
<td>5</td>
<td>Hemorrhagic corpus luteum cyst</td>
</tr>
<tr>
<td>6</td>
<td>Torsion of the adnexa (fallopian tube and/or ovary)</td>
</tr>
<tr>
<td>7</td>
<td>Ruptured ovarian cyst</td>
</tr>
<tr>
<td>8</td>
<td>Acute gastroenteritis</td>
</tr>
<tr>
<td>9</td>
<td>Ruptured endometrioma, endometriosis</td>
</tr>
<tr>
<td>10</td>
<td>Diverticulitis</td>
</tr>
</tbody>
</table>

Clinical Presentations

The patient's clinical presentation depends on the integrity of her fallopian tube. Ectopic pregnancy can present with mild cramping and vaginal spotting or with frank hemorrhagic shock. The classic triad of vaginal bleeding, delayed menses, and severe lower abdominal pain is associated with tubal rupture and is now a fairly infrequent presentation, because early diagnosis is more routine. In general, there are two distinctly different constellations of signs and symptoms that are expressed by women with ectopic pregnancies, each of which dictates different action plans.

Acute Presentation: Classic, Ruptured Ectopic Pregnancy

**Symptoms** The patient who presents with an acutely ruptured ectopic pregnancy has the following symptoms:

1. Sudden onset of extreme, sharp, or stabbing unilateral pelvic pain, as well as shoulder pain. The shoulder pain is referred pain resulting from subdiaphragmatic irritation caused by the hemoperitoneum.
2. Dizziness, lightheadedness, or loss of consciousness from acute intraperitoneal hemorrhage.
3. Abnormal menses: The patient may have missed her menses and/or experienced several days of abnormal vaginal spotting and/or bleeding, as well as vague pelvic pain before the onset of her acute symptoms.
4. Pregnancy symptoms: The patient may also have noticed nausea, vomiting, or other early symptoms of early pregnancy.
5. Hemoglobin and hematocrit: Rapid assessment of hematocrit and hemoglobin. The blood bank should be prepared to provide packed red blood cells for replacement if necessary.
6. Coagulation factors: Coagulation factors should be sent.
7. Rh factor: A blood sample should also be sent for Rh and antibody screening to assess the need for Rh immunoglobulin later.
8. Ultrasound: An ultrasound is not necessary if the patient is hemodynamically unstable. In an emergency, if this study will delay getting the patient to an operating theater, it should not be performed. If ultrasound is performed, however, the most remarkable finding will be free fluid and clots in the pelvis; blood may fill the entire abdominal cavity. A corpus luteum cyst may be seen. The endometrium will be thickened with decidual material. Unless there is a heterotopic pregnancy, there should be no intrauterine pregnancy. It is not necessary to visualize the pregnancy in the tube.

Laboratory Tests

Laboratory testing requirements are minimal and are necessary to prepare for surgery and to rule out other pathologies.

1. Pregnancy testing: Sensitive urine pregnancy test results should be positive.
2. Hemoglobin and hematocrit: Rapid assessment of hematocrit and hemoglobin. The blood bank should be prepared to provide packed red blood cells for transfusion.
3. Coagulation factors: Coagulation factors should be sent.
4. Rh factor: A blood sample should also be sent for Rh and antibody screening to assess the need for Rh immunoglobulin later.
5. Ultrasound: An ultrasound is not necessary if the patient is hemodynamically unstable. In an emergency, if this study will delay getting the patient to an operating theater, it should not be performed. If ultrasound is performed, however, the most remarkable finding will be free fluid and clots in the pelvis; blood may fill the entire abdominal cavity. A corpus luteum cyst may be seen. The endometrium will be thickened with decidual material. Unless there is a heterotopic pregnancy, there should be no intrauterine pregnancy. It is not necessary to visualize the pregnancy in the tube.

Therapy

1. Fluids: The patient will require large-bore intravenous lines and hydration. Transfusion may be started if clinically indicated, but surgery should not be delayed by the need to give the patient a transfusion to some arbitrary hemoglobin level; often the patient is losing blood internally at a rate faster than it is possible to replace her blood by transfusion.
2. Emergency surgery is required: At surgery, it may be possible to preserve at least a portion of the affected fallopian tube, but often the trauma inflicted by the rupture may have left little viable tissue and a unilateral salpingectomy may be required. An oophorectomy is not indicated unless the ovary is bleeding uncontrollably or has other pathology.

Subacute Presentations: Probable Ectopic Pregnancy and Possible Ectopic Pregnancy

A pregnant woman who presents with cramping, abnormal vaginal spotting or bleeding, and lower abdominal/adnexal pain should be suspected of having an ectopic pregnancy, particularly if the diagnosis is supported by physical findings of cervical motion tenderness, a closed cervix, adnexal tenderness, and (possibly) an adnexal mass. Women who present in early pregnancy with complaints of vaginal spotting or bleeding and cramping without those suspicious physical findings must also be evaluated to rule out an ectopic pregnancy, although their diagnosis is more likely to be threatened abortion. The workup and treatment depend on the woman's risk factors and her pregnancy intentions.

In a stable patient with reliable access to follow-up, the diagnosis of ectopic pregnancy can be evaluated using serial measurements of serum b-hCG levels and transvaginal ultrasonography over a period of days. The patient with a suspected ectopic pregnancy is considered stable if she has normal vital signs, reference-range hematocrit values, and few complaints. Figure 56.1 outlines a common diagnostic algorithm used in these circumstances.
Serum levels of b-hCG should increase by at least 66% every 48 hours in a normally progressing intrauterine pregnancy within the first 30 days after implantation (Pittaway et al., 1985). Only 15% of normal intrauterine pregnancies will fail to have this appropriate increase in b-hCG levels. If b-hCG measurements are unchanged or increasing more slowly than normal, the pregnancy is abnormal; it may be an abnormal intrauterine pregnancy (destined to abort), or it may be an ectopic pregnancy. Pregnancies that have inappropriately low b-hCG levels are more likely to be ectopic.

2. Ultrasound studies at appropriate b-hCG levels are diagnostic. Although ectopic pregnancies can have characteristic appearances on ultrasound (Frates and Laing, 1995), ultrasound is not used to visualize the tubal pregnancy, but to identify a pregnancy within the uterine cavity. Every normal intrauterine pregnancy should be visible within the endometrial cavity by the time the serum b-hCG levels reach the so-called discriminatory zone. The numeric value of the discriminatory zone depends on local expertise with transvaginal ultrasound and on the international standard (Second International Standard or Third International Standard) that the laboratory uses to report its results (Kadar et al., 1994; Nyberg et al., 1985). Although an intrauterine pregnancy may be detected at lower levels, the possibility that the pregnancy in question is intrauterine cannot be excluded until the b-hCG levels reach the discriminatory range.

Ectopic pregnancies are diagnosed if no intrauterine pregnancy is found when the b-hCG reaches the discriminatory zone. However, the gestational sac for twin pregnancies would not become visible on ultrasonography until higher levels of b-hCG are achieved.

Outpatient Workup

After Serial b-hCG Levels

1. Declining b-hCG levels: If the b-hCG levels are declining 50%–66% every 3 days, it can be assumed that the patient has experienced a complete spontaneous abortion. As long as the patient's vaginal bleeding is minimal and there is no evidence of retained products of conception, no further follow-up is necessary.

2. Increasing b-hCG levels: If the b-hCG levels are increasing by at least 66% every 2–3 days, they should be followed in a mildly symptomatic patient until they reach the discriminatory zone and her diagnosis can be made ultrasonographically.

3. Abnormally changing b-hCG levels: If the b-hCG levels are declining or rising at an inappropriate rate, the pregnancy is abnormal; it can be an abnormal intrauterine pregnancy (blighted ovum or missed abortion) or an ectopic pregnancy.

   a. If her b-hCG levels are above the discriminatory level, an ultrasound should be obtained to localize the pregnancy. If it is not seen within the endometrial cavity, the pregnancy is presumed to be ectopic.

   b. If her b-hCG levels are less than the discriminatory range, the presence of an abnormal uterine pregnancy can be ruled out by performing an outpatient (office) dilation and curettage (D & C). The material obtained from the endometrium can be inspected for the presence of villi, which would indicate that the pregnancy is intrauterine. However, because 10%–15% of intrauterine pregnancies have no villi found, and because pathology reports are often not available for several days, it has been suggested that to more rapidly confirm an intrauterine pregnancy after D & C, a b-hCG level, obtained 12–24 hr after the procedure, should be compared with a prepregnancy level (Lipscomb et al., 2000). If levels drop by 50% in that time, an ectopic pregnancy can be ruled out.

4. However, because methotrexate may be therapeutic for abnormal intrauterine pregnancies, some investigators have suggested forgoing the D & C and immediately using the methotrexate therapy (see later discussion) to treat the abnormal pregnancy (Tulandi, 1999).

5. If the patient declines a D & C because she does not want to risk interfering with a possible intrauterine pregnancy, other diagnostic approaches are possible. Continued serum b-hCG measurements can be offered to document pregnancy progress or failure. If the b-hCG levels are higher than the threshold level, but lower than the discriminatory level (the earliest time it may be possible to see an intrauterine pregnancy), an ultrasound may be indicated if the patient has problems returning and may have to be hospitalized for observation (Counselman et al., 1998; Dart et al., 1997). In about 25% of women with b-hCG levels in the transition area between threshold and discriminatory, a diagnosis of ectopic can be made (e.g., complex adnexal mass), and in many more, an intrauterine pregnancy can be visualized. However, the high false-negative and false-positive rates make this test very costly (Barnhart et al., 1999). Diagnostic laparoscopy may be used to determine pregnancy location, but it does not have 100% sensitivity with small ectopics (see later discussion).

Other Diagnostic Modalities

1. Serum progesterone levels: Other investigators have included serum progesterone level measurements in their diagnostic protocols (Stovall and Ling, 1993). A progesterone level <5 mL can identify an abnormal pregnancy more rapidly than following serial b-hCG levels. Progesterone levels >25 ng/mL are diagnostic of normal intrauterine pregnancies in 98% of cases. However, in most situations, the progesterone levels have not been found to make any significant clinical contributions, because most patients will present with progesterone levels in the range of 10–20 ng/mL.

2. Culdocentesis to determine if there is blood in the cul-de-sac is rarely used today. It has been replaced by ultrasonic imaging.

3. Color and pulsed Doppler imaging may increase the sensitivity of vaginal sonography but are not standard of care.

4. Some authors have recommended gestational age as a starting point for the diagnostic workup. In this approach, the first step in the evaluation is an ultrasound if the gestational age is at least 6 weeks. However, the last menstrual period is often not a reliable or secure data point, particularly in adolescents who may have irregular cycles or postpone recalculations of their menstrual dates. Gole et al. (1990) reported that in 19 adolescents who presented with the ectopic pregnancies with a mean gestational age of 8.5 weeks, 10 patients denied knowing they were pregnant. Mol et al. (1999b) reviewed 354 patients evaluated for ectopic pregnancy and found that gestational age did not discriminate between intrauterine and ectopic pregnancy. Quantitative b-hCG levels have more reproducibility and, therefore, are used as the basis of most management protocols.

5. It is important to note that these general outpatient protocols, which rely on the detection of an intrauterine pregnancy to rule out an ectopic implantation, are not appropriate for patients who have undergone IVF, who have a 1% risk of a heterotopic pregnancy. Similarly, methotrexate is inappropriate to treat tubal pregnancies that coexist with desired normal intrauterine ones. Laparoscopy for diagnosis and treatment are more frequently needed for these patients: in one study, local injection of potassium chloride into the ectopic pregnancy resulted in a 67% delivery rate of the untreated intrauterine pregnancy (Lau and Tulandi, 1999).

Surgical Evaluation and Therapy

If there is any question about the patient's diagnosis, her longer term hemodynamic stability, or her ability to follow up with outpatient follow-up, surgery is the default option for both diagnosis and therapy. Virtually every hemodynamically stable patient can be approached laparoscopically (DeCherney and Diamond, 1987), although it is acknowledged that laparoscopy has a 2% to 5% misdiagnosis rate (false-negative results from early ectopics and false-positive results from clotted blood).

Types of Surgery

The surgery selected depends on the portion of the fallopian tube involved, the extent of tubal damage, and the patient's preferences for future fertility. Salpingectomy, partial salpingectomy, and salpingostomy are all effective therapies.

1. Linear salpingostomy is preferred if the ectopic pregnancy is in the ampulla of the fallopian tube.

2. Segmental resection is more appropriate for isthmic ectopics.

3. Wedge resection is the minimal procedure needed for an interstitial pregnancy.
4. Expression of the ectopic products of conception from the tube is associated with an unacceptably high rate of residual disease except when aborted ectopic tissue can be easily lifted from the fimbria.

Laparoscopy has the potential to shorten hospital stays compared with laparotomy, although operating times and complication rates are roughly equivalent between these two approaches. Gray et al. (1995) evaluated the cost-effectiveness of therapeutic laparoscopy and open laparotomy for treatment of laparoscopically diagnosed ectopic pregnancy and found that the initial procedure eliminated trophoblastic activity without major complications in 81% of 52 patients who underwent laparoscopy versus 95% of 57 patients who underwent laparotomy. However, residual trophoblasts or complications were successfully treated in all. Therefore, the authors concluded that laparoscopy produced final outcomes equivalent to those of laparotomy at lower costs. Unfortunately, Learman and Grimes (1997) found that many laparoscopically treated patients were not being discharged home early, and that the cost advantages of laparoscopy were being lost in practice.

Medical Treatment Early diagnosis of ectopic pregnancy using laboratory and sensitive imaging techniques has significantly reduced the mortality and morbidity of this condition. It has also enabled the use of outpatient therapy in lieu of surgical intervention, which in time has reduced hospitalization costs and operative complications.

Systemic Methotrexate Most stable ectopic pregnancies in appropriate candidates (Table 56.2) are now treated on an outpatient basis with single-dose methotrexate without citrovorum rescue (Table 56.3). Methotrexate disrupts cytotrophoblast syncytialization and blunts $b$-hCG production, thus decreasing support for progesterone secretion by the corpus luteum (Creinin et al., 1998). Metaanalysis of outpatient methotrexate treatment for appropriate candidates demonstrated a cure rate of 92% (Slaughter and Grimes, 1995). At least 85% of those women successfully complete therapy, although 5% to 16% may require a second dose of methotrexate (Henry and Gentry, 1994). Only 2.7% require three or more doses. Failure rates are higher with higher initial $b$-hCG levels. One study found that the failure rate was 32% when the presenting $b$-hCG levels were more than 15,000 but 6% when the pretreatment $b$-hCG level was less than 10,000 (Lipscomb et al., 1999).

The side effects attributable to methotrexate ( stomatitis, conjunctivitis, dermatitis, and pleuritis ) are generally mild and transient, but they may occasionally be quite serious. The most frequent serious problem with medical management is tubal rupture; even after the trophoblasts have stopped dividing, bleeding into the tube can continue, and the pressure of the expanding clot against a weakened fallopian wall can cause tubal rupture. Rupture has been reported in 3% to 4% of all cases. For this reason, patients taking methotrexate must understand the signs and symptoms of acute rupture and be advised to seek immediate medical attention if any of them develops. However, many women experience a worsening of abdominal pain for 1 to 2 days after injection because of the increasing intraluminal pressure. Warning them of this eventually, teaching them to distinguish this pressure from rupture, and providing acetaminophen prophylaxis reduces the need for subsequent surgical intervention (Lipscomb et al., 2000). Other important patient instructions are listed in Table 56.4.

Outpatient methotrexate therapy is less expensive than surgical intervention if the initial $b$-hCG level is less than 1,500 mIU/ml; between 1,500 and 3,000 mIU/ml, surgery and medical management are equally cost-effective. Surgery is most cost-effective when $b$-hCG levels present more than 3,000 mIU/ml if laparoscopy is used to make the diagnosis (Hajenius et al., 2000; Mol et al., 1999a). In general practice, outpatient medical therapy is less expensive than surgery—even at higher $b$-hCG levels—when the diagnosis is made clinically without surgery.

Combined Systemic and Local Methotrexate Systemic methotrexate therapy has been combined with local methotrexate injection under laparoscopic visualization. Although this increased subsequent pregnancy rates and tubal patency in one study (Debby et al., 2000), the cost and need for surgical intervention have limited the appeal of this combined approach.
Some authors advocate routine use of multiple doses of methotrexate with citrovorum rescue; this increases the success of medical management but increases the incidence of side effects. Other medical management procedures have also been attempted. The most common has been real-time ultrasound-guided injection of methotrexate through the bladder into the gestational sac (Yao et al., 1996). Other agents such as hypertonic saline or prostaglandins have also been injected with various degrees of success into the sac to induce abortion or resorption of the products of conception. In general, these procedures do have fewer side effects but are considerably more complicated than systemic therapy with methotrexate and their success is much more operator dependent. Other systemic agents, such as mifepristone, have been shown to be ineffective in treating ectopic pregnancies.

**Expectant Management** Early diagnosis of ectopic pregnancy has also introduced the possibility of expectant management, particularly in cases in which the levels of b-hCG are initially quite low (less than 1,000 to 2,000 mIU/mL) and do not rise. It must be clear that the ectopic pregnancy is tubal and measures less than 3 cm, and that there has been no significant blood loss. About 25% of ectopic pregnancies may be managed this way. Meta-analysis showed that 69% of such ectopies can be successfully observed without further intervention, but very careful consent and very reliable follow-up are required.

**Follow-up** Complete resolution of the ectopic pregnancy must be documented, because residual trophoblastic tissue proliferation can cause clinical problems. Overall, with salpingotomy, almost 5% of women undergoing laparotomy and 8% to 15% of women who are treated laparoscopically will develop persistent trophoblastic tissue (Seifer et al., 1993). In this situation, it is prudent to ensure that the b-hCG levels completely clear. b-hCG levels should be measured 6 days postoperatively. If the sixth day value is greater than 15% of the baseline value obtained at the time of surgery, persistent disease is presumed. Some have suggested that postoperative day 1 determinations replace the more delayed follow-up measurements; if day 1 serum b-hCG levels are decreased by 90%, there is an 85% probability that persistent trophoblastic tissue will not occur, and that the patient has been adequately treated (Spandorfer et al., 1997). Removal of aborting ectopic tissue has most frequently been associated with residual disease; nearly 25% of these women have persistent disease. Careful postoperative monitoring in these cases is critical. Obviously, women treated with methotrexate or expectant management will require weekly (or more frequent) quantitative b-hCG determinations until the levels of that hormone become undetectable. If persistent disease is diagnosed, treatment is necessary; options include salpingectomy, methotrexate (Graczykowski and Mishell, 1997), or occasionally, expectant management.

It is important to remind the patient that she should avoid intercourse until her b-hCG levels are significantly reduced. Also, provide her effective contraception during her recovery period, not only to prevent a second pregnancy from complicating the b-hCG results but also to allow the tubal tissue to heal and reduce the risk of a second ectopic pregnancy. Initiation of birth control should be immediate; as soon as methotrexate is started, condoms, pills, or depot medroxyprogesterone acetate should be given. Waiting until the b-hCG levels "zero out" puts a woman at jeopardy for pregnancy because ovulation often precedes complete b-hCG clearance.

Some authors have suggested that women who are diagnosed with intrauterine pregnancies should be imaged with serial ultrasound studies until "viability" is established. This may be appropriate as part of quality antepartum care, but it is not required to resolve the acute problem. Providing the patient with threatened abortion precautions is adequate.

**Rh Considerations** Unsensitized Rh-negative women with gestational age of greater than 8 weeks should be given an appropriate dose of Rh immunoglobulin (50 µg if gestational age is 8 to 12 weeks; 300 µg if more) promptly unless the father of the baby is known to be Rh negative.

**IMPACTS ON FUTURE FERTILITY**

Classically, it has been estimated that about two thirds of women are able to conceive after one ectopic pregnancy; 8% to 15% of those conceptions are ectopic; and one sixth result in spontaneous abortions (Yao and Tulandi, 1997). Younger women have higher subsequent fertility rates than these numbers reflect, except in the case of the woman whose first pregnancy is ectopic; that woman has only a 35% chance of future fertility, and one third of second pregnancies are ectopic. However, women who are diagnosed before tubal rupture and who are treated with conservative management have higher fertility rates; 82% subsequently conceived if they had no underlying infertility problems (Langer et al., 1990). Tubal patency after medical management has been demonstrated to be comparable to tubal pregnancy surgery, but long-term fertility studies of medically managed ectopic pregnancies are not available. The rate of recurrent ectopic pregnancies after a single ectopic pregnancy ranges from 8% to 27%, with a mean of about 20%.

**WEB SITES**

For Teenagers and Parents


For Health Professionals


**REFERENCES AND ADDITIONAL READINGS**


Galactorrhea, the inappropriate secretion of a clear or milky fluid from one or both breasts, is nonphysiological because it is not related to pregnancy or breast feeding. Yellow, greenish, or blood-tinged fluid is suggestive of local breast disease. Galactorrhea is often accompanied by amenorrhea and warrants evaluation in any nulliparous female or in a parous woman if one or more years have elapsed since the last pregnancy or weaning.

ETIOLOGY

Prolactin secretion is necessary for normal lactation, with the breast being the primary target for prolactin secreted by lactotroph cells of the anterior pituitary under the neuroendocrine control of hypothalamic prolactin-releasing factors and prolactin-inhibiting factors. Regulation is predominantly mediated by dopamine, which traverses the hypothalamic-pituitary portal vasculature and binds to the lactotrophs, where it inhibits prolactin secretion. Transection or compression of the pituitary stalk, which typically decreases secretion of nearly all pituitary hormones, increases prolactin secretion via interference with dopamine's ability to reach the lactotrophs. Psychotropic drugs, such as phenothiazines and butyrophenones (including haloperidol), interfere with dopamine's inhibition of prolactin by blocking dopamine receptors. Prolactin is also stimulated by a number of other releasing factors, including serotonin, vasoactive intestinal peptide, and hypothalamic thyrotropin-releasing hormone (TRH), which explains the occurrence of galactorrhea in cases of primary hypothyroidism. A schema of prolactin control is shown in Fig. 57.1.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis for hyperprolactinemia is listed in Table 57.1. The differential diagnosis for galactorrhea may be complex due to numerous factors that control prolactin secretion in preparation for pregnancy and lactation. Galactorrhea has been reported in males attempting to rid themselves of "functional" gynecomastia by means of excessive breast manipulation.

| TABLE 57.1, Differential diagnosis for hyperprolactinemia |
Exogenous estrogen (e.g., high-estrogen-content birth control pills) has been linked to mild hyperprolactinemia and galactorrhea. Oral contraceptives, however, are incapable of producing pituitary adenomas, and the lower dose pills currently used have a lower prevalence of galactorrhea. Galactorrhea related to estrogens, antipsychotics, and other medication does not usually persist longer than 3 to 6 months after discontinuation of the offending drug.

**DIAGNOSIS**

Multiple factors must be considered in the evaluation and treatment of hyperprolactinemia-induced galactorrhea (Fig. 57.2). Because prolactin is secreted in pulsatile fashion, augmented by breast stimulation or examination, exercise, stress, and eating, serum elevations should be confirmed by several repeated samples drawn in a fasting state avoiding the previously mentioned precipitants. Persistent hyperprolactinemia unassociated with pregnancy, renal failure, hypothyroidism, or the use of medications known to induce hyperprolactinemia warrants a cranial magnetic resonance imaging (MRI) study with gadolinium enhancement to evaluate the pituitary.

![Flowchart of evaluation for galactorrhea.](image)

**FIG. 57.2.** Flowchart of evaluation for galactorrhea.

Symptoms in women tend to be proportional to circulating prolactin concentrations. A given level of hyperprolactinemia is less likely to produce galactorrhea in a male, because estrogen levels must be sufficiently high to prime the mammary glands and ducts. Men may experience infertility or impotence and typically present later in the course of a macroadenoma when the mass effect from a growing tumor induces headaches or visual field changes. Delay in pubertal development may occur in either sex via the GnRH suppression induced by elevated prolactin.

The level of serum prolactin is somewhat useful for predicting diagnosis:

1. Reference-range prolactin levels in a patient with galactorrhea and normal menses virtually rule out a pituitary tumor. Prolactin levels <100 ng/mL are often unassociated with a discrete tumor, and any tumor found is unlikely to be composed of lactotrophs. The hyperprolactinemia is probably the result of compressive interference with dopamine pathways. Levels of 100–250 ng/mL are more often associated with a microadenoma (<10 mm diameter).
2. Levels >250 ng/mL are usually secondary to macroadenomas (>10 mm diameter).

Kane et al. (1994) evaluated the signs, symptoms, and outcomes of 56 children and adolescents with pituitary adenomas, as did Colao et al. (1998) in 26 patients diagnosed at age 7 to 17 years.

1. Types of adenoma: Macroadenomas were more common than microadenomas in both studies. The tumor histochmistry of the 56 patients in the series by Kane et al. (1994) was as follows:
   a. Prolactin alone, 41
   b. Prolactin and growth hormone, 8
   c. Multiple hormones, 6
   d. Glycoproteins, 1
2. Prevalence by sex
   a. No males had microadenomas in the study by Kane et al. (1994); in the review by Colao et al. (1998), one male had a microadenoma presenting with arrested skeletal growth.
   b. Females outnumbered males by a ratio of 3:3:1. All of the females in the study by Colao et al. (1998) presented with primary or secondary amenorrhea.
3. Symptoms: Headache, menstrual dysfunction, galactorrhea, and symptoms related to hypopituitarism were most frequent. Macroadenomas were found in all but one of the patients who presented with hypopituitarism.

**THERAPY**

1. Oral contraceptives: 40% of patients using oral contraceptives have mildly elevated basal prolactin levels (20–40 ng/mL) and most do not have galactorrhea. If galactorrhea occurs, the oral contraceptive should be stopped for 1 month and prolactin levels retested.
2. Psychotropic medications: If galactorrhea is secondary to psychiatric drug therapy, the offending drug should be changed unless the galactorrhea is tolerable and no alternative psychiatric drug is effective. Among the antipsychotics, the dibenzodiazepine, clozapine, is less likely to cause galactorrhea.
3. Hypothyroidism: If galactorrhea is related to primary hypothyroidism, treatment with thyroid hormone should be initiated immediately. If galactorrhea persists, the oral contraceptive must be stopped for 1 month and prolactin levels retested.
4. Prolactinoma: In hyperprolactinemia associated with prolactinoma
   a. Microadenoma: Consider whether or not to treat. If estrogen levels are within the reference range, menses are unaltered, and the galactorrhea itself is tolerable, the patient may choose no therapy, with follow-up prolactin level tests and serial imaging. If medication is preferred, the initial drug of choice is bromocriptine or cabergoline, which should lead to a return of menses in 2–3 months, with resolution of galactorrhea in about 3 months. A second MRI should be done in 6 months and then every 2–3 years.
   b. Macroadenoma: Pharmacological treatment is the primary therapy for macroadenomas, with surgery reserved for refractory cases or when mass effects persist. Pituitary adenomas, in general, are slow growing even without treatment.

In a prospective study, 30 hyperprolactinemic women were followed for 3–7 years without therapy. Serum prolactin levels increased in 6 patients, decreased in 10, and remained unchanged in 14. Decreased serum prolactin level and restoration of normal menses were more likely to occur in women who presented with oligomenorrhea or normal menses, rather than amenorrhea. Of 27 patients who had serial imaging studies, 2 showed evidence of tumor progression and 4, who had normal imaging at the beginning of the study, developed radiographic evidence of a pituitary microadenoma. No patients reached the macroadenoma size (Schlechte et al., 1989).

**Specific Therapeutic Options**

1. Bromocriptine: This ergot derivative and dopamine receptor agonist has been shown to lower prolactin levels, eliminate galactorrhea, and return menses to normal ovulatory cycles.
   a. Outcome: Bromocriptine normalizes prolactin levels and restores fertility in about 90% of individuals with a prolactinoma and often does so before curtailing the galactorrhea. Tumor diameter is reduced in 60%–79% of patients within 3–12 months. Symptoms may return after the drug is withdrawn, and for some patients, medical therapy may be lifelong. Pediatric pituitary tumors did not appear to be more invasive or more aggressive than adult pituitary tumors (Kane et al., 1994).
   b. Dosing: Therapy may be started at 1.25 mg at bedtime, increasing to 2.5 mg 1 week later. A dose increase of 1.25 mg may be made weekly. A final dose of 5–10 mg/day is almost always adequate.
   c. Side effects: Hypotension, nausea, vomiting, lethargy, dizziness, and nasal congestion are usually not problematic after the first few weeks of therapy.
   d. Pregnancy risk: Bromocriptine usually restores ovulatory cycles and fertility. Low-dose oral contraceptives (estrogen dose ≤35 μg/day) may be prescribed.
e. Tumor size: Prolactinomas may grow despite a reduction of prolactin levels in bromocriptine-treated patients. Follow-up evaluations and repeated MRIs are necessary.

f. Bromocriptine improves but may not normalize bone density in amenorrheic and oligomenorrheic patients with osteopenia.

2. Cabergoline is a long-acting dopamine agonist that is highly effective in twice-weekly doses of 0.25–1.0 mg. It is an extremely well tolerated but expensive drug.

In the series by Colao et al. (1998), the children and adolescents who failed to respond adequately to bromocriptine invariably responded to cabergoline.

3. Pergolide is an ergot-derived dopamine receptor agonist effective in the 0.025–0.05-mg/day dose range. The major advantage is once-a-day dosing, which may improve compliance and decrease side effects.

4. Surgery: Neurosurgical intervention, preferably via the transphenoidal approach, may be required for rapidly growing prolactinomas that threaten vision or fail to respond to medical therapy. Successful vision outcomes have been reported with medical therapy alone in cases of proptosis and visual impairment. Medical therapy with cabergoline should be the initial treatment in such patients.

WEB SITES

For Teenagers and Parents


For Health Professionals

- http://www.echt.chm.msu.edu/courseware/blockII/Pathology/Pituitary_5.html. Prolactinoma case and slides.

REFERENCES AND ADDITIONAL READINGS


Hirsutism is defined as increased growth of terminal (long, coarse, and pigmented) hair in a young woman, in an amount more than is cosmetically acceptable in a certain culture. The condition commonly refers to an increase in length and coarseness of the hair, in a male pattern, including predominantly midline hair of the upper lip, chin, cheeks, inner thighs, lower back, and periareolar, sternal, abdominal, and intergluteal regions. Virilism implies the development of male secondary sex characteristics in a woman. This may include the following:

1. Defeminizing symptoms: Vaginal wall atrophy, decreased vaginal secretions, decreased breast tissue, oligomenorrhea, and amenorrhea
2. Masculinizing symptoms: Hirsutism, deepened voice, increased libido, increased muscle mass, clitoromegaly (>5-mm diameter), temporal balding, and acne

Hypertrichosis implies the predominance of excessive vellus hair on the body, particularly the forehead, forearms, and lower legs.

Androgen excess, or hyperandrogenism, results in appearance changes in a young woman and can be associated with abnormal menstrual patterns, infertility, and metabolic disturbances that include decreased high-density lipoprotein cholesterol level, insulin resistance, decreased sex hormone-binding globulin (SHBG), and alterations in the balance between thromboxane and 2-prostacyclin (Haseltine et al., 1994). A common cause of hyperandrogenism, polycystic ovary syndrome (PCOS), can increase a patient’s risks for developing obesity, type 2 diabetes mellitus, and cardiovascular disease (Gordon, 1999). These young women can also have increased levels of plasminogen-activator inhibitor-1, which inhibits fibrinolysis and is a risk factor for myocardial infarction (Ehrmann et al., 1997).

Androgen disorders must be evaluated, particularly in female adolescents, because appropriate interventions are now available. The evaluation does not require complicated, expensive procedures; and if untreated, the hyperandrogenism will persist and can lead to excess morbidity and psychosocial dysfunction. It is also important to delineate the etiology of the hyperandrogenism so an appropriate management plan can be developed around a specific diagnosis (e.g., PCOS and late-onset congenital adrenal hyperplasia).

HAIR PHYSIOLOGY

Hair grows from hair follicles that develop at 8 weeks of gestation. All hair follicles are developed in utero, and no new follicles develop during life. The concentration of hair follicles per unit area of skin is similar in males and females but differs between races and ethnic groups. Whites have a greater concentration than Asians, and Mediterranean people have a greater concentration than individuals of Nordic descent. Hair grows in cycles according to the following phases:

1. Anagen phase: Growing phase
2. Catagen phase: Rapid involution phase
3. Telogen phase: Resting phase

Hair length is determined by the duration of the growing phase. Factors influencing hair growth include the following:

1. Androgens: Androgens initiate hair growth and increase hair diameter and pigmentation. These changes occur secondary to dihydrotestosterone (DHT) conversion of vellus hair to terminal hair. Once hair growth is established, the pattern may continue despite androgen withdrawal, albeit at a slower rate. Once the androgen level is reduced, there may be a lag time of 6–9 months before a significant change is noticed, as old terminal hairs fall out and are replaced by new vellus hairs.
2. Estrogens: Estrogens retard initiation and the rate of hair growth and may prolong the anagen phase.

The effects of sex hormones and other factors on hair development and distribution can be more easily understood by considering the pilosebaceous unit (Fig. 58.1). The clinical manifestations of androgen excess vary depending on end-organ sensitivity to androgens, as is shown. Hirsutism can result either from overproduction or increased sensitivity of hair follicles to androgens. Terminal hair growth is stimulated by the increased conversion of testosterone to DHT from excess 5a-reductase within this unit or the presence of more numerous hair follicles.

**FIG. 58.1.** Effect of ovarian androgens on the pilosebaceous unit. Within the ovarian theca cell, insulin and LH may stimulate cytochrome P450c17a activity, resulting in increased 17α-hydroxylase and 17,20-lyase activity, as denoted by asterisks above. These two enzymes comprise the P450c17a complex. Ovarian testosterone, along with DHT from 5a-reductase within the pilosebaceous unit, stimulates the androgen receptors at the hair follicle and sebaceous glands. Hirsutism and acne can result. (From Gordon CM. Menstrual disorders in adolescents: excess androgens and the polycystic ovary syndrome. *Pediatr Clin North Am* 1999;46:519–543, with permission.)

ANDROGEN PHYSIOLOGY
Androgens are synthesized during the metabolic pathways of progesterone, cortisol, and estrogen (Fig. 58.2).

**Fig. 58.2.** Ovarian steroid biosynthetic pathways. The following enzymes are required where indicated: (a) 20-hydroxylase, 22-hydroxylase, and 20,22-desmolase; (b) 3b-hydroxysteroid dehydrogenase and D^{5b\to D^{4b}}-isomerase; (c) 17a-hydroxylase; (d) 17,20-lyase; (e) 17b-hydroxysteroid dehydrogenase; and (f) aromatizing enzyme system. (From Goebelsmann U. Steroid hormones. In: Mishell DR Jr, Davajan V, eds. Infertility, contraception, and reproductive endocrinology. Oradell, NJ: Medical Economics, 1986, with permission.)

1. Circulating androgenic steroids in females
   a. 17-Ketosteroids (17-KSs)
      - Dehydroepiandrosterone sulfate (DHEAS)
      - Dehydroepiandrosterone (DHEA)
      - Androstenedione
   b. 17b-Hydroxysteroids
      - Testosterone
      - DHT
      - Androstenediol
      - 3b-Androstenediol

2. Metabolism: Androgens originate in the adrenal gland and ovaries, either via direct secretion or peripheral conversion of precursors. DHEAS, DHEA, and androstenedione, which are mainly produced in the adrenal gland, exert their androgenic activity after peripheral conversion to testosterone or its metabolites.
   a. Adrenal secretion: Androgens are by-products of cortisol synthesis.
      - 17-KSs: Most of the 17-KSs are generated from adrenal sources. This includes a daily secretion of 7 mg of DHEAS (90% of total daily secretion), 5.5 mg of DHEA, and 1.8 mg of androstenedione (50% of total daily secretion). All of these compounds have low androgenic activity because they are precursors of testosterone.
      - Testosterone: 25% is derived from adrenal secretion, or a total of 0.06 mg/day is secreted from the adrenal gland. Testosterone is a potent androgen, although the most potent androgen is DHT, formed after conversion by 5a-reductase.
   b. Ovarian secretions: Androgens from the ovary are metabolized as intermediates in the production of estrogen and progesterone. Androgenic hormones secreted by the ovary include the following:
      - Testosterone: About 25% of total daily secretion (0.06 mg/day)
      - Androstenedione: About 50% of total daily secretion (1.7 mg/day)
   c. Peripheral conversion: About 50% of testosterone is derived from peripheral conversion of androstenedione in liver, fat, and skin cells.
   d. Testosterone is 95.5% bound to SHBG in females; only the free portion is active. During pregnancy, about 99% is bound. In healthy males, 92.8% of testosterone is bound.

DIFFERENTIAL DIAGNOSIS

1. Idiopathic hirsutism: As the pathophysiology behind specific causes of hyperandrogenism is better delineated, the percentage of hirsute women with idiopathic hirsutism has continued to fall.
2. Ovarian causes
   a. PCOS or hyperthecosis (see Chapter 52)
   b. Tumor: Sertoli-Leydig cell tumor, lipid cell tumors, hilar cell tumor
   c. Pregnancy: Luteoma
3. Adrenal causes
   a. Congenital adrenal hyperplasia: 21-hydroxylase or 11-hydroxylase deficiency, classic or nonclassic, late-onset
   b. Tumors: Adenomas and carcinomas
   c. Cushing syndrome
4. Nonandrogenic causes of hirsutism
   a. Genetic: Racial, familial
   b. Physiological: Pregnancy, puberty, postmenopausal
   c. Endocrine: Hypothyroidism, acromegaly
   d. Porphyria
   e. Hamartomas
   f. Drug-induced: Drugs that cause hirsutism by increasing androgenic activity include testosterone, DHEAS, danazol, corticosterone, high-dose corticosteroids, metyrapone, phenothiazine derivatives, anabolic steroids, androgenic progestins, and acetazolamide. Nonandrogenic drugs that can cause hirsutism include cyclosporine, phenytoin, diazoxide, triamterene-hydrochlorothiazide, minoxidil, hexachlorophene, penicillamine and psoralens, and minoxidil. Valproate is also associated with menstrual disturbances and hyperandrogenism (Isojarvi et al., 1993).
   g. Central nervous system lesions: Multiple sclerosis, encephalitis
   h. Congenital lesions: Hurler syndrome, de Lange syndrome

Ehrmann et al. (1992) examined 40 women with hyperandrogenism and found that 25% had ovarian dysfunction, 33% combined ovarian and adrenal dysfunction, and 25% adrenal dysfunction alone. Only one patient had adult-onset adrenal 21-hydroxylase deficiency. Overall, most diagnostic tests including luteinizing hormone (LH) and follicle-stimulating hormone (FSH) and stimulation tests were not highly specific.

DIAGNOSIS

Indications for Evaluation

1. Rapid onset of signs and symptoms
2. Viritization
3. Onset of hirsutism or virilism that is not peripubertal
4. Symptoms suggesting Cushing syndrome (e.g., weight gain, weakness, or hypertension)

Consider hyperandrogenism in any female with either premature pubarche, severe acne, hirsutism, or androgenetic alopecia.

History
Menstrual history, evaluating for amenorrhea or oligomenorrhea

Physical Examination

1. Extent of hirsutism: Grading systems are available that enable a clinician to quantitate the degree of hirsutism in a patient. One method is illustrated and discussed in Hatch et al. (1981), based on grading nine areas of the body from one to four. The Ferriman-Gallwey hirsutism scoring system (Ferriman and Gallwey, 1961) is another frequently used system that enables clinicians to quantify the extent of hirsutism by circling an individual's appearance on a flow sheet and recording the total score on the patient's chart. These scores can be helpful for making comparative assessments between visits and for appraising the efficacy of a particular therapy. Some terminal hair on the lower abdomen, face, and around the areola is normal, but hair on the upper back, shoulders, sternum, and upper abdomen suggests more marked androgen activity.

2. Stigmata of Cushing syndrome.

3. Signs of virilization: Check clitoral diameter or index. A clitoral diameter >5 mm is abnormal. The clitoral index is the product of the vertical and horizontal dimensions of the glans. The normal range is 9–35 mm²; a clitoral index >100 mm² suggests a serious underlying disorder.

4. Presence of ovarian or adrenal masses.

5. Evidence of ovarian or adrenal masses.

Laboratory Evaluation

The goals of the laboratory evaluation include demonstrating androgen excess and locating the source of the excess.

1. Measuring androgen excess
   a. Plasma testosterone is the most important measurement, although this is a subject of debate in the diagnostic work-up of these patients. Levels >150–200 ng/dL suggest serious disease.
   b. Other important indicators
      • DHEAS (levels >700 mg/dL suggest an ovarian or adrenal tumor)
      • 17-hydroxyprogesterone (17-OHP): This hormone should only be measured in the morning (ideally between 7 and 9 a.m.). This is characteristically elevated in patients with congenital adrenal hyperplasia due to 21-hydroxylase deficiency. One can also measure 11-deoxycortisol in the morning to rule out 11-hydroxylase deficiency.
      • Free testosterone: Free testosterone may be elevated in the presence of normal total testosterone. However, free testosterone will be elevated in the presence of hirsutism, so it is not a specific test. Total testosterone tests are less expensive and may be enough to point the diagnosis toward an ovarian cause.
      • c. 17-KS: This is a nonspecific test, because some 17-KSs are nonandrogenic and the potent 17b-hydroxysteroids are not measured.
      • d. If the teen has either amenorrhea or oligomenorrhea, prolactin and thyroid-stimulating hormone should be measured and a pregnancy test performed.

2. Locating the source of androgen excess
   a. If male levels of testosterone are obtained or a mass is felt on examination, perform an ultrasound or computed tomography (CT) scan of adrenal glands and ovaries. Markedly elevated serum testosterone and DHEAS levels suggest an adrenal tumor and the need for an ACTH scan, whereas markedly elevated serum testosterone and normal DHEAS levels suggest an ovarian source and the need for ultrasound of the ovaries.
   b. If any of the androgens are elevated or signs suggest hypercortisolism, perform a dexamethasone suppression test.
      • An ovarian source is suggested by cortisol suppression but a lack of androgen suppression. An ultrasound of the ovaries is helpful in this instance.
      • Both adrenogenital syndrome and idiopathic hirsutism are suggested by suppression of cortisol and androgens after dexamethasone administration.
      • Cushing syndrome or an adrenal tumor is suggested by lack of cortisol suppression.

   Indicators of suppression after dexamethasone (0.5 mg q.i.d. for 5–7 days)

1. Free testosterone level <8 pg/mL
2. Total testosterone level <58 ng/dL
3. Free plasma 17b-hydroxysteroid level <42 pg/mL
4. Decrease in DHEAS level of at least 50%
   c. If 17-OHP is elevated, perform an adrenocorticotropic hormone (ACTH) stimulation test. This is helpful in differentiating normal and idiopathic hirsute females from those with late-onset congenital adrenal hyperplasia due to incomplete 21-hydroxylase deficiency.
      • To perform the test: Measure a baseline 17-OHP and repeat a serum level 60 minutes after 0.25 mg of ACTH is administered intravenously. In a positive result, there is an increase in the serum level to >30 ng/mL, whereas in normal or idiopathic hirsute females, the levels are usually <5 ng/mL. This test can also be used to rule out less common forms of late-onset congenital adrenal hyperplasia due to 11-hydroxylase or 3b-hydroxysteroid dehydrogenase deficiency.

3. Specific diagnoses
   a. Idiopathic hirsutism: These women generally ovulate regularly and have normal levels of androgens. As hyperandrogenism is better understood, the number of women with a hyperandrogenic state ascribed to idiopathic hirsutism will decline. The underlying mechanism remains to be identified, with the following possible causes of androgen excess:
      • Altered gonadotropin secretory patterns
      • Exaggerated adrenal androgen secretion
      • Increased prolactin levels, augmenting adrenal androgen secretion
      • Alteration of SHBG (decreased SHBG level, resulting in elevation of free testosterone level)
      • Obesity
      • Hyperinsulinism
      • Altered skin metabolism of androgens
   b. Ovarian tumors
      • Palpable adnexal mass
      • Testosterone level >200 ng/mL
      • Nonsuppression of androgens with dexamethasone
   c. PCOS or ovarian hyperthecosis
      • Hirsutism, infertility, menstrual irregularities, obesity
      • Slight elevations in androgen levels
      • Increase in LH level and LH : FSH ratio: LH and FSH have been suggested as markers for PCOS with a high LH and low-normal FSH level (ratio >3 : 1), but this test is neither sensitive nor specific, because only approximately 50% of patients with PCOS exhibit these abnormalities.
   d. Congenital adrenal hyperplasia: Elevated 17-OHP, with large increase after ACTH administration is diagnostic of incomplete 21-hydroxylase deficiency. This condition is often recognized during adolescence with presentation similar to PCOS syndrome. Elevated 11-deoxycortisol or DHEAS and 17-hydroxyprogrenolone levels are found in 11-hydroxylase and 3b-hydroxysteroid dehydrogenase deficiencies.
   e. Adrenal tumors
      • Androgen-secreting tumors: Rare and associated with rapid defeminization
      • Adrenal mass: Palpable in many individuals
      • Elevated 17-KS, DHEAS, and DHEA levels
      • Subnormal suppression with dexamethasone administration
Drug-induced hirsutism: The cause of nonandrogen drug-induced hirsutism is not well understood. The pattern is not restricted to androgen-dependent areas, and the hair is usually vellus in nature.

Anabolic steroid abuse.

H A I R-AN syndrome: This includes the following characteristic features: hyperandrogenism, insulin resistance, and acanthosis nigricans. This syndrome may lead to the clinical and metabolic features of PCOS, as well as myocardial hypertrophy. Insulin receptor mutations, circulating antibodies to the insulin receptor, and postreceptor signaling defects have been described in variants of this syndrome. These individuals have fasting basal insulin levels of >80 mU/mL compared with reference-range levels of about 7–8 mU/mL, as well as peaks of >1,000 mU/mL compared with about 60 mU/mL in healthy individuals.

THERAPY

1. Tumor: Remove the androgen source.
2. Drug-induced: Stop medication.
3. Congenital adrenal hyperplasia: Replace cortisol with oral hydrocortisone or prednisone. In rare instances, use low-dose dexamethasone (0.25 mg q.d.).
4. Functional ovarian hyperandrogenism (e.g., PCOS).

a. Hirsutism
   - Cosmetic approaches: Standard treatments include camouflaging with heavy makeup, bleaching, and removal with physical methods, such as rubbing, cutting, shaving, plucking, or waxing. Chemical depilatories are designed to use on specific body locations. Most of these methods last hours to days. Electrolysis or thermodestruction of the hair follicle relapses regrowth for days to weeks and can permanently remove hair. Electrolysis can be expensive, time-consuming, and uncomfortable. Photothermodestruction with a laser is a new hair removal technique. It is expensive but can offer long periods between regrowth and can lead to permanent hair loss. All of these methods can cause skin irritation, folliculitis, and pigment abnormalities.
   - Weight loss: Weight loss in obese girls with PCOS and hirsutism can reduce hirsutism. Weight loss can reduce insulin levels, thereby reducing testosterone.
   - Estrogen/progesterone: Oral contraceptives work in 60%–100% of hirsute girls. Medical therapy is slow and requires 6–12 months to judge effectiveness. Lag time occurs because of the delay before terminal hair falls out and is replaced by thinner less pigmented hair. Combination pills that contain low androgenic progestins such as norethindrone or norgestimate should be used. Oral contraceptives also provide contraception for women on other antiandrogenic medications that might be teratogenic. Combinations of oral contraceptives and antiandrogenic medications may enhance therapeutic effectiveness and prolong remission. Oral contraceptives decrease androgen production by doing the following:
     - Lowering LH levels, thus decreasing androgen production
     - Increasing SHBG, thereby lowering free androgens
     - Decreasing adrenal androgen production
     - Decreasing 5a-reductase activity

   This is an off-label use of oral contraceptives.

   a. Antiandrogenic agents: Antiandrogenic agents include drugs that block androgen cytochrome P-450 receptors, resulting in decreased testosterone, DHT, and DHEAS levels, and drugs that inhibit 5a-reductase, reducing conversion of testosterone to DHT. Spironolactone and cyproterone acetate (investigational) have been used. Spironolactone competes at the androgen receptor peripherally and inhibits 5a-reductase. The starting dose is usually 50 mg/day and is typically effective between about 75 and 200 mg/day. The medication can be increased by 25 mg every 1–2 weeks. However, the maximal response is not seen for 6 months to 1 year. Side effects are minimal but can include dry mouth, diuresis, fatigue, and menstrual spotting. The drug is contraindicated during pregnancy, because it can lead to feminization of the male fetus. In Europe, flutamide (a nonsteroidal antiandrogen) and 5a-reductase inhibitors (such as finasteride) have been used, but reports of severe hepatotoxicity prohibit its use in teenagers.
   - Combination therapy: The combination of low-dose oral contraceptives and spironolactone is very effective.
   - Future directions: Therapies will probably include insulin-sensitizing agents, topical antiandrogens, inhibitors of the enzyme 5a-reductase, and long-acting GnRH agonists. The efficacy of insulin-sensitizing agents (e.g., metformin) in patients with PCOS is an area of intensive research. GnRH agonists are alternative agents for patients with PCOS, but should be reserved for severe cases of hyperandrogenism, because they are fraught with adverse side effects. Carr et al. (1995) compared the use of oral contraceptives alone, GnRH agonists alone, or the two in combination. They found that by 6 months, measurements of hirsutism were not different between the groups. GnRH agonists alone had a negative impact on bone density. If GnRH agonists are used, it is best to use them with oral contraceptives to avoid the hypoestrogenic state that GnRH agonists can induce when used as monotherapy.

b. Menstrual abnormality
   - Cyclic progestin
   - Combined oral contraceptives

c. Infertility (referral to infertility specialist)
   - Clomiphene citrate
   - Dexamethasone
   - Human choric gonadotropin
   - Insulin-sensitizing agents plus/minus clomiphene citrate (their use in adolescents is currently experimental)

WEB SITES

For Teenagers and Parents

http://www.obgyn.net/pcos/articles/hairissue_article.htm. OB-GYN.net handout on hirsutism.
http://www.pcosupport.org/. PCOS Association Web site includes facts and figures on PCOS, as well as on-line support.
http://www.pcosupport.org/pcoteen. PCO Teenlink home page is dedicated to teenagers with PCOS. Includes a chat room and bulletin board so teens can share their thoughts on the disease.

For Health Professionals


REFERENCES AND ADDITIONAL READINGS


Barth JH. How hairy are hirsute women? Clin Endocrinol 1997;47:255.


Breast Disorders
Lawrence S. Neinstein

Although breast cancer is uncommon during the adolescent years, breast concerns and problems among adolescent females are a common occurrence. Breast development often is the first sign of beginning puberty. This chapter reviews breast disorders that can occur in female adolescents and young adults. These include disorders such as asymmetrical breast development, accessory breast tissue, macromastia, benign and malignant breast tumors, and nipple discharges. Galactorrhea (abnormal lactation) is discussed in Chapter 57.

**BREAST DEVELOPMENT AND ANATOMY**

A mammary ridge or milk line forms from the ectodermal layer in the 20-day-old embryo extending from the forelimb to hind limb. The nipple and areola, which form in the 6th week of fetal life, overlie a bud of breast tissue composed of both the primary mammary ducts and a loose fibrous stroma. Approximately 15 to 25 secondary buds develop, which bifurcate into tubules forming the basis of the duct system. Each duct system opens separately into the nipple.

There is a small amount of breast tissue present in prepubertal children and this usually undergoes no change before puberty. Occasionally, a prepubertal male or female develops enlargement of one or both breasts. This usually consists of a soft, mobile subareolar nodule of uniform consistency. In these individuals, usually the areola and nipple are not developed or pigmented and there are no associated signs of puberty. Spontaneous resolution usually occurs after a few weeks or months. Biopsy should not be performed because this could eliminate pubertal breast development. In some prepubertal individuals, these changes may be the first sign of precocious puberty.

The physiology of breast development during puberty is complex and involves both hormonal levels and the binding of hormones to breast tissue. Multiple hormones are involved including estrogen, progesterone, corticosteroids, and thyroxine. Estrogen, mainly estradiol, has the major influence on ductal development while progesterone influences additional lobular alveolar development. The physiological influences that terminate further breast development are not well understood.

Breasts are usually similar in males and females until puberty. In female adolescents, breast development (thelarche) is usually the first sign of puberty and full breast development often is the first sign of beginning puberty. This chapter reviews breast disorders that can occur in female adolescents and young adults. These include disorders such as asymmetrical breast development, accessory breast tissue, macromastia, benign and malignant breast tumors, and nipple discharges. Galactorrhea (abnormal lactation) is discussed in Chapter 57.

**DEVELOPMENTAL ANOMALIES**

Asymmetrical Breast Development

In most females, one breast is slightly larger than the other, usually with the left breast larger than the right. However, pubertal breast development does not always occur symmetrically, and for unknown reasons, some adolescents have more significant asymmetry than others during puberty. Much of this corrects by adulthood. Occasionally, when notable asymmetry is present, corrective surgery can be performed with augmentation or reduction of one breast. This can be done in stages with...
an implant placed in one side that allows for increasing amounts of saline to match growth on the other side. After puberty, this implant is replaced with a permanent implant. One can monitor differences in breast sizes by measuring breast units, which equal vertical distance multiplied by horizontal distance. Some teens may wish to use bra pads for the smaller breast for cosmetic reasons. Breast asymmetry may also be caused by a large mass that may distort breast tissue such as a giant fibroadenoma; these should be followed during the visit. Pseudoasymmetry may result for deformities of the rib cage such as pectus excavatum.

Accessory Breast Tissue (Polymastia)

Accessory breast tissue is the most common breast anomaly, found in 1% to 5% of males and female. Polythelia refers to supernumerary nipples and polymastia to any accessory breast elements. The accessory tissue is usually located along the embryonic milk line anywhere from the midclavicular or axillary area to the middle of the inguinal ligament in the groin. Accessory breast tissue below the umbilicus is extremely rare. This condition has been occasionally associated with cardiovascular and genitourinary anomalies. Although the problem is usually of no significance, the extra nipples may become engorged postpartum and create painful swellings. The extra nipples can be excised for cosmetic reasons. It is important to remember that breast diseases can occur in accessory breast tissue.

Absence of Breast Tissue (Amastia and Athelia)

Amastia is the total absence of one breast. The condition is often associated with an anomaly in the chest wall, including the absence of the pectoralis major or other muscles. Poland syndrome involves a combination of amastia with an ipsilateral rib deformity, webbed fingers, and radial nerve palsy. Certainly, amastia can be extremely disrupting to an adolescent. As described already, surgical correction for amastia can be performed in stages. Atelea is the absence of the nipple on one or both sides. Surgical correction is an option for this condition also.

Atrophy

Atrophy of breast tissue may also occur during puberty. The most common cause of this disorder is a significant loss of fat and supportive glandular tissue related to dieting and eating disorders. Other possible causes include premature ovarian failure, androgen excess (tumors and anabolic steroids), and chronic diseases leading to significant weight loss such as diabetes mellitus, inflammatory bowel disease, and others.

Tuberous Breast Deformity

This deformity involves protuberant and overdeveloped areolae with hypoplasia of other breast areas. It is a benign condition that requires either reassurance or plastic surgery if the defect is severe.

Macromastia

The definition of “normal breast size” is difficult to define accurately and can be a function of society that changes over time. One categorization of breast size (Corriveau and Jacobs, 1990) uses the following:

- “ideal breast size”: 250–300 mL
- moderate hypertrophy: 400–600 mL
- rather significant hypertrophy: 600–800 mL
- significant hypertrophy: 800–1,000 mL
- gigantomastia: >1,500 mL

There is a strong association between macromastia with obesity and a strong familial incidence. Most cases of macromastia start at the time of puberty, with 80% of cases beginning in adolescence. Macromastia may occur over months to years and may occur before or after menarche.

Female adolescents and their parents usually complain of the psychological effects of macromastia. This is in distinction to female adults who usually complain of breast pain, shoulder grooving, and back pain. No relationship has been found between circulating hormonal levels in these teens and macromastia. However, there may be differences in hormone-receptor affinity.

There are no definitive guidelines for surgical intervention. It is generally preferred to wait for surgical interventions until after the breasts have matured, but this may be difficult in extreme cases. The outcome of reduction mammoplasty was evaluated in 16 female adolescents by Evans and Ryan (1994). All patients were satisfied with the surgical results and experienced relief of their symptoms. Subjective nipple sensation was the same or increased in 60% of the group. In another review of reduction mammoplasty, Boschet et al. (1996) evaluated the outcome in 72 women available for long-term follow-up and found a significant reduction in symptoms post-surgery and a significant increase in exercise and other physical and social activities.

Virginal or Juvenile Hypertrophy

An extreme case of macromastia is virginal breast, or juvenile, hypertrophy, which is defined as a significant diffuse enlargement of the breast that is usually symmetrical occurring near the time of menarche.

1. Etiology: The cause of juvenile hypertrophy is not well understood but may represent an abnormal response of the breast to normal serum estrogen levels. Results from hormonal studies are normal in these individuals. The condition has also been reported to occur at pregnancy (gravid hypertrophy) and with exogenous estrogen, androgens, corticosteroids, and insulin.

2. Clinical Manifestations
   a. Pendulous and diffusely firm breasts without any discrete mass lesions. The breasts can get as large as 30–50 pounds.
   b. Although usually symmetrical, the condition has also been reported as a unilateral condition.
   c. The breast tissue may be soft but sometimes has diffuse ropelike thickenings.
   d. Neck and back strain may be associated problems.
   e. The hypertrophy may cause significant psychological problems and embarrassment.
   f. In contrast to the giant fibroadenoma, there is less thinning of the skin, less prevalence of enlarged veins, and less displacement of the nipple or areola.

3. Treatment: No definite therapeutic guidelines have been developed. Although it is preferable to delay any surgery until the breasts have matured, this may not be practical in some adolescents if breast size or weight is unbearable. Four modalities of treatment have been recommended (Bauer et al., 1987):
   a. Reduction mammoplasty: This is the most common therapy, but many adolescents may continue to have breast enlargement after this procedure.
   b. Subcutaneous mastectomy with implantation of a prosthesis: This may be the surgical procedure of choice in individuals with massive recurrent enlargement.
   c. Hormonal manipulation: This includes treatment with either medroxyprogesterone, dydrogesterone, or danazol (Danocrine). Dydrogesterone may suppress the secretion of growth hormone and could interfere with the development of secondary characteristics. Teratogenic and carcinogenic effects have also been a concern with these medications.
   d. A combination of medications and surgery: This includes surgery plus the postoperative use of the dydrogesterone to prevent recurrences.

### BREAST TUMORS

#### Types of Tumors

In reviewing 15 retrospective studies involving breast lesions in adolescents and young adults younger than 22 years, the following prevalences were found (studies include Bauer et al., 1987; Bower et al., 1976; Daniel and Mathews, 1968; Farrow and Ashikari, 1969; Gogas et al., 1979; Goldstein and Miller, 1982; Neinstein et al., 1993; Raju, 1985; Sandison and Walker, 1968; Seashore, 1975; Simmons and Wold, 1989; Simpson and Barson, 1969; Skiles and Seltzer, 1980; Stone et al., 1977; Turbery et al., 1975):

<table>
<thead>
<tr>
<th>Type of Lesion</th>
<th>Number (n = 1,791)</th>
<th>Percentage of Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibroadenoma</td>
<td>1,227</td>
<td>68.3</td>
</tr>
<tr>
<td>Abscessed Lesion</td>
<td>1,227</td>
<td>68.3</td>
</tr>
</tbody>
</table>
Fibrocystic changes/mastodynia 332 18.5
Abscess or mastitis 67 3.7
Juvenile hypertrophy 34 1.9
Other breast lesion 26 1.4
Cyst 21 1.2
Intraductal papilloma 22 1.2
Other benign tumor 22 1.2
Giant fibroadenoma 19 1.0
Cancer 16 0.9

As expected from surgical studies, fibroadenomas were the most common lesion found (68.3%), with most of the remaining being fibrocystic changes (18.5%). Malignancies were very uncommon (0.9% of surgical cases). Of the 12 malignant lesions reported in the above-mentioned studies, 5 were primary breast cancer. The practitioner should remember that these prevalences reflect surgically excised lesions. Fibrocystic disease or proliferative breast changes are probably more common than represented here. In a review of breast lesions, 4.5% of 400 adolescents had palpable breast lesions (3.25% with a discrete mass and 1.25% with other benign changes (Neinstein et al., 1993)).

Benign Breast Disease

Physiological Swelling and Tenderness The breasts of most reproductive-age women have a nodular texture representing the glandular units or lobules of the breast. Under hormonal stimulation during each menstrual cycle, these lobules undergo proliferative changes. This results in changes varying from a feeling of fullness in the breast to distinct masses suggestive of a pathological process. Such physiological changes account for as many as 50% of breast complaints in female adolescents. If treatment is needed, analgesics or the use of a well-fitting brassiere worn both day and night can be tried.

Mastalgia (Severe Pain, Either Cyclic or Noncyclic) Moderate to severe breast pain is another relatively common and occasionally distressing breast symptom. Although the prevalence in female adolescents is unknown, mastalgia is reported in as many as 66% of women (Maddox and Mansel, 1989). These symptoms have not been correlated to any histological changes. The most common type of breast pain is associated with the menstrual cycle (cyclic mastalgia) and is associated with maximal pain premenstrually. Cyclic mastalgia is usually bilateral, poorly localized pain. It is often described as a soreness or heaviness radiating to the axilla and arm, which usually subsides after menses. It is difficult to consider this condition as pathological because cyclic pain and nodularity are so common among early reproductive-age women in their twenties and thirties. The better term for this condition is benign breast changes and not fibrocystic disease or mastitis. Some women have noncyclic mastalgia characterized by a spot that hurts all the time, most commonly in the upper outer quadrants of one or both breasts. Noncyclic mastalgia is more common in women in their forties.

Many modalities have been tried in the treatment of mastalgia. These have included heat, firm support, analgesics, hormonal therapy, evening primrose oil, and diuretics, and in adults, danazol, bromocriptine, and tamoxifen. These latter drugs are not recommended for adolescents. Most adolescents only require reassurance and analgesics, such as the nonsteroidal antiinflammatory agents. Exclusion diets, diuretics, and vitamins B, B6, and E have not shown significant benefits. Evening primrose oil has been used predominantly in Europe with an overall response rate of 44% on two 500-mg capsules three times a day (Maddox and Mansel, 1989; Pye et al., 1985). A trial usually consists of 3 months and then another 2 months if the response is positive.

Proliferative Breast Changes (Nodularity, Fibrocystic Changes) Most nodularity in adolescents and young adults is associated with benign, proliferative breast changes or in less preferable terminology, fibrocystic changes. Some authorities consider this condition a nonexistent and recommend elimination of the term fibrocystic disease.

1. Prevalence: The prevalence in adolescents is unknown. If examined carefully, probably more than 50% of women in the reproductive-age group have some degree of proliferative breast changes. The prevalence increases during the third and fourth decade. At autopsy, as many as 90% of women of virtually all ages have histological changes associated with the fibrocystic changes.

2. Pathophysiology: The exact cause of breast nodularity or fibrocystic changes is unknown. However, an imbalance between estrogen and progesterone has been implicated (Vorherr, 1986). With relatively higher estradiol-to-progesterone levels, connective and epithelial tissue proliferation occurs. Some women with proliferative breast changes also have obstruction and persistent secretory material in alveoli and terminal ducts causing alveolar enlargement and cyst formation. In some studies, methyloxanthines (caffeine) have been implicated to worsen the condition; however, several case-control and randomized trials have failed to confirm this.

a. Proliferative breast changes usually occur in stages that correlate to the individual's age. Adolescents and women in their twenties have minimally symptomatic fibrocystic tissue changes, particularly in the upper outer quadrants of the breasts. Changes in women in their thirties and forties usually include multiple small cysts, with a diffuse increase in glandular tissue and increasing complaints of pain. Single large cysts are more common in women 35 years of age or older.

3. Clinical manifestations
   a. Proliferative breast changes are usually found either as painless lumps on examination or because of pain or discomfort.
   b. Symptoms, including tenderness, are most common about 1 week before menstruation and are often relieved by menstruation.
   c. Characteristic nodularity consists of hard and tender areas of a few millimeters to 1 cm in diameter.

4. Treatment: Many modalities have been suggested for treating proliferative breast changes. In most adolescents, the symptoms are not severe enough to warrant aggressive measures.
   a. Supportive measures include well-padded brassieres, in addition to mild analgesics.
   b. Hormonal modalities: Oral contraceptives can help in up to 70%-90% of individuals while medroxyprogesterone acetate (Provera) (10 mg on days 15–25 of the menstrual cycle) has had success in up to 85% of women (Cox, 1985).
   c. Caffeine: A decrease in caffeine intake is advocated by some; however, because of its very questionable effects, heavy restriction of diet should not be encouraged.
   d. Vitamin therapy, including vitamins B, A, and E, has been used, but a beneficial effect has not been proven.
   e. Danazol: Although danazol has been used in adult women for severe proliferative breast changes, there is little experience with its use in female adolescents.

Fibroadenomas and Other Benign Breast Masses

Common Fibroadenomas

1. Definition: A fibroadenoma is a benign neoplasm of mammary gland that microscopically has stromal proliferation surrounding aggregates of compressed or uncompressed, elongated, and distorted ducts. Although classified as benign neoplasms, they are almost an aberration of normal development. Fibroadenomas can be divided into the following groups:
   a. Common fibroadenomas
   b. Giant/juvenile fibroadenomas
   c. Phyllodes tumors

2. Prevalence: Common fibroadenomas are the most common breast tumor found in adolescents in surgical reports, comprising 90%-90% of benign breast lesions. Most adolescents with this condition are older than 14 years, with a large increase in prevalence in 15- and 16-year-olds. The condition has been
Clinical manifestations

1. Fibroadenomas are frequently discovered by the adolescent, often while bathing.
2. Associated symptoms, other than the presence of a breast mass, are unusual. However, some adolescents will complain of breast discomfort during menstruation or pregnancy.
3. The average duration of symptoms is about 5 months.
4. On examination, the mass is usually a rubbery, firm, mobile, well-demarcated, and nontender lesion. It is usually easy to distinguish the mass from surrounding breast tissue.
5. Commonly, there is only one fibroadenoma, with the largest prevalence in the upper outer quadrant of the breast. Thirty-three percent are in the lateral quadrants. Fibroadenomas are multiple in 10%–25% of cases and bilateral in about 10%.
6. Fibroadenomas range in size from <1 cm to >10 cm, with an average size of 2–3 cm.
7. Diagnosis: Usually the diagnosis can be made with a combination of clinical examination; sonography; and fine-needle aspiration (FNA) cytology, core biopsy, or excision biopsy.
8. Treatment: Treatment for fibroadenomas may involve either careful follow-up, particularly if diagnosis has been confirmed by FNA cytology, or elective surgical excision. Surgical intervention in adolescents diagnosed by examination, sonography, FNA, or core biopsy usually involves considering the size of the lesion and the breast cancer concerns of the teen and her family. These operations can often be performed under local anesthesia and sedation on an outpatient basis sparing teens the risk of general anesthesia. However, general anesthesia is recommended in adolescents with undue anxiety, with large pendulous breasts, or with deep lesions.
9. Prognosis: Most fibroadenomas do not increase in size and some may get smaller or disappear. In one study of 25 women diagnosed with fibroadenomas by examination, cytology, and sonography, 52% decreased in size, 16% did not change, and 32% increased in size over at least a 5-year period (Carty et al., 1995). This was also confirmed in 65 women with fibroadenomas diagnosed by examination and cytology, with a 46% probability of disappearance at 5-year follow-up (Carty et al., 1995), as well as in a study by Neinstein et al. (1993) in which 39% of lesions resolved.

Giant or Juvenile Fibroadenoma

Some fibroadenomas, labeled juvenile or giant fibroadenomas, have much more rapid growth with a greater degree of stromal cellularity and the potential to grow to a size large, usually larger than 5 cm in diameter. Giant fibroadenomas, although uncommon, are found most commonly in young adolescents, with a greater prevalence in African-American teens. The mass is benign but may cause distortion of normal breast tissue. The mass has a rapid and asymmetrical growth pattern, which may cause compression of adjacent breast tissue. The area may feel warmer due to the increased blood supply of the tumor. Although encapsulated, the tumor may have a consistency similar to that of normal breast tissue, which may make it difficult to differentiate from normal tissue or unilateral virginal hypertrophy. Treatment of giant fibroadenomas is by simple excision, sparing as much mammary tissue as possible. A simple mastectomy for this lesion is not warranted.

Phyllodes Tumors (Cystosarcoma Phylloides)

Cystosarcoma phylloides tumors usually present as a bulky mass in the breast and are the least prevalent cause of massive breast lesions in adolescents. The lesions tend to be large, up to 20 cm, and sharply circumscribed. The mass is firm, mobile, and smooth or irregular. Overlaying skin may be stretched and shiny, with distended veins from the rapid growth of the tumor. Compared with juvenile or giant fibroadenoma, this lesion is more firm and more discrete. The lesion is almost always benign, but malignant lesions have been reported in adolescents.

Both Briggs et al. (1983) and Rajan et al. (1998) review phyllodes tumors in female patients. In one study, the mean size was 6 cm, and 4.6 cm in the other series. However, the range was up to 13 cm. In the series by Rajan et al. (1998), 34 were benign and 11 were malignant. Microscopically, benign phyllodes tumors are similar to fibroadenomas containing both epithelial and connective tissue elements, but with a more cellular, hyperplastic stroma. Phyllodes tumors lack complete encapsulation and extend into surrounding tissue in multiple projections of varying size. The classification of benign or malignant depends on the stromal findings of cellular atypia, anaplasia, and increased mitotic activity. Treatment recommendations range from simple excision to radical mastectomy, but little evidence exists to support the use of mastectomy as initial therapy (Mollit et al., 1987). Most adolescents and adults are cured by excision alone. The lesion should be excised completely with a surrounding rim of normal breast tissue. There is no need for a mastectomy unless the tumor is found to be malignant. There is also no reason for adjuvant chemotherapy or radiation in the absence of metastatic disease.

Cysts

Large cysts are another cause of benign breast masses. Cysts larger than 1 cm usually occur in women in their forties. Cysts are associated with few symptoms and on examination feel like a well-circumscribed, small, freely movable mass. These can usually be diagnosed and treated by FNA.

Nipple Discharge

A discharge from the nipple can represent many different conditions. Nipple discharge in adolescents may include galactorrhea, Montgomery tubercles, intraductal papillomatosis, or duct ectasia. Generally, milky, green, gray, or black discharges that can be expressed from several ducts are not suggestive of cancer. In teens, even most bloody nipple discharges are not secondary to a malignancy. Cytology analysis of nipple discharge is neither useful nor cost-effective in teens.

The type of discharge may be helpful in the differential diagnosis.

Milk: Galactorrhea (see Chapter 57)

Multicolored/sticky: Duct ectasia

Purulent: Mastitis

Watery: Papilloma, cancer

Serous/serosanguineous: Intraductal papilloma, benign proliferative changes, cancer, duct ectasia

Many conditions can lead to galactorrhea including pregnancy, past abortion, postpartum, pituitary adenomas, hypothyroidism, and medications such as oral contraceptives, phenothiazines, spironolactone, estrogen, and methyltestosterone. The evaluation of galactorrhea is reviewed in Chapter 57.

Montgomery Tubercles

A nipple discharge may also be associated with Montgomery tubercles or Mongagni tubercles. These may arise from sebaceous glands associated with a lactiferous duct. Individuals with Montgomery tubercles present with small soft papules around the areola, which tend to enlarge with pregnancy and are involved with lactation. The teen usually complains of an episodic, thin, clear to brown discharge. Breast examination results will usually either be normal or show a small lump under the areola. The condition usually resolves without intervention, with the discharge disappearing in 3 to 5 weeks and the lumps within 4 months.

Intraductal Papilloma

An intra ductal papilloma arises from an abnormal proliferation of cells in mammary ducts. The lesion is usually small and most frequently microscopic, consisting of simple proliferations of duct epithelium projecting into a dilated lumen. Because the proliferated epithelium is supported by a vascular stalk, slight local trauma may rupture this stalk, leading to a bloody discharge. The proliferation of cells may grow large enough so a mass may be palpable. A bloody discharge associated with a soft mass in a teen has a 95% chance of being an intraductal papilloma.

1. Infrequent finding in the adolescent: The lesion is most frequent in women in their twenties through forties. In the author's series, these lesions made up 1.2% of biopsied lesions in adolescents (Neinstein, 1994).
2. May present with a bloody nipple discharge: In the largest series of adolescents, only 3 of 13 teens noted a spontaneous bloody nipple discharge (Farow and Ashkari, 1969) and 9 of 13 presented with an abnormal thickening or breast enlargement.
3. Examination: Many individuals with this condition have well-defined nodules or thickenings near the areola. The lesions are often multiple and located in ducts near the periphery of the breast and less frequently near the areola.
4. Treatment: These lesions are uniformly benign and amenable to local excision.

Infections and inflammations

Infections and inflammations include subareolar abscess, lactational mastitis, duct ectasia, and breast abscess.
A breast abscess or cellulitis can occur secondary to bacteria introduced from the skin into the ductal system or from cutaneous infections, foreign bodies, epidermal cysts, and trauma, such as shaving parierreolar hair or trauma related to sexual play.

1. Breast abscesses are not common in adolescents, with most being related to lactation. In retrospective chart reviews of adolescent breast lesions, about 3%–4% are related to an inflammatory cause (Diedel and Kaplan, 1965; Neinstein, 1994).

2. Abscesses usually present similarly to an abscess elsewhere on the body, leading to the sudden onset of a tender or fluctuant mass with skin erythema.

3. Organisms: Staphylococcus aureus is the most common organism, followed by Escherichia coli and pseudomonas. Other organisms include group B beta-hemolytic streptococcus and anaerobes.

4. Risk factors: Preceding factors may include trauma, ductal obstruction, or a preexisting cyst.

5. Treatment: Treatment involves the use of warm compresses and antibiotics.

**Mastitis**


2. Etiology: Mastitis results from abrasions on the nipple that allow for infection and the clogging of lactiferous ducts, allowing for the stasis of milk.

3. Clinical manifestations: Pain, tenderness, induration, and fever. The abscess may be subcutaneous, subareolar, intramammary, or retromammary.

4. Organisms: The most common bacteria involved is *S. aureus*. However, other organisms include streptococcus*, Micrococcus dyogenes*, E. coli, *Pseudomonas* species, and others.

5. Diagnosis: An infection is likely with a leukocyte count from breast milk of $>10^7$ per mL plus $>10^3$ bacteria per mL on culture. Culture and sensitivity of breast milk of the affected breast is helpful in identifying the organism and choosing an appropriate antibiotic.

6. Treatment: Heat and antibiotics are used in the treatment. Nursing or breast pumping can be continued using the unaffected breast. Nursing on the affected side can be quite painful.

**Mondor Disease**

Mondor disease is a superficial thrombophlebitis of the breast. It is an uncommon and self-limited condition. Usually the condition presents with an inflammation in a vertical linear pattern. The linear mass is often painful. Treatment involves analgesics and hot compresses. Rarely, a residual, long, linear skin retraction persists after the inflammation resolves.

**Cancer of the Breast**

**Prevalence** During the past 70 years, there have only been sporadic reports of breast cancer in females younger than 20 years (Hammar, 1981; Oberman and Stephens, 1971; Seltzer and Skiles, 1980; Winchester, 1996). Fewer than 1% of all breast tumors in adolescents are cancerous, and 98% of breast cancer occurs in women older than 25 years. Of breast cancer cases in adolescents, about one third are primary tumors of breast tissue and the rest are either a tumor of nonbreast tissue or some form of metastatic cancer. Fibrosarcoma and liposarcoma are the most frequent type of breast sarcoma. Other malignancies occurring in the breasts of female adolescents include lymphomas, Hodgkin disease, leukemia, and multiple myeloma. In tabulation of English mortality data including more than 70,000 deaths from breast cancer, there was 1 case of a child younger than 5 years, 1 between age 10 and 14 years, 5 between age 15 and 19 years, and 27 between age 20 and 24 years (Close and Maximov, 1965). In another 20-year review of all patients with breast cancer younger than 35 years at Hahnemann University Hospital in Philadelphia, there were 81 patients, with only 2 patients (2%) being younger than 20 years and 3 patients (4%) being 21 to 25 years of age (Sariego et al., 1995).

**Clinical Manifestations** Schuytloer (1982) found that 90% of children and adolescents with breast cancer present with a breast mass. The mass is usually hard, most commonly subareolar, and frequently fixed to the deep tissues. The size varies from 1 to 2.5 cm, with both breasts equally affected. Symptoms are uncommon with axillary lymphadenopathy present in only a few cases. Up to 30% of affected teens have a family history of breast cancer, and the tumor tends to occur earlier in the daughter than in the mother.

**Prognosis** There is some controversy over whether patients with breast cancer younger than 35 years have a better, worse, or similar prognosis to that of older patients. It appears that premenopausal patients have more aggressive breast tumors (based on histology), but it is unclear if this leads to a poorer prognosis or worse long-term survival (Anderson et al., 1995; Croye et al., 1994; Sariego et al., 1995).

**DIAGNOSIS AND EVALUATION OF BREAST MASSES IN ADOLESCENTS**

**History**

A thorough risk assessment is important, but 75% of women with recently diagnosed breast cancer have no known risk factors. Important risk information includes age, family history, prior malignancies and radiation exposure, age at first pregnancy, and age at menarche.

1. Age: Breast cancer increases with age, with a very low risk in the adolescent population.

2. Family history of breast tumors (both benign and malignant): The history should include any first-degree relatives (i.e., mothers, sisters, or daughters) and breast cancer and the age at diagnosis. A teen with a premenopausal first-degree relative with breast cancer has a threefold to fourfold greater risk (Cady et al., 1996). This risk is increased to eightfold or tenfold if the relative had bilateral cancer before menopause or if breast cancer developed premenopausally in more than one first-degree relative.

3. Genetics: At least eight candidate susceptibility genes have been identified. Probably the most important that lead to striking family clusters of breast cancer are mutations of BRCA1 and BRCA2, accounting for almost 80% of hereditary breast cancer and about 5%–6% of all breast cancers (Greene, 1997). Although these mutations are rare in the general population (5–50/100,000), they may occur in about 1% of all Jewish women of Ashkenazi descent (Fitzgerald et al., 1996).

4. Radiation screening of BRCA1 is not warranted because of the difficulty in evaluating the multiple mutations, social discrimination issues such as insurance, and the lack of appropriate preventive strategies. However, genetic testing for cancer risk is likely to change dramatically in the coming years. Elger and Harding (2000) discuss testing for BRCA1 in the adolescent population and the importance of making distinctions between testing children and adolescents.

5. Radiation exposure: Radiation exposure of the breast during childhood may be associated with a significantly higher risk of cancer. Childhood-onset Hodgkin disease is associated with an increased risk of breast cancer and is the second most common solid malignancy found in women with prior Hodgkin disease (75-fold risk). In the study by Bhalla et al. (1996) of breast cancer in teens with childhood Hodgkin disease, of the 17 women with breast cancer, 7 had prior history of radiation therapy alone and 10 had a history of a combination of radiation and chemotherapy. The women with breast cancer in this study had a median age of 31.5 years (range, 16–42 years).

6. Physical activity: Different findings have been found relative to physical activity and risk of breast cancer. Some studies have found that physical activity has no protective effect on the risk of breast cancer in young women (Chen et al., 1997). On the other hand, Verloop et al. (2000) found that women who were more active than their peers had a reduced risk of breast cancer, compared with inactive women (odds ratio = 0.70; 95% confidence interval, 0.56–0.88).

7. Oral contraceptives: Although there have been obvious benefits of oral contraceptives in the risk of endometrial and ovarian cancer, their impact on breast cancer has been more controversial. Almost all epidemiological studies of present and past oral contraceptive users demonstrate risk ratios whose confidence intervals cluster around 1.0 or include 1.0 without statistically significant increased risk. Some studies have indicated a slight increased risk in selected subgroups. Both the Centers for Disease Control and Prevention (CDC) Cancer and Steroid Hormone Study and a World Health Organization study of 5,000 women found no increased risk of breast cancer with duration of use. Overall, there is no conclusive evidence that oral contraceptives increase a woman's risk of breast cancer. See Chapter 43 for a more in-depth discussion.

**Breast Examination**

A thorough examination of the breast is important in the evaluation of a breast lesion in an adolescent or young adult. This includes both inspection and palpation. It is important to be sensitive to the adolescent's concerns about this examination. If the teen has never had a breast examination, then an explanation of the procedure...
and the reason for the examination is critical. It is also important for there to be a chaperon present during the breast examination; some younger teens may prefer their mother. Otherwise, a medical assistant or nurse would be appropriate, particularly for a male examiner. Teaching the breast self-examination (BSE) as part of the examination may help in reducing the anxiety level of the teen. It is useful to explain to the teen that she may be the best person to identify any changes in her breasts. A gown should be used to reduce unnecessary exposure of the breast. In addition, it is reassuring to teens to be told that the breast has many lumps and bumps that may change, particularly with menstrual cycles.

**Inspection** This consists of inspection of both breasts to observe for asymmetry or skin retraction. Traditionally, this has been performed with the individual seated and in three different positions: leaning forward, extending her arms over her head, and pressing her hands against her hips (Sapira, 1990). However, these three positions are seldom helpful in the screening examination unless a mass is palpated. For this reason and the potential discomfort to the adolescent, I recommend skipping this maneuver for the screening examination. This does not exclude observing the breasts in either the sitting or the supine position for size, symmetry, and any observable lesions.

**Palpation** The examiner should next palpate the breast for a mass or discharge. Palpation is performed while the teen is in the supine position. First, the teen’s arm on the side to be examined should be placed behind her head. The examiner can also place a pillow or folded sheet under the posterior ribs. The breast should be palpated in an orderly fashion. The examiner can examine the breast in one of several ways.

1. Spokes of a wheel: In the first method, the examiner uses a pattern similar to the spokes of a wheel. Starting with the tail of the breast in the axilla, the examiner moves in a straight line to the nipple. Using straight lines from the outer boundary of the breast to the nipple, the examiner can work around the whole breast.

2. Concentric circles: A second method involves covering the breast in either concentric circles or a spiral pattern around the breast.

3. Vertical strips: A third method involves covering the breast by examining vertical strips. In a study by Atkins et al. (1991), this was found to be the most effective method.

Whichever method is used, the entire anterior chest wall should be palpated, applying varying degrees of pressure with the pads of the second, third, and fourth fingers and rotating in small dime-sized circles. Particular attention should be given to the nipple and areolar areas, as 15% of breast cancers are located here. The areola should be compressed to a firm nipple discharge. The examiner should also palpate for supraclavicular, infraclavicular, and axillary nodes. Occasionally, using talc in palpating the breast may be helpful.

The presence of masses should be documented regarding size, location, mobility, and consistency. Masses larger than 1 cm may be best felt by compressing them between the thumb and index finger. A fibroadenoma is suggested by the palpation of a firm, rubbery, and mobile mass with a smooth or slightly irregular surface. Rapidly enlarging tumors of the breast are usually either a juvenile fibroadenoma or phyllodes tumor.

Barton et al. (1999) reviewed controlled trials and case-control studies in which clinical breast examination (CBE) was part of the screening. CBE alone detected between 3% and 45% of the breast cancers that screening mammography missed. The preferred technique included use of a vertical strip template. The value of inspection was not demonstrated.

**Breast Self-examination** Controversies still exist over the use and benefits of BSE for breast cancer screening, particularly as it applies to adolescents. The benefit of BSE has not been proven. In a study by Harvey et al. (1997) of the effects of BSE, there was a 2.84 odds ratio of death from breast cancer in women who did not perform BSE compared with those who performed inspection and palpation. Although there may be a benefit in teaching this technique to adolescents in regards to education about their body and in lowering concern during the breast examination, disadvantages may include raising anxiety and decreasing time available for other risk assessment and health-promotion activities.

**Diagnostic Procedures**

**Mammography** Although mammography is an excellent screening tool in adult women, particularly those older than 40 to 50 years, it is neither generally helpful nor recommended in adolescents and young women. The very dense breast tissue of young adults and the low prevalence of cancer in young women lead to a low sensitivity and specificity of mammography in this age group. A poor correlation between mammographic diagnosis and tissue diagnosis exists for women younger than 30 years because masses may be hidden in dense breast parenchyma. Mammography should be reserved for women younger than 30 years who have a clinical impression of a malignancy on examination. Glaziov et al. (1995) reviewed seven trials that included 159,465 women with 8 to 9 years of follow-up and found that the benefit of mammographic screening is small or nonexistent in women younger than 50 years.

**Sonography** Ultrasound of the breast is mainly used to differentiate between a solid or cystic mass. Sonograms should not be used either as a screening tool or to differentiate a benign from a malignant solid mass. In addition, a sonogram may be useful in guiding a needle into an abscess or cyst.

**Fine-needle Aspiration** This is the primary technique for evaluation of breast masses in many centers even without sonography. If the aspiration shows nonbloody fluid, it is considered benign and not sent for cytology. In this case, the clinician should recheck the teen for recurrence in 4 to 6 weeks. If the FNA shows a solid mass, then the aspirate is performed with a cytological smear made up for evaluation. While the role of FNA is still not defined; in some centers, it has become the diagnostic modality of choice for triaging younger women to either observation or open biopsy. There are others who use FNA as a triage between outpatient excision biopsy versus an inpatient biopsy and frozen section for those with positive biopsy results.

FNA is dependent on obtaining a good cytological specimen and having an experienced cytopathologist. Although the false-positive rate of FNA is very low, the false-negative rate may be as high as 10% to 20%. There is a suggestion that the accuracy of FNA for breast tumors 2.0 cm or smaller is improved when combining with sonography from 65% to 86.9% (Hatada et al., 1996). Younger women may also have a higher false-positive rate.

Individuals with benign cytology can be followed, whereas those with malignant cytology need a definitive surgical procedure and those with suspicious cytology need an open excision biopsy. Carli et al. (1997) evaluated the accuracy of FNA in 321 women with the clinical diagnosis of fibroadenoma, all who underwent both FNA and excision biopsy. There were four cases of carcinoma in this group and a 68% prevalence of fibroadenoma. The FNA showed carcinoma on cytology on three of four and suspicious cells in the fourth. In addition, the patients were asked their views of nonoperative treatment, and only 21% preferred conservative management in the future and 7% would have preferred conservative management rather than their recent excision. Pacinda and Ramzy (1998) evaluated FNA in women younger than 21 years. In this study, 49% of the breast FNAs were diagnosed as fibroadenomas and no cases of malignant breast disease or phyllodes tumors were encountered. The FNA appears to be a useful and reliable tool in the evaluation and management of masses in the adolescent breast. Hindle (private communication) found that most younger women in their breast center are comfortable with the FNA result without doing an excision biopsy in those with benign cytology. Although a conservative approach appears to be safe in women younger than age 25 years, it might not be acceptable to some women. An open biopsy should be considered in women who either have a large or rapidly growing mass, have significant high-risk factors for carcinoma, or prefer excision.

**Core Biopsy** Breast core biopsy is another popular method of obtaining a tissue diagnosis for breast masses while avoiding excision biopsy in most women. This method is often used in the evaluation of nonpalpable breast masses found on screening mammography in older women. The correlation to surgical biopsy is excellent. Image-guided core biopsy can also be used as an adjunct to FNA, if the result is inadequate or equivocal, or can be used instead of FNA in centers without expertise in FNA or with more experience in core biopsies.

**Other Modalities** Thermography has no role in either breast cancer screening or diagnostic evaluation. Other modalities are being explored in their role in the diagnosis of breast lesions including contrast-enhanced magnetic resonance breast imaging, digital mammography, computer-aided diagnosis, scintimammography, position emission tomography, and single photon emission planar computed tomographic scan imaging.

**Management** Compared with women older than 30 or 40 years, in whom the usefulness of mammography in evaluating breast lesions is well documented, the management of breast masses in adolescents is more controversial. Palpation cannot definitively diagnose a breast mass, so there may be a need for an FNA or biopsy in a teen.
Although the risk of an underlying malignancy in this population is low, it is not zero; however, because of the rarity of malignant breast tumors, excision biopsies should not be an urgent procedure. Fibroadenomas are likely to be the most common solid mass in this age group of young women. Options available to the clinician to evaluate a mass include: observation, additional imaging examinations (ultrasound, mammography), FNA, core biopsy, open biopsy, or some combination of these. Few articles address the specific evaluation of breast lesions in teens, and there are very few studies that have prospectively followed this group of girls. In one prospective study of 52 women with a clinical diagnosis of a benign mass younger than 25 years, 29 had masses resolving over 2 to 12 months and 23 had benign biopsy results (Furnival et al., 1983).

Three studies have commented on the correlation of fibroadenomas in many individuals and the lack of development of cancer in these lesions (Cant et al., 1987; Carty et al., 1996; Neinstein et al., 1993). These findings have led to recommendations that breast masses in adolescents be observed through at least one complete menstrual cycle. Although an excision biopsy has been the traditional diagnostic test for a persistent breast mass or one that continues to grow, an increasingly popular alternative is the FNA, which avoids the surgical risks and scars of excision biopsies. An excision biopsy is recommended for a hard mass, fixed mass, or if there is skin dimpling, edema, ulceration, or fixation to the chest wall, patient or parental anxiety about the mass, or a strong positive family history. Multiple or recurrent lesions that are stable in size should not be excised. If feasible, cysts can be aspirated and the fluid, if bloody, sent for cytological examination. Mammography may be of some benefit in adolescents with highly suspicious lesions on clinical examination.

A common diagnostic approach in adults has been the diagnostic triad of examination, mammography, and FNA. The accuracy of confirming a benign lesion if all three test results are negative is 98% to 99%. However, another diagnostic approach in young women is the modified triple test (MTT) (physical examination, ultrasonography instead of mammography, and an FNA). In one study, no patients with MTT results in which all the elements were concordant and benign had cancer developing at follow-up (negative predictive value and specificity of 100%) (Vetel et al., 1996). FNAs and examination were more accurate than ultrasound in the seven cases in which MTT results were nonconcordant. This approach could help eliminate open biopsies in most cases and reduce costs. Hindle found that in evaluation of breast masses in younger women in his breast center, examination and FNA are sufficient for accurate diagnosis (William Hindle, personal communication, August 1998). They found that mammography added no information in patients younger than 30 years, and that ultrasound was rarely necessary if a needle aspiration was being performed. FNAs that show either atypical or suspicious cytology should lead the clinician to recommend an open biopsy. Those individuals having malignant cytology on FNA should have a definitive surgical procedure with frozen section.

The following is thus recommended:

1. Clinical examination should be performed. If the lesion is not suspicious of a malignancy, it should be evaluated again in 4–8 weeks.
2. A suspicious mass or persistent discrete mass would then be subject to an FNA or core biopsy. An optional ultrasound could be performed but is not necessary if an FNA is done.
3. If the results of the examination and the FNA or core biopsy are benign, the patient can be observed without excision biopsy.
4. If the results of the FNA or core biopsy are suspicious, then an open excision biopsy should be performed.
5. If the examination and FNA or core biopsy results are concordant for malignancy, then the individual should proceed directly to definitive therapy with confirmatory frozen section without an open biopsy.

SUMMARY

Breast lesions are common in adolescent girls and young adult women including mastalgia, benign proliferative changes, and benign masses including fibroadenomas. Breast cancer is rare in women younger than 20 years and uncommon in women younger than 30 years. Although discrete masses in teens and adults younger than 30 years that do not feel suspicious on examination can be observed for 1 to 2 months, persistent masses should be evaluated with an FNA to differentiate benign versus potentially malignant lesions. FNA can help in determining which masses can be observed versus the need for excision biopsy. Mammography has little role in women younger than 30 years, except in those individuals with a highly suspicious lesion on examination.

WEB SITES

For Teenagers and Parents


http://webmd.lycos.com/content/dmik/dmik_article_57969. WebMD article.


http://www.drkoop.com/conditions/ency/article/003152.htm. Dr. Koop has several sections on breast disease problems.


http://www.goaaskalice.columbia.edu/about.html. Go Ask Alice Web site including questions from young adults about medical issues.

For Health Professionals

http://www.cdc.gov/cancer/NBCCEDP. The CDC Women's Health page.

REFERENCES AND ADDITIONAL READINGS


Thomas DB. The WHO collaborative study of neoplasia and steroid contraceptives: the influence of combined oral contraceptives on risk of neoplasms in developing and developed countries. Contraception 1991;43:895.


From a clinical and public health perspective, sexually transmitted diseases (STDs) are one of the visible tracks marking the occasionally obscure developmental trails of sexuality through adolescence. Sexual activity itself occupies an uncomfortable, ambiguous position among the health challenges of adolescence: development of healthy sexuality balanced against the fear and stigma associated with STDs and their genuine threats to health.

The key clinical considerations include direct attention to issues of sexuality within the adolescent's developmental path, attention to behaviors that increase or reduce risk of acquiring an STD, screening by physical examination and laboratory testing, treatment of identified infections, and counseling for partner treatment and prevention of infections. Annual attention to these issues is recommended and some experts suggest even more frequent risk-reduction counseling and STD screening, particularly in teens involved in higher risk sexual behaviors. STD screening provides an opportunity to discuss risk of human immunodeficiency virus (HIV) testing and prevention.

STDs are associated with significant disease burden among adolescents. In 1998, 15- to 19-year-old girls had the highest gonorrhea and chlamydia rates of any age group. Gonorrhea rates among male and female adolescents generally declined during the early years of the decade of the 1990s, but this decline appears to have reversed in the later years of the decade. Chlamydia rates are typically 6% to 18% among adolescent women, although rates decrease when aggressive screening and treatment policies are implemented. Trichomonas vaginalis rates are up to 14% in adolescent women and 3% to 5% of asymptomatic males. Serological studies show positivity rates for herpes simplex virus (HSV) of up to 30% for some groups of adolescents; most do not have symptomatic infection. Evidence for human papillomavirus (HPV) infection may be seen in up to one third of some clinical samples.

The elevated STD risk of adolescents is almost certainly multifactorial in origin. Developmental susceptibility of the reproductive tract of adolescent women, the substantial rates of sex partner infections, and inconsistent or incorrect condom use are likely contributors. Socioenvironmental risks such as high endemic STD rates, sexual and physical abuse, social chaos, poverty, drug trafficking and use, and inadequate health care access also contribute and may be more powerful explanations of STD risk than developmental or individual behaviors.

Diagnostic possibilities for many STDs, particularly gonorrhea and chlamydia, have been revolutionized by nucleic acid amplification techniques (NAATs). NAATs have superior sensitivity and specificity compared with culture or other diagnostic tests such as direct fluorescent antibody (DFA) or DNA probe tests. NAATs also allow use of urine and vaginal specimens, in addition to cervical or urethral specimens. Higher initial costs, compared with other tests, may be offset by reductions in morbidity. Table 60.1 summarizes currently available NAATs and approved specimen sources.

<table>
<thead>
<tr>
<th>Nucleic acid amplification tests for diagnosis of gonorrhea and chlamydia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Table 60.1</td>
</tr>
</tbody>
</table>

In view of the fact that most adolescents complain of a particular set of symptoms and not a specific organism, a list of presenting symptoms for the STDs is also included (Table 60.2). As a broad overview, the appendix to this chapter summarizes the clinical features and treatments of many of the well-known STDs. The remaining chapters in Section XIII focus on individual STDs in more detail.

<table>
<thead>
<tr>
<th>Sexually transmitted diseases by presenting symptom</th>
</tr>
</thead>
<tbody>
<tr>
<td>Table 60.2</td>
</tr>
</tbody>
</table>

WEB SITES

For Teenagers and Parents

http://www.iwannaknow.org/. The American Social Health Association Web site designed specifically for teens. Sexuality and STD prevention are directly and explicitly addressed.


For Health Professionals


APPENDIX 60.1

Sexually Transmitted Diseases Summary

Note: Adapted from the Centers for Disease Control and Prevention, Department of Health and Human Services. 1998 guidelines for treatment of sexually transmitted diseases. MMWR Morb Mortal Wkly Rep 1997;47(RR-14), with permission. For a copy of this publication, write to CDC, Technical Information Services, Atlanta, GA 30333. Copies and updates are also available on-line, at http://www.cdc.gov/nchstp/dstd.

NONGONOCOCCAL URETHRITIS (NGU)

bi Etiological Agents

Chlamydia trachomatis (15%–40%)
Ureaplasma urealyticum (10%–40%)
Mycoplasma genitalium (5%–15%)
T. vaginalis (2%–5%)

HSV on occasion

TYPICAL CLINICAL PRESENTATION

Men usually have dysuria, frequency, and mucoid-to-purulent urethral discharge. Some men have asymptomatic infections.

Urethral discharge associated with NGU tends to occur 1–5 weeks after infection and produce less discharge and dysuria than gonococcal urethritis.

However, no symptoms or signs reliably distinguish gonococcal urethritis from NGU or among various etiological causes of NGU.

PRESumptive Diagnosis

(Warrants full treatment and follow-up.)

Mucopurulent or purulent discharge.

Absence of gram-negative intracellular diplococci and ≥5 polymorphonuclear (PMN) leukocytes per oil immersion field on a smear of an intraurethral swab specimen.

Positive leukocyte esterase test (LET) results on first-void urine or microscopic examination of first-void urine demonstrating ≥10 PMN leukocytes per high-power field. Positive LET results should be always be confirmed with a Gram stain of a urethral swab specimen and gonorrhea and Chlamydia testing.

Asymptomatic men with negative gonorrhea test results are presumed to have NGU if they have ≥5 PMN per oil immersion field on an intraurethral smear.

DEFINITIVE DIAGNOSIS

An agent etiologically associated with NGU is recovered from the male urethra. Specific diagnostic tests for organisms other than gonorrhea and chlamydia are not indicated in the evaluation of males with urethritis.

Note that coinfection by multiple organisms is common.

THERAPY

Recommended Regimen: Azithromycin (1 g PO in a single dose), OR

Doxycline (100 mg PO b.i.d. for 7 days).

Alternative Regimens:

Erythromycin base, 500 mg PO q.i.d. for 7 days, OR

Erythromycin ethylsuccinate, 800 mg PO q.i.d. for 7 days, OR

Ofloxacin, 300 mg PO b.i.d. for 7 days, OR Levofloxacin 500 mg orally once a day for seven days.

If patient cannot tolerate high-dose erythromycin schedules, one of the following regimens can be used:

Erythromycin base, 250 mg PO q.i.d. for 14 days, OR

Erythromycin ethylsuccinate 400 mg PO q.i.d. for 14 days.

COMPLICATIONS AND SEQUELAE

Urethral strictures

Prostatitis

Epididymitis

Reiter syndrome

Chlamydial NGU may be transmitted to female sex partners, resulting in mucopurulent endocervicitis, pelvic inflammatory disease (PID), and other adverse outcomes. (See entries related to these conditions in the succeeding pages.)

OTHER CONSIDERATIONS

Follow-up: Regimens for persistent/recurrent urethritis have not been rigorously evaluated. Noncompliant patients and those with reexposure to untreated partners should be re-treated with the initial regimen. Patients with objective evidence of persistent/recurrent urethritis should be evaluated for T. vaginalis infection. A
recommended treatment for persistent/recurrent urethritis is as follows:

Metronidazole, 2.0 g PO in a single dose, PLUS
Erythromycin base, 500 mg PO q.i.d. for 7 days, OR
Erythromycin ethylsuccinate, 800 mg PO q.i.d. for 7 days.

Management of Sex Partners: Sex partners should be referred for evaluation and treatment.

HIV Infection: Patients with HIV infection should receive the same treatment as patients without HIV.

EPIDIDYMIS

Etiological Agents

C. trachomatis
Neisseria gonorrhoeae
Coliform/enteric bacteria

TYPICAL CLINICAL PRESENTATION

Scrotal, inguinal, or flank pain and scrotal swelling. Subacute onset is typical, but acute symptoms are not uncommon. Most patients with epididymitis associated with sexually transmitted organisms have accompanying dysuria, urethral discharge, or both.

PRESCRIPTIVE DIAGNOSIS

Requires ruling out testicular torsion. Gram stain of urethral secretions may show PMN leukocytes and gram-negative intracellular diplococci. Urinalysis is often positive for white blood cells (WBCs).

DEFINITIVE DIAGNOSIS

Definitive bacterial diagnosis may be made after ruling out testicular torsion. Positive Chlamydia test result (culture, direct immunofluorescence assay, DNA probe, or NAAT) or a positive gonorrhea test result (culture, DNA probe, or NAAT). Rarely, epididymal aspiration is used to establish a diagnosis before surgery.

THERAPY

For epididymitis most likely caused by gonococcal or chlamydial infection:
Ceftriaxone, 250 mg IM in single dose, PLUS
Doxycycline, 100 mg PO b.i.d. for 10 days.

For epididymitis most likely caused by coliform/enteric organisms:
Ofloxacin, 300 mg PO b.i.d. for 10 days, OR Levofloxacin 500 mg orally once a day for 10 days.

COMPLICATIONS AND SEQUELAE

Testicular/scrotal abscess
Testicular infarction
Chronic epididymitis
Infertility

OTHER CONSIDERATIONS

Follow-up: Failure to improve within 3 days requires reevaluation.

Management of Sex Partners: Sex partners should be managed as appropriate for the identified STD. Partners of presumptively treated patients should be notified, evaluated, and treated for infections identified or suspected in the index patient.

HIV Infection: Patients with HIV infection should receive the same treatment as patients without HIV infection. Fungal and mycobacterial causes are more common among immunosuppressed patients and should be considered if initial treatment fails.

MUCOPURULENT CERVICITIS

Etiological Agents

N. gonorrhoeae
C. trachomatis

In most cases, neither of these organisms are isolated.

TYPICAL CLINICAL PRESENTATION

Most patients are asymptomatic. Symptomatic patients may complain of yellow vaginal discharge or abnormal vaginal bleeding (e.g., after coitus).

PRESCRIPTIVE DIAGNOSIS

MPC is not a sensitive and specific predictor of infection by C. trachomatis or N. gonorrhoeae.

The presence of yellow mucopurulent endocervical discharge or the finding of yellow discharge on a white cotton-tipped swab of endocervical secretions suggests infection.

The presence of increased numbers of PMN leukocytes on a Gram stain of endocervical mucus is not standardized and has low predictive value. This evaluation is
DEFINITIVE DIAGNOSIS

Definitive diagnosis is made by a positive Chlamydia test result (culture, direct immunofluorescence assay [DFA], DNA probe, or NAAT) or a positive gonorrhea test result (culture, DNA probe, or NAAT).

THERAPY

Treatment is based on the results of chlamydia and gonorrhea testing. If the patient is unreliable or in an area of high likelihood of gonorrhea or chlamydial infection, treat presumptively with coverage for both gonorrhea and chlamydia.

COMPLICATIONS AND SEQUELAE

Complications are those associated with etiological microbiological agents.

OTHER CONSIDERATIONS

Follow-up: Follow-up should be appropriate for identified sexually transmitted organisms.

Management of Sex Partners: Sex partners should be managed as appropriate for the identified STD. Partners of presumptively treated patients should be notified, evaluated, and treated for infections identified or suspected in the index patient.

HIV Infection: Patients with HIV infection should receive the same treatment as patients without HIV infection.

GONORRHEA

Etiological Agent

N. gonorrhoeae

TYPICAL CLINICAL PRESENTATION

When symptomatic, men complain of dysuria, urinary frequency, and purulent urethral discharge. Variable degrees of edema and erythema of the urethral meatus are often present.

Many infections are asymptomatic. Symptoms include abnormal vaginal discharge, intermenstrual bleeding, menorrhagia, or dysuria.

Symptoms of rectal gonococcal infection include mild anal pruritus, painless mucopurulent discharge, and mild bleeding. Symptoms of severe proctitis sometimes occur.

Pharyngeal infections are usually asymptomatic.

PRESumptive DIAGNOSIS

(Warrants full treatment and follow-up.)

Identification of typical gram-negative intracellular diplococci on smear of urethral discharge (men) or endocervical mucus (women). Gram stain is insufficiently sensitive for diagnosis in girls and should be supplemented (if used) by culture, DNA probe, or NAAT confirmation.

DEFINITIVE DIAGNOSIS

Growth on selective medium demonstrating typical colonial morphology, positive oxidase reaction, and typical Gram stain morphology.

NAATs are highly sensitive and specific for the diagnosis of gonorrhea. Tests based on several methods are Food and Drug Administration (FDA)-approved and commercially available. Approved specimen sources include urethral and cervical discharge/mucus and urine. Provider and self-obtained vaginal swabs show high sensitivity and specificity in research settings but are not FDA-approved specimen sources.

THERAPY

Uncomplicated Urogenital or Anorectal Gonococcal Infections

Cefixime, 400 mg PO in a single dose, OR
Ceftriaxone, 125 mg IM at one time, OR
Ciprofloxacin, 500 mg PO in a single dose, OR
Ofloxacin, 400 mg PO in a single dose, OR
Levofloxacin 250 mg orally in a single dose.

Treatment of coinfection by C. trachomatis should be added unless appropriate diagnostic test results are negative for chlamydia.

Uncomplicated Pharyngeal Infections

Ceftriaxone, 125 mg IM at one time, OR
Ciprofloxacin, 500 mg PO in a single dose, OR
Ofloxacin, 400 mg PO in a single dose, OR Levofloxacin 250 mg orally in a single dose.

Concomitant treatment for pharyngeal chlamydial infection is recommended, although coinfection is unusual.

Alternative Regimens

Spectinomycin, 2 g IM a single dose.

Injectable cephalosporin regimens such as ceftriaxone (500 mg IM in a single dose), cefotaxime (500 mg IM in a single dose), cefotetan (1 g IM in a single dose), and cefoxitin (2 g IM in a single dose).

Quinolone regimens other than ciprofloxacin and ofloxacin such as enoxacin (400 mg PO in a single dose), lomefloxacin (400 mg PO in a single dose), and...
norfloxacin (800 mg PO in a single dose). None of these regimens offers advantage over ciprofloxacin or ofloxacin regimens.

COMPLICATIONS AND SEQUELAE

Ten percent to 20% of women develop PID and are at risk for its sequelae (see entry following).

Men are at risk for epididymitis, sterility, urethral stricture, and infertility. Newborns are at risk for ophthalmia neonatorum, scalp abscess at the site of fetal monitors, rhinitis, pneumonia, or anorectal infections.

All infected, untreated persons are at risk for disseminated gonococcal infection (includes septicemia, arthritis, dermatitis, meningitis, and endocarditis).

OTHER CONSIDERATIONS

Patients treated for gonorrhea should be screened for syphilis by serological testing. Infections acquired in Asia or the Pacific including Hawaii: avoid the use of quinolones.

**Pregnant Women:** Should not be treated with tetracycline or quinolones.

**Follow-up:** No test of cure is needed for patients with uncomplicated gonorrhea who are treated with one of the regimens in these guidelines. Treatment failures are most likely due to reinfection, although quinolone resistance is increasingly common.

**Management of Sex Partners:** Sex partners should be referred for evaluation and treatment. Sexual intercourse should be avoided until the patient and partner are cured.

**HIV Infection:** Patients with HIV infection should receive the same treatment as patients without HIV infection.

**CHLAMYDIA**

**Etiological Agent**

*C. trachomatis*

**TYPICAL CLINICAL PRESENTATION**

Many patients are asymptomatic. Symptomatic women complain of dysuria or abnormal vaginal discharge. Symptomatic men usually have dysuria, urinary frequency, and a mucopurulent urethral discharge.

**PRESumptive Diagnosis**

(Warrants full treatment and follow-up.)

**Women:** Sexual contact with a partner with diagnosed nongonococcal or chlamydial urethritis. Mucopurulent cervicitis (MPC) is sometimes used as presumptive diagnosis of cervical chlamydial infection.

**Men:** Sexual contact with partners with urogenital chlamydial infection. NGU (i.e., typical clinical symptoms and ≥5 PMN leukocytes per oil immersion field on a smear of an intraurethral swab specimen).

**DEFINITIVE DIAGNOSIS**

Definitive diagnosis is made with a positive *Chlamydia* test result (culture, DFA, or NAAT).

**THERAPY**

**Recommended Regimens**

Azithromycin, 1 g PO in a single dose, OR Doxycycline, 100 mg PO b.i.d. for 7 days.

**Alternative Regimens**

Ofloxacin, 300 mg PO b.i.d. for 7 days, OR Levofloxacin 500 mg orally once a day for 7 days, ORERYTHROMYCIN BASE, 500 MG PO Q.I.D. FOR 7 DAYS, ORERYTHROMYCIN ETHYLsuccinate, 800 MG PO Q.I.D. FOR 7 DAYS.

**COMPLICATIONS AND SEQUELAE**

Ascending infections may lead to symptomatic or asymptomatic endometritis and salpingitis and subsequent infertility. Ascending infection during pregnancy may lead to adverse obstetric outcomes, conjunctivitis, or pneumonia in the infant, and to puerperal infection.

**OTHER CONSIDERATIONS**

**Pregnant Women:** Doxycycline, ofloxacin, and levofloxacin are contraindicated for use during pregnancy. Azithromycin is a Class B drug, so its safety for pregnant and lactating women is not known. However, there is now extensive clinical experience with azithromycin treatment during pregnancy.

**Recommended Regimen for Pregnant Women**

ERYTHROMYCIN BASE, 500 MG PO Q.I.D. FOR 7 DAYS, ORAMOXICILLIN, 500 MG PO T.I.D. FOR 7 DAYS.

**Alternative Regimens**

ERYTHROMYCIN BASE, 250 MG PO Q.I.D. FOR 14 DAYS, ORERYTHROMYCIN ETHYLsucinate, 800 MG PO Q.I.D. FOR 7 DAYS, ORERYTHROMYCIN ETHYLsucinate, 400 MG PO Q.I.D. FOR 14 DAYS.

**Follow-up:** No need for retesting after completing treatment with doxycycline or azithromycin. Retesting at 3 weeks after completion of therapy may be useful for pregnant women because none of the regimens are highly efficacious and erythromycin side effects may prevent compliance. Reinfection is common in women with
C. trachomatis and rescreening in 3–4 months after treatment is recommended, particularly in adolescents.

Management of Sex Partners: Sex partners should be referred for evaluation and treatment.

HIV Infection: Patients with HIV infection should receive the same treatment as patients without HIV infection.

**PELVIC INFLAMMATORY DISEASE**

**Etiological Agents**

In most cases, sexually transmitted organisms, especially *N. gonorrhoeae* and *C. trachomatis*, are implicated. However, other microorganisms that can be part of vaginal flora, such as anaerobes, *Gardnerella vaginalis*, *Haemophilus influenzae*, enteric gram-negative rods, and *Streptococcus agalactiae* can cause PID. *Mycoplasma hominis* and *U. urealyticum* may also play a role.

**TYPICAL CLINICAL PRESENTATION**

The spectrum of PID includes any combination of endometritis, salpingitis, tuboovarian abscess (TOA), and pelvic peritonitis. The patient may present with pain and tenderness involving the lower abdomen, cervix, uterus, and adnexa. Fever, chills, elevated WBC count, and elevated erythrocyte sedimentation rate (ESR) are often absent.

**PRESumptive diagnosis**

The clinical diagnosis of PID is difficult because of the wide variation of symptoms and signs. No combination of symptoms, signs, or laboratory findings is both sensitive and specific for PID. Because delay in treatment increases the potential for damage to the reproductive health of the woman with PID, a low threshold for the diagnosis of PID is necessary.

**Minimum Criteria**

- Adnexal tenderness, OR
- Cervical motion tenderness

Empirical treatment of PID should be initiated in sexually active young women and others at risk for STDs if the minimum criteria are present and no other cause(s) for the illness can be identified. Although PID occurs during pregnancy, patients with positive pregnancy tests require careful evaluation for ectopic pregnancy as a cause for pelvic pain.

**Additional Criteria**: Additional criteria may increase the specificity of the diagnosis.

**Routine Criteria**

- Oral temperature >38.3°C
- Abnormal cervical or vaginal discharge
- Presence of white blood cells on saline microscopy of vaginal secretions
- Elevated ESR
- Elevated C-reactive protein
- Laboratory documentation of cervical infection with *N. gonorrhoeae* or *C. trachomatis*

**Elaborate Criteria**

- Histopathological evidence of endometritis on endometrial biopsy
- TOA on sonography
- Laparoscopic abnormalities consistent with PID

**Definitive Diagnosis**

Direct visualization of inflamed (edema, hyperemia, or tubal exudate) fallopian tube at laparoscopy or laparotomy makes the diagnosis of PID definitive. A culture of tubal exudate establishes the etiology.

**THERAPY**

Some experts recommend that all patients with PID be hospitalized to initiate parenteral antibiotics. Hospitalization of patients with PID is particularly recommended in the following circumstances:

1. The diagnosis is uncertain; and surgical emergencies such as appendicitis and ectopic pregnancy cannot be excluded.
2. A pelvic abscess is suspected.
3. The patient is pregnant.
4. The patient is an adolescent.
5. The patient has HIV infection.
6. Severe illness or nausea and vomiting preclude outpatient management.
7. The patient is unable to follow or tolerate an outpatient regimen.
8. The patient has failed to respond to outpatient therapy.
9. Clinical follow-up within 72 hours of starting antibiotic treatment cannot be arranged.

**Outpatient Treatment**

Little information is available from clinical trials on intermediate and long-term outcomes using outpatient regimens. If patients do not respond within 72 hours to outpatient regimens, they should be hospitalized to confirm diagnosis and receive parenteral treatment.

**Regimen A**

- Ofloxacin, 400 mg PO b.i.d. for 14 days, OR Levofloxacin, 500 mg orally once daily; WITH or WITHOUT Metronidazole, 500 mg PO b.i.d. for 14 days.

**Regimen B**

- Ceftriaxone, 250 mg IM once, OR
- Cefoxitin, 2 g IM, plus probenecid, 1 g concurrently, OR
- Other parenteral third-generation cephalosporin such as ceftriaxone or cefotaxime, PLUS
- Doxycycline, 100 mg PO b.i.d. for 14 days.
INPATIENT TREATMENT

Regimen A
Cefoxitin, 2 g IV q6h, or cefotetan, 2 g IV q12h, PLUS Doxycycline, 100 mg IV or PO q12h.

Regimen B
Clindamycin, 900 mg IV q8h, PLUS Gentamicin loading dose, IV or IM 2 mg/kg of body weight, followed by a maintenance dose, 1.5 mg/kg q8h.

These regimens should be continued for at least 48 hours after the patient demonstrates improvement. Thereafter, doxycycline (100 mg PO b.i.d.) or clindamycin (450 mg PO q.i.d.) should be continued for 14 days. When TOA is present, many health care providers use clindamycin for continued therapy, rather than doxycycline, because clindamycin provides more effective anaerobic coverage.

Alternative Parenteral Regimens: Few data support the use of other parenteral regimens, but the following three regimens have been investigated in at least one clinical trial, and they have broad-spectrum coverage.

Ofloxacin, 400 mg IV q12h or levofloxacin 500 mg IV once daily WITH or WITHOUT,
Metronidazole, 500 mg IV q8h, OR Ampicillin/sulbactam, 3 g IV q6h; PLUS Doxycycline, 100 mg IV or PO q12h.

COMPLICATIONS AND SEQUELAE

Life-threatening complications include ectopic pregnancy and pelvic abscess. Other complications are involuntary infertility, recurrent PID, chronic PID, chronic abdominal pain, pelvic adhesions, premature hysterectomy, and depression.

OTHER CONSIDERATIONS

Pregnant Women: Should be treated as inpatients.

Follow-up: Hospitalized patients should show substantial clinical improvement within 3–5 days or require further diagnostic workup. Patients treated as outpatients should follow up within 72 hours and after significant clinical improvement. Some experts recommend retesting for \textit{N. gonorrhoeae} and \textit{C. trachomatis} 4–6 weeks after completing therapy.

Management of Sex Partners: Sex partners should be referred for evaluation and treatment. Treatment should include coverage for both \textit{N. gonorrhoeae} and \textit{C. trachomatis} infections. Sexual intercourse should be avoided until the patient and partner are cured.

HIV Infection: Patients with HIV infection should be managed aggressively including hospitalization.

VAGINITIS

\textbf{Etiological Agent}

\textit{T. vaginalis}

Bacterial vaginosis (sometimes incorrectly called nonspecific vaginitis or \textit{G. vaginalis}-associated vaginitis). Clinical syndrome resulting from replacement of normal vaginal flora with anaerobic bacteria, \textit{G. vaginalis}, and \textit{M. hominis}.

Fungal vaginitis (predominantly \textit{Candida albicans} or occasionally by other \textit{Candida} species).

Other vaginitides (vaginitis caused by other infectious, chemical, allergenic, and physical agents).

TYPICAL CLINICAL PRESENTATION

Presentations vary from no signs or symptoms to erythema, edema, and pruritus of the external genitalia. Excessive or malodorous discharge is a common finding. Symptoms and clinical findings do not reliably distinguish among etiologies.

Male sex partners may develop urethritis, balanitis, or cutaneous lesions on penis.

PRESCRIPTIVE DIAGNOSIS

(Warrants full treatment and follow-up.)

The diagnosis of vaginitis is made by vaginal pH and microscopic examination of fresh samples of the discharge.

\textit{T. vaginalis Vaginitis}

Small, punctate cervical hemorrhages called “colpitis macularis” or “strawberry cervix” are highly specific for the diagnosis of vaginal trichomoniasis. However, this finding is present on routine speculum examination in fewer than 5% of women.

Vaginal pH level is almost always >4.5 and wet mount examination often shows many WBCs.

Bacterial Vaginosis: The clinical criteria include three of the following:

- A homogenous gray or white noninflammatory discharge that adheres to vaginal walls
- Vaginal pH level >4.5
- A fishy odor from vaginal fluid before or after addition of 10\% potassium hydroxide (KOH)
- Presence of “clue cells” on microscopic examination

Vulvovaginal Candidiasis: The presumptive criteria are the typical symptoms of vaginitis or vulvitis and microscopic identification of yeast forms (budding cells or hyphae) in Gram stain or KOH wet mount preparation of vaginal discharge.
DEFINITIVE DIAGNOSIS

T. vaginalis Vaginitis

A vaginal culture is positive for T. vaginalis, OR
Typical motile trichomonads are identified in a saline wet mount of vaginal discharge.

NAATs are currently under development but are commercially unavailable.

Bacterial Vaginosis: Gram stain demonstration of few or no lactobacilli, with a predominance of G. vaginalis plus other organisms resembling gram-negative Bacteroides sp., anaerobic gram-positive cocci, or curved rods.

Vulvovaginal Candidiasis: Culture may be useful when signs and symptoms are suggestive but when the fungus cannot be identified by direct microscopy. Therapy of apparent treatment failures is best guided by culture.

THERAPY

T. vaginalis Vaginitis

Recommended regimen: Metronidazole, 2 g PO in a single dose.

Alternative regimen: Metronidazole, 500 mg b.i.d. for 7 days.

Both regimens have cure rates of approximately 95%. Metronidazole resistance is reported, but its prevalence is not known. Metronidazole gel is associated with unacceptably high failure rates.

Bacterial Vaginosis

Recommended Regimen

Metronidazole, 500 mg PO b.i.d. for 7 days, OR
Clindamycin cream 2%, one applicator (5 g) intravaginally at bedtime for 7 days, OR
Metronidazole gel 0.75%, one applicator (5 g) intravaginally q.d. or b.i.d. for 5 days.

Alternative Regimens

Metronidazole, 2 g in a single oral dose, OR Clindamycin, 300 mg PO b.i.d. for 7 days.

Vulvovaginal Candidiasis

Intravaginal Agents

Clotrimazole, miconazole nitrate, terconazole, or butoconazole creams or vaginal tablets are recommended. Regimens range from 1 to 14 days of treatment. Several are available for over-the-counter purchase. Some contain oils that may weaken latex condoms.

Oral Agent

Fluconazole, 150-mg tablet in a single dose.

COMPLICATIONS AND SEQUELAE

Secondary excoriations are common.

Recurrent infections are common.

Bacterial vaginosis and trichomoniasis are associated with infectious complications of pregnancy, such as chorioamnionitis and puerperal infection, and with polymicrobial upper genital tract infections in nonpregnant women, such as endometritis and salpingitis. Intravaginal preparations are not recommended during pregnancy.

Vulvovaginal candidiasis in pregnancy increases the risk of neonatal oral thrush.

OTHER CONSIDERATIONS

Pregnant Women

Metronidazole may be used during pregnancy in a single dose of 2 g.

Clindamycin vaginal cream should be avoided during pregnancy.

Vulvovaginal candidiasis should be treated with topical azole therapies during pregnancy. Many experts recommend 7 days of therapy.

Follow-up:

Bacterial vaginosis: No follow-up visits are necessary.

Trichomoniasis: Follow-up is unnecessary for patients who become asymptomatic after treatment.

Vulvovaginal candidiasis: Follow-up is unnecessary for patients who respond to therapy.

Management of Sex Partners

Bacterial Vaginosis: Treatment of partners is not recommended.

Trichomoniasis: Sex partners should be treated and sexual contact should be avoided until the patient and partner are cured.
Vulvovaginal candidiasis: Treatment of sex partners is not routinely warranted unless male sex partner has balanitis.

**HIV Infection:**

Bacterial vaginosis, trichomoniasis, and vulvovaginal candidiasis: Patients with HIV infection should be managed in the same manner as patients without HIV infection.

**CONDYLOMATA ACUMINATA (GENITAL WARTS)**

**Etiological Agent**

Human papillomavirus

More than 70 types have been identified and more than 20 types infect the genital tract. Certain types (usually 6 and 11) cause exophytic benign genital and anal warts. Other types (e.g., 16, 18, 31, 33, and 35) are associated with several types of anogenital carcinomas.

**TYPICAL CLINICAL PRESENTATION**

Condylomata acuminata present as single or multiple soft, fleshy, papillary or sessile, painless growths around the anus, vulvovaginal area, penis, urethra, or perineum.

**PRESUMPTIVE DIAGNOSIS**

(Warrants full treatment and follow-up.)

A diagnosis is made on the basis of the typical clinical presentation.

Colposcopy may also aid in the diagnosis of certain cervical lesions.

Condylomata lata can be excluded by dark-field microscopy or a serological test for syphilis.

**DEFINITIVE DIAGNOSIS**

A biopsy, although usually unnecessary, can make a definitive diagnosis. Atypical lesions, in which neoplasia is a consideration, should be biopsied before initiating therapy.

A Papanicolaou (Pap) smear of cervical lesions shows typical cytological changes of koilocytosis. Direct DNA immunofluorescence staining techniques can diagnose certain types of HPV.

A hybrid capture test for detection of high-risk HPV types is now FDA-approved for triage of atypical squamous cells of undetermined significance (ASCUS). Women with ASCUS by Pap smear and a positive hybrid capture test result can be further evaluated by colposcopy. The role of HPV screening among women with low-grade squamous intraepithelial lesions is under investigation. This test is not approved for routine screening for infection with high-risk HPV.

**THERAPY**

The goal of therapy is removal of exophytic warts and alleviation of signs and symptoms, not the eradication of HPV.

**External Genital Warts**

*Patient Applied*

Podofilox 0.5% solution or gel: Apply to visible warts b.i.d. for 3 days, followed by 4 days without therapy. Repeat as necessary up to four cycles. Total area treated should not exceed 10 cm² and total volume should not exceed 0.5 mL/day.

Imiquimod 5% cream: Apply to visible warts at bedtime, three times per week. Treatment area should be washed with soap and water 6–10 hours after application.

*Provider Applied*

Cryotherapy with liquid nitrogen or cryoprobe: For vaginal warts, do not use cryoprobe (to avoid perforations), OR Podophyllin 10%–25% in compound tincture of benzoin: Wash off in 1–4 hours to reduce irritation, OR Trichloroacetic acid (TCA) or bichloracetic acid 80%–90%: Weekly for maximum of 6 weeks, OR Electrodesiccation or electrocautery.

**Cervical Warts:** Cervical dysplasia must be excluded before treatment is begun. Management is complicated and should be carried out in consultation with an expert.

**Vaginal Warts:** Cryotherapy with liquid nitrogen, TCA, or podophyllin. Podophyllin treatments should be limited to £2cm² and the treated area should be dry before speculum removal.

**Anal or Oral Warts:** Cryotherapy with liquid nitrogen or TCA or surgical removal.

**COMPLICATIONS AND SEQUELAE**

Lesions may enlarge and produce tissue destruction. Giant condyloma, although histologically benign, may stimulate carcinoma. Cervical lesions are with neoplasia.

In pregnancy, warts enlarge, are extremely vascular, and may obstruct the birth canal, necessitating cesarean section.

**OTHER CONSIDERATIONS**

**Pregnant Girls:** Use of podophyllin and podofilox are contraindicated. The safety of imiquimod during pregnancy is not established.

**Follow-up:** Not necessary after warts have responded to therapy. Annual cytological screening is recommended for women with or without genital warts.

**Management of Sex Partners:** Routine referral of partners for examination and treatment is not recommended. Partners may wish to be treated for clinical lesions. Reinfection from a partner is unusual. Use of condoms reduces but does not eliminate transmission to uninfected partners.

**HIV Infection:** Patients with HIV may not respond to therapy for HPV, as well as persons without HIV. Cervical dysplasia may progress more rapidly among
HIV-infected persons.

**HERPES GENITALIS**

**Etiological Agents**

HSV types 1 and 2

**TYPICAL CLINICAL PRESENTATION**

Single or multiple vesicles appear anywhere on the genitalia. Vesicles spontaneously rupture to form shallow ulcers that may be very painful. Lesions resolve spontaneously without scarring. The first occurrence is termed initial infection (mean duration, 12 days). Subsequent, usually milder, occurrences are termed recurrent infections (mean duration, 4–5 days). The interval between clinical episodes is termed latency. Viral shedding occurs intermittently and unpredictably during latency.

**PRE SUMPTIVE DIAGNOSIS**

(Warrants full treatment and follow-up.)

When typical genital lesions are present or a pattern of recurrence has developed, herpes infection is likely. A presumptive diagnosis is further supported by direct identification of multinucleated giant cells with intranuclear inclusions in a clinical specimen prepared by Pap smear or other histochemical stain; or typical HSV morphology by electron microscopy; or detection of HSV antigens by monoclonal antibody detection systems. Primary HSV infection is presumed if an initially negative serological titer becomes significantly detectable in convalescent serum.

Several sensitive and specific type-specific relatively rapid screening tests are commercially available or under development. These test results are usually negative until 3 weeks after initial infection.

**DEFINITIVE DIAGNOSIS**

An HSV tissue culture demonstrates the characteristic cytopathic effect after inoculation of a specimen from the cervix, the urethra, or the base of a genital lesion. The isolates can be identified as type 1 or type 2 by fluorescent antibody, neutralization, or other serological techniques.

**THERAPY**

**First Clinical Episode of Genital Herpes**

Acyclovir, 400 mg PO t.i.d. for 7–10 days, OR
Acyclovir, 200 mg PO 5 times daily for 7–10 days, OR
Famciclovir, 250 mg PO t.i.d. for 7–10 days, OR
Valacyclovir, 1 g PO b.i.d. for 7–10 days.

Treatment may be extended if healing is incomplete after 10 days of therapy.

**First Clinical Episode of Herpes Proctitis**

Acyclovir, 400 mg PO 5 times a day for 10 days or until clinical resolution is attained.

Famciclovir and valacyclovir may also be effective, but clinical experience is lacking.

**Episodic Treatment of Recurrent Episodes of Genital Herpes and Herpes Proctitis:** When treatment is started during prodrome or within 1 day of onset of lesions, many patients experience shortened duration of symptoms.

Acyclovir, 400 mg PO t.i.d. for 5 days, OR
Acyclovir, 200 mg PO 5 times daily for 5 days, OR
Acyclovir, 800 mg PO b.i.d. for 5 days, OR
Famciclovir, 125 mg PO b.i.d. for 5 days, OR
Valacyclovir, 500 mg PO b.i.d. for 3–5 days, OR
Valacyclovir, 1.0 g PO once a day for 5 days.

**Daily Suppressive Therapy of Genital Herpes and Herpes Proctitis:** Daily suppressive therapy can reduce frequency of HSV recurrences by at least 75% with patients with six or more recurrences per year.Suppressive therapy reduces but does not eliminate viral shedding.

Acyclovir, 400 mg PO b.i.d., OR
Famciclovir, 250 mg PO b.i.d., OR
Valacyclovir, 250 mg PO b.i.d., OR
Valacyclovir 1 mg PO q.d.

**COMPLICATIONS AND SEQUELAE**

**Boys and Girls:** Neuralgia, meningitis, ascending myelitis, urethral strictures, and lymphatic suppuration may occur.

**Neonates:** Virus from an active genital infection may be transmitted during vaginal delivery, causing neonatal herpes infection, which has a high case fatality rate, and many survivors have ocular or neurological sequelae.

**OTHER CONSIDERATIONS**

**Pregnant Women:** The safety of systemic acyclovir and valacyclovir during pregnancy has not been established. Girls who receive acyclovir or valacyclovir during pregnancy should be reported to a registry at 800-722-9292, ext. 38465.

**Management of Sex Partners:** Patients should abstain from sexual activity while lesions are present. Sexual transmission of HSV can occur during periods without evidence of lesions. The use of condoms should be encouraged during all sexual contact. Sex partners may require evaluation and counseling.

**HIV Infection:** HSV lesions are common among HIV-infected patients. Intermittent or suppressive therapy with oral acyclovir may be required.

**SYphilis**

**Etiological Agent**
**TYPICAL CLINICAL PRESENTATION**

**Primary:** The classic chancre is painless, indurated, and located at the site of exposure. Genital chancres are often accompanied by tender inguinal lymphadenopathy.

**Secondary:** Patients may have a macular, maculopapular, or papulosquamous skin rash. Other signs include mucous patches and condylomata lata.

**Tertiary:** Patients have cardiac, neurological, ophthalmic, auditory, or gummatous lesions.

**Latent:** Patients are without clinical signs.

**PRESumptive DIAGNOSIS**

(Warrants full treatment and follow-up.)

Presumptive diagnosis relies on both nontreponemal serological tests for syphilis (STS) (e.g., Venereal Disease Research Laboratories or rapid plasma reagin) and treponemal tests (fluorescent treponemal antibody-absorption or microhemagglutination- T. pallidum test). Nontreponemal test antibody titers usually correlate with disease activity.

**Primary:** Patients have typical lesions and either a newly positive STS or STS titer at least fourfold greater than the last, or syphilis exposure within 90 days of lesion onset.

**Secondary:** Patients have the typical clinical presentation and a strongly reactive STS.

**Latent:** Patients have serological evidence of untreated syphilis without clinical signs.

**HIV-infected patients:** When clinical findings suggest syphilis is present, but serological test results are negative, alternative tests, such as biopsy, dark-field examination, and DFA staining of lesion material, should be employed.

**DEFINITIVE DIAGNOSIS**

Demonstration of characteristic spirochetes with dark-field microscopy of serous transudate from genital lesions. DFA of material from a chancre, regional lymph node, or other lesion.

**THERAPY**

**Primary and Secondary Syphilis:** Penicillin G benzathine, 2.4 million units IM in a single dose

*Penicillin-allergic Patients*

Doxycycline, 100 mg PO b.i.d. for 2 weeks, OR

Tetracycline, 500 mg PO q.i.d. for 2 weeks.

**Latent Syphilis**

*Early latent (<1 year) syphilis:** Penicillin G benzathine, 2.4 million units IM in a single dose.

*Late latent (>1 year) syphilis or latent syphilis of unknown duration:** Penicillin G benzathine, 7.2 million units total, administered as three doses of 2.4 million units IM each at 1-week intervals.

**Late Syphilis:** Patients with gumma or cardiovascular syphilis but not neurosyphilis: Penicillin G benzathine, 7.2 million units total, administered as three doses of 2.4 million units IM at 1-week intervals.

**Neurosyphilis**

*Recommended regimen:* Aqueous crystalline penicillin G, 18–24 million units daily, administered as 2–4 million units IV q4h for 10–14 days.

*Alternative regimen:* 2.4 million units procaine penicillin IM daily, plus probenecid 500 mg PO q.i.d., both for 10–14 days.

**COMPLICATIONS AND SEQUELAE**

Both late syphilis and congenital syphilis are complications, because they are preventable with prompt diagnosis and treatment of early syphilis. Sequelae of late syphilis include neurological (general paresis, tabes dorsalis, and focal neurological signs), cardiovascular syphilis (thoracic aortic aneurysm, aortic insufficiency), and localized gumma formation.

**OTHER CONSIDERATIONS**

**Pregnant Women:** Pregnant girls should receive the same therapy as listed earlier, except that tetracycline, doxycycline, and erythromycin should not be used. Pregnant girls with a history of penicillin allergy should be skin tested, desensitized if allergy is documented, and then treated with penicillin.

**Follow-up:** Patients should be reexamined clinically and serologically at 3 and 6 months for primary and secondary syphilis and 6 and 12 months for latent syphilis.STS results become negative or reactive only in low titers (<1:8) in most successfully treated patients.

**Management of Sex Partners:** Persons exposed to a patient with primary, secondary, or early latent syphilis within 90 days should be treated presumptively. Those exposed >90 days should be treated presumptively if serological tests are not available immediately or follow-up is uncertain. Partners considered at risk are those exposed within 3 months plus duration of symptoms for primary syphilis, within 6 months plus duration of symptoms for secondary syphilis, and within 1 year for early latent syphilis.

**HIV Infection:** Unusual serological response may occur in HIV-infected persons. Penicillin regimens should be used whenever possible. Some authorities recommend cerebrospinal fluid examination or treatment with a regimen appropriate for neurosyphilis for all patients infected with syphilis and HIV. Patients should be followed clinically and serologically at 1, 2, 3, 6, 9, and 12 months after therapy.

**CHANCROID**
Etiological Agent

**Haemophilus ducreyi**

A gram-negative bacillus with rounded ends, commonly observed in small clusters along strands of mucus. On culture, the organism tends to form straight or tangled chains.

**TYPICAL CLINICAL PRESENTATION**

Usually a single (but sometimes multiple), superficial, painful ulcer surrounded by a erythematous halo. Ulcers may also be necrotic or severely erosive with ragged serpiginous borders. Accompanying adenopathy is usually unilateral. A characteristic inguinal bubo occurs in 25% to 60% of cases.

**PRESUMPTIVE DIAGNOSIS**

(Warrants full treatment and follow-up.)

Chancroid is the third most common sexually transmitted cause of genital ulcer in the United States, although it is far less frequently seen than genital herpes or primary syphilis. Presumptive diagnosis depends on a clinically consistent lesion, a negative dark-field examination of lesion fluid, and absence of serological evidence of syphilis.

**DEFINITIVE DIAGNOSIS**

Culture identification of *H. ducreyi*.

**THERAPY**

Recommended Regimens

- Azithromycin, 1 g PO in a single dose, OR
- Ceftriaxone, 250 mg IM in a single dose, OR
- Ciprofloxacin, 500 mg PO b.i.d. for 3 days, OR
- Erythromycin base, 500 mg PO t.i.d. times daily for 7 days.

**COMPLICATIONS AND SEQUELAE**

Systemic spread is not known to occur.

Lesions may become secondarily infected and necrotic.

Buboes may rupture and suppurate, resulting in fistulae.

Ulcers on the prepuce may cause paraphimosis or phimosis.

**OTHER CONSIDERATIONS**

**Pregnant Women:** Safety of azithromycin during pregnancy has not been established. Ciprofloxacin is contraindicated during pregnancy.

**Follow-up:** Successfully treated ulcers are clinically improved by 7 days after institution of therapy. If the condition does not improve, the clinician should consider whether antimicrobials were taken as prescribed; the *H. ducreyi* is resistant to the prescribed antimicrobial; the diagnosis is correct; there is a coinfection with another STD; or the patient is infected with HIV.

**Management of Sex Partners:** Partners who had contact within 10 days before the onset of symptoms should be examined and treated.

**HIV Infection:** Patients with HIV infections should be closely monitored and may require longer courses of therapy.

---

**LYMPHOGRANULOMA VENEREUM**

**Etiological Agent**

*C. trachomatis*

An obligate intracellular organism of immunotypes L1, L2, or L3.

**TYPICAL CLINICAL PRESENTATION**

The primary lesion of lymphogranuloma venereum (LGV) is a 2- to 3-mm painless vesicle or nonindurated ulcer at the site of inoculation. Patients commonly fail to notice this primary lesion. Regional adenopathy follows a week to a month later and is the most common clinical presentation.

Sensation of stiffness and aching in the groin, followed by swelling of the inguinal region, may be the first indications of infection for most patients. Adenopathy may subside spontaneously or proceed to the formation of abscesses that rupture to produce draining sinuses or fistulae.

**PRESUMPTIVE DIAGNOSIS**

(Warrants full treatment and follow-up.)

The LGV complement-fixation test result is typically positive, with titers of 1:64 or higher. Cross-reactions due to other chlamydial infections may be misleading. Because the sequelae of LGV are serious and preventable, treatment should be provided pending laboratory confirmation.

**DEFINITIVE DIAGNOSIS**

A definitive diagnosis requires isolation of *C. trachomatis* from an appropriate specimen and confirmation of the isolate as an LGV immunotype. However, such laboratory diagnostic capabilities are not widely available.

**THERAPY**
**Recommended regimen:** Doxycycline, 100 mg PO b.i.d. for 21 days.

**Alternative regimen:** Erythromycin, 500 mg PO q.i.d. for 21 days.

**COMPLICATIONS AND SEQUELAE**

Dissemination may occur with nephropathy, hepatomegaly, or phlebitis.

Large polyoid swellings of the vulva, anal margin, or rectal mucosa may occur.

The most common severe morbidity results from rectal involvement; perianal abscess and rectovaginal or other fistulae are early consequences, and rectal stricture may develop 1–10 years after infection.

**OTHER CONSIDERATIONS**

**Pregnant Women:** Pregnant patients should be treated with the erythromycin regimen.

**Follow-up:** Patients should be followed clinically until signs and symptoms have resolved.

**Management of Sex Partners:** Persons having had sexual contact with a patient who has LGV within 30 days before onset of the patient's symptoms should be examined and treated.

**HIV Infection:** Patients with HIV infection are managed in the same manner as patients without HIV infection.

---

**MOLLUSCUM CONTAGIOSUM**

**Etiological Agent**

*Molluscum contagiosum virus*

The largest DNA virus of the poxvirus group.

**TYPICAL CLINICAL PRESENTATION**

Both sexual and nonsexual transmission modes are likely. Lesions are 1–5 mm, smooth, rounded, shiny, firm, flesh-colored to pearly white papules with umbilicated centers. They are most commonly seen on the trunk and anogenital. Itching or tenderness is occasionally noted but most patients are asymptomatic. Extensive skin involvement is seen in immunocompromised hosts, particularly those with advanced HIV disease. Dissemination does not occur.

**PREVIOUS DIAGNOSIS**

(Warrants full treatment and follow-up.)

Usually diagnosed on the basis of the typical clinical presentation.

**DEFINITIVE DIAGNOSIS**

Microscopic examination of lesions or lesion material reveals the pathognomonic molluscum inclusion bodies.

**THERAPY**

Lesions resolve spontaneously; most within 2 months. However, they may be removed by curettage after cryoanesthesia.

Caustic chemicals (podophyllin, TCA, silver nitrate) and cryotherapy (liquid nitrogen) have been used successfully. Self-applied podophyllotoxin may also be effective. Recurrence is reported in 15%–35% of cases.

**COMPLICATIONS AND SEQUELAE**

Secondary infection, usually with *Staphylococcus*, occurs.

Lesions rarely attain a size >10 mm in diameter.

**OTHER CONSIDERATIONS**

**Pregnant Women:** Podophyllin should be avoided during pregnancy.

**Follow-up:** Patients should return for evaluation 1 month after treatment so any new lesions can be removed.

**Management of Sex Partners:** Sex partners should be examined.

**HIV Infection:** Patients with HIV infection should be managed in the same manner as patients without HIV infection.

---

**PEDICULOSIS PUBIS**

**Etiological Agent**

*Pthirus pubis* (pubic or crab louse)

A grayish ectoparasite that is 1–4 mm long with segmented tarsi and claws for clinging to hairs.

**TYPICAL CLINICAL PRESENTATION**

Symptoms range from slight discomfort to intolerable itching. Erythematous papules, nits, or adult lice clinging to pubic, perineal, or perianal hairs are present and often noticed by patients.
**PRESumptive Diagnosis**

(Warrants full treatment and follow-up.)

A presumptive diagnosis is made when a patient with a history of recent exposure to pubic lice has pruritic, erythematous macules, papules, or secondary excoriations in the genital area.

**Definitive Diagnosis**

A definitive diagnosis is made by finding lice or nits attached to genital hairs.

**Therapy**

- Permethrin 1% creme rinse applied to affected areas and washed off after 10 minutes, OR
- Lindane 1% shampoo applied for 4 minutes and then thoroughly washed off (not recommended for pregnant or lactating women or for children younger than 2 years), OR
- Pyrethrins with piperonyl butoxide applied to the infested area and washed off after 10 minutes.

The recommended regimens should not be applied to the eyes. Involvement of the eyelashes should be treated by applying occlusive ophthalmic ointment to the eyelid margins b.i.d. for 10 days.

Clothing and linen should be disinfected by washing them in hot water, by dry-cleaning them, or by removing them from human exposure for at least 72 hours.

**Complications and Sequelae**

Secondary excoriations; lymphadenitis; pyoderma

**Other Considerations**

- **Pregnant Women:** Lindane is contraindicated in pregnant or lactating women.
- **Follow-up:** Patients should be evaluated after 1 week if symptoms persist. If lice are found or if eggs are observed at the hair-skin junction, re-treatment may be necessary.
- **Management of Sex Partners:** Sex partners within the last month should be treated.
- **HIV Infection:** Patients with HIV infection are managed in the same manner as patients without HIV infection.

**Scabies**

**etiological Agent**

*Sarcoptes scabiei*

The female is 0.3–0.4 mm; the male is somewhat smaller. The female burrows under the skin to deposit eggs.

**Typical Clinical Presentation**

Symptoms include itching, often worse at night, and the presence of erythematous, papular eruptions. Excoriations and secondary infections are common. Reddish-brown nodules are caused by hypersensitivity and develop 1 or more months after infection has occurred. The primary lesion is the burrow. When not obliterated by excoriations, burrows are usually seen on the fingers, penis, and wrists.

**PRESumptive Diagnosis**

(Warrants full treatment and follow-up.)

The diagnosis is often made on clinical grounds alone. Exposure to a person with scabies within the previous 2 months supports the diagnosis.

**Definitive Diagnosis**

Definitive diagnosis is made by microscopic identification of the mite or its eggs, larvae, or feces in scrapings from an elevated papule or burrow.

**Therapy**

- **Recommended Regimen:** Permethrin cream 5% applied to all areas of the body from the neck down and washed off after 8–14 hours.

**Alternative Regimens**

- Lindane (1%) 1 ounce of lotion or 30 g of cream applied thinly to all areas of the body from the neck down and washed off thoroughly after 8 hours. Lindane should not be used after a bath and should not be used by persons with extensive dermatitis, pregnant or lactating women, and children younger than 2 years. Not recommended for pregnant or lactating women, or infants and young children. OR
- Ivermectin 200 µg/kg orally, repeated in two weeks.

**Complications and Sequelae**

Secondary bacterial infection occurs, particularly with nephritogenic strains of streptococci. Norwegian or crusted scabies (with up to 2 million adult mites in the crusts) is a risk for patients with neurological defects and the immunologically compromised.

**Other Considerations**

- **Pregnant Women:** Lindane is contraindicated in pregnant or lactating women.
- **Follow-up:** Pruritus may persist for several weeks. Re-treatment should be considered in patients who are symptomatic after 1 week, particularly if live mites are observed.
Management of Sex Partners: Sex partners and close personal or household contacts within the last month should be examined and treated.

HIV Infection: Patients with HIV infection are managed in the same manner as patients without HIV infection.

HEPATITIS B

Etiological Agent

Hepatitis B virus (HBV)

A DNA virus with multiple antigenic components.

Sexual transmission accounts for an estimated one third to two thirds of the estimated 200,000–300,000 new HBV infections that occur annually in the United States.

TYPICAL CLINICAL PRESENTATION

Hepatitis B is clinically indistinguishable from other forms of hepatitis. Most infections are clinically inapparent. Clinical symptoms and signs include various combinations of anorexia, malaise, nausea, vomiting, abdominal pain, and jaundice. Skin rashes, arthralgias, and arthritis can also occur.

PREVIOUS DIAGNOSIS

(Warrants full treatment and follow-up.)

HBV infection is clinically indistinguishable from other forms of viral hepatitis and many times from hepatitis caused by toxins or drugs. The diagnosis should be considered in a symptomatic patient with symptoms suggestive of an acute viral illness and with an occupational exposure or sexual history that places the patient in a high-risk group.

Groups at high risk of acquiring infection include immigrants or refugees from areas of high HBV endemicity, patients in institutions for the mentally retarded, persons with multiple sex partners, users of illicit parenteral drugs, men who have sex with men, household contacts of HBV carriers, and patients of hemodialysis units.

DEFINITIVE DIAGNOSIS

Serodiagnosis of HBV infection is the only method for clinicians to reach a definitive diagnosis. A positive result for hepatitis B surface antigen (HBsAg) indicates active infection with HBV, either acute hepatitis B or the chronic carrier state. Hepatitis B e antigen (HBeAg) correlates with infectivity. Antibody to HBsAg (anti-HBs) usually indicates past infection with present immunity.

THERAPY

No specific therapy is available for the various types of acute hepatitis, whether sexually transmitted or not. Vaccination is recommended for all persons with multiple sex partners within the past 6 months, intravenous drug users, men and women diagnosed as having recently acquired another STD, and residents of correctional or long-term care facilities.

For immunization recommendations, refer to Chapter 31.

COMPLICATIONS AND SEQUELAE

Long-term sequelae include chronic persistent and chronic active hepatitis, cirrhosis, hepatocellular carcinoma, hepatic failure, and death. Rarely, the course may be fulminant with hepatic failure, resulting in early death. Infectious chronic carriers may be completely asymptomatic.

OTHER CONSIDERATIONS

Oral contraceptives are contraindicated for women with active hepatitis.

Pregnant Women: Pregnancy is not a contraindication to HBV or hepatitis B immune globulin (HBIG) vaccine administration.

Management of Sex Partners: Susceptible persons who have been exposed to HBV through sexual contact with a person who has acute or chronic HBV infection should receive postexposure prophylaxis. This should include 0.06 mL/kg of HBIG in a single IM dose within 14 days of their last exposure. This should be followed with the standard three-dose immunization series with HBV vaccine.

HIV Infection: Patients with HIV infection who have HBV are more likely to develop a chronic HBV state. HIV infection may also impair the response to HBV vaccine. HIV-infected persons should be tested for anti-HBs 1–2 months after the third vaccine and revaccinated with one or more doses in those who have not responded.

ENTERIC INFECTIONS

Etiological Agent

Proctitis: N. gonorrhoeae, C. trachomatis, T. pallidum, and HSV.

Proctocolitis: Campylobacter sp., Shigella sp., Entamoeba histolytica, and rarely C. trachomatis.

Enteritis: Giardia lamblia. Among HIV-infected patients, others include cytomegalovirus (CMV), Mycobacterium avium-intracellulare, Salmonella sp., Cryptosporidium, microsporidia, and Isospora.

These are particularly common among persons who participate in anal intercourse (proctitis) or whose sexual practices include oral-fecal contact (enteritis).

TYPICAL CLINICAL PRESENTATION

Infections are frequently asymptomatic or minimally symptomatic. Symptoms include the following:

Proctitis: Anorectal pain, tenesmus, and rectal discharge.

Proctocolitis: Symptoms of proctitis plus diarrhea or abdominal cramps.

Enteritis: Diarrhea and abdominal cramping.

PREVIOUS DIAGNOSIS
The typical clinical findings suggest enteric infection. Examination of a fresh stool specimen can be helpful. The finding of WBCs on direct microscopy of a suspension of fresh stool or the finding of occult or grossly bloody stools supports the diagnosis.

DEFINITIVE DIAGNOSIS
Definitive diagnostic tests vary according to the agent and site of infection involved.

THERAPY
Treatment of proctitis and enteritis should be based on etiological diagnosis. Some asymptomatic infected individuals for whom anal-oral contact is a sexual practice should be treated in accordance with recommendations for symptomatic individuals, as should persons whose work or social situation is associated with a likelihood of transmission (e.g., food handlers, hospital workers, day-care center employees). Until laboratory test results are available, persons with acute proctitis who have recently practiced receptive anal intercourse and have either anorectal pus on examination or PMN leukocytes on a Gram stain should receive treatment for anogential gonorrhea and doxycycline (100 mg PO b.i.d. for 7 days).

COMPLICATIONS AND SEQUELAE
Complications and sequelae vary with the disease agent, health of the host, therapy, and other factors. Spontaneous cures are common. Morbidity may be severe, requiring hospitalization and intravenous hydration. Infections may become systemic (such as gram-negative septicemia) or distantly localized (amebic hepatic cyst). Some infections may rarely be fatal (hepatitis A, disseminated bacterial disease).

OTHER CONSIDERATIONS
Follow-up: Follow-up should be based on severity of clinical symptoms and specific etiological agent involved.

Management of Sex Partners: Sex partners should be evaluated for any diseases diagnosed in the index patient.

HIV Infection: Patients with HIV infection should be managed in the same manner as patients without HIV infection. HIV-infected patients are at risk for infections not commonly found in non-HIV-infected patients.

HIV infections and Acquired Immunodeficiency Syndrome

<table>
<thead>
<tr>
<th>Etiological Agent</th>
<th>HIV-1 or HIV-2</th>
</tr>
</thead>
</table>

HIV-1 and HIV-2 are members of one of seven genera of retroviruses.

TYPICAL CLINICAL PRESENTATION
The range of symptoms associated with HIV infection extends from an acute illness shortly after infection to the full clinical syndrome of acquired immunodeficiency syndrome (AIDS). Acute HIV infection includes a mononucleosis-like syndrome consisting of headache, myalgia, sore throat, rash, diarrhea, fever, and lymphadenopathy. The acute HIV retroviral syndrome is reported 1 to 3 weeks after initial infection and resolves within a few weeks. This is a period of high levels of viral replication and viremia, with great potential for transmission. A latent or asymptomatic stage, lasting from a year to a decade or more, often follows. Disease progression appears inevitable, with ongoing destruction of the host immune system, followed by wasting and weight loss, symptoms specific to opportunistic infections (e.g., shortness of breath and cough from Pneumocystis carinii pneumonia [PCP] infection), or purple to bluish skin lesions associated with Kaposi sarcoma. Virtually all organ systems are affected by advanced HIV disease.

PREUMPTIVE DIAGNOSIS
Presumptive diagnosis of HIV infection is made usually by clinical evidence, supported by tests for antibodies to HIV infection. Screening tests are based on enzyme immunoassay, with positive results confirmed by immunoblot (Western blot). Rapid serological tests are now available that provide results within 15 to 30 minutes, although these tests always require confirmation by immunoblot. Screening may also be done with either saliva or urine. These tests increase the ease of screening, but their results should be confirmed by immunoblot. Clinicians and patients should keep in mind that the median time between infection and confirmed seropositivity is 3 months and may be as long as 6 months. Retesting is recommended when suspicion is high, particularly when the clinical presentation is consistent with the acute HIV syndrome.

DEFINITIVE DIAGNOSIS
Currently, isolation of the virus from body fluids is the most highly specific means to make a definitive diagnosis of HIV infection. Only very few research laboratories have the technology to perform viral isolation. Results from reactive enzyme immunoassay tests, confirmed by immunoblot (Western blots) or other confirmatory tests, are considered diagnostic. Indeterminate tests are usually resolved by retesting, combined with examination of the pattern of the indeterminate Western blot and a careful risk-assessment interview.

THERAPY
To date, no treatments eradicate either HIV-1 or HIV-2. A number of antiretroviral drugs are used to limit viral replication, restore immunocompetence, and delay onset of AIDS-related illness.

Acute Retroviral Syndrome
Immediate initiation of antiretroviral treatments improves prognosis of HIV-related infection. The optimal regimen is not known. Single-drug therapy with zidovudine may be effective, but many experts recommend two nucleoside reverse-transcriptase inhibitors and a protease inhibitor.

Antiretroviral therapy is central to the treatment of HIV disease. Three classes of antiretroviral agents are available and are typically used in combination. Therapy can be monitored with highly sensitive viral load assays. Tuberculin skin testing, review of vaccination status, provision of pneumococcal and influenza vaccines, and serological tests for syphilis are all important aspects of comprehensive therapy. PCP prophylaxis with trimethoprim-sulfamethoxazole, dapsone, or aerosolized pentamidine should be instituted for adolescents and adults with <200 CD4-positive T cells/mL, or after an initial episode of PCP. Prophylaxis should be continued for the lifetime of the patient. Prophylaxis for individuals seropositive for Toxoplasma gondii and CD4+ counts <100 T cells/mL includes trimethoprim-sulfamethoxazole, or dapsone with pyrimethamine.

COMPLICATIONS AND SEQUELAE
Most people with HIV will eventually have symptoms related to the infection. Aggressive antiretroviral therapy improves disease-free survival, but relapse is expected.
when therapy is stopped. Many HIV-infected persons may have years even decades before development of AIDS-related condition.

OTHER CONSIDERATIONS

**Management of Sex Partners:** Sex partners should be notified either by their partners or through a referral to health department partner-notification programs. Partners should receive counseling and testing.
Gonorrhea is one of the most important sexually transmitted diseases (STDs) in adolescents because of its high incidence and serious complications.

**ETIOLOGY**

Gonorrhea is an STD caused by *Neisseria gonorrhoeae*, which has the following characteristics:

1. The organisms are nonmotile, nonspore-forming cocci, occurring in pairs, with abutting flattened sides.
2. The organisms are gram-negative and are usually located within or associated with polymorphonuclear (PMN) leukocytes.
3. The organisms grow optimally at 35°C–37°C, with an ambient carbon dioxide concentration of 5%.
4. *N. gonorrhoeae* is an oxidase-positive diplococcus, which can be differentiated from other *Neisseria* species in that it can only use glucose, lactate, and pyruvate but not other carbohydrates. Iron is mandatory for growth of this organism.
5. Types of organisms: There are >70 different strains. *N. gonorrhoeae* species have been differentiated by several characteristics:
   a. Presence or absence of pili: Pili increase adhesion of gonococci to tissues and are associated with small colonies and increased virulence.
   b. Opaque or transparent: Opaque growing colonies have an outer-membrane protein, opacity-associated protein (Opa), formerly called protein II. Opa proteins increase cell adherence in colonies and gonococcal adhesion to host cells.
   c. Auxotyping: This is determined by the nutritional requirements of the organism including amino acids, purines, and pyrimidines. Different auxotypes are resistant to killing in human serum; more likely to cause asymptomatic infection in males; and more likely to disseminate.
   d. Serotyping: This technique measures the ability of the organism to react to monoclonal antibodies to outer-membrane protein I (Por). There are two serogroups, PorA and PorB.
   e. Genotyping: This technique uses DNA analysis techniques to perform Opa typing, which can detect sequence variations between strains.

**EPIDEMIOLOGY**

**Incidence**

1. Gonorrhea remains one of the most common reportable diseases in the United States. Approximately 350,000 cases are reported per year. However, reported cases may only represent £50% of all cases. The number of cases declined 72% between 1975 and 1998. Adolescents (age 10–19 years) and young adults (age 20–24 years) continue to be at high risk for acquiring this disease. As detailed later in this chapter, the rates of gonorrhea are far from uniform and vary dramatically among adolescents from different racial/ethnic backgrounds and practice settings.
2. Sixty percent of all cases in men and women occur between the ages of 15 and 24. The number of cases is equally divided at 30% between the 15–19-year-old and 20–24-year-old age groups. Adolescent girls age 15–19 years account for almost 40% of reported cases in females. In contrast, adolescent boys age 15–19 years only account for 20% of reported cases in males, whereas men age 20–24 years account for 30% of the cases.
3. Although overall for both sexes, the 20–24-year-old and 15–19-year-old age groups have approximately the same number of cases, almost twice as many individuals are sexually active in the 20–24-year-old age group as in the 15–19-year-old age group. When the incidence rate is corrected for this bias, the incidence in sexually active 15–19-year-olds is twice that of 20–24-year-olds.
4. The reasons for the high incidence in 15–19-year-old adolescents include biological and psychosocial factors.
   a. Psychosocial factors
      - The increased rates of sexual activity and decreased age at first intercourse
      - The lack of consistent use of condoms, spermicidal agents, and diaphragms, which can provide some protection against STDs
      - Lack of clinical services in settings convenient to adolescents or environments that can ensure confidentiality
      - The high incidence of asymptomatic carriers and the low use by adolescents of preventive medical care to detect these carriers
      - The lack of compliance with therapy by the patient and his or her partner
   b. Biological factors
      - The larger degree of cervical ectopy in adolescents: *N. gonorrhoeae* preferentially infects columnar epithelial cells. Adolescents have more of this tissue exposed on the ectocervix.
5. Seasonal variation: Higher incidence rates occur in late summer.
6. Prevalence: The prevalence rates vary on routine screening for gonorrhea, depending on both the reporting facility and possibly the bias toward individuals who seek care at public STD clinics, in particular certain racial and ethnic minorities. Adolescents from private practice settings have lower rates than those from inner-city health clinics.
   a. STD clinics: *15%* are positive for gonorrhea.
   b. Health departments: About *3%* are positive for gonorrhea.
   c. Selected family planning clinics (27 nationally, 15–24-year-old women): 0%–5.2%.
   d. Job Corps (12 states, 16–24-year-old women): 1.4%–8.4%.
   e. Student health centers: <1%–2% are positive for gonorrhea.
   f. Juvenile detention facilities (girls): 3%–18%.
   g. Adolescent clinics: Approximately 3–6% are positive for gonorrhea.
7. Correlation with drug use: Schwarcz et al. (1992) found that 32% of female adolescents with gonorrhea in San Francisco had received money or drugs in exchange for sex, compared with no cases of gonorrhea in a control group of female adolescents who had not reported exchanging sex for drugs or money. In addition, 89% of the teens who had received money or drugs in exchange for sex reported using crack cocaine.
8. Trends: Although the number of cases and incidence have fallen in the past 10 years to less than half the cases in 1978 (Table 61.1), there was a reversal in this trend in 1998.
9. Race: In 1998, about 77% of the reported cases occurred in the African-American population. Incidence rates in the African-American population have fallen since the late 1970s and early 1980s from >2,000 cases per 100,000 to about 862 per 100,000 in 1998, still about six times the overall national rate. The incidence in Hispanic (74/100,000), white (28/100,000), and other populations are each <100 per 100,000. However, when focusing on adolescents, one finds the rates more alarming. In 1998, there were 3,852 per 100,000 cases in 15–19-year-old black females and 2,076 per 100,000 cases in 15–19-year-old black males. These rates are 23 times higher than those for white adolescents in the same age group. The rates among 20–24-year-old African-Americans is 27 times higher than those for 20–24-year-old whites.

10. Geography: The incidence rates of gonorrhea vary widely by state, from rates of 200–300 per 100,000 in each of the southeastern states except Florida (130/100,000) and Maryland (221/100,000). Rates per 100,000 were 169 in Texas and 392 in Mississippi. States with rates of 10 per 100,000 or less include Montana, Maine, Vermont, New Hampshire, and Wyoming. Examples of rates per 100,000 from other states include the following:

**Host**
Humans are the only natural host for *N. gonorrhoeae*.

**Transmission**
Transmission is virtually exclusively through oral, vaginal, or anal sexual contact. The exception is gonococcal ophthalmia, which usually occurs in newborns but has been reported in physicians, laboratory technicians, and the general adult population presumably when direct contact of the organism with the eye through hand transmission has occurred. Transmission risk from a single exposure is higher from males to females than from females to males.

**PATHOPHYSIOLOGY**

*N. gonorrhoeae* causes disease by direct invasion and spread on mucosal and glandular structures lined by columnar or cuboidal noncornified epithelium. Adherence of the organism to the mucosa, mediated by pili and surface proteins, is followed by mucosal cell damage and submucosal invasion. Although gonococci do not attach to ciliated cells, ciliary cell function is impaired by gonococcal lipooligosaccharide (LOS) (toxin activity). The results are an inflammatory response characterized by edema, a PMN leukocyte response, submucosal microabscesses, and purulent exudate. Transmission to the upper genital tract may occur via adherence to sperm or with refluxed blood during menses. Blood is also a good culture medium for *N. gonorrhoeae*. The loss of the endometrium and cervical mucous plug during menses may also contribute to the spread into the upper genital tract.

**Virulence**

The virulence of the infection may be related to certain characteristics of the organism.

1. Pili: Gonococcal pili are the main mediators of adherence of the organism to epithelial cells. Organisms with pili attach more successfully than nonpiliated forms to columnar epithelial cells and neutrophils. Pili also decrease the ability of neutrophils to ingest and kill the organism.

2. Colony morphology: Cells with Opa have an “opaque” colony morphology, whereas strains without Opa are “transparent.” Opaque colonies are more often found in specimens from males with gonococcal urethritis and in cervical isolates obtained from females at about midcycle. Transparent colonies appear to represent the invasive form of *N. gonorrhoeae* and are usually found in cervical cultures from women around the time of menses.

3. Auxotype: Growth requirements of *N. gonorrhoeae* organisms may relate to pathogenicity. Strains requiring arginine, hypoxanthine, and uracil are associated with asymptomatic urethral infection in males, disseminated gonococcal infection (DGI), and increased susceptibility to penicillin. The strains that do not require any substrates are called prototrophic.

4. Other virulence factors
   a. Reduction-modifiable protein (Rmp): Rmp is found on pathogenic gonococci and is a target for blocking antibodies that prevent bactericidal activity of serum antibodies.
   b. LOS: Depending on the type of LOS on the surface of the gonococcus, the organism has different abilities to either invade epithelial cells or resist serum antibodies.
   c. Other possible molecular mechanisms: Immunoglobulin A (IgA)1 protease, peptidoglycan, and iron-repressible proteins

**Clinical Manifestations**

Clinical manifestations are similar to those caused by *Chlamydia trachomatis*, and both *C. trachomatis* and *N. gonorrhoeae* occur frequently together in the same individual. Susceptible sites are usually mucosal columnar epithelial areas. Both organisms produce urethritis in males and dysuria-pyuria syndrome and cervicitis in females. In both sexes, proctitis and conjunctivitis can occur. Both *N. gonorrhoeae* and *C. trachomatis* cause epididymitis, Bartholinitis, endometritis, salpingitis, and perihepatitis (Fitz-Hugh-Curtis syndrome). In prepubertal females, both organisms can infect vaginal epithelium, causing vaginitis. In addition, both organisms can cause a systemic arthritis-dermatitis syndrome and conjunctivitis. The spectrum of gonococcal infections includes the following:

1. Asymptomatic infections: Asymptomatic urethral and cervical infections may persist for months if untreated. Asymptomatic infection in women ranges from 25%–90% depending on the population. In a study of males in a juvenile detention facility, 84% of those with gonorrhea by ligase chain reaction (LCR), self-reported having no symptoms (Pack et al., 2000). In another study of symptoms in males diagnosed with gonorrhea, 10.2% who were evaluated did not have symptoms (Sherard et al., 1996). Studies have shown that <10% of rectal infections are symptomatic, but these studies have been criticized for sample bias and failure to recognize subtle symptoms. Because symptomatic individuals seek treatment and most asymptomatic individuals do not, asymptomatic individuals accumulate in the population. However, the presence of symptoms does not necessarily lead to abstinence as demonstrated in a study by Upchurch et al. (1989), 38% of men and 46% of women with symptoms attributable to *N. gonorrhoeae* remained sexually active while awaiting treatment.

Asymptomatic infections include the following:
   a. Urethritis: Only 1%–3% of general population asymptomatic
   b. Endocervix
   c. Rectum
   d. Pharynx
   e. Conjunctiva

2. Symptomatic uncomplicated infections
   a. Urethritis
   b. Cervicitis
   c. Proctitis
   d. Pharyngitis
e. Bartholinitis
f. Conjunctivitis

3. Local complications
a. Salpingitis
b. Epididymitis
c. Bartholin gland abscess
d. Lymphangitis
e. Periurethral abscess
f. Prostatitis
g. Perihepatitis: Complication of salpingitis

4. Systemic complications
a. DGI

**Genitourinary Infections**

The most common clinical manifestation of gonorrhea is a genitourinary infection.

**Males**

1. Urethritis
   a. Follows a 2–5-day incubation period (range, 1–14 days)
   b. Dysuria
c. Profuse purulent urethral discharge: Approximately 25% have scant minimally purulent discharge

2. Infection can spread and cause prostatitis, epididymitis, seminal vesiculitis, and infection of Cowper and Tyson glands.
   a. Epididymitis: 10% to 30% of untreated men develop this complication, which is manifested by the following:
      - Urethral discharge and dysuria
      - Scrotal pain and tenderness, usually unilateral
      - Scrotal swelling and erythema
      - Pain in the inguinal area and flank pain in severe cases
   b. Prostatitis: Prostatitis is a rare complication of gonorrhea. Signs and symptoms include the following:
      - May be asymptomatic
      - Chills, fever, malaise, myalgia
      - Rectal pain and discomfort
      - Lower back pain
      - Lower abdominal pain, suprapubic discomfort
      - Dysuria, urinary frequency, and occasionally acute urinary retention

3. Risk of infection: Risk of infection is approximately 20% for a male after a single exposure through vaginal intercourse with an infected female.

**Females**

Signs and symptoms are less specific in females than in males. Often the teen may complain of vaginal discharge, dysuria, or frequency. The incubation period is more variable than in males, but symptoms usually appear within 10 days of exposure. Common local problems include the following:

1. Endocervicitis
   a. Increased vaginal discharge, often purulent
   b. Dyspareunia
c. Erythema, edema, and friability of cervix
d. Risk of infection: Estimated at 50%–90% for a female after exposure to an infected male, but studies accounting for mean time to transmission and number of exposures are lacking.

2. Urethritis
   a. Dysuria
   b. Urinary frequency
c. Exudate from urethra or periurethral glands (Skene gland)
d. Suprapubic pain

3. Bartholinitis: Pusulent exudate from Bartholin gland

4. Bartholin gland abscess: Labial pain and swelling. The most common complication in females apart from pelvic inflammatory disease (PID) is abscess of the Bartholin gland.

5. Spread of infection can extend into the following areas:
   a. Uterus: Endometritis
   b. Fallopian tubes: Salpingitis (see Chapter 63). Salpingitis occurs in as many as 10%–20% of females with acute urogenital gonorrhea. Strains causing PID vary; some are more likely to have auxotypes different from those causing cervical or disseminated infections; some are more likely to be resistant to penicillin than disseminated strains; and others almost always grow in transparent colonies. In addition to abdominal pain, symptoms of salpingitis can include intermenstrual bleeding, menorrhagia, and dyspareunia. Patients with gonococcal salpingitis are often more ill and febrile and have the onset on symptoms within 7 days of the menstrual cycle.
   d. Ovary: Tuboovarian abscess

**Extragenital Sites**

1. Pharyngitis
   a. Pharyngeal involvement is usually asymptomatic in >90% of infected individuals.
b. Pharyngitis may be manifested by a sore throat 3–7 days after exposure and occasionally with fever and cervical adenopathy.
c. Positive pharyngeal cultures are found in 3%–7% of heterosexual males, 10%–20% of heterosexual females, and 10%–25% percent of homosexual males with genital gonorrhea, but the pharynx is the sole site of infection in <5% of individuals, regardless of gender or sexual orientation. The infection is transmitted to the pharynx by orogenital sexual contact. Fellatio is a more effective mode of transmission than cunnilingus. Pharyngeal infection may be a significant cause of urethral gonorrhea in males who have sex with other males. In a study of pharyngeal gonorrhea in female adolescents, Brown et al. (1989) found positive pharyngeal cultures in none of 240 adolescents from a hospital adolescent clinic and 3.4% in a group of adolescents from an STD public health clinic. In only 2 of 20 adolescents with pharyngeal gonococcal infection was the pharynx the only infected site. There was a significant relationship between concurrent pharyngeal and genital gonorrhea.
d. Spontaneous elimination of the organism usually occurs in 12 weeks.
e. Significance of infection: The clinical significance is controversial. However, infected individuals may be at risk for dissemination of gonorrhea.

2. Rectal gonorrhea
   a. Prevalence rates
      - Rectal cultures are positive in 35%–50% of females with cervicitis and homosexual males with gonorrhea. Most anorectal infections in females occur without a history of anogenital sexual contact and are thought to be related to infected perineal secretions. In studies conducted before awareness about human immunodeficiency virus (HIV) infection, 40% of males engaged in homosexual activity had infection isolated to the rectum. It is the sole site of infection in approximately 5% of women. Rectal infections are uncommon in heterosexual males.
b. Rectal gonorrhea can produce the following:
   - Proctitis with anal discharge
   - Rectal bleeding
   - Anorectal pain
Most anorectal infections in females are asymptomatic. The examination may show a purulent exudate, erythema, edema, friability, or other inflammatory changes of the rectal mucosa. The differential diagnosis for infections involving the first 5–10 cm of the rectum causing proctitis is chlamydia, herpes, and syphilis. Inflammation extending more than 15 cm and causing proctocolitis is usually caused by either Shigella, Campylobacter, Entamoeba histolytica, or Salmonella.

3. Conjunctivitis is usually severe with high risk of sequelae
4. Otitis externa (Pareek, 1979)

**Disseminated Disease** About 0.5% to 3.0% of individuals with gonorrhea develop disseminated disease (DGI) characterized by arthritis/arthralgia, tenosynovitis, and dermatitis. Certain strains of *N. gonorrhoeae* are more likely to disseminate. These strains tend to cause asymptomatic urogenital infection and are more resistant to complement-mediated bacterial activity in serum. DGI is more prevalent in females in general (about 4 : 1) and in particular in pregnant females and those who had menses in the previous 7 days. This is probably related to hormonal influences or alternation in the pH level of the vaginal secretions. Other risk factors for dissemination include pharyngeal gonorrhea, complement deficiency disease, and other immune-altering disease states such as lupus erythematosus. Commonly, disseminated disease develops in individuals with asymptomatic pharyngeal or anogenital infections.

**Arthritis-dermatitis Syndrome**

1. Arthritis is the most common systemic complication of *N. gonorrhoeae* and usually occurs within 1 month of exposure. About 25% of patients complain of pain in a single joint, whereas up to two thirds have migratory polyarthralgias or tenosynovitis. The knee is the most common site of purulent gonococcal arthritis.
2. Sixteen percent of the arthritis-dermatitis infections occur in the 10–19-year-old age group.
3. Clinical presentation of arthritis-dermatitis syndrome
   a. Most have fever, chills, leukocytosis. Up to 40% are afebrile.
   b. Arthritis or tenosynovitis: Migratory arthritis/arthralgias and tenosynovitis usually involve multiple joints. Around 60% of patients present without a detectable synovial effusion and >90% of these will have a skin rash and/or tenosynovitis often together with nonsuppurative arthritis. Arthralgias and tenosynovitis are more common than frank arthritis. Tenosynovitis commonly involves the extensor and flexor tendons and sheaths of the hands and feet. Arthritis is most common in the wrist, metacarpophalangeal, ankle, and knee joints.
   c. Skin lesions
      • Dermatitis is the second most common complication of DGI. Variable presentations include erythematosus macules or papules, as well as pustules or vesicles with erythematous halos and necrotic centers and purpura.
      • Often tender
      • Usually <30 lesions on the body
      • Frequently occur on distal portions of extremities including palms, fingers, and soles; occasionally the trunk; rarely on the face.
      • Gram stain results and cultures are usually negative, but direct immunofluorescent stains in research studies on biopsy specimens of skin identify gonorrhea in more than half the specimens.
   d. Positive cultures from blood in 20%–30% of patients, but cultures should be done in the first few days of the illness. Tenosynovitis, arthralgia, and dermatitis tend to occur early in the course when there is greater likelihood of positive blood cultures. Arthritis with effusion occurs later. This sequence is not universal and some patients have isolated monoarticular arthritis. Joint cultures are rarely positive, but polymerase chain reaction (PCR) has been used on joint fluid to make the diagnosis (Liebling et al., 1994).
   e. Gonococci have been found on mucosal surfaces 80% of the time despite negative blood, skin, and joint fluid cultures.
4. Monoarticular septic arthritis
   a. Monoarticular septic arthritis is found in less than one half of the cases of DGI.
   b. Monoarticular septic arthritis may present without preceding dermatitis or tenosynovitis.
   c. Knees are the most frequently involved joints, but all joints including the hip and shoulder have been affected. Sacroiliac, temporomandibular, and sternoclavicular joints are rarely involved.
   d. Synovial fluid cultures are positive in about 25% of patients. Blood cultures are rarely positive by the time the infection is in a joint.
   e. Monoarticular septic arthritis is more likely than tenosynovitis to have a negative blood culture and a positive joint culture. Cultures are usually negative from synovial fluid containing <20,000 leukocytes/mm³, and are more often positive if >40,000 leukocytes/mm³.
5. Differential diagnosis of gonococcal arthritis
   a. Infections: Meningococcemia, bacteremia, endocarditis, infectious arthritis, and infectious tenosynovitis
   b. Seronegative arthralgias: Reiter syndrome, ankylosing spondylitis, psoriatic arthritis
   c. Lupus erythematosus
   d. Allergic reaction to drugs

**TABLE 61.2. Comparison of acute gonococcal arthritis and acute Reiter syndrome**

Other sites of dissemination include the following:

1. Perihepatitis: May be a complication of salpingitis, but occasionally may be caused by hematogenous dissemination of the disease
2. Mild hepatitis: Found in up to 50% of patients, but not usually clinically suspected
3. Gonococcal meningitis (Sayeed et al., 1972): Rare complication that can be indistinguishable clinically from meningococcal infection
4. Myopericarditis
5. Complete heart block (Garn et al., 1977)
6. Gonococcal endocarditis (Cooke et al., 1979)
7. Gonococcal osteomyelitis (Gantzi et al., 1976)
8. Pneumonia
9. Adult respiratory distress syndrome (Belding and Carbone, 1991)

**DIAGNOSIS**

**Gonococcal Urethritis: Males**

1. Microscopic demonstration of typical gram-negative intracellular diplococci on smear of urethral exudate constitutes sufficient basis for diagnosis of gonorrhea.
2. Sensitivity of a Gram stain approaches 100% in symptomatic men but is 50%–70% for asymptomatic infections. Specificity is >95%. Sensitivity and specificity of
If the Gram stain result is negative or if urethral exudate is absent, a culture of a specimen taken from the anterior urethra should be done. One should use a LCR and TMA are approved for both asymptomatic and symptomatic males on urine and urethral specimens. PCR is approved for asymptomatic and symptomatic males on urine and only symptomatic males from the urethra. SDA is approved for symptomatic males from urine and urethra but not on asymptomatic males (Table 61.5).

Gonococcal Endocervicitis: Females

TABLE 61.3. Sensitivity and specificity of Gram-stained smears

<table>
<thead>
<tr>
<th>Site</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mid urethral-pelvic</td>
<td>96-100</td>
<td>95-100</td>
</tr>
<tr>
<td>Mid urethral-pelvic</td>
<td>96-100</td>
<td>95-100</td>
</tr>
<tr>
<td>Endocervix</td>
<td>80-90</td>
<td>95-100</td>
</tr>
<tr>
<td>Uncultured urethral</td>
<td>80-90</td>
<td>95-100</td>
</tr>
<tr>
<td>Proximal urethral</td>
<td>80-90</td>
<td>95-100</td>
</tr>
<tr>
<td>Anal canal</td>
<td>80-90</td>
<td>95-100</td>
</tr>
<tr>
<td>Bilateral</td>
<td>80-90</td>
<td>95-100</td>
</tr>
<tr>
<td>Amniotic fluid specimen</td>
<td>70-80</td>
<td>95-100</td>
</tr>
</tbody>
</table>

TABLE 61.4. FDA-approved nucleic acid diagnostic tests for C. trachomatis and N. gonorrhoeae

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NAATs</td>
<td>90-100</td>
<td>90-100</td>
</tr>
<tr>
<td>LCR</td>
<td>92.7</td>
<td>99.9</td>
</tr>
<tr>
<td>PCR</td>
<td>92.7</td>
<td>99.9</td>
</tr>
<tr>
<td>TMA</td>
<td>92.7</td>
<td>99.9</td>
</tr>
<tr>
<td>SDA</td>
<td>92.7</td>
<td>99.9</td>
</tr>
</tbody>
</table>

TABLE 61.5. Comparison of DNA amplification tests for Neisseria gonorrhoeae

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NAATs</td>
<td>90-100</td>
<td>90-100</td>
</tr>
<tr>
<td>LCR</td>
<td>92.7</td>
<td>99.9</td>
</tr>
<tr>
<td>PCR</td>
<td>92.7</td>
<td>99.9</td>
</tr>
<tr>
<td>TMA</td>
<td>92.7</td>
<td>99.9</td>
</tr>
<tr>
<td>SDA</td>
<td>92.7</td>
<td>99.9</td>
</tr>
</tbody>
</table>

Gonococcal Endocervicitis: Females

1. Cultures should be obtained from the endocervical canal and inoculated on Thayer-Martin medium to diagnose gonorrhea. Do not use a lubricant during the pelvic examination, because this may be toxic to the organism. Place a swab in the cervical os for 20–30 seconds and rotate. For screening purposes, only endocervical cultures are recommended. A single culture is 80%–95% sensitive in detecting gonorrhea. If gonorrhea is suspected, a separate swab can be used in the anal canal. About 5% of females have positive culture from this site only. The swab can be inserted about 2 cm, avoiding fecal mass, and moved side to side for 20–30 seconds. Although anal culture will increase the yield, it should be optional based on a history of anal exposure, clinical symptoms, and available resources.

2. Gram stain smears from the endocervix are not recommended, except as an adjunct to culture or in symptomatic females. Such smears are only 50%–70% sensitive in uncomplicated endocervical infection.

3. Newer diagnostic methods include nucleic acid probe assays and NAATs (LCR, PCR, TMA, SDA). The LCx assay TMA, SDA, and Amplicor CT/NG PCR test...
Diagnosis requires a positive culture from the pharynx. As with anal infection, nucleic acid detection techniques are not considered appropriate.

Penicillin

Each of these regimens appears to cure >97% of anal and genital infections.

Recommended regimens

- Tetracycline: Tetracycline-resistant
- Cefixime has the advantage of a one-time oral dose. The serum levels are not as high as with ceftriaxone or as sustained. Its effectiveness against N. gonorrhoeae isolates was also resistant to tetracycline. One percent of isolates had intermediate or total resistance to ciprofloxacin. Intermediate resistance to ciprofloxacin was found throughout the country, with rates of 29.5% in the samples from Cleveland and 25% in those from Atlanta. Resistant strains were seen in Cincinnati, San Francisco, and Hawaii. In 1999, fluoroquinolone resistance was again noted in Hawaii, with decreased susceptibility to azithromycin in strains from Missouri.

Spectinomycin

125 mg of ceftriaxone appears to be as effective as 250 mg, and no ceftriaxone-resistant strains of N. gonorrhoeae have been reported.

Anorectal Gonorrhea

Positive cultures from the rectum are required for diagnosis of anorectal gonorrhea. The nucleic acid assays have not been adequately studied for this site.

Gonococcal Pharyngitis

1. Diagnosis requires a positive culture from the pharynx. As with anal infection, nucleic acid detection techniques are not considered appropriate.
2. Several studies have indicated that routine pharyngeal screening in adolescents is not cost-effective (Brown et al., 1989; Roohvarg and Lovchik, 1991). It is probably more cost-effective to treat adolescents with genital infections with medications than treat both genital and pharyngeal gonorrhea.

Systemic Infection

1. Typical signs such as tenosynovitis and classic skin lesions.
2. Positive cultures from the urethra, endocervix, pharynx, rectum, skin lesions, synovial fluid, or blood. Nucleic acid tests of the urethra or endocervix can also be used.

THERAPY

Treatment of gonorrhea should take into account that strains of N. gonorrhoeae resistant to traditional treatment are rising, that chlamydial infections often coexist with gonorrhea, and that serious complications can arise from both gonococcal and chlamydial infections.

Resistance

The incidence of isolates of N. gonorrhoeae resistant to antibiotics has increased dramatically since the early 1980s. The forms of antibiotic resistance include the following:

1. Plasmid mediated
   a. Penicillin: Penicillinase-producing N. gonorrhoeae (PPNG)
   b. Tetracycline: Tetracycline-resistant N. gonorrhoeae (TRNG)
2. Chromosomally mediated resistant N. gonorrhoeae (CMRNG)
   a. Penicillin
   b. Tetracycline
   c. Cefoxitin
   d. Spectinomycin

In 1976, PPNG was first recognized in the United States. The mechanism of acquisition was a new plasmid that carried genes for producing a β-lactamase capable of breaking the essential penicillin β-lactam ring. This problem rose slowly until 1980, at which time, cases increased dramatically. PPNG became endemic in many parts of the United States, particularly in New York, California, and Florida, but other areas were affected as well. Penicillin has not been used to treat N. gonorrhoeae since the early 1990s. Data from the Gonococcal Isolate Surveillance Project showed that in 1998, only 3% were PPNG. Another form of plasmid-mediated resistance, first isolated in 1985, is tetracycline (TRNG). In 1998, 6.6% of the isolates were TRNG and this rate has been stable for the past decade. Plasmid-mediated resistance to both penicillin and tetracycline was low (0.7%) in 1998.

CMRNG was the reason for the rising doses of penicillin required between 1950 and the 1970s. However, in 1983 a higher level of this resistance was ascribed to penicillin and tetracycline. The mechanism of resistance involves multiple chromosomal mutations that cause alterations in the cell membrane to antibiotics and changes in penicillin-binding proteins. CMRNG also involves some second-generation cephalosporins and spectinomycin (rare in the United States). N. gonorrhoeae isolates, which require 1 µg/mL or more of penicillin for inhibition, and which do not produce β-lactamase, have been designated as CMRNG. In 1998, chromosomal-mediated resistance to penicillin was 5.1%, up from 0.5% in 1988. Resistance to tetracycline was 6.8%, which represented a relatively stable rate since 1989. Resistance to both penicillin and tetracycline was 7.2%, an increase of 4.2% in the past decade.

In 1998, the Gonococcal Isolate Surveillance Project found that 29.4% of isolates collected from patients at 28 cities were resistant to penicillin. There was no resistance that year to spectinomycin or ceftriaxone. Some decreased sensitivity to ceftriaxone was noted in isolates from St. Louis and Philadelphia, and two of these isolates were also resistant to tetracycline. One percent of isolates had intermediate or total resistance to ciprofloxacin. Intermediate resistance to ciprofloxacin was found throughout the country, with rates of 29.5% in the samples from Cleveland and 25% in those from Atlanta. Resistant strains were seen in Cincinnati, San Francisco, and Hawaii. In 1999, fluoroquinolone resistance was again noted in Hawaii, with decreased susceptibility to azithromycin in strains from Missouri. Treatment with ciprofloxacin is not recommended in Hawaii. The percentage of PPNG, TRNG, and CMRNG, although widespread, varies widely from city to city.

Treatment Recommendations

Recommendations from the Centers for Disease Control and Prevention (CDC, 1997) 1998 STD guidelines (which can be found at www.cdc.gov/nchstp/dstd/1998_STD_Guidelines/1998_guidelines_for_the_treatment.htm) include the following:

1. Uncomplicated urethral, endocervical, or rectal infections in adolescents and adults:
   a. Recommended regimens
      - Cefixime, 400 mg PO in a single dose, OR
      - Cefuroxime, 125 mg IM at one time, OR
      - Ciprofloxacin, 500 mg PO in a single dose, OR
      - Ofloxacin, 400 mg PO in a single dose, OR
      - Levofloxacin, 250 mg PO in a single dose,
      - Doxycycline (100 mg PO b.i.d. for 7 days)
   b. Alternative regimens
      - 1. Each of these regimens appears to cure >97% of anal and genital infections.
      - 2. Cefixime has the advantage of a one-time oral dose. The serum levels are not as high as with ceftriaxone or as sustained. Its effectiveness against incubating syphilis is not known. Cefixime is the current recommendation in Hawaii because of the resistance to ciprofloxacin.
      - 3. Quinolones are contraindicated for pregnant or nursing women and for persons younger than 18 years. Quinolones should also not be used for infections acquired in Asia and the Pacific including Hawaii.
      - 4. 125 mg of ceftriaxone appears to be as effective as 250 mg, and no ceftriaxone-resistant strains of N. gonorrhoeae have been reported.
Special considerations

HIV infection: Teens infected with HIV and treated as follows:

- Ceftriaxone, 125 mg IM in a single dose, OR
- Oral cephalosporins other than cefixime (400 mg): These include cefuroxime axetil (1 g PO in a single dose) and cefpodoxime proxetil (200 mg PO in a single dose). These appear to have less antibiotic activity than cefixime (400 mg).
- Quinolones other than ciprofloxacin (500 mg) and ofloxacin (400 mg): These include enoxacin (400 mg PO in a single dose), lomefloxacin (400 mg PO in a single dose), and norfloxacin (800 mg PO in a single dose). None appears to offer any advantage over ciprofloxacin (500 mg) or ofloxacin (400 mg).

These regimens should be followed with a therapy that treats chlamydia. Although, azithromycin (2 g as a single dose) is effective for uncomplicated gonococcal infection, the expense and gastrointestinal side effects make it difficult to use. The 1-g dose is not considered effective.

2. Special considerations
   a. Individuals with gonorrhea should have a serological test for syphilis. In addition, the practitioner should consider offering testing for HIV infection.
   b. Adolescents who have documented syphilis coexistent with gonorrhea should have the syphilis treated with a regimen outlined in Chapter 64.
   c. Some practitioners mix 1% lidocaine with ceftriaxone to reduce the discomfort associated with the injection.

3. Treatment of sex partners: All adolescents exposed to gonorrhea should be examined, cultured, and treated presumptively. The sex partner(s) of symptomatic patients should be evaluated and treated if their last sexual contact with the patient was within 60 days of onset of the patient’s symptoms. This is also the time period for evaluation if the patient is asymptomatic. Teens should be told to refer sex partners for evaluation and treatment. Teens should avoid sexual intercourse until they and their partners are cured.

4. Follow-up: Because of the efficacy of recommended regimens, routine follow-up cultures are not needed for persons treated for uncomplicated gonorrhea. Adolescents should be told to return for an examination if symptoms or signs persist after therapy. These individuals should be evaluated by culture for N. gonorrhoeae, including testing for antimicrobial susceptibility. Most treatment failures are due to reinfection.

5. Pharyngeal gonococcal infection: Gonococcal infection of the pharynx may be more difficult to eradicate than urethral and anorectal sites. Few regimens have consistent cure rates >90%. Recommended regimens include the following:

a. Ceftriaxone, 125 mg IM in a single dose, OR
b. Ciprofloxacin, 500 mg PO in a single dose, OR
c. Ofloxacin, 400 mg PO in a single dose, OR
   PLUS treatment for chlamydia including either:
   - Azithromycin, 1 g PO in a single dose, OR
   - Doxycycline, 100 mg PO b.i.d. for 7 days

   Cefixime is not considered effective enough for pharyngeal infection.

6. Treatment in pregnant adolescents: Pregnant adolescents should be screened for gonorrhea, chlamydia, and syphilis at the first prenatal care visit, with tests repeated in the third trimester. Quinolones and tetracyclines should be avoided during pregnancy. N. gonorrhoeae should be treated with one of the recommended cephalosporin regimens. Spectinomycin (2 g IM) can be used alternatively. Erythromycin is recommended to treat C. trachomatis during pregnancy.

7. HIV infection: Teens infected with HIV and N. gonorrhoeae should receive the same treatment as those not infected with HIV.


9. Acute epididymitis: In sexually active adolescents, epididymitis is most likely caused by N. gonorrhoeae or C. trachomatis. Recommended therapy after appropriate cultures for gonorrhea and chlamydia includes the following:

   a. Ceftriaxone, 250 mg IM once, PLUS
   b. Doxycycline, 100 mg b.i.d. for 10 days
   c. Alternatively, ofloxacin (300 mg PO b.i.d. for 10 days) can be used in individuals who are 18 years or older.

10. DGI: Hospitalization for intravenous treatment is recommended for initial therapy. This is particularly important in individuals who have an uncertain diagnosis, in adolescents in whom there is uncertain compliance with therapy, and in teens with purulent synovial effusions or other serious complications.

   a. Recommended initial regimen
      - Ceftriaxone, 1 g IV every 24 hr
   b. Alternative initial regimens
      - Cefixime, 1 g IV every 8 hr, OR
      - Cefotaxime, 1 g IV every 8 hr
      - Spectinomycin (2 g IM every 12 hr) should be used in those adolescents allergic to b-lactam drugs. For those teens older than 18 years, ciprofloxacin (500 mg IV every 12 hr) or ofloxacin (400 mg IV every 12 hr) can be used.
   c. Duration of therapy: Adolescents may be discharged 24–48 hr after resolution of symptoms to finish a week total of antibiotic therapy with an oral regimen of either:
      - Cefixime, 400 mg PO b.i.d., OR
      - Ciprofloxacin, 500 mg PO b.i.d., OR
      - Ofloxacin (400 mg PO b.i.d.)

   Quinolones should not be used in pregnant and lactating women and those under 18 years of age.

11. Meningitis and endocarditis: These serious complications require high-dose intravenous therapy with an antibiotic effective against the causative strain. The recommended initial regimen is 1–2 g of ceftriaxone IV every 12 hours. Although optimal duration is not known, most authorities treat gonococcal meningitis for 10–14 days and endocarditis for at least 4 weeks.

12. Adult gonococcal ophthalmia: For adolescents and children weighing >20 kg, the treatment includes ceftriaxone (1 g IM once), and eye irrigation once with buffered ophthalmic solution should be performed to help clear the discharge. All of these individuals should be followed by careful ophthalmological examination, including slit-lamp examination. Simultaneous infection with C. trachomatis should be considered if the individual does not respond to antibiotics.

13. Doses in adolescents: Adolescents weighing >45 kg should be treated with the adult doses, as already outlined. Adolescents who weigh <45 kg should be treated as follows:

   a. For uncomplicated vulvovaginitis, cervicitis, urethritis, pharyngitis, and proctitis
      - Ceftriaxone (125 mg IM once), or if not tolerated
      - Spectinomycin (40 mg/kg of body weight IM [maximum 2 g] once).
   b. Adolescents and children older than 8 years should be given doxycycline (100 mg b.i.d. for 7 days) in addition to the previously described regimen.
   c. For meningitis
      - Ceftriaxone (50 mg/kg as a single daily dose [maximum 2 g] IV/IM for 10–14 days)

   Adolescents with documented gonorrhea but no history of sexual activity should be carefully evaluated for sexual abuse.

PUBLIC HEALTH ISSUES

1. Relative high prevalence in adolescents, compared with other age groups
2. High prevalence in certain groups including inner-city populations, female adolescents, men in their early twenties, prostitutes, and substance-abusing individuals
3. High coinfection rates with other STDs, particularly C. trachomatis
4. Rapid emergence of multiple types of antibiotic resistance to gonorrhea
5. Large number of asymptomatic gonococcal infections, with a growing number in males

WEB SITES

For Teenagers and Parents
Chlamydia trachomatis

Mary-Ann Shafer and Athena Countouriotis

ETIOLOGY

The genus Chlamydia is divided into four species with specific subtypes known as serovars: Chlamydia psittaci, C. pecorum, C. pneumoniae, and C. trachomatis.

1. C. psittaci is responsible for the zoonosis, psittacosis, an infection contracted by humans from infected birds, which is characterized by interstitial pneumonitis.
2. C. pecorum affects domestic animals.
3. C. pneumoniae causes pneumonia, pharyngitis, and bronchitis and most recently has been associated with possible etiological factors in coronary artery disease. Epidemiological studies have revealed that C. pneumoniae (TWAR serovar) is a relatively common cause of infection in school age children, and it is probably the most common cause of community-acquired pneumonia in this age group.
4. C. trachomatis is associated with a spectrum of diseases. This species contains 18 serologically distinct variants known as serovars. Chlamydial genital infections and neonatal disease (pneumonia and conjunctivitis) are caused by serovars B, D, E, F, G, H, I, J, and K. Table 62.1 outlines the major serotypes of Chlamydia. C. trachomatis itself is easily differentiated by two laboratory tests: iodine-staining glycogen containing inclusions in chlamydial infected cells, and the less reliable testing for sulfonamide susceptibility (C. trachomatis strains are susceptible).

<table>
<thead>
<tr>
<th>Species</th>
<th>Design</th>
<th>Cave</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlamydia psittaci</td>
<td>[image]</td>
<td>[image]</td>
</tr>
<tr>
<td>Chlamydia pneumoniae</td>
<td>[image]</td>
<td>[image]</td>
</tr>
<tr>
<td>Chlamydia trachomatis</td>
<td>[image]</td>
<td>[image]</td>
</tr>
</tbody>
</table>

TABLE 62.1. Serotypes of Chlamydia

DEVELOPMENTAL CYCLE AND PATHOGENESIS

1. Developmental cycle: Chlamydial disease is characterized by a unique developmental cycle, which lasts between 48 and 72 hours and is characterized by transformation between two morphologically distinct infectious and reproductive forms (Schachter, 1999). The extracellular infectious form, the elementary body, attaches to a susceptible epithelial cell and is ingested. Susceptible host cells seem to have a specific receptor that facilitates attachment to Chlamydia and facilitates its ingestion. The trachoma biovar responsible for human genital infections may have a very specific attachment site, which may help to explain its restricted host range. Once within an endocytotic vesicle, the elementary body reorganizes into the replicative form, the reticulate body. As the reticulate body divides, it fills the endosome, now a cytoplasmic inclusion, with its progeny. After 48 hours, multiplication ceases and the reticulate bodies transform to new infectious elementary bodies. The elementary bodies then are released from the cell by cytolysis or by a process of exocytosis or extrusion of the entire inclusion, which often results in the destruction of the host cell (Fig. 62.1).
Predilection for columnar epithelium: Of particular importance to the young female adolescent, *C. trachomatis* has a predilection for columnar epithelium commonly found on the cervix of young women. This tissue involves with increasing age.

3. Immune response: The signs and symptoms associated with infection, particularly in females, are mainly secondary to tissue destruction and the body’s immunopathogenic response to the infection.
   a. Major outer membrane protein (MOMP): A very important component in the immune response is the presence of a 40-kd MOMP of *C. trachomatis* that is capable of inducing both a neutralizing antibody and a T-cell mediated immune response. Antibody to MOMP neutralizes chlamydial infectivity both in cellular and animal models. However, the MOMP gene appears capable of frequently developing “polymorphism” and this mechanism may serve as a type of escape from the neutralizing antibodies mounted by the host. The ability of this polymorphism to actually protect the chlamydiae from inactivation by the host is not known but would have an important impact on the design and development of potential future vaccines.
   b. Heat shock protein: Another important chlamydial protein is the *C. trachomatis* heat shock protein, which is a 60-kd protein, and it has shown to be 50% homologous with heat shock proteins from humans. This homology, which could potentially cause cross-reactive immune responses with healthy human tissues as a part of the body’s mounting a defense against the infecting chlamydiae, could help to explain the apparent tissue immune-mediated destruction associated with chlamydial infections, such as the scarring of the fallopian tubes as a result of pelvic inflammatory disease (PID). Most of the damage caused by genital chlamydial infections may be due to immune processes.

**EPIDEMIOLOGY**

*C. trachomatis* is the most common reported bacterial sexually transmitted infection in the United States, with an estimated 4 to 5 million cases reported annually. This includes an estimated 2.6 million symptomatic infections in female patients, 1.8 million in male patients, and 0.25 million in infants. These estimates do not include the large number of people with asymptomatic infection. Many men and most women who are infected with *C. trachomatis* are either asymptomatic or minimally symptomatic, and presentation for diagnosis is a result of screening or symptoms developing in a sexual contact. Adolescents and young adults are at substantial risk of contracting chlamydial infections and are the highest risk group being infected. Peak incidence of genital *C. trachomatis* infections is among sexually active adolescent women younger than 20 years. Overall, national rates reported by the CDC in 1999 are as follows (CDC, 2000):

1. Data from 49 states (not New York), New York City and District of Columbia reported 659,441 cases
2. Overall rate in the United States was 254/100,000
   a. 403/100,000 women
   b. 75/100,000 men
   c. 2,484/100,000 females age 15–19 years
   d. 344/100,000 males age 15–19 years
   e. 5.5% (2.6%–15%) rate in women age 15–24 years attending family planning clinics
3. A 62% decrease in infection rate was reported after the introduction of a screening program among 15–44-year-old women attending family planning clinics in Health and Human Services Region X (1998–1999).

Overall, rates for chlamydial infection are greatest among young women and men 15 to 24 years of age. Although there are numerous studies of young females, information about rates in males is limited. Rates vary by gender and target population, among other factors. Since the introduction of nucleic acid amplification techniques (NAATs) such as ligase chain reaction (LCR) and polymerase chain reaction (PCR), for example, differences by testing techniques have been minimized. Selected chlamydial prevalences among adolescent populations are reviewed in Table 62.2.

**TABLE 62.2.** Recent chlamydial prevalence rates by population and type of testing

<table>
<thead>
<tr>
<th>Category</th>
<th>Population</th>
<th>Prevalence Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Females</td>
<td>Young</td>
<td>5.5% (2.6%–15%)</td>
</tr>
<tr>
<td>Males</td>
<td>Young</td>
<td>62% decrease</td>
</tr>
</tbody>
</table>

**Risk Factors**

*C. trachomatis* infection is related to a number of risk factors including young age (peak infection rates at age 15–24 years), prior history of STDs, new sex partner, multiple sex partners, oral contraceptive use, condom use (inconsistent findings), nonwhite race and/or ethnicity (African-American predominance), female gender, pregnancy, presence of ectopy (common in adolescents), unmarried, and young age at sexual debut (Berman and Hein, 1999; Boyer et al., 1999; Marrazzo et al., 1997; Orr et al., 1994; Stamm, 1999a, 1999b).

**Transmission**

1. *C. trachomatis* is sexually transmitted in adolescent populations.
2. 60%–75% of females with male sex partners who have chlamydial urethritis test positive for chlamydial infection (Lycke et al., 1980; Quinn et al., 1995).
3. 25%–50% of male sex partners of females with a mucopurulent cervicitis (MPC) or PID test positive for chlamydial infection. In one study, male partners of women who had chlamydial cervicitis were found to be infected 28% of the time (Lycke et al., 1980).
4. Male to female transmission may be more efficient due to increased pathogen contact time in females infected by sexual intercourse with men and/or the female endocervix is more efficiently infected than the male urethra (Bolan et al., 1999).
5. Recent male to female transmission data among partnerships using the newer NAATs suggest that the transmission after multiple sexual encounters may actually be equivalent (Quinn et al., 1996).
6. 15%–30% of males with urethritis have simultaneous gonorrheal and chlamydial infection.
The clinical manifestations of *C. trachomatis* are similar to those of *Nesseria gonorrhoeae* (Table 62.3). Both organisms preferentially infect columnar or transitional epithelium of the urethra, with extension to the epididymis, the endocervix, with extension to the endometrium, salpinx, and peritoneum; and the rectum. Both organisms can invade deeper tissue, causing extensive subepithelial inflammation, epithelial ulceration, scarring; and PID. PID is responsible for most of the serious acute illness and long-term economic cost related to chlamydial infections. Most infections caused by *C. trachomatis* infections are asymptomatic or have few or no symptoms, compared with gonococcal infections. For example, it is estimated that 70% to 90% of endocervical infections have no symptoms (Brunham and Peeling, 1994).

**TABLE 62.3.** Comparison of clinical manifestations of Chlamydia trachomatis and Neisseria gonorrhoeae

### Male Infections

Studies of infected male patients have historically been limited to those who were symptomatic attending STD clinics and who were diagnosed with nongonococcal urethritis (NGU). Screening rates for male adolescents were difficult to ascertain due to the invasiveness of urethral swabs for culture. The first attempt to screen asymptomatic males was published in 1984 and used urethral culture to screen chlamydial and gonococcal infection (Adger, 1984; Shafer et al., 1993). With the advent of the newer urine-based NAATs, it has been possible to screen a broader range of young male populations. Rates among male adolescent populations range from 2% among males attending a Health Maintenance Organization to 14% among those screened in detention clinics. Young enlisted military boys screened before leaving for a foreign deployment in a nondesign setting yielded a 3.4% rate of chlamydial infection (Brodine et al., 1998) using the newer urine-based NAATs (Table 62.2). Like young women, men younger than 25 years have the highest reported rates of chlamydial infection. Complications other than urethritis, epididymitis, proctitis, and Reiter syndrome are unusual in males. However, male infertility has also been associated with chlamydial infection.

### Urethritis

1. Urethritis is the most common problem associated with *C. trachomatis* in males.
2. *C. trachomatis* causes about 40%–60% of NGU cases in males.
3. Urethritis infection is more often asymptomatic than gonococcal urethral infection, and when symptoms occur, they are milder with chlamydial urethritis.
4. Most males with asymptomatic chlamydial urethral infection have a persistent inflammatory response shown by urethral leukocytosis (more than four polymorphonuclear [PMN] leukocytes per ×1,000 field on Gram stains of urethral secretions and/or white cells in a first-void urine).
5. There is a 7–21-day incubation period from infection to development of symptoms.

### Epididymitis

1. *C. trachomatis* and *N. gonorrhoeae* infections are responsible for most of the cases of epididymitis among men younger than 35 years. In particular, chlamydial are responsible for 70% of cases in adolescent and young men.
2. The pathogenesis of chlamydial epididymitis is unclear.
3. Chlamydial urethritis, both symptomatic and asymptomatic, often accompanies the epididymitis among sexually active young males.
4. Onset is usually gradual but can be sudden.
5. Complaints include severe scrotal pain, inguinal pain, and when severe flank pain.
6. Complaints of dysuria are present in less than half of men with epididymitis.
7. Differential diagnosis in young males with scrotal pain includes testicular torsion and hemorrhage into a mass or tumor.
8. To differentiate between tumor, mechanical torsion of the testicle and infectious epididymitis, a urinalysis, and tests for chlamydial and gonorrheal infections should be done, and a Doppler ultrasound or radionuclide scan should be considered (see Chapter 29 for further description of the workup for scrotal pain).

### Prostatitis

Despite continued study, the role of *C. trachomatis* in causing nonbacterial prostatitis remains controversial. Although definitive studies are lacking, *C. trachomatis* has been isolated from prostatic secretions and transrectal prostatic biopsies from some patients with prostatitis.

### Proctitis

Most of the information about chlamydia and proctitis comes from studies of homosexual men. Either the non-LGV strains or the genital strains D through K are responsible for the development of proctitis. The LGV strains can produce a primary ulcerative proctitis and a histopathological picture of giant cell formation and granulomas similar to those seen in acute Crohn disease, whereas the non-LGV immunotypes produce more mild disease, from no symptoms present to rectal bleeding, diarrhea, and rectal discharge.

### Reiter Syndrome

Reiter syndrome (conjunctivitis, dermatitis, urethritis, and arthritis), arthritis, or reactive tenosynovitis without the other characteristics of Reiter syndrome have been associated with chlamydial infection of the genital tract. More than 80% of men with the classic signs of Reiter syndrome (untreated at the time of study) give a prior history of having or have a current *C. trachomatis* infection (Stamm, 1999a, 1999b). Most individuals who develop Reiter syndrome are HLA-B27 positive.

### Female Infections

#### Cervicitis

1. Approximately 70% of women infected with *C. trachomatis* are asymptomatic or have mild symptoms such as vaginal discharge, vaginal spotting, mild abdominal pain, or dysuria. On examination, the cervix may appear normal or exhibit “hypertrophic” ectopy that appears edematous, and may bleed easily (easy friability) when touched by a swab. There may be a mucopurulent discharge from the cervical os.
2. Ectopy, the presence of columnar epithelial cells on the ectocervix, is a common and normal finding of the developing adolescent cervix. It occurs in 60%–80% of adolescent cervixes. Although causality has not been shown, besides young age, ectopy is associated with birth control use. It may be that more adolescents use birth control pills than older adults, that birth control pills retard the maturation and involution of the columnar epithelia into the endocervical canal, or that birth control pills actually do stimulate the formation of ectopy. However, it is known that *C. trachomatis* infection is greater in young women with ectopy than in those without ectopy. Ectopy is not synonymous with the inflammatory reaction of the cervix to infection or cervicitis.
3. Chlamydial and gonococcal cervicitis is associated with the finding of more than 30 PMN leukocytes per high-power field (HPF) of Gram stains of cervical secretions.
4. There is currently controversy regarding any association between chlamydial infections of the cervix and low-grade squamous intraepithelial lesion changes on Papanicolaou smears.
Urethritis

1. Screening studies in STD clinics suggest that C. trachomatis-positive women have chlamydialia isolated from the endocervix and urethra 50% of the time and are positive in 25% from either site alone (Stamm, 1999a, 1999b). Women with C. trachomatis isolated from both the cervix and the urethra were more likely to complain of dysuria than women with vaginal infection alone.
2. The acute urethral syndrome is associated with the finding of sterile pyuria for urine pathogens in the face of symptoms of dysuria and frequency in sexually active young women. Although most females with chlamydial infections do not experience urethral symptoms, the presence of MPC in a woman with dysuria and frequency should suggest the diagnosis.

Pelvic Inflammatory Disease

1. PID, particularly chlamydial-related disease, is most often a disease of adolescents. The risk for a 15-year-old female to develop PID is ten times the risk for a 24-year-old young woman.
2. C. trachomatis has been associated with 20%–50% of the PID cases in the United States (similar rates for N. gonorrhoeae in surveys of a number of studies) (CDC, 2000).
3. It is estimated that 10% of endocervical infections ascend and develop into PID.
4. Most studies of PID including fallopian tube sampling for chlamydial infection were completed before 1990 and thus before the advent of the more accurate NAATs.
5. The spectrum of PID associated with C. trachomatis infection ranges from acute, severe disease with perichephalis (right-upper-quadrant pain and tenderness) to asymptomatic or "silent" disease.
6. As much as one-third of ectopic pregnancies have been related to prior chlamydial infections.
7. C. trachomatis infection is related to postpartum and postabortal endometritis. Postpartum PID occurs in 19%–34% of infected pregnant females who deliver vaginally. PID has also been reported in 10%–28% of pregnant females with untreated C. trachomatis infections who had recently undergone an induced abortion (CDC, 1993, 1998).

Perinatal Chlamydial Infections

1. 33% of exposed infants develop conjunctivitis. Neonatal chlamydial infection is the most common cause of neonatal conjunctivitis, which peaks in incidence in 5–14 days of life.
2. Approximately 10%–20% of infants born to infected mothers develop pneumonia due to C. trachomatis. Approximately 50% of affected infants with pneumonia will have a history of conjunctivitis (Darville, 1998).

Perihepatitis (Fitz-Hugh and Curtis Syndrome) This syndrome may be associated with chlamydial and gonococcal salpingitis. Signs and symptoms include right-upper-quadrant pain and tenderness, fever, nausea, and vomiting. Signs and symptoms of salpingitis are usually present. Although usually related to STD infections in females, perihepatitis has been described in males in rare cases.

Other Infections and Complications, Male and Female

1. C. trachomatis is isolated from the pharynx but causes few problems. It is present in 3.7% of males and 3.2% of females at risk. In a study by Neilstein and Anderson (1986), the organism was only isolated in 1 of 100 adolescents examined.
2. Rare cardiac complications include endocarditis (Dimmitt et al., 1985; Jones et al., 1982b) and myocarditis.
3. Chlamydial infections cause obstructive infertility and ectopic pregnancy in female patients. Undetected, untreated fallopian tube infections can be an important cause of infertility and ectopic pregnancy. Two studies of chlamydia and PID in fertile female patients demonstrated PID as the cause of the infertility in half the patients and found that antichlamydial antibody was strongly associated with a tubal problem associated with infertility (Jones et al., 1982a; Kelver and Nogamani, 1989). Many of these females denied a past history of salpingitis. Undetected or "silent" cases of salpingitis may also be a contributor to ectopic pregnancies.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of a reproductive-related problem is dependent on the symptom complex of the patient (e.g., urethritis, cervicitis, epididymitis, or PID). The reader is best directed to the chapters in this book dealing with these individual problems.

Although most cases of chlamydia in female patients are asymptomatic, a common problem in those with chlamydia is MPC, which can also be caused by the following:

1. Infections such as N. gonorrhoeae, Trichomonas vaginalis, herpes simplex, and other organisms such as Escherichia coli
2. Intrauterine device
3. Allergic reaction to contraceptive foam, gel, or film
4. Idiopathic disease, such as local irritation due to feminine hygiene products, perfumes, and others

The most common problem in males is urethritis, which can also be caused by the following:

1. Infections such as N. gonorrhoeae, Ureaplasma urealyticum, T. vaginalis, and herpes simplex
2. Allergic reaction to contraceptive foam, gel, or film
3. Idiopathic disease (see earlier description)

DIAGNOSIS

Until recently, the diagnosis of C. trachomatis was difficult to make because of the lack of readily available, highly sensitive, inexpensive, and noninvasive screening tests. Case finding was directed at the symptomatic male patient attending STD clinics and female patients who had genitourinary symptoms. As more specific and accurate testing became available, the focus for testing changed to screening the infected individual without symptoms. However, there are some clinical signs and symptoms that, although not diagnostic of a chlamydial infection, do indicate that one may be present.

Clinical Diagnosis

C. trachomatis infections should be suspected in all sexually active adolescents, particularly those with multiple partners or signs and symptoms of genitourinary infection including urethritis, cervicitis, epididymitis, or PID. This includes female patients with an edematous friable cervix, mucopurulent endocervical discharge, and white blood cells (WBCs) on the wet mount or patients with a urethritis with Gram stains or cultures not consistent with gonococcal infection. In asymptomatic male patients, the urinary leukocyte esterase dipstick test (LET) on a first-catch urine sample is a good screening test for further evaluation for C. trachomatis or N. gonorrhoeae. It must be emphasized that approximately 70% of females and 25% or more males with chlamydia are asymptomatic. By treating only presumptive symptomatic cases, at least one third more of infected teenagers will be missed.

Collection of Specimens

The reliability of the results of a Chlamydia test are as accurate as the sum of the components of the testing process, including the presence of symptoms in the patient, the source of the specimen (urine, endocervix, urethra, vagina, rectum, pharynx, or conjunctiva), collection technique, storage and transportation of specimens, and finally processing and type of test used. Because C. trachomatis is an obligate intracellular organism infecting columnar epithelium, the practitioner must obtain columnar epithelial cells from the endocervix or the urethra. Precleaning the endocervix with a large swab allows the endocervix to be exposed for proper
sample collection. The preferred method of collection is dictated by the particular test's manufacturer's directives.

Collection Sites

Endocervix

The endocervix is currently the preferred site for screening specimens during pelvic examination collection. This site should theoretically yield the highest number of positive results of any female site. After cleaning the exocervix, the physician inserts a small swab approximately 0.5 to 1 cm into the os and rotates it several times to collect the specimen. All types of Chlamydia testing techniques can be applied to the cervix.

Urethra

This is the main site of infection in the male patient but is also a site of infection in a subset of women infected with Chlamydia, either alone or in conjunction with an endocervical infection. Except for urethral swabs for Gram stain differentiation of gonococcal and nongonococcal urethral infection by Gram stain in male patients, urethral swabs for Chlamydia testing are being replaced by the noninvasive NAATs applied to the first-part urine specimen. Again, all types of Chlamydia tests have been applied successfully to urethral specimens as well.

Urinary (Urethra and Perineal/Vaginal "Reflux Wash")

With the acceptance and dissemination of the NAATs, the noninvasive urine-based testing is becoming widely used to screen asymptomatic adolescent males and females for chlamydial infection. The urine has the potential for "outperforming" the endocervical swab in females because it is really a "multiple-site" sampling technique due to the inevitable "reflux wash" during first-part urination. The urine sample can be optimized for identification: If it is a "dirty" sample, it is a first-part sample (first 15 to 20 ml of micritution), and there has been an extended time since the prior urination (more than 2 hours). The benefit to the male patient is obvious, as it essentially eliminates the need for the painful urethral swab.

Vagina

Although the myriad NAATs available for Chlamydia testing are not currently licensed to be used on vaginal specimens, the performance of LCR on vaginal samples in our hands and others has been excellent and may exceed the performance of the endocervical sample (Fig. 62.2). Progress toward licensing for this purpose is now under way. The benefit of using vaginal samples include that they can be accurately self-collected and do not require a pelvic examination to obtain; that the use of a swab sample eliminates an additional step in laboratory processing required by the urine-based sampling; and that they are as accurate or even more accurate when compared with the other sampling sites in detecting the presence of chlamydial infection. This sampling is particularly adapted to the NAATs.

Conjunctival specimens are excellent sources for specimens for NAATs. In prepubertal girls, particularly in sexual abuse cases, cultures are the preferred testing technique for vaginal, nasopharyngeal, and rectal specimens. Rectal specimens when needed for any purpose have not proved to be amenable to NAATs due to inhibitors present in rectal specimens.

Laboratory Diagnosis

The newly introduced NAATs present the clinician with an almost "ideal" diagnostic tool. Their introduction has also led to a redefinition of the gold standard from Chlamydia culture to a combination of the testing techniques, which include the highly sensitive NAATs. The impetus for developing nonculture tests was the result of the difficulties with using the culture technique, including expense, intense processing protocols, nonavailability, false-negative results, length of time required for processing, lack of applicability to urine specimens, among other problems. It must be remembered that the lower the prevalence rate, particularly less than 5%, the higher the potential for a false-positive test result among the nonculture techniques for testing.

Chlamydia-specific Tests

1. Direct fluorescent antibody (DFA) or enzyme immunoassay (EIA): The first generation of specific nonculture tests were the fluorescent monoclonal antibody stains (i.e., DFA) and EIAs. Although the test performances were slightly poorer than culture in the best laboratories, the DFA and EIA tests could be applied to urine.

2. Nonamplified DNA probes: The first-generation nucleic acid DNA probes included the nucleic hybridization tests (nonamplified DNA probes). However, the performance of these nonamplified nucleic acid probes was not significantly better than that of DFA, EIA, and culture (Fig. 62.2).

3. NAATs: The amplified nucleic acid tests have revolutionized Chlamydia screening because they have increased sensitivity and can be applied to noninvasive specimens such as urine in both male and female patients. Differing in their approach to amplification of nucleic acid, examples of such tests applied to Chlamydia detection include PCR, LCR, and transcription-mediated amplification assay. Although more sensitive, these newer nucleic tests are currently more expensive than the older tests. However, it is likely that costs will decrease as more types of tests are available and used in screening for chlamydial infections.

Comparison of performance of different test types by type of specimen is outlined in Fig. 62.2.

Nonspecific Tests Indicative of Possible Chlamydial Infection

1. LET: Although sometimes forgotten in the excitement of the development of the sensitive but relatively expensive NAATs, the LET still has a place in screening among the asymptomatic male patient. Originally applied to Chlamydia screening in young males by Shaffer et al. (1989), the performance of the LET to detect Chlamydia among 948 asymptomatic adolescent males is as follows: sensitivity, 72%; specificity, 93%; positive predictive value, 58%; and negative predictive value, 96%. These findings are supported by a recent study of largely asymptomatic men attending an STD clinic who provided urine samples for LET and NAATs screening (using PCR). Results showed the same high negative predictive value (96%) (Bowden, 1998). Such a widely available and inexpensive test can be used in a simple algorithm to decide which men need further definitive testing, that is, those with a positive LET result (more than or equal to one reading).

2. Cytology: Cytological specimens are unsatisfactory to detect chlamydial infection.

3. Serology: There is no use for the application of serology in acute genital infection with Chlamydia. Epidemiological studies linking the presence of antibody to tuberculosis infection and most recently to possibly cervical cancer have been of some clinical usefulness.

![Fig. 62.2](image-url)
Who Should Be Tested for Chlamydia?

The major approach recommended by the CDC and most professional health services and policy organizations (e.g., the American Academy of Pediatrics, the American Medical Association, Health Plan Employer Data and Information Set [HEDIS], American College of Obstetricians and Gynecologists, among others) is that all sexually active adolescent females should be screened for Chlamydia at least once a year. Attempts to identify risk factors to develop algorithms have not proven fruitful among this at-risk population. The greatest factor besides sexual activity is simply young age. In addition to the obvious teenage male or female who has genitourinary symptoms, adolescents on the street, in detention, who are paid for sex, who use intravenous drugs, who are pregnant, who are victims of sexual assault, who have chosen to have a therapeutic abortion, who have had prior STDs, who have new and multiple partners, and who do not use barrier contraception consistently should be considered for screening.

TREATMENT

Principles of Chlamydial Treatment

Treatment guidelines and recommendations were derived for the most part from the CDC (1998). A number of principles should guide the treatment of C. trachomatis in adolescents and young adults. These range from understanding the basic biology and epidemiology to transmission and recent advances in antibiotic treatment of chlamydia. Some of these important factors are listed:

- Emergence of resistance to current regimens is not a problem, which is unlike that found with gonococcal infections.
- Most data accrued on uncomplicated chlamydial infections are based on young male populations, particularly those who are symptomatic and attend STD clinics.
- NGU is eradicated by the appropriate dosing with tetracyclines, erythromycin, trimethoprim-sulfamethoxazole, ofloxacin, and possibly amoxicillin (high dose).
- Most single-dose regimens for treatment of gonorrhea do not eradicate concomitant chlamydial infections.
- "Recurrence" occurs in 3%-15% of men treated for NGU with appropriate 7-day tetracycline regimens, which represents recurrence, reinfection, or nongonococcal/nonchlamydial urethritis not sensitive to tetracycline.
- Single-dose oral azithromycin is an effective treatment for uncomplicated chlamydial infections; however, sexual abstinence for 7 days is still needed to ensure effective treatment and reduce reinfection between partners.
- Single-dose oral azithromycin is recommended as an alternative regimen for treatment of pregnant women, because only preliminary data indicate its safety and effectiveness in pregnancy.
- The new urine-based NAATs have rendered much "syndromic" treatment unnecessary in girls, except in select cases in which the risk is very high and follow-up is very low; in men, it is still possible to determine most chlamydial urethritis rapidly by Gram stain criteria when urine-based NAATs are not possible.

Empirical Treatment

Definitive testing and subsequent appropriate disease-specific treatment should be the rule regarding chlamydial treatment. Empirical treatment is reserved for specific situations in the adolescent client:

- **Urethritis:** Adolescents with symptoms but no documentation of urethritis who are at high risk for infection (e.g., those with prior STD infections and multiple partners) are unlikely to return for follow-up should receive empirical treatment. ("Documentation" here would include the presence of mucopurulent/purulent urethral discharge, Gram stain consistent with chlamydial or gonococcal infection, positive LET results on first-catch urine sample, or >10 WBCs/HPF on first-catch urine who have multiple partners.)
- **MPC:** Presence on examination if the prevalence of chlamydial infection in the population is high (15%) and follow-up is unlikely.
- **PID:** All three minimal clinical criteria for PID are met including lower abdominal tenderness and adnexal tenderness and cervical motion tenderness.

Regimens

Recommended Regimens

Uncomplicated urethral, endocervical, or rectal infection in adults and adolescents should be treated with one of the following:

1. Azithromycin 1 g orally in a single dose, OR
2. Doxycycline 100 mg orally b.i.d. for 7 days

Alternative Regimens

Alternative regimens are as follows:

1. Erythromycin base, 500 mg by mouth q.i.d. for 7 days, OR
2. Erythromycin ethylsuccinate, 800 mg by mouth q.i.d. for 7 days, OR
3. Ofloxacin, 300 mg orally b.i.d. for 7 days, OR
4. Levofloxacin, 500 mg orally once a day for 7 days

Azithromycin has the advantage of single-dose administration. With increased use, its price is becoming competitive with other traditionally cheaper regimes. It is approved as an alternative regimen for use during pregnancy because its safety and efficacy have been shown in preliminary studies. Ofloxacin is also very effective but may be more expensive and not approved for use during pregnancy or for adolescents younger than 18 years. (However, another quinolone, ciprofloxacin, is commonly used in cystic fibrosis in children without adverse effects.) Erythromycin has more gastrointestinal toxicity but is inexpensive and can be used during pregnancy.

Follow-up

When taken as directed, azithromycin, doxycycline, and ofloxacin are highly effective (more than 95%). If one of these regimens is used, posttreatment tests of cure are not required unless symptoms persist or reinfection is suspected. Posttreatment testing 3 weeks after completion of treatment should be considered if erythromycin is used. Retesting before 3 weeks after completion of therapy can lead to false-positive results. Patients with positive posttreatment test results should be re-treated with one of the preceding regimens, because resistant chlamydiae have not been described. Partners should also be re-treated. If urethritis symptoms in males persist, the addition of nongonococcal/nonchlamydial infection not responsive to tetracycline.

Adolescents with chlamydial infections appear to be twice as likely to have a recurrent chlamydial infection compared with young adult women. Among the few available studies that were largely conducted before the era of the more sensitive NAATs, reported recurrence rates were from 18% to 50%, with most recurring within 1 year (Burstein, 1998b; Hillis, 1994; Fortenberry et al., 1999). Applying PCR technology on adolescents attending STD community and school-based clinics in the Baltimore area, Burstein et al. (1998b) reported the median time to reinfection to be 6.3 months. Because of the concern about increased tissue damage with 1 year (Burstein, 1998b; Hillis, 1994; Fortenberry et al., 1999). Applying PCR technology on adolescents attending STD community and school-based clinics in the Baltimore area, Burstein et al. (1998b) reported the median time to reinfection to be 6.3 months. Because of the concern about increased tissue damage with

Sex Partners

All sex partners should be referred for evaluation and treatment. The exact time intervals for exposure have not been well evaluated. The CDC recommends referring sex partners of symptomatic patients who have had exposure within 30 days. This should be extended to 60 days if the patient is asymptomatic. The last sex partner
should be treated even if the time interval is more than 60 days. Sex partners of mothers with infected newborns should also be evaluated and treated.

Patients should avoid sexual contact until they and their partners are treated and are assumed cured. With the increasing use of single-dose azithromycin, it is prudent to remain sexually abstinent for a minimum of 7 days after completing treatment of both (or all) partners.

**Pregnant Patients**

**Recommended Regimen During Pregnancy**

1. Erythromycin base 500 mg by mouth q.i.d. for 7 days, OR
2. Amoxicillin 500 mg by mouth t.i.d. for 7 days

**Alternative Regimens**

1. Erythromycin base 250 mg by mouth q.i.d. for 14 days, OR
2. Erythromycin ethylsuccinate 800 mg q.i.d. for 7 days, OR
3. Erythromycin ethylsuccinate 400 mg q.i.d. for 14 days

Doxycycline, ofloxacin, levofloxacin, and erythromycin estolate are contraindicated during pregnancy. Preliminary studies have shown the safety and efficacy of azithromycin use in pregnancy and the CDC now recommends it as an alternative regimen in the treatment of pregnant women with chlamydial infection.

**HIV Infection**

Adolescents with HIV and chlamydial infections should receive the same treatments listed for those without HIV infection.

**PREVENTION**

1. **Goal**
   a. To prevent overt and “silent” chlamydial PID and its sequelae
   b. To prevent perinatal and postpartum infections
   c. To prevent adverse consequences of chlamydial infections at other anatomical sites
   d. To prevent recurrence of infection in young women, which is linked to increased upper reproductive tract tissue damage

2. **Prevention strategies**
   a. **Primary prevention**
      - Behavioral changes include reduction of the number of sex partners, delaying age at first intercourse, and the use of condoms. Chlamydia is often neglected in discussions of HIV risk and sexual behaviors. Information about chlamydia should be incorporated into educational materials and discussions regarding risk behaviors. Specific areas to cover include the following:
        - Chlamydia is the most common reported STD, particularly among adolescents and young adults
        - Adverse consequences of chlamydia in self, current, and future partners (e.g., PID and infertility, question of link to cervical cancer in women)
        - Symptoms and signs of infection in self and partner (and other STDs)
        - Asymptomatic or “silent” infection, particularly the link to undetected PID
        - Need for discussion with and treatment of sex partners
        - Referrals and services available in the community for testing and treatment of partners
        - Discussion of the link between substance use (particularly alcohol and marijuana), poor decision making, and acquisition of STDs including chlamydia
   
   b. **Secondary prevention**
      - Screen females to identify and treat asymptomatic chlamydial infections at least once a year and more often if risky behaviors are identified in the interim.
      - Rescreening: retest of index-positive cases 3–4 months after treatment.

   A high prevalence of *C. trachomatis* infection is found in women who have had chlamydial infection in the preceding several months. Most post-treatment infections result from reinfection, often occurring because patient’s sex partners were not treated or because the patient resumed sex among a network of persons with a high prevalence of infection. Repeat infection confers an elevated risk of PID and other complications when compared with initial infection. Therefore, recently infected women are a high priority for repeat testing for *C. trachomatis*. For these reasons, clinicians and health care agencies should consider advising all women with chlamydial infection to be rescreened 3–4 months after treatment. Some experts believe rescreening is an especially high priority for teens. Providers are also strongly encouraged to rescreen all women treated for chlamydial infection whenever they next present for care in the following 12 months, regardless of whether or not the patient believes that her sex partners were treated.

   Rescreening is distinct from early retesting to detect therapeutic failure (test-of-cure). Except in pregnant women, test-of-cure is not recommended for persons treated with the recommended regimens, unless therapeutic compliance is in doubt.

   - Track and treat all positive clients and their partners.
   - Recognize chlamydia-associated syndromes such as MPC and treat as appropriate.

3. **Target populations**
   a. Sexually active adolescents and young adults
      - Female patients: It is recommended to screen sexually active adolescent and young adult females younger than 25 years for Chlamydia at least annually. With the advent of urine-based testing, the goal should be to screen for *Chlamydia* first and perform a pelvic examination only when necessary—not just for Chlamydia screening purposes. Because of the high rate of recurrence, it is advisable to consider rescreening a young woman with a positive Chlamydia test result within 3–4 months after treatment of the index infection or whenever increased risk presents itself (e.g., unprotected sex or multiple new sex partners).
      - Males patients: The urinary LET has been shown to be a useful “first step” among lower risk sexually active male adolescents and young adult males. If positive, it is then more efficacious to perform a more definitive Chlamydia screening test such as a NAAT.
   b. Pregnant women and those before receiving an induced abortion
   c. Adolescents, particularly females, in detention facilities or attending an STD clinic

**CHLAMYDIA-associated Syndromes**

**Nongonococcal Urethritis**

Criteria for NGU include objective evidence of urethritis in a patient with negative test results for *N. gonorrhoeae*. Stripping the urethra in suspected males by exerting pressure on the penis with the forefinger and thumb and moving from the base to the meatus three times will help demonstrate a discharge. Objective evidence of NGU includes the following:

1. A mucopurulent/purulent urethral discharge and/or
2. Gram stain of urethral secretions containing 5 WBCs/HPF oil immersion. If no gram-negative intracellular diplococci (GNID) are present, NGU is diagnosed; or
3. GNID are present, gonococcal infection is diagnosed and chlamydial infection is considered likely (about 50%) with subsequent treatment for dual infection.

The LET is frequently used to screen urine from asymptomatic males for evidence of urethritis. For those adolescents with a positive LET result, the diagnosis should be confirmed with a Gram stained smear from the urethra or a more definitive test such the urine-based NAAT for *Chlamydia* and testing for gonorrhea (culture, NAATs, Gram stain). The etiology of uncomplicated urethritis is discussed earlier in this chapter. Treatment is discussed earlier also with the treatment of uncomplicated infections.
If symptoms persist, the teen should be re-treated with the initial regimen if noncompliant, if the individual had sexual contact with an infected partner before 7 days after both completed treatment, or if the individual had a new partner. If the teen was compliant and was not reexposed, then a urethral swab specimen should be obtained and the specimen should be tested for *T. vaginalis* using a wet mount or direct culture. The recommended empirical treatment of the non-reexposed and compliant patient is as follows:

Metronidazole 2 g by mouth once, AND
Erythromycin base 500 mg by mouth q.i.d. for 7 days, OR
Erythromycin ethylsuccinate 600 mg by mouth q.i.d. for 7 days

**Mucopurulent Cervicitis**

MPC is known by the presence of a mucopurulent/purulent endocervical discharge from the endocervical os. There is disagreement on the definition and meaning of the finding. Although both *C. trachomatis* and *N. gonorrhoeae* have been related to the presence of MPC, in most cases, neither is identified on testing. In most cases of documented chlamydial and gonococcal cervical infection, MPC is not found on examination. Other organisms associated with discharge and friability of the cervix include herpes simplex virus and human papillomavirus. However, it is not unusual to be unable to identify any cause of the finding of MPC in some women. Some findings associated with MPC as are as follows:

1. Mucopurulent secretion from the endocervix, usually yellow or green, particularly when viewed on a white cotton-tipped swab (positive swab test)
2. More than 10 PMN leukocytes per oil immersion field on a Gram stained smear of endocervical secretions
3. Cervical friability (bleeding when the first swab culture is taken)
4. Erythema or edema within a zone of cervical ectopy

MPC has been associated with adverse pregnancy outcome. Nugent and Hillier (1992) found that female patients with more than or equal to 30 PMN leukocytes per high-powered oil immersion field were twice as likely to deliver a low-birth-weight infant.

Empirical treatment of MPC should be considered only in a female patient who is suspected to be infected with a gonococcal or a chlamydial infection if both the prevalence of these infections is more than 15% in the targeted population and if follow-up with the individual will be difficult. Treatment should follow the parameters for chlamydial and gonococcal infection treatment. If after investigation and empirical treatment MPC persists, management is unclear.

**Treatment of Sex Partners** Males exposed to females with mucopurulent discharge should be evaluated for an STD and treated with the same regimen as their sex partner.

**Pelvic Inflammatory Disease**

Because many cases of PID are caused by more than one organism, treatment regimens must include broad coverage. Evaluation and treatment of PID are discussed in detail in Chapter 63.

**Acute Epididymoorchitis**

Most epididymoorchitis infections that affect sexually active adolescents and young adults are often associated with urethritis due to *C. trachomatis* (most frequent), *N. gonorrhoeae*, and gram-positive cocci. In young postpubertal men, coliform and *Pseudomonas aeruginosa* are less common and occur in zero to about one third of men. Gram-negative enteric organisms occur more frequently in men older than 35 years. In homosexual males, epididymitis may also be caused by sexually transmitted organisms such as *E. coli* among the insertive partners involved in anal intercourse. Males with epididymitis usually complain of unilateral testicular pain and tenderness, and a hydrocele or swelling of the epididymis is usually present. However, it must be remembered that the most common cause of an acute painful scrotal swelling in the sexually active male adolescent is torsion of the spermatic cord, which is a surgical emergency—and not epididymitis. Therefore, the workup for torsion and an infectious etiology must be done in concert and must be done with urgency. The diagnosis is based on a dual diagnostic workup for infection and torsion.

**Infection** A painful scrotal mass with a purulent urethral discharge is likely due to epididymitis in this age group until proven otherwise. The workup includes the following:

1. A Gram stained intraurethral swab sample to evaluate for GNID and for more than five PMNs per oil immersion field
2. Testing of an intraurethral swab specimen or first-part urine for *N. gonorrhoeae* and *C. trachomatis*
3. Culture and/or testing of urine for WBC counts and for other urogenital pathogens associated with epididymitis

**Torsion of Spermatic Cord** A painful scrotum, particularly with pain of sudden onset not accompanied by a urethral discharge, is likely due to a mechanical torsion in the male adolescent.

1. Same workup as for urethritis/epididymitis described in items 1–3
2. Radionuclide or Doppler scan
   a. If normal to increased uptake/pulsations: Torsed testicular appendix or epididymitis requiring conservative treatment for torsed appendix and antibiotics for epididymitis.
   b. If decreased uptake/pulsations: Spermatic cord torsion needing emergent surgical intervention.
   c. Surgery may be the first diagnostic approach depending on the length of time of the pain because scans and Doppler are not 100% sensitive in the diagnosis and the testicular salvation decreases markedly with increased time before intervention.

**Treatment** Treatment should be initiated before culture results are known.

**Regimen of Choice**

1. Ceftriaxone 250 mg intramuscularly once AND
2. Doxycycline 100 mg orally b.i.d. for 10 days

Bed rest and elevation of the scrotum are also recommended.

**Alternative Regimen**

Ofloxacin (300 mg orally b.i.d. for 10 days) is not approved for use in individuals younger than 18 years.

These regimens are similar in HIV-infected teens. However, in immunocompromised adolescents fungal and mycobacterial causes are more common. Those teens who fail to respond within 3 days require close reevaluation of the diagnosis and therapy.

**Sex Partners**

Sex partners should be examined for an STD and treated with a regimen effective against uncomplicated gonococcal and chlamydial infections. Both partners should avoid sexual contact until therapy is completed and both individuals are asymptomatic.
For Teenagers and Parents


For Health Professionals


REFERENCES AND ADDITIONAL READINGS


Pelvic inflammatory disease (PID) is an ascending polymicrobial genital tract infection of sexually active females. It includes an array of inflammatory disorders, including endometritis, parametritis, salpingitis, oophoritis, tuboovarian abscess (TOA), peritonitis, and perihisatilis. Neisseria gonorrhoeae and Chlamydia trachomatis are usually the causative agents of PID, but vaginal and enteric microorganisms contribute to its pathogenesis. In addition to the pain and risk accompanying the acute infection, nearly 20% of women with PID experience at least one long-term consequence, such as chronic pelvic pain, ectopic pregnancy, or infertility. Intervention efforts aimed at PID during adolescence focus on primary prevention of all sexually transmitted disease (STD) and secondary prevention through aggressive screening and early treatment of gonorrhea and chlamydia. The rates of U.S. cases of gonorrhea, chlamydia, and hospitalization for PID decreased during the 1990s. Although it is likely that the overall rate of PID decreased, there may have been some shift in the management of PID from the inpatient to the outpatient setting.

Etiology

Risk Factors

1. Age: The risk of PID among sexually active females is highest during early adolescence, with twice as many cases reported at age 12 years than at age 28 years. Adolescents account for 33% of all cases of PID, and women younger than 25 years account for 70% of cases. The tenfold risk of PID and threefold risk of gonorrheal or chlamydial infection among sexually active adolescents compared with that of adults are explained by both biology and behavior.
   a. Cervical ectropion: The erythematous ring around the cervical os that is commonly seen on pelvic examination of adolescent patients represents the transitional zone between the columnar and squamous epithelium. Cells in this zone are highly susceptible to sexually transmitted infections. During childhood, the transitional zone is located in the distal vagina. By adulthood, it usually recedes into the more protected environment of the endocervical canal.
   b. Cervical secretory immunoglobulin A: The levels are lower during adolescence than adulthood due to the lower prevalence of past exposure to immunogenic factors.
   c. Sexual risk behaviors
   d. Age at first intercourse: Risk for all STDs is inversely related with adolescent age at coitarche.
2. Sex partners: The risk of PID in females with multiple partners is 4.6 times higher than that for females with one partner. The risk for both STDs in general and PID is highest within 3 months of contact with a new partner.
3. Previous PID: A history of previous PID increases the risk of subsequent PID 2.3 times. At least one in five females with PID will experience a subsequent episode.
4. Race: Nonwhite adolescents are 2.5 times more likely to develop PID than white adolescents.
5. Contraceptive methods
   a. Condom: Increased use among adolescents in the United States since 1991 has contributed to the declining rates of gonorrheal and chlamydial infections.
   b. Spermicide: Nonoxynol 9 promotes cell wall destruction of N. gonorrhoeae and C. trachomatis.
   c. Oral contraceptive: Oral contraceptive use decreases the risk of PID sevenfold by thickening the cervical mucus and by decreasing cervical dilation, uterine contraction, and blood flow during menses.
   d. Intrauterine device (IUD): Use of the IUD increases the risk of PID seven to nine times among nulliparous women and two to four times among all women. However, the risk is concentrated in the weeks after insertion and then declines rapidly. In addition, IUDs developed recently seem to carry a lower risk than the earlier systems.
   e. Vaginal douching: Increases the risk of PID twofold.
6. Bacterial vaginosis: Bacterial vaginosis has been associated with PID after first-trimester therapeutic abortion, as well as third-trimester preterm delivery.
7. Substance use: Use of alcohol, marijuana, and other illicit drugs is associated with increased rates of sexual risk behaviors and STDs in general.

Microbiology

PID is a polymicrobial infection that usually begins with a sexually transmitted organism such as gonorrhea or chlamydia but involves other organisms as well, such as anaerobes. Normally, the upper genital tract (uterus, fallopian tubes, ovaries) is sterile. Organisms isolated from the upper genital tract of women with PID include the following:

1. N. gonorrhoeae: 25%–50% of women with PID have evidence of upper tract gonococcal infection, and of these, 40% have evidence of chlamydial infection. The likelihood of positive endocervical test results for gonorrhea is three times higher among women with PID who present within the first 24 hours of symptoms than among women who present after 48 hours.
2. C. trachomatis: 10%–43% of women with PID have reported to have evidence of upper tract chlamydial infection. However, laboratory testing for Chlamydia has improved dramatically over the past decade and it is likely that the rates are higher than those previously reported.
3. Bacteroides species and other anaerobes: 50% of women with PID have evidence of upper tract infection with anaerobic organisms.
4. Escherichia coli, Streptococcus species, and other facultative bacteria
5. Mycoplasma hominis and Ureaplasma urealyticum

Pathogenesis

1. After lower tract infection with N. gonorrhoeae or C. trachomatis, the normal vaginal lactobacilli are supplanted by anaerobes, facultative bacteria, and genital mycoplasmas.
2. Inflammatory disruption of the cervical barrier facilitates ascension of the inciting sexually transmitted pathogens and other microorganisms from the vagina into the normally sterile environment of the uterus. Plasma cell infiltration of the endometrium is the hallmark of PID.
3. Menstrual fluid is believed to facilitate ascension of microorganisms for the following reasons:
   a. Cervical os is open.
   b. Mucous plug is absent.
   c. Blood in the endometrial cavity supports growth of microorganisms.
   d. Myometrial contractions propel spread of infection from the uterus to tubes.
4. Decreased tubal motility secondary to inflammation results in collection of fluid (hydrosalpinx) or pus (pyosalpinx) within the tube.
5. Spillage of infected contents from the tubal fimbriae into the peritoneal cavity may result in the following:
   a. Peritonitis
   b. Perihepatitis (Fitz-Hugh-Curtis syndrome): Injected material tracks along the paracolic gutter. Inflammation of the hepatic capsule and diaphragm cause right-upper-quadrant (RUQ) pain and referred right subscapular pain. Liver function study results are normal or minimally elevated.
   c. TOA: Develops if resolution of the upper tract infection is delayed or if previous tubal scarring occludes the tube. The abscess can form in the tube or between the tube and ovary. Estimates of TOA formation range from 7%–19% of women with PID.
   d. Adhesions: As PID resolves, scar tissue may form in the tube, between the tube and ovary, or in the peritoneal cavity. Adhesions are the cause of subsequent infertility, ectopic pregnancy, and chronic pain.

PRESENTING SYMPTOMS

1. Abdominal pain: More than 80% of adolescents with PID present with abdominal pain, and 50%–75% of those with pain present within 7 days of menses. The pain is usually pelvic, but 5%–15% of women with PID may present with RUQ pain alone or accompanying pelvic pain. The pelvic pain of PID is constant, cramping, and exacerbated by walking and intercourse.
2. Abnormal vaginal bleeding: The endometritis of PID is associated with menorrhagia, metromenorrhagia, or menometrorrhagia in 35% of patients with PID. Unlike anovulation, which is the most common cause of irregular bleeding during adolescence, bleeding due to PID is painful.
3. Vaginal discharge: Cervicovaginitis and/or vaginitis cause an abnormal discharge in about 50% of patients with PID.
4. Gastrointestinal (GI) symptoms: Peritonitis may cause an ileus with anorexia, nausea, or vomiting; most patients, however, do not complain primarily of GI symptoms.
5. Subclinical: Women undergoing evaluations for infertility who recall no symptoms suggestive of PID have been found to have tubal scarring and serum antibodies to C. trachomatis or N. gonorrhoeae. This suggests that some cases of PID are subclinical. Decreased severity of symptoms does not translate into decreased likelihood or severity of sequelae, particularly because milder presentation may delay diagnosis and treatment.

Findings on Physical Examination

1. Vital signs: Temperature higher than 38°C is present in 40% of patients with laparoscopically verified PID. Tachycardia secondary to the pain and fever is common.
2. Abdomen: Tenderness to palpation of the lower abdomen, with or without rebound and guarding.
3. Pelvic examination
   a. Abnormal vaginal or cervical discharge
   b. Foul, inflamed cervix
   c. Cervical motion tenderness is present in more than 80% of patients with PID.
   d. Adnexal tenderness may be unilateral or bilateral.
   e. Palpation of an adnexal mass varies widely across studies, from 5%–60%.
   f. Uterine tenderness is common and may be elicited on both the pelvic and rectal examinations.

Laboratory Findings

The following laboratory findings support the diagnosis of PID, but their absence does not exclude the diagnosis. All laboratory study results may be normal in patients with PID, and no single test is diagnostic of PID.

1. Pregnancy test: If positive, ectopic pregnancy must be considered.
2. White blood cell (WBC) count: Elevated in 30%–50% of patients with PID.
3. Erythrocyte sedimentation rate (ESR): An ESR of >15 mm/hr is found in 75% of patients with PID.
4. Wet mount: Saline and microscopic examination of the cervical discharge will show >10 WBCs per high-power field if cervicitis is present.
5. Microbiological tests: Positive results for N. gonorrhoeae or C. trachomatis support but do not confirm the diagnosis of PID because cervicitis may exist without endometritis, salpingitis, or peritonitis. Furthermore, presumptive diagnosis and treatment of PID should not await microbiological test results.
   a. Samples should be collected and sent to the laboratory before initiating antibiotic therapy.
   b. Because a pelvic examination is required for the diagnosis of PID, endocervical, rather than vaginal or urine samples, are preferred.
   c. The specimens should be examined for N. gonorrhoeae and C. trachomatis, but not for anaerobes, mycoplasmas, or enteric organisms that normally colonize the vagina.
   d. The preferred test for N. gonorrhoeae in patients with PID is either endocervical cell culture (sensitivity and specificity both exceed 95%) or ligase chain reaction (LCR), which has a sensitivity of 92%–97% and a specificity of 97%–100%.
   e. The preferred test for C. trachomatis in patients with PID is endocervical LCR, which has a sensitivity and specificity of 97%–100%.
6. Urinalysis and urine culture: Most patients with suspected PID should also be evaluated with urinalysis and urine culture for urinary tract infection.
7. T. gondii: Human immunodeficiency virus (HIV) testing: All patients with STDs warrant discussion about the risk of HIV infection and should be offered counseling and testing.
8. Pelvic ultrasonography: Can help narrow the differential diagnosis or confirm suspected ectopic pregnancy or TOA. Images should be obtained both transabdominally and transvaginally in the patient.
9. Laparoscopy: Surgical intervention is rarely necessary to establish the diagnosis of PID. It may be indicated diagnostically in the patient whose pain does not respond to antibiotic therapy, and therapeutically in the patient with a persistent TOA.

DIAGNOSIS

The timely and accurate diagnosis of PID is essential in preventing sequelae. The positive predictive value of a clinical diagnosis of PID, using laparoscopic diagnosis as the gold standard, ranges from 65% to 90%, depending on the criteria used and the epidemiological characteristics of the patient population. Thus, it is important to remember that no one symptom or sign is specific or pathognomonic for PID. Although the differential diagnosis is broad (Table 63.1), the most important prevalent conditions to consider in adolescents are appendicitis, ectopic pregnancy, corpus luteum cyst rupture or hemorrhage, and endometriosis.

TABLE 63.1. Differential diagnosis of pelvic inflammatory disease

The Centers for Disease Control and Prevention (CDC) has recently revised recommendations on the use of minimum and elaborate criteria for the diagnosis of PID (Table 63.2). These recommendations for diagnosing PID are intended to help health care providers recognize when PID should be suspected and when additional information is needed to increase diagnostic certainty. PID should be considered as a likely diagnosis in any woman with pelvic tenderness and signs or symptoms of lower genital tract inflammation. Empirical treatment should be initiated in young women at risk for STDs if the following minimum criteria are present and no other
cause(s) for the illness can be identified:

TABLE 63.2. Centers for Disease Control and Prevention diagnostic criteria for pelvic inflammatory disease

<table>
<thead>
<tr>
<th>Centres for Disease Control and Prevention diagnostic criteria for pelvic inflammatory disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uterine or adnexal tenderness, or</td>
</tr>
<tr>
<td>Cervical motion tenderness.</td>
</tr>
<tr>
<td>Treatment may be indicated based on a patient's profile of risk factors.</td>
</tr>
<tr>
<td>More elaborate diagnostic criteria are often needed, because incorrect diagnosis and management might cause unnecessary morbidity. These additional criteria may be used to enhance the specificity of the minimum criteria. Additional criteria that support a diagnosis of PID include the following:</td>
</tr>
<tr>
<td>1. Oral temperature &gt;101°F (&gt;38.3°C)</td>
</tr>
<tr>
<td>2. Abnormal cervical or vaginal mucopurulent discharge</td>
</tr>
<tr>
<td>3. Presence of white blood cells (WBCs) on saline microscopy of vaginal secretions</td>
</tr>
<tr>
<td>4. Elevated erythrocyte sedimentation rate</td>
</tr>
<tr>
<td>5. Elevated C-reactive protein</td>
</tr>
<tr>
<td>6. Laboratory documentation of cervical infection with *N. gonorrhoeae or C. trachomatis.</td>
</tr>
<tr>
<td>Of note, most women with PID have mucopurulent cervical discharge or evidence of WBCs on a microscopic evaluation of a saline preparation of vaginal fluid. If the cervical discharge appears normal and there are no white blood cells noted on the saline wet prep, the diagnosis of PID is unlikely and alternative causes of pain should be sought.</td>
</tr>
<tr>
<td>The most specific criteria for diagnosing PID, which are warranted in selected cases, include the following:</td>
</tr>
<tr>
<td>1. Endometrial biopsy with histopathologic evidence of endometritis</td>
</tr>
<tr>
<td>2. Transvaginal sonography or magnetic resonance imaging techniques showing thickened fluid-filled tubes with or without free pelvic fluid or tubo-ovarian complex</td>
</tr>
<tr>
<td>3. Laparoscopic abnormalities consistent with PID.</td>
</tr>
<tr>
<td>The CDC urges, however, that clinicians maintain a low threshold for the diagnosis and empirical treatment of PID.</td>
</tr>
</tbody>
</table>

THERAPY

PID requires treatment with broad-spectrum antibiotics as soon as a presumptive diagnosis is made. CDC criteria for hospitalization are as follows:

1. Surgical emergencies such as appendicitis cannot be excluded.                   |
2. Pregnancy                                                                      |
3. Poor response to oral antimicrobial therapy.                                    |
4. Inability to follow or tolerate an outpatient oral regimen.                     |
5. Severe illness, nausea and vomiting, or high fever                            |
6. TOA (at least 24 hours inpatient followed by home parenteral therapy)         |
7. Immunodeficiency (i.e., HIV infection with low CD4 counts, immunosuppressive therapy) |

Whether treatment is indicated as an inpatient or outpatient, the following general recommendations hold:

1. Patients should be educated about the importance of completing a full 14-day course of antibiotics. The duration of treatment does not depend on the result of any laboratory test. |
2. All sex partners within the preceding 60 days require treatment of gonorrhea and chlamydia, regardless of patient or partner test results for \*C. trachomatis and \*N. gonorrhoeae. |
3. The use of nonsteroidal antiinflammatory drugs is recommended to treat abdominal pain or cramping. |
4. In the setting of TOA, clindamycin or metronidazole with doxycycline is used as continued therapy for expanded anaerobic coverage. |
5. Single-dose azithromycin has not been shown to be effective for the treatment of PID. |

CDC-recommended treatment regimens for PID are summarized in Table 63.3 and Table 63.4

<table>
<thead>
<tr>
<th>TABLE 63.3. Centers for Disease Control and Prevention recommended parenteral antibiotic regimens</th>
</tr>
</thead>
</table>

TABLE 63.4. Recommended Hospitalization Regimens for Pelvic Inflammatory Disease

<table>
<thead>
<tr>
<th>Hospitalization Regimens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inpatient Parenteral</td>
</tr>
<tr>
<td>TOA (24 hours inpatient followed by home parenteral)</td>
</tr>
<tr>
<td>Single Dose Azithromycin</td>
</tr>
<tr>
<td>Clindamycin or Metronidazole with Doxycycline</td>
</tr>
</tbody>
</table>

Table 63.3 and Table 63.4 summarize CDC-recommended treatment regimens for PID.
Patients who do not improve clinically within 72 hours require further testing or surgical intervention.

Communities must prioritize the establishment and maintenance of comprehensive STD control strategies that include health promotion, as well as education about the signs and symptoms of STDs, the consequences of STDs, and behaviors that increase or decrease the risk should begin early.

Primary prevention involves education about STD prevention and aggressive screening of all sexually active adolescents.

Recurrence: Reported rates vary from 12% to 33%. Risk is inversely correlated with treatment of sexual contacts.

Infertility: One episode of PID is associated with a 13%–21% risk; two episodes, a 35% risk; and three or more episodes, a 55%–75% risk. Care must be taken in counseling an adolescent who has had PID about the risk of infertility. Although it is important that she understand the complications associated with infection, she should not assume that she is unable to conceive.

Ectopic pregnancy: PID is the single most common predisposing factor for ectopic pregnancy. One episode of PID increases the risk sixfold to tenfold.

Chronic abdominal pain: Dysmenorrhea and dyspareunia occur in up to 18% of women after one episode of PID.

SECONDARY PREVENTION

Adolescents with PID who are treated as outpatients should have a follow-up examination within 72 hours to document defervescence and improvement in pain. Repeated screening to document cure of C. trachomatis and N. gonorrhoeae infection is optional. It is not indicated if the baseline test results are negative. If a baseline test result is positive by LCR, test of cure should be delayed for at least 1 month after completion of therapy.

CONSEQUENCES

1. Recurrence: Reported rates vary from 12% to 33%. Risk is inversely correlated with treatment of sexual contacts.

2. TOA: May occur in as many as one third of individuals hospitalized with salpingitis. Physical examination may not detect all individuals with a TOA. Antibiotic therapy is effective in 42%–92% of cases. Surgical therapy is indicated for rupture or ultrasound evidence of increasing size or nonresponse.

3. Infertility: One episode of PID is associated with a 13%–21% risk; two episodes, a 35% risk; and three or more episodes, a 55%–75% risk. Care must be taken in counseling an adolescent who has had PID about the risk of infertility. Although it is important that she understand the complications associated with infection, she should not assume that she is unable to conceive.

4. Eclectic pregnancy: PID is the single most common predisposing factor for ectopic pregnancy. One episode of PID increases the risk sixfold to tenfold.

5. Chronic abdominal pain: Dysmenorrhea and dyspareunia occur in up to 18% of women after one episode of PID.

PREVENTION

PID can be a life-changing event in adolescence. For many young women, it is a first experience with severe pain, illness, and hospitalization. For others, it leads to prolonged suffering and disappointment about reproductive expectations. Unfortunately, few studies exist that evaluate prevention strategies. However, the CDC has published recommendations for both individuals and health providers to prevent STDs and PID. The emphasis for all adolescents should be on primary and secondary prevention.

1. Primary prevention involves education about STD prevention and aggressive screening of all sexually active adolescents.

   a. Education about the signs and symptoms of STDs, the consequences of STDs, and behaviors that increase or decrease the risk should begin early.

   b. Communities must prioritize the establishment and maintenance of comprehensive STD control strategies that include health promotion, as well as confidential clinical service.

2. Secondary prevention focuses on those adolescents with a history of PID.

   a. Counseling should begin with the initiation of antibiotic therapy. If the adolescent is hospitalized, the inpatient stay provides an important opportunity for intense education and discussion.

   b. Sex partners should be included in secondary counseling and education.

   c. Prevention continues after treatment, with the promotion of secondary abstinence or safer sexual behaviors.

WEB SITES

For Teenagers and Parents

http://www.niaid.nih.gov/factsheets/stdpid.htm, National Institutes of Health handout on PID.

http://www.mckinley.uiuc.edu/health-info/womwnhth/pid.html, University of Illinois health center handout.

http://depts.washington.edu/hhpcc/women/PID.html, University of Washington handout on PID.

http://www.4woman.gov/faq/stdpids.htm, National Women's Health Information Center site.


http://webmd.lycos.com/content/asset/adam_disease_oophoritis, WebMD information on PID.

For Health Professionals


http://edcenter.med.cornell.edu/CUMC_PathNotes/Female_Genital_Tract/FGT_2.html, Cornell University teaching slides on female genital tract.


REFERENCES AND ADDITIONAL READINGS


ETIOLOGY
The agent causing syphilis is *Treponema pallidum*, a motile, spiral microorganism 6 to 20 µm in length and 0.10 to 0.18 µm in diameter. The organisms do not stain well and are best visualized by dark-field microscopy. *T. pallidum* does not grow in artificial media.

EPIDEMIOLOGY

Hosts
Human beings are the only known natural host. Experimental infections are produced in rabbits, monkeys, and chimpanzees.

Transmission
Most infections are contracted during sexual contact, including kissing and sexual intercourse. Rare cases occur from direct contact with infectious cutaneous or mucous membrane lesions. Rashes are not infectious if the skin is intact. Other modes of transmission include congenital and transfusion-related transmission. The estimated rate of transmission after sexual exposure to a person with a chancre is 30%. The risk of transmission persists during the first 4 years of untreated syphilis.

Incidence
Syphilis incidence shows a cyclical waxing and waning, with peaks at intervals of approximately 7 to 10 years. Syphilis incidence rates peaked in 1990 at about 60 per 100,000 individuals, both men and women, age 20 to 24 years. The 1990 incidence rates for 15- to 19-year-olds was about 18 per 100,000 for men and 42 per 100,000 for women. During the remainder of the 1990s, rates declined to less than 15 per 100,000 for all age groups. Epidemiologically, syphilis shows substantial geographical concentration, with more than 50% of primary and secondary cases reported from fewer than 1% of U. S. counties. The southeastern section of the United States bears an especially heavy burden of syphilis. Although most new cases are found among young adults age 20 to 30 years, adolescents participating in commercial sex work, in cocaine and crack cocaine distribution or use, or in other social or sexual networks are important foci in localized outbreaks.

The current nadir in incidence of syphilis cases and the geographical clustering has prompted the Centers for Disease Control and Prevention (CDC) to target syphilis for elimination in the United States during the first decade of the 21st century.

PATHOGENESIS
*T. pallidum* enters the body via minute abrasions in the skin and exposure to sera of moist, mucocutaneous lesions. The infection is spread via lymphatics and blood vessels. The spirochetes cause cellular infiltrates, granuloma formation, and an obliterative endarteritis. This can lead to necrosis, with resultant ulcerations and erosions. In later stages tissue hypersensitivity becomes prominent and can lead to gummas. Syphilitic lesions heal by scar formation so that in tertiary lesions scarring is considerable.

CLINICAL MANIFESTATIONS

Primary Syphilis
Syphilis should be considered in the differential diagnosis of any ulcerating lesion of the anogenital or oral areas. Less frequently affected areas are breasts and fingers. After an incubation period of 9 to 90 days with an average of 21 days, the primary lesions appear. Syphilis is characterized by a chancre at the point of inoculation. Characteristics of the syphilitic chancre are as follows.

1. Location
   a. Ninety-five percent are on the external genitalia.
   b. Single lesions are typical but multiple lesions are common.
   c. Lesions may also appear as “kissing lesions,” chancres that touch each other across a fold of skin.
   d. Other primary sites include the cervix, mouth, anus, lips, face, breast, and fingers.
2. Size: 1 to 2 cm.
3. Chancre: Starts as a painless papule eroding to an indurated, painless ulcer. The ulcer typically has a punched out, clean appearance, with slightly elevated, firm margins.
4. Regional lymphadenopathy accompanies the lesion. The nodes are firm, nonsuppurative, and bilateral and may be painless.
5. Healing: The chancre heals in 3 to 6 weeks.

The primary infection may manifest with an inconspicuous lesion, particularly in women. Infection may occur with no papule or ulcer at all, particularly in previously infected patients.

Secondary Syphilis

Approximately 6 to 8 weeks (maximum, 6 months) after exposure and 4 to 10 weeks after the onset of the chancre, the manifestations of secondary syphilis appear. During this stage, *T. pallidum* can be identified in lesions and body fluids. The signs and symptoms of secondary syphilis usually disappear after weeks or months. Up to 25% of patients with untreated secondary syphilis develop relapses of secondary disease, with about one fourth of these having multiple relapses. Secondary syphilis lesions are infectious if the lesions are open (e.g., on mucous membranes, in intertriginous areas). Signs and symptoms of secondary syphilis include the following:

1. **General skin eruption:** Most common manifestation, affecting 90% of individuals with secondary syphilis
   a. Eruption involves the trunk and extremities with a predilection for palms and soles. The lesions on the palms and soles may be scaly and hyperkeratotic, and they may be the last to clear.
   b. Eruption involves skin as well as mucous membranes.
   c. Eruption tends to follow the lines of cleavage.
   d. Eruption is bilateral and symmetrical.
   e. Individual lesions are sharply demarcated, 0.5 to 2.0 cm in diameter with a reddish-brown hue.
   f. Eruption is most commonly macular, papular, or papulosquamous. Less common are follicular rashes. Vesicular and pustular rashes are rare.
   g. Lesions are typically nonpruritic, but pruritus is not infrequent.
   h. Eruption may last a few weeks to 12 months.
   i. Variety: Almost any type of rash can occur with syphilis, including acneform lesions, herpetiform lesions, and lesions similar to psoriasis. Lesions in intertriginous areas may erode and fissure, especially in the nasolabial folds and near the corners of the mouth. In warm, moist areas, hypertrophic granulomatous lesions (condylomata lata) may occur. These lesions usually occur near the area of the original chancre and have a broad, flat appearance.

2. **General or regional lymphadenopathy** (about 70%)
   a. Nonpainful nodes
   b. Rubbery, hard feeling; discrete; with no suppuration
   c. Occasional hepatosplenomegaly

3. **Flu-like syndrome (about 50%)**
   a. Sore throat and malaise most common
   b. Headaches
   c. Lacrimation
   d. Nasal discharge
   e. Arthralgias and myalgias
   f. Weight loss
   g. Fever

4. **Syphilis alopecia** (uncommon): Moth-eaten—appearing alopecia of the scalp and eyebrows

5. **Other rare manifestations**
   a. Arthritis or bursitis
   b. Hepatitis
   c. Iritis and anterior uveitis
   d. Glomerulonephritis

**Late Syphilis**

The early latent period is defined as the first year of infection. Early syphilis includes primary, secondary, and early latent syphilis. The late latent stage refers to the period after this first year unless late (tertiary) syphilis occurs. Latent syphilis is characterized by the following:

1. Absence of clinical signs and symptoms of syphilis
2. Repeated positive serological tests (Venereal Disease Research Laboratory [VDRL] and fluorescent treponemal antibody absorption [FTA-ABS]) for syphilis
3. Negative results from serological tests of the spinal fluid

**Neurosyphilis**

Neurosyphilis develops in 10% to 20% of patients with untreated syphilis but is uncommon in adolescents. Neurological involvement may become evident within 2 years after the initial infection. Most cases of neurosyphilis in adolescents are asymptomatic or manifest as acute syphilitic meningitis. Meningovascular syphilis is rare.

1. **Asymptomatic neurosyphilis:** Characterized by abnormal cerebrospinal fluid (CSF), including pleocytosis, elevated protein, and positive CSF-VDRL
2. **Acute syphilitic meningitis**
   a. Usually occurs during secondary syphilis or the early latent period
   b. Common symptoms: Fever, headache, photophobia, and meningismus
   c. Cranial nerve palsies (40%)
   d. Less frequent symptoms: Confusion, delirium, and seizures
   e. CSF: Increased protein, lymphocytic pleocytosis, and sometimes lowered glucose
3. **Meningovascular syphilis**
   a. Rare in adolescents (occurs 5 to 12 years after initial infection)
   b. Symptoms and signs from a syphilitic endarteritis producing local areas of infarction
   c. Symptoms: Headache, dizziness, mood changes, memory loss
   d. Signs: Hemiparesis, hemiplegia, aphasia
   e. Other signs of parenchymal nervous system damage: Argyll-Robertson pupils (accommodation, but no response to light); injury to the posterior column of the spinal cord, causing tabes dorsalis

**Late Syphilis**

Signs and symptoms of late syphilis may occur 2 to 10 years after initial exposure in untreated or inadequately treated patients. This includes individuals with gummas and cardiovascular syphilis but not neurosyphilis. Late syphilis has not been reported in adolescents.

Cardiovascular syphilis usually occurs 10 to 30 years after exposure.

Gummas are granulomatous lesions of late syphilis that involve skin, soft tissue, viscera, or bones. They are usually few in number, asymmetrical, indolent, and not contagious.

**Congenital Syphilis**

The fetus becomes susceptible to infection after the 4th month of gestation. Therefore, adequate treatment of the mother before the 16th week of gestation prevents...
infection of the fetus. The risk of infection of the fetus during untreated early maternal syphilis is about 80% to 95%. Approximately 25% of infants infected in utero die before birth, and 25% die shortly after birth, if untreated. The remainder develop either early or late lesions.

1. Early congenital syphilis lesions (lesions occurring during the first 2 years of life and usually by 3 months of age)
   a. Vesicular and vesiculobullous eruptions
   b. Superficial desquamation
   c. Rhinitis
   d. Hepatosplenomegaly
   e. Hemolytic anemia, thrombocytopenia
   f. Skeletal involvement: Osteochondritis with periarticular swelling
   g. Neurosyphilis
   h. Ocular: Glaucoma, uveitis, chorioretinitis
   i. Nephropathy: Uncommon

2. Late congenital syphilis: This type of syphilis corresponds to tertiary syphilis in adults. In 60% of cases the infection remains latent, and in the rest the lesions can be divided into the following categories.
   a. Inflammatory or hypersensitivity lesions
   b. Gummas
   c. Neurosyphilis
   d. Intestinal keratitis
   e. Clutton joints: Symmetrical, painless swelling of knees
   f. Palatal deformations
   g. Paroxysmal cold hemoglobinuria

3. Unique stigmata
   a. Hutchinson incisors: Centrally notched, screwdriver-shaped upper incisors
   b. Abnormal facies: Saddlenose, frontal bossing
   c. Eighth nerve deafness
   d. Scaphoid scapulas
   e. Hutchinson triad: Malformed incisors, eighth nerve deafness, and interstitial keratitis

DIFFERENTIAL DIAGNOSIS

Primary Syphilis

Sexually Transmitted Causes of Genital Ulcers The most common sexually transmitted genital ulcers in the United States are herpes, syphilis, and chancroid, in that order. Lymphogranuloma venereum and donovanosis (granuloma inguinale) are rare in the United States.

1. Herpes simplex: Usually painful, multiple lesions beginning as vesicles on an erythematous base. Primary lesions are usually bilateral, extensive, and associated with tender adenopathy, and recurrent lesions are usually unilateral without significant adenopathy. The vesicles break down into ulcers with nonindurated borders.

2. Chancroid: Usually painful lesions with a deep purulent base and often erythematous borders. Local lymph nodes are often fluctuant and tender.

3. Lymphogranuloma venereum: The primary lesion may be a nonindurated, herpetiform ulcer that heals rapidly. Many patients present with advanced disease including fever and massive regional adenopathy.


Nonsexually Transmitted Causes of Genital Ulcers The most common nonsexually transmitted cause is trauma.

1. Traumatic lesions: There should be a history of appearance of the lesion at the time of the trauma. However, many patients attribute genital ulcers to trauma without a specific history of injury.

2. Fixed drug reaction: There may be history of a similar lesion after prior drug exposure. Lesions may start as reddish plaque and become hyperpigmented, edematous, or eroded.

3. Candida balanitis.

4. Behçet syndrome: Not limited to genital area.

5. Psoriasis, if excoriated.

6. Lichen planus, if excoriated.

7. Erythema multiforme, if excoriated.


Secondary Syphilis

1. Psoriasis

2. Pityriasis rosea

3. Drug eruptions

4. Tinea versicolor

5. Alopecia areata

6. Lichen planus

7. Viremia

8. Lupus erythematosus

9. Scabies

10. Pediculosis

11. Rosacea

12. Infectious mononucleosis

13. Keratodermia blennorrhagica

14. Condyloma acuminatum

Although the clinical history and appearance of these conditions can often separate them from secondary syphilis, a VDRL or rapid plasma reagin (RPR) test should be performed whenever doubt exists.

DIAGNOSIS

Syphilis screening is an important element of routine health care for sexually experienced adolescents. Adolescents should also be screened during pregnancy or when diagnosed with other sexually transmitted infections. However, as the prevalence falls in certain lower-risk groups, such as college students, the criteria for screening syphilis serology will have to be reevaluated.

Laboratory Findings

**Dark-field Examination** The dark-field examination is essential in evaluating moist ulcers and lesions such as a chancre or condyloma lata. Technique is as follows.

1. Clean lesion with saline and gauze.

2. Abrade gently with dry gauze. Avoid inducing bleeding, which makes dark-field examination more difficult.

3. Squeeze lesion (with gloves) to express serous transudate.

4. Place a drop of transudate on a slide.
5. Place a drop of saline on transudate and cover with a cover slip.
7. Procedure must be repeated on 3 successive days before it is considered negative.
8. For internal lesions, a bacteriological loop can be used to transfer the fluid to a slide.
9. For lymph node aspirations: Clean the skin, inject 0.2 mL or less of sterile saline, and aspirate the node. Place the fluid on a slide.

**Direct Fluorescent Antibody** Specimens from primary lesions can also be sent to reference laboratories or some state health departments for direct fluorescent antibody (DFA) staining. These specimens can be collected as described previously; however, saline should not be added to the slides, and they should be allowed to air-dry.

Both dark-field microscopy and DFA staining are very specific except for oral specimens, but sensitivity depends on many factors, including collection technique, age of lesions, and experience of laboratory personnel.

### Serological Tests

1. **Nontreponemal antibody tests:** Tests for a nonspecific anti-cardiolipin antibody that forms in response to surface lipids on the treponeme
   - a. Types
      - Agglutination: RPR (qualitative test)
      - Flocculation: VDRL (quantitative test) used for screening or to monitor therapy
   - b. Use: Nontreponemal tests are used to monitor treatment success. Nontreponemal test titers correlate with disease activity and fall after treatment. If a positive qualitative test is confirmed by a treponemal test, a quantitative VDRL should be obtained, titered out to the highest point, and monitored over time. A fourfold change in titer, equivalent to a change of two dilutions (e.g., from 1:8 to 1:32 or 1:16 to 1:4), demonstrates a substantial change if the same serological test is used.

2. **Specific treponemal antibody tests**
   - a. Types
      - Immunofluorescence: FTA-ABS is used to confirm a positive result from RPR or VDRL.
      - Microhemagglutination: The microhemagglutination–T. pallidum (MHA-TP) test has replaced the FTA-ABS test in many laboratories as the specific treponemal test to confirm a positive result from VDRL.
      - Immobilization: T. pallidum immobilization (TPI)
   - b. Use: Treponemal tests are specific and sensitive, but because of their expense and more difficult technical requirement, they are typically used to confirm positive results from a screening test. Once an individual tests positive on treponemal tests, he or she usually remains positive for life. Titer are unrelated to disease activity or treatment. Treponemal antibody titters therefore should not be quantitated but recorded as reactive, nonreactive, or minimally reactive. A minimally reactive test result may represent a false-positive finding, and the test should be repeated.

3. **Tests in development:** These include treponeme-specific immunoglobulin M (IgM) antibody tests and polymerase chain reaction (PCR) tests.

### Sensitivity

- a. The sensitivity of nontreponemal tests (RPR and VDRL) in primary syphilis ranges from 60% to 90% depending on the duration of infection and the population under study. Results are positive at the following times:

<table>
<thead>
<tr>
<th>Onset of primary chancre</th>
<th>About 25% of individuals are positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 weeks after chancre appearance</td>
<td>50% are positive</td>
</tr>
<tr>
<td>3 weeks after chancre appearance</td>
<td>75% are positive</td>
</tr>
<tr>
<td>4 weeks after chancre appearance</td>
<td>100% are positive</td>
</tr>
</tbody>
</table>

- b. Treponemal tests (MHA-TP and FTA-ABS) are positive in 80% to 100% of primary syphilis. Sensitivity of nontreponemal and treponemal tests approaches 100% in secondary syphilis.

5. **False-positive serology test results:** About 20% to 40% of all positive nontreponemal test results are false-positive results, as shown by a nonreactive treponemal test. Most false-positive nontreponemal test results show a low titer (dilution less than 1:8), and the probability of a false-positive finding decreases with increasing titer. The causes of false-positive test results include the following.

- a. Acute infection: Viral infections, chlamydial infections, Lyme disease, Mycoplasma infections, nonsyphilitic spirochetal infections, and various bacterial, fungal, and protozoal infections
- b. Autoimmune diseases
- c. Narcotic addiction
- d. Aging
- e. Hashimoto thyroiditis
- f. Sarcoidosis
- g. Lymphoma
- h. Leprosy
- i. Cirrhosis of the liver
- j. Human immunodeficiency virus (HIV) infection: Can lead to unusually high, unusually low, or fluctuating titers
- k. False-positive findings can occasionally arise in treponemal tests. However, most of these are reported as borderline and not positive. Only a positive TPI provides conclusive proof of past or present infection. The TPI, however, is reserved for research purposes and difficult diagnostic cases.

6. **Tests most commonly used**
   - a. RPR (screening and quantitative measurement of clinical activity)
   - b. VDRL (quantitative measurement to assess clinical activity and response to therapy or qualitative test for screening)
   - c. MHA-TP or FTA-ABS (to confirm diagnosis in a patient with a positive result from VDRL or RPR)
   - d. Other tests under development are based on PCR, enzyme immunoassay, or enzyme-linked immunosorbent testing for treponeme-specific antibody–secreting cells. Clinical experience with these tests is limited, and they have not replaced existing modes of screening and confirmation.

### Diagnosis by Stage

#### Primary Syphilis

1. **Definitive diagnosis of early syphilis requires a positive dark-field examination or DFA test of lesion transudate or tissue.**
2. **Presumptive diagnosis relies on a positive nontreponemal test (VDRL or RPR) with a high titer (1:8 or higher) or rising titer (more than two dilutions) and a positive treponemal test result (e.g., FTA-ABS or MHA-TP).**

Adolescents with a positive dark-field examination should be treated, as should those with a typical lesion and a positive serological test result. Sexual partners (within the previous 90 days) of persons with documented infection should also be treated. If the initial serological test result is negative, it should be repeated 1 week, 1 month, and 3 months later in suspected cases. An FTA-ABS or MHA-TP test should be used to confirm a positive nontreponemal test result.

Lumbar puncture is not recommended for routine evaluation of primary syphilis unless clinical signs and symptoms of neurological involvement are present. The role of lumbar puncture in the care of HIV-infected persons with primary syphilis is controversial.

#### Secondary Syphilis

1. **Dark-field examination of material from lesions or lymph nodes**
2. **VDRL or RPR**

An adolescent should be treated if the dark-field examination result is positive or if the patient has typical findings of secondary syphilis and a positive result from VDRL or RPR. Adolescents with atypical findings or a quantitative nontreponemal titer less than 1:16 should have a second quantitative nontreponemal test and an FTA-ABS or MHA-TP test. Positive nontreponemal tests should be confirmed with an FTA-ABS or MHA-TP test.
Neurosyphilis The standard test is the CSF-VDRL. It is a specific but not a sensitive test for active neurosyphilis. On the other hand, the FTA-ABS is sensitive but not specific for neurosyphilis. Serum antibody may diffuse into the CSF and may not be reflective of active central nervous system (CNS) disease. However, a nonreactive FTA-ABS probably indicates the absence of active neurosyphilis. Pleocytosis in the CSF is another good indicator of active disease.

The CDC, in their 1998 treatment guidelines for sexually transmitted diseases (STDs), listed the following indications for CSF examination:

1. Neurological or ophthalmological signs or symptoms
2. Treatment failure
3. Serum nontreponemal test titer greater than or equal to 1:32
4. Other evidence of active syphilis (aortitis, gumma, iritis)
5. Nonpenicillin therapy planned unless duration of infection is known to be less than 1 year
6. HIV infection

Spinal fluid tests should include cell count, protein, and VDRL. There are no perfect tests for evaluating neurosyphilis. The cell count is usually elevated in the presence of neurosyphilis and is an excellent marker for assessing treatment. The VDRL is the standard and most specific test on spinal fluid, but it has a sensitivity of only 60% to 70%. Although the FTA-ABS is highly sensitive, the false-positive rate may be 0% or greater because of transfer of antibodies across the blood-brain barrier. Some experts order both tests. If the FTA-ABS result is negative, the likelihood of neurosyphilis is very small.

Latent Syphilis A RPR/VDRL and a FTA-ABS test should be given. The FTA-ABS is essential in latent and late syphilis because the nontreponemal tests are only about 70% sensitive in these states. The adolescent should be treated if the FTA-ABS result is positive and there is no documentation of appropriate prior treatment.

Examination of spinal fluid in individuals with late latent syphilis and a negative neurological examination is controversial. If a lumbar puncture is not performed, the concern is whether the standard 3-week treatment for latent syphilis will be adequate for the treatment of asymptomatic neurosyphilis.

Syphilis in Pregnancy All pregnant adolescents should be screened early in pregnancy. Seropositive subjects should be considered infected unless a prior history documents recent treatment and serological titers have appropriately declined. Screening should be repeated in the third trimester and again at delivery in areas or populations with a high prevalence of syphilis. A female delivering a stillborn infant after 20 weeks’ gestation should also be tested for syphilis.

Congenital Syphilis

1. Evaluation recommendations: Who? The CDC recommends evaluating infants born to seropositive mothers who:
   a. Have untreated syphilis
   b. Had treated syphilis in pregnancy but the treatment was less than 1 month before delivery, involved a nonpenicillin regimen, or was accompanied by a lack of appropriate decrease in serological titers
   c. Do not have a well-documented history of syphilis treatment
   d. Have a documented treatment regimen but undocumented serological follow-up after therapy
2. Evaluation recommendations: How? The CDC recommends the following evaluation of infants born to women in the preceding situations:
   a. Thorough physical examination, looking for evidence of congenital syphilis
   b. Quantitative nontreponemal serological test for syphilis performed on the infant's sera (not cord blood)
   c. CSF analysis for cells, protein, and VDRL
   d. Long-bone x-ray examination
   e. Other tests if clinically indicated (e.g., chest radiographic examination, complete blood count, liver function tests)
   f. For infants who have no evidence of congenital syphilis by this evaluation, determination of the presence of specific antitreponemal IgM antibody by a CDC-recognized method
   g. Pathological examination of the placenta or amniotic cord using specific fluorescent antitreponemal antibody staining.
3. Treatment recommendations: Who? The CDC recommends treating infants if they have any of the following:
   a. Clinical evidence of active disease
   b. Radiographic evidence of active disease
   c. Reactive CSF-VDRL
   d. Abnormal CSF findings such as elevated cell count or protein even in the presence of nonreactive CSF-VDRL for infants born to seroconvertive mothers
   e. Quantitative nontreponemal serological titers fourfold higher than that of the mother
   f. Specific antitreponemal IgM antibody detected by a testing method given provisional or standard status by the CDC
   g. Mother with untreated early syphilis or who had evidence of relapse or reinfection after treatment

Syphilis and HIV Ulcerative lesions such as syphilitic chancres increase the risk of transmission of HIV. There is also evidence that infection with HIV alters the serological response to syphilis. There have been reports of patients who were coinfected with HIV and syphilis and had unusual serological responses. Many of these reports involved higher than expected serological titers, but false-negative serological test results have also been reported. Most treponemal and nontreponemal serological tests for syphilis are accurate for the majority of individuals with both syphilis and HIV infection. If serological tests are not consistent with clinical findings, alternative tests, such as biopsy and DFA staining of lesion material, should be considered. HIV-infected individuals with neurological disease should be evaluated for neurosyphilis.

Problem Sera

1. Positive nontreponemal test and negative treponemal test results
   a. False-positive nontreponemal test: Most likely explanation without strong clinical suspicion for syphilis
   b. False-negative treponemal results: Rare
2. Negative nontreponemal test and positive FTA-ABS results
   a. Early and late syphilis: May have negative nontreponemal test results
   b. Adequately treated syphilis: Most treated patients remain positive for treponemal tests for life
   c. False-positive treponemal test results: Rare
3. Negative nontreponemal and negative treponemal test results
   a. Absence of disease: Most likely unless strong clinical suspicion of syphilis is present
   b. Incubating or early syphilis: Recent sexual contact (within 90 days) with a partner with primary, secondary, or early latent syphilis; should be treated even if nontreponemal and treponemal tests are negative
4. Persistently positive nontreponemal results
   a. Untreated or inadequately treated syphilis
   b. Adequately treated syphilis but positive serological test results: such “serofast” results are usually low titer; decline in titer after treatment is always seen in adequately treated patients even if nontreponemal test results remain positive in low titer.
5. Borderline FTA-ABS results
   a. May indicate syphilis or a false-positive finding
   b. Test should be repeated; if results are still borderline, TPI should be performed

THERAPY

Penicillin is the optimal antibiotic for syphilis treatment. It is the only proven therapy for neurosyphilis, congenital syphilis, and syphilis during pregnancy. For individuals in these categories with a history of penicillin allergy, skin testing and desensitization, if indicated, are recommended. Because minor determinants of penicillin allergy are not commercially available, clinicians should be aware that 3% to 10% of patients with otherwise negative skin test responses are penicillin allergic. No adequately controlled comparative trials have been conducted to guide optimal penicillin regimens, including dose, duration, and preparation. The dose of penicillin is controversial in certain situations, particularly in regard to CNS involvement and in individuals who are immunocompromised. The cure of syphilis probably
Benzathine penicillin G: The total recommended dose is 2.4 million units intramuscularly (IM) at a single session.

Ceftriaxone 250 mg IM daily for 10 days is probably effective, but careful follow-up is mandatory; optimal dose and duration have not been established, and experience has been limited.

Late latent syphilis or latent syphilis of unknown duration: Benzathine penicillin G 7.2 million units total administered as three doses of 2.4 million units IM each.

Individuals with symptomatic late syphilis should have a CSF examination before therapy begins.

Other considerations:
- All patients with syphilis should be tested for HIV. For high-risk patients or in high-prevalence areas, patients with primary syphilis should be retested for HIV after 3 months.
- Those individuals with signs or symptoms that suggest neurological or ophthalmic disease should be evaluated by CSF analysis or slit-lamp examination, respectively. Routine lumbar puncture is not recommended for individuals with primary or secondary syphilis unless clinical signs and symptoms suggest neurological involvement.
- Follow-up:
  - Infected individuals should be reexamined clinically, and serological test results should be checked at 3 and 6 months. Quantitative nontreponemal tests should be used for follow-up, because the FTA-ABS results usually remain positive throughout the individual's life. If signs or symptoms persist or nontreponemal antibody titers have not decreased fourfold by 6 months, the patient should have a CSF examination and HIV test and be retreated. Most individuals with primary syphilis are seronegative by 3 to 12 months, and 75% to 95% of individuals with secondary syphilis are seronegative by 1 year. The drop in titers for primary and secondary syphilis applies only to first episodes of primary or secondary syphilis; those with reinfections have less predictable serological drops.
  - Individuals are at risk for treatment failure if their nontreponemal titers have not declined fourfold by 3 months after treatment for primary or secondary syphilis. HIV testing should be performed at 3 months in these individuals.
  - Retreatment should probably include three weekly injections of benzathine penicillin G 2.4 million units IM unless neurosyphilis is present.

Latent Syphilis

Early latent syphilis is defined as disease acquired during the past year (based on documented seroconversion—that is, a fourfold or greater increase in titer of a nontreponemal serological test) and absence of clinical signs of primary, secondary, or tertiary syphilis. Late latent syphilis identifies a disease duration of 1 year or longer. The term latent syphilis of unknown duration is used when the timing of the initial infection cannot be established.

There are two regimens for patients who are not allergic to penicillin and who have normal CSF examinations:

1. Early latent syphilis: Benzathine penicillin G 2.4 million units IM in a single dose.
2. Late latent syphilis or late syphilis of unknown duration: Benzathine penicillin G 7.2 million units total administered as three doses of 2.4 million units IM each at 1-week intervals.
3. Penicillin-allergic patients: No clinical data exist that adequately document the efficacy of drugs other than penicillin for syphilis of more than 1 year's duration. CSF examinations should be performed before therapy with these regimens. Suggested regimens are doxycycline 100 mg orally twice a day, or tetracycline 500 mg orally four times a day. Either is given for 2 weeks to individuals with early latent syphilis or 4 weeks for other individuals. If the CSF examination shows any evidence of neurosyphilis, the patient should be treated for neurosyphilis.

Other considerations:
- All individuals with latent syphilis should be evaluated for tertiary disease including neurosyphilis, aortitis, iritis, and gummata.
- All patients with syphilis should be tested for HIV.

5. Follow-up:
- Quantitative nontreponemal serological titers should be done at 6 and 12 months after treatment. If titers increase fourfold or initial high titers (1 : 32 or greater) fail to decrease fourfold (two dilutions) within 12 to 24 months, or if signs or symptoms of syphilis occur, the individual should be evaluated for neurosyphilis and retreated appropriately.
- Approximately 75% of the patients with early latent disease (duration 4 years or less) become seronegative by 5 years; the remaining 25% have positive serology for life.

Late Syphilis

The term late syphilis describes patients with gumma disease or cardiovascular involvement but not neurosyphilis.

1. Recommended regimen: Benzathine penicillin G 7.2 million units IM or 2.4 million units IM daily for 10 days.
2. Penicillin-allergic patients: Treat with regimens similar to those listed for late latent syphilis.
3. Other considerations:
   - All individuals with symptomatic late syphilis should have a CSF examination before therapy begins.
   - All patients with syphilis should have HIV testing.
   - Approximately 25% of the patients with late disease become seronegative within 5 years, and the rest remain seropositive for life.

Neurosyphilis

Neurosyphilis can occur during any stage of syphilis. Patients with syphilitic eye involvement should be treated with regimens covering neurosyphilis. Individuals with neurological symptoms should have a CSF examination.

1. Recommended regimen for neurosyphilis or syphilitic eye disease in individuals not allergic to penicillin: Aqueous crystalline penicillin G 18 to 24 million units daily administered as 2 to 4 million units intravenously (IV) every 4 hours for 10 to 14 days.
2. Penicillin-allergic patients: Patients should be desensitized to penicillin, if necessary, and treated with penicillin. No alternatives have been adequately evaluated.
3. Follow-up:
   - If the initial CSF examination showed an increased cell count, the examination should be repeated every 6 months until the cell count is normal. If the count has not decreased at 6 months or is not normal by 2 years, retreatment should be strongly considered.

Syphilis in Pregnancy

All pregnant women should receive penicillin doses appropriate for their stage of syphilis. Although penicillin is effective in preventing transmission to the fetus and in treating infections in the fetus, the exact optimal penicillin regimens have not been adequately studied. Some experts recommend additional therapy, such as a second dose of benzathine penicillin G 2.4 million units IM given 1 week after the first dose, particularly for women in their third trimester with secondary syphilis. Tetracycline should not be used, because it is contraindicated in pregnancy. Erythromycin has a high risk of failure to cure the fetus. Therefore, pregnant women with a history of an allergy to penicillin should be skin tested and either treated or desensitized. A Jarisch-Herxheimer reaction during the second half of pregnancy can
induce premature labor or fetal distress.

Congenital Syphilis

1. Treatment should consist of either of the following two regimens:
   a. Aqueous crystalline penicillin G 100,000 to 150,000 units/kg/day (50,000 units/kg IV every 12 hours during the first 7 days of life and every 8 hours thereafter) for 10 to 14 days
   b. Procaine penicillin G 50,000 units/kg/day (IM once a day) for 10 to 14 days (14 days if neurosyphilis is present)
   c. If more than 1 day of therapy is missed, the course should be restarted.
   d. If findings from the infant's evaluation are normal but the mother was either (a) treated for syphilis during pregnancy or by erythromycin, (b) treated for syphilis less than 1 month before delivery, or (c) treated with penicillin appropriately but did not have an adequate serological response, the infant should be treated with 50,000 units/kg of benzathine penicillin G IM in a single dose.
   e. Penicillin-allergic children should be treated with penicillin after desensitization, if necessary.

2. Follow-up
   a. Seropositive infants untreated during the perinatal period: These infants must be observed closely at 1, 2, 3, 6, and 12 months after therapy.
   b. Treated infants: These infants also must be monitored closely every 2 to 3 months. The titers should become nonreactive by 6 months of age, but they may fall more slowly in infants treated after the neonatal period. Infants with cells in the CSF on initial examination should have a second CSF examination at 6 months or until the cell count is normal. The infant should be retreated if the cell count does not show a downward trend or is not normal by 2 years. The CSF-VDRL should also be checked at 6 months and the infant retreated if the test is still reactive.

HIV-infected Individuals

Among HIV-positive individuals, there have been reports of higher rates of neurological complications and treatment failures with traditional regimens for syphilis. There have also been cases in HIV-positive patients of rapid progress of syphilis into secondary and tertiary stages. However, no treatment regimens have yet been demonstrated to be more effective in treating HIV-infected individuals than those used in patients without HIV infection. HIV-positive patients with syphilis require careful evaluation for late and unusual manifestations of syphilis, including CSF evaluation. These patients require careful follow-up after therapy.

1. Penicillin regimens should be used whenever possible. Skin testing and desensitization can be used as appropriate.
2. Primary and secondary syphilis in HIV-infected patients: The CDC recommends no change in therapy for early syphilis in HIV-infected patients. Some experts recommend adding multiple doses of benzathine penicillin G, similar to the dosages used to treat late syphilis, or adding other antibiotics.
3. Patients with HIV and latent syphilis should have a CSF examination before treatment begins.
4. Identification of at-risk sex partners: Time periods used to determine partners at risk are as follows:
   a. Three months plus duration of symptoms for primary syphilis
   b. Six months plus duration of symptoms for secondary syphilis
   c. One year plus duration of symptoms for early latent syphilis

PREVENTION

To prevent the rising spread of syphilis, recommendations include screening in the following high-risk groups:

1. All women of childbearing age: In high-risk areas pregnant women should be screened several times: at the first visit, during the third trimester, and at the time of delivery. A cord blood sample should also be drawn and held pending maternal results.
2. All sexually active teens: Especially at risk are those with multiple partners, those with a substance abuse history, and those with another STD. Screening in lower-risk sexually active adolescents will have to be reevaluated as the prevalence rate of syphilis continues to fall in this group.
3. All men and women with two or more sex partners in 6 months
4. All persons who use illicit drugs
5. All persons who have had sexual contact with prostitutes
6. All patients who have another STD or are HIV positive: Positive cases should be reported to the local health department.

To prevent congenital syphilis, recommendations include the following:

1. All pregnant women, especially those with no history of prenatal care and women using illicit drugs, should be tested. High-risk mothers should be screened as outlined previously.
2. A postpartum mother should not be released from the hospital until the serological results have been reviewed.
3. The diagnosis of syphilis should be considered in any case of stillbirth or miscarriage and in any infant with symptoms, including snuffles, osteochondritis or periostitis, hepatosplenomegaly, rash, pneumonia, failure to thrive, jaundice, lymphadenopathy, neurological signs, fissures of the lips or other cutaneous lesions, or rinitis.
4. All infants of women diagnosed with syphilis within 1 year before delivery should be evaluated for congenital syphilis. Conversely, mothers of infants diagnosed with congenital syphilis should be evaluated and treated for syphilis.
5. All pregnant women with positive results from serological examination and all confirmed cases of congenital syphilis should be reported to the local health department.
6. HIV testing should be considered for all women and children diagnosed with syphilis, because more aggressive treatment may be required in patients who are
Herpes simplex virus is the cause of 90% of all vesiculoulcerative lesions of the genitalia. After human papillomavirus, it is the second most prevalent sexually transmitted disease. Herpes labialis: Between 16% and 45% of all adults report at least one episode during their lifetime, with 28% having recurrences at least twice a year. Infection is most prevalent in the 2- to 4-year-old age group. HSV-1: Primary infections with HSV-1 usually cause herpetic gingivostomatitis. HSV-2: This type most commonly causes genital herpes. Antibodies are not routinely detected until puberty, when antibody levels correlate with past sexual activity. Recurrent infections: Between 70% and 90% of patients infected with HSV-2 have a recurrence, compared with 50% of those infected with HSV-1. Recurrences vary by site and viral type. About 97% of recurrent genital infections are caused by HSV-2 and 3% by HSV-1. Therefore, identification of the type of infecting strain may have some prognostic importance to the individual and may be useful in counseling.

Pathogenesis

Virus particles can be shed in salivary, cervical, and seminal secretions of infected individuals. The virus gains entry to the body via mucosal surfaces or abraded skin and replicates in the epithelial and dermal cells of a susceptible host. After replication, the virus spreads via contiguous cells to mucocutaneous projections of sensory nerves.

In oral herpes the virus lodges in the trigeminal ganglion; in genital herpes the sacral dorsal root (S2 to S4) ganglion is the target site. Centrifugal spread can then
occur through peripheral sensory nerves back to the skin surface, so that large areas may be involved.

After resolution of the primary disease, the virus becomes latent. Latency appears to be lifelong but is interrupted by periods of viral reactivation, leading to silent viral shedding or clinically apparent recurrence. Reactivation of latent virus leads to transport of viral genomes to the skin surface, where replication occurs in the dermis and epidermis. Factors involved in activating latent virus may include fever, local trauma, exposure to sunlight, and stress.

Clinical Manifestations

Definition of Terms

1. **Primary infection**: Genital herpes in a patient seronegative for antibody to HSV-1 or HSV-2.
2. **Nonprimary first episode**: First clinically noted infection in an individual seropositive for HSV-1 or HSV-2.
3. **First clinical episode**: This term includes both primary infections and nonprimary first episodes; it should be used when the practitioner cannot clinically classify the patient's infection as a primary infection or a nonprimary first episode.
4. **Recurrence**: Return of genital HSV lesions in a patient with a previously documented episode of symptomatic genital herpes.

Primary Infection

1. **Incubation period**: 1 to 45 days, average 6 to 8 days.
2. **Duration a.** Time from onset of lesions to complete healing: approximately 3 weeks.
   b. Viral shedding: 11 days (median), can be much longer.
3. **Symptoms** start with paresthesias or burning sensations in the genital area, followed by the appearance of 1- to 2-mm vesicles on erythematous bases. Women are more likely to have symptoms when acquiring a new HSV infection (Langenberg et al., 1999).
4. Herpetic lesions can be extensive and can involve the vulva, perineum, vagina, and cervix or, in males, large areas of the penis. Early lesions are vesicular and then erode to become shallow ulcers. The lesions may coalesce, producing large ulcerated areas with surrounding edema, erythema, and secondary infection. Painful lesions are present in 95% of men and 99% of women with primary HSV infection.
5. Healing follows crusting of unbroken lesions and reepithelialization of ulcers.
6. **Primary infections** are usually more severe. They are characterized by significant local symptoms, multiple lesions (usually six or more), and enlarged, tender regional nodes. Lesions in primary infections are bilateral, whereas those appearing in recurrences tend to be unilateral.
7. Constitutional symptoms occur in more than half of patients with primary infection. Systemic complaints including fever, malaise, and myalgias are reported by almost 40% of men and 70% of women with primary HSV-2 disease. Neurological signs and symptoms (headaches, stiff neck, photophobia) are also common.
8. Dysuria, urinary retention, and dyspareunia may occur. Dysuria appears in 83% of women and 44% of men. Urethral discharge and dysuria are noted in about one third of men with primary HSV-2 infection. Herpes can be misdiagnosed as urinary tract infection (UTI). Therefore, inquire about genital sores and pain in a teen presenting with UTI symptoms.
9. Cervical involvement occurs in 90% of primary infections and 12% to 20% of recurrences. Rarely, a primary infection is manifested by necrotizing cervicitis.
10. **Course**: Systemic symptoms appear early, peak within the first 3 to 4 days, and recede over the next several days. The clinical symptoms of pain and irritation increase over the first 6 to 7 days, are maximal between days 7 and 11, and recede over the second week. Lesions persist 4 to 15 days, ending with crusting and reepithelialization. Scarring is uncommon. Tender inguinal adenopathy usually appears during the second and third week and is often the last symptom to resolve. Total duration is about 21 days, with a gradual worsening over the first 10 days and a 12-day healing period. Primary episodes of HSV-1 genital infection are similar in duration and character to those of HSV-2 genital infection.

Recurrent Episodes

1. The herpes virus lies dormant in the sensory neurons of the involved area until reactivation. This can occur frequently, infrequently, or never. The primary infection is the most severe, but recurrences are more likely to cause chronic anxiety and sexual dysfunction.
2. **Duration**
   a. Average time from onset of symptoms to complete resolution is 1 week.
   b. Viral shedding lasts 2 to 7 days.
3. **Symptoms**: About 50% of infected individuals have prodromal symptoms, ranging from mild tingling sensations to shooting pains in the buttocks, legs, or hips, hours to days before eruption. Lesions are similar to those seen in primary infection but are smaller in size and number. They tend to occur unilaterally, with the involved area being smaller, about one-tenth that of the primary infection. Systemic signs are minimal. Pain, lesion size, and virus shedding peak within 2 days after onset.
4. The typical course is 2 to 4 days of worsening symptoms, followed by 4 to 5 days of healing.
5. Recurrent herpes, like primary herpes, tends to be more severe in women.
6. Characteristics of recurrent episodes include predominantly nonmucosal skin involvement, small numbers of lesions (fewer than three), clustering of lesions, and resolution in 5 to 10 days.
7. After the first year, recurrences tend to decrease in frequency. Benedetti et al. (1994) examined recurrence rates of genital herpes after symptomatic first-episode infection. In their study of 457 patients with HSV-2 infection, 89% had at least one recurrence during follow-up. During the first year of follow-up, 38% had at least 6 recurrences and 20% had more than 10. However, 26% of women and 8% of men had no recurrences or only one recurrence in year 1. Patients who had severe primary HSV-2 infection (duration, 35 days or longer) had recurrences almost twice as often. Men with genital HSV-2 infection had about 20% more recurrences than did women. Benedetti et al. also looked at long-term recurrence rates of genital herpes in a 1999 study. The median recurrence rate in the first year after primary infection was 1 for HSV-1 infection (n = 59) and 5 for HSV-2 (n = 151). In the second year, the median was zero for HSV-1 and 4 for HSV-2. The rate of recurrences continued to drop in subsequent years, even for patients observed for more than 3 years. However, one third of patients experienced no decrease in recurrences over a 5-year period, and 25% of patients had more recurrences in year 5 than in year 1.

Table 65.1 shows a comparison of initial infections and reactivation, and Table 65.2 shows a comparison of serological types.

<table>
<thead>
<tr>
<th>Table 65.1</th>
<th>Table 65.2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Serological Type</strong></td>
<td><strong>Initial Infection</strong></td>
</tr>
<tr>
<td>HSV-1</td>
<td></td>
</tr>
<tr>
<td>HSV-2</td>
<td></td>
</tr>
</tbody>
</table>

TABLE 65.1. Comparison of initial infection and reactivation of herpes genitalis
DIFFERENTIAL DIAGNOSIS

Herpes genitalis lesions must be differentiated from early syphilis, chancroid, lymphogranuloma venereum, granuloma inguinale, excoriations, allergic and irritant contact dermatitis, molluscum contagiosum, warts, scabies, pediculosis, and genital lesions of Behçet syndrome.

DIAGNOSIS

Clinical History and Examination

The presence of symptoms and typical lesions is noted. A history of prior episodes or recent contact with an infected partner is helpful but not necessary to establish the diagnosis.

Dark-field examination and syphilis serology should be obtained if ulcers have an atypical appearance.

Laboratory Diagnosis

1. A Tzanck smear shows multinucleated giant cells. This test is inexpensive and rapid, but its sensitivity ranges from 30% to 80%, depending on the type of lesion and the experience of the observer. The technique was reviewed in detail by Cohen (1994).

2. A Papanicolaou (Pap) smear is also rapid and inexpensive but only 40% sensitive.

3. Viral culture is the gold standard of diagnosis at present, and it differentiates between HSV-1 and HSV-2. As the lesions progress through pustule, ulcer, and crusting, the sensitivity falls. Sensitivities in various stages are maculopapular, 25%; vesicular, 94%; pustular, 87%; ulcer, 70%; crusting, 27%. In clinically obvious cases of herpes, a viral culture is not absolutely necessary. However, knowledge of infection type (HSV-1 versus HSV-2) is helpful in predicting recurrences. In addition, most patients appreciate having a confirmed laboratory diagnosis, so cultures should be obtained when feasible.

a. Method of obtaining HSV cultures

   i. If intact vesicles are present: Aspirate vesicle fluid using a fine-gauge needle (best yield) or, if vesicles are too small to aspirate, gently unroof the vesicle and swirl fluid and debris. Use cotton or Dacron swabs rather than calcium alginate, which inactivates the virus. Immediately place the specimen in transport medium.

   ii. Pustules: Unroof the pustule and wash away purulent material with sterile saline; then swirl the base of the lesion.

   iii. To culture a ruptured vesicle or ulcers: Swab base of lesion.

b. When swabbing the base of a lesion, remember that friction must be used to obtain cells. Avoid contaminating the specimen with alcohol, soap, blood, or stool. If transport medium is not available, substitute sterile distilled water (minimally decreased yield). Leave the swab in the transport medium if transport time is less than 8 hours. If transport time is longer, swirl the swab vigorously in the medium and remove. If a laboratory courier is used, refrigerate the specimen before pickup.

c. With high-titer virus specimen cultures, results may be positive in 24 to 48 hours, but with lower titers the culture may require up to 7 days. Because cultures can be negative in the presence of herpes, use caution in reporting negative results to patients.

4. An enzyme-linked immunosorbent assay (ELISA) is available, with a sensitivity of 70% to 90% compared with viral isolation. ELISA does not reliably differentiate between virus types.

5. Immunofluorescence techniques can differentiate between HSV-1 and HSV-2, have excellent sensitivity and specificity, and are rapid, but they require an experienced technologist. These techniques are most often used when an immediate diagnosis is needed.

6. DNA probes and polymerase chain reaction (PCR) techniques are highly sensitive and specific but not widely available.

7. Type-specific Serologic Tests: Both type-specific and nonspecific antibodies to HSV develop during the first several weeks following infection and persist indefinitely. Because almost all HSV-2 infections are sexually acquired, type-specific HSV-2 antibody indicates anogenital infection, but the presence of HSV-1 antibody does not distinguish anogenital from oral/oral infection. Accurate type-specific assays for HSV antibodies must be based on the HSV-specific glycoprotein G2 for the diagnosis of infection with HSV-2 and glycoprotein G1 for diagnosis of infection with HSV-1. Such assays first became commercially available in 1999, but older assays that do not accurately distinguish HSV-1 from HSV-2 antibody, despite claims to the contrary, remain on the market. Therefore, the serologic type-specific gG-based assays should be specifically requested when serology is performed.

Currently the FDA-approved gG-based type-specific assays include: Dia gnostics POckit HSV-2, Focus Technology, Inc., HSV-1 or HSV-2 gG ELISA, and HSV-1 and HSV-2 Differential Hemglobin. The POckit HSV-2 assay is a point-of-care test that provides results for HSV-2 antibodies from capillary blood or serum during the clinic visit. The Focus Technology assays are laboratory-based. The sensitivities of these tests for detection of HSV-2 antibody vary from 80% to 98% and false-negative results may occur, especially early after infection. The specificities of these assays are >98%; false-positive results can occur, especially in patients with low likelihood of HSV infection. Therefore, repeat testing or a confirmatory test (e.g., an immunoblot assay if the initial test was an ELISA) may be indicated in some settings.

As false-negative HSV cultures are common, especially in patients with recurrent infection or with healing lesions, type-specific serologic tests are useful in confirming a clinical diagnosis of genital herpes. Additionally, they can be used to diagnose persons with unrecognized infection and to manage sexual partners of persons with genital herpes. While serologic assays for HSV-2 should be available for persons who request them, screening for HSV-1 or HSV-2 infection in the general population is not indicated.

THERAPY

We have used the guidelines from the Centers for Disease Control and Prevention (CDC, 2001) for dosing recommendations. Practitioners are encouraged to use regimens with less dosing per day to encourage compliance when at all possible.

Systemic antiviral drugs including acyclovir, valacyclovir, and famciclovir partially control signs and symptoms of herpes episodes when used to treat first clinical episodes or recurrent episodes or when used as daily suppressive therapy. However, none of these medications eliminates latent virus, nor do they affect the risk, frequency, or severity of recurrences when the medication is stopped. All three of these medications provide benefit for genital herpes. Acyclovir is the oldest approved antiviral for this indication and has the largest body of supporting research. Valacyclovir is a valine ester of acyclovir with increased absorption after oral intake. Topical use of acyclovir is less effective and is not recommended.

Indications

Oral antivirals are indicated for the treatment of initial episodes and for management of recurrences in certain individuals. Patients with primary episodes are more likely to benefit if the treatment is started promptly (while new lesions are forming) and if the episode is severe. Topical antiviral ointment is recommended only for
herpes labialis and should be discouraged in genital herpes.

Drug Action

Acyclovir is a guanosine analogue that inhibits viral replication of HSV-1 and HSV-2 by interfering with viral DNA polymerase. Valacyclovir is an acyclovir prodrug that is designed to improve on the relatively low bioavailability of acyclovir after oral administration. Valacyclovir is rapidly absorbed from the gastrointestinal tract and is converted to acyclovir and L-valine by first-pass metabolism in the intestines and liver. Famciclovir is converted to penciclovir and inhibits viral replication in a similar manner to acyclovir. It has high bioavailability and a much longer half-life than acyclovir.

Efficacy

First Clinical Episodes

Antivirals decrease:

1. Duration of viral shedding: Shortened by about 10 days.
2. New lesion formation: 44% of those taking a placebo develop new lesions, compared with 4% of those taking acyclovir.
3. Duration of pain: Decreased by about 25% (3 days for valacyclovir versus 4 days for placebo).
4. Time to healing (crusting): Reduced by 4 to 9 days.
5. Proctitis symptoms: Rompalo et al. (1988) examined the effect of acyclovir in the first episode of HSV proctitis and found the median duration of rectal lesions and viral excretion to be significantly shorter in treated patients. Duration of local signs and symptoms of proctitis was also shorter.
6. There is no effect on the subsequent rate of recurrences of first clinical herpes infections treated with antivirals.

Recurrent Episodes

Effective episodic treatment of recurrent herpes requires initiation of therapy within 1 day of lesion onset, or during the prodrome that precedes some outbreaks. The patient should be provided with a supply of drug or a prescription for the medication with instructions to self-initiate treatment immediately when symptoms begin.

Episodic Therapy

1. Viral shedding: Reduced by approximately 1 day.
2. Healing time: Reduced by an average of 1 full day by all three antivirals. A more pronounced effect is noted when therapy is self-initiated early in the course of a recurrent episode.
3. Duration of symptoms: Itching, burning, pain, lesion tenderness, and tingling are all significantly shortened with penciclovir (Sacks et al., 1994).
4. Recurrent episodes are not prevented if antivirals are used only on a periodic basis.

Suppressive Therapy

There is a significant reduction in frequency and duration of recurrent episodes when antivirals are used in a prophylactic fashion. With daily use, the frequency of recurrent infections is reduced by more than 75% in individuals with frequent recurrences (i.e., six or more per year). Suppressive therapy also reduces but does not eliminate asymptomatic viral shedding.

Dose

1. First-episode genital herpes
   a. Recommended regimens
      - Acyclovir (Zovirax or generic) 400 mg three times daily for 7 to 10 days (until clinical resolution).
      - Acyclovir 200 mg orally five times a day for 7 to 10 days, OR
      - Famciclovir (Famvir) 250 mg three times daily for 7 to 10 days, OR
      - Valacyclovir (Valtrix) 1 g orally twice daily for 7 to 10 days, OR
   b. The clinician may wish to treat longer than 10 days if healing is incomplete.
2. Recurrent genital herpes
   a. Recommended regimens for episodic recurrent infection
      - Acyclovir 400 mg three times daily for 5 days, OR
      - Acyclovir 200 mg orally five times a day for 5 days, OR
      - Acyclovir 500 mg orally twice a day for 5 days, OR
      - Famciclovir 125 mg twice daily for 5 days, OR
      - Valacyclovir 500 mg twice daily for 5 days, OR
      - Valacyclovir 1.0 g orally once a day for 5 days
   b. Recommended regimens for daily suppressive therapy: In general, consider suppressive therapy if the patient is having six or more recurrences per year. This approach may also be considered in patients with fewer but more severe recurrences and in patients who are in herpes-discordant relationships. Because recurrences tend to decrease over time, try discontinuing the medication every 1 to 2 years and observe.
      - Acyclovir 400 mg twice daily
      - Famiclovir 250 mg twice daily
      - Valacyclovir 500 mg orally once a day
      - Valacyclovir 1,000 mg orally once a day
3. Herpes labialis (oral herpes): Penciclovir (Denavir) cream every 2 hours (while awake) for 4 days. Alternatively, oral antivirals listed for treatment of genital herpes may be used in the same dosages. For recurrences, 3 or 4 days of treatment is usually adequate.
4. Immunocompromised patient: Because immunocompromised individuals have prolonged and/or severe herpetic episodes, intermittent or suppressive therapy with oral antiviral agents can be of benefit. The exact dosing in these individuals has not been well documented but higher dosing appears to be of some benefit, such as acyclovir 400 mg three to five times a day orally for 7 to 14 days or until clinical resolution. For severe cases, acyclovir 5 mg/kg intravenously (IV) every 8 hours may be needed (famciclovir and valacyclovir are not available as injectables).
5. Proctitis: It may be that higher doses are needed, such as acyclovir 400 mg five times a day orally for 10 days or until clinical resolution occurs. Valacyclovir and famciclovir are also probably effective for acute HSV proctitis.
6. For severe disease or complications requiring hospitalization (e.g., pneumonia, hepatitis): Acyclovir 5 to 10 mg/kg IV every 8 hours for 5 to 7 days or until clinical resolution occurs. For encephalitis: acyclovir 10 mg/kg IV every 8 hours for 14 to 21 days.
7. Acyclovir-resistant strains: Foscarnet (Foscavir) 40 mg/kg IV every 8 hours.

Toxicity

All three drugs have an excellent safety profile and are remarkably well tolerated. Acyclovir-resistant strains are not commonly recovered from immunocompetent patients during acyclovir therapy; nor does there seem to be a high frequency of resistance after 4 months of suppressive therapy. Safety and efficacy have been demonstrated in individuals receiving suppressive therapy with acyclovir for longer than 6 years. Other treatment considerations:

1. Keep lesions clean and dry.
2. Tap water compresses or sitz baths are soothing in the vesicular and pustular stages. A light application of petroleum jelly may relieve the discomfort of crusting and fissuring.
3. Use antiviral medication early in primary infections.
4. Avoid lesion contact with fingers or eyes.
5. Avoid sexual activity for at least 10 days after lesions heal and preferably until lesions have completely reepithelialized (about 16 to 20 days).
PREVENTION

Patients with active lesions during a first or recurrent episode should abstain from intercourse until the lesions are clearly healed. Because viral shedding can occur in the absence of lesions, recommend regular use of condoms to any patient who has had an episode of genital herpes. There is currently no available herpes vaccine, although research appears promising.

COMPLICATIONS

1. Significant psychological distress: Initially, denial, shock, fear, guilt, feelings of social isolation, and anger at the partner are common. Anxiety and depression also occur and may persist in some patients, especially with recurrences.
2. Local complications: These include secondary bacterial infection of lesions, phimosis (males) or labial adhesions (females), urinary retention, constipation, and occasionally impotence. Sacral radiculopathy can also occur, causing paresthesias in the lower extremities.
3. Proctitis: This is common in homosexual men. Presenting complaints may include rectal bleeding, mucoid discharge, constipation, myalgias, fever, and occasionally impotence.
4. Herpes keratitis: This is predominantly associated with HSV-1 infection.
5. Encephalitis and meningitis: Encephalitis is primarily caused by HSV-1 infection, with about 250 to 500 cases per year in the United States. The case-fatality rate exceeds 70% without treatment. Aseptic meningitis and transverse myelitis occurs in as many as 36% of women and 13% of men with primary genital HSV-2 infections. However, hospitalization is required for clinically overt aseptic meningitis in a minority of these cases.
6. Neonatal herpes virus infection
   a. Neonatal infection is most commonly caused by HSV-2, with a case-fatality rate of about 50%. There are an estimated 1,000 cases per year in the United States. The mechanisms of infection include spread from the lower to upper genital tract, delivery through an infected birth canal, and transmission from nursery personnel with recurrent labial disease. Most babies born vaginally to mothers with primary genital herpes acquire disseminated infection.
   b. Infants of pregnant women with primary herpes infections are at much greater risk than those born to mothers who have recurrences.
      • Initial infections: Brown et al. (1987) examined the effects on infants of initial episodes of genital herpes infections during pregnancy. In mothers with a primary first episode of genital HSV-2 infection, 6 of 15 infants had serious perinatal morbidity; in contrast, none of 14 infants with mothers who had nonprimary first episodes were affected. Asymptomatic cervical shedding of HSV-2 was detected in 10.8% of weekly visits made after a primary first episode in only 0.5% of visits after a nonprimary first episode.
      • Recurrent infections: Prober et al. (1987) studied infants who were born to mothers with recurrent genital HSV infections and exposed to virus at delivery: Of 34 such infants, none acquired an HSV infection; in addition, all of 33 infants tested possessed neutralizing antibody to HSV-2. Practitioners should reassure pregnant patients with recurrent infections that the risk of neonatal herpes is very small and that most infants can be safely delivered vaginally.
      c. Of those infants with neonatal herpes, 35% have no history of an infection in their mother or father; and in 90% of such infants there are no signs or symptoms in their mother at delivery.
   d. Preliminary data on the use of acyclovir in pregnancy (more than 500 women studied by the CDC acyclovir registry) are favorable, with no adverse outcomes linked to the drug. There are no comparable data to support the use of famciclovir or valacyclovir in pregnancy.
   e. The American College of Obstetricians and Gynecologists practice bulletin currently recommends antiviral therapy for women with primary HSV infection during pregnancy (Prebooth, 2000). Antiviral therapy can also be considered for women at 36 weeks or more of gestation with either a first-episode HSV infection occurring during the current pregnancy or a history of recurrent HSV infection.
   f. Congenital HSV results from intrauterine infection. The syndrome is well described but rare and includes skin lesions and scars, chorioretinitis, and central nervous system involvement (microcephaly or hydranencephaly).

OBSTETRIC MANAGEMENT

Recommendations for obstetric management include obtaining HSV type-specific serology at the initial visit. Women without signs or symptoms of herpes at the time of delivery may deliver the infant vaginally. Cesarean delivery is currently recommended for women with recurrences who have genital lesions or prodromal symptoms (Prebooth, 2000).

A 1998 study of 42,000 women by Brown et al. found that women with HSV-2 recovered from the genital tract during labor were at very low risk for transmission to the fetus if they had already become HSV-2 seropositive. This was not true for HSV-1–infected women. The authors suggested that women who are experiencing recurrence and are HSV-2 seropositive may be considered for vaginal delivery. If an HSV-2–seropositive woman delivers vaginally, the pediatrician should be informed and the parents or caregivers should be educated to observe the infant for lethargy, poor feeding, fever, or lesions.

PATIENT RESOURCES


SUGGESTIONS FOR MANAGING A FIRST EPISODE OF GENITAL HERPES

1. Obtain a culture if possible.
2. Screen for other STDs. Cervical sampling in female patients may need to be deferred to a subsequent visit due to pain. HIV testing should be suggested, but it may be desirable to discuss this at the follow-up visit.
3. An important aspect of management in teens with genital herpes is counseling regarding the implications of a herpes infection. Briefly explain how the virus is transmitted, including asymptomatic shedding and sexual transmission, the possibility of recurrences, and treatment. Anticipate that the patient will be upset by the diagnosis; take time to comfort the patient and answer questions.
4. Prescribe analgesics, tap water compresses or sitz baths, and topical petrolatum if fissures or crusting is bothersome. Advise the patient to keep lesions clean and dry.
5. If within 6 days after onset, prescribe antiviral medication.
6. Advise the patient to abstain from sex while lesions are present.
7. Give the patient written information to take home.
8. Recommend a follow-up visit in 1 week. Suggest that the patient bring a list of questions and that the partner attend the visit if possible.

At the follow-up visit:
1. Confirm the diagnosis.
2. Assess the need to continue antiviral medication.
3. Ask about the patient's emotional state.
4. Answer questions and review information about transmission and recurrence. The teen should be advised to avoid sexual activity during the prodromal symptom period or during the presence of active lesions.
5. Discuss the need for safer sex to prevent acquisition of other STDs as well as transmission of herpes. This includes the use of condoms during all sexual exposures with new or uninfected sex partners.
6. Suggest that the partner have an examination. If available, consider obtaining HSV type-specific serology from the partner. (Serological assays that are not type-specific should not be used.)
7. Teens need to be aware of the availability of treatment for episodic infections and the possibility for suppressive antiviral therapy for prevention of recurrent episodes.
WEB SITES

For Teenagers and Parents


http://www.iwanmaknow.org/, Teen information site on STDS.


http://www.pediatrics.columbia.edu/Cul7.html, Go Ask Alice site with questions and answers oriented for college students and older adolescents.


http://www/herpeshelp.com/, Glaxo Wellcome patient education site.

http://www.cafeherpes.com/, Information site from Novartis Pharmaceuticals.

For Health Professionals


REFERENCES AND ADDITIONAL READINGS


Infection by the human papillomavirus (HPV), a small nonenveloped, double-stranded DNA virus of the PAPova group, is the most prevalent sexually transmitted disease in the United States. Most individuals infected with HPV display no manifestations of infection (Fig. 66.1). Others develop external and internal anogenital warts, or cervical dysplasia, or both. This chapter reviews the epidemiology of HPV infection and the diagnosis and treatment of anogenital warts. HPV associated cervical dysplasia is reviewed in Chapter 64.

More than 100 genotypes of HPV have been identified, and at least 35 of them infect primarily genital epithelium. Distinct genotypes must share less than 50% homology of the 7,800- to 7,900-base sequence. HPV types with a predilection for the genital areas are classified as low risk (types 6, 11, 42, 43, and 44) or high risk (16, 18, 31, 33, 35, 52, 55, and others), depending on whether they are associated with anogenital cancers. Although some HPV types (e.g., 6, 11) are predominately associated with external genital warts (EGWs), they may also cause warts in the anus, urethra, or vagina and/or on the cervix. Conversely, types 16, 18, 31, 33, and 35, which are strongly correlated with cervical dysplasia, may cause external anogenital warts and have been linked to external genital squamous intraepithelial neoplasia. In low-risk HPV-associated lesions, the HPV genome usually exists separately (as an episome or plasmid) from the host cell's DNA; in contrast, viral DNA from malignancies associated with HPV type 16 or 18 is usually incorporated into the host cell's chromosomes.

Epidemiology

Prevalence Among women, the prevalence of HPV infection detected by polymerase chain reaction (PCR) detection methods varies from 1.5% among those who were never sexually active to 46% among sexually active university women. Rates of detection among men are generally somewhat lower, with recovery of HPV from about one in four men. However, careful testing of male partners of women with high rates of HPV infection identified evidence of HPV in 39% to 80% (Schneider et al., 1988). In one study, viral types between partners were identical in almost 90%.

Transmission Transmission of the HPV types that cause genital infection occurs primarily through sexual contact (Ferenczy, 1995a). Infectivity rate of contacts is high. In a prospective study after the Korean War of women presumably uninfected with HPV, 85% developed genital warts within 8 months after sexual contact with returning infected soldiers (Ferenczy, 1995b). External genital condylomata may be contracted by autoinoculation or inoculation with HPV DNA from skin warts and from viral exposure during delivery. HPV types that cause skin warts are transmissible by fomites. The virus is recoverable from tanning couches, underwear, examination gloves, biopsy forceps, and smoke plumes; transmission has now been demonstrated from sauna benches. Whether fomites represent an important source of transmission of genital HPV types is unknown. Condylomata acuminata have been reported in premenarcheal children and in nonsexually active adolescents. However, the evidence for nonsexual transmission in most cases is questionable. Young people with infections should be questioned and examined for evidence of sexual abuse.

Marrazzo et al. (2000) reviewed the epidemiology of sexual transmission of HPV between women who have sex with women. Transmission has been suggested on the basis of reports of abnormal Papanicolaou (Pap) smears in women without a history of sex with men. A review of studies performed provided limited data that HPV transmission may occur between women. There are also data to suggest that Pap smear screening in these women may be suboptimal compared with screening in heterosexual women.

Incubation Period Lesions usually appear within 3 months after infection, but the range is 3 weeks to 8 months. Recent data, however, suggest that the viral latency period can in fact be much longer, with lesions first appearing years after the moment of infection (Beutner et al., 1997).

Risk Factors The major risk factors for acquisition of HPV relate to sexual behavior.

1. Multiple sex partners: There is a 5.4 times greater relative risk in individuals with three to five partners compared to individuals with one. There should be almost no risk in nonsexually active persons or in HPV-negative couples who are strictly monogamous. Having intercourse with a male partner who has had multiple
2. Age at first coitus: Although early age at first intercourse was previously linked to increased risk, this most likely reflects the increased risk that results from a greater number of lifetime sex partners. However, Shew et al. (1994) examined the relationship between HPV infection and the time interval from menarche to first intercourse. The prevalence of HPV infection was 19.2% in the 108 adolescents. After controlling for number of lifetime partners, first sexual intercourse within 18 months after menarche was associated with a significantly higher risk of HPV infection, in comparison with the risk in adolescents who postponed first intercourse until 3 to 4 years after menarche.

3. Smoking: The relationship between smoking and HPV infection is tenuous. Although a few studies appear to demonstrate a link, most have failed to establish any correlation between the two.

4. Increased frequency of intercourse is also linked to increased risk of HPV infection.

5. The presence of genital warts on a partner increases risk.

6. Contraceptive use: Current evidence suggests that oral contraceptive pills affect the progression of HPV infection and not a woman’s risk for contracting HPV. Failure to use a condom increases a man’s risk for contracting HPV; the relationship is less clearcut for women.

Pathophysiology

HPV infects the basal layer of epithelial cells. The virus requires access to actively dividing epithelial basal cells. Areas where such activity predominates include the transformation zone of the cervix and genital areas susceptible to microtrauma or increased friction during sexual activity (Table 66.1). The virus multiplies exclusively in the nuclei of the basal cells.

<table>
<thead>
<tr>
<th>Gender</th>
<th>Year</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>2000</td>
<td>20.3</td>
</tr>
<tr>
<td>Female</td>
<td>2000</td>
<td>20.6</td>
</tr>
</tbody>
</table>

TABLE 66.1. Distribution of genital human papillomavirus infection in infected individuals by gender

Clinical Manifestations

1. Four major types of venereal warts occur.
   a. Condylomata acuminata: The classic cauliflower-shaped growths with a granular surface and finger-like projections. They usually have highly vascular cores that produce punctuated or loop-like patterns unless obscured by overlying keratinized surfaces.
   b. Papular warts: Flesh-colored, smooth, dome-shaped papules that are 1 to 5 mm in diameter and lack finger-like projections.
   c. Keratotic warts: These have a thick, horny (crustlike) layer; they resemble common warts or seborrheic keratoses.
   d. Flat-topped warts: These appear macular to slightly raised and are invisible to the naked eye. Flat-topped warts are estimated to be twice as common as the other three kinds, both on the cervix and in the anogenital area.

The genital area of humans consists of two types of skin: fully keratinized skin (both hair-bearing and non–hair-bearing) and partially keratinized non–hair-bearing skin (often erroneously referred to as “moist” skin). Condylomata acuminata tend to occur on partially keratinized skin surfaces; flat warts can occur on any skin surface; and the keratotic or smooth papular types are found on fully keratinized skin.

2. Location: Typical sites for involvement with HPV are shown in Table 66.1; other studies show a somewhat different distribution, depending on the population studied and the technique for detecting HPV. Circumcised men are more likely to have involvement of the shaft. The urethral meatus is involved in about 5% of women and up to one fourth of males. Condylomata can be multifocal (one or more lesions at one anatomic site) or multicentric (lesions at multiple separate anatomic sites).

3. Color: Pinkish, red, gray, or white
4. Symptoms: Usually asymptomatic but may cause pruritus, burning, fissuring, pain, or bleeding
5. Aggravating factors: Pregnancy, skin moisture, vaginal or anal discharge
6. Differential diagnosis
   a. Microspapillomatosis labialis of labia minora: Lesions with separate bases that do not converge as do the papillae of condylomata acuminata
   b. Condylomata lata: Secondary syphilis with positive dark-field examination and serology
   c. Molluscum contagiosum: Dome-shaped globular lesion with central umbilication that contains excretable cheesy material
   d. Granuloma inguinale: Rare disease; Donovan bodies found in crushed tissue smears
   e. Seborrheic keratosis
   f. Intraepithelial and invasive neoplasia
   g. Benign neoplasias: including fibromas, lipomas, hidradenomas, and adenomas
   h. Pink pearly papules (in males): Parallel rows of lesions at the corona of the penis that demonstrate hypertrophic papillae histologically; normally present in approximately 15% of the male population.

Diagnostic Considerations

According to a 1998 consensus conference on genital warts sponsored by the American Medical Association, clinical inspection without use of instruments is adequate for the diagnosis of EGWs in most circumstances. A bright light and a magnifying glass may assist in the diagnosis. Speculum examination is mandatory for all women with EGWs. Men and women with recurrent perianal warts and/or a history of anoreceptive intercourse should undergo anoscopy. Men with warts at the terminal urethra who have terminal meataluria or an altered urinary stream are candidates for urethroscopy.

In general, the use of dilute acetic acid solutions (usually 3% to 5% or white vinegar) to diagnose subclinical warts is not recommended. The positive predictive value is low, the false-positive rate (seen in psoriasis, balanoposthitis, vulvovaginitis, eczema, herpes, traumatic microabrasions) is as high as 25%, and the diagnostic utility has not been established. HPV typing plays no role in management of EGWs, although it may play an important role in management of abnormal Pap smears (see Chapter 64). Biopsy of suspicious lesions is almost never indicated.

What benefit screening of the sex partners of patients with EGWs confers is unclear. A screening visit provides the opportunity for the clinician to look for visible warts, screen for other sexually transmitted diseases (STDs), and teach about HPV and EGWs. However, it is unknown whether treatment of the male partner or partners of a woman with cervical HPV infection alters the natural history of her disease.

Treatment

Spontaneous clearance of visible warts is a well-described phenomenon, but the probability of regression in a given patient cannot be predicted with any degree of uncertainty. While one waits for the wart or warts to clear, it is also entirely possible that existing warts will grow in size or new lesions will appear, making treatment more difficult or painful. Longitudinal studies of women testing positive for HPV show a median duration of new infections of 8 months (95% confidence interval, 7 to 10 months); another study demonstrated that 70% of women had regression of the infection by 24 months. Infection with a high-risk type of HPV (e.g., 16, 18) was associated with longer duration of infection.
The goal of therapy for EGWs is the removal of symptomatic warts. It is not clear whether treatment alters the natural history of the infection or reduces the infectivity of the individual patient. Treatment may render the patient wart free, but virus may persist in surrounding normal-appearing tissue. Most patients have up to 10 genital warts with a surface area of 0.5 to 1.0 cm². Most warts are responsive to most treatment regimens; hence, treatment should be guided by the patient’s preferences, the type and extent of the lesions, the site of the warts, and available resources. Patient-applied therapies require that the patient can adequately visualize the lesions to be treated and can adhere to the specified schedule of treatment.

General treatment considerations include the following goals:

1. Eliminating any predisposing factors
2. Treating any coexisting vaginitis and/or cervicitis
3. Decreasing tissue trauma at coitus
4. Keeping the genital area dry
5. Keeping diabetes mellitus under tight control

Specific treatments for EGWs can broadly be classified as patient applied or clinician applied. The various types, with their initial treatment success and recurrence rates, are summarized in Table 66.2. In general, warts located on moist surfaces respond better to treatment than warts on dry surfaces. Studies evaluating the outcome for each therapy vary widely in their methodology, including patient selection, type of wart treated, duration of therapy, length of follow-up, and whether additional therapies were also used in the treatment. Some treatment modalities have been evaluated in only a few clinical studies. The figures in the table should therefore be viewed as a general guide to treatment efficacy rather than a guarantee of outcome. The advantages and disadvantages of the various treatment regimens are presented in Table 66.3. Clinicians should be familiar with at least one clinician-applied and one patient-applied therapy. A particular treatment should be changed if the patient fails to notice substantial improvement after three provider-applied treatments or complete resolution is not achieved with six treatments. Some clinicians simultaneously use two or more of the treatments discussed later in an attempt to improve or hasten outcome. Combining treatments may increase the risk of side effects, and there is at present no credible evidence to support this approach.

**TABLE 66.2. Initial clearance and recurrence rates by treatment for external genital warts**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Initial Clearance (%)</th>
<th>Recurrence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5% Podofilox</td>
<td>10</td>
<td>30</td>
</tr>
<tr>
<td>5% Imiquimod</td>
<td>20</td>
<td>50</td>
</tr>
<tr>
<td>5% Cryotherapy</td>
<td>30</td>
<td>70</td>
</tr>
<tr>
<td>5% Podophyllint</td>
<td>40</td>
<td>80</td>
</tr>
</tbody>
</table>

**TABLE 66.3. Advantages and disadvantages of treatment regimens for genital warts**

The choices of therapy include the following:

1. **Patient applied**
   a. **Imiquimod**: Imiquimod stimulates keratinocytes and other cells to produce interferon and other cytokines that inhibit viral replication and promote cell-mediated immune response to infection. The 5% cream (provided in individual packets) is applied at bedtime, left on overnight (6 to 10 hours), and then washed off. It is used three times per week for 16 weeks or until all lesions have disappeared. Local irritation is the major side effect, being characterized as severe in 5.7% of patients in one study. A 1-week treatment-free holiday may be implemented should severe irritation occur. Sexual contact should be avoided while imiquimod cream is on the skin; the patient should wash the cream off if he or she anticipates having sex. The cream may weaken condoms or diaphragms. Whether imiquimod is safe for use during pregnancy is unknown.
   b. **Podophyllin**: Podophyllin is a popular chemical agent used to treat anogenital warts. Use weekly treatments with 20% to 25% podophyllin in tincture of benzoin. Do not apply to mucosal surfaces. This treatment is relatively ineffective on dry warts (penile shaft, scrotum, and labia majora).

2. **Clinician applied**
   a. **Liquid nitrogen or cryotherapy**: These treatments can be used on dry and moist warts. It is often the preferred method for penile lesions and resistant vulvar lesions. It can be used on anal warts and during pregnancy. Liquid nitrogen may be used to treat vaginal warts but use of a cryoprobe is not recommended because of the risk of vaginal perforation or fistula formation. Wound cotton on an applicator (but not the typical cotton swab) should be used. The swab is placed in liquid nitrogen for 2 to 3 seconds and then quickly applied with gentle pressure to the wart to be treated and 2 to 3 mm of surrounding skin for 2 to 3 seconds. The surface of the wart should briefly turn white and then return to its normal color. The process should be repeated once or twice. Treated warts may begin to redden at the end of the application.
   b. **Topical chemotherapies**: These are most effective for the sessile lesions. Older, more keratinized lesions are more refractory to topical agents.
      - **Bichloroacetic acid (BCA) or trichloroacetic acid (TCA)**: These treatments are best used on small dry or moist warts and can be used during pregnancy.
        - **Technique**: Apply occlusive ointment to the healthy tissue surrounding the lesion. Touch the lesion with 50% to 90% acid solution to cause blanching. Dry the lesion rapidly to minimize pain (a blow dryer is helpful). Powder with baking soda to remove unreacted acid, if possible. Careful application is advised, because the treatment also desiccates normal tissue on contact.
        - **There is no need to wash off the solution after treatment.**
        - **Repeat the process weekly until the lesion has resolved.**
      - **Podophyllin**: Podophyllin is a popular chemical agent used to treat anogenital warts. Use weekly treatments with 20% to 25% podophyllin in tincture of benzoin. Do not apply to mucosal surfaces. This treatment is relatively ineffective on dry warts (penile shaft, scrotum, and labia majora).
One can place occlusive ointment on the areas surrounding the lesions to protect normal skin; however, if the podophyllin is properly applied, this is not necessary.

Paint the lesions with podophyllin (use of the back end of a cotton swab allows for precise application). Be sure the solution is air-dried before allowing the patient to resume a normal position.

Instruct the patient to wash off the podophyllin in 1 to 4 hours.

If lesions are resistant, one can either leave the podophyllin on longer, use a 50% podophyllin solution, or use another modality.

Because it may contain mutagenic compounds, podophyllin is contraindicated during pregnancy.

c. **Surgery:** Surgical therapies include excision with the loop electrocautery excision procedure (LEEP), laser ablation, and cold knife excision (rarely performed today); these treatments usually are reserved for large or resistant lesions.

d. **Immunotherapy:** Immunotherapy with intralesional injections of interferon is very expensive and perhaps is best reserved for recurrent lesions or those resistant to other therapies.

3. **Vaginal, urethral, and perianal warts may be treated with various topical and surgical modalities.**

   a. **Vaginal warts:** Cryotherapy with liquid nitrogen (but not a cryoprobe); TCA/BCA; podophyllin (10% to 15%). Some experts caution against the use of podophyllin in the vagina.

   b. **Urethral meatus warts:** Cryotherapy with liquid nitrogen or podophyllin. Treated warts must be dry before contact with normal mucosa.

   c. **Anal warts:** Cryotherapy with liquid nitrogen; TCA/BCA; surgical removal

4. Patients must be advised that partners do require evaluation for visible lesions, but treatment of the partner does not affect the patient's response or risk of recurrence.

5. Patients should be reminded that infections are forever: recurrence is possible, and involvement of nonvulvar areas possible. Frequent (at least annual) Pap smears are recommended. Safer sex practices should be emphasized.

**MOLLUSCUM CONTAGIOSUM**

**Etiology**

Molluscum contagiosum is a skin disease caused by a member of the poxvirus group.

**Epidemiology**

Transmission is by direct person-to-person contact, with an incubation period of 30 days to several months. The disease is also spread by autoinoculation. Prevalence is increasing among sexually active adolescents.

**Clinical Manifestations**

1. **Location:** The lesions commonly occur on the face, arms, legs, and chest. In sexually active adolescents, the lesions are commonly seen on the genital and perineal areas.

2. **Appearance:** Lesions are firm, flesh-colored, raised, waxy, dome-shaped, globular nodules with central umbilication. There are usually between 1 and 20 lesions, each 3 to 7 mm in diameter; they often occur in clusters.

3. **Symptoms:** The lesions are usually asymptomatic, but inflammatory changes can occur.

**Diagnosis**

1. The clinical appearance is usually diagnostic.

2. If the lesions are sprayed with ethyl chloride, a distinct central area of darkness appears that is not found in warts.

3. Expressible cheesy material on potassium hydroxide preparation or with methylene blue shows intracytoplasmic inclusions (molluscum bodies).

4. Unroofing of the lesion with a 27-guage needle reveals the presence of a white “pearl.”

5. Biopsy is rarely necessary.

**Therapy**

1. Unroofing of the lesion, expression of cheesy material, or application of TCA or podophyllin to the base will help.

2. Liquid nitrogen applied to lesions is an alternative.

3. Light electrodesiccation may be used.

4. Topically applied 1% imiquimod cream has also been shown to be effective.

5. Patient should be observed again in 30 days to check for new lesions that may have been incubating at the time of the initial treatment.

**WEB SITES**

For Teenagers and Parents

National STD Hotline: 1-800-227-8922, Spanish speaking 1-800-344-7432 (8 a.m. to 2 a.m. EST). Teletype service 1-800-243-7889 (10 a.m. to 10 p.m. EST).

http://www.ashe STD.org/stdflags/hpv.html. American Social Health Association site on STDs including HPV.


http://www.kff.org/content/2000/3002/. Specific HPV fact sheet from the Kaiser Family Foundation.


http://www.hc-sc.gc.ca/hpb/lcdc/bah/epi/hpv_e.html. Health Canada (Bureau of HIV/AIDS, STD and TB) with information sheet on HPV.


For Health Professionals


http://cybermed.ucsd.edu/derm1/Warts/dermweb1.htm#venereal. Course with pictures on warts and genital warts from University of California, San Diego Dermatology Department.


**REFERENCES AND ADDITIONAL READINGS**


Scabies and pediculosis are ubiquitous and highly contagious parasitic skin infections that have been present since antiquity and are distributed worldwide. Infections occur both in individuals and in clusters such as school children, homeless people, staff in hospitals, and immunocompromised persons. Difficulties in management have returned scabies and pediculosis to the limelight.

PEDICULOSIS PUBIS

Etiology

Pediculosis pubis is caused by the pubic crab louse, *Pthirus pubis*, a wingless, oval, yellow-gray insect 1 to 4 mm in length. It has 12 prestomal teeth and stylets used for sucking blood. There are hundreds of millions of cases of pediculosis worldwide each year.

Epidemiology

1. Transmission: The parasites are transmitted by close bodily contact, chiefly by sexual contact, frequently in coexistence with another sexually transmitted disease (STD), but it can also be transmitted by clothing and bedding. There is a 95% chance of acquiring disease after one sexual exposure. Transmission of pubic lice is not prevented by condoms. At present there is no evidence linking ectoparasites to transmission of human immunodeficiency virus (HIV).
2. Life cycle: The parasite spends its life on skin and feeds on blood. It dies in about 24 hours without animal contact. The female pubic louse lays about three eggs per day, which are attached to hair shafts as nits. The nits hatch in 8 to 10 days. Adult life expectancy is about 1 month.

Clinical Manifestations

1. Asymptomatic: Lice are found by patient, friend, or contact.
2. Symptoms occur 1 to 2 weeks after contact, more rapidly if the patient had a prior infestation.
   a. Pruritus related to a bite as a probable hypersensitivity reaction
   b. Secondary infections from scratching
3. Common areas of infection: Pubic hair; hairs of abdomen, thighs, axilla, and perianal area; and occasionally eyebrows and lashes. Nits may appear on terminal hair on trunk, thighs, axillary region, bearded area, and eyelashes.
4. After prolonged infestation, small blue maculae called maculae caeruleae may appear on thighs and abdomen. These are uncommon but specific for pubic lice. They represent feeding sites of the louse.
5. Thirty-seven percent of cases of pediculosis pubis had coexisting STD (Opaneye et al., 1993).

Diagnosis

1. Clinical history
2. Finding nits (eggs) or lice: Nits are small, yellowish-white, glistening, oval kernels attached to hair shafts. (Adult lice were described earlier.)

Therapy

1. Recommended regimens
   a. Lindane 1% shampoo applied for 4 minutes and then thoroughly washed off (not recommended for pregnant or lactating women).
   b. Permethrin 1% creme rinse (Nix) applied to affected area and washed off after 10 minutes.
   c. Pyrethrins and piperonyl butoxide (nonprescription RID, R & C Lice treatment, Clear, Pronto) applied to the affected area and washed off after 10 minutes.
   d. Note: Lindane cream and lotion are no longer recommended for the treatment of pubic lice. Lindane shampoo is the least expensive treatment. The side effects of seizures and aplastic anaemia have not been reported when treatment is limited to the recommended 4-minute period.
2. Retreatment is indicated after 7 days if lice are found or eggs are observed at the hair-skin junction.
3. Clothing or bed linen coming in contact with the patient within the past 2 days should be washed or dried by machine (hot cycle) or dry cleaned. Fumigation is not necessary.
4. Residual nits should be removed with a fine comb. For nits that are difficult to remove, use a solution of vinegar and water to loosen them.
5. Sexual contacts within the last month should be treated as described.
6. Pregnancy: Use permethrin or pyrethrins with piperonyl butoxide.
7. HIV infection: Use the same therapy as for a noninfected adolescent.
8. Pediculosis of eyelashes: Treat with application of occlusive ophthalmic ointment to the eyelid margins two times a day for 10 days. This smothers the lice and nits. Do not apply lindane or other medications to the eyes.

SCABIES

Scabies, a highly contagious ectoparasitic infection, is a common cause of pruritus and rash in adolescents. It is one of the most widespread infestations in the world, with about 300 million cases of scabies worldwide each year.

Etiology

Scabies is caused by a small mite, *Sarcoptes scabiei* var. *hominis*. The adult mite has a rounded body, has four pairs of legs, and measures 400 µm in length. This parasite is host-specific for humans.

Epidemiology
Transmission: The mite is transmitted to the host after close personal contact. Because it is transmitted by skin-to-skin contact, sexual transmission is common.

Clinical Manifestations
1. Incubation: Symptoms occur 3 to 5 weeks after first exposure and 1 to 2 days after re-exposure.

2. Lesions: Scabies is an intensely pruritic papular eruption. The host may present with only pruritus, which is often worse at night or after a hot bath. The rash is usually a symmetrical polymorphous eruption, including red papules with or without excoriations, vesicles, pustules, or crusted lesions. This is caused by a cell-mediated immune reaction to the mite and its byproducts. The burrows, if seen, appear as short wavy lines a few millimeters to 1 cm in length.

3. Involved areas: Scabies involves finger webs, flexor surfaces of wrists, axillary folds, nipples, umbilicus, belt-line area, buttocks, thighs, knees, and ankles. In the male, the penis and scrotum are common areas of involvement. Scabies usually spares the face, neck, and scalp except in children.

4. Differential diagnosis: The lesions can become secondarily infected and eczematized and thus confused with eczema, atopic or contact dermatitis, or impetigo. Papulovesicular lesions may be confused with papular urticaria, chickenpox, drug eruptions, folliculitis, or dermatitis herpetiformis.

Diagnosis
1. Clinical picture of pruritus with lesions in distribution as outlined earlier: Diagnosis is often made based on the distribution of lesions alone. A similar clinical history in family members or close contacts is helpful. Burrows are virtually pathognomonic for human scabies.

2. Isolation of mite: Scrape the lesion or burrow with a no. 15 blade and mineral oil. Look for ova, feces, or organism. Do not use potassium hydroxide, because it dissolves the mite’s body and feces. An alternative method is a shave biopsy of the superficial layer of skin. The specimen is examined with immersion oil on low power. The shave biopsy specimen has a higher sensitivity than the skin scraping specimen.

Therapy
1. Recommended regimens
   a. Topical 5% permethrin cream (Elimite) applied to all areas of the body from the neck down and washed off by bath or shower after 8 to 14 hours. The treatment should be careful to apply underneath fingernails and skin folds. The cream can be applied at bedtime and removed by bathing the next morning.
   b. Ivermectin 200 µg/kg orally, repeated in two weeks.

2. Alternative regimens
   a. Lindane (1%) (Kwell) 1 ounce of lotion or 30 g of cream applied thinly to all areas of the body from the neck down and washed off thoroughly after 8 hours. Include web spaces of digits and under fingernails. No preapplication shower is necessary; in fact, a shower may increase unnecessary systemic absorption. Prescribe only the required amount, which is usually 1 ounce per treatment. Do not prescribe refills. Note: Lindane should not be used after a bath and not with extensive dermatis. Pregnant or lactating women and children younger than 2 years of age should not use lindane. If the patient has a bad infestation, a second treatment is recommended 1 week later. Permethrin is highly effective and safer than lindane (Kwell) but costs more. Lindane resistance has been reported in some areas of the United States.

   b. Ivermectin 200 µg/kg orally, repeated in two weeks.

3. The patient should not be contagious after 24 hours of treatment.

4. Bedding and clothing should be machine washed and crotamiton is the soap and dry cleaned, or removed from body contact and set aside in a sealed plastic bag for at least 72 hours. Fumigation of living areas is not necessary.

5. Follow-up: Pruritus may persist for several weeks. The practitioner may either retreat those who are symptomatic or retreat only if live mites are observed.

6. Sex partners: Sex partners, as well as close personal or household contacts within the last month, should be treated.

7. Pregnant women: Pregnant or lactating women should not use lindane but should use permethrin or crotamiton regimens.

8. Oral steroids may be used for severe systemic or local reactions.

9. Antipruritics such as hydroxyzine (Atarax), trimperazine tartrate (Temaril), or promethazine (Phenergan) may be used for pruritus. Crotamiton (Eurax) is also antipruritic.

10. HIV infection: HIV-infected individuals should use the same treatment. HIV-infected individuals are at increased risk for Norwegian scabies, a disseminated infection.

11. Norwegian scabies is more difficult to treat; particularly in those who are immunosuppressed, several treatments with scabicides and sometimes sequential use of several agents may be required.

Therapy Problems
Treatment problems are usually manifested by continued pruritus.

1. Examination reveals continued infestation, which could be the result of inadequate therapy (all skin below neck areas may not have been treated), reinfestation, or resistance to therapy. Continued infestation requires retreatment, using the same or another agent.

2. Examination suggests no scabies but dry or irritated skin, which could be the result of irritation or sensitization from therapy or residual sensitization from the mite or its products. Use topical steroids or antipruritic drugs.

WEB SITES
http://www.goaskalice.columbia.edu/0894.html. Go Ask Alice site from Columbia University on public lice.

REFERENCES AND ADDITIONAL READINGS


Chancroid, lymphogranuloma venereum (LGV), and granuloma inguinale constitute the classic minor sexually transmitted diseases. In the United States, most patients with genital ulcers have genital herpes or syphilis, herpes being the most common. About 3% to 10% of patients with genital ulcers have more than one of these conditions present. All three of these diseases are uncommon but should be considered in the differential diagnosis of genital ulcers. In 1998, a total of 189 cases of chancroid were reported to Centers for Disease Control and Prevention (CDC), for a rate of 0.07 cases per 100,000 population. This reflects a 23% decline from 1997 and a continuing decline since 1987. However, because chancroid is difficult to culture and often is not considered, the condition may be substantially underdiagnosed. With the use of DNA amplification tests (not commercially available), the CDC has identified this infection in cities where it was previously undetected. Genital ulcerative infections are associated with increased risk for human immunodeficiency virus (HIV) infection.

**CHANCOID**

Chancroid is a genital ulcer infection caused by *Haemophilus ducreyi*. Although it is endemic in some parts of the United States and also is associated with discrete outbreaks, it is most commonly found in developing countries, with the highest prevalence in southern, central, and eastern Africa. Chancroid is a known risk factor for heterosexual HIV transmission in developing countries. In addition, as many as 10% of patients with chancroid may be coinfected with *Treponema pallidum* or herpes simplex virus (HSV).

Chancroid is an acute ulcerative disease that involves the genitalia. In as many as 30% of cases, chancroid is associated with a painful unilateral inguinal adenitis known as a bubo. Men typically have single ulcers, whereas affected women usually have multiple lesions. Unlike a syphilitic chancre, which is painless, the chancroidal ulcer is painful and tender although not indurated. Chancroid must be considered in the differential diagnosis for any adolescent with a painful genital ulcer, especially if it is associated with enlarged, tender inguinal adenopathy.

**Etiology**

Chancroid is caused by *H. ducreyi*, a gram-negative coccobacillus.

1. Incidence: The global incidence of chancroid may exceed that of syphilis. Chancroid is common in several areas of the world including Africa, the Caribbean basin, and southwest Asia. In Kenya, Gambia, and Zimbabwe, chancroid is considered to be the most common cause of genital ulceration. Chancroid has been considered a disappearing disease in developing countries. Outbreaks of chancroid occur in certain areas of the United States, and 85% of the 243 cases in 1997 were reported in New York, California, Texas, and South Carolina. Given that the diagnosis of chancroid based on morphological features alone has an accuracy rate of only 30% to 50%, there may be significant underrecognition of this pathogen.
2. Race: The incidence is increased in African-American and Hispanic patients.
4. Transmission: Transmission is through sexual contact. Most cases have been contracted through heterosexual contact. Because sexual contact is the only known route of transmission, sexual abuse should be considered if the diagnosis of chancroid is made in an adolescent with severe developmental delay.
5. Relation to crack cocaine: A number of studies have established a link between the incidence of syphilis and use of cocaine, specifically crack cocaine. A similar link appears to be present for chancroid.
6. Socio-demographic factors: Chancroid is associated with poverty and urban prostitution in the United States. It has become endemic to certain areas of the United States and also occurs in discrete outbreaks.
7. Coinfection: Coinfection with syphilis or HSV serves as a cofactor for HIV transmission.

**Clinical Manifestations**

1. Incubation period: 3 days to 2 weeks
2. Presentation: A small inflammatory papule or pustule arises at the site of inoculation. Within days, the lesion erodes to form an extremely painful, deep ulceration. The characteristic ulcer is soft, friable, and nonindurated with ragged undermined margins, a foul-smelling yellow-gray exudative covering, and surrounding erythema. Several of these lesions may be present in a patient. Within 1 to 23 weeks, painful inguinal lymphadenitis, most often unilateral, develops in 30% to 60% of patients. Twenty-five percent of patients have progression of the lymphadenitis into a suppurative bubo, which may rupture and ulcerate. If this occurs, the patient can develop autoinoculation with bilateral opposing ulcers, known as “kissing lesions.”
3. Location
   a. In males: Prepuce, coronal sulcus, and frenulum
   b. In females: Labia, clitoris, and perianal region
   c. Extragential sites: Lip, tongue, and finger
4. Other presentations: Chancroid may be associated with a variety of presentations.
   a. The classic form just described has ulcers ranging in diameter from 3 to 20 mm.
   b. Transient chancroid consists of an ulcer that rapidly resolves in 4 to 6 days, followed by suppurative inguinal lymphadenitis, which develops in 10 to 20 days.
   c. Follicular chancroid has ulcerations in hair-bearing areas.
   d. The dwarf variety manifests as one or more herpetiform ulcerations with or without inguinal adenopathy.
   e. Giant chancroid consists of multiple small ulcerations that rapidly expand and coalesce to form a single large destructive ulceration. This form can produce widespread necrosis and may closely resemble granuloma inguinale.
5. Constitutional signs: Although fever and malaise may occur, spread to distant sites is very unusual.

6. Females: Many females are carriers without disease or have asymptomatic lesions of the vagina or cervix. There have been no reports of adverse effects on pregnancy outcome or on the fetus.

7. HIV-infected patients: Although relatively few studies have evaluated chancroid in HIV-positive patients, the clinical presentation appears only slightly different from that in seronegative patients, and the rate of treatment failure may be slight increased in HIV-positive patients. Ulcer size was consistently unaffected by HIV serostatus in all studies. The only differences reported were a longer ulcer duration and a greater number of ulcers at initial presentation in HIV-positive patients. Nonetheless, atypical presentations can occur, as evidenced by one HIV-positive patient who had chancroid that manifested as a chronic penile ulcer accompanied by ulcers on his legs and digits. Chancroid in HIV-positive patients may manifest as large ulcerations, extragenital lesions, less prominent regional adenopathy, and delayed healing.

Differential Diagnosis

Chancroid may be confused with or coexist with herpes genitalis, primary syphilis, LGV traumatic lesions, Behçet syndrome, or fixed drug eruptions. The prevalence of genital ulcers in adolescents would be in the following order, from highest to lowest: herpes, nonspecific trauma, syphilis, and then chancroid.

1. In syphilitic chancres, the ulcers are nonpainful and have indurated borders. A dark-field examination and serological examination are needed for confirmation.

2. In LGV, the lesions are nonpainful. The adenopathy develops after the lesions have healed.

3. In herpes, the lesions start as vesicles, which are usually painful, are more superficial, are more numerous, and are surrounded by a narrower zone of erythema.

Adenopathy is usually bilateral. Constitutional symptoms and lymphadenopathy may occur in first-time infections. Culture or antigen test for HSV should be performed.

Diagnosis

The diagnosis may be difficult because it is often made only on clinical grounds. All individuals with genital ulcers should receive a serological test for syphilis and possibly other tests including a dark-field examination or direct immunofluorescence test for T. pallidum, a culture or antigen test for HSV, and a culture for H. ducreyi.

1. Clinical appearance, which is accurate in 33% to 53% of cases.

2. Smears: Direct smear from an ulcer or aspiration material from an infected lymph node (bubo) is required for diagnosis. The lesion is cleaned thoroughly and serous exudate is collected on a cotton-tipped applicator from the undermined border of an ulcer. This is carefully rolled in one direction onto a glass slide and Gram-stained. The bacteria arrange themselves in parallel short chains, described as “schools of fish.” A promising test in the future is the immunofluorescence test of the ulcer material. Sensitivity of microscopy is between 5% and 63%.

3. Culture: A culture may be attempts from lesions, buboes, or blood, but the organism is difficult to grow in vitro. Sensitivity of culture is 35% to 75% compared with clinical diagnosis and 35% to 75% compared with polymerase chain reaction (PCR). Specificity is 94% to 100% compared with PCR.

4. Immunodiagnostic, DNA probe, and PCR tests are being investigated but are not routinely available. Sensitivity ranges from 56% to 100%.

5. CDC case-definition criteria for chancroid include the following:
   a. Definite: Recovery of H. ducreyi from an individual, regardless of site of recovery or symptoms.
   b. Probable: One or more painful ulcers, with no evidence of T. pallidum on dark-field examination or by a serological test for syphilis performed at least 7 days after onset of ulcers, and either a clinical presentation of ulcers that is not typical of disease caused by HSV or a negative result on testing for HSV.

   The combination of a painful ulcer with tender inguinal adenopathy is suggestive of chancroid, and when accompanied by suppurative inguinal adenopathy it is almost pathognomonic.

6. HIV testing should be considered in the management of patients with genital ulcers, especially those with syphilis or chancroid. If the initial testing is negative, then repeat testing should be performed in 3 months.

Therapy

1. Recommended regimens
   a. Azithromycin 1 g orally in a single dose
   b. Ceftriaxone 250 mg intramuscularly (IM) in a single dose
   c. Erythromycin base 500 mg orally three times a day for 7 days
   d. Note: Azithromycin and ceftriaxone have the advantage of single-dose therapy.

2. Alternative regimens
   a. Amoxicillin 500 mg plus clavulanic acid 125 mg orally three times a day for 7 days
   b. Ciprofloxacin 500 mg orally twice a day for 3 days
   c. Note: These alternative regimens have not been studied as extensively as the recommended regimens. Ciprofloxacin is contraindicated for pregnant and lactating women, children, and adolescents younger than 18 years of age.

3. Aspirate fluid from ulcer and lymph node, and from a site of overlying normal skin tissue. Traditionally, this technique has been advised to decrease the risk for development of chronic draining sinuses; however, incision and drainage may be preferred because of the decreased need for subsequent procedures.

4. Follow-up: Follow-up with infected individuals should occur within 3 to 7 days after initiation of therapy and should continue weekly until resolution of symptoms. There should be subjective improvement within 3 days and objective improvement within 7 days. If there is no improvement, the practitioner must consider whether the diagnosis is correct, there is a coinfection with another STD, the individual is infected with HIV, treatment compliance is poor, or there is resistance to the prescribed antimicrobial. Large ulcers may require more than 2 weeks to resolve, and fluctuant lymphadenopathy heals even more slowly than ulcers. Healing may also occur more slowly if the ulcers are under the foreskin of an uncircumcised male patient. Adenopathy may progress to fluctuation despite successful therapy and does not represent treatment failure.

    5. No sexual activity while clinical disease is present.
    6. Sexual partners: Treat recent sexual partners. Because the incubation period is usually not longer than 10 days, treating partners who had intimate contact within that time period is usually sufficient.
    7. Pregnancy: The safety of azithromycin for pregnant and lactating women has not been established. Ciprofloxacin is contraindicated during pregnancy.
    8. HIV-infected patients: These individuals may require longer courses of therapy, and healing may be slower. Treatment failures do occur. The 7-day erythromycin regimen may be better unless very close follow-up is possible.

LYMPHOGRAVANULA VENEREUM

LGV is a systemic infectious disease that is usually sexually transmitted. Worldwide, LGV is an uncommon disease, although it may account for 2% to 10% of genital ulcers and ulcers in areas of India and Africa. In the United States, the rate of LGV is 1 case per million population. LGV is characterized by a primary ulcer or granulomatous lesion, followed by suppurative of regional lymph nodes and constitutional signs and symptoms. The disease is of interest in the adolescent because it is a rare cause of genital ulcerative lesions and lymphadenopathy.

Etiology

The causative agent of LGV is an obligate intracellular organism of the genus Chlamydia. LGV is caused by L1, L2, and L3 strains of Chlamydia trachomatis. Strains A through C cause trachoma, and strains D through K cause genital infections and inclusion conjunctivitis. Strains causing LGV are more invasive in the host and therefore cause systemic disease, rather than being restricted to mucous membrane surfaces.

Epidemiology

1. Frequency: There were 113 known cases in the United States in 1997. This prevalence may be falsely low because of underreporting and misdiagnosis.

2. Age: Peak incidence: 15 to 40 years of age

3. Male-to-female ratio: 3:4:1

4. Transmission: The disease usually is sexually transmitted but can occasionally be contracted from fomites. The reservoir of disease has not been proven, but transmission has been attributed largely to female carriers.
Clinical Manifestations

1. Incubation period: 3 to 30 days (usually 7 to 12 days)
2. Primary lesion
   a. LGV usually takes one of four forms: a papule; a small, painless, nonindurated ulcer on the penis, labia, vagina, or anus; a herpeticform lesion; or urethritis or cervicitis. The most common of the four is a herpeticform ulcer at the site of infection. This lesion typically heals without scarring within 1 week and often remains unnoticed by the affected person. In one study of a limited sample of patients with LGV in more advanced stages, only 5 of 27 patients were able to recall having a genital lesion within the past several weeks.
   b. An associated mucopurulent discharge may be present, affecting the urethra in men and the cervix in women.
   c. Rectal intercourse can lead to a primary rectal infection with consequent diarrhea, rectal discharge, and tenesmus.
   d. Females usually have primary involvement of the rectum, vagina, and cervix, which drain to deep iliac or perirectal nodes that may result in lower back or abdominal pain.
3. Secondary manifestations: LGV is primarily a disease of the lymphatic system that progresses to lymphangitis. The infected macrophages drain the regional lymph nodes, typically producing unilateral enlargement, infection, and necrotic abscesses. Painful regional adenopathy is the most common manifestation of secondary disease and the most common lesion in heterosexual individuals. The syndrome usually occurs 1 to 6 weeks after the primary lesion. It is referred to as the inguinal stage or inguinal syndrome. The node enlargement begins as discrete adenopathy, after which the nodes can become matted and fluctuant. This produces the characteristic bubo. The skin overlying the bubo often becomes attached to the underlying lymph nodes and takes on a characteristic deep reddish blue color. The buboes may become fluctuant and rupture in as many as one third of patients. However, most buboes heal without problems and without the development of sinus tracts. Inguinal lymphadenopathy occurs in only 20% to 30% of women with LGV. Because most women tend not to develop inguinal lymphadenopathy, only one third present with secondary-stage signs, whereas most men present during this stage. Inguinal adenopathy is unilateral in 70% of cases. The “groove” sign is the result of enlarged inguinal nodes above Poupart ligament and femoral nodes below it. The organism may spread and cause the following:
   a. Constitutional symptoms, including headache, fever, chills, and myalgias. LGV can present as a fever of unknown origin.
   b. Systemic complications, including arthritis, hepatitis and pneumonitis. Rarer complications include cardiac involvement, aseptic meningitis, and ocular inflammatory disease.
4. Stage 3: Genitanoarectal syndrome. This is uncommon but occurs more often in females who were asymptomatic during previous stages of the disease.
   a. Proctocolitis and hyperplasia of intestinal and perirectal lymphatic tissue (lymphorrhoids): The majority of anorectal disease occurs in females and in homosexual males.
   b. Perirectal abscesses
   c. Rectovaginal and anorectal fistulas
   d. Rectal strictures, often manifested by constipation, ileus, weight loss, and abdominal distention
   e. Elephantiasis of genitals 1 to 20 years after onset (rare)
   f. Scarring of pelvis and resultant infertility

Differential Diagnosis

1. Genital-inguinal lesion
   a. Syphilis
   b. Herpes simplex
   c. Chancre
   d. Granuloma inguinale
   e. Pyogenic infection
   f. Cat-scratch fever
2. Rectal fistulas
   a. Inflammatory bowel disease
   b. Chronic rectal infections: Gonorrhea, amebiasis, tuberculosis
   c. Granuloma inguinale

Diagnosis

The diagnosis of LGV is increased by the difficulty of culturing the organism and the cross-reactivity of serology between several serotypes.

1. Clinical manifestations
2. Culture: Culture for Chlamydia can be obtained on isolation of the organism and cell typing of the isolate or from a node aspirate. The recovery rate is less than 30%. A swab of the lesion may also be obtained.
3. Complement fixation: Titers higher than 1:16 and particularly those higher than 1:64 indicate active or recent infection. Acute and convalescent titers are required for complete interpretation. Titers are also positive after Chlamydia urethritis, psittacosis, or trachoma, but in those cases they are rarely higher than 1:16. Disease severity does not correlate with antibody titers. The microimmunofluorescence test is more sensitive than complement fixation but is not routinely available. In summary, with an appropriate clinical presentation, a complement fixation titer of greater than 1:64 is considered diagnostic for LGV.
4. Cytology: Direct immunofluorescence techniques are available to identify Chlamydia, although they are not specific for LGV strains.
5. Biopsy of node: A biopsy is useful if needed to rule out lymphoma.

Therapy

1. Recommended regimen: Doxycycline 100 mg two times a day for 21 days.
2. Alternative regimens
   a. Erythromycin 500 mg orally four times a day for 21 days
   b. Sulfamethoxazole 500 mg orally four times a day for 21 days
3. Aspiration, incision and drainage, and surgery: Occasionally, aspiration of a fluctuant node or incision and drainage of an abscess is required for prevention of ulcer formation or relief of inguinal pain. The late complications of LGV may necessitate surgical repair after antibiotic treatment is complete.
4. Follow-up: Patients should be monitored clinically until signs and symptoms have resolved.
5. Sex partners: Sexual contacts within 30 days before onset of symptoms should be examined, tested for urethral or cervical chlamydial infection, and treated.
6. Pregnancy and lactation: Pregnant and lactating women should be treated with the erythromycin regimen.
7. HIV infection: HIV-infected adolescents should be treated with the same regimens as for noninfected adolescents.

GRANULOMA INGUINALE

Granuloma inguinale is extremely uncommon in the United States, with only eight reported cases in 1997, but is in the differential diagnosis of STDs that cause chronic progressive ulcerative disease of the genital and anal areas.

Etiology

Granuloma inguinale is caused by Calymmatobacterium granulomatis, a nonmotile, obligate-intracellular, encapsulated, gram-negative coccobacillus.

1. Frequency: Extremely uncommon in the United States, with peak incidence between 20 and 40 years of age. Indigenous granuloma inguinale is no longer present in the United States or most other developed countries. Cases that occur in the United States are imported.
2. Sex: Prevalence in males is greater than in females.
3. Geographic prevalence: In this country, more common in the southern United States; highest incidence is in underdeveloped countries, particularly those in tropical and subtropical environments.
4. Transmission: Primarily through sexual contact, most commonly from a person with active infection but possibly also from a person with asymptomatic rectal
infection. The disease is only mildly contagious, requiring several exposures for clinical disease; autoinoculation also leads to spread.

5. Incubation period: 8 to 80 days

Clinical Manifestations

1. Granuloma inguinale has a variety of presentations and atypical lesions, which makes identification a challenge.
   a. Ulcerovegetative or ulceroceruminomatous forms: Most common form; produces large, extensive, nonindurated ulcerations with beefy-red, friable granulation tissue that bleeds easily.
   b. Nodular form: Consists of soft red nodules or plaques that erode to form ulcerations.
   c. Verrucous form: Consists of dry vegetative masses that resemble condylomata acuminata.
   d. Necrotic form: Less common; produces extensive destruction of tissue with gray, foul-smelling exudate. These ulcerations are often painful, unlike the other variants of granuloma inguinale.
   e. Sclerotic form: Rare; consists of dry, nonbleeding ulcers that expand into plaques with band-like scarring. Because of the formation of strictures, lymphedema can occur.

2. True inguinal lymphadenopathy does not occur with granuloma inguinale unless bacterial superinfection develops. Pseudobuboes can result from inguinal enlargement related to subcutaneous granulomas.

3. Sites involved
   a. Granuloma inguinale is limited to local tissue.
   b. Granuloma inguinale usually does not produce constitutional symptoms.
   c. Systemic symptoms may suggest hematogenous dissemination, which may be associated with a grave prognosis.
   d. C. granulomatis organisms may also involve extragenital sites (mouth) through autoinoculation, or bone, bowel, or bladder.

Differential Diagnosis

The disease in its early stages may be confused with syphilis, herpes simplex, chancroid, or pyogenic infection.

DIAGNOSIS

1. The clinical appearance is highly suggestive.
2. Giemsa or Wright stain: A piece of clean granulation tissue is spread against a slide and stained with Giemsa or Wright stain. Intracytoplasmic rods (Donovan bodies) in large mononuclear cells are indicative of granuloma inguinale. The microorganism also can be detected by histological examination of biopsy specimens.
3. Currently under development is a serological test that uses an indirect immunofluorescence technique applied to paraffin-embedded tissue sections of lesions containing Donovan bodies. The test has a sensitivity of 100% and a specificity of 98%. This test may prove valuable, because there is no culture method for C. granulomatis.
4. Lesions should be cultured for H. ducreyi to exclude chancroid (pseudogranuloma inguinale). Granuloma inguinale frequently is misdiagnosed as carcinoma, which can be excluded by histological examination of tissue or by response of the lesion to antibiotics.

Therapy

1. Recommended regimens
   a. Trimethoprim-sulfamethoxazole, one double strength tablet orally twice a day for a minimum of 3 weeks
   b. Doxycycline 100 mg orally twice a day for a minimum of 3 weeks or until resolution.
2. Alternative regimens
   a. Ciprofloxacin 750 mg orally twice a day for a minimum of 3 weeks
   b. Erythromycin base 500 mg orally 4 times a day for a minimum of 3 weeks
   c. An aminoglycoside may be added to any of the regimens if lesions are not responding within the first few days.
   d. Gentamicin and ciprofloxacin are not recommended for use in pregnant women or children younger than 18 years of age; they are effective but should be reserved for resistant cases.
   e. Follow-up: Patients are monitored until resolution of signs and symptoms. If there is a response, partial healing will be noted within the first week. Relapse can occur, especially if the antibiotic is stopped before the primary lesion has healed completely.
   f. Sexual partners: Sexual partners should be treated if they had contact with the patient during the 60 days before the onset of symptoms or if they clinically are symptomatic.
   g. Pregnancy: Erythromycin should be used in pregnant and lactating women.
   h. HIV-infected patients: A parenteral aminoglycoside should be strongly considered in addition to one of the recommended regimens.

WEB SITES

For Teenagers and Parents

http://www.niaid.nih.gov/factsheets/stdother.htm#std1, National Institutes of Health handout on chancroid.
Calgary Birth Control Association information on chancroid.

For Health Professionals

http://www.emedicine.com/, E-medicine Web site with clinical information (search for the disease).
http://www.stdservices.on.net/std/chancroid/management.htm, LGV diagnosis and management information.

REFERENCES AND ADDITIONAL READINGS


Lewis DA. Diagnostic tests for chancroid. Sex Transm Infect 2000;76:137.


Ridgway GL. Quinolones in sexually transmitted diseases. Drugs 1993;45[Suppl 3]:134.


Overview of Drug Use and Abuse

Lawrence S. Neinstein and Bruce S. Heischober

Definitions

Drug Use among Adolescents increased explosively in the 1960s and 1970s. Although drug use by teenagers declined from the late 1970s until 1991, the use of drugs among American secondary school students has been rising since 1991 among 8th grade students and since 1992 among 10th and 12th graders. This chapter provides an overview on the epidemiology of drug use and abuse in adolescents and young adults.

1. In 2000, it was estimated that 54% of American youth try an illicit drug before they finish high school.
2. By 12th grade, almost one third (29%) of adolescents have used illicit drugs other than marijuana.
3. About 6% of high school seniors actively smoke marijuana on a daily basis.
4. Rise in drug use: The prevalence of 8th graders taking any illicit drug in the prior 12 months almost doubled between 1991 and 2000 (from 11% to 19.5%). Between 1992 to 2000, the prevalence for use of any illicit drug in the prior 12 months increased by almost two thirds among 10th graders (from 20.4% to 36.4%) and by almost half among 12th graders (from 27.1% to 40.9%). The use of other drugs, including LSD, other hallucinogens, inhalants, stimulants, barbiturates, and caffeine and crack, also rose between 1991 and 1997 but appeared to level off between 1997 and 2000.
5. In the year 2000, about 2.9% of high school seniors drink alcohol daily; when surveyed, 30.0% reported they had had five or more drinks in a row at least once in the previous 2 weeks.
6. The biggest recent increase in use has occurred with MDMA (Ecstasy). This usage has been tracked from 1996 on, and its use in the past 12 months among high school seniors rose from 4.6% in 1996 to 8.2% in 2000. The increase from 1999 to 2000 in 8th graders was from 1.7% to 3.1%.

Health care providers should be aware of drug effects, the health consequences of drugs, and the management of drug abuse. If the practitioner is uncomfortable with management, he or she should be prepared to refer the teenager to appropriate local resources.

DEFINITIONS

Some definitions of terms are useful to keep in mind when one is dealing with the issue of drugs. A task force of the Panels on Alcoholism and Drug Abuse of the American Medical Association's Council on Scientific Affairs conducted a survey of substance abuse experts to help develop standard definitions (Rinaldi et al., 1988).

1. Drug abuse: Any use of drugs that causes physical, psychological, economic, legal, or social harm to the individual user or to others affected by the drug user's behavior.
2. Drug intoxication: Changes in physiological functioning, psychological functioning, mood states, cognitive processes, or all of these, as a consequence of excessive consumption of a drug, usually disruptive.
3. Drug addiction: Chronic disorder characterized by the compulsive use of a substance that results in progressive physical, psychological, or social harm to the user and by continued use despite that harm.
4. Psychological dependence: The emotional state of craving a drug, either for its positive effect or to avoid negative effects associated with its absence.
5. Physical dependence: A physiological state of adaptation to a drug, usually characterized by the development of tolerance to drug effects and the emergence of a withdrawal syndrome during prolonged abstinence.

Categories of Commonly Abused Drugs

1. Cannabinoids: Cannabinoids include marijuana and hashish.
2. Depressants: Depressants include sedatives and minor and major tranquilizers.
   a. Sedatives: Drugs that reduce anxiety and induce sleep. Sedatives can lead to physical and psychological dependence.
      i. Alcohol
      ii. Barbiturates (Amytal, Nembutal, Seconal, phenobarbital)
      iii. Methaqualone (Quaalude)—no longer legally available
      iv. Glutethimide (Doriden)
      v. Flunitrazepam (Rohypnol)
   b. Minor tranquilizers: Drugs that reduce anxiety. Included in this group are diazepam (Valium), alprazolam (Xanax), chlordiazepoxide (Librium), triazolam (Halcion), and lorazepam (Ativan). Physical and psychological dependence commonly occurs with these drugs.
   c. Major tranquilizers: This group includes the phenothiazines, such as thioridazine (Mellaril), trifluoperazine (Stelazine), and chlorpromazine (Thorazine).
3. Stimulants: Stimulants produce tolerance and strong psychological dependence. Physical dependence was previously thought to occur only to a mild degree or not at all. It is now well established that a physical withdrawal syndrome indicating physical dependence occurs with this class of drugs. In addition, these drugs are clearly able to affect the mesolimbic reward systems of the central nervous system (CNS) in such a way as to induce intense cravings and profoundly influence preconscious drives to use. The CNS stimulants, which cause increased alertness and activity, include:
   a. Amphetamines: including dexamfetamine methamphetamine ("speed"), pemphetamine methamphetamine (Desoxyn), and amphetamine (Biphetamine, Adderall, Dextroamphetamine)
   b. Nicotine
   c. Caffeine
   d. Cocaine
   e. MDMA (methyleneedioxymethamphetamine; "Ecstasy")—has both stimulant and hallucinogenic properties
   f. Methylenediamine (Ritalin)
   g. Betel nut
4. Hallucinogens: These drugs affect sensations, emotions, and awareness, causing distortion of perceived reality. They can produce tolerance and psychological dependence but do not result in physical dependence.
   a. LSD (3,4-lysergic acid diethylamide)
   b. Mescaline
   c. DMT (dimethyltryptamine)
   d. DOM (2,5-dimethoxy-4-methylamphetamine)
   e. PCP (phencyclidine hydrochloride), also categorized as a dissociative anesthetic
   f. Psilocybin/psilocin
   g. MDA (methylenedioxyamphetamine)
   h. MDMA (methylendioxymethamphetamine)—has both stimulant and hallucinogenic properties

5. Opioids and morphine derivatives: Opiates are used to relieve pain. They produce tolerance and strong physical and psychological dependence. Included in this class of drugs are
   a. Morphine
   b. Heroin
   c. Codeine
   d. Meperidine (Demerol)
   e. Methadone
   f. Fentanyl (Actil, Duragesic, Sublimaze)
   g. Opium

6. Dispersive anesthesics: This group includes ketamine (Ketalar SV) and phencyclidine (PCP) and their analogues.

7. Volatile solvents: These drugs have a general depressant effect on the CNS and may create hallucinogenic experiences. They include solvents (paint thinners, gasoline, glues); gases (butane, propane, aerosol propellants, nitrous oxide); and nitrites (isooamyl, isobutyl, cyclohexyl). They can produce tolerance and psychological dependence but no true physical dependence.

8. Anabolic-androgenic steroids: These drugs are synthetic derivatives of testosterone, engineered by chemists to have a longer half-life (testosterone activity is measured in minutes) and less androgenic activity. Most in use today are orally active alkylated testosterone analogues or injectable testosterone esters (Anadrol, Oxandrin, Durabolin, Depo-Testosterone, Equipoise). They are used in cycles of 6 to 12 weeks, with combining of oral and injectable agents (called "stacking").

**PREVALENCE OF DRUG USE**

It is easier than in prior years to access up-to-date information on adolescent drug use and trends from several national studies. These include the following:

1. Monitoring the Future (MFT): MTF is a long-term study of American adolescents, college students, and young adults. The study is conducted by the University of Michigan's Institute for Social Research and is supported by grants from the National Institute on Drug Abuse (NIDA). This survey (Johnston et al., 2000) includes approximately 50,000 students from 400 public and private high schools. In addition, since 1977, a total of 1,200 college students and 11,000 young adult high school graduates have been surveyed. Information on use and trends has been analyzed yearly since 1975 and is accessible at the study Web site: http://www.monitoringthefuture.org/

It is important to remember that data from MTF do not include high school dropouts, who constitute about 15% to 20% of an age group by the end of senior year. Very few students have left school by 8th grade and relatively few by the end of 10th grade, so data from those classes may be more generalizable to the majority of that age group.

2. Youth Risk Behavior Surveillance (YRBS): The YRBS surveys are conducted every 2 years and monitor six categories of priority health-risk behaviors among youth and young adults that contribute to unintentional and intentional injuries, including use of tobacco, alcohol, and other drugs. A summary of this information for 1999 is available at the Centers for Disease Control and Prevention (CDC) Web site: http://www.cdc.gov/mmwr/preview/mmwrhtml/ls4905a1.htm. General YRBS information is available at http://www.cdc.gov/mmwr/dash/yrbst/. The YRBS interviews also include only students in school and not those who have dropped out.

3. National Household Survey on Drug Abuse (NHSDA): This survey is conducted by the U.S. Department of Health and Human Services. Since 1969, the NHSDA was expanded almost fourfold from previous years to enhance understanding of substance abuse and to provide state-level data on estimated use of illicit drugs, alcohol, and tobacco (NHSDA, 2000). Information on this survey is available at their Web site: www.samhsa.gov/oas/nhsda.

**Monitoring the Future**

The year 2000 was the fourth year in a row in which illicit drug use among 8th, 10th, and 12th graders remained lower or steady in some cases (Johnston et al., 2000). Since 1999, cigarette smoking has decreased in all three grade levels. Although reductions occurred in cocaine, hallucinogens, inhalants, and methamphetamine, there were significant increases in the use of Ecstasy and anabolic steroids among 10th graders and heroin among 12th graders.

1. Perceived risk of harm and disapproval: In past years, it was noted that perceived risk correlated in a negative fashion with usage. Among 10th graders overall, the perceived risk of smoking one or more packs of cigarettes per day increased between 1999 and 2000, but the perceived risk of occasional use of crack decreased; for 12th graders, the perceived risk of taking anabolic steroids decreased. The perceived availability of Ecstasy increased among 12th graders, from 40.1% in 1999 to 51.4% in 2000.

2. Comeback drugs: Another finding in the 2000 MTF survey was that, although some drugs are new to the scene, others are being "rediscovered" by adolescents and young adults. These include drugs like LSD, methamphetamine, heroin, and PCP.

3. Overview of use in college students and young adults: Volume II of the MTF national survey reviews data for college students and adults age 19 to 40 years.

This analysis examines both young adult high school graduates age 19 to 32 years and college students. Overall, there was little increase in illicit drug use in the young adult population age 19 to 28 years. Between 1991 and 2000, their use of illicit drugs stayed stable at the same time that adolescent drug use rose. However, this finding is not true for every drug and every group. For example:

a. In 1998 and 1999, while smoking was declining among secondary school students at all grades, smoking increases significantly for college students.

b. Marijuana use among college students increased much more gradually (from 27% in 1991 to 34% in 2000) than among high school students in the 1990s, and there was even less change among young adults who were not college students (from 24% in 1991 to 28% in 2000).

c. Daily marijuana use rose substantially among college students between 1992 and 2000 but less so among young adults who were not in college.

d. Use of LSD among college students and young adults peaked in 1995 and declined in both groups through 2000.

e. Between 1982 and 1992, amphetamine use declined among college students, from 21% in 1982 to 4% in 1992. Amphetamine use increased modestly among college students in the 1990s, and the rates were about half those for 10th and 12th graders.

f. Crack cocaine use did not show much of an increase among college students in the 1990s.

g. MDMA (Ecstasy) had a substantial increase in use among college students starting in 1995. Use in last year increased from 2.4% in 1997, 3.9% in 1998, 5.5% in 1999, and 9.1% in 2000.

h. For five classes of illicitly used drugs—marijuana, cocaine, amphetamines, LSD, and inhalants—their respective annual prevalence rates in 2000 for high schools seniors and college students were as follows:

<table>
<thead>
<tr>
<th>Age</th>
<th>Marijuana</th>
<th>Cocaine</th>
<th>Amphetamines</th>
<th>LSD</th>
<th>Inhalants</th>
</tr>
</thead>
<tbody>
<tr>
<td>High school seniors</td>
<td>36.5%</td>
<td>5.0%</td>
<td>10.0%</td>
<td>6.6%</td>
<td>5.9%</td>
</tr>
<tr>
<td>College students</td>
<td>34.0%</td>
<td>4.8%</td>
<td>6.6%</td>
<td>4.3%</td>
<td>2.9%</td>
</tr>
</tbody>
</table>

i. American college students (whether in 2-year or 4-year schools) show annual usage rates similar to those of high school graduates of the same age, including the categories of any illicit drug, marijuana, inhalants, hallucinogens other than LSD, and narcotics other than heroin. College students have lower rates than their age peers for any illicit drug other than marijuana, hallucinogens, LSD, cocaine, crack cocaine, heroin, amphetamines, ice, barbiturates, and tranquilizers.

j. In general, the trends since 1980 for illicit substance use among American college students have paralleled those of their same-age peers who were not in
National Household Survey of Drug Abuse

In 1999, an estimated 14.8 million Americans were users of illicit drugs (i.e., used an illicit drug at least once during the 30 days before survey) (NHSDA, 2000). In 1979, the figure was 25 million. Among this 14.8 million, usage included 57% marijuana only, 18% marijuana and some other drug, and 25% another drug and no marijuana.

The highest rate of illicit drug use was found among 18- to 20-year-olds (20% to 21%). The next highest group was the 16- to 17-year-olds, followed by the 21- to 25-year-olds. Rates declined in each successive age group, with only 1.7% of persons age 50 to 64 years and 0.6% of those age 65 and older using illicit drugs. The only exception to this decline with age was among those age 40 to 44 years, who had a rate of 8.6%, which was higher than for the 30- to 39-year-old group. Persons in this age group were teenagers during the 1970s, when drug use peaked.

Among youth age 12 to 17 years, 10.9% reported current use of an illicit drug in 1999. Marijuana was the most common drug used (7.7% were current users). The rate in this age group was higher for males (11.3%) than for females (10.5%).

Illicit drug use rates remained highly correlated with educational status. College graduates had the lowest rate of current use (4.8%, compared with 7.1% among those who did not complete high school). Nevertheless, individuals who had completed 4 years of college had higher rates of having tried an illicit drug in their lifetime (45.6%) compared with those who had not completed high school (30.0%). The rate of current illicit drug use among the college-age population was the same for those who were full-time undergraduate students (19.4%) as for other persons of the same age group (18 to 22 years).

Employment status was also highly correlated with current use of an illicit drug—16.5% of unemployed adults age 18 years and older were users, compared with 6.5% of those who were employed full-time.

Current illicit drug use in the United States was highest in the West (7.9%) and lowest in the South (5.6%).

There are numerous charts in this chapter that help summarize the epidemiology of drug use among adolescents and young adults:

Table 69.1 shows the prevalence of drug use among 8th, 10th, and 12th graders in 2000.

Table 69.2, Table 69.3, Table 69.4 and Table 69.5 illustrate, respectively, the trends in lifetime prevalence, annual prevalence, 30-day prevalence, and 30-day daily prevalence of drug use among high school seniors.

Table 69.1. Prevalence of use of various drugs for 8th, 10th, and 12th graders, 2000

Table 69.2. Long-term trends in lifetime prevalence of use of various drugs for 12th graders (% ever used)

Table 69.3. Long-term trends in annual prevalence of use of various drugs for 12th graders (% who used in last 12 mo)
Table 69.4. Long-term trends in 30-day prevalence of use of various drugs for 12th graders (% who used in last 30 days)

Table 69.5. Long-term trends in 30-day prevalence of daily use of various drugs for 12th graders (% who used daily in last 30 days)

Table 69.6 shows trends in lifetime prevalence for various types of drugs among college students at 1 to 4 years beyond high school.

Table 69.6. Trends in lifetime prevalence of various types of drugs among college students 1–4 years beyond high school (% who used in lifetime)

Table 69.7 illustrates 1999 drug use by grade level from YRBS data.

Table 69.7. 1999 drug use in youth by grade from Youth Risk Behavior Survey, 1999

Table 69.8 includes data on high school seniors disapproving of regular drug use in 2000.

Table 69.8. High school seniors disapproving of regular use of drugs, 2000

Table 69.9 includes long-term trends in disapproval of drug use by 12th graders.
Figure 69.1 illustrates the lifetime prevalence and recency of use for 12 types of drugs among high school seniors in the class of 2000.

Figure 69.2 shows trends in lifetime prevalence of marijuana use and use of any illicit drug among high school seniors in 2000.

Figure 69.3 displays trends in the annual prevalence of illicit drug use in comparison with use of illicit drugs other than marijuana among 8th, 10th, and 12th graders for 2000.

Figure 69.4 shows trends in annual prevalence of an illicit drug use index for 8th, 10th, and 12th graders.
Figure 69.4. Trends in annual prevalence of an illicit drug use index among 8th, 10th, and 12th graders. (From Johnston LD, O’Malley PM, Bachman JG. Monitoring the Future study: national results on adolescent drug use. Overview of key findings, 2000. Washington, DC: U.S. Department of Health and Human Services, 2001.)

Figure 69.5 illustrates trends in the annual use of selected drugs by grade from 1976 to 2000.

Figure 69.5. Trends in annual use of selected drugs by grade, 1976–2000, and percentage of use in last 12 months among 8th, 10th, and 12th graders. (From Johnston LD, O’Malley PM, Bachman JG. Monitoring the Future study: national results on adolescent drug use. Overview of key findings, 2000. Washington, DC: U.S. Department of Health and Human Services, 2001.)

Figure 69.6 illustrates the trends in perceived availability, perceived risk of regular use, and prevalence of use for marijuana among 12th graders.


Figure 69.7 illustrates the trends in perceived availability, perceived risk of regular use, and prevalence of use for cocaine among 12th graders.


Figure 69.8 shows trends in annual prevalence of use of alcohol, marijuana, and cocaine among college students.
Cigarette Use

The 2000 MTF survey found that cigarette smoking among teens has begun to drop. For example, use within the past month among 8th graders declined from 17.5% in 1999 to 14.6% in 2000. Similar drops were found for 10th and 12th graders. In addition, perceived risk of harm from smoking a pack or more of cigarettes per day increased among high school students. However, still almost 63% of teens have tried cigarettes by the 12th grade, and almost one third (31%) are current smokers. Significant cigarette use starts even earlier: 41% of teens have tried cigarettes by the 8th grade, and 15% are current smokers in the 8th grade.

The YRBS 1999 survey found that 70.4% of students had tried cigarettes and 25.3% had smoked every day for the previous 30 days. Overall, white students (29.3%) were significantly more likely than Hispanic students (19.6%) or black students (11.2%) to report lifetime daily cigarette use. White students (38.6%) and Hispanic students (32.7%) were more likely than black students (19.7%) to report current cigarette use. Nationwide, 16.6% of students had smoked on 20 or more days in the 30 days preceding the survey (i.e., current frequent cigarette use). Nationwide, 7.8% of students had used smokeless tobacco on at least 1 day in the 30 days preceding the survey.

In the NHSDA for 1999, current cigarette smoking rates increased steadily by age, from 2.2% at 12 years to 43.5% at age 20. Overall, 14.9% of youths age 12 to 17 years in 1999 smoked cigarettes currently. Current use was much higher in the 18- to 25-year-old age group. Smoking within the past month was highest among Native Americans and lowest in the Asian population. Young adults enrolled full-time in college were less likely than their peers who were not enrolled to report current cigarette use. Use was lowest in the Pacific portion of the West (21.9%) and highest in the East South Central part of the country (30.5%). Three brands of cigarette accounted for most cigarette smoking by adolescents age 12 to 17 years: 54.5% smoked Marlboro, 21.6% Newport, and 9.8% Camel.

For more information on use of tobacco by adolescents, see Chapter 71.

Alcohol Use

Alcoholic drinks have been the most widely used substances by adolescents and adults for many years. In the MTF survey, alcohol use remained stable over the past several years through the year 2000. Among 8th graders, daily drinking in past month decreased significantly. In 2000, the percentages of 8th, 10th, and 12th graders who drank an alcoholic beverage in the past month were 22%, 41%, and 50%, respectively. Potentially the most serious drinking is episodic heavy drinking, defined in the MTF study as consumption of five or more drinks in a row during the previous 2-week period. The prevalence of binge drinking appears to have peaked in about 1979; it declined in 12th graders from 41% in 1983 to 28% in 1992 and has remained fairly constant since, with a small rise. Still, in 2000, more than 14% of 8th graders, 26% of 10th graders, and 30% of high school seniors had participated in episodic heavy drinking at least once during the previous 2 weeks.

In the 1999 YRBS survey, 61% of students reported having had at least one drink during their lifetime. Fifty percent of all students had had at least one drink within the past 30 days, and 31.5% had had at least five drinks at one occasion during the past 30 days. Overall, rates of heavy drinking were higher in males (34.9%) than in females (28.1%) and higher in white students (35.8%) and Hispanic students (32.1%) than in black students (16.0%).

In the 1999 NHSDA, the prevalence of current alcohol drinking increased with age, from 3.0% at 12 years to a peak of 65.6% among 21-year-olds. However, unlike use of cigarettes and illicit drugs, current alcohol use remained steady among older age groups. Among teens age 12 to 17 years, 18.6% had used alcohol in the month before the survey interview, 10.9% were binge drinkers, and 2.5% were heavy drinkers (defined as consuming five or more drinks at one occasion on at least 5 of the past 30 days). Binge alcohol rates were 1.7% for 12-year-olds, 3.7% for 13-year-olds, and 7.3% for 14-year-olds. Young adults age 18 to 22 years who were enrolled full-time in college were more likely than their peers who were not enrolled full-time to report drinking, binge drinking, and heavy drinking.

Marijuana Use

Marijuana use rose sharply until about 1979, at which point it seemed to peak. The trend toward declining use persisted until 1992, when a sharp reversal developed. This reversal continued until about 1996 in 8th graders and 1997 in 10th and 12th graders. Since then there has been a modest decline through 2000. For all 25 years of the MTF survey, marijuana was the most widely used illicit drug. In 2000, 48.8% of high school seniors reported past or current use of marijuana; this is still a distinct increase from the low of 32.6% by seniors in 1992. The proportion of seniors who reported marijuana use in the past 12 months declined from 50.8% in the class of 1979, to 22% in the class of 1992, only to increase to 38.5% in 1997 and then lower to 36.5% in 2000. In 2000, the proportion of students reporting any use of marijuana in the past 12 months was 15.6% for 8th graders, 32.2% for 10th graders, and 36.5% for 12th graders.

In the 1999 YRBS, 47.2% of students were found to have used marijuana during their lifetime, and 26.7% had used marijuana at least once in the past 30 days. Overall, male students (30.8%) were more likely than female students (22.6%) to report current marijuana use. Current use ranged from 10.6% in Utah to 33.7% in the East South Central part of the country.

In the 1999 NHSDA, an estimated 2.3 million Americans reported using marijuana for the first time in 1998. This number had increased from 1.4 million in 1990 to 2.6 million in 1996 and then dropped in 1997 and 1998. The rise in new users in the 1990s was particularly evident among younger age groups. Among 8th graders, 26% of 10th graders, and 30% of high school seniors had participated in episodic heavy drinking at least once during the previous 2 weeks.

Other Drugs

According to the 2000 MTF survey, 29% of the class of 2000 had used some illicit drug other than marijuana (compared with 23.1% of 10th graders and 15.8% of 8th graders). The overall prevalence rate for use of any illicit drug declined from a peak level of 65.6% in 1981 to a nadir of 40.7% in 1992. This trend reversed in 1992 and increased until 1999 with a rate of 54.7%. There was a small decline to 54.0% in 2000. Other than marijuana, the most prevalent illicit drugs used by adolescents were stimulants, inhalants, cocaine, hallucinogens, tranquilizers, and sedatives. One of the most frequently used illicit drugs other than marijuana in the year 2000 was Ecstasy.

Illicit Drugs Increasing in Use

Based on the MTF, the most important increase was observed for MDMA (Ecstasy). This increase was seen for all three grade levels, and although the 1999 increase was mainly in the Northeast, the increase in the 2000 survey was primarily in the other three regions. Ecstasy use is now more prevalent among American teens than use of cocaine. Use of Ecstasy in the past 12 months ranged from 3.1% of 8th graders to 8.2% of 12th graders. The other drugs that had significant increases were anabolic steroids and heroin. In the YRBS 1999 report, 3.7% of students had used illegal steroids during their lifetime (5.2% of males and 2.2% of females; 4.1% of whites and 2.2% of blacks). In the same year, 2.4% of students reported having used heroin in their lifetime (3.5% of males and 1.3% of females).

The annual prevalence of cocaine use among high school seniors rose in the 1970s and remained stable through the first half of the 1980s before a dramatic decline...
between 1986 (12.7%) and 1992 (3.1%). The rate increased between 1992 and 1996, when it peaked at 6.2% before falling off again to 5.0% in 2000. Current use (within the past 30 days) dropped from a peak level of 6.7% in 1985 to 1.3% in 1993 before rising to 2.6% in 1999 and falling again to 2.1% in 2000. In the YRBS 1999 report, 9.5% of students had used a form of cocaine during their lifetime and 4.0% of students had used cocaine at least once in the past 30 days. Males were even more likely than females to have used cocaine in the past 30 days (5.2% versus 2.9%). Overall, Hispanic students (6.7%) and white students (4.1%) were significantly more likely than black students (1.1%) to report current cocaine use. In the 1999 NHSDA, the rate of initiation among 12- to 17-year-olds increased from 5.1 per 1,000 in 1992 to 13.1 per 1,000 in 1996. Historically, the highest rates of first time use of cocaine has been in young adults, age 18 to 25 years.

Amphetamines and other stimulants have had relatively high prevalence of use in youth for many years. The downward trend in the use of stimulants, which began in 1982, continued to a low in 1992, after which a sudden reversal developed. Use peaked again among 8th and 10th graders in 1996 and among 12th graders in 1997. Since then, use has declined in among 8th and 10th graders. In the 2000 MTF survey, 10.5% of high school seniors reported using amphetamines in the past year, compared with 11.1% of 10th graders and 6.5% of 8th graders. In the 1999 YRBS report, 9.1% of students reported using methamphetamine during their lifetime (11.3% of Hispanics, 10.3% of whites, and 1.7% of blacks).

Use of hallucinogens declined between 1975 and 1988; however, in 1989 there was a slight increase in use, and the 1996 MTF data showed that 10.1% of high school seniors had used these drugs in the past year—the highest rate in more than a decade. Since 1996, use has declined for all grades, with 8.1% of the class of 2000 reporting use of hallucinogens in the past year.

### Daily Use

The 30-day prevalence of daily use of drugs among high school seniors in 2000 includes the following percentages:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cigarettes</td>
<td>20.6%</td>
</tr>
<tr>
<td>Alcohol</td>
<td>2.9%</td>
</tr>
<tr>
<td>Marijuana</td>
<td>6.0%</td>
</tr>
<tr>
<td>Inhalants</td>
<td>0.2%</td>
</tr>
<tr>
<td>Cocaine</td>
<td>0.2%</td>
</tr>
<tr>
<td>Stimulants</td>
<td>0.5%</td>
</tr>
<tr>
<td>Hallucinogens</td>
<td>0.2%</td>
</tr>
<tr>
<td>Sedatives</td>
<td>0.1%</td>
</tr>
<tr>
<td>Tranquilizers</td>
<td>0.1%</td>
</tr>
<tr>
<td>Heroin</td>
<td>0.1%</td>
</tr>
</tbody>
</table>

### Age and Drug Use

Table 69.1 and Table 69.2 and Fig. 69.3, Fig. 69.4, and Fig. 69.5 illustrate the relationship between grade in school and drug use. According to these data, the majority of experimentation with illicit drugs occurs during high school. However, for marijuana, alcohol, and cigarettes, many of the initial experiences take place before high school. Inhaled users, in particular, often have their first experience before the 10th grade. Initial experience with cocaine is more common in the 10th grade and beyond.

### Drug Beliefs Among Adolescents

#### Harmfulness of Drugs

The majority of high school seniors perceive regular use of illicit drugs as entailing harmfulness to the user. According to the MTF (2000), the percentages of seniors responding in such a manner in regard to regular use of various drugs were as follows:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Harmfulness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marijuana</td>
<td>74.8%</td>
</tr>
<tr>
<td>Inhalants</td>
<td>69.9%</td>
</tr>
<tr>
<td>Heroin</td>
<td>89.2%</td>
</tr>
<tr>
<td>LSD</td>
<td>75.0%</td>
</tr>
<tr>
<td>Cocaine</td>
<td>86.2%</td>
</tr>
<tr>
<td>Barbiturates</td>
<td>52.3%</td>
</tr>
<tr>
<td>Amphetamines</td>
<td>66.3%</td>
</tr>
</tbody>
</table>

Regular use of cigarettes was judged to be a great risk to the user by 73.1% of the respondents. Only 21.7% considered one or two daily alcoholic drinks to carry great risk, and only 42.7% considered five or more drinks once or twice a weekend to constitute a risk of harming themselves.

#### Extent of Disapproval

The great majority of high school seniors do not approve of the regular use of any illicit drug. The percentages that disapprove of regular use of various drugs are outlined in Table 69.8. Seventy percent of high school seniors disapproved of taking one or two alcoholic drinks almost every day. The overall trend in all categories is toward diminished disapproval of drug use, particularly in relation to marijuana, LSD, and stimulants including cocaine (Table 69.9). The environment of decreased perceived risk and less disapproval from peers correlates with some of the increased patterns of substance use in the middle to late 1990s.

### Etiology for Drug Use and Abuse

Adolescent substance abuse is a complex phenomenon that includes diverse drugs, diverse usage patterns, and diverse etiologies. Although drug use appears to be a function of social and peer factors, substance abuse is more correlated with particular biological and psychological factors.

For many clinicians the term “addiction medicine” is an oxymoron because of the lack of basic science or clinical research to support the existence of a well-defined disease state. In adolescence, certain patterns of substance use are seen as normative, and some studies show that specific adolescent uses of drugs and alcohol do not predict adult abuse and addiction. This has led to concern about labeling an adolescent an “addict” and consigning a nonsupervised “12-Step” treatment plan. In addition, there has been a lack of consensus regarding terminology, etiology, prevention, and treatment as well as the application of conceptual frameworks developed for adults to the adolescent population.

Recent research has focused on both risk and protective factors and multiple etiological pathways, particularly the biological aspects. Support has developed for the view that addiction is a CNS disease that involves identifiable structural and functional changes within specific anatomical brain structures or pathways that are genetically programmed and environmentally triggered (i.e., by the substance). NIDA has championed this theory through research and collaboration with other clinical and research groups. The explosion of information on receptors, neurotransmitters, and other brain functions continues to become more important clinically as their roles and their impacts on interventions become better understood.

### Neurobiology of Addiction Disorders

Increased dopamine levels are postulated as the underlying cause of positive reinforcement that leads to addiction. Dopamine has been implicated in the incentive motivational effects of food, sex, and several drugs of abuse. All drugs of abuse stimulate the brain’s limbic system. The limbic system is a group of well-defined structures that communicate with each other in the regulation of memory, learning, and emotions. The limbic system networks with the hypothalamus, which coordinates the interactions among many brain structures. The limbic system also communicates with the frontal lobe, which is the central area for perceptions,
feelings, and speech. The perception of pleasure is centered structurally in the nucleus accumbens of the limbic system. Sleep, level of alertness, perceptions, emotions, movement, judgment, and attention all are affected by any psychoactive drug through these structural areas of the brain.

Genetics

Knowledge of the genetics of drug abuse also appears to be rapidly advancing (Weinberg et al., 1998). Two possible pathways have been suggested: (a) parental alcohol use predicts substance abuse in offspring, and (b) antisocial personality disorder in biological parents leads to higher rates of conduct disorders and aggression in offspring, resulting in substance abuse disorders.

No single gene for substance abuse disorders has been isolated. Clearly numerous drugs of abuse have effects on the CNS that are highly addicting. There appear to be individual susceptibilities to these influences that are probably genetically determined. Resilience factors may help protect the adolescent; these include positive self-esteem, supportive family relationships, positive role models, and problem-solving ability.

Cultural and Social Factors

Adolescents and researchers report a multitude of reasons for use of drugs by teenagers, including the following:

1. Use of the drugs by family and peers
2. Exploration and experimentation
3. To gain social acceptance
4. As a result of low self-esteem
5. To seek a change in consciousness or in perceptions or mood
6. To enhance the ability to act socially
7. To relieve a stressful situation
8. As a challenge to parents or authority
9. As a response to messages in the media regarding tobacco and alcohol that convey the idea that these drugs are important for one's body image and sexual identity
10. As a rite of passage
11. To enhance one's sexuality
12. As a reaction to boredom

Affluence and Poverty

One should avoid assuming that levels of drug and alcohol use correlate predominantly with poverty and that the highest risk occurs in the lowest-income communities. Use of many substances increases with increasing levels of income.

Immigrants and Refugees

There are many large concentrations of immigrants and/or refugees in North America. Typically, rates of substance abuse are lower during an initial period of several years after immigration, which is followed by increased rates. Young immigrants are often ignorant of the dangers related to abuse of substances not present in their country of origin. Economic pressures and lack of parallel acculturation on the part of parents or other responsible adults can place these youth at risk. Western physicians may also be unaware of the existence and dangers of substances that are commonplace only within a given refugee community (e.g., krat, betel nut) (see Chapter 74).

Religious Beliefs

A personal relationship with "God" (a higher spiritual power) or affiliation with a fundamentalist denomination has been associated with lower rates of alcohol and illicit drug abuse or dependence (Kendler et al., 1997; Wallace et al., 1998).

Ceremonial Use

When culturally sanctioned substance use is modeled in family-centered, multigenerational ritual or ceremonial settings, abuse of the given substance is low. Youth are put at increased risk of addiction when substance use becomes a rite of passage in a deviant, secretive, peer-led ritual.

STAGES OF DRUG USE

MacDonald (1987) suggested five stages of adolescent substance abuse, as follows:

Stage 0: Showing curiosity. At this stage the teen usually is normal but may have low self-esteem and a strong desire for peer acceptance. Given a natural curiosity and tendency to exhibit a sense of immortality, the teenager decides to try a mood-altering chemical. Often the result is feeling good and suffering no dire consequences, and the teen enters stage 1.

Stage 1: Learning about drug-induced mood swings. The teen learns more about use of drugs, but use is limited to group settings, usually on weekends. Peer pressure is frequently intense and is a prime reason for continuance. The teen's discomfort with family, school, or social problems is often relieved temporarily by the drug use.

Stage 2: Seeking the drug-induced mood swings. Having learned that the drugs can alleviate perceived pain and anxiety, the adolescent now seeks the highs of drug use. The teen may acquire a supply of drugs and paraphernalia. The drugs are now used more to relax than as part of the social scene. The teen becomes a regular weekend and occasional weekday user. Behavioral changes may occur during this stage, including a decrease in school performance and abandonment of extracurricular interests.

Stage 3: Being preoccupied with the drug-induced mood swings. The teen loses control of his or her life and is concerned only with getting high. The behavioral changes are more pronounced and more obvious. New behaviors may also include stealing, school truancy, and lying. Drug dealing, to obtain the money necessary for continued drug use, may start.

Stage 4: Burnout. At this point the teen is using drugs just to feel normal. Drugs may no longer produce euphoria. "Zombies" and "space cadets" are common terms used by adolescents to describe this group.

An estimated 2.8 million people in the United States received some kind of drug or alcohol treatment in the 12 months before the 1999 NSHDA interviews. This included 1.3% of youth 12 to 17 years of age and 2.0% of young adults age 18 to 25. Chapter 70, Chapter 71, Chapter 72, Chapter 73 and Chapter 74 of this book focus on specific drugs, concentrating on drug use patterns and effects on health. Chapter 75, the final chapter in this section, discusses approaches to managing drug abuse.

WEB SITES

http://www.monitoringthefuture.org/. MTF home page with detailed information and data from this comprehensive longitudinal study.
http://www.nida.nih.gov/drugpages/stats.html. Information on trends from NIDA.
http://www.lycaeum.org/live/. Lycaeum is a site about drug use by individuals with experience in drug use. It has useful information on various aspects of drug use from an alternative point of view. The site offers an extensive database of psychoactive substances and community-based discussion forums. It has images of many chemical formulas, pills, plants, and drug paraphernalia.
http://www.erowid.org/psychoactives/. Erowid is another site about drug use and drugs by individuals with experience in drug use. The site offers a database of...
psychoactive substances, many images of drugs and plants, and so on.

REFERENCES AND ADDITIONAL READINGS


MacDonald DI. Drugs, drinking, and adolescents. Chicago: Year Book Medical, 1984.


MacDonald DI. High school cocaine use declines. JAMA 1988;259:1615.


Alcohol is the most widely used drug in the United States. Readily available and inexpensive, it has been used by 80% to 90% of adolescents by the time they reach 18 years of age. The monthly prevalence of alcohol use among high school seniors in 2000 was 50% and 73.2% for use in the past year. About 3% of high school seniors used alcohol daily in 2000 (Johnston et al., 2000). Thirty percent of high school seniors reported that they had consumed more than five drinks in a row during the previous 2 weeks. Sixty-two percent of high school seniors have been drunk. Figure 70.1 depicts trends in alcohol use prevalence among 8th, 10th, and 12th graders between 1993 and 2000.


MORBIDITY AND MORTALITY

An estimated 4.6 million adolescents age 14 to 17 years have alcohol-related problems. Motor vehicle accidents caused by driving under the influence of alcohol are the leading cause of death in the 15- to 24-year-old age group. Alcohol-related motor vehicle accidents result in 8,000 adolescent deaths and 45,000 injuries each year. Thirty-three percent of students nationwide have ridden with a driver who had been drinking, and 13% have driven a car after drinking. Alcohol use is also involved in approximately 40% of the 10,000 annual nonautomotive accidental deaths of adolescents and in a significant number of the 5,500 suicides and 5,000 homicides of adolescents each year. Alcohol use may be related to acquisition of sexually transmitted diseases (STDs). A study reported in Morbidity and Mortality Weekly Report suggested that higher alcohol taxes and higher minimum legal drinking ages are associated with lower incidence of STDs among adolescents and young adults (Anonymous, MMWR 2000). A 1999 Office of Juvenile Justice and Delinquency Prevention (OJJDP) study estimated that the costs of underage drinking in America totals more than $56 billion annually. Alcohol use is not limited to healthy teens. Adolescents with chronic illnesses such as sickle cell disease or cystic fibrosis engaged in risk-taking behaviors such as smoking, sexual activity, and drug and alcohol use. They may use at lower rates than their peers, but they still should be screened for health-risk behaviors. Health care providers should not underestimate the effects of alcohol use on adolescents or its consequences.

ALCOHOL AND ITS EFFECTS

Although alcohol is a central nervous system (CNS) depressant, at low doses it has behavioral stimulant properties, particularly for persons with an alcoholic diathesis. The principal ingredient of all alcoholic beverages is ethanol. Most beers and wines contain between 3% and 20% alcohol. Moderate doses of alcohol in the nontolerant individual induce sedation, euphoria, decreased inhibitions, and impaired coordination. As the dose and corresponding blood alcohol level increase, ataxia, decreased mentation, poor judgment, labile mood, and slurred speech occur. Heavy use of alcohol can induce unconsciousness, anesthesia, respiratory failure, coma, and death (Table 70.1).

TABLE 70.1. Effects of alcohol consumption in the nontolerant individual
Although alcohol can adversely affect many organ systems of the body, adolescent alcohol abusers usually are spared the complications of prolonged alcohol use, such as cirrhosis, alcoholic hepatitis, and pancreatitis. Acute withdrawal symptoms such as delirium tremens (DTs) or seizures also are unusual in adolescents. Farrow et al. (1987) examined the health and nutritional status of adolescent alcohol abusers. Any significant health or nutritional disability from the abuse related primarily to poor dietary habits. These teens’ hematological status, liver function test (LFT) results, and growth parameters were normal. However, Strauss et al. (2000), in a study of obese children and adolescents with elevated LFT values secondary to fatty liver, showed a significant increase in LFTs with the addition of the alcohol. Defects in retrieval of verbal and nonverbal information and in visuospatial functioning were found in adolescents with histories of heavy drinking during early and middle adolescence (Brown, 2000).

**FACTORS CONTRIBUTING TO TEENAGE ALCOHOL USE**

Adolescent alcohol use is an individual as well as a social problem. Available literature points to several variables that appear to be associated with the use of alcohol by adolescents. Although the conclusions reached in these studies sometimes differ, the hypothesized contributing factors include the following.

1. **Family and parental factors**
   a. Genetic: Twin adoption studies support a genetic predisposition for alcoholism.
   b. Parents as role models: Parental attitudes about alcohol and parental drinking practices influence adolescent alcohol use, especially during early adolescence.
   c. Style of parenting: Extreme parenting styles (authoritarian or permissive) and inconsistent discipline seem to contribute to increased alcohol use among adolescents.
   d. Perceived family support: High levels of perceived family support are correlated with low levels of alcohol and drug use. Cohen et al. (1994) found that children who reported that parents spent more time with them and communicated with them more frequently had lower onset rates of alcohol and tobacco use in the preceding month.

2. **Peer influence**
   a. Peer pressure to maintain alcohol abuse: Although parental factors contribute to initiation of alcohol use, peer attitudes and behavior contribute even more significantly to the maintenance of alcohol use and abuse.
   b. Group acceptance: As adolescents separate from their family, they often associate with peers who have attitudes and beliefs similar to their own. Studies indicate that an individual's alcohol and drug use closely parallels that of his or her peer group.
   c. Group norms: There is a tendency within certain peer groups to excuse drunken behavior and to minimize the physical consequences of heavy drinking. These groups also tend to negate any fear of consequences or punishment.
   d. Desire to attain adult status: The adolescent's desire to imitate adult behavior and society's identification of drinking as an adult privilege contribute to adolescent alcohol abuse. In addition, alcohol use is often seen as a rite of passage to achieve adult status.
   e. Sexuality socialization: As adolescents learn to establish relationships and explore their sexuality, they simultaneously become concerned with body image, social behavior, and developing sexual arousal. Alcohol lessens inhibitions, enabling the adolescent to focus less on being socially incompetent and facing possible rejection. Alcohol use also enables the adolescent to blame social awkwardness on his or her drinking. However, alcohol use leaves the adolescent less able to make complex decisions regarding sexual behavior.

3. **Reasons for drinking**

   - Curiosity
   - Peer conformity
   - Enjoyment
   - Escape
   - Parental encouragement to take first drink to celebrate a special occasion

**PROBLEM DRINKING AMONG ADOLESCENTS**

Problem drinking has been defined as having been drunk six or more times in the past year or acknowledging problems in at least three of the following areas because of drinking:

1. Trouble with a teacher or principal
2. Difficulties with friends
3. Driving after drinking
4. Criticism by dates
5. Trouble with the police

**Incidence of Adverse Consequences of Alcohol Use**

Nationally in the year 2000, 14% of 8th graders and 30% of 12th graders were classified as heavy drinkers (five or more drinks in a row during the previous 2 weeks) (Johnston, 2000). Adolescents may have little insight into the significance of their excessive alcohol intake. A study of 3,395 Arkansas middle school students showed that 13% (455) were heavy drinkers, but only 16% (65) of these youth acknowledged having an alcohol use problem. These statistics did not include school dropouts, and there is evidence that dropouts use alcohol more heavily than their counterparts who have stayed in school. Problem drinking can seriously interfere with successful completion of the developmental tasks of adolescence, resulting in a maturation arrest.

Harrison and Luxenberg (1995) reported on alcohol and drug use among Minnesota adolescents. They found a continued trend in the proportion of students who reported at least three adverse consequences of alcohol and drug use, including 1% of 6th graders, 7% of 9th graders, and 16% of 12th graders. Alcohol was the primary substance of abuse among students. The most commonly reported consequences included tolerance, blackouts, violence, and school or job absence/ism. The problem users were 2 to 7 times more likely than comparable students with a lesser or no drug history to report parental alcohol or other drug problems, physical abuse, and sexual abuse. They were also 2 to 15 times more likely to have low self-esteem and emotional distress, to exhibit antisocial behavior, and to have made suicide attempts.

**Binge Drinking (Heavy Drinkers)**

Binge drinking is defined as having consumed five or more consecutive drinks during the previous 2 weeks. The 2000 high school senior survey data indicated that 30% of 12th graders are binge drinkers. Figure 70.2 graphically depicts the trends in binge drinking, disapproval of binge drinking, and perceived risk of binge drinking between 1976 and 2000. It appears that disapproval and perceived risks vary inversely with rate of binge drinking. Wechsler et al. (2000), in a national survey of 14,000 college students, reported that 44% were binge drinkers; almost one fifth of the students were frequent binge drinkers. Although this was the same rate this group found in 1993, the rates of both abstention and frequent binge drinking had increased significantly since then. In 1999, 19% were abstainers and 23% were frequent binge drinkers. Other studies have also demonstrated high levels of college binge drinking. In this study of college students, binge drinkers, and particularly frequent binge drinkers, were more likely than other students to experience alcohol-related problems. Almost half (47%) of the frequent binge drinkers had
experienced five or more different drinking-related problems, such as sustaining injuries and engaging in unplanned sex, since the beginning of the school year. This group of drinkers were three times as likely as nonbinge drinkers to engage in unplanned sexual activity, six times as likely to drive after consuming large amounts of alcohol, and twice as likely to ride with an intoxicated driver. Male bingers were four times as likely to be involved in arguments or fights.


DIAGNOSIS

The medical practitioner must be acutely aware of the differing patterns of use manifested in adolescence to be able to formulate accurate diagnostic impressions and thereby use therapeutic interventions with the greatest likelihood of improving outcome. Alcoholism and problem drinking during adolescence can have similar manifestations and consequences. Problem drinking can develop as an attempt to escape the psychic distress resulting from a distinct primary psychiatric disorder such as major depression. It may result in acting out in response to unique psychodynamic circumstances or an evolving personality disorder. In these circumstances, the use usually subsides if the primary disorder is properly identified and treated. However, if the adolescent does in fact have alcoholism, attempts to treat the secondary psychiatric manifestations will do little or nothing to prevent the evolution of this progressive disorder. Because the manifestations of alcoholism in adolescence may be only very subtly distinguished from those of problem drinking, it is exceedingly important to have a clear understanding of the defining features of the diagnosis of alcoholism.

Alcoholism is a primary, chronic disease with genetic, psychosocial, and environmental factors influencing its development and manifestations.

Characteristics of Alcoholism

1. The disease is often progressive and may be fatal.
2. The individual has impaired control over drinking, progressive preoccupation with alcohol use despite significant adverse consequences, and distortions in thinking, most notably denial.
3. Adverse consequences include impairments in work or school functioning, negative influences on interpersonal relationships, and legal or health-status ramifications.
4. A family history of alcoholism is present in the majority of cases.
5. Research suggests that genetics is a major determinant in the risk of alcoholism. The biological features of these genetic determinants create an environment in the dopaminergic mesolimbic reward systems that may predispose a person to progressive use of alcohol and, in addition, may facilitate potent biological reinforcement by substances other than alcohol that also stimulate this region of the brain. Cocaine and amphetamines are two such compounds with a great potential for dependency. Similarly, there appear to be unique elements of the endorphin system in the alcoholic brain that may result in a predisposition to opiate dependency. Although alcoholism is not the only route to dependency on these substances, experimentation with these drugs by an adolescent with suspected alcoholism suggests a more treacherous clinical circumstance and a need for immediate intervention by the health care provider.

The biopsychosocial consequences of drug use during adolescence are often the same, whether or not addictions are present. However, the natural history of the clinical situation and the effectiveness of specific treatments are clearly a function of the specificity of the diagnostic circumstances.

Further confounding diagnostic accuracy is the fact that adolescents who use large amounts of alcohol generally deceive the physicians with whom they come in contact. Because of the teen’s (and family’s) denial, the physician often does not recognize the alcohol dependence. The serious medical illnesses and somatic complaints associated with long-term adult drug or alcohol use are usually not available as clues when one is assessing the adolescent. Therefore, the physician is largely dependent on the history to recognize and diagnose adolescent alcohol abuse.

Behavioral Changes

The following behavioral changes (Table 70.2) can arouse the suspicion of alcohol or other drug abuse (but none of them is an absolute indicator of excessive drinking):

TABLE 70.2. Developing signs of alcoholism in teenagers

<table>
<thead>
<tr>
<th>Signs of Alcoholic Abuse in Teenagers</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Changes in activity, such as loss of interest in school, play, home, or work</td>
</tr>
<tr>
<td>2. Changes in sleeping patterns</td>
</tr>
<tr>
<td>3. Changes in eating patterns</td>
</tr>
<tr>
<td>4. Changes in personality: May be reflected in mood changes, fighting with friends and family members, or truancy</td>
</tr>
<tr>
<td>5. Manifestations of depression, such as poor attention span, difficulty concentrating, lack of interest, and boredom</td>
</tr>
<tr>
<td>6. Trouble with the law enforcement system</td>
</tr>
<tr>
<td>7. Multiple or frequent accident-related injuries</td>
</tr>
<tr>
<td>8. School failure</td>
</tr>
<tr>
<td>9. Blackouts</td>
</tr>
</tbody>
</table>
Screening Instruments

Determining the extent of alcohol abuse and diagnosing alcoholism in the adolescent is crucial. The HEADSS psychosocial profile, as outlined in Chapter 3, is a helpful interview technique for eliciting a history of substance abuse. Several screening devices are also available to help make this diagnosis. The Michigan Alcoholism Screening Test (MAST) (Fig. 70.3) is the most widely used screening test. A shorter instrument is the CAGE questionnaire (Fig. 70.4). Other available instruments include:

1. Adolescent Alcohol Involvement Scale (AAIS)
2. Drinking Analysis Questionnaire (DAQ)
3. Adolescent Alcohol Abuse Questionnaire
4. MacAndrew Alcoholism Scale
5. Addiction Severity Index (ASI)
6. Severity of Alcohol Dependence Questionnaire (SADQ)
7. Perceived Benefit of Drinking Scale

Many of these screening instruments are reviewed in the publication by the National Institute on Alcohol Abuse and Alcoholism (NIAAA), *Assessing Alcohol Problems* (NIAAA, 1995). A family history of alcoholism or addiction also places the adolescent at high risk for abuse of an addictive substance and subsequent addiction, for the reasons described earlier. The Children of Alcoholics Screening Test (CAST) may help to identify the adolescent child of an alcoholic or addict and may give reason for increased suspicion that the adolescent has or may develop an alcohol or other drug problem (Dinning and Dark, 1989).

Werner et al. (1994) examined several scales and variables in an attempt to predict problem drinking among female college freshman. The CAGE questions, the Perceived Benefit of Drinking Scale, the student's tobacco use, the student's best friend's drinking pattern, and the age at which the student first started drinking showed some potential, as a group, to constitute a clinically useful screening measure for predicting subsequent problem drinking. Knight et al. (2000) reviewed the reliability of short substance abuse screening tests and found the Simple Screening Instrument for Alcohol and Other Drug Abuse (SSIAOD) had good internal consistency and test-retest reliability.

Fiellin et al. (2000) reviewed performance characteristics of screening methods for alcohol problems through 38 studies conducted between 1966 and 1998. Overall, the Alcohol Use Disorders Identification Test (AUDIT) was most effective in identifying subjects with at-risk, hazardous, or harmful drinking (sensitivity, 51% to 97%; specificity, 78% to 96%), although the CAGE questions proved better for discovering alcohol abuse and dependence (sensitivity, 43% to 94%; specificity, 70% to 97%). The authors concluded that these two screening instruments consistently performed better than other methods. However, these tests were not specifically examined in adolescents.

CONSEQUENCES OF HEAVY DRINKING

The following may result from the intake of large amounts of alcohol at a single setting:

1. Acute intoxication
2. Acute gastritis
3. Acute pancreatitis
4. Decrease in sexual functioning
5. Blackouts (amnesia)
6. Motor vehicle accidents: Blood alcohol concentrations lower than 0.05% are considered "legally safe" for driving and those of 0.08% to 0.15% are considered "legally intoxicated" in some states.
7. Nonautomotive accidents and trauma
8. Coma and death

Alcohol use can also interfere with the treatment of chronic medical conditions, such as diabetes mellitus and seizure disorders. Furthermore, it can interfere with medications that the adolescent may be taking.

Fetal Alcohol Syndrome

Fetal alcohol syndrome is the most common cause of teratogenic mental retardation, and it is also the most preventable. There is no known safe level of alcohol use during pregnancy. Alcohol readily crosses the placenta and can result in the fetal alcohol syndrome, which is characterized by the following:

1. Abnormal facies: Microcephaly; short, upturned nose; thin upper lip; short palpebral fissures; and hypoplastic maxilla
2. Cardiac abnormalities: Especially atrial and ventricular septal defects
3. Renal abnormalities: Deformed kidneys
4. Genital abnormalities: Hypospadias and labial hypoplasia
5. Skeletal abnormalities: Contractures of the extremities; pectus excavatum
6. Hirautism
7. CNS abnormalities: Electroencephalographic changes, mental retardation
8. Abnormal size: Small for gestational age
9. Behavior: Irritability in infancy; hyperactivity in childhood

TREATMENT

The American Medical Association Guidelines for Adolescent Preventive Services (GAPS), Bright Futures, and the American Academy of Pediatrics Policy Statement on Substance Abuse all recommend that every adolescent be screened during history taking for alcohol, tobacco, and other drug abuse (ATODA) as part of routine care. If the screen is positive for alcohol, then the clinician must decide what to do next. Research shows that brief interventions in physicians' offices can be effective in assisting patients in changing their behavior.

Stages of Change

In 1979, Prochaska identified common themes in therapies used to promote behavioral change and found that individuals who make changes on their own also exhibited similar processes. He and his colleagues developed a transtheoretical model which entailed (a) a cyclical pattern of movement through six specific stages of change; (b) a common set of processes of change; and (c) a systematic integration of the stages and processes of change. They designated six stages of change: precontemplation, contemplation, determination, action, maintenance, and relapse (Table 70.3).

| TABLE 70.3. Stages of change and intervention tasks |

Motivational Enhancement Therapy

Motivational Enhancement Therapy is a systemic intervention approach for evoking change in behavior (Miller et al., 1991). It is based on the principles of motivational psychology and is designed to produce rapid, internally motivated change. This technique can be used to assist an adolescent in increasing his or her motivation to alter a behavior. This treatment strategy is not a roadmap for the patient to follow but a method for mobilizing the patient's own resources.

Five Principles of Motivational Enhancement Therapy

1. Develop discrepancy.
2. Avoid argumentation.
3. Roll with resistance.
4. Express empathy.
5. Support self-efficacy.

Tasks for each of these principles include the following.

1. Develop discrepancy.
   a. Be aware of consequences.
   b. Balance risks and benefits.
   c. Assist the patient in contrasting current behavior with future goals.
   d. Motivation for change occurs when people perceive a discrepancy between where they are and where they want to be.
   e. Have the patient develop reasons for change.
2. Avoid argumentation.
   a. Arguments signal loss of control and are counterproductive.
   b. Argumentation breeds defensiveness and resistance.
   c. Denial is reflection of confrontation.
   d. Resistance means it isn't working; drop it and try a new tack.
   e. The patient, not the clinician, voices the arguments for change.
3. Roll with resistance.
   a. Help the patient problem-solve.
   b. Investigate and encourage new perspectives and approaches.
   c. Keep the discussion going.
   d. Solutions are to be from the patient, not from the physician.
4. Express empathy.
   a. Show respect for the patient.
   b. Acceptance facilitates change.
   c. Reflective listening is key.
   d. Listen rather than tell.
   e. Ambivalence is normal and to be expected.
   f. Blend support with knowledge.
5. Support self-efficacy.
   a. Belief in the possibility of change is an important motivator.
   b. The patient is responsible for choosing and carrying out personal change.

Components of Successful Treatment of Adolescent Alcohol Abuse and Dependence

1. Accurate diagnosis and assessment: Treatment of any primary psychiatric disturbances that may be identified. If the patient meets criteria for a diagnosis of alcoholism or addiction, then proceed with interventions listed later. If the diagnosis is uncertain, always proceed with these suggestions. Reassessment of psychiatric symptoms should be undertaken after a minimum of 30 days. Very often, prominent psychiatric symptoms remit spontaneously with abstinence.
2. Disease concept of recovery: Viewing alcoholism as a primary progressive disease implies a long-term, ongoing recovery process that requires abstinence and learning to live without alcohol and drugs. The recovery process also helps to expose and deal with accumulated feelings of guilt and shame, while rebuilding coping skills and self-esteem.
3. Positive alternatives: Treatment requires that the adolescent learn substitute activities that provide pleasure and reward to replace the "highs" of drug use. These activities should be realistic and attainable.

4. Support systems: Sober peer-support systems are essential for recovery. Alcoholics Anonymous, Cocaine Anonymous, and Narcotics Anonymous provide 12-step programs that are useful for recovering adolescents.

5. Family involvement: Alcoholism is a family illness. The substance abuse of one member of the family system affects the other members. Dysfunctional coping trends are established. Recovery and treatment should help establish a new, healthier equilibrium. Family members should be encouraged to attend Al-Anon or Alateen, which are 12-step self-help groups for family members. Referrals: The clinician should also be able to provide appropriate referrals for substance abuse services in the community.

RESOURCES

Organizations
Al-Anon/Alateen Family Group Headquarters, Inc., P.O. Box 862 Midtown Station, New York, NY 10018-0862, telephone 1-212-302-7240 or 1-800-334-2666 (U.S.) or 1-800-443-4525 (Canada).

Boys and Girls Clubs of America, 771 First Avenue, New York, NY 10017, telephone 1-212-351-5900.

Friday Night Live, California Friday Night Life Partnership, 2637 W. Burrel, P.O. Box 5091, Visalia, CA 93278-5091, telephone 1-559-733-6496, fax 1-559-737-4231, E-mail: mjs@tsce.k12.ca.us.

National Association for Children of Alcoholics, 11426 Rockville Pike, Suite 100, Rockville, MD 20852, telephone 1-301-468-2600 or 1-800-729-6686.

National Association of Teen Institutes, 8790 Manchester Road, St. Louis, MO 63144, telephone 1-314-962-3456.

National Clearinghouse for Alcohol and Drug Information, P.O. Box 2345, Rockville, MD 20852, telephone 1-301-468-2600 or 1-800-729-6686.


National Council on Alcoholism and Drug Dependence, 12 West 21st Street, 7th Floor, New York NY 10010, telephone 1-800-622-2255.

National Families in Action, 2296 Henderson Mill Road, Suite 300, Atlanta, GA 30345, telephone 1-404-934-6364.

Parent Resources Institute on Drug Education (PRIDE), Suite 126 Woodruff Building, 100 Edgewood Avenue NE, Atlanta, GA 30303, 1-231-652-4400.


Publications and Other Resource Materials

Resources for Teens Contact SAMHSA's National Clearinghouse for Alcohol and Drug Information at 1-800-729-6686 or http://www.samhsa.gov/centers/clearinghouse/clearinghouses.html for the publications and videotapes listed here.

Publications
Alcohol Alert No. 37: Youth Drinking—Risk Factors and Consequences
Alcohol Impairment Chart (for both men and women)
Alcohol, Tobacco, and Other Drugs and the College Experience (ML003)
Alcoholism Tends to Run in Families (PH318)
Children of Alcoholics: Important Facts (NACoA)
Drugs of Abuse: Alcohol
A Guide for Teens: Does Your Friend Have an Alcohol or Other Drug Problem? (PHD688)
How To Cut Down on Your Drinking
Straight Facts about Alcohol
Sex Under the Influence of Alcohol and Other Drugs (ML005)

Resources for Families Contact SAMHSA's National Clearinghouse for Alcohol and Drug Information at 1-800-729-6686 or http://www.samhsa.gov/centers/clearinghouse/clearinghouses.html for the publications and videotapes listed here.

Publications
If Someone Close Has a Problem with Alcohol or Other Drugs (PH317)
TAP 6: Empowering Families, Helping Adolescents: Family-Centered Treatment of Adolescents with Alcohol, Drug Abuse, and Mental Health Problems (BKD81)
Parents, Guardians and Caregivers (MS503)
Alcohol Alert No. 37: Youth Drinking—Risk Factors and Consequences (PH376)
Alcoholism Tends to Run in Families (PH318)
Children of Alcoholics: Important Facts

Videocassettes
Poor Jennifer, She's Always Losing Her Hat (VHS65). Designed to educate adults about the issues faced by children of alcoholics. Cost recovery fee, $12.50.

Resources for Professionals Contact SAMHSA's National Clearinghouse for Alcohol and Drug Information at 800-729-6686 or http://www.samhsa.gov/centers/clearinghouse/clearinghouses.html for the publications and videotapes listed here.

Publications
TIP 3: Screening and Assessment of Alcohol- and Other Drug-Abusing Adolescents (BKD108)
TIP 4: Guidelines for the Treatment of Alcohol- and Other Drug-Abusing Adolescents (BKD109)
TIP 21: Combining Alcohol and Other Drug Abuse Treatment with Diversion for Juveniles in the Justice System (BKD169)
TIP 28: Naltrexone and Alcoholism Treatment (BKD268)
TIP 11: Screening and Assessing Adolescents for Substance Abuse Disorders (BKD306)
TAP 1: Approaches in the Treatment of Adolescents with Emotional and Substance Abuse Problems (PHD580)
The Physician's Guide to Helping Patients with Alcohol Problems. NIAAA, 1995 (PHD380)
Changing Lives: Programs that Make a Difference for Youth at High Risk. Center for Substance Abuse Prevention (CSAP), 1995 (PHD714)
The Young and Restless: Generation X and Alcohol Policy (RPO993)
Children at Risk Because of Parental Substance Abuse. AOS Working Paper. (RPO965)
Prevention Pipeline: Focus on Youth Prevention—Science and Practice in Action (July/August, 1997). Prevention Pipeline is an award winning bimonthly magazine
References and Additional Readings


Decker MD, Gralitzer PL, Schaffner W. Reduction in motor vehicle fatalities associated with an increase in the minimum drinking age. JAMA 1988;260:3604.


Cigarette smoking is the chief, single avoidable cause of death in our society and the most important public health issue of our time.

—C. Everett Koop, M.D.

This statement made by Dr. Koop when he was United States Surgeon General (1981–1989) remains equally true at the beginning of the new millennium. The World Health Organization (WHO) estimates that by the year 2025, some 500 million people worldwide will have died from a tobacco-related disease. In the United States, more than 450,000 deaths each year—the equivalent of three 747 fatal airline crashes per day—can be attributed to cigarette smoking. This figure is almost triple the annual number of deaths due to illegal drugs, homicide, alcohol, acquired immunodeficiency syndrome, suicide, and motor vehicle accidents combined (Fig. 71.1).

The financial cost for smoking-related health care per year in the United States is approximately $70 billion, or approximately 10% of total medical expenditures. Additionally, cigarettes are the leading cause of the many hundreds of fire-related deaths and many thousands of fire-related injuries in this country each year, costing approximately $7 billion annually. More than 80% of all cigarette smokers start before the age of 18 years; almost 5% of youth first began smoking by 8 years of age, and another approximately 20% before their 13th birthday. Estimates derived from smoking rates of the mid-1990s indicate that about 5 million persons age 17 years of age or younger in 1995 will die prematurely from a smoking-related illness. Therefore, tobacco use can also be considered a pediatric disease. Clinicians can play an important role in preventing cigarette use by their patients and helping their patients who are already smoking to stop.


PREVALENCE

Use Among Adolescents

Tobacco use by adolescents remains a serious problem, with approximately 3,000 American teenagers becoming regular smokers each day. Despite all the new information concerning the negative health consequences of tobacco use, the addictive properties of nicotine, and the misinformation of the tobacco industry, use of tobacco products by adolescents increased significantly in the early and middle 1990s, although they did start to decline in the few years after that (Fig. 71.2 and Fig. 71.3). In addition, cigarette smoking by young adults (age 18 to 24 years) increased by 16% between 1995 and 1997. This young adult population, which represents the youngest legal targets of tobacco industry marketing, may also be initiating tobacco use in larger numbers. This trend, if continued, threatens to reverse the decline in smoking prevalence among U.S. adults that has occurred during the past half century.

FIG. 71.2. Use of tobacco products by adolescents, percentage who have smoked in past 30 days.

FIG. 71.3. Use of tobacco products by adolescents, percentage who have smoked in past 7 days.
Prevalence data are gathered from a number of sources; three major sources are the following:

1. National Youth Tobacco Survey (sponsored by the American Legacy Foundation and the Centers for Disease Control and Prevention Foundation); information available at http://www.cdc.gov/tobacco/nyts2000.htm
2. Youth Risk Behavior Survey (sponsored by the Centers for Disease Control and Prevention [CDC]); information available at http://www.cdc.gov/nccdphp/dash/yrbs/
3. Monitoring the Future (sponsored by the University of Michigan Institute for Social Research and the National Institute of Drug Abuse); information available at http://www.monitoringthefuture.org/

The latest data available from these three sources are discussed here. All three use school-based samples, and the rates of tobacco use shown would probably be even greater if high school dropouts had been included in the study samples.

The 2000 Monitoring the Future data revealed that about 15% of 8th graders, 24% of 10th graders, and 31% of 12th graders reported current smoking (i.e., smoking one or more cigarettes during the previous 30 days). Furthermore, 7% of 8th graders, 14% of 10th graders, and 21% of 12th graders were daily smokers in 2000. The 1999 Youth Risk Behavior Survey data revealed the rates of lifetime daily cigarette use (i.e., ever smoked at least one cigarette every day for 30 days), to be 18.5%, 27.0%, 25.7%, and 31.5% in grades 9, 10, 11, and 12, respectively. Smoking has increased among white, black, and Hispanic teens. Smoking rates are now similar for adolescent girls and adolescent boys in the 12th grade. The 1999 National Youth Tobacco Survey data revealed that 15.4% of middle school students and 29.1% of high school students were current smokers, smoking at least six cigarettes per day on each day that they smoked cigarettes. The 2000 National Youth Tobacco Survey data revealed that students of Asian descent had the lowest smoking rates in middle school (5.5%) but the highest smoking rates in 12th grade (33%).

A fourth source is the National Household Survey on Drug Abuse (sponsored by the Substance Abuse and Mental Health Sciences Administration), a home-based survey on alcohol and other drugs available at http://www.samhsa.gov/oas/nhsda.htm#NHSDAinfo.

### Use Among College Students

Smoking also continues to be a problem on college campuses. Tobacco use among college students increased significantly during the 1990s and 2000; in the year 2000, 32.9% of college students currently use a tobacco product; with a gender breakdown of 37.9% males and 29.7% females. For both male and female college students, cigarettes are the most commonly used tobacco product, followed by cigars, smokeless tobacco, and pipes. Whites have the highest use of tobacco products, followed by Hispanics, Asians, and African-Americans. College students who use tobacco are more likely to be single, white, and engaged in other risky behaviors involving substance use and sexual activity. They are also more likely to value social life over educational achievement, athletic participation, or religion.

Table 71.1 shows current use of tobacco products from the 1999 National Youth Tobacco Survey. Note that use of a variety of tobacco products was studied: cigarettes, smokeless tobacco (snuff and chewing tobacco), cigars, pipes, bidis, and kreteks. As can be seen from this table, adolescents used all of these products. Bidis, produced in India and other Southeast Asian countries, are hand-rolled cigarettes consisting of tobacco wrapped in a tendu or temburi leaf. Bidis are available in various flavors such as chocolate, cherry, and mango. Kreteks are cigarettes that contain 30% to 40% cut cloves; they are produced in Indonesia. Both bidis and kreteks are relatively new to the American market and are promoted as “safe” alternatives to cigarettes, as are “clove cigarettes.” However, these products contain tobacco and may have even higher levels of nicotine, tar, and carbon monoxide than regular tobacco products.

### Table 71.1. Percentage of middle school and high school students who were current users of any tobacco product, cigarettes, cigars, smokeless tobacco, pipes, bidis, or kreteks, by sex and race/ethnicity—National Youth Tobacco Survey, 1999

Table 71.2, Table 71.3, and Table 71.4 are from the 1999 Youth Risk Behavior Survey. Note that the rates of current frequent (primarily daily) cigarette use and likely addiction (10 or more cigarettes smoked a day) were studied. Half of current smokers in middle school and high school reported that they want to quit smoking. However, one fourth of middle and high school students who had never smoked cigarettes stated that they might try smoking in the next year. This study also revealed that exposure to environmental tobacco smoke (second-hand smoke) is very high: 9 of every 10 current smokers and 1 of every 2 students who had never smoked were exposed to environmental tobacco smoke (ETS) in the previous week. The authors also noted that even though the purchase of cigarettes by minors is illegal, the majority of these adolescent smokers were able to buy cigarettes without proof of age.
TABLE 71.2. Percentage of high school students who used tobacco, by sex, race/ethnicity, and grade—United States, Youth Risk Behavior Survey, 1999

TABLE 71.3. Percentage of high school students who used smokeless tobacco, smoked cigars, and used any tobacco product, by sex, race/ethnicity, and grade—United States, Youth Risk Behavior Survey, 1999

TABLE 71.4. Percentage of high school students aged <18 years who were current cigarette smokers and usually obtained their own cigarettes by purchasing them in a store or gas station and who purchased cigarettes without being asked to show proof of age, by sex, race/ethnicity, and grade—United States, Youth Risk Behavior Survey, 1999

WHY DO ADOLESCENTS USE TOBACCO?

Adolescent Development

Tobacco use in adolescence can be understood in terms of biopsychosocial development during adolescence. Major developmental tasks during adolescence include establishing independence and autonomy, developing meaningful peer relations, negotiating the changes associated with physical development and puberty, and establishing a coherent self-identity. Cigarette smoking may, for example, be viewed as a means of attaining maturity and autonomy, since smoking is a legal adult behavior. Smoking may also be viewed as a social event and a means of fitting in with a peer group. Research has shown that peer influence (e.g., smoking status of best friends) is the most significant and consistent predictor of adolescent smoking. The price of tobacco products also correlates with adolescent tobacco use: a significant price increase leads to a decrease in adolescent tobacco use.

Psychosocial Factors

Psychosocial factors related to smoking initiation for both genders include low educational aspirations or attainment; low self-esteem, low self-image, or depression; risk-taking; minimizing perceived hazards of smoking; and favorable attitudes toward smoking or smokers. Other variables associated with adolescent smoking include parental or sibling smoking, perceived support for smoking by parents or peers, and having lower socioeconomic status or parental educational attainment. There are also gender-specific factors associated with smoking. For example, adolescent girl smokers are more likely to be socially skilled, outgoing, and self-confident. In contrast, adolescent boy smokers may be more insecure in social settings. Teenage girls may use cigarette smoking as a method of weight control and maintenance of a thin appearance. Teenage boys may smoke for a sense of adventure and recreation as well as daring. Youth who identify themselves as gay, lesbian, or bisexual smoke at rates more than 50% higher than those of their straight counterparts, and they are four times more likely to use smokeless tobacco products.

Advertising

Tobacco industry advertising plays an important role in inducing adolescents to smoke. One study found that 86% of 10th graders and 88% of 12th graders who purchase their own cigarettes bought one of the three most heavily advertised brands: Marlboro, Camel, and Newport. In comparison, less than 50% of adults buy these same three brands. Until 1999, when parts of the master settlement agreement between the tobacco companies and the states' attorneys general went into effect, cigarettes were the most heavily advertised product in the outdoor (billboard) media, including the newest and growing form of outdoor advertising: the neighborhood-based bus-stop shelter illuminated billboard. The tobacco industry is now focusing on print media such as magazines with a youth or young-adult-focus, electronic media, and movies, so adolescents are constantly exposed to the messages promoted by these advertisers. The tobacco industry is also now sponsoring concerts in bars and clubs, specifically targeting young adults of legal age. The associated messages virtually ignore all health concerns and use themes that appeal to young people. In the messages, use of cigarettes is associated with healthy activities involving adventure and recreation, independence, sexual attractiveness, professional success, confidence in social settings, and weight control and physical appearance. Advertising tobacco in the context of other businesses and services (e.g., household detergents, movies, clothing) helps legitimize tobacco use. The internal documents of tobacco companies demonstrate targeting of youth, women, and minorities. Promotional offerings and "contests," as well as offers of "free" items (e.g., hats, jackets) that usually are redeemable after sending in a specified number of empty cigarette packs, are also inducements to youth to start and continue smoking. In March 1997, the Liggett Tobacco Company, in a precedent-setting legal case, submitted documents to the Arizona Attorney General admitting that (a) nicotine is addictive, (b) cigarettes cause cancer, and (c) the tobacco industry targets children and teenagers.
NICOTINE ADDICTION AND HEALTH CONSEQUENCES

Addiction

In addition to being a potent pesticide, nicotine is one of the most addictive substances known. Tobacco use by adolescents, which may have started primarily for psychosocial reasons, may over time become a serious drug addiction. Initial symptoms of nicotine dependence occur in some teens within days to weeks after onset of use.

Modes of Action

Nicotine seems to function as a positive reinforcer through its actions on nicotinic acetylcholine receptors in the mesocorticolimbic dopamine pathway. Stimulation of brain dopamine systems is of great importance for the rewarding and dependence-producing properties of nicotine. Abstinence from nicotine is associated with depletion of dopamine and other neurotransmitters, which may cause numerous withdrawal symptoms including anxiety, irritability, and cravings (Fig. 71.4). Relapse rates for persons attempting to quit use of nicotine are comparable to those for quitting heroin (Fig. 71.5).


**FIG. 71.5.** Relapse over time for heroin use, smoking, and alcohol abuse. (From National Center for Chronic Disease Prevention and Health Promotion, Office of Smoking and Health. The health consequences of smoking: nicotine addiction. A report of the Surgeon General. Washington, DC: U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, 1988.)

**Pharmacology**

- Each cigarette contains 6 to 11 mg of nicotine, and smokers absorb 1 to 3 mg of nicotine per cigarette.
- Each cigarette contains 10 to 12 doses (puffs) of nicotine; someone who smokes half a pack per day therefore inhales approximately 200 doses of the drug daily.
- One pack per day equals 20 to 40 mg of nicotine absorbed per day.
- Each dose of the drug acts on the user within seconds after being inhaled.

Plasma concentrations of nicotine decline in a biphasic manner. Typically the initial half-life is 2 to 3 minutes, and the terminal half-life is 30 to 120 minutes. Most nicotine is metabolized in the liver to cotinine and nicotine-1'-oxide. Cotinine has a plasma half-life that varies from approximately 10 to 40 hours. Nicotine and its metabolites are excreted by the kidneys; about 10% to 20% of the nicotine is eliminated unchanged in the urine.

**Effects of Other Compounds in Cigarettes**

Besides nicotine, cigarettes contain tar, a toxic compound. Cigarettes usually contain literally thousands of other chemicals, many poisonous and cancer causing, including ammonia, cadmium, carbon monoxide, cyanide, formaldehyde, nitrosamines, and polynuclear aromatic hydrocarbons. The tobacco industry is actively fighting disclosure of the chemical ingredients in cigarettes, including pesticides and flavor additives, arguing that they are "trade secrets."

**Systemic Effects of Tobacco**

Use of tobacco products can adversely affect virtually every organ system in the body.

1. Cardiovascular: Smokers have significantly higher rates of ischemic heart disease, cerebrovascular disease, and peripheral vascular disease.
2. Cancer: Numerous cancers are increased in smokers including lung, head and neck, esophageal, gastric, colorectal, bladder, renal, prostate, and cervical cancers. Approximately 85% of lung cancers and 30% of all cancer deaths are attributable to smoking.
3. Endocrine: Hormone-related disorders, which are caused by an antiestrogenic effect of nicotine, are increased; these include menstrual disorders, early menopause, and decreased bone mineral density. The most common cause of erectile dysfunction (i.e., impotence) is tobacco use.
4. Pulmonary: Smokers have higher rates of chronic obstructive pulmonary disease (COPD). Small airway disease is present in smokers even before evidence of chronic lung disease is demonstrable. Approximately 80% to 90% of deaths caused by COPD are in smokers.
5. Gastrointestinal: Rates of gastroesophageal reflux and peptic ulcer disease are increased.
6. Dermatologic: There is evidence of premature wrinkling of the skin in smokers.
7. Ophthalmologic: The rate of macular degeneration is increased, and it occurs at a younger age.
8. Immune system: There is evidence of adverse effects on natural killer cells and other immune modulators.
9. Pregnancy complications: Women who smoke during pregnancy have significantly higher rates of low-birth-weight babies. Intrauterine growth retardation and small-for-gestational-age babies are also more common. Other pregnancy-related complications in smokers include higher rates of spontaneous abortion, ectopic pregnancy, and premature rupture of membranes. Sudden infant death syndrome (SIDS) is more common in babies whose mothers smoked during pregnancy.

Smokeless Tobacco
Smokeless tobacco users, besides suffering from many of the same systemic adverse effects as smokers due to nicotine, have higher rates of various cancers, including oral, prostate, pancreas, and cervical cancers. Smokeless tobacco use is associated with numerous dental, periodontal, and oral soft tissue problems, including gingival recession, periodontal attachment loss, tooth staining, halitosis, and leukoplakia. Inflammatory bowel disease is more common in smokeless tobacco users.

**Environment Tobacco Smoke**

Environmental tobacco smoke has numerous adverse health effects (Table 71.5). Children exposed to ETS may have development of and/or worsening of asthma, higher rates of lower respiratory tract infections (e.g., bronchitis, pneumonia), and higher rates of otitis media. Heart disease, lung cancer, and nasal sinus cancer are also more common with exposure to ETS, as are pulmonary hypertension of the newborn and postanesthesia pulmonary complications.

**TABLE 71.5. Health effects associated with exposure to environmental tobacco smoke (ETS)**

<table>
<thead>
<tr>
<th>Health Effect</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Development of and/or worsening of asthma</td>
<td>Higher rates of lower respiratory tract infections (e.g., bronchitis, pneumonia)</td>
</tr>
<tr>
<td>More common of heart disease, lung cancer, and nasal sinus cancer</td>
<td>Higher rates of otitis media</td>
</tr>
<tr>
<td>Pulmonary hypertension of the newborn</td>
<td>Postanesthesia pulmonary complications</td>
</tr>
</tbody>
</table>

**PREVENTION AND TREATMENT**

**Brief Practitioner Interventions**

Although smoking onset and maintenance by adolescents are complex psychosocial and biological phenomena, as noted earlier, research has demonstrated that 3-minute discussions of tobacco use (brief interventions) can have a significant impact on smoking prevention or smoking cessation. Busy practitioners can still address the smoking issue in a meaningful way in a short period of time. There are two types of 3-minute interventions: those directed toward patients (Fig. 71.6) and those directed toward parents (Fig. 71.7). Strong and direct language is purposefully used, and these kinds of messages have been found to be very helpful. Given the medical problems associated with passive or second-hand smoke, and given the important role modeling of parents to their teens, pediatricians must also provide smoking cessation referrals and/or interventions for the parents of their patients. It is much more likely for an adolescent to start smoking, and much more difficult for an adolescent to successfully quit smoking, if he or she is living with siblings or parents who smoke. Therefore siblings and parents need to be encouraged to quit too. Parents should be encouraged to maintain smoke-free homes.

**FIG. 71.6. Patient 3-minute pointers. (Adapted from Ammerman SD. Helping kids kick butts. Contemporary Pediatrics 1998;15[2]:64.)**

**FIG. 71.7. Parent 3-minute pointers. (Adapted from Ammerman SD. Helping kids kick butts. Contemporary Pediatrics 1998;15[2]:64.)**

**Intensive Smoking Cessation Interventions**

More intensive smoking cessation interventions may be more effective in helping addicted smokers quit. These more intensive interventions may involve a medical clinician to discuss health issues and prescribe pharmacotherapy and a nonmedical clinician to focus on additional psychosocial or behavioral issues.

**Antismoking Messages**

The antismoking message should be varied according to the smoking status, age, and developmental stage of the patient. Prevention starts with the prenatal visit and continues throughout childhood (as noted earlier, children may start smoking by the age of 8 years) and during the preteen, teen, young adult, and adult years. Anticipatory guidance should always include tobacco use counseling.

1. **Nonsmokers:** Nonsmoking should be praised and the behavior normalized. Urge continuation of nonsmoking: “Keep making smart choices.”

2. **Individuals who are considering starting:** For someone who is considering smoking and who lives in an environment with exposure to smokers (e.g., parents, siblings, friends who smoke), offer praise for nonsmoking to date, healthy alternatives to smoking, and role-playing of methods to gracefully bow out of smoking among peers. For example, the teen may refuse opportunities to smoke by saying, “No thanks, I’m not in the mood right now” or “I feel like I’m getting a sore throat and smoking will make it worse” or “I don’t want to put all those nasty chemicals in my body.”
Patients who smoke: For patients who are smoking, the sooner treatment is begun, the more likely successful quitting will occur. The estimates of quit rates for teen smokers, quitting on their own without help, range from zero to 11%. For someone who is experimenting with tobacco use, immediate quitting should be encouraged and a quit date set. For someone who is regularly using tobacco, quitting should be encouraged. If the patient wants to quit, the clinician can be more assertive and set a quit date. If the patient does not want to quit, the physician must be less assertive but should raise quitting as an important issue, provide motivational literature, and follow up at subsequent visits.

United States Public Health Service Clinical Guidelines

The U.S. Public Health Service originally published guidelines that stressed the five “R’s” for enhancing motivation to quit tobacco use: (a) indicating why quitting is personally Relevant; (b) identifying the Risks of tobacco use; (c) identifying the medical and psychosocial Rewards of quitting; (d) identifying Roadblocks to quitting and how to overcome them; and (e) Repeating the motivational intervention at every clinic visit.

In 2000, the clinical practice guideline for treating tobacco use and dependence was revised. The five “A’s”—Ask, Advise, Assess, Assist, and Arrange—are used for smoking cessation counseling. There are very few published (and even fewer methodologically sound) studies concerning smoking cessation in teens. Therefore these treatment guidelines are based primarily on the adult literature.

1. First, Ask systematically about smoking at each visit, just as vital signs are taken at every visit. Smoking status can change quickly in teenagers, and a previous nonsmoker may be smoking by the time of the next visit—or a regular smoker who did not wish to quit in the past may now wish to quit smoking. Because teens often come in sporadically for health care, the tobacco issue should be raised at every office visit, no matter what the chief complaint. In addition to cigarette use, it is important to inquire about the use of other tobacco products. Teens may use cigars, chewing tobacco, snuff, bidis, or kretek, and they may not realize that these products are harmful. Additionally, adolescents who use tobacco products may also be using alcohol and other drugs. Therefore, an alcohol and other drug use history should be obtained. Concomitant use of tobacco with alcohol or other drugs may make it more difficult for the teen to stop tobacco use without also stopping alcohol or other drug use; this needs to be addressed directly in smoking cessation counseling.

2. Second, strongly Advise all smokers to quit. Advice that is clear and personally relevant is most effective. Physicians are looked on as authoritative figures, even by teens, and giving a consistent cessation message is important.

3. Third, Assess patient willingness to make a quit attempt (as noted earlier).

4. Fourth, Assist the patient in stopping smoking.

   a. Motivational steps: Setting a quit date has been shown to be an important and effective first step in smoking cessation. An actual calendar date should be chosen and agreed upon by the patient and physician. See Fig. 71.8 for an example of a “quit date” form. Once the quit date has been selected (usually 2 to 4 weeks away), the patient can prepare to become a nonsmoker. Preparation to quit smoking has physical, psychological, and emotional components. For example, in getting ready to quit (before the quit date), the patient should keep a journal noting when and why and how much he or she smokes, as well as any routine activities in which smoking plays a part, such as drinking coffee or alcohol. The patient can attempt to change smoking routines by keeping cigarettes in a different place, smoking with the other hand, or smoking only in self-designated areas. The patient should occasionally chew gum or drink a glass of water instead of smoking a cigarette; he or she will notice that the smoking craving usually subsides within a few minutes. Gum, hard candy, sunflower seeds, or toothpicks can be carried around and used as cigarette substitutes. By the quit date, the patient’s environment should be rid of cigarette cues. For example, clothes, the living space, and the inside of the car should all be cleaned to get rid of the tobacco smell. Ashtrays and all cigarettes should be got rid of. The patient should make it a point to find nonsmoking spaces to be in and to stay away from places in which smoking occurs (e.g., bars). Patients need to think of themselves as nonsmokers, and they should literally say to themselves that being a nonsmoker is important. Patients should try to remember the benefits of nonsmoking! Writing down the benefits on a 3 × 5 card that the patient can carry around and look at in tempting situations may be helpful. To maintain the quit effort, patients need to know that withdrawal symptoms are common but transient and that pharmacotherapy is available if necessary. Mild-to-moderate exercise, such as walking or riding a bicycle, can help attenuate withdrawal symptoms. Suggest that the patient start a money jar with the money saved from not buying cigarettes. This will add up quickly, and the patient can reward himself or herself by buying new music, going to the movies, and so on. The patient should actively elicit support from friends and family. Going through the process with a “buddy” who is also willing to quit simultaneously can make the whole cessation process easier and should be encouraged. The clinician should provide self-help materials, such as the “quit tips” listed in Table 71.6.

   b. Pharmacotherapy: Pharmacotherapy includes nicotine replacement products (patch, gum, inhaler, or nasal spray), and bupropion (Zyban). These modalities may be very helpful for addicted smokers. Addiction is usually defined as smoking half a pack of cigarettes or more per day, smoking the first cigarette of the day within 1 hour after awakening, or having had withdrawal symptoms during a previous quit attempt. Nicotine dependence criteria are listed in the American Psychiatric Association’s Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) (Table 71.7). Withdrawal symptoms and cravings may make quitting very difficult and may be mitigated in large part with use of pharmacotherapy. Prescribing instructions for these medications can be found in Table 71.8. Note that nicotine patches and gum are now over-the-counter medications.

FIG. 71.8. A firm quit date is an important step in quitting smoking. (Adapted from Ammerman SD. Helping kids kick butts. Contemporary Pediatrics 1998;15[2]:64.)

TABLE 71.6. Guide for patients: How to stop smoking

<table>
<thead>
<tr>
<th>Step</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Identify smoking routines</td>
</tr>
<tr>
<td>2. Prepare to quit</td>
</tr>
<tr>
<td>3. Set a quit date</td>
</tr>
<tr>
<td>4. Keep a journal</td>
</tr>
<tr>
<td>5. Change smoking routines</td>
</tr>
<tr>
<td>6. Rid environment of cigarette cues</td>
</tr>
<tr>
<td>7. Chew gum or drink water</td>
</tr>
<tr>
<td>8. Avoid temptation</td>
</tr>
<tr>
<td>9. Maintain cessation</td>
</tr>
<tr>
<td>10. Elicit support from friends and family</td>
</tr>
</tbody>
</table>

TABLE 71.7. Nicotine Dependence Criteria

<table>
<thead>
<tr>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking half a pack of cigarettes or more per day</td>
</tr>
<tr>
<td>Smoking the first cigarette of the day within 1 hour after awakening</td>
</tr>
<tr>
<td>Having had withdrawal symptoms during a previous quit attempt</td>
</tr>
</tbody>
</table>

TABLE 71.8. Medications for smoking cessation

<table>
<thead>
<tr>
<th>Medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nicotine patches</td>
</tr>
<tr>
<td>Nicotine gum</td>
</tr>
<tr>
<td>Nicotine inhaler</td>
</tr>
<tr>
<td>Nicotine nasal spray</td>
</tr>
<tr>
<td>Bupropion (Zyban)</td>
</tr>
</tbody>
</table>
TABLE 71.7. DSM-IV Criteria of nicotine withdrawal

<table>
<thead>
<tr>
<th>Symptom</th>
<th>DSM-IV Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Restlessness</td>
<td>Caffeine physical dependence</td>
</tr>
<tr>
<td>2. Irritability and Marked Anger</td>
<td>Caffeine physical dependence</td>
</tr>
<tr>
<td>3. Nausea, Diarrhea, or Vomiting</td>
<td>Caffeine physical dependence</td>
</tr>
<tr>
<td>4. Insomnia</td>
<td>Caffeine physical dependence</td>
</tr>
<tr>
<td>5. Psychomotor agitation</td>
<td>Caffeine physical dependence</td>
</tr>
</tbody>
</table>

TABLE 71.8. Pharmacotherapeutic aids

1. Select a smoking cessation coordinator. This person is in charge of all antismoking efforts and may be anyone who is interested in the project (e.g., receptionist, nurse, aide, doctor). The immediate goal is to create a smoke-free office.
2. Select a date to make the office smoke free. This is the office employees' equivalent of the individual patient's quit date.
3. Post "No Smoking" signs in all office areas. Prominently display smoking cessation materials and information in your waiting and examination rooms.
4. Eliminate all tobacco advertising from your waiting room, either by not subscribing to magazines that carry tobacco advertisements and thereby support the tobacco industry (the Maryland Medicine Society, http://www.smokefreemd.org/, has a list of magazines that do not carry any tobacco ads) or by having the office smoking coordinator write over cigarette ads or place stickers with slogans such as, "Don't fall for this" or "This is a rip-off." Stickers are available for purchase from Doctors Ought to Care () to place on tobacco advertisements in magazines.
5. Have prominent office campaigns to publicize the "Great American Smoke-Out," which is always the Thursday before Thanksgiving, and "World No-Tobacco Day," which is always May 31. These are particularly high-profile public events to encourage smoking cessation.

Billing Issues

Concerning billing issues for follow-up, if smoking cessation per se is not covered, there is almost always a related medical issue that may be billed, such as asthma, bronchitis, cough, pharyngitis, or an upper respiratory infection.

Educational Materials

Educational materials for teens, parents, and physicians are available from a variety of sources either free or for nominal fees. The Web sites listed in this section and at the end of the chapter all offer educational materials and provide hyperlinks to many other tobacco control groups. These include local chapters of the American Cancer Society (http://www.cancer.org/) and the American Lung Association (www.lungusa.org/tobacco); the American Academy of Pediatrics (http://www.aap.org/); the U.S. Department of Health and Human Services (http://www.hhs.gov/topics/smoking.html); the National Cancer Institute (http://www.nci.nih.gov/); and the Agency for Health Care Policy and Research, now called the Agency for Health Care Research and Quality (http://www.ahrq.gov/), which also provides free smoking cessation guidelines for physicians and guides for patients. Finally, the federal government's CDC, in conjunction with the Office on Smoking and Health and the National Center for Chronic Disease Prevention and Health Promotion (www.cdc.gov/tobacco), offers educational materials, posters, hypertext links, and other information.

ADVOCACY ISSUES

The most successful tobacco control efforts involve a number of concerted actions. These include increasing the cost of tobacco products through higher taxes on the products; litigation against the tobacco industry to hold corporations financially responsible for the disease and death their products cause; ending government subsidies to the tobacco industry (which currently exceed $100 million dollars per year); banning advertising of tobacco products in youth-oriented media and youth-oriented activities such as sporting events; enforcing laws that ban minors from buying tobacco products; banning cigarette vending machines; promoting adoption of clean indoor air laws and smoke-free facilities such as schools, day care centers, office buildings, restaurants, and bars; getting pharmacies to stop selling tobacco products; advocating for divestment of tobacco industry stocks by state and local government investment agencies; shareholder efforts to change tobacco industry behavior; and giving the federal government regulatory oversight of tobacco as a drug.

Advocacy organizations such as Action on Smoking and Health (http://ash.org/), Americans for Nonsmokers' Rights (http://www.no-smoke.org/), and the Center for Tobacco-Free Kids (http://www.tobaccofreekids.org/) have many useful fact sheets, educational materials, and up-to-date information on various aspects of the tobacco wars. The American College Health Association published a position statement on tobacco use on college and university campuses; this is available at www.acha.org/info_resources/tobacco_statement.pdf. "Smokescreen" (http://www.smokescreen.org/) is another excellent tobacco advocacy site. It offers daily e-mail updates on a wide variety of tobacco issues, from the latest science to the latest legal battles. In addition, information received from this site can be personalized to one's own areas of interest. Features include tobacco-related news from individual states and a daily document from the tobacco industry files, which were long suppressed by the tobacco industry until 1999. A companion site, http://www.tobacco.org/, features daily updates of "tobacco in the news," as well as related documents and health information. The American Legacy Foundation (http://www.americanlegacy.org/) was founded as part of the master settlement agreement and
particularly involves youth in its tobacco control activities. The University of California, San Francisco (www.library.ucsf.edu/tobacco) provides online access to the Tobacco Control Archives Print Collection, tobacco industry Web sites and documents, state-by-state reports on tobacco industry activities, and the "Cigarette Papers."

Internationally, the tobacco industry has not changed its tactics. It has shifted its efforts elsewhere around the globe, and particularly increased them in developing countries, where tobacco control efforts may not be as well established. The tobacco industry continues to aggressively market its damaging and deadly products. To fight this global epidemic of tobacco-related disease, the World Health Organization (http://www.tobacco.who.int/) is developing a treaty on tobacco control, the International Framework Convention on Tobacco Control. For more information on this important development, contact the Web site at http://tobacco.who.int/.

RESEARCH ISSUES

A number of questions concerning tobacco use prevention and cessation in adolescents are being actively investigated in the research setting, including the following:

1. What are the best methods to prevent or delay onset of tobacco use in the pediatric population?
2. What is the natural history of adolescent cessation?
3. How should successful treatment be defined—for example, is significant decrease in use, as opposed to total quitting, a reasonable treatment outcome for adolescents?
4. Are smoking patterns in adolescents similar to those in adults?
5. How valid is self-reporting of tobacco use, including self-report measures in adolescents?
6. Does biochemical verification (e.g., breath carbon monoxide, salivary or urinary cotinine) significantly increase the validity of self-reporting?
7. What are accurate cutoff points for biochemical verification of smoking status?
8. How should relapse be defined for adolescents?

The Society for Nicotine Research and Treatment (http://www.srnt.org/) publishes its own research journal.

SUMMARY

Tobacco prevention and cessation counseling is one of the most important steps pediatricians can take to improve the short-term and long-term health of patients and their parents. Smoking is a very serious disease with potentially lifelong and life-shortening consequences. Practitioners are in a unique position to help prevent smoking onset or to intervene early to stop smoking by adolescents.

WEB SITES

For Teenagers

http://www.thetruth.com/, American Legacy Foundation site for patients.
http://www.lung.org/smokefreeclass, American Lung Association site for and by teens.
http://www.ymmn.org/, Youth Media Network.

For Parents

http://www.cdc.gov/tobacco/slam.htm, and www.cdc.gov/tobacco/smokescreen.htm, CDC sites and advocacy sites.
http://www.drkoop.com/wellness/tobacco, Dr. Koop site on tobacco.

For Clinicians

http://www.cdc.gov/tobacco/cdc site on tobacco.
http://www.smokescreen.org/, Smokescreen, a national advocacy Web site.

REFERENCES AND ADDITIONAL READINGS

California Department of Health Services, Cancer Prevention Program. Does tobacco advertising influence teens to start smoking? Chapter 10: Tobacco use in California: a focus on preventing uptake.


Tobacco control archives. University of California, San Francisco, Library and Center for Knowledge Management. Available at [www.library.ucsf.edu/tobacco](http://www.library.ucsf.edu/tobacco).


Marijuana is the most widely abused illicit drug in the United States, and its effects on physical and mental health remain controversial. The rate of use of marijuana within the previous year among 8th graders was 61% and among high school seniors in 1979 and declined until 1992, when it hit a low of 22%. However, use increased in the 1990s and in 1997 rose to 38.5% among high school seniors. Use fell slightly to 36.5% by 2000. The lifetime prevalence among high school seniors increased from 32.6% in 1992 to 48.8% in 2000. During the period between 1992 and 2000, the annual use of marijuana more than doubled (from 7.2% to 15.6%) among 8th graders; it increased also among 10th graders (from 15.2% to 32.3%) and 12th graders (from 21.9% to 36.5%). Of particular concern is the rise in daily use of marijuana. Active daily use of marijuana more than doubled, from 1.9% among high school seniors in 1992 to 6.0% in 2000.

Marijuana is no longer considered a benign drug. It has been shown to have negative effects on both physical and psychological health and is associated with the possible development of tolerance, dependence, and a withdrawal syndrome. The frequent use and abuse of marijuana must be taken seriously, because regular use can have adverse effects on learning, with possible psychological and cognitive impairment.

**THE DRUG**

Marijuana is derived from the flowering tops and leaves of the plant, *Cannabis sativa*. The resinous oil is extracted. The content of D-9-tetrahydrocannabinol (THC) is highest in the flowering tops and declines in leaves, stems, and seeds. Marijuana joints obtained mainly from the flowering tops and leaves usually have a THC content of 0.5% to 5.0%, and hashish, which consists of dried cannabis resin and compressed flowers, contains 2% to 20%. Hashish oil may contain 15% to 30% THC. Marijuana contains more than 60 cannabinoids, but the major psychoactive ingredient appears to be THC.

Dronabinol is chemically synthesized THC that is prepared as gelatin capsules for medical uses.

1. Preparations: Marijuana is usually smoked but may be eaten, brewed in tea, or swallowed in a pill form.
   a. Joint: This form of marijuana usually consists of chopped up leaves and stems of the plants, which are rolled into cigarettes and smoked. A typical joint contains between 0.5 g and 1.0 g of cannabis.
   b. Cookies and brownsies: Marijuana is sometimes baked into cookies or brownies and ingested orally.
   c. Pipe: Loose marijuana is often smoked in pipes or bongs, sometimes in combination with other drugs such as cocaine or phencyclidine (PCP).
   d. Hashish: This preparation is the strongest form of marijuana. It is composed of a pure resin derived from the leaves and flowers of the female plant and is usually pressed into a “brick” and smoked.
2. Slang names include grass, pot, weed, do, bud, endo, and blunts (hollowed-out small cigars refilled with marijuana).
3. Active ingredient and mechanism of action: THC is the active ingredient in all forms of marijuana. Cannabinoid biology and especially neurobiology has advanced in recent years. Marijuana appears to stimulate the dopamine pathway from the ventral tegmental area to the nucleus accumbens. This is believed to be the reward center of the brain. Two endogenous cannabinoid receptors have been found: CB1 (found mainly in the brain) and CB2 (found only in peripheral tissues, especially in the immune system). In the brain, the receptors are most prevalent in the cerebral cortex, hippocampus, basal ganglia, and cerebellum. The location of these receptors helps explain the cognition, motor coordination, memory, and mood changes produced by marijuana. Endogenous cannabinoids, anandamide and 2AG, have been discovered; they are part of the cannabinoid neurotransmission system in the brain. It appears that cannabinoids may have a natural role in pain modulation, control of movement, cognition, and memory. Studies demonstrate that the brain can develop tolerance and dependence on cannabinoids. There appears to be a role for cannabinoids in the immune system, but it is yet to be defined.
4. Potency: In the 1960s the average potency was 0.1% to 0.5% THC. Recent analysis shows that today most marijuana averages 4% to 5% THC. Samples of sensimilla, a potent marijuana cultivated to obtain high THC levels, average 7% to 9% but have tested as high as 14%. Hash oil may contain 20% to 30% THC. This increase in potency may be a factor in the recent increase in reports of side effects. The potency of marijuana appears to depend on the way it is prepared. Ganja is about three times more potent than marijuana, while hashish is five to eight times more potent.
5. Metabolism: THC is metabolized primarily in the liver through the cytochrome P-450 system. Peak plasma levels of THC are reached within about 10 minutes after smoking marijuana. Effects last 2 to 3 hours. The drug is fat soluble and therefore can accumulate for long periods in the body. Smoked marijuana produces 5 to 10 times the bioavailability of the ingested drug.
6. Excretion: Cannabinoid metabolites are carried by the enterohepatic circulation to the intestinal lumen and excreted in the feces (65%) or are carried through the renal circulation and excreted in the urine (35%). Carboxy and hydroxy cannabinoids are the major metabolites detected in urine drug screening tests. The cannabinoid metabolites may be detected for 3 to 10 days in the occasional user and for 1 to 2 months in chronic users. Because this compound is stored in fat tissue, changes in activity or diet that mobilize fat may cause sudden increases in levels of cannabinoids detected in urine. Interpretation of urine drug screening results depends somewhat on the level detected:
   a. Less than 20 ng/mL: Considered negative
   b. 20 to 50 ng/mL: May not distinguish recent use in the occasional user from past use in the long-term user.
   c. Higher than 50 ng/mL: May be detected in long-term users for up to 2 weeks after last use.
   d. Higher than 400 ng/mL: Indicates recent heavy use.
7. Effects of intoxication
   a. Physical reactions: Increase in heart rate, reddening of the conjunctivae, dry mouth and throat, dilated pupils, sleepiness
   b. Distortion of time sense
   c. Auditory and visual enhancement or distortions
d. Impaired learning and cognitive functions
   e. Increase in appetite
   f. Low to moderate doses produce euphoria, time distortion, increased talking, and the physical reactions described earlier.
g. High doses produce mood fluctuations, depersonalization, and hallucinations.
   h. Potential toxic reactions: Anxiety, panic, organic brain syndrome, psychoses, delusions, hallucinations, and paranoia
   i. Marijuana may precipitate seizures in epileptic individuals.
   j. Marijuana may precipitate psychotic episodes in schizophrenic individuals.

**ADVERSE EFFECTS**

Although some side effects are known, others are postulated but not yet conclusively documented in well-controlled studies. The risk of adverse effects increases with increased potency, amount used, frequency of use, and length of exposure to marijuana. Early age at onset also increases the risk of negative effects.
Marijuana smoking results in a substantially greater respiratory burden of carbon monoxide and tar than does cigarette smoking (Wu et al., 1988).

- Reduced testicular size

Cannabis psychosis: There is little evidence for the existence of a cannabis psychosis. However, the drug may precipitate several types of mental dysfunction in chronic marijuana users.

- Amotivational syndrome: A syndrome associated with chronic heavy marijuana use and consisting of a state of passive withdrawal from usual work and recreational activities.

- Acute changes: This primarily includes the acute psychological effects, many of which are pleasurable although some may be unpleasurable and or disabling.

- Male fertility: Heavy use of marijuana causes a decrease in sperm count and motility and an increase in the number of sperm with abnormal morphologic features.

- Mild decrease in exercise capacity, which could potentially be harmful in cardiac patients (Tashkin et al., 1976).

- Menstrual function: An increase in anovulatory cycles occurs in heavy users, increasing the risk of menstrual disorders and infertility (Smith et al., 1979; Mueller et al., 1991). Long-term use may impair memory, learning ability, and perception (Dupont, 1985; Miller et al., 1977). Also of concern with long-term use is dependence and possible withdrawal syndrome on cessation. Some marijuana users develop dependence that includes a lifestyle revolving around procurement and use of marijuana and other drugs.

- Cardiovascular Effects

1. Tachycardia (Tashkin et al., 1976)
2. Mild decrease in exercise capacity, which could potentially be harmful in cardiac patients (Tashkin et al., 1976).

- Endocrine and Immune Function Effects

1. Antagonistic effects on insulin, which could potentially cause problems, including ketoadiposis, in adolescents with diabetes (Lantner et al., 1980).

- Effects on the Reproductive System

Chronic administration of high doses of THC in animals lowers testosterone secretion; impairs sperm production, motility, and viability; and alters the menstrual cycles. It is unclear if these effects occur in humans. Reports have included the following effects:

1. Menstrual function: An increase in anovulatory cycles occurs in heavy users, increasing the risk of menstrual disorders and infertility (Smith et al., 1979; Mueller et al., 1990).
2. Abortion: Monkeys have an increased rate of abortions with moderate to heavy use (40% with use versus 8% without) (Sassenrath et al., 1979).
3. Male fertility: Heavy use of marijuana causes a decrease in sperm count and motility and an increase in the number of sperm with abnormal morphologic features (Hembree et al., 1979).
4. Testosterone levels: A drop in testosterone level may occur as a result of marijuana's effects on luteinizing hormone or on Leydig cells in the testes. This has not been confirmed by all researchers (Kolody et al., 1974; Mendelson et al., 1974).
5. Gynecomastia
6. Reduced testicular size
7. Decreased libido

- Central Nervous System Effects

One significant area of concern has been central nervous system effects, including acute, subacute or long-term effects that may extend to months or possibly may be permanent.

1. Acute changes: This primarily includes the acute psychological effects, many of which are pleasurable although some may be unpleasant and or disabling. Most of these were listed previously in the discussion of marijuana intoxication. Impairments in reaction time and judgment may contribute to the risk of motor vehicle or other accidents.
2. Subacute effects: Regular heavy use of marijuana may lead to a subacute encephalopathy. Because marijuana has a long half-life and persists in body tissues, the effects on nerve function may persist after the immediate effects have disappeared. Pope et al. (1995, 1996) reviewed the neuropsychological effects of cannabis. Their review included both drug administration studies, in which known amounts of cannabis were administered to volunteers, and naturalistic studies, in which heavy marijuana users were tested after some period of abstinence. The results suggested a “drug residue” effect on attention, psychomotor tasks, and short-term memory during the 12- to 24-hour period immediately after cannabis use. However, the evidence was not yet sufficient to support or refute either a more prolonged drug residue effect or a toxic effect on the central nervous system that might persist after drug residues have left the body. Short-term use can also lead to decreases in reading comprehension and problem-solving ability (Miller et al., 1977; Lantner et al., 1980). In a study of human couples, marijuana use led to a decrease in interpersonal skills between the pairs studied (Jansky et al., 1979).
3. Long-term effects: Pope et al. (1995) reported that marijuana use may lead to permanent impairment of cognitive function and behavior. Chronic buildup of cannabinoids may produce impaired ability to focus attention, impaired ability to filter out irrelevant information, and impaired ability to compromise (Solowij et al., 1991, 1995; Leon-Carrion, 1990; Tunving, 1985). Long-term use may impair memory, learning ability, and perception (Dupont, 1985; Miller et al., 1977). Also of concern with long-term use is dependence and possible withdrawal syndrome on cessation. Some marijuana users develop dependence that includes restlessness, irritability, mild agitation, insomnia, nausea, cramping, and sleep electroencephalographic disturbances (Crowley et al., 1998).
4. Amotivational syndrome: A syndrome associated with chronic marijuana use and consisting of a state of passive withdrawal from usual work and recreational activities was outlined by Schwartz (1987a), who identified seven components:
   a. Loss of interest, general apathy, and passivity
   b. Loss of desire to work consistently and loss of productivity, accompanied by a lack of concern about the poor work performance
   c. Loss of energy and tiredness
   d. Moodiness, sullenness, and inability to handle frustration
   e. Impairment in concentration and inability to process new material
   f. Bizarre habits and appearance
   g. A lifestyle revolving around procurement and use of marijuana and other drugs
5. Cannabis psychosis: There is little evidence for the existence of a cannabis psychosis. However, the drug may precipitate several types of mental dysfunction in susceptible individuals, including a brief toxic psychosis resembling the delirium of a high fever, a short-lived acute anxiety state, and an acute depressive reaction.

Controversy exists concerning the presence of these behavioral changes, including the amotivational syndrome. Because heavy drug users may already have underlying behavioral problems and may already be depressed, alienated, or bored, it is difficult to distinguish whether marijuana is the cause or whether the behaviors are preexistent. In one long-term study, Shedler and Block (1990), examined this issue in 101 children who were evaluated and given personality tests at 7, 11, and 18 years of age. By the end of the study, three groups could be distinguished: abstainers, experimenters (tried marijuana no more than once a month), and frequent users (smoked marijuana at least once a week and had used at least one other drug). The study demonstrated marked personality differences among the three groups, with many of the changes noted long before any drug use occurred. The frequent users got along poorly with other children, lacked self-confidence, and were insecure, alienated, impulsive, and unpredictable. The abstainers were more inhibited, conventional, shy, neat, and anxious. The experimenters were more likely to be responsive, curious, active, and open.

- Motor Performance

Marijuana causes a decrease in both psychomotor functions and reaction times. This poses a dangerous problem for the adolescent who drives after getting high (Institute of Medicine, 1981). Specific functions related to driving skills that are impaired include:

1. Tracking: The ability to follow a moving object and to control the position of a car in relation to the highway
2. Signal detection: The ability to quickly notice and respond to lights or other unpredictable stimuli
3. Glare recovery time: The ability to see clearly after exposure to bright lights such as headlights

The impairment of these driving skills, in conjunction with marijuana-induced decreased judgment, impaired time and distance estimation, and impaired motor performance, makes driving under the influence of marijuana dangerous. There is good evidence that marijuana causes lingering effects on memory and coordination. Striking changes in the ability of pilots to operate a landing simulator persisted 24 hours after exposure to cannabis, during which time the pilots reported no awareness of marijuana aftereffects (Leirer and Yesavage, 1991).

Drug Interactions
1. Marijuana potentiates sedation when used with alcohol, diazepam, antihistamines, phenothiazines, barbiturates, or narcotics.
2. Marijuana potentiates stimulation when used with cocaine or amphetamines.
3. Marijuana is antagonistic with the effects of phenytoin, propranolol, and insulin.

TREATMENT

Treatment of marijuana use in the adolescent involves differentiation between experimental or occasional use and the abuse of marijuana. After initially experimenting with marijuana, many adolescents do not use it again or use it very infrequently. However, physicians should not overlook the negative effects of marijuana use in teenagers. Frequent marijuana use can interfere with the cognitive, emotional, and social development of adolescents. Deterioration in school performance, family and social problems, accidents, and legal difficulties suggest the need for intervention and treatment. Chapter 75 discusses management in more detail.

MEDICAL MARIJUANA

Dronabinol is chemically synthesized THC for medical uses. It is formulated in sesame oil and supplied in 2.5-, 5- and 10-mg gelatin capsules. There is still significant debate over the uses of medical THC. The medicinal use of THC as an anesthetic may become even less clear with the advent of serotonin antagonists.

Dronabinol is predominantly labeled for use in the treatment of anorexia associated with weight loss in patients with the acquired immunodeficiency syndrome (AIDS) or for nausea and vomiting associated with chemotherapy. It is usually prescribed after other medications have failed. It has also been used off-label for treatment of glaucoma and epilepsy and to help decrease tremors, ataxia, and spasticity in patients with multiple sclerosis. Watson et al. (2000) summarized the scientific evidence for benefits and risks of marijuana as a medicine in a study by the Office of National Drug Control Policy. In this report there was the call for heavier investment in research on the biology of cannabinoid systems, careful clinical studies of cannabinoids in clinical syndromes, analysis of cannabinoids' psychological effects on symptoms, and evaluations of the health consequences of heavy marijuana use. There was also a recommendation against the use of smoked marijuana in medicine and for the development of a medical cannabinoid inhaler.

WEB SITES

http://www.forreal.org/. From the Center for Substance Abuse Prevention.
http://www.health.org/govpubs/phd8411. National Clearinghouse for Alcohol and Drug Information (NCADI), Center for Substance Abuse Prevention. This resource was produced as part of the Girl Power! program for girls age 9 to 14 years. The fact sheet presents a general overview of marijuana use; the short- and long-term effects of marijuana use, and other related facts.
http://www.health.org/realitycheck. NCADI, Center for Substance Abuse Prevention. Reality Check is a national public education campaign designed to counter increases in marijuana use by youth. This Web site provides information and activities for parents and other concerned adults working to prevent marijuana use in their homes and communities. A link is provided to a companion site for teens: http://www.forreal.org/.
http://www.drugabuse.gov/GoestoSchool/NIDA_Quest/index7.htm. National Institute on Drug Abuse, NIH. Sara’s Quest is a science-based drug abuse educational game. Players search out the correct answers to questions about how marijuana affects the brain. You get a free poster if you complete the “quest” and get right answers.

REFERENCES AND ADDITIONAL READINGS

Capalini L, Tashkin D, Vlensky W. Does marijuana have a place in medicine. JAMA 1988;299:11.


Hallucinogens

Lawrence S. Neinstein and Bruce S. Heischober

The hallucinogen class of drugs includes LSD (d-lysergic acid diethylamide tartrate), peyote, mescaline, psilocybin, certain mushrooms, DMT (dimethyltryptamine), morning glory seeds, STP (dimethoxy-4-methylamphetamine), jimsonweed, and PCP (phencyclidine). The term hallucinogen (“producer of hallucinations”) is actually a misnomer, because prototypical hallucinogens such as LSD, mescaline, and psilocybin at typical dosage levels do not cause hallucinations (sensory perception changes without a corresponding environmental stimulus) but rather illusions (perceptual distortion of a real environmental stimulus) or distortions of perceived reality. True hallucinations do occur with the use of volatile solvents such as gasoline. Set (the user’s attitudes and expectations) and setting (the drug-taking environment) greatly influence a user’s experience with this class of drugs. With the exception of the hallucinogenic amphetamines, physical withdrawal does not occur.

TYPES OF HALLUCINOGENS

The following is a subgrouping of hallucinogens based on distinctive psychoactive effects and structure-activity relationship similarities.

1. Psychedelics: prominent hallucinations/synesthesias with mild distortion of time and reality, impaired attention/concentration, mild disruption in ego structure
   a. Indolealkylamines: LSD, psilocybin (“magic mushrooms”), dimethyltryptamine (DMT), beta-carbolines (harmaline)
   b. Phenylalkylamines: mescaline (peyote)
2. Entactogens: structural similarities to psychedelics (mescaline) and amphetamines; unique characteristics psychoactively include improved communication, empathy with others, and positive mood enhancement
   a. Methylenedioxyamphetamine (MDMA, or “Ecstasy”) (see Chapter 74)
   b. 4-Methylenedioxyamphetamine (EVE)
3. PCP: also a dissociative anesthetic
4. Marijuana (see Chapter 72)

PREVALENCE

Overall, the prevalence of hallucinogen use decreased in the late 1970s and early 1980s and then began a slow but definite rise in the late 1980s that continued into the 1990s until about 1997, after which rates fell through 2000. Approximately 13.0% of the 2000 seniors in the Monitoring the Future Study of high school seniors had used hallucinogens; 11.1% had used LSD; and 3.4% had used PCP (Johnston et al., 2001). Among high school seniors in 2000, 8.1% had used a hallucinogen within the past 12 months and 2.6% within the past 30 days, and 0.2% had daily use. The lifetime prevalence rates for college students in 1999 were 14.8% for hallucinogens and 12.7% for LSD (Johnston et al., 2001). Among high school seniors in 2000, 8.1% had used a hallucinogen within the past 12 months and 2.6% within the past 30 days, and 0.2% had daily use. The lifetime prevalence rates for college students in 1999 were 14.8% for hallucinogens and 12.7% for LSD (Johnston et al., 2001). The 1999 National Household Drug Survey showed the following hallucinogen prevalence rates for past month use and trends:

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>12–17</td>
<td>1.1</td>
<td>1.7</td>
<td>2.0</td>
<td>1.9</td>
<td>1.8</td>
<td>1.6</td>
</tr>
<tr>
<td>18–25</td>
<td>1.8</td>
<td>2.3</td>
<td>2.3</td>
<td>2.5</td>
<td>2.7</td>
<td>3.5</td>
</tr>
</tbody>
</table>

Two trends emerging from the “pop culture” scene are partially responsible for the resurgence of LSD and the emergence of the use of MDMA (ecstasy), a hallucinogenic methamphetamine derivative. “Rave” or “house” parties involve alternative forms of rock music played in coordination with colorful, pulsating light effects and augmented by the use of LSD or MDMA. Frequently the drugs are supplied as part of the admission price or by the organizers of the event. There has also been a revival of interest in the 1960s psychedelic movement, from music to memorabilia, dress, and lifestyle.

It is important to emphasize that one should not label an adolescent because of his or her dress or music; yet, especially in early adolescence, information about the peer group can give insights into the thinking and behaviors of the identified patient. There is also the suggestion that familiarity with an adolescent's music preference can open avenues of communication, allowing more effective data collection by the clinician.

An extremely important fact should be remembered in regard to the current wave of LSD use. In the 1960s, doses of up to 500 µg were not unusual. According to the U.S. Drug Enforcement Agency (DEA) and Sheriffs Crime Laboratory data, the average current dose is in the 20- to 80-µg range. Most users today describe a seemingly mild “trip” with colorful visual “tracers,” enhancement of sound, and light sensations. Psychiatric emergency services are not seeing the same level of acuteness as was seen in the 1960s. There is clearly a disregard for and underestimation of the dangers of LSD because of the lower dose. However, even at this lower dosage level, one is at risk for chronic psychiatric problems, acute physical trauma, and other consequences of risk-taking behaviors that might occur under the influence of the drug.

LSD
Although LSD use peaked in the 1960s, the drug has had a major increase in the 1990s. Lifetime prevalence among high school seniors in the Monitoring the Future survey fell from 11.3% in 1975 to 7.2% in 1986 only to increase to 13.6% in 1997 and then fall again to 11.1% in 2000. In the 2000 Monitoring the Future Study (Johnston et al., 2001), 6.6% of high school seniors had used LSD within the previous year, 1.6% had used it within the 30 days before the survey; and 0.1% used LSD daily. In 1999, among college students, 12.7% had used LSD at least once, 5.4% within the past year, and 1.2% within the past 30 days. LSD is making a comeback nationwide among white middle-class high school and college students. Increases have been noted in LSD-related arrests and in seizures of larger quantities of LSD. LSD-related visits to emergency departments by adolescents have also increased. The risk attributed to occasional use of LSD by high school students has fallen.

Origin
LSD is derived from an alkaloid found in rye fungus. It is made by mixing lysergic acid with diethylamide, freezing the mixture, and then extracting the resulting LSD. The procedure is not easy; therefore, much of the LSD sold on the street is either adulterated or contains no LSD. In one survey of LSD samples submitted to the Los Angeles County Street Drug Identification Program, 11% contained no LSD.

Action
LSD is the most potent psychoactive drug. It inhibits the release of serotonin and gives rise to a nonspecific stress response and autonomic changes. The drug is rapidly absorbed from the gastrointestinal tract, with onset of action in 30 to 40 minutes. LSD has a half-life of 3 hours and is not detected on standard urine drug screens. Tolerance develops rapidly but is short-lived. Some daily users of LSD describe the practice of "doubling up" (doubling the previous day's dose when using on consecutive days) to counteract tolerance.

1. Physiological effects: These occur within 30 minutes to several hours after use and usually resolve within 6 hours.
   a. Conjunctival injection
   b. Ataxia
   c. Increase in blood pressure, heart rate, and temperature
   d. Mydriasis, lacrimation, and piloerection
   e. Flushing and sweating
   f. Decrease in urine output
   g. Decrease in appetite
   h. Dry mouth
   i. Blurred vision
   j. Tremors and incoordination

2. Psychological effects: The major effects of LSD and the reason for its abuse are the psychological effects, which may last up to 14 hours or longer.
   a. Depersonalization
   b. Loss of time sense and of the relationship between current impressions and past experience
   c. Loss of ego boundaries between the user and his or her surroundings
   d. Loss of muscle coordination and pain perception
   e. Decrease in judgment
   f. Visual and auditory illusions, including synesthesia (a secondary sensation caused by an actual perception of a different sense, such as sound producing the sensation of color)
   g. Impairment of attention, motivation, and concentration
   h. Possibly anxiety, depression, paranoia, confusion, and fragmentation

A fairly typical description of the effects of LSD was given by its discoverer, Dr. Albert Hoffman, a Swiss chemist:

I lost all control of time. Space and time became more and more disorganized, and I was overcome with fears that I was going crazy. The worst part of it was I was clearly aware of my condition, though I was not able to stop it. Often I felt that I was outside of my body. I thought I had died. My ego was suspended somewhere in space, and I thought my body was lying dead on the sofa. I observed and registered clearly that my “alter ego” was moving about the room moaning. . . . I became dizzy and delirious with fantastic visions of extraordinary vividness accompanied by a kaleidoscopic play of intense coloration.

—Albert Hoffman, quoted by Jenkins and Brody, 1974

Dr. Hoffman’s description of the sense of being an observer is frequently reported by LSD users and distinguishes LSD psychosis from schizophrenia.

Dose
The usual dose of LSD is between 20 and 80 µg. Anything more than 250 µg is considered especially dangerous. The drug is commonly distributed as a soluble powder or liquid. It is usually colorless, odorless, and tasteless in its manufactured state, but it is most often colored when sold. It is sold as cylindrical tablets or gelatin squares or applied to small pieces of paper; these preparations are known on the street, respectively, as microdots, windowpanes, and blotters. LSD is also sold as decals or stickers.

Slang Names
Slang names for LSD include acid, beast, big D, black, blue barrels, blotters, blue cheer, boomers, brown dot, cubes, fry, microdots, orange sunshine, panes, sugar, sunshine, trips, while lightning, window panes, and yellow sunshine.

Effects
1. Symptoms of intoxication
   a. General: Anorexia, nausea, flushing, elevated temperature
   b. Neurological: Dizziness, paresthesia, dilated pupils, hyperactive reflexes, tremor
   c. Psychiatric: Labile affect, anxiety, body image changes, euphoria, floating feeling, illusions, restlessness, sleep disturbance, paranoia, and depersonalization
   d. Cardiovascular: Elevated blood pressure, tachycardia

2. Symptoms of overdosage
   a. General: Dry mouth, perspiration, elevated temperature, flushing
   b. Neurological: Grand mal seizures, dilated pupils, hyperactive reflexes, tremor, dizziness, coma
   c. Psychiatric: Toxic psychosis, suspiciousness, anxiety, body distortions, irritability, delirium, illusions
   d. Cardiovascular: Tachycardia, hypertension, circulatory collapse
   e. Gastrointestinal: Anorexia, nausea, vomiting, abdominal cramps
   f. Hematological: Coagulopathies

3. Tolerance and psychological dependence: No physical dependence occurs.

4. Bad trips: Negative emotional responses, often triggered by environmental factors (setting) or feelings within the user (set). These responses terrify the user and may produce a sense of panic, fragmentation, or “going crazy.” The most significant characteristic of a bad trip is fear.

5. Flashbacks: Recurrence of the LSD-induced state after the effects of the drug have worn off. Flashbacks may occur spontaneously for variable lengths of time after original drug ingestion. Concurrent use of selective serotonin reuptake inhibitor agents may induce or worsen the LSD flashback syndrome (Markel et al., 1994), possibly as a result of the similarity in neuroreceptor physiology for LSD and serotonin.

6. Chronic adverse effects may include psychosis, depression, and personality changes. The use of a hallucinogen should be considered in the differential diagnosis of an adolescent who presents with the new onset of psychosis.
Treatment of a Bad Trip and of Overdose

Treatment of a bad trip should be done by someone with experience in this area. Important components include the following:

1. Provide an appropriate setting. Often the setting, such as a room with loud music, induces a bad trip. Changing the setting to a peaceful, calm area often alleviates the problem.
2. Help to restore contact with reality. The person dealing with the user should try to calm the user by talking to him or her about familiar things. The user should be reassured that his or her unusual sensations will cease when the drug wears off. The helping individual should listen carefully to the user and respond sympathetically. If the user is high on PCP, then talking the user down will be counterproductive and should be avoided (see later discussion of PCP).
3. Avoid the use of any medications, if possible.
4. Avoid discussing reasons for use of the drug or personal problems of the user during a bad trip.
5. Support respiration and circulation as needed.
6. Treat hyperthermia.
7. Treat seizures.
8. Treat hypertension.
9. Look for other causes of symptoms—an overdose of LSD is not common.
10. Monitor the cycles of lucidity and periods of intense reactions to the drug. If the cycles are frequent, then the individual is probably early in the course of experiencing effects of the drug; if the cycles are less frequent, the drug effects may have peaked.

MDMA (ECSTASY)

MDMA has both stimulant and hallucinogenic properties. For a discussion of this drug, see Chapter 74.

PEYOTE AND MESCALINE

Peyote is a cactus (Lophophora) that grows in the southwestern United States and in Mexico. The tops of the cactus contain numerous alkaloids, including mescaline (3,4,5-trimethoxyphenethylamine). Although many drugs are sold as mescaline, of the 459 samples submitted to the Los Angeles County Street Drug Identification Program in 1980, 96% contained no mescaline. Most mescaline capsules contained either LSD or both LSD and PCP. Peyote is sold either as buttons derived from the cactus or as capsules containing ground peyote. Street names include big chief, buttons, cactus, mesc, and mescal.

Action

Mescaline has its onset of action within 30 minutes to 2 hours after ingestion, and the effects last for 6 to 12 hours. The mescaline high differs from the LSD high in several ways:

1. LSD creates a more intense experience than mescaline does.
2. Mescaline intensifies body sense, whereas LSD tends to have a stronger effect on the mind.
3. Mescaline is less disorienting than LSD.
4. Mescaline use is frequently accompanied by unpleasant side effects such as nausea and vomiting.

Doses

The usual human dose ranges from 100 to 500 mg.

Side Effects

Tolerance and psychological dependence can occur with mescaline, but no physical addiction occurs. Bad trips are less severe and less frequent with mescaline than with LSD.

PSILOCYBIN

Mushrooms containing psilocybin and psilocin produce effects similar to those of the other hallucinogens. The mushrooms are ingested orally, and there is a rapid onset of effects in about 15 minutes. The effects peak at 90 minutes, begin to wear off in 2 to 3 hours, and disappear after about 5 or 6 hours. The average dose is 4 to 10 mg of psilocybin. Street names for psilocybin mushrooms include ‘shrooms, mushrooms, Silly Putty, magic Mexican mushrooms, and psychedelic mushrooms.

DIMETHYLTRYPTAMINE

DMT is a natural constituent of the seeds of several plants found in the West Indies and South America. DMT is usually prepared as an orange liquid in which either tobacco, marijuana, or parsley is soaked and then smoked; it is inactive orally. This drug has effects similar to those of other hallucinogens, except that the “trip” is short, lasting only 1 to 3 hours. DMT is known on the street as businessman's special or businessman's lunch.

MORNING GLORY SEEDS

The seeds of some members of the bindweed family, including the morning glory (Rivea corymbosa and Ipomoea), have been used for centuries for their hallucinogenic effects. Morning glory seeds are legally available on seed racks, but, to prevent spoilage, seeds intended for planting are usually coated with dangerous chemicals such as methyl mercury. The active principal ingredient in the seeds is similar to LSD but about one tenth as potent. The effects of morning glory seeds are similar to those of LSD; however, there is an increase in side effects such as nausea, dizziness, and diarrhea, and there is an extremely bitter taste.

NUTMEG

Nutmeg is extracted from the dried seed kernels of an evergreen tree found in the South Pacific Islands. This common spice is ubiquitous in household pantries, and outbreaks of its use usually follow media reports of its hallucinogenic properties. It has long been used by prison inmates. Nutmeg contains lysergide as well as several other hallucinatory alkaloids. The presence of an extremely potent emetic, geraniol, has discouraged widespread use.

STP

STP (also known as the “serenity tranquility peace pill”) is related to mescaline but about 100 times more potent. Its effects are also similar to those of other hallucinogenic drugs, with the exception that with STP the incidence of unpleasant sensations is increased and the effects seem to last longer, up to 72 hours.

JIMSONWEED

Jimsonweed (Datura stramonium) has anticholinergic and hallucinogenic properties. It grows wild throughout the United States but especially in the Southwest. Adolescents make tea from the seeds. Users may have an anticholinergic syndrome at presentation for medical evaluation.

PHENCYCLIDINE

The use of PCP steadily declined in the 1980s, from a high of 12.8% in 1979 to a low of 2.4% in 1992. However, PCP use later increased, to a high of 4.0% in 1996.
before declining to 3.4% in 2000. The 2000 Monitoring the Future Study of high school seniors (Johnston et al., 2001) found that 3.4% of the seniors had used PCP at some time, 2.3% had used it within the past year, and 0.9% were current users (within the previous 30 days). Daily use occurred among 0.2% of the seniors. These data have shown no statistically significant change in the 1990s.

PCP was introduced in the 1950s as a general anesthetic. Clinical trials revealed PCP to be an effective anesthetic, but during surgical recovery it caused excessive agitation, excitement, and disorientation. In 1965, the drug was discontinued as an investigational drug for human use. In the late 1960s, its use increased in San Francisco as an experimental psychedelic drug, called the “peace pill.” It was unpopular at that time because of excessive reports of bad trips. However, during the middle and late 1970s its popularity increased tremendously, and it became one of the nation’s major drugs of abuse. Until 1978 the drug was still legally manufactured as Semylan for veterinary anesthesia. PCP is still an unsafe and commonly abused drug among adolescents, especially in urban areas. There is an increasing awareness that dextromethorphan, an OTC cough suppressant, can have similar effects to PCP, when taken in high doses.

Metabolism

PCP is the hydrogen chloride salt of phencyclidine. It is related to the anesthetic ketamine. The drug is rapidly inactivated by hepatic metabolism and is excreted in the urine as the monopiperidine conjugate. Because PCP is fat soluble, it has the ability to remain in the body for prolonged periods. Its urinary excretion is highly dependent on urine pH, with significantly higher excretion rates at an acidic pH. The half-life of PCP is 3 days. The active ingredient is the phencyclidine itself, not the metabolites.

Action

PCP is a dissociative anesthetic with analgesic, stimulant, depressant, and hallucinogenic properties. The drug acts on the thalamus, midbrain, and sensory cortex to impair proprioception and the brain’s ability to organize input. Its physiological effects are more fully discussed later in this chapter. PCP usually induces one of several clinical states:

1. Acute intoxication
2. Acute or prolonged delirium: Disorientation, clouded consciousness, and abnormal cognition
3. Schizophreniform psychosis: Hallucinations, thought disorder, and delusions
4. Mania: Hallucinations, elevated mood, and elevated self-attitude
5. Depressive reactions: May occur after long-term use of PCP

Dose

PCP may be packaged as a liquid, powder, tablet, leaf mixture, or rock crystal. It can be used intravenously, intramuscularly, or orally, or it can be snorted or smoked. Examples of methods of using the drug and associated doses are listed as follows:

<table>
<thead>
<tr>
<th>Modality</th>
<th>Average Dose (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking (joint)</td>
<td>3</td>
</tr>
<tr>
<td>Snorting (powder)</td>
<td>5</td>
</tr>
<tr>
<td>Swallowing (tablet)</td>
<td>5</td>
</tr>
<tr>
<td>Injection (liquid)</td>
<td>10</td>
</tr>
<tr>
<td>Eyedrops (liquid)</td>
<td>Unknown</td>
</tr>
<tr>
<td>Rectally (liquid)</td>
<td>Unknown</td>
</tr>
<tr>
<td>Vaginally (liquid)</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

Dose ranges vary tremendously, from 0.1 to more than 150 mg in one survey. In addition, approximately 20% of drug samples sold as PCP contained no PCP. In terms of potency, less than 5 mg is considered a low dose, 5 to 10 mg a moderate dose, and more than 10 mg a high dose.

Street Names

Street names for PCP include the following:

angel dust
dust
lovely
caffle

angel mist
elephant tranquilizer
lovely dust mist
shermans

animal
embalming fluid
magic dust
shermers

animal tranquilizer
flakes
mist
snorts

aurora borealis
goon
monkey dust
soma

busy bee
goon dust
orange crystal
star dust

Cadillac
gorilla biscuits
parsley
super grass

CJ
green tea
peace
super joint

columbo
hag
peace pill
super weed

crystal
jet fuel
Peter Pan
super X

crystal joints
juice
pip
surfer

cyclones
kaps
pits
whack whack

Detroit pink
KJ crystal
polvo
worn

devil's dust
kool 5
roker
zombie weed

dipper
Lemmon 714
puffy
zoom

dummy dust
live ones
rocket fuel

Clinical Manifestations

The clinical symptoms of PCP use vary with the dose, the route of administration, and the experience of the user. Intravenous, intramuscular, and oral routes of administration are more difficult to regulate than the smoking of PCP. In addition, inexperienced users have more side effects than experienced users do. The following list describes the clinical manifestations by dosage.

1. Low dose (less than 5 mg)
   a. Blank stare
   b. Horizontal and vertical nystagmus
   c. Gait ataxia
   d. Increased blood pressure
   e. Increased deep tendon reflexes
   f. Decreased proprioception and sensations
   g. Miosis or midposition, reactive pupils
   h. Diaphoresis
   i. Flushing
   j. Behavioral disorders
      • Disorganized thought processes
      • Distortion of body image and of objects
      • Amnesia
      • Agitated or combative behavior
      • Unresponsive behavior
      • Disinhibition of underlying psychopathology
- Schizophrenic reactions
- Catalepsy, catatonia
- Illusions
- Anxiety, excitement

2. Moderate dose (5 to 10 mg)
   a. Hypertension
   b. Vertical and horizontal nystagmus
   c. Myoclonus
   d. Midposition pupil size
   e. Dysarthria
   f. Diaphoresis
   g. Fever
   h. Hypersalivation
   i. Mutism
   j. Amnesia
   k. Anxiety, excitement
   l. Delusions
   m. Behavior: Stupor or extreme agitation; violent or psychotic behavior can occur

3. High dose (more than 10 mg)
   a. Unresponsive, immobile state
   b. Eyes that may remain open during coma
   c. Hypertension
   d. Arrhythmias
   e. Increased deep tendon reflexes
   f. Muscle rigidity
   g. Decerebrate posturing
   h. Convulsions
   i. Spontaneous nystagmus
   j. Miosis
   k. Decreased urine output
   l. Dysarthria
   m. Diaphoresis and flushing
   n. Fever
   o. Amnesia
   p. Mutism
   q. Behavior: Stupor or extreme agitation; violent or psychotic behavior can occur

4. Massive oral overdose (more than 500 mg)
   a. Prolonged coma
   b. Extensor posturing
   c. Seizures
   d. Hypoventilation
   e. Hypertension or hypotension
   f. Prolonged and fluctuating confusional state after recovery from coma

Recovery
Recovery usually occurs within 24 hours but can proceed for days, depending on the dose and the acidity of the urine. With higher doses the coma can last 5 to 6 days and can be followed by a prolonged recovery period marked by behavioral disorders. Cognitive, memory, and speech disorders may last up to 1 year after the last use of PCP. Flashbacks may occur, as with LSD.

Diagnosis
The diagnosis of PCP use should be suspected in all adolescents with a distorted thought process, especially when there is evidence of analgesia or nystagmus. Any individual with open-eye coma, horizontal and vertical nystagmus, hypertension, and rigidity should be considered to have taken PCP.

1. Common symptoms for diagnosis
   a. Vertical and horizontal nystagmus: PCP is the only drug of abuse that causes a characteristic vertical nystagmus, however it can also cause horizontal or rotatory nystagmus.
   b. Ataxia
   c. Miotic but reactive pupils
   d. Disorientation with either a catatonic or an agitated state
   e. Increased blood pressure
   f. Increased deep tendon reflexes
   g. Severe intoxication: Seizure, coma, rigidity, and decerebrate posturing

2. Identification: PCP can be found in the blood, urine, and gastrointestinal secretions; the best fluid to sample is the urine.
   a. Blood level: A serum concentration of 25–100 ng/mL may be found in patients who are in an acute confusional state; a level of more than 100 ng/mL may be found in those in a comatose state.
   b. Urinary level: The concentration may vary in different clinical states. Excretion in the urine is highly pH dependent and decreases dramatically as the pH becomes alkaline. It is important to determine the pH of urine sent for analysis.
   c. Method: PCP can be detected by gas chromatography, thin-layer chromatography, or gas chromatography-mass spectrometry. The latter method is the most accurate.

3. Differential diagnosis: Table 73.1 compares PCP overdose with that of other drugs.

<table>
<thead>
<tr>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Death: Death can occur during PCP use. Death usually is caused by injuries sustained during periods of analgesia and aggression directed at self or others.</td>
</tr>
</tbody>
</table>
Death also can occur as a result of convulsions and cerebral hemorrhage.

2. Seizures: Generalized motor seizures may be early or delayed in appearance (Burns and Lerner, 1975).

3. Hypertension: Although the hypertension is mild, there was one reported case of hypertensive cerebral hemorrhage in a 13-year-old adolescent (Eastman and Cohen, 1975).

4. Renal failure: This complication can occur as a result of rhabdomyolysis and myoglobinuria (Cogen et al., 1978; Patel et al., 1979).

5. Fetal effects: One case report described an infant with abnormal behavior and abnormal facies born to a mother who used PCP (Golden et al., 1980).

6. Psychosis: This can last several weeks in patients with PCP overdose and is usually more common in adolescents who have underlying psychological problems.

**Treatment**

1. Use extreme caution: PCP users are unpredictable and often have little awareness of the consequences of their behavior.

2. Reduce stimulation: Reducing the levels of light, sound, and other external stimuli can rapidly bring down a PCP user. In an emergency, one can cover the user with a blanket.

3. Remove all hazards; however, do not forcibly take an object from a PCP user.

4. Do not enter water to save a PCP user; use some other first-aid technique such as a life preserver.

5. Do not use Maes.

6. Do not corner or touch a PCP user.

7. Restraints are not recommended; they may cause the PCP user to harm himself or herself in an attempt to escape.

8. Do not attempt to talk to a patient who has recently used PCP.

9. Try to avoid administering other medications, but, if necessary, diazepam (Valium) 2.5 mg given intravenously or lorazepam (Ativan) 1.0 to 2.0 mg given intramuscularly or intravenously can be used to treat seizures.

10. Theoretically, alkalization of the urine increases elimination, but the possible renal complications outweigh the small potential benefit.

11. Support respiratory and cardiovascular functions if necessary.

12. In addition to basic cardiopulmonary resuscitation, it is essential to check for signs of head, neck, back, and internal injuries, which can occur because of the behavioral effects of the drug. Unconscious victims should be placed on the side so that aspiration does not occur.

13. Treat hypotension with nitroprusside, labetalol, or phentolamine (see Chapter 74).

14. Severe agitation and psychosis can be treated with haloperidol. Avoid phenothiazine use because of the risk of excessive orthostatic hypotension and the potential for enhancing the cholinergic imbalance. As noted in the sections on cocaine and amphetamines, some authorities recommend that neuroleptic agents be avoided in favor of benzodiazepines alone. If the agitation is severe, then the differential diagnosis and initial management should be the same as for the delirious patient (see the section on cocaine in Chapter 74).

15. Treat hyperthermia as indicated.

16. Use intravenously administered diphenhydramine for dystonias.

17. Excessive salivation may need sucralfate.

18. Diuresis: Although there is no evidence to support diuresis, some authors recommend use of furosemide (20 to 40 mg) and intravenous administration of fluids to maintain urine output at more than 250 mL/hr.

19. During the recovery phase, an adolescent may have paranoia, regressive behavior, and a slow phase of reintegration. Adolescents may need inpatient psychiatric support through this period.

20. Referral to a drug rehabilitation program is indicated for any adolescent whose drug use causes significant life problems.

**SUMMARY**

It is important to remember that one cannot rely on the history when managing alleged use of a hallucinogen. Especially in this class of drugs, adulteration and misrepresentation of the substance are common. In addition, in the case of a patient with clowned sensorium and fever, even with a history of ingestion of LSD, the differential diagnosis must include central nervous system infection, endocrine disorder, drug or alcohol withdrawal syndrome, and ingestion of an unknown toxin.

Another dilemma occurs in the situation of the combative patient with a history of drug use. Although chemical and physical restraints are discouraged, if more passive means of calming the patient have not been effective, restraints must be used to facilitate further clinical evaluation and diagnostic testing. It is essential that every clinician become adept at using at least one sedative and one major tranquilizer. Alprazolam is probably the best suited of the benzodiazepines because it can be given intramuscularly, intravenously, or orally and is more effective than Valium as an anticonvulsant. Haloperidol (Haldol) and droperidol are superior to the neuroleptics because they have fewer cardiovascular side effects such as hypotension. Droperidol has come into favor recently because of its more rapid onset of action and shorter half-life and because it is approved for intravenous use. It is also more sedating than haloperidol. All major tranquilizers lower the seizure threshold.

**WEB SITES**


http://www.nih.gov/Infofax/MIND/Minddex.html


http://www.nida.nih.gov/Infofax/DrugsAbuse.html


http://www.nida.nih.gov/Infofax/InfofaxPCP.html

http://www.nida.nih.gov/Infofax/LSD.html

http://www.nida.nih.gov/Infofax/Abuse.html


**REFERENCES AND ADDITIONAL READINGS**


Death also can occur as a result of convulsions and cerebral hemorrhage.


Los Angeles County Street Drug Identification Program. Los Angeles: Department of Health Services, County of Los Angeles, 1980.


This chapter discusses a wide variety of miscellaneous drugs, including stimulants, cocaine, inhalants, opiates, depressants, anabolic steroids, and designer drugs such as “ecstasy.”

**STIMULANTS**

Stimulants include drugs such as nicotine (see Chapter 71), caffeine, cocaine, and amphetamines. Cocaine and amphetamines are discussed in this section.

**Cocaine**

Cocaine (benzoylmethylecgonine) is a stimulant made from an alkaloid contained in the leaves of the coca bush, *Erythroxylon coca*. Its use goes back to the Inca people 3,000 years ago.

Crack or rock cocaine is a ready-to-smoke, potent, relatively inexpensive, and highly addictive freebase form of cocaine that is popular with adolescents and young adults. The use of crack by adolescents is associated with rapid addiction and with serious behavioral and medical complications.

**Prevalence**

Cocaine has been tried by about 8.6% of the seniors of the class of 2000, according to national survey results from the Monitoring the Future Study (Johnston et al., 2000); this represents a decrease from 17.3% in 1985 but an increase from 5.9% in 1994. The figures for use in the past year and 30-day use have increased slightly in the past several years. The annual use rate for seniors went from 4.0% in 1995 to 5.0% in 2000. The 30-day use changed from 1.8% in 1995 to 2.1% in 2000. **Figure 74.1** shows trends by region of the country.

![Figure 74.1](http://www.cdc.gov/mmwr/preview/mmwrhtml/ss4905a1.htm)


Crack cocaine had been used by 3.9% of high school seniors in 2000. The 1999 National Household Survey on Drug Abuse found that the annual number of new users of any form of cocaine rose between 1994 and 1998 from 514,000 to 934,000. However, this was less than during the early and middle 1980s, when the number of new initiates was about 1.6 million. The rate of initiation increased among youth 12 to 17 years of age, from 5.1 per 1,000 potential new users in 1992 to 13.1 in 1996, and remained level through 1999.

The highest rate of initiation of cocaine use has been in young adults age 18 to 25 years. The number of new users for this age group fell from a high of 872,000 in 1983 to 275,000 in 1994 and then increased to 444,000 in 1998. The new users of crack cocaine increased in the 12- to 17-year-old age group, from 92,000 in 1991 to 339,000 in 1998.

Data from the 1999 Youth Risk Behavior Survey (YRBS) ([http://www.cdc.gov/mmwr/preview/mmwrhtml/ss4905a1.htm](http://www.cdc.gov/mmwr/preview/mmwrhtml/ss4905a1.htm)) indicated that 9.5% of students had used some form of cocaine during their lifetime. White and Hispanic students (9.9% and 15.3%, respectively) were significantly more likely than black students (2.2%) to report lifetime cocaine use. In addition, male students were more likely to report lifetime cocaine use, with the highest rate found among male Hispanics (18.3%). Use rose with grade level, from 5.8% in grade 9 to 13.7% in grade 12. Nationwide, 4.0% of students had used cocaine at least once during the past 30 days. Current use was highest among Hispanic males (8.0%) and lowest for black males (1.0%). Most high school seniors surveyed believed that it would be very easy for them to obtain...
Cocaine: Routes of administration

<table>
<thead>
<tr>
<th>InjectionSite</th>
<th>Route of Administration</th>
<th>Start Time</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intramuscular</td>
<td>Injection Site</td>
<td>15 minutes</td>
<td>4 hours</td>
</tr>
<tr>
<td>Intranasal</td>
<td>Injection Site</td>
<td>15 minutes</td>
<td>3 hours</td>
</tr>
</tbody>
</table>

### 3. Mechanisms of Action

a. Stimulation of the presynaptic neurons releases neurotransmitters (primarily dopamine, serotonin, and norepinephrine) into the synaptic cleft, activating postsynaptic neurons.

b. Cocaine blocks reuptake of the neurotransmitters, causing synaptic entrapment. This entrapment leaves an excess of neurotransmitters in the synapse, where they continue to stimulate the postsynaptic receptors. Depletion occurs as entrapped neurotransmitters are broken down by enzymes. Depletion leaves the user feeling dysphoric, with feelings of irritability, restlessness, and depression. This downside can be so intense that it leads to repeated use to overcome the dysphoric feeling. This can rapidly lead to cycles of highs and lows.

c. Cocaine increases the sensitivity of the postsynaptic receptor sites. The central nervous system (CNS) stimulation leaves the user alert, full of self-confidence, and feeling immune to outside influences.

d. Similarities between cocaine and amphetamines: Both drugs achieve their reinforcing effects via profound stimulation of the mesolimbic/mesocortical dopaminergic neuronal system, which consists of the ventral tegmental area, nucleus accumbens, ventral pallidum, and medial prefrontal cortex. Repeated exposure results in either sensitization or tolerance depending on dose and pattern of use. Intake of either drug causes neuroadaptation, a process that explains many of the disease aspects of addiction. Sensitization is mediated by the D1 and D2 dopamine receptors. The study of the neurochemical pathways underlying these neuroadaptations is facilitating new approaches to treatment, such as N-methyl-D-aspartate (NMDA) receptor antagonists that block both dopaminergic and reinforcing effects.

### 4. Street Names

Street names include coke, Bernice, blow, bump, C, candy, Charlie, flake, nose candy, rock, toot, base, snow, crack, and gold dust. Various drug combinations are in use:

- **Speedball:** Heroin and cocaine. The term was synonymous with intravenous use but now can refer to administration of any opiate with cocaine in close temporal proximity by any route. Other names for this combination include Belushi, birdie powder, dynamite, foo-foo stuff, joy powder, junk, lace, and leaf.
- **Primo:** Cocaine and marijuana, smoked
- **Space base:** Cocaine and phenycyclidine (PCP), smoked
- **Caviar or champagne:** Rock or crack cocaine and marijuana, smoked
- **Jim Jones:** Marijuana cigarette dipped in PCP
- **Snowcap:** Cocaine sprinkled on a bowl of marijuana. Other names for this combination include banana, blunt, bush, cocoa puff, hoofer, and woolas.
- **Space baring:** Rock or crack cocaine with PCP and tobacco
- **Whacking:** Rock or crack cocaine with PCP and tobacco, smoked
- **Blotter:** Cocaine combined with LSD
- **C and M:** Cocaine combined with morphine
- **Snow seals or turkey:** Cocaine and amphetamines

### 5. Clinical Use

Cocaine is used primarily by otolaryngologists, plastic surgeons, and emergency medicine physicians to provide local anesthesia and vasoconstriction of...
Symptoms of intoxication (Table 74.2)

1. Symptoms of intoxication (Table 74.2)

a. General: Hyperalert state, increased talking, restlessness, elevated temperature, anorexia, nausea, dry mouth, dilated pupils, sweating
b. Neurological: Seizures, dizziness, paresthesias, hyperactive reflexes, tremor
c. Psychiatric: Labile affect, insomnia, delirium, aggression, elation, euphoria, hallucinations, agitation, irritability, anxiety, skin picking (the act of picking at imagined bugs under the skin, formication), suspicious feelings
d. Cardiac: Arrhythmias, hypertension, tachycardia

2. Symptoms of overdose
a. General: Dry mouth, nausea, vomiting, anorexia, dilated pupils, excessive sweating, increased talking, flushing, increased temperature, respiratory failure
b. Neurological: Seizures, paresthesias, hyperactive reflexes, tremor, pinprick analgesia, facial grimaces, headache, coma
c. Psychiatric: Toxic psychosis, skin picking, paranoid behavior, anxiety, delirium, body image change, hallucinations, irritability
d. Cardiac: Tachycardia, angina, arrhythmias, chest pain, hypertension, cardiovascular collapse
3. Complications: Until recent years, cocaine overdose was thought to be rare. However, particularly with the advent of crack cocaine use, many deaths caused by cardiovascular or respiratory collapse have been reported. The pathogenesis of these cardiovascular complications has not been fully elucidated, but it may be related to the combination of sympathomimetic and membrane anesthetic effects of cocaine.
a. Cardiovascular: Chest pain, arrhythmias, hypertension, myocardial infarction, cardiomyopathy, myocarditis, stroke
b. Psychiatric: Depression, schizophrenia, psychosis, toxic delirium, anxiety, paraesthesia, suicide
c. Neurological: Seizures, headaches, cerebral hemorrhage, cerebral infarctions, cerebral vasculitis
d. Malnutrition
e. Hyperpyrexia
f. Obstetric: Placental abruption, lower infant weight, prematurity, microcephaly
g. Pulmonary: Pneumothorax, pneumomediastinum, pneumopericardium, pulmonary edema, pulmonary hemorrhage
h. Skin: Burns and skin infection
i. Head and neck: Erosion of dental enamel, gingival ulceration, keratitis, chronic rhinitis, perforated nasal septum, midline granuloma, altered olfaction, optic neuropathy, osteolytic sinusitis
j. Sexual dysfunction
k. Renal: Rhabdomyolysis
l. Endocrine: Hyperprolactinemia
m. Gastrointestinal
   • Acute ischemic syndromes are the most prominent gastrointestinal complication of cocaine use. Severe ischemia can result from intense activation of α-adrenergic receptors in the mesentery. This can lead to gastroparesic ulcers, gangrene, perforation of both small and large intestines, and colitis.
   • Massive overdose has occurred after rupture of small bags of cocaine swallowed by an individual in an attempt to transport the cocaine; this type of overdose has been called “body packer syndrome.”
   • Several cases of acute hepatotoxic effects and hepatocellular necrosis from cocaine use have also been reported (Gourgoutis and Das, 1994).
4. Symptoms of post-cocaine-use dysphoria: Depression, sadness, crying spells, suicidal ideation, melancholia, apathy, inability to concentrate, delusions, anorexia, insomnia, and paranoia (especially regarding police).
5. Symptoms of cocaine abstinence or withdrawal (Table 74.2)
a. These symptoms include depression, anhedonia, irritability, aches and pains, restless but protracted sleep, tremors, nausea, weakness, intense cravings for more cocaine, slow comprehension, suicidal ideation, lethargy, and hunger.
b. Cocaine causes strong dependence, as evidenced by the resulting cravings to alleviate depression and irritability when the drug’s effects wear off.
c. There is currently no widely accepted treatment of cocaine withdrawal. Although many uncontrolled studies have been reported in the literature, no drug has been proven effective in controlled studies.
6. Tolerance
a. Because of cocaine’s powerful euphoriant effects and its short half-life, repeated use leads to rapid development of tolerance; addicts can progress from small doses to large daily quantities in a short period.
b. No tolerance develops to the cardiovascular side effects.
7. Metabolism
a. About 80% of cocaine is metabolized by hepatic esterases and plasma cholinesterase to benzoylecgonine and ergonine methylester; both are metabolically active and can result in significant morbidity or mortality.
b. Anything that decreases hepatic perfusion, such as hypotension or low cardiac output, results in increased cocaine levels. Plasma cholinesterase activity is lower in pregnant women, fetuses, infants, and patients with liver disease. Plasma cholinesterase can also be low as a result of genetic or nutritional causes.
   In these patients adverse reactions or sudden death can occur after seemingly small doses of cocaine.
c. Between 10% and 15% of cocaine is metabolized by hepatic N-demethylation into norcocaine. In addition to being metabolically active, norcocaine has greater vasocostrictive activity than cocaine or other metabolites. Progesterone increases hepatic N-demethylation, resulting in increased formation of norcocaine. Therefore, as a result of hormonal potentiation, women may be more sensitive to the cardiotoxic effects of cocaine.

**TABLE 74.2. Effects of stimulants**

<table>
<thead>
<tr>
<th>Effect</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neurological</td>
<td>Seizures, dizziness, paresthesias, hyperactive reflexes, tremor</td>
</tr>
<tr>
<td>Psychiatric</td>
<td>Toxic psychosis, skin picking, paranoid behavior, anxiety, delirium, body image change, hallucinations, irritability</td>
</tr>
<tr>
<td>Cardiac</td>
<td>Tachycardia, angina, arrhythmias, chest pain, hypertension, cardiovascular collapse</td>
</tr>
<tr>
<td>Obstetric</td>
<td>Placental abruption, lower infant weight, prematurity, microcephaly</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>Pneumothorax, pneumomediastinum, pneumopericardium, pulmonary edema, pulmonary hemorrhage</td>
</tr>
<tr>
<td>Skin</td>
<td>Burns and skin infection</td>
</tr>
<tr>
<td>Head and neck</td>
<td>Erosion of dental enamel, gingival ulceration, keratitis, chronic rhinitis, perforated nasal septum, midline granuloma, altered olfaction, optic neuropathy, osteolytic sinusitis</td>
</tr>
<tr>
<td>Sexual</td>
<td>Dysfunction</td>
</tr>
<tr>
<td>Renal</td>
<td>Rhabdomyolysis</td>
</tr>
<tr>
<td>Endocrine</td>
<td>Hyperprolactinemia</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>Acute ischemic syndromes are the most prominent gastrointestinal complication of cocaine use. Severe ischemia can result from intense activation of α-adrenergic receptors in the mesentery. This can lead to gastroparesic ulcers, gangrene, perforation of both small and large intestines, and colitis.</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>Chest pain, arrhythmias, hypertension, myocardial infarction, cardiomyopathy, myocarditis, stroke</td>
</tr>
<tr>
<td>Psychiatric</td>
<td>Depression, schizophrenia, psychosis, toxic delirium, anxiety, paraesthesia, suicide</td>
</tr>
<tr>
<td>Neurological</td>
<td>Seizures, headaches, cerebral hemorrhage, cerebral infarctions, cerebral vasculitis</td>
</tr>
</tbody>
</table>

**Treatmen of Cocaine Toxicity**

1. A, B, C (Airway, Breathing, Circulation): Support respiratory and cardiovascular functions. Frequent monitoring of vital signs, cardiac monitoring, intravenous access, and pulse oximetry should be used.
2. Remove any residual cocaine from the patient’s nostrils.
3. Any patient with altered mental status or acute psychiatric signs or symptoms should have a blood glucose determination as soon as possible (stat) to rule out hypoglycemia, followed by 50 mL of 50% dextrose in water (D50W) plus 100 mg of thiamine.
4. Treat arrhythmias: Controversy remains regarding appropriate therapy. Recommendations are derived from Guidelines 2000 for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care, which is available at www.currentsonline.com/adobe/fall2000.pdf for details.
   a. Atrial tachydysrhythmias: Treat with immediate oxygen and sedation (benzodiazepines) and the use of labetalol. Benzodiazepine caution: Decrease dose when medications inhibiting the metabolism and clearance of benzodiazepines (e.g., nicotine, cimetidine [Tagamet]) are used by the patient. Also note the precaution (later in this chapter) regarding the use of β-blockers in patients with potential cardiac ischemia and cocaine toxicity.
   b. Ventricular arrhythmias: Guidelines 2000 recognizes the theoretical contraindications of lidocaine in the setting of cocaine poisoning; however, the recommendations based on extensive clinical experience state that lidocaine is safe and effective. The guidelines state that in most cases of drug-induced ventricular fibrillation or monomorphic ventricular tachycardia, lidocaine is the antiarrhythmic of choice (following advanced cardiac life support protocols).
   c. Ventricular ectopy
      • Usually transient
      • Treat with careful observation and escalating doses of benzodiazepine in an attempt to blunt thehypersympathetic state.
d. Malignant ventricular ectopy and perfusing ventricular tachycardia: Treatment includes oxygenation; benzodiazepine; antidysrhythmic medications (e.g., bretylium); and, if ventricular arrhythmias still persist, defibrillation.

e. Paroxysmal supraventricular tachycardia, atrial flutter, and rapid atrial fibrillation.
   • Generally short-lived
   • With drug-induced hemodynamically significant tachycardia (HST), adenosine and synchronized cardioversion should be avoided, because the tachycardia is likely to recur or to be refractory. Benzodiazepines are usually safe and effective for patients with drug-induced HST.

5. Cocaine-associated chest pain: Treatment includes nitroglycerin and benzodiazepines; Guidelines 2000 recommends phenotolamine as a second-line agent.

6. Thrombolysis indications
   a. ECG results consistent with an acute MI. Early repolarization changes on ECG can be difficult to distinguish from acute MI changes.
   b. Absence of conventional contraindications
   c. Up to 43% of patients with cocaine-related chest pain meet standard ECG criteria for thrombolysis despite being cardiac marker-negative for infarction.
   d. Thrombolysis contraindications: Hypertension or CNS vasculitis, in which percutaneous transluminal coronary angioplasty (PTCA) is safer

7. Hypertension secondary to cocaine use
   a. Direct CNS stimulation by cocaine: Treat with intravenous benzodiazepines.
   b. Peripheral a-agonist effects: Treat with vasodilator, nitroglycerin, or nitroprusside.
   c. Hypertension associated with chest pain: Nitroglycerin is the drug of choice.


10. Benzphetamine (Didrex): Yellow (25 mg) or pink (50 mg) tablets.

11. Methamphetamine (Desoxyn): Often referred to as speed, crystal, or meth

12. Amphetamine (Dexedrine), amphetamine hydrochloride (Vicks Inhaler). Methamphetamine HCl is much more versatile than the hydrochloride salt of cocaine. It has high bioavailability in the salt form by any route of administration, and illicit production occurs in homes, workshops, recreational vehicles, and rural cabins. Methamphetamine is a derivative of phenylethylamine. The substances differ structurally in that a methyl group attaches to the terminal nitrogen to form methamphetamine. The federal government and some states have enacted laws decreasing the availability of necessary precursor chemicals. Many of these agents can still be obtained in neighboring states or countries.

13. Bretylium; and, if ventricular arrhythmias still persist, defibrillation.

Note: Use of b-blockers in the subset of patients with acute coronary syndromes and cocaine toxicity has been associated with coronary vasocnstriction and should be avoided. Instead, nitrates should be the first line of therapy as well as benzodiazepines. a-Adrenergic blocking agents may induce tachycardia and hypotension and should be reserved for patients who do not respond to nitrates and benzodiazepines.

Cocacethylene

When alcohol is used in conjunction with cocaine, a third substance, cocacethylene, is formed in the liver (Rose, 1994). Cocacethylene increases the toxicity of cocaine, particularly on the heart. When alcohol is ingested and metabolized along with cocaine, the risk of sudden cardiac death is increased 25 times. In animal models cocacethylene is more likely to result in seizure activity. The half-life of cocacethylene is 2 hours, compared with 38 minutes for cocaine, and it is also able to block dopamine reuptake, thereby extending the period of intoxication and toxicity.

Amphetamines, Methamphetamine, and "Look-Alikes"

Amphetamines are CNS stimulants that work as sympathomimetic drugs. Amphetamines act on the CNS to cause the release of neurotransmitters from presynaptic neurons, and they directly stimulate postynaptic catecholamine receptors. They also prevent reuptake of neurotransmitters and act as a mild monoamine oxidase inhibitor. Routes of administration include oral ingestion, snorting, and intravenous administration. The characteristics of amphetamines are similar to those of cocaine.

Production and Synthesis

By the late 1970s, it was thought that the vast majority of street methamphetamine was actually "look-alike" methamphetamine comprising caffeine, ephedrine, and phenylpropanolamine. During the early 1980s, a process using ephedrine to synthesize methamphetamine became popular. Synthesis is relatively easy, and illicit production occurs in homes, workshops, recreational vehicles, and rural cabins. Methamphetamine is a derivative of phenylethylamine. The substances differ structurally in that a methyl group attaches to the terminal nitrogen to form methamphetamine. The federal government and some states have enacted laws decreasing the availability of necessary precursor chemicals. Many of these agents can still be obtained in neighboring states or countries.

The methamphetamine reduction by ephedrine is an acidic-soluble pure base form that is fairly volatile and can evaporate if left exposed to room air. This product is converted to the water-soluble form, methamphetamine HCI salt. Illicitly synthesized methamphetamine may be contaminated by organic or inorganic impurities. Poisoning from heavy metals (e.g., lead, mercury) or from solvents used in the synthesis process have been reported. Exposures to carcinogenic materials have been noted. Street methamphetamine may be mixed with many drugs, including cocaine. Studies show that 8% to 20% of street-available stimulants contain both drugs. In a report on cocaine intoxication, 7% of patients sought medical help because of the concurrent use of cocaine and amphetamines.

The production process described here results in a high yield of D-methamphetamine, which is cortically more active than the L-isomer (the active ingredient in Vicks Inhaler). Methamphetamine HCI is much more versatile than the hydrochloride salt of cocaine. It has high bioavailability in the salt form by any route of administration, such as snorting, smoking, ingesting by mouth, or passing across other mucous membranes such as the vaginal mucosa. "Ice" consists of pure crystals of D-methamphetamine. There is no difference between smoking street speed and smoking ice.

There are areas in the western and southwestern United States where methamphetamine is the predominant stimulant of abuse. Look-alikes containing combinations of caffeine, ephedrine, and phenylpropanolamine are particularly dangerous. A much larger dose is necessary to achieve the same level of cortical stimulation, as with amphetamines. This combination has greater cardiovascular stimulation to begin with, so abuse of look-alikes puts the user at great risk for stroke, MI, or hypertensive crisis.

Dose, Medical Use, and Street Names

The most common dosage forms of amphetamines include the following:

1. Dextroamphetamine sulfate (Dexedrine): Orange, heart-shaped tablets, often referred to as hearts, oranges, or dexies
2. Methamphetamine (Desoxyn): Often referred to as speed, crystal, or meth
3. Amphetamine sulfate (benzphetamine sulfate): Rose-colored, heart-shaped tablets, often called hearts or peaches, or as oval tablets called footballs
4. Benzphetamine (Didrex): Yellow (25 mg) or pink (50 mg) tablets
5. Most "cross-tops": Now actually ephedrine
6. Smoking form: Smoking methamphetamine is becoming very common. On the streets, this form is sometimes referred to as "ice," or as "crack" if it is mixed with crack cocaine. Smoking crack (methamphetamine (ice) may be more addictive and more potent than snorting or ingesting it; smoking produces higher concentrations of drug in the brain for a shorter period. One reason for the popularity of smoked methamphetamine is the immediate clinical euphoria that results from rapid absorption in the lungs and deposition in the brain. The user places methamphetamine HCI powder, crystals, or ice into a piece of aluminum foil that has been molded into the shape of a bowl, a glass pipe, or a modified light bulb and heats it over the flame of a cigarette lighter or torch; then the volatile methamphetamine fumes are inhaled through a straw or pipe.

In terms of medical use, various forms of amphetamines have been used for weight loss, behavioral disorders of children, and narcolepsy. Their efficacy for weight loss is questionable.

Street names for amphetamines include A’s, meth, speed, crystal, cartwheel, copilots, footballs, magnums, powder, 20-20, whites, white crosses, crank, ice, ups,
Symptoms of intoxication, overdose, and abstinence are similar to those of cocaine. The mortality associated with amphetamines is related to use of amphetamines has also been associated with assaults, suicides, homicides, accidents, driving impairment, and renal failure related to use of amphetamines. It has been demonstrated that rates of subsequent substance abuse in adolescents are decreased by appropriate therapeutic use of amphetamine.

Complications of amphetamine overdose resemble those of cocaine. However, cocaine and the amphetamines are structurally dissimilar. Cocaine is an ester of benzoic acid; as a local anesthetic, it has pronounced effects on nerve membranes and therefore on conduction. Amphetamines are phenylisopropylamines with no direct cell membrane effects. Arrhythmias, seizures, and other medical complications are not as common with amphetamines, although the addiction potential is no less. Serious side effects include the following:

- Cardiac: Tachycardia, hypertension, atrial and ventricular arrhythmias, and MI. Cardiac ischemia may be secondary to thrombus formation or may result from amphetamine-induced hypertension and necrosis. Necrotizing angitis with arterial aneurysms and sacculations have been observed in kidney, liver, pancreas, and small bowel of methamphetamine drug abusers. Similarly, acute aortic dissections and arterial aneurysms have been associated with methamphetamine abuse.

- CNS effects: Seizures, psychosis, choreoathetoid movement disorders, cerebrovascular accidents due to hemorrhage or vasospasm, cerebral edema, and cerebral vasculitis.

- Respiratory effects: Pneumoniediastinum, pneumothorax, and pneumopericardium; acute noncardiogenic pulmonary edema; and pulmonary hypertension.

- Renal effects: Renal failure related to hypoxemia, rhabdomyolysis, necrotizing angitis, and cardiovascular shock with subsequent acute tubular necrosis.

- Hepatic effects: Hepatocellular damage has been reported with amphetamines, malondialdehyde (MDA), and 3, 4-methylenedioxyamphetamine (MDMA) after acute and chronic abuse. Direct toxic effects (e.g., hypotension, hepatotoxicity, effects of contaminants, hepatic vasoconstriction, lipid peroxidation, occult viral causes, necrotizing angitis) have been postulated as mechanisms for the amphetamine-induced hepato-cellular toxicity.

- Gastrointestinal effects: Absence of amphetamine also has been associated with the formation of giant gastrointestinal ulcers and ischemic colitis.

- Mortality: Deaths related to use of amphetamines have also been associated with assaults, suicides, homicides, accidents, driving impairment, and maternal-fetal and infant exposures. In one study in Belgium of drug abuse and alcohol consumption related to motor vehicle accidents, methamphetamine was the most commonly found drug other than alcohol.

**Treatment of Amphetamine Toxicity** (Further information is provided in the section on treatment of cocaine toxicity.)

1. Support respiratory and circulatory function.
2. If the clinical presentation suggests significant ingestion or possible coinjection, aggressive use of a large-bore (40 Fr) orogastric tube and multiple-dose activated charcoal (1 g/kg body weight) is mandatory.
3. Agitation
   - a. Because of the ability of methamphetamine to cause significant CNS and psychiatric activation, patients who present to emergency departments for acute intoxication may require pharmacological intervention.
   - b. Hyperactive or agitated persons should be treated with droperidol or haloperidol. These are butyrophenones and dopamine-blocking agents that specifically antagonize the central behavioral effects of methamphetamine. Multiple clinical reports attest to the efficacy of droperidol and haloperidol in acute amphetamine toxicity.
   - c. Patients with acute choreoathetoid syndrome associated with use of amphetamines may show rapid improvement with haloperidol.
   - d. The doses of these medications should be titrated to the symptoms and administered intravenously.
   - e. Droperidol instead of diazepam or lorazepam: Diazepam was found to be highly effective in antagonizing the toxic effects of cocaine but not as effective against amphetamines in animal models. In a recent study of 146 patients presenting to an emergency department, agitated, violent, or psychotic reactions from methamphetamine responded better to droperidol than to lorazepam, with more rapid and more profound sedation (Richards et al., 1998). Both drugs produced clinically significant reductions in pulse, systolic blood pressure, respiration rate, and temperature over a 60-minute period.
   - f. Avoid chlorpromazine (Thorazine) because of the possibility of a severe drop in blood pressure, anticholinergic crisis, or seizure activity (see earlier discussion of cocaine toxicity treatment). Beyond 5 to 10 mg of haloperidol or droperidol, the sedating benefit is minimal and benzo diazepines should be added.
   - g. Treat arrhythmias: Arrhythmias are not as common or as severe as in the cocaine-related disorders. The arrhythmias usually respond to sedation (see Agitation).

5. Hyperesthesia: Treat hyperesthesia as described previously.
   - a. If sedation fails, several antihypertensive agents, including short-acting intravenous b-blockers or direct short-acting vasodilators, are effective in reversing some methamphetamine-induced hypertension.
   - b. Theoretically, intravenous labetalol would be the best agent because of its combined anti-a-adrenergic and anti-b-adrenergic effects. However, when given intravenously, labetalol loses much of its anti-a-adrenergic effect. These drugs should be given in small intravenous doses and titrated to effect. However, some methamphetamine-induced hypertension.
   - c. Monitor suicide potential after toxic condition has lessened.

Ritalin (Methylphenidate)

With the increase in diagnosis of attention deficit hyperactivity disorder (ADHD) in children and in adults more methylphenidate (Ritalin) is being diverted as a drug of abuse. The drug is frequently nasally inhaled by adolescents. Case reports of sudden death have been described. The CNS effects are comparable to those of the amphetamines. It has been demonstrated that rates of subsequent substance abuse in adolescents are decreased by appropriate therapeutic use of this and other CNS stimulants.
stilnt medications in patients with the diagnosis of ADHD.

Khat (Cathine, Cathinone)

Cathinone is chemically similar to d-amphetamine, and cathine (p-norisoephedrine) is a milder form of cathinone. These compounds are the active ingredients in khat leaves (Catha edulis), which are used as a tea or chewed for their euphoriant and stimulant effects by persons in Africa, the Middle East, and corresponding immigrant and refugee communities in developed nations. The plant grows as a large flowering evergreen shrub or tree. If left unrefrigerated, the cathinone degrades within 48 hours, explaining the preference for fresh leaves. The U.S. Drug Enforcement Agency has classified cathinone as a schedule IV narcotic, whereas cathine remains a schedule IV controlled substance. The most common uses of khat are by African or Arab sellers and is used within cultural norms with little evidence of abuse. Khat-induced psychosis is rare but has been described in the literature; it most commonly occurs in the context of nonculturally sanctioned polydrug abuse. Western physicians are frequently unaware of the widespread use of and availability of khat in certain African and Arabian communities. Susceptible children and adolescents in these communities are at risk because khat can potentially act as a gateway substance when the protective context of culture and family are absent.

In Russia, methcathinone synthesis from ephedrine in makeshift home laboratories is widespread, and it is one of the most common drugs of abuse, after alcohol and tobacco. When ephedrine is reduced, the hydroxy group is lost and methamphetamine results. When this group is oxidized, methcathinone is produced. Clandestine laboratories producing this substance appeared in the midwestern United States in the 1990s, yet production has been limited and methcathinone has failed to achieve the abuse status of other substances. In Russian immigrant and refugee communities, knowledge of and possibly experience with methcathinone may predispose at-risk individuals to seek out methamphetamine or other stimulants. In either population, abuse of khat or methcathinone or a family history of such should be suspected in the substance-abusing adolescent from a representative community.

Betel Nut

Though betel nut is unknown to most Western physicians, it is chewed on a daily basis by 15% of the world’s population (600 million people). It is chewed alone or more commonly, in a “quid.” The quid consists of betel nut, catechu gum (produced from the sap of the Malaysian acacia tree), and calcium hydroxide paste (produced by burning limestone, reef coral, or shells) wrapped in betel leaf. This combination is placed in the lateral gingival pocket, and the strongly alkaline salvia-generated calcium hydroxide solution activates enzymes in the catechu gum, releasing eugenol (betel oil) from the betel leaf. Eugenol contains two psychotropic phenols, betel-phenol and chavicol, and an alkaloid stimulant called cadinene that has cocaine-like properties. Betel nut releases arecoline, a volatile cholinergic alkaloid and CNS stimulant. Tobacco is frequently added to the quid.

More than 4% of the U.S. population is of Asian or Pacific Island descent, and the use of betel nut (with or without tobacco) is culturally accepted in these communities. Most youth in these communities have experimented with this substance by adolescence. Dependence occurs rapidly, and if the individual leaves the community, transition to tobacco products is common. Once again, a knowledge of traditional cultural practices is key to diagnosis.

INHALANTS

General

Inhalants can be classified as volatiles, aerosols/propellants, and anesthetics. Included are spray paints, plastic cement (model-airplane glue), rubber cement, typewriter-correction fluid, gasoline, nitriles, and nitrous oxide. Fluorinated propellants are no longer used in hair sprays and deodorants, although other propellants have been abused (e.g., isobutane). They are often the first mood-altering substance used by children. Use of inhalants decreases with increasing age, but studies show that inhalant abusers are at increased risk for abuse of alcohol and illicit drugs.

Prevalence

The 2000 national survey on drug use from the Monitoring the Future Study (Johnston et al., 2001) found that 14.2% of the 12th graders had tried inhalants; 5.9% had used them within the year and 2.2% within the month before the survey. Use within the past year was highest among 8th graders (9.4%, versus 7.3% of 10th graders and 5.9% of 12th graders). Use in 8th graders was down from recent years (10.3% in 1999, 11.1% in 1998, 11.8% in 1997). The 1999 YRBS showed that 14.6% of high school students had ever used inhalants. The use rate ranged from 16.5% of 9th graders to 11.3% of 12th graders. Use was high among Hispanic and white students (16.4% and 16.1%, respectively) and much lower among black students (4.5%). “Fad” use also occurs sporadically and may occur after news reports of a certain trend or a media portrayal of inhalant use. In addition, new types of volative abuse have emerged in factory workers exposed to solvents, who may take them home for use on weekends or evenings. In addition, amyl nitrate (poppers), butyl nitrite vials (rush), and nitrous oxide have become popular.

Pathophysiology

Inhalants are attractive to adolescents because of their rapid onset of action, low cost, and easy availability. They are typically used by inhaling from a plastic bag containing the substance (“bagging”) or by inhaling a cloth saturated with the substance (“huffing”). The initial effect is stimulation and excitation, which then progresses to a depressant effect on the CNS. Of the myriad products and substances abused, toluene is the most common volatile component. It is present in spray paint, airplane glues, rubber cement, cleaning fluids, inks (magic markers), and lacquer thinner.

Symptoms of Intoxication

1. General: Lacrimation, rhinorrhea, salivation, irritation of the mucous membranes, anorexia, vomiting, sleepiness
2. Neurological: Dizziness, headaches, slurred speech, ataxia, diplopia
3. Psychiatric: Euphoria, decreased inhibition, decreased judgment
4. Symptoms Caused by Specific Inhalant Groups
   a. Solvents: Bronchitis, liver damage, renal damage, CNS damage, coma, cardiac arrhythmias
   b. Amyl and butyl nitriles: Methemoglobinemia
   c. Gasoline: Lead poisoning
   d. Aerosol sprays: Giddiness and hallucinations lasting 5 to 10 minutes
5. Trauma and accidental injury may also occur during inhalant abuse.

Symptoms of Overdose

1. Slow and shallow respirations
2. Delirium
3. Arrhythmias
4. Stupor
5. Seizures
6. Loss of consciousness
7. Cardiopulmonary arrest and death
8. Sudden sniffing-death syndrome
   a. Not associated with toluene
   b. Has occurred after inhalation of fluorocarbons or halogenated hydrocarbons
   c. Postulated mechanism involves sensitization of the myocardium by the solvent to the arrhythmogenic effects of epinephrine and increased sympathetic outflow, which occurs during the initial brief excitatory phase of intoxication.

Treatment

Treatment is aimed at control of arrhythmias and respiratory and circulatory support. Although tolerance to inhalants may develop, withdrawal symptoms do not usually occur.

Nitrous Oxide

Also known as laughing gas, nitrous oxide (N₂O) has long been abused by health care personnel. More recently there has been a resurgence of interest in the adolescent population. It is most commonly sold in small balloons or inhaled from whipped-cream cans, in which it is used as a propellant. Occasionally, individual
Symptoms of narcotic overdose

Induce analgesia
Cardiac: Hypertension, tachycardia
Cause vasodilation, with a resultant fall in blood pressure
Cardiac: Circulatory collapse and hypotension
Induce constriction of the pupils
General: Muscle aches, chills, coryza, flulike symptoms, lacrimation, muscle spasms, nausea, vomiting, piloerection, sweating, increased respiratory rate and
Cause sedation, narcosis, or stupor
Protracted abstinence syndrome includes miosis, hyposensitive respiratory center, decreased pulse, decreased blood pressure, decreased temperature, poor
Neurological: Paresthesia, tremors, ejaculation/orgasm, mydriasis
Increase nonpropulsive contractions of the intestines
General: Pinpoint pupils, slow and shallow respirations, decreased temperature, pulmonary edema, constipation, cyanosis
Symptoms of intoxication: Anxiety, slow comprehension, euphoria, floating feeling, flushing, hypotonia, pinpoint pupils, skin picking, sleepiness, and constipation
Gastrointestinal: Abdominal cramps, diarrhea
Newer synthetic narcotics, such as fentanyl, are 80 times more potent than morphine (see
Psychiatric: Delirium
Psychiatric: Anxiety, sleep disturbances, supplicating behavior, irritability, restlessness
d. Cardiac: Hypertension, tachycardia
e. Gastrointestinal: Abdominal cramps, diarrhea
Complications

users gain access to a tank of nitrous oxide. Deaths have occurred after prolonged inhalation of 100% N₂O in a closed space.

Nitriles

Amyl, butyl, and isobutyl nitrite are examples of nitriles. They are volatile liquids abused for their vasodilatory action and subjective feeling of light-headedness
(which is known as the "rush"). Amyl nitrite requires a prescription and is currently indicated in cyanide poisoning to produce methemoglobin. Butyl and isobutyl nitrite are
available over the counter (commonly in "head shops") as a room deodorizer, cologne, or liquid incense.

Individuals abusing nitriles rarely seek medical attention for complications of abuse. The most common side effects are severe headache, dizziness, orthostatic hypotension,
and occasional syncope. These effects are a result of smooth muscle relaxation. Clinically significant methemoglobinemia is extremely rare as a
complication of nitrite abuse. Definitive evidence linking nitriles, immunosuppression, Kaposi sarcoma, and infection with human immunodeficiency virus are lacking.

OPIOIDS

Opium has been known and used for centuries. The term opioid refers to all drugs, natural and synthetic, with morphine-like activity, as well as antagonists that bind to
opioid receptors. All opiates are derived from the opium poppy. Papaver somniferum. The plant is grown primarily in the Middle East and in the Far East. Crude opium
is obtained from the seed pods of the poppy. From this crude opium, morphine, codeine, and heroin are manufactured. The cost of heroin addiction in the United
States is more than $3 billion per year. In general, the drug is unpopular among adolescents; however, the recent trend of smoking heroin provides a route of
administration that is familiar to many, and heroin use appears to be on the increase. Heroin dependence, regardless of the chosen route of administration, creates
intense addictive disease and carries at best a guarded prognosis.

Physical toxic symptoms of all opioids include pupillary constriction, drowsiness or coma, decreased respiratory rate, decreased heart rate, pulmonary edema, slurred speech, and impairment in attention. Psychiatric toxicity symptoms include initial euphoria, apathy, dysphoria, psychomotor agitation or retardation, impaired
judgment, impaired social functioning, and impaired occupational functioning.

Equivalent doses of various opioids is reviewed in Table 74.3.

TABLE 74.3. Equivalent doses of opioids

Heroin

Action, Dose, and Street Names Heroin is morphine treated with acetic acid. It has a stronger and faster onset of action than morphine and acts on both the CNS
and the peripheral nervous system to

1. Induce analgesia
2. Cause sedation, narcosis, or stupor
3. Act as a respiratory depressant
4. Block the cough reflex
5. Cause vasodilation, with a resultant fall in blood pressure
6. Increase nonpropulsive contractions of the intestines
7. Induce constriction of the pupils

Heroin in the United States is usually only about 5% pure. It is commonly mixed with sugar, talcum powder, Epsom salt, or quinine. This mixture is usually heated into
a solution and injected intravenously. Besides leg and arm veins, the veins between the toes, the veins under the tongue, and the dorsal vein of the penis are often
used for injection. Heroin is sometimes injected under the skin ("skin popping") or snorted in the same manner as cocaine; the effect is less intense with any of these
methods than with intravenous use. The duration of the effects of intravenously injected heroin is 3 to 6 hours.

Street names for heroin include smack, scat, junk, horse, H. Jones, shit, hard stuff, brown, chiva, do-jea, estufa, hombre, mud, polvo, and stofa.

Prevalence Heroin use, particularly noninjection use, has increased significantly in past 10 years. There has been a trend toward increased snorting and smoking of
opiate derivatives among adolescents. In the Monitoring the Future survey (Johnston et al., 2001), the rate of "ever use" (lifetime use) among 12th graders increased
from 0.9% in 1991 to 2.4% in 2000. This was the highest reported use rate since the beginning of the study. Use was much higher without a needle than with a needle
(2.4% versus 0.8%). Among high school seniors, use was 1.5% within the past year, 0.7% within the past 30 days, and 0.1% for daily use.

Effects

1. Symptoms of intoxication: Anxiety, slow comprehension, euphoria, floating feeling, flushing, hypotonia, pinpoint pupils, skin picking, sleepiness, and constipation
2. Newer synthetic narcotics, such as fentanyl, are 80 times more potent than morphine (see Table 74.3) and pose an increased danger of death by overdose.
3. Symptoms of narcotic overdose
   a. General: Pinpoint pupils, slow and shallow respirations, decreased temperature, pulmonary edema, constipation, cyanosis
   b. Neurological: Pinprick analgesia, ataxia, stupor, slow comprehension, hypotonia, diminished reflexes, coma
c. Psychiatric: Delirium
d. Cardiac: Circulatory collapse and hypotension
4. Symptoms of withdrawal include
   a. General: Muscle aches, chills, coryza, flulike symptoms, lacrimation, muscle spasms, nausea, vomiting, piloerection, sweating, increased respiratory rate and
temperature, yawning, hot and cold flashes
   b. Neurological: Paresthesia, tremors, ejaculation/orgasm, mydriasis
c. Psychiatric: Anxiety, sleep disturbances, supplanting behavior, irritability, restlessness
d. Cardiac: Hypertension, tachycardia
e. Gastrointestinal: Abdominal cramps, diarrhea
5. Protracted abstinence syndrome includes miosis, hyposensitive respiratory center, decreased pulse, decreased blood pressure, decreased temperature, poor
stress tolerance, decreased self-image, weakness, depression, fatigue, and hyposensitivity to carbon dioxide.

Complications
1. Pronounced tolerance: Physical and psychological dependence
2. Cutaneous: Abscesses, cellulitis, lymphadenitis, phlebitis, and tongue and penile lesions from injections
3. Pulmonary: Foreign fibers (talc, cotton), arteritis and thrombosis of the pulmonary vessels, septic emboli, lung abscesses, pulmonary fibrosis, pulmonary hypertension, pneumonia, and respiratory depression
4. Cardiac: Pulmonary edema, arrhythmias caused by quinine, and bacterial endocarditis
5. Infections: Hepatitis, endocarditis, septic arthritis, osteomyelitis, tetanus, tuberculosis, and acquired immunodeficiency syndrome (AIDS)
6. Myositis ossificans: Extraosseous metaplasia of muscle caused by needle manipulation
7. Neurological: Coma, seizures, transverse myelitis, polyneuropathy, cerebrovascular accidents, deafness, and infections (abscesses, meningitis, myotic aneurysm)
8. Crush injuries caused by immobility
9. Renal lesions: Nephrotic syndrome caused by hepatitis or foreign injected matter and focal glomerulosclerosis
10. Endocrine: Increased incidence of amenorrhea and infertility
11. Immunological: Hypergammaglobulinemia, false-positive VDRL test result in 23% of addicts, false-positive latex fixation result in 21% of addicts, and a defect in cellular immunity characterized by a decrease in lymphocyte responsiveness
12. Chronic constipation
13. Fetal effects: Opiate withdrawal during pregnancy threatens viability of fetus. Methadone maintenance is recommended.
14. Neonatal effects: Withdrawal in 70% of neonates, manifested by tremors, jitters, seizures, and tachypnea; 40% prevalence of low birth weight in neonates; respiratory compromise at birth

Treatment

1. Treatment of heroin overdose
   a. Support respiratory and circulatory function and assure an adequate airway.
   b. Treat hypoxia.
   c. Treat pulmonary edema with positive pressure.
   d. Treat hypothermia with volume expanders and pressors.
   e. Treat arrhythmias.
   f. Give naloxone (Narcan), 0.4 mg to 2 mg (usually 2 mg) intravenously; dose may be repeated every 5 minutes if no reaction occurs, up to 10 mg maximum. Usually, if there is no response after three intravenous doses, this indicates that the individual has an opioid overdose. Repeated doses may be needed in 2 to 3 hours as the naloxone wears off. It is important to remember that naloxone lasts for about 1 or 2 hours, most opioids last 3 to 6 hours, and methadone lasts 24 to 36 hours. Naloxone does not reverse hypotension that is caused by opiate-induced histamine release. Always observe the patient for at least 6 hours after the initial response to naloxone, because opiates, especially propoxyphene and methadone, have a longer half-life. The patient should be admitted to the hospital for observation. Longer-acting opiate antagonists will be available soon.
   g. Look for evidence of other drug involvement.
   h. Treat hypoglycemia, if present, with 50 mL of 50% glucose solution given intravenously.
   i. Look for and treat any infectious complications.
2. Treatment of withdrawal
   a. General support and reassurance
   b. Detoxification protocols
      • Methadone substitution with gradual detoxification—this requires a special state and federal Drug Enforcement Agency license. Methadone may be used by physicians for temporary maintenance or detoxification when an addicted individual is admitted to a hospital for a nonopioid addiction illness.
      • Clonidine detoxification: after 10 days, follow with naltrexone.
      • Clonidine detoxification without naltrexone.
   c. Symptomatic treatment of abdominal cramping (with dicyclomine [Bentyl]), bone pain, and insomnia
   d. Supportive treatment of chemical dependency with 12-step meetings, group therapy (see Chapter 75).
3. Methadone
   a. The use of methadone is strictly regulated by the federal government. The U.S. Food and Drug Administration (FDA) requires that detoxification, rather than methadone maintenance, be used for patients who have been dependent on opiates for less than 1 year. Patients who have been dependent on heroin for more than one year are eligible for methadone maintenance. Methadone should, however, be reserved for the most recalcitrant cases. The methadone withdrawal syndrome is protracted and extremely unpleasant. Perhaps not unjustifiably, methadone-dependent patients have a pathological fear of withdrawal. It is difficult to treat the methadone-dependent patient. Many patients also continue to use heroin, further confounding the potential for successful treatment. With the advent of AIDS, there has been a renewed public health interest in methadone programs. In some cities, clean needles, bleach, and condoms have been distributed in an attempt to curb the spread of AIDS among abusers of intravenous narcotics.

   Although methadone has been the major medication used for opioid maintenance, both levomethadyl acetate and buprenorphine are also similarly effective. Levomethadyl acetate, a synthetic opioid, was approved for treatment by the FDA in 1993. Levomethadyl acetate has a longer half-life than methadone, so it can be given three times a week rather than daily. Buprenorphine is a partial opioid agonist and therefore may have some advantages, including fewer withdrawal symptoms and a lower risk of overdose. It also is long-acting and can be used three times per week. In a study by Johnson et al. (2000), treatment with either of these three medications was effective in reducing illicit opioid use.
   b. Goals of methadone maintenance
      • Suppression of abstinence syndrome
      • Avoidance of euphoria and sedation
      • Inclusion of the individual in the treatment effort
      • Removal of the individual from criminal activity
      • Improvement of health status
      • Reduction of the risk of infection (AIDS, Hepatitis)
   c. Methadone maintenance is the treatment of choice for the person with intractable addiction.
   d. Methadone is the safest opiate during pregnancy.

DEPRESSANTS

The CNS depressants include the barbiturates; the nonbarbiturate hypnotic drugs such as glutethimide (Doriden) and methaqualone (Quaalude); the major tranquilizers (phenothiazines) and minor tranquilizers (benzodiazepines); and the carbamates such as meprobamate (Equanil and Miltown). Another depressant drug of concern has been flunitrazepam (Rohypnal).

Overall physical symptoms of sedative-hypnotic intoxication include slurred speech, incoordination, unsteady gait, nystagmus, decreased reflexes, impaired attention or memory, and stupor or coma. Overall psychiatric symptoms of intoxication include inappropriate behavior, mood lability, impaired judgment, impaired social functioning, and impaired occupational functioning.

Barbiturates

Barbiturates are hypnotic and sedative drugs derived from barbituric acid. More than 50 types of pills containing barbiturates are available in the United States. The most frequently abused barbiturates are secobarbital and pentobarbital.

Action, Dose, Type, and Street Names

Barbiturates are CNS depressants. Low doses result in mild sedation, higher doses result in hypnosis, and still higher doses result in anesthesia and possible death. Long-acting barbiturates have a strong anticonvulsant action and are popular antiseizure medications (i.e., phenobarbital).

Barbiturates are usually taken orally, although some users inject them intravenously. Many of the pills are made in Mexico and contain varying amounts of secobarbital.

Barbiturates are divided into ultrashort-acting, short-acting, intermediate-acting, and long-acting types. Equivalent doses of sedatives and hypnotics are presented in
1. Ultrashort-acting: Thiopental (Pentothal) and methohexital (Brevital), usually used for anesthesia
2. Short-acting: Secobarbital (Seconal) and pentobarbital (Nembutal), usually used as sleeping pills
3. Intermediate-acting: Amobarbital (Amytal) and butabarbital (Butisol)
4. Long-acting: Phenobarbital (Luminal)

Street names include reds, red devils, yellow jackets, tooies, blue heavens, purple hearts, Mexican reds, nebbies, nimbies, bluebirds, blue devils, blues, yellows, Christmas trees, trees, bars, beans, goofballs, and stumblers.

**Prevalence** The 2000 Monitoring the Future Study (Johnston et al., 2001) found that 9.2% of high school seniors interviewed had used barbiturates at some time in their life. Of reporting seniors, 5.8% had used barbiturates during the previous 12 months, and 3.0% had used them in the previous 30 days. Barbiturate use among high school seniors fell from 16.9% in 1975 to a low of 5.5% in 1992, after which the lifetime use increased to 9.2% in 2000.

**Side Effects**

1. Symptoms of intoxication
   a. General: Muscle aches, anorexia, fatigue, floating feeling, sleepiness, yawning
   b. Neurological: Ataxia, slow comprehension, diplopia, dizziness, dysmetria, hypotonia, poor memory, lateral nystagmus, slurred speech
   c. Psychiatric: Anxiety, delirium, depressed mood, euphoria, irritability, “toxic” psychosis, violent behavior
   d. Cardiac: Orthostatic hypotension
2. Symptoms of overdose include pinprick analgesia, ataxia, slow comprehension, delirium, orthostatic hypotension, hypotonia, irritability, lateral nystagmus, slow and shallow respirations, and bradycardia; coma, shock, and death are possible.
3. Physical dependence occurs with a severe withdrawal syndrome after the drug is stopped. The withdrawal syndrome can be fatal. The severity of the withdrawal syndrome parallels the strength of the drug, the dose used, and the duration of prior abuse. Withdrawal symptoms include:
   a. General: Abdominal cramps, flushing, nausea, sweating, increased temperature, weakness
   b. Neurological: Convulsions, headaches, grand mal seizures, hyperactive reflexes, tremor
   c. Psychiatric: Anxiety, delirium, hallucinations, irritability, “toxic” psychosis, sleep disturbance
   d. Cardiac: Tachycardia, orthostatic hypotension, circulatory collapse
4. Tolerance to barbiturates occurs through increased metabolism of the drug and by adaptation of the CNS to the drug’s effects. However, the lethal dose does not increase. Cross-tolerance to other depressant drugs can also be seen.
5. Physical dependence occurs with a severe withdrawal syndrome after the drug is stopped. The withdrawal syndrome can be fatal. The severity of the withdrawal syndrome parallels the strength of the drug, the dose used, and the duration of prior abuse. Withdrawal symptoms include:
   a. General: Abdominal cramps, flushing, nausea, sweating, increased temperature, weakness
   b. Neurological: Convulsions, headaches, grand mal seizures, hyperactive reflexes, tremor
   c. Psychiatric: Anxiety, delirium, hallucinations, irritability, “toxic” psychosis, sleep disturbance
   d. Cardiac: Tachycardia, orthostatic hypotension, circulatory collapse
4. Tolerance to barbiturates occurs through increased metabolism of the drug and by adaptation of the CNS to the drug's effects. However, the lethal dose does not increase. Cross-tolerance to other depressant drugs can also be seen.
6. Allergic reactions: Asthma, urticaria, dermatitis, fever, and angioneurotic edema can be caused by barbiturates.
7. Dermatological reactions: Cutaneous lesions and bullae are possible side effects.

**Treatment of Overdose**

1. A, B, Cs: Maintain adequate airway, respirations, and circulation. Use mechanical ventilation and treat shock as necessary. Supportive care is outlined in Chapter 75.
2. Remove unabsorbed toxins by gastric lavage if ingestion is recent; then use activated charcoal.
3. Remove absorbed toxins by alkaline diuresis or dialysis.
4. Consider use of naloxone (Narcan) to treat any possible coexisting narcotic overdose.
5. Avoid CNS stimulants.
6. Lethal dose
   a. Short-acting barbiturates: Ingestion of more than 3 g, or blood level greater than 2 mg/dL.
   b. Long-acting barbiturates: Ingestion of more than 6 to 9 g, or blood level greater than 11 to 12 mg/dL.

**Treatment of Withdrawal**

1. Give supportive care as needed.
2. The goal of treatment is to relieve symptoms of withdrawal and prevent progression of the withdrawal. Wesson and Smith (1977) recommended the following protocol:
   a. Give a 200-mg oral pentobarbital challenge dose and assess neurological changes after 60 minutes.
   b. The daily (24-hour) pentobarbital requirement is calculated on the basis of the neurological examination after 60 minutes:

<table>
<thead>
<tr>
<th>Neurological Status</th>
<th>24-Hour Pentobarbital Requirement (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asleep but arousable</td>
<td>None</td>
</tr>
<tr>
<td>Drowsy; slurred speech</td>
<td>400–600</td>
</tr>
<tr>
<td>Marked intoxication</td>
<td></td>
</tr>
<tr>
<td>Comfortable, fine lateral nystagmus</td>
<td>800</td>
</tr>
<tr>
<td>the only sign of intoxication</td>
<td></td>
</tr>
<tr>
<td>No signs of drug effects; no intoxication</td>
<td>1,000–1,200</td>
</tr>
<tr>
<td></td>
<td>or more</td>
</tr>
</tbody>
</table>

3. Other detoxification protocols are also available.

**Nonbarbiturate Hypnotic Drugs**

This group includes drugs such as glutethimide (Dolotid) and methaqualone (Quaalude) that are similar in effect to short-acting barbiturates. These drugs have high
abuse potential and are not good therapeutic agents. Tolerance and psychological and physical dependence can all occur. The effects of the drugs include a sense of euphoria, a loss of concern for self, and withdrawal from reality. Heavy use leads to intoxication, with unsteadiness, tremors, loss of memory, irritability, and delirium, and may result in coma and cardiovascular and respiratory failure. Withdrawal from these drugs is dangerous and can result in seizures, coma, and death. Treatment is similar to that for barbiturate abuse.

**Tranquilizers**

Tranquilizers include the major tranquilizers, such as the phenothiazines, and the minor tranquilizers, such as diazepam (Valium) and alprazolam (Xanax). The major tranquilizers are the most frequent drugs of abuse among adolescents. The minor tranquilizers have the potential for psychological and physical dependence. However, abuse of these drugs is more common in adults than in adolescents. The minor tranquilizers are fairly safe in regard to overdose, with minimal serious side effects after ingestions of 50 to 100 times the daily dosage. However, these drugs have serious lethal potential when combined with alcohol, barbiturates, or other drugs with depressant effects. Equivalent doses are reviewed in Table 74.4. Tranquilizer use among high school seniors went from 17.0% in 1975 to a low of 6.4% in 1992 before increasing to 8.9% in 2000 (Johnston et al., 2001).

**Detoxification**

Detoxification from benzodiazepine dependence can be accomplished in several ways:

1. Slow, gradual outpatient detoxification lasting 2 to 3 months; decreasing the dose by one sixth every 10 days
2. Rapid inpatient detoxification using the phenobarbital substitution method for 10 to 14 days
3. Rapid inpatient detoxification using long-acting benzodiazepines such as chlordiazepoxide for 10 to 14 days

**Benzodiazepine Receptor Antagonist**

Flumazenil is the first specific benzodiazepine receptor antagonist to become available. It is an imidazobenzodiazepine available for intravenous injection only. Indications include benzodiazepine overdose. It is given in incremental doses of 0.2 mg/min. If a clinical effect is not seen after 5 doses have been given, it is unlikely that higher doses will be helpful. In patients who have been long-term users and those who have taken an overdose of an agent with a long half-life, redosing may be necessary. Deaths have occurred in overdose patients when the antidote half-life was not compared with the effective half-life of drug “on board.”

In mixed overdoses involving tricyclic antidepressants, flumazenil is contraindicated. In this setting it can cause seizure activity. It is also contraindicated in individuals who are physically dependent on benzodiazepines. This dependence can occur rapidly. In one study of healthy adults treated for 2 weeks with therapeutic doses of lorazepam, use of flumazenil precipitated a full-blown benzodiazepine withdrawal state (agitation, tremor, flushing).

An antidote is at best an adjunct in the management of the patient with a drug overdose. A secure airway, intravenous access, cardiac monitoring, and pulse oximetry are never to be overlooked.

**Flunitrazepam (Rohypnol) and “Date Rape” Drugs**

Flunitrazepam (Rohypnol), gamma-hydroxybutyrate (GHB), and ketamine are predominantly CNS depressants. These drugs are often colorless, tasteless, and odorless and therefore have been added to beverages and ingested by individuals unknowingly. These drugs have a reputation as the so-called “date rape” drugs. In 1996, federal legislation was passed that increased penalties for the use of any controlled substance to aid in sexual assault.

Flunitrazepam probably has the widest reputation as a “date rape” drug. If mixed with alcohol, it can incapacitate victims and prevent them from resisting sexual assault. This drug can be lethal when combined with alcohol and other depressants. Beside its sedative-hypnotic effects, flunitrazepam can produce physical and psychological dependence. This drug is not approved for use in the United States, and it is illegal to import flunitrazepam into the United States.

Use of flunitrazepam begin in Europe in the 1970s and appeared in the United States in the early 1990s. Street names include rophies, roofies, roach, and rope. The Monitoring the Future survey included questions on Rohypnol in 1996. In that year, 1.2% of seniors had used Rohypnol at some time; this figure rose to 3.0% in 1998 before falling to 1.5% in 2000. Occasionally clonazepam (Klonopin) is sold as roofies. GHB, abused for its euphoric, sedative, and anabolic effects, also has been associated with sexual assaults.

Information and educational materials on Rohypnol and GHB directed toward college students are available from the Rape Treatment Center at Santa Monica—UCLA Medical Center at 1-800-END-RAPE (1-800-363-7273). Information is also available at http://www.nida.nih.gov/Infofax/RohypnolGHB.html.

**ANABOLIC STEROIDS**

Anabolic steroids are synthetic derivatives of testosterone. Though a steroid dependence syndrome is not listed in the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV), abusers of this class of drug exhibit tolerance, withdrawal, and psychological dependence. Treatment may require detoxification and a rehabilitation phase comparable to traditional drug treatment.

The numerous agents fit into two basic categories: the oral agents are 17a-methyl derivatives of testosterone, and the injectable agents are esters of testosterone and 19-nortestosterone. The ideal anabolic steroid would have minimal androgenic activity and a longer half-life than the parent compound, testosterone. The 17a-alkylated steroids have a half-life of 8 to 10 hours, whereas the injectable forms have half-lives in the range of 21 days. Although these agents have less androgenic activity in lower dosage ranges, this activity is lost at higher doses. Many abusers use 10 times the usual therapeutic dose and use combinations of oral and injectable agents concurrently in 6- to 12-week cycles (“stacking”).

**Prevalence**

The 2000 Monitoring the Future Study reported a lifetime prevalence in seniors of 2.5%. In the 1999 YRBS survey, 3.7% of students had used illegal steroids during their lifetime (5.2% of the boys and 2.2% of the girls).

**Side Effects**

1. **Cardiovascular** (Sullivan et al., 1998):
   a. The high-density lipoprotein cholesterol concentration is decreased, and that of low-density lipoprotein cholesterol is increased.
   b. Hypertension, ventricular remodeling, myocardial ischemia, and sudden death have each been both temporally and causally associated with anabolic steroid use. The effects of anabolic steroids persist for years after use has been stopped.
2. **Endocrine**
   a. Premature epiphyseal closure
   b. Female virilization
   c. Hypogonadism
3. **Hepatic**: Hepatocellular carcinoma
4. **Psychiatric**
   a. Psychosis
   b. Mania
   c. Mood swings
   d. Violence syndrome (hyperaggressiveness)
   e. Depression during withdrawal
5. **Addictive**: Dependence syndrome, including
   a. Tolerance
   b. Withdrawal symptoms
   c. Inability to cut down or control use
Continued use despite adverse consequences

TREATMENT OF WITHDRAWAL OR DEPENDENCE

Patients exhibiting psychotic behavior or severe depression require inpatient care. Appropriate pharmacological intervention with antipsychotic, antidepressant, and anxiolytic agents may be indicated, usually for a short period. For the patient meeting DSM-IV criteria (3 of 12 listed) for substance dependence, a traditional drug treatment approach is indicated. Attending 12-step meetings and "working a program" are ideal methods to provide the adolescent with a conceptual framework to work through this problem.

DESIGNER AND CLUB DRUGS

Designer drug is an imprecise term that originated with a fentanyl analogue that was synthesized in a clandestine laboratory and sold on the street as heroin. The intent of the "chemists" was to synthesize a substance that was closely related to the controlled substance and yet technically legal. Legislation has closed this loophole, but the term "designer drug" persists. Common designer drugs include the following:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Method of Use</th>
<th>Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dextromethamphetamine</td>
<td>Smoked</td>
<td>Impulsiveness, fearlessness, paranoia</td>
</tr>
<tr>
<td>MDA (&quot;love drug&quot;)</td>
<td>Oral</td>
<td>Feelings of euphoria and empathy without hallucinations</td>
</tr>
<tr>
<td>MDMA (&quot;Ecstasy&quot; or &quot;Adam&quot;) and MDEA</td>
<td>Oral</td>
<td>Feelings of euphoria and empathy mild visual hallucinations, increased self-esteem, anorexia, bruxism, hypertension, tachycardia, diaphoresis, ataxia</td>
</tr>
<tr>
<td>&quot;Evergreen&quot; a-Methylfenanyl (&quot;synthetic heroin&quot;)</td>
<td>Injected</td>
<td>Analgesia, miosis, CNS depression, respiratory depression respiratory depression</td>
</tr>
<tr>
<td>&quot;china white&quot;)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The term club drugs was coined to describe a number of primarily synthetic drugs that are preferred by adolescent and young adult attendees at "raves," nightclubs that stay open all night, and "circuit parties." Drugs used at raves include Ecstasy, LSD, ketamine, PCP, crystal methamphetamine, GHB, GBL, fentanyl, Rohypnol, cocaine, and marijuana. Club drug use appears to be increasing in many cities in the United States, with Atlanta, Seattle, Chicago, Detroit, Miami, and Newark, reporting widespread use at rave and club scenes. This section focuses on the drugs MDMA (Ecstasy) and GHB. In addition, raves are described in further detail.

Raves

Raves are essentially all-night dance parties or mass gatherings of 10,000 to 70,000 individuals who listen to loud, syncopated, "techno" music being "spun" by a DJ band, often in coordination with laser effects and other visual and auditory stimuli. Another component to raves has been the liberal use of drugs such as Ecstasy (MDMA), GHB, and ketamine. MDMA started to become more popular in the 1980s, and several features of the drug specifically shaped virtually all aspects of the rave. The intense motor restlessness and stimulation of the "stereotypic behavior" portions of the brain occur as a side effect of MDMA and are relieved by group "movement" (dancing) and "wandering" from one stage area to another. In addition, because of the hallucinogenic properties of MDMA and the predictable occurrence of "seeing tracers," the light show or laser effects are coordinated with the music.

Raves first appeared in Britain and the United States in the mid-1980s and have since spread to many other countries including Australia, India, Belgium, Egypt, and Canada. There is very little in the medical literature on raves, although Weir (2000) has a review article on the rave culture and the associated drugs.

The rave music at raves is usually computer generated, without vocals, and noncommercial in nature. The music is usually generated by independent record companies with no packaging and distributed directly to DJs. The music is a "techno" sound that is repetitive, loud, and fast and is described as "surgery past the listener in mind-numbing waves" (Weir, 2000). The rave typically begins at 9 p.m. and ends at 6 a.m., curiously close to the duration of the MDMA "trip." Circuit parties are large-scale dance parties lasting from one to several days and primarily attended by gay and bisexual men in their thirties and forties. Because alcohol usually is not available at raves, there is often no age restriction on admission. Raves are usually held at different venues each time and may not occur as announced, to deter police surveillance. Exact locations may be released only hours before an event takes place. Most attendees are between 15 and 25 years of age, and often they are from middle socioeconomic backgrounds. The activity can be expensive, because admission can run from $10 to $50 and the drugs may cost $10 to $40 per night. Ravers often consider raves to be safe havens for outcasts or "computer geeks."

Although not all attendees use drugs, drugs are used liberally and many illicit drugs are available at raves. As mentioned previously, alcohol is usually absent from raves. Ecstasy is probably the best known drug used at raves, but marijuana is also a popular drug. Others include LSD, PCP, ketamine, crystal methamphetamine, and GHB.

Gamma-Hydroxybutyrate

GHB ("liquid Ecstasy") is a CNS depressant that acts through a metabolite of the inhibitory neurotransmitter g-aminobutyric acid (GABA) and can function as a neurotransmitter itself. GHB triggers the release of an opiate-like substance and can mediate sleep cycles, temperature regulation, memory, and emotional control. In some countries, GHB is used as an anesthetic and for narcolepsy. It is rapidly absorbed after ingestion.

The illicit use of GHB has grown in North America among both body builders and ravers. Body builders claim that it metabolizes fat and builds muscles. Ravers use it as an euphoriant. It has also been mentioned as one of the several "date rape" drugs. It has been sold as a strength enhancer, euphoriant, and aphrodisiac. Some of the common street names include liquid ecstasy, somatomax, scoop, Georgia Home Boy, and grievous bodily harm. The drug comes in both liquid and powder form.

Raves are essentially all-night dance parties or mass gatherings of 10,000 to 70,000 individuals who listen to loud, syncopated, "techno" music being "spun" by a DJ band, often in coordination with laser effects and other visual and auditory stimuli. Another component to raves has been the liberal use of drugs such as Ecstasy (MDMA), GHB, and ketamine. MDMA started to become more popular in the 1980s, and several features of the drug specifically shaped virtually all aspects of the rave. The intense motor restlessness and stimulation of the "stereotypic behavior" portions of the brain occur as a side effect of MDMA and are relieved by group "movement" (dancing) and "wandering" from one stage area to another. In addition, because of the hallucinogenic properties of MDMA and the predictable occurrence of "seeing tracers," the light show or laser effects are coordinated with the music.

Raves first appeared in Britain and the United States in the mid-1980s and have since spread to many other countries including Australia, India, Belgium, Egypt, and Canada. There is very little in the medical literature on raves, although Weir (2000) has a review article on the rave culture and the associated drugs.

The rave music at raves is usually computer generated, without vocals, and noncommercial in nature. The music is usually generated by independent record companies with no packaging and distributed directly to DJs. The music is a "techno" sound that is repetitive, loud, and fast and is described as "surgery past the listener in mind-numbing waves" (Weir, 2000). The rave typically begins at 9 p.m. and ends at 6 a.m., curiously close to the duration of the MDMA "trip." Circuit parties are large-scale dance parties lasting from one to several days and primarily attended by gay and bisexual men in their thirties and forties. Because alcohol usually is not available at raves, there is often no age restriction on admission. Raves are usually held at different venues each time and may not occur as announced, to deter police surveillance. Exact locations may be released only hours before an event takes place. Most attendees are between 15 and 25 years of age, and often they are from middle socioeconomic backgrounds. The activity can be expensive, because admission can run from $10 to $50 and the drugs may cost $10 to $40 per night. Ravers often consider raves to be safe havens for outcasts or "computer geeks."

Although not all attendees use drugs, drugs are used liberally and many illicit drugs are available at raves. As mentioned previously, alcohol is usually absent from raves. Ecstasy is probably the best known drug used at raves, but marijuana is also a popular drug. Others include LSD, PCP, ketamine, crystal methamphetamine, and GHB.

Gamma-Hydroxybutyrate

GHB ("liquid Ecstasy") is a CNS depressant that acts through a metabolite of the inhibitory neurotransmitter g-aminobutyric acid (GABA) and can function as a neurotransmitter itself. GHB triggers the release of an opiate-like substance and can mediate sleep cycles, temperature regulation, memory, and emotional control. In some countries, GHB is used as an anesthetic and for narcolepsy. It is rapidly absorbed after ingestion.

The illicit use of GHB has grown in North America among both body builders and ravers. Body builders claim that it metabolizes fat and builds muscles. Ravers use it as an euphoriant. It has also been mentioned as one of the several "date rape" drugs. It has been sold as a strength enhancer, euphoriant, and aphrodisiac. Some of the common street names include liquid ecstasy, somatomax, scoop, Georgia Home Boy, and grievous bodily harm. The drug comes in both liquid and powder form. Before February 2000, GHB was not illegal to possess, but now it is a schedule I drug. GHB has not been sold over the counter in the United States since 1992. However, products containing gamma-butyrolactone (GBL), a chemical that is converted by the body into GHB, are used in a number of dietary supplements in health food stores and gyms.

Adverse effects include:

1. Cardiorespiratory: Bradycardia, respiratory depression, and increases or decreases in blood pressure; respiratory depression is particularly common if GHB is combined with other drugs such as alcohol.
2. Hypothermia
3. Neurological: Confusion, sedation, dizziness, weakness, ataxia, vertigo, dysarthria, short-term amnesia, hallucinations, coma, tonic-clinic seizures
4. Psychiatric: Aggression and impairment in judgment
5. Gastrointestinal: Vomiting
6. Endocrine: Mild hyperglycemia
7. Acute respiratory acidosis
8. Withdrawal effects include insomnia, anxiety, tremors, and sweating.

Heavy doses can lead to coma and respiratory depression, which can be exacerbated by the use of alcohol. The FDA has issued a warning about GHB because the products have been linked to at least 122 serious illnesses and at least 6 deaths (O'Connell, 2000). There is no antidote for GHB overdose; the treatment is supportive care.

Ketamine

Ketamine ("Special K") is a rapid-acting anesthetic that combines sedative-hypnotic, analgesic, hallucinogenic, and amnesic effects. It also produces a "dissociative" state. Ketamine is used as a veterinary anesthetic, and it entered the rave scene in the early 1990s. Its use has been growing in North America and in the United Kingdom. Accidents are often of greater threat to the individual than toxicity secondary to the loss of physical control. Ketamine is similar to PCP, but it has a more rapid onset and is less potent. Ketamine is reported to be used as an alternative to cocaine, and it is often snorted. The drug is also often sold in tablets similar to
“Ecstasy,” and users may take ketamine thinking they are using MDMA. Ketamine has also been abused as a “date rape” drug.

**Ecstasy**

MDMA was first patented in 1912 as an appetite suppressant by a scientist working on chemical structures found in methamphetamine. However, it was never manufactured and sold commercially, although it did resurface in the 1950s as a potential psychotherapeutic agent for psychoanalysis. In 1985, MDMA was classified as a schedule I drug by the FDA after reports were published of neurotoxicity in laboratory animals. Since the mid-1980s, it has become a popular drug at raves, where most MDMA use occurs.

MDMA shares both amphetamine-like and hallucinogenic drug effects. Its effects are mediated through activity on the dopaminergic and serotonergic pathways and last about 3 to 6 hours. The drug is sold as a tablet or capsule, often with a symbol printed on it. Street names include “Adam” and “XTC” among others. MDMA ingestion has been associated with severe toxic side effects. MDMA’s onset of action is related to the route of administration; for the oral dose, onset usually occurs within 30 to 45 minutes. The effects last about 4 to 6 hours, but a noticeable decrease in effect occurs within 2 to 3 hours.

**Usage**

Use of MDMA by American adolescents has continued to rise sharply. Johnston et al. (2000) reported a sharp increase in Ecstasy use among 10th and 12th graders in 1999, which continued in 2000. The drug appears to becoming popular also among 8th graders. According to Monitoring the Future data (www.monitoringthefuture.org), use among 8th graders in 1999 to 2000 increased from 1.7% to 3.1%, among 10th graders from 4.4% to 5.4%, and among 12th graders from 5.6% to 8.2%. At present, Ecstasy is used by more American adolescents than cocaine is. The study also found an increase in use in the 19- to 22-year-old population. Use of the drug appears to be concentrated in teens and young adults who are involved in raves, clubs, and party scenes. In college students, Ecstasy use in the last 12 months rose from 0.5% in 1994 to 5.5% in 1998. Although the perceived toxicity among teens has risen by only a small degree, availability has jumped, from 22% of 12th graders who could get Ecstasy easily in 1989 to 40% in 1999 and 51% in 2000.

Users describe feelings of enhanced well-being and empathy. Teens taking Ecstasy describe taking it to lower inhibitions; enhance feelings of love and affection, and increase energy.

**Adverse Effects**

### Cardiovascular
- Tachycardia, increased blood pressure

### Motor
- Sweating, muscle spasms including involuntary teeth clenching

### General
- Fatigue, nausea, blurred vision, faintness, chills, and rapid eye movements

### Dermatological
- Rash

### Neurological
- Confusion, depression, sleep problems, anxiety and paranoia. In addition, some research links MDMA to long-term damage to areas of the brain that are critical to thought and memory. In experiments on monkeys, exposure to MDMA for 4 days caused brain damage that was evident 6 years later (www.nida.nih.gov/infofax/ecstasy.html).

### Hepatic
- May produce severe hepatic damage. Several cases requiring liver transplantation have been described (Brauer et al., 1997; Andreu et al., 1998; Schwab et al., 1999). In a review by Andreu et al. (1998), Ecstasy was the second most common cause of liver injury in patients younger than 25 years of age. It accounted for 20% of the cases in this group of patients—35% of viral hepatitis was excluded. Full recovery occurred in all cases in 3 to 12 months.

### Skin
- Severe side effects: There have been reports of toxicity and death associated with Ecstasy use. The mechanisms of death appear to be related to fatal hyperthermia, disseminated intravascular coagulation, rhabdomyolysis, renal failure, cardiac arrhythmias, hyponatremia, and seizures. Other reports have also described hyperthermia, cerebral infarction, and cerebral hemorrhage. The most common severe reaction to toxic ingestion is a syndrome of altered mental status, tachycardia, tachypnea, profuse sweating, and hyperthermia. This syndrome can appear similar to acute amphetamine overdose.

### Possible Long-term Neurological Damage

- Brain imaging has been associated with severe toxic side effects. MDMA’s onset of action is related to the route of administration; for the oral dose, onset usually occurs within 30 to 45 minutes. The effects last about 4 to 6 hours, but a noticeable decrease in effect occurs within 2 to 3 hours.

**Treatment of Overdose**

The treatment of toxic ingestions of MDMA is supportive and similar to that for amphetamine overdose:

1. Support of airway, breathing, and circulation.
2. Assessment and treatment of ventricular dysrhythmias, hypertension or hypotension, and tachycardia. There should also be serial assessment of vital signs and level of consciousness using either:
   - AVPU (alert, responds to voice, responds to pain, unconscious), or
   - Glasgow Coma Score
3. Treat hyperthermia with cooling blankets and intravenous fluids. In addition, dantrolene is recommended by some individuals for treatment of hyperthermia.
4. Oral charcoal if ingestion occurred within the last 30 to 60 minutes.
5. Close monitoring of blood chemistry and urine output (a Foley catheter may be necessary) as well as liver function. Initial studies should include a complete blood count, blood chemistry analysis, liver function tests, cardiac enzyme measurements, creatine kinase measurements, and urine toxicology screening.
6. Possible use of muscle relaxants, anticonvulsants, and sedative medications, particularly benzodiazepines.
7. Use of fluids, mannitol, or bicarbonate for rhabdomyolysis.
8. Head CT/MRI if seizures or prolonged alteration of mental status.

Although most individuals who take Ecstasy do not have complications, there is considerable controversy regarding the safety of this drug. The numerous concerns include the following:

1. Possible contaminants in drugs sold as MDMA: In one report, approximately 10% of drugs sold as Ecstasy contained no active ingredient, and others contained a mixture of substances including amphetamines, ephedrine, caffeine, and aspirin. In addition, the concentration of MDMA may vary 70-fold or more among tablets sold.
2. Severe toxicity including death, as described earlier.
3. Possible long-term neurological damage associated with use. Curran (2000) reviewed the research on MDMA neurotoxicity in both rodents and nonhuman primates. Her conclusions were that MDMA has been shown to cause serotonergic neuronal toxicity in every animal species tested, although recovery occurred in some. Direct evidence in humans has been more difficult to demonstrate because of the problems with study methods in humans. Kish (2000) reported that striatal levels of serotonin and hydroxyindoleacetic acid (HIAA) were depleted by 50% to 80% in the brains of chronic users of MDMA. Gerra et al. (2000) found long-lasting impairment of the 5-hydroxytryptamine (5-HT) system in past users of MDMA. Bolla et al. (1998) found evidence of verbal and visual memory impairment in abstinence MDMA users. Parrott (2000) found that users of Ecstasy had several cognitive functions impaired, including reduced memory for new information, impaired higher executive processing, and heightened impulsivity. Despite methodological problems, the pattern of cognitive changes is consistent with animal data showing serotoninergic damage after MDMA use.

**Methods for Teens to Reduce Harm at Raves**

1. Replenish fluids and electrolytes; too much water can be dangerous.
2. Avoid alcohol.
3. Ensure that a medical team is on-site.
4. Don't attend a rave alone; have a partner so that each of you can look out for the other.
5. Take dance breaks.
6. Monterey individuals are advised against the use of MDMA, there is information available that discusses a safer dosage of MDMA if it is used. The dosage "recommended" is 2 mg/kg as an initial dose, with a booster dose of 0.5 to 1 mg/kg after 3 to 4 hours (Rochester et al., 1999).
7. [http://www.dancesafe.org/](http://www.dancesafe.org/) is a controversial Web site that promotes health and safety in the rave and nightclub community through safer use of drugs.

**WEB SITES**


**REFERENCES AND ADDITIONAL READINGS**


Bolla KI, McCann UD, Ricaute GA. Memory impairment in abstinent MDMA (Ecstasy) users. Neurology 1998;51:1532.


75
Approaches to the Management of Drug Abuse
Lawrence S. Neinstein, Drew Pinsky, and Bruce S. Heischober

Physician Responsibilities

HISTORY TAKING

Indications for Testing

6. To be well informed regarding current drugs of abuse and their pharmacology. (The Internet can be a valuable tool in keeping abreast of advances in epidemiology and treatment trends as well as drug related fads and activities, etc. See list of Web sites at end of chapter.)

2. To understand one's own limitations and use community resources as needed.

To be aware of available community resources for emergency medical services, crisis intervention, residential treatment programs, counseling services, legal services, vocational counseling, and housing and recreational facilities.

3. To develop relationships with emergency departments at local hospitals, working with them on identification and referral of adolescents who are at high risk for substance abuse or identified as substance abusers. Because most teens will not participate in follow-up for a substance abuse issue when simply handed a telephone number, it is important to try other approaches. An example is the ASSEERT Program at Boston City Hospital Emergency Department, in which multicultural health promotion advocates are used to screen, assess readiness to change, and enlist the patient in an active referral process.

4. To become familiar with laws related to drug abuse.

5. To be able to manage acute drug ingestion, including knowledge of toxic syndromes and early consultation with a poison control center when appropriate.

6. To provide drug education to schools, youth organizations, adolescents, and parents. It is often useful to establish a profile in the community as an expert, because many parents, teens, and organizations feel that there are no resources available to them in this area.

7. To provide drug education to schools, youth organizations, adolescents, and parents. It is often useful to establish a profile in the community as an expert, because many parents, teens, and organizations feel that there are no resources available to them in this area.

8. To provide supportive counseling to the adolescent.

9. To be aware of the unique problems of chemically dependent adolescents who are in recovery.

10. To identify the child or adolescent at high risk for chemical dependency and to intervene appropriately.

11. With the increase in raves aside from rock concerts, to be aware of the increasingly important area of event medicine. It is important to consider developing a rave medicine program with the emergency medicine department. At the same time, guidelines should be developed for the prehospital, hospital, and follow-up care of intoxicated youth.

12. For those providers with a strong interest in substance abuse care, have a working knowledge of the first five steps of the 12 Steps of the Anonymous programs and be able to communicate information about these steps at the specific developmental level of the teen or young adult.

HISTORY TAKING

In taking the adolescent's history, the health care provider should keep the following points in mind:

1. To be well informed regarding current drugs of abuse and their pharmacology. (The Internet can be a valuable tool in keeping abreast of advances in epidemiology and treatment trends as well as drug related fads and activities, etc. See list of Web sites at end of chapter.)

2. To understand one's own limitations and use community resources as needed.

3. To be aware of available community resources for emergency medical services, crisis intervention, residential treatment programs, counseling services, legal services, vocational counseling, and housing and recreational facilities.

4. To develop relationships with emergency departments at local hospitals, working with them on identification and referral of adolescents who are at high risk for substance abuse or identified as substance abusers. Because most teens will not participate in follow-up for a substance abuse issue when simply handed a telephone number, it is important to try other approaches. An example is the ASSEERT Program at Boston City Hospital Emergency Department, in which multicultural health promotion advocates are used to screen, assess readiness to change, and enlist the patient in an active referral process.

5. To become familiar with laws related to drug abuse.

6. To be able to manage acute drug ingestion, including knowledge of toxic syndromes and early consultation with a poison control center when appropriate.

7. To provide drug education to schools, youth organizations, adolescents, and parents. It is often useful to establish a profile in the community as an expert, because many parents, teens, and organizations feel that there are no resources available to them in this area.

8. To provide supportive counseling to the adolescent.

9. To be aware of the unique problems of chemically dependent adolescents who are in recovery.

10. To identify the child or adolescent at high risk for chemical dependency and to intervene appropriately.

11. With the increase in raves aside from rock concerts, to be aware of the increasingly important area of event medicine. It is important to consider developing a rave medicine program with the emergency medicine department. At the same time, guidelines should be developed for the prehospital, hospital, and follow-up care of intoxicated youth.

12. For those providers with a strong interest in substance abuse care, have a working knowledge of the first five steps of the 12 Steps of the Anonymous programs and be able to communicate information about these steps at the specific developmental level of the teen or young adult.

The physician's responsibilities in dealing with drug-abusing adolescents are:

1. To be well informed regarding current drugs of abuse and their pharmacology. (The Internet can be a valuable tool in keeping abreast of advances in epidemiology and treatment trends as well as drug related fads and activities, etc. See list of Web sites at end of chapter.)

2. To understand one's own limitations and use community resources as needed.

3. To be aware of available community resources for emergency medical services, crisis intervention, residential treatment programs, counseling services, legal services, vocational counseling, and housing and recreational facilities.

4. To develop relationships with emergency departments at local hospitals, working with them on identification and referral of adolescents who are at high risk for substance abuse or identified as substance abusers. Because most teens will not participate in follow-up for a substance abuse issue when simply handed a telephone number, it is important to try other approaches. An example is the ASSEERT Program at Boston City Hospital Emergency Department, in which multicultural health promotion advocates are used to screen, assess readiness to change, and enlist the patient in an active referral process.

5. To become familiar with laws related to drug abuse.

6. To be able to manage acute drug ingestion, including knowledge of toxic syndromes and early consultation with a poison control center when appropriate.

7. To provide drug education to schools, youth organizations, adolescents, and parents. It is often useful to establish a profile in the community as an expert, because many parents, teens, and organizations feel that there are no resources available to them in this area.

8. To provide supportive counseling to the adolescent.

9. To be aware of the unique problems of chemically dependent adolescents who are in recovery.

10. To identify the child or adolescent at high risk for chemical dependency and to intervene appropriately.

11. With the increase in raves aside from rock concerts, to be aware of the increasingly important area of event medicine. It is important to consider developing a rave medicine program with the emergency medicine department. At the same time, guidelines should be developed for the prehospital, hospital, and follow-up care of intoxicated youth.

12. For those providers with a strong interest in substance abuse care, have a working knowledge of the first five steps of the 12 Steps of the Anonymous programs and be able to communicate information about these steps at the specific developmental level of the teen or young adult.

PHYSICIAN RESPONSIBILITIES

The physician's responsibilities in dealing with drug-abusing adolescents are:

1. To be well informed regarding current drugs of abuse and their pharmacology. (The Internet can be a valuable tool in keeping abreast of advances in epidemiology and treatment trends as well as drug related fads and activities, etc. See list of Web sites at end of chapter.)

2. To understand one's own limitations and use community resources as needed.

3. To be aware of available community resources for emergency medical services, crisis intervention, residential treatment programs, counseling services, legal services, vocational counseling, and housing and recreational facilities.

4. To develop relationships with emergency departments at local hospitals, working with them on identification and referral of adolescents who are at high risk for substance abuse or identified as substance abusers. Because most teens will not participate in follow-up for a substance abuse issue when simply handed a telephone number, it is important to try other approaches. An example is the ASSEERT Program at Boston City Hospital Emergency Department, in which multicultural health promotion advocates are used to screen, assess readiness to change, and enlist the patient in an active referral process.

5. To become familiar with laws related to drug abuse.

6. To be able to manage acute drug ingestion, including knowledge of toxic syndromes and early consultation with a poison control center when appropriate.

7. To provide drug education to schools, youth organizations, adolescents, and parents. It is often useful to establish a profile in the community as an expert, because many parents, teens, and organizations feel that there are no resources available to them in this area.

8. To provide supportive counseling to the adolescent.

9. To be aware of the unique problems of chemically dependent adolescents who are in recovery.

10. To identify the child or adolescent at high risk for chemical dependency and to intervene appropriately.

11. With the increase in raves aside from rock concerts, to be aware of the increasingly important area of event medicine. It is important to consider developing a rave medicine program with the emergency medicine department. At the same time, guidelines should be developed for the prehospital, hospital, and follow-up care of intoxicated youth.

12. For those providers with a strong interest in substance abuse care, have a working knowledge of the first five steps of the 12 Steps of the Anonymous programs and be able to communicate information about these steps at the specific developmental level of the teen or young adult.

HISTORY TAKING

In taking the adolescent's history, the health care provider should keep the following points in mind:

1. To be well informed regarding current drugs of abuse and their pharmacology. (The Internet can be a valuable tool in keeping abreast of advances in epidemiology and treatment trends as well as drug related fads and activities, etc. See list of Web sites at end of chapter.)

2. To understand one's own limitations and use community resources as needed.

3. To be aware of available community resources for emergency medical services, crisis intervention, residential treatment programs, counseling services, legal services, vocational counseling, and housing and recreational facilities.

4. To develop relationships with emergency departments at local hospitals, working with them on identification and referral of adolescents who are at high risk for substance abuse or identified as substance abusers. Because most teens will not participate in follow-up for a substance abuse issue when simply handed a telephone number, it is important to try other approaches. An example is the ASSEERT Program at Boston City Hospital Emergency Department, in which multicultural health promotion advocates are used to screen, assess readiness to change, and enlist the patient in an active referral process.

5. To become familiar with laws related to drug abuse.

6. To be able to manage acute drug ingestion, including knowledge of toxic syndromes and early consultation with a poison control center when appropriate.

7. To provide drug education to schools, youth organizations, adolescents, and parents. It is often useful to establish a profile in the community as an expert, because many parents, teens, and organizations feel that there are no resources available to them in this area.

8. To provide supportive counseling to the adolescent.

9. To be aware of the unique problems of chemically dependent adolescents who are in recovery.

10. To identify the child or adolescent at high risk for chemical dependency and to intervene appropriately.

11. With the increase in raves aside from rock concerts, to be aware of the increasingly important area of event medicine. It is important to consider developing a rave medicine program with the emergency medicine department. At the same time, guidelines should be developed for the prehospital, hospital, and follow-up care of intoxicated youth.

12. For those providers with a strong interest in substance abuse care, have a working knowledge of the first five steps of the 12 Steps of the Anonymous programs and be able to communicate information about these steps at the specific developmental level of the teen or young adult.
PHYSICAL EXAMINATION

1. General appearance: Look for evidence of malnutrition and infection.
2. Vital signs: Check the following:
   a. Blood pressure: Increased with amphetamines, phencyclidine (PCP), d-lysergic acid diethylamide (LSD), and drug withdrawals; decreased with narcotic use
   b. Pulse: Increased with hallucinogens, stimulants, and drug withdrawal; bradycardia with GHB
   c. Respiration: Depressed with barbiturates, opiates, and tranquilizers. GHB has been observed to cause respiratory depression to the point of apnea
      interspersed with periods of violent agitation; this has been described in the literature as appearing like a drowning swimmer flailing for air.
   d. Temperature: Increased with PCP, MDMA, and amphetamines; decreased with morphine or barbiturates
3. Skin: Assess for evidence of needle tracks in the antecubital fossa, inguinal and jugular areas, and dorsal vein of the penis. Assess for nodules, abscesses, cellulitis, and cigarette stains and burns. Postural acne may occur with the use of barbiturates, LSD, or stimulants or withdrawal from opiates; cyanosis with opiates and sedatives; and flushed skin with PCP and LSD. Burns on lips may occur as a result of smoking volatilized chemicals. Because of formation and delusional preoccupations, stimulant abusers have multiple small ulcerations in various stages of healing, sometimes called "picker's syndrome."
4. Lymphatic vessels: Explore for lymphadenopathy caused by the injection of foreign material. Look for evidence of lymphangitis caused by injected substances.
5. Eyes: Tennant (1988) described a rapid eye test to detect current drug intoxication
   a. General observation: Look for conjunctival injection, ptosis, retracted upper lid (white sclera visible above the iris, causing the appearance of a blank stare), glazing, excessive tearing of eyes, and swelling of eyelids.
   b. Pupil size: Look for dilation (more than 6.5 mm) or constriction (less than 3.0 mm).
   c. Pupil reaction to light: Look for slow, sluggish, or absent response.
   d. Nystagmus: Hold examining finger in a vertical position and have the teen follow the finger as it is moved to the side, in a circle, and up and down. A positive test result is failure to hold the gaze or jerkiness of eye movements.
   e. Convergence: The teen is unable to track or hold the cross-eyed position after an examining finger is moved from 1 foot away from teen's nose to 1 inch and held there for 5 seconds.
   f. Convergence: The teen is unable to track or hold the cross-eyed position after an examining finger is moved from 1 foot away from teen's nose to 1 inch and held there for 5 seconds.
   g. Rapid eye test: Results are considered suggestive of drug influence only if two or more of the five primary eye signs (ptosis, abnormal pupil size, nonreactive pupil, nystagmus, and nonconvergence) are present. The following list of common eye signs to determine the use of various drugs is adapted from Tennant (1988).
      ● Marijuana
         - Normal-sized pupil
         - Slow or no reaction of pupil to light
         - Nonconvergence
         - Convergent injection
         - Glazing of cornea
         - Horizontal nystagmus
         - Swollen eyelids
         - Watering
      ● Heroin
         - Constricted pupil
         - Nonreactive pupil
         - Ptosis
         - Glazing of cornea
         - Decreased corneal reflex
         - Swollen eyelids
      ● Alcohol or benzodiazepines
         - Normal-sized pupil
         - Slow or no reaction of pupil to light
         - Nystagmus
         - Redness of conjunctiva
         - Glazing of cornea
         - Nonconvergence
      ● Cocaine or amphetamines
         - Dilated pupil
         - Slow or no reaction of pupil to light
         - Decreased corneal reflex
      ● Phencyclidine (PCP)
         - Normal-sized pupil
         - Slow or no reaction of pupil to light
         - Vertical and horizontal nystagmus
         - Retracted upper eyelid
         - Decreased corneal reflex
         - Swollen eyelids
      ● Amphetamines
         - Dilated pupils
         - Nonreactive pupil
         - Barbiturates
         - Lateral nystagmus
6. Nasopharynx: Check for nasal mucosal injury and perforation caused by nasal insufflation of drugs: methamphetamine, heroin, cocaine. Also check for bruxism (amphetamines).
7. Cardiovascular system: Explore for evidence of pneumonitis caused by aspiration, chemically induced alveolitis, or infection; pulmonary hypertension; arrhythmias; and signs of endocarditis. Ischemic injury is not uncommon with use of stimulants, particularly cocaine.
8. Gastrointestinal system: Check for the following:
   a. Weight loss: Amphetamines, cocaine, and often heroin
   b. Vomiting: Alcohol, opiates, and peryode
   c. Constipation: Opiates
   d. Diarrhea: Alcohol, marijuana, or opiate withdrawal
   e. Abdominal pain: Alcohol, hallucinogens, or amphetamines; opiate withdrawal
9. Musculoskeletal system: Check for the following:
   a. Tremors: Hallucinogens or stimulants; long-term use of alcohol, sedatives, or opiates
   b. Rigidly: PCP and Ecstasy
10. Central nervous system (CNS): Check for the following:
    a. Seizures: Can occur during withdrawal from alcohol, barbiturates, glutethimide, or tranquilizers or as a result of intoxication with stimulants or GHB
    b. Slurred speech: Caused by alcohol, barbiturates, GHB, opiates, and solvents
    c. Hyperreflexia: Caused by hallucinogens, stimulants, and drug withdrawal
    d. Hyporeflexia: Caused by sedatives and narcotics
    e. Truncal ataxia: Caused by PCP and Ecstasy
    f. Mental status: Overt psychoses with hallucinogens, amphetamines, or cocaine (the paranoid delusions associated with cocaine use essentially always focus on uniformed officials, whereas those associated with amphetamine focus on close relations such as family, friends, or neighbors); depression resulting from

Other questionnaires include the Adolescent Assessment/Referral System (AARS) and the Problem-Oriented Screening Instrument for Teenagers (POSIT) (Rahdert, 1991).

Assess for evidence of associated medical problems.

1971), have been developed. The MAST has been tested in older adolescents, but many other questionnaires have not been tested in adolescents. Leccese and Waldron (1994) reviewed measurement instruments used in the assessment of substance abuse in adolescents.

6. Other questionnaires include the Adolescent Assessment/Referral System (AARS) and the Problem-Oriented Screening Instrument for Teenagers (POSIT) (Rahdert, 1991).

barbiturates or withdrawal from stimulants; hallucinations from LSD, PCP, barbiturates, or stimulants; panic states caused by marijuana, stimulants, or hallucinogens; visual hallucination and formation from alcohol withdrawal

**DIAGNOSTIC CLUES BY DRUG CLASS (TOXIDROMES, OR POISONING SYNDROMES)**

1. Sympathomimetics: Delusions, paranoia, restlessness, agitation, tachycardia, hypertension, hyperpyrexia, diaphoresis, mydriasis and hyperreflexia, dry mouth, diaphoresis, mydriasis and hyperreflexia.
2. Hallucinogens: Bizarre behavior, psychosis, hallucinations.
3. Opiates: Coma, hypotension, bradycardia, hypothermia, hyporeflexia, miosis, respiratory depression, miosis, bradycardia, hypothermia, hyporeflexia.
4. Phenothiazines: Miosis, hypotension, tremors, extrapyramidal movements, cardiac arrhythmias.
5. Anticholinergics (e.g., tricyclics, antidepressants, jimsonweed): Delirium with mumbling speech, tachycardia, dry flushed skin, dilated pupils, myoclonus, decreased bowel sounds, hypotension, arrhythmias, increased QRS-complex duration, chooreoathetoid movements, urinary retention ("mad as a hatter, blind as a bat, red as a beet, hot as a hare, and dry as a bone.").
6. Cholinergics (e.g., Amanita muscaria mushrooms): SLUDGE (salivation, lacrimation, urination, defecation, gastrointestinal upset and emesis); also bronchonrhea, miosis, confusion, seizures, or coma.

**Note:**
The emergence phenomena seen after ketamine ingestion may not fit a toxidrome. These patients appear to be having an ongoing "nightmare" and are noncommunicative with normal or near-normal vital signs and no clear signs or symptoms suggestive of a toxidrome or withdrawal state.

**DRUG SCREENING**

The technology for drug screening and identification has greatly expanded in recent years. Inexpensive, reliable, and rapid tests are currently available. Drug tests can provide reliable and useful information in the diagnosis and management of substance abuse in adolescents, and they are the only objective tests available to evaluate chemical abuse and dependency. Keep in mind that false-positive and false-negative results do occur and that positive results on screening tests should be confirmed with more specific tests. The practitioner faces many dilemmas with drug testing. Questions such as the circumstances in which it is ethical to order such tests, the confidentiality of the results, and the action plan for handling positive test results are often more difficult than the actual technical aspects of the tests. Occupational, school, and sports-participation drug screening tests are becoming more common.

**Resources**

Practitioners involved in drug screening may wish to consult the following resources:

3. Seminars for prospective medical review officers: Contact the American Society of Addiction Medicine, 4601 North Park Avenue, Arcade, Suite 101, Chevy Chase, MD 20815, telephone 1-301-656-3920, fax 1-301-656-3815, or visit their Web site at [http://www.asam.org/](http://www.asam.org/).

**Indications for Testing**

1. Psychiatric symptoms
2. Significant changes in performance or behavior in daily activities or school
3. Sudden changes in behavior
4. Recurrent unexplained accidents
5. Recurrent unexplained respiratory ailments
6. Monitoring of compliance during recovery program
7. Emergency department evaluations of trauma victims, automobile accidents, or unexplained illness in an adolescent with risk factors

Testing should always be undertaken with a clear plan of action in mind, including appropriate referrals. A single positive test result cannot be ignored but does not determine the frequency and extent of drug use. By the same token, a negative test provides only a "snapshot" of the recent use of some drugs. It must always be kept in mind that drug testing is not a substitute for parental monitoring or for professional assessment and intervention.

**Techniques**

The best time to collect urine specimens is early morning. Monday morning is a good time, although Sunday collections might be even more revealing. Teens with suspected drug abuse may need to be observed during the collection to prevent substitution or addition of liquids of other adulterating agents.

**Types of Tests**

1. Color spot: Rapid but not highly sensitive or specific.
2. Immunoassay screening tests, such as the enzyme-multiplied immunoassay technique (EMIT), radioimmunoassay (RIA), fluorescent polarization immunoassay (FIPA), and latex agglutination test. The EMIT is the most widely used immunoassay method and is a good screening test, but positive results should be confirmed by a more specific technique. There are also a variety of new specific assays, such as Ontrak, a second-generation latex agglutination immunoassay that is simple to perform and does not require expensive instrumentation.
3. Thin-layer chromatography (TLC): Widely used technique for drug screening. Problems can occur with sensitivity and specificity.
5. High-performance liquid chromatography (HPLC): Mainly used for determination of serum levels of therapeutic agents, but increasingly used for identification of illicit drugs.
6. Gas chromatography—mass spectrometry (GC-MS): Used for confirmation of positive screening results; highly sensitive and specific.

**Duration of Detectability of Drugs in the Urine**
Duration (Hr)

<table>
<thead>
<tr>
<th>Drug or Drug Class</th>
<th>Alcohol</th>
<th>Amphetamine and methamphetamine</th>
<th>Barbiturates</th>
<th>Pentobarbital</th>
<th>Secobarbital</th>
<th>Phenobarbital</th>
<th>OXAZEPAM</th>
<th>Cocaine</th>
<th>HEROIN</th>
<th>CODEINE</th>
<th>Propoxyphene</th>
<th>MARIJUANA</th>
<th>Methaqualone</th>
<th>Phencyclidine</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>12</td>
<td>48</td>
<td></td>
<td>24</td>
<td>24</td>
<td>900</td>
<td>72</td>
<td>48–72</td>
<td>48</td>
<td>24</td>
<td></td>
<td>48</td>
<td>112–570</td>
<td>192</td>
</tr>
<tr>
<td><strong>Duration (Hr)</strong></td>
<td>900</td>
<td>48</td>
<td></td>
<td>24</td>
<td>24</td>
<td>900</td>
<td>72</td>
<td>48–72</td>
<td>48</td>
<td>24</td>
<td></td>
<td>48</td>
<td>112–570</td>
<td>192</td>
</tr>
</tbody>
</table>

Interpretation of the duration of the detectability must take into account multiple variables such as drug metabolism and half-life; the subject's physical condition, fluid balance, and state of hydration; and the route and frequency of ingestion. For instance, it is not uncommon for intermediate-acting benzodiazepines given to chronic alcoholics for withdrawal to persist in urine for 2 weeks. These are to be considered general guidelines only.

**MANAGEMENT**

**Overall Principles**

It is important to consider the basic principles laid out by the NIDA that characterize effective drug abuse treatment. These can be further explored in detail in NIDA’s *Principles of Drug Addiction Treatment: A Research-based Guide*, which is available at [http://www.nida.nih.gov/DrugsofAbuse.html](http://www.nida.nih.gov/DrugsofAbuse.html). The extensive selection of books and materials located at this Web site is described at the end of the chapter.

1. **No single treatment is appropriate for all individuals.** Matching of treatment settings, interventions, and services to each patient's problems and needs is critical.
2. **Treatment needs to be readily available to avoid losing interested individuals.**
3. **Effective treatment attends to multiple needs of the individual, not just his or her drug use.** Other areas must be addressed, including medical, psychological, social, vocational, and legal problems.
4. **At different times during treatment, a patient may develop a need for medical services, family therapy, vocational rehabilitation, and social and legal services.**
5. **Treatment must be continued for an adequate time period.** This period varies with the individual, but most patients need at least 3 months for significant improvement. Programs should include strategies to prevent patients from leaving treatment prematurely.
6. **Individual and/or group counseling and other behavioral therapies are critical components of effective treatment for addiction.** Behavioral therapy also facilitates interpersonal relationships.
7. **Medications are an important element of treatment for many patients**, especially when combined with counseling and other behavioral therapies. This can include use of methadone and levo-a-acetylmethadol (LAAM) for individuals addicted to opiates, naltrexone for both opiate addiction and alcohol dependence, and nicotine patches or bupropion for nicotine addiction.
8. **Addicted or drug-abusing individuals with coexisting mental disorders should have both disorders treated in an integrated way.**
9. **Medical detoxification is only the first stage of addiction treatment and by itself does little to change long-term drug use.**
10. **Treatment does not need to be voluntary to be effective.** Sanctions or enticements in the family, employment setting, or criminal justice system can significantly increase treatment entry, retention, and success.
11. **Possible drug use during treatment must be monitored continuously.**
12. **Treatment programs should provide assessment for HIV/AIDS, hepatitis B and C, tuberculosis, and other infectious diseases, as well as counseling to help patients modify or change behaviors that place them or others at risk for infection.**
13. **Recovery from drug addiction can be a long-term process and frequently requires multiple episodes of treatment.** As with other chronic illnesses, relapses to drug use can occur during or after successful treatment episodes.

**Considerations in the Teen** In the treatment of drug abuse in adolescents, it is important to remember the following.

1. **Adolescents may use drugs for self-medication to deal with negative feelings or to treat underlying psychiatric conditions.** In this setting, treatment of the primary condition is essential. Substance use may subside if the appropriate primary condition is properly treated. It is difficult to get an adolescent to stop abusing drugs unless his or her denial is broken and alternative solutions are offered.
2. **Family involvement: Well-meaning family members may unknowingly enable an adolescent to continue abusing drugs by rescuing him or her from the consequences of drug use.**
3. **Treatment programs: Involvement with an outpatient drug clinic or an inpatient treatment program is often necessary for the drug-abusing adolescent.**

**Indications for Inpatient Treatment**

1. An adolescent is unable to stop using drugs in an outpatient setting.
2. An adolescent’s behavior is out of control.
3. An adolescent has significant life problems warranting intervention.
4. Legal involvement dictates residential treatment as a condition of probation.
5. An adolescent’s home environment is not supportive for stopping drug use.
6. Psychiatric symptoms require inpatient stabilization.

A residential treatment program can provide the adolescent an opportunity to develop positive relationships, during which the community itself functions as the primary therapeutic process.

**Selection of a Drug Treatment Program**

The following program characteristics combine recommendations from the American Academy of Pediatrics Committee on Substance Abuse (1985) and Center for Substance Abuse Treatment’s Treatment Improvement Protocol Series 32, *Treatment of Adolescents with Substance Use Disorders* (1999).

1. **A program’s staff should view drug and alcohol use as a primary disease, not as only a symptom of some other emotional problem, although substance abuse may be coexistent with a psychiatric disorder.**
2. **Recovering staff should have 2 to 5 years of sobriety and should have fulfilled the same formal training requirements as nonrecovering staff members in that position.** In addition, intimate teen-counselor interactions should be considered; a staff:patient ratio of no smaller than 1:6 should be maintained.
3. **Scheduled staff education and training with subsequent evaluation should be ongoing.** Adolescent-specific issues should be addressed.
4. **Formal orientation is critical as a first step in the treatment of the substance-abusing adolescent; it clearly defines the nature of the program and the formal expectations and boundaries.**
5. **Contracts: Substance-free and behavioral contracts are effective and should include clearly stated goals, consequences, and time frame.** In addition to providing a measure of progress, they benefit adolescents by giving them a sense of participation in and control over their treatment. Family contracts also provide...
clariﬁcation for members of chaotic or dysfunctional families, and they give the adolescent “identiﬁed patient” reassurance that changes in the entire family unit will occur and facilitate the transition from a higher to a lower level of care.
6. An aftercare program should be an integral part of the treatment. For example, support groups such as Alcoholics Anonymous (AA), Narcotics Anonymous (NA), Cocaine Anonymous (CA), ALANON, and ALATEEN, commonly called 12-step programs, should be incorporated into the treatment plan before the youngster leaves the program. The AA 12-step program is a fundamental part of the program because it provides the teen with good tools for change during and after treatment.
7. Drug or alcohol addiction is a family disease, so the program must include involvement and treatment of the whole family and important relationships.
8. A locally based program should be chosen if a good one exists.
9. Cost of the program should be considered.
10. Inquiry should be made into the type of therapy used.
11. The program should assist adolescents in progressively reconstituting each area of life, including family, school, friendships, and leisure-time activities.
12. Separate units for adolescents and adults are essential.
13. A school program should be an integral part of the program.
14. If the program is hospital based, it should be accredited by the Joint Commission for the Accreditation of Healthcare Organizations (JCAHO).

Components of a Drug Treatment Program

Treatment of chemical dependency involves abstinence, rehabilitation, use of tools for recovery, and extended care. Necessary components include the following.

1. Abstinence from all mood-altering substances is essential because of cross-addiction. Many of the disturbances of thought, behavior, and affect remit with sustained abstinence alone.
2. The teen should become actively enrolled in a 12-step program such as AA, NA, or CA. These programs offer a sponsor who acts as a guide to recovery and as a source of support and encouragement for the adolescent. If the patient has a bona fide addiction, involvement in such a program is essential to avoid the progressive natural history of addiction. Most 12 step programs focus on the ﬁrst ﬁve steps during primary treatment, with the remaining ones attended to during aftercare. Included here is a summary of the ﬁrst ﬁve steps with special considerations for adolescents and their developmental needs.
   a. Step 1: We admitted we were powerless over drugs and alcohol—that our lives had become unmanageable. Internalizing and accepting powerlessness is not a developmentally sound goal in adolescence; an acknowledgement of the “wrackage of the past” caused by the use of drugs and/or alcohol is a sufﬁcient goal.
   b. Step 2: We came to believe that a Power greater than ourselves could restore us to sanity. To convey this message, allow new clients to interact with those who have been successful in treatment and leaving the program. Providers must help adolescents with coexisting mental illnesses or cognitive disabilities to understand that Step 2 refers to obtaining help to stop drug seeking and use behavior, identifying the group and the 12-step process as the higher power, and recognizing the changes made by other group members who are further ahead in treatment through “working a program.”
   c. Step 3: We made a decision to turn our will and our lives over to the care of God as we understood Him. Translation: take the advice and accept the help of others in recovery; admitting your own “stinking thinking” that got you here.
   d. Step 4: We made a searching and fearless moral inventory of ourselves and Step 5: We admitted to God, to ourselves, and to another human being the exact nature of our wrongs. Steps 4 and 5 address accountability and acceptance of responsibility; experientially, the adolescent feels acceptance and a sense of self-worth.
3. Positive alternative leisure activities that are realistic and agreeable to the adolescent should be explored.
4. Vocational and educational assistance is needed because drug use can interfere with achievement.
5. Contact between the adolescent and non-drug-using peers should be encouraged. Outpatient treatment programs, 12-step programs, and activities such as “sobber” dances are sources of new friends for the recovering adolescent.
6. Family therapy is needed, because chemical dependency in one family member has an impact on other family members. Family members should also be required to go to a 12-step program such as ALANON or ALATEEN.
7. The parents and the adolescent should have a contract specifying expected behavior on the part of the teen, with appropriate privileges and consequences.
8. Individual therapy should be given to the teen for work on self-esteem, assertiveness skills, and expression of feelings.
9. The severity of illness should determine the type and intensity of treatment rendered. Assessment of illness severity based on a biopsychosocial view of addiction includes evaluation for the following.
   a. Acute intoxication and/or withdrawal
   b. Biomedical conditions and complications
   c. Emotional and behavioral conditions or complications
   d. Treatment resistance versus acceptance
   e. Relapse potential
   f. Recovery environment to which the adolescent is returning
   g. Concomitant psychiatric disorders
   h. Continuing treatment and aftercare plans
10. Linkages to the local community become important for the patient who is in transition to community-based 12-step programs, particularly those who are involved with multiple agencies such as juvenile justice or child welfare.

Third-party payers use these assessment dimensions to determine the “medical necessity” for speciﬁed levels of intensity of treatment. Addiction treatment today involves placing patients on a continuum of care, from comprehensive inpatient to outpatient modalities. A quality program should assist in determining the appropriate level of care and moving the patient as seamlessly as possible through levels of care, always matching the intensity of service to the particular patient’s needs.

Practitioners should remember that treatment for adolescent substance abuse does work. Studies have demonstrated clear improvements in substance-use frequency and in the number of substances used 1 year after treatment and also have shown sharp reductions in school and legal problems (Bergmann et al., 1995). However, substance abuse treatment must entail more than the formal treatment episode, such as continuing attendance at support groups, family support, and help with reentry at school. Identiﬁcation of adolescent substance abuse and referral are key roles for primary care providers.

Therapeutic Communities

As the need for addiction treatment for adolescents has increased and the existence of the so-called hospital-based Minnesota model program has essentially vanished, therapeutic communities (TCs) have proliferated. Once reserved for the atypical and most severely affected youth, they now speciﬁcally address the needs of the “typical” substance-abusing adolescent with evidence of progression to the abuse/dependence stage, comorbidity, and poor family/social structure. Although TCs have trained staff, they are fundamentally different from other residential treatment programs in that the community takes on a role in treatment and the program is largely self-reliant.

In addition to their more traditional roles, the TC staff are participating members of the community. The highly structured nature of the TC along with its dynamic role in providing continuous teaching and therapy is ideally suited to the typical adolescent patient and offers the added beneﬁt of experiencing, maybe for the ﬁrst time, a functioning “family” unit.

Modiﬁcations that are generally made in the TC model for treatment of adolescents can be summarized as follows:

1. The TC is focused on adolescents rather than adults.
2. There is a shorter length of stay (12 to 16 months is optimal).
3. The treatment program addresses developmental needs of the adolescent.
4. Adolescents have less autonomy, they are not confronted as aggressively, and there is greater oversight by staff of community activities.
5. Screening for comorbid disorders, history of abuse (physical, sexual), and learning disabilities such as attention deﬁcit hyperactivity disorder (ADHD) is provided.
6. Education/school time decreases the work schedule.
7. There is a focus on family issues and therapy.
8. The level system incorporates the behavioral theory model of adolescent behavior change; modeling the desired behavior as well as rewarding it is key.
Early Intervention

Early intervention is another area of substance-abuse intervention that is being implemented and evaluated. Unlike prevention, which is directed at the general population, early intervention targets individuals who are just beginning to have problems related to their substance abuse or a family member’s abuse. Unlike treatment, early intervention provides low-intensity service to individuals who are experimenting with substances or who have substance-related problems that are not yet severe. Early intervention programs and strategies are being implemented across the United States, but evaluation has not been extensive. Effectiveness of the programs has not been well demonstrated, and the potential for labeling some adolescents inappropriately as substance abusers is a consideration.

Juvenile Drug Courts

The success of adult drug courts and the increasing prevalence of substance abuse in the adjudicated adolescent population has resulted in the institution of dozens of juvenile drug court programs in more than 30 states. Because the juvenile justice system was established to specifically address the multiple needs of the adolescent, the concept of finally recognizing and addressing substance abuse in this population was intuitive. Juvenile drug courts should do the following:

1. Recognize that multiple risk factors prevail.
2. Recognize and address a range of developmental changes that inevitably occur during what is typically an extended period of “supervision.”
3. Address the adolescent and interventions in the context of the family, with awareness of the high level of family dysfunction, substance abuse, and impaired parenting skills.
4. Understand and develop proficiency in dealing with the unmotivated, conduct-disordered, substance-abusing teen.
5. Comply with juvenile confidentiality laws without hindering evaluation or referral.

A successful juvenile drug court will use the case management system, which provides a more “user-friendly” interface with the adolescent and family. Continuity beginning with intake assessment is best provided by this model. Members of the team should include the court, school representative, health care provider, social services representative, and substance abuse treatment staff member. There should be positive reinforcement for compliance as well as clearly outlined consequences that are swiftly enforced for violation of court-ordered program guidelines.

STREET NAMES FOR DRUGS

In treating adolescents for drug use, it is important for the practitioner to be familiar with drug slang. Drug slang constantly changes, and no listing is ever up-to-date. In addition, communities often have their own terms for drugs, and the translation may vary from one locality to another.

Slang Drug Terms

The following is a listing of slang words that seem to be used widely and frequently.

<table>
<thead>
<tr>
<th>Slang</th>
<th>Translation</th>
</tr>
</thead>
<tbody>
<tr>
<td>A’s</td>
<td>amphetamine</td>
</tr>
<tr>
<td>Acapulco gold</td>
<td>high-grade marijuana</td>
</tr>
<tr>
<td>acid</td>
<td>LSD (5-lysergic acid diethylamide tartrate)</td>
</tr>
<tr>
<td>adam</td>
<td>methylenedioxymethamphetamine (MDMA) (psychedelic)</td>
</tr>
<tr>
<td>angel dust</td>
<td>dimethyltryptamine (DMT) or PCP sprinkled over parsley or tobacco</td>
</tr>
<tr>
<td>Apache</td>
<td>fentanyl</td>
</tr>
<tr>
<td>babo</td>
<td>nalorphine</td>
</tr>
<tr>
<td>bag</td>
<td>packet of drugs, particularly heroin</td>
</tr>
<tr>
<td>bagging</td>
<td>sniffing glue in a bag</td>
</tr>
<tr>
<td>balloon</td>
<td>commonly sold unit of heroin</td>
</tr>
<tr>
<td>bars</td>
<td>methamphetamine</td>
</tr>
<tr>
<td>barbites</td>
<td></td>
</tr>
<tr>
<td>base</td>
<td>cocaine</td>
</tr>
<tr>
<td>Beast (The)</td>
<td>LSD</td>
</tr>
<tr>
<td>bennies</td>
<td>Benzedraine (brand of amphetamine sulfate)</td>
</tr>
<tr>
<td>Bernice</td>
<td>cocaine</td>
</tr>
<tr>
<td>bhang</td>
<td>marijuana</td>
</tr>
<tr>
<td>big chief</td>
<td>mescaline</td>
</tr>
<tr>
<td>Big D</td>
<td>LSD</td>
</tr>
<tr>
<td>black</td>
<td>LSD</td>
</tr>
<tr>
<td>black beauty</td>
<td>methamphetamine</td>
</tr>
<tr>
<td>blow</td>
<td>cocaine</td>
</tr>
<tr>
<td>blotter</td>
<td>LSD</td>
</tr>
<tr>
<td>blue angels</td>
<td>amobarbital sodium</td>
</tr>
<tr>
<td>bluebirds</td>
<td>amobarbital sodium</td>
</tr>
<tr>
<td>blue devils</td>
<td>amobarbital sodium</td>
</tr>
<tr>
<td>blue heaven</td>
<td>amobarbital sodium</td>
</tr>
<tr>
<td>blues</td>
<td>amobarbital sodium</td>
</tr>
<tr>
<td>Blue Cheer</td>
<td>type of LSD</td>
</tr>
<tr>
<td>blue racers</td>
<td>barbiturates</td>
</tr>
<tr>
<td>blues-and-reds</td>
<td>(see rainbows)</td>
</tr>
<tr>
<td>blue velvet</td>
<td>paregoric in combination with amphetamine or antihistamine such as Pyribenzamine (brand of tripelennamine)</td>
</tr>
<tr>
<td>bombers</td>
<td>large marijuana cigarettes</td>
</tr>
<tr>
<td>bombido</td>
<td>injectable amphetamine</td>
</tr>
<tr>
<td>boo</td>
<td>marijuana</td>
</tr>
<tr>
<td>boom</td>
<td>hashish</td>
</tr>
<tr>
<td>booze</td>
<td>alcohol</td>
</tr>
<tr>
<td>brown</td>
<td>heroin</td>
</tr>
<tr>
<td>brown dot</td>
<td>LSD</td>
</tr>
<tr>
<td>BT-72s</td>
<td>phenylpropanolamine</td>
</tr>
<tr>
<td>buds</td>
<td>marijuana</td>
</tr>
<tr>
<td>bullets</td>
<td>Seconal (brand of secobarbital sodium)</td>
</tr>
<tr>
<td>buscusso</td>
<td>cocoa paste</td>
</tr>
<tr>
<td>bush</td>
<td>marijuana</td>
</tr>
<tr>
<td>businessman's trip</td>
<td>DMT</td>
</tr>
<tr>
<td>buttons</td>
<td>dried tops of the Lophophora cactus (peyote)</td>
</tr>
<tr>
<td>cactus</td>
<td>mescaline</td>
</tr>
<tr>
<td>candy</td>
<td>barbiturates or benzodiazepines</td>
</tr>
<tr>
<td>cap</td>
<td>capsule</td>
</tr>
<tr>
<td>Captain Cody</td>
<td>codeine</td>
</tr>
<tr>
<td>cartwheel</td>
<td>white, round, double-scored amphetamine tablet</td>
</tr>
<tr>
<td>cat</td>
<td>Valium (ketamine)</td>
</tr>
<tr>
<td>caviar</td>
<td>rock or crack cocaine with marijuana, smoked</td>
</tr>
<tr>
<td>chalk</td>
<td>methamphetamine hydrochloride, powder form</td>
</tr>
<tr>
<td>Term</td>
<td>Description</td>
</tr>
<tr>
<td>----------------------</td>
<td>------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>champagne</td>
<td>rock or crack cocaine with marijuana, smoked</td>
</tr>
<tr>
<td>Charlie</td>
<td>cocaine</td>
</tr>
<tr>
<td>Chicano green</td>
<td>type of dark green marijuana</td>
</tr>
<tr>
<td>china white</td>
<td>heroin, fentanyl</td>
</tr>
<tr>
<td>chipping</td>
<td>periodic use of intravenously used drugs</td>
</tr>
<tr>
<td>Christmas tree</td>
<td>Tuinal (brand of amobarbital sodium and secobarbital sodium)</td>
</tr>
<tr>
<td>Chronic</td>
<td>marijuana</td>
</tr>
<tr>
<td>crystal</td>
<td>methamphetamine</td>
</tr>
<tr>
<td>Cody</td>
<td>codeine</td>
</tr>
<tr>
<td>coke</td>
<td>cocaine (extract of dried leaves of <em>Erythroxylon coca</em>)</td>
</tr>
<tr>
<td>cooke</td>
<td>cocaine addict</td>
</tr>
<tr>
<td>Cookie</td>
<td>PCP</td>
</tr>
<tr>
<td>coplots</td>
<td>amphetamines</td>
</tr>
<tr>
<td>crank</td>
<td>methamphetamine hydrochloride</td>
</tr>
<tr>
<td>crasp</td>
<td>heroin</td>
</tr>
<tr>
<td>Cristina</td>
<td>methamphetamine hydrochloride</td>
</tr>
<tr>
<td>crosses</td>
<td>amphetamines</td>
</tr>
<tr>
<td>crystal</td>
<td>methamphetamine hydrochloride, powdered or crystalline form</td>
</tr>
<tr>
<td>cubes</td>
<td>LSD</td>
</tr>
<tr>
<td>DET</td>
<td>diethyltryptamine</td>
</tr>
<tr>
<td>dexies</td>
<td>Dexamphetamine (brand of dextroamphetamine sulfate)</td>
</tr>
<tr>
<td>DMT</td>
<td>dimethyltryptamine</td>
</tr>
<tr>
<td>dolly</td>
<td>Dolophine (brand of methadone hydrochloride) tablets</td>
</tr>
<tr>
<td>DOM</td>
<td>dimethoxymethylamphetamine (see also STP)</td>
</tr>
<tr>
<td>doobie</td>
<td>marijuana cigarette</td>
</tr>
<tr>
<td>downers</td>
<td>nonnarcotic CNS depressants</td>
</tr>
<tr>
<td>dust</td>
<td>cocaine, PCP</td>
</tr>
<tr>
<td>dynamite</td>
<td>high-grade heroin</td>
</tr>
<tr>
<td>Ecstasy</td>
<td>dimethoxymethamphetamine (MDMA)</td>
</tr>
<tr>
<td>E</td>
<td>dimethoxymethamphetamine</td>
</tr>
<tr>
<td>Eve</td>
<td>freebase cocaine</td>
</tr>
<tr>
<td>fatty</td>
<td>large marijuana cigarette</td>
</tr>
<tr>
<td>flake</td>
<td>cocaine</td>
</tr>
<tr>
<td>footballs</td>
<td>amphetamine tablets (oval shaped)</td>
</tr>
<tr>
<td>G</td>
<td>g-hydroxybutyrate (GHB)</td>
</tr>
<tr>
<td>gage</td>
<td>marijuana (term seldom used)</td>
</tr>
<tr>
<td>ganja</td>
<td>hashish, marijuana</td>
</tr>
<tr>
<td>gee-head</td>
<td>paregoric user</td>
</tr>
<tr>
<td>geeze</td>
<td>inject heroin</td>
</tr>
<tr>
<td>gold dust</td>
<td>cocaine</td>
</tr>
<tr>
<td>goofballs</td>
<td>barbiturates</td>
</tr>
<tr>
<td>grass</td>
<td>marijuana (dried leaves, seeds, and stems of <em>Cannabis sativa</em>)</td>
</tr>
<tr>
<td>greenies</td>
<td>ethchlorvynol</td>
</tr>
<tr>
<td>H</td>
<td>heroin (diazetyl morphine)</td>
</tr>
<tr>
<td>Harry</td>
<td>heroin (diazetyl morphine)</td>
</tr>
<tr>
<td>Harvey Wallbanger</td>
<td>STP-LSD (see STP)</td>
</tr>
<tr>
<td>hash</td>
<td>hashish (resin from <em>Cannabis</em>)</td>
</tr>
<tr>
<td>hay</td>
<td>marijuana</td>
</tr>
<tr>
<td>hearts</td>
<td>Dexamphetamine (brand of dextroamphetamine sulfate)</td>
</tr>
<tr>
<td>hogs</td>
<td>PCP</td>
</tr>
<tr>
<td>honk</td>
<td>spray-paint inhalation</td>
</tr>
<tr>
<td>horse</td>
<td>heroin (diazetyl morphine)</td>
</tr>
<tr>
<td>huffing</td>
<td>inhaling hydrocarbons, especially glue or gasoline</td>
</tr>
<tr>
<td>hyke</td>
<td>Hycoadan (brand of hydrococodone)</td>
</tr>
<tr>
<td>J</td>
<td>marijuana cigarette</td>
</tr>
<tr>
<td>Jim Jones</td>
<td>marijuana cigarette laced with cocaine dipped in PCP</td>
</tr>
<tr>
<td>joint</td>
<td>marijuana cigarette</td>
</tr>
<tr>
<td>jug</td>
<td>ampule of injectable drugs</td>
</tr>
<tr>
<td>juice</td>
<td>PCP or anabolic steroids</td>
</tr>
<tr>
<td>junk</td>
<td>heroin (diazetyl morphine)</td>
</tr>
<tr>
<td>junkie</td>
<td>heroin user</td>
</tr>
<tr>
<td>key</td>
<td>kilogram of marijuana</td>
</tr>
<tr>
<td>KJ</td>
<td>marijuana and PCP</td>
</tr>
<tr>
<td>lemons</td>
<td>methaqualone</td>
</tr>
<tr>
<td>lid</td>
<td>one ounce of marijuana (approximately)</td>
</tr>
<tr>
<td>liquid Ecstasy</td>
<td>GHB</td>
</tr>
<tr>
<td>Llesia</td>
<td>Mexican term for marijuana</td>
</tr>
<tr>
<td>locoweed</td>
<td>Jimsonweed (<em>Datura stramonium</em>)</td>
</tr>
<tr>
<td>ludes</td>
<td>Quaule (methaqualone)</td>
</tr>
<tr>
<td>M</td>
<td>morphine sulfate</td>
</tr>
<tr>
<td>mad dog</td>
<td>cheap wine</td>
</tr>
<tr>
<td>magic mushroom</td>
<td>mushroom (<em>Psilocybe mexicana</em>) containing psilocybin</td>
</tr>
<tr>
<td>magnums</td>
<td>amphetamines</td>
</tr>
<tr>
<td>mesc</td>
<td>mescaline</td>
</tr>
<tr>
<td>mese</td>
<td>mescaline (resin from <em>Lophophora cactus-peyote</em>)</td>
</tr>
<tr>
<td>meth</td>
<td>methamphetamine</td>
</tr>
<tr>
<td>Mexican brown</td>
<td>brown marijuana from Mexico</td>
</tr>
<tr>
<td>Mexican Valium</td>
<td>flunitrazepam (Rohypnol)</td>
</tr>
<tr>
<td>Mickey, or Mickey Finn</td>
<td>combination of alcohol and chloral hydrate</td>
</tr>
<tr>
<td>Miss Emma</td>
<td>morphine sulfate</td>
</tr>
<tr>
<td>MJ</td>
<td>marijuana</td>
</tr>
<tr>
<td>mota</td>
<td>Mexican term for good marijuana</td>
</tr>
<tr>
<td>mushroom</td>
<td>psilocybin (psychedelic)</td>
</tr>
<tr>
<td>nembies</td>
<td>pentobarbital sodium</td>
</tr>
<tr>
<td>number</td>
<td>marijuana cigarette</td>
</tr>
<tr>
<td>orange</td>
<td>STP-LSD (see also STP)</td>
</tr>
<tr>
<td>orange sunshine</td>
<td>form of LSD</td>
</tr>
<tr>
<td>Panama red</td>
<td>potent grade of marijuana from Panama</td>
</tr>
<tr>
<td>pasta</td>
<td>cocoa paste</td>
</tr>
<tr>
<td>peace pill</td>
<td>Sernylan (brand of phencyclidine [PCP]), originally used as an anesthetic for dogs</td>
</tr>
<tr>
<td>peanuts</td>
<td>barbiturates</td>
</tr>
<tr>
<td>PG</td>
<td>paregoric</td>
</tr>
<tr>
<td>Substance</td>
<td>Sample Street Names</td>
</tr>
<tr>
<td>---------------------------</td>
<td>----------------------------------------------</td>
</tr>
<tr>
<td>Hashish</td>
<td>boom, chronic, gangster, hash, hash oil, hemp</td>
</tr>
<tr>
<td>Marijuana</td>
<td>blunt, dope, ganja, grass, herb, joints, Mary Jane, pot, reefer, sinsemilla, skunk, weed</td>
</tr>
<tr>
<td>Depressants</td>
<td></td>
</tr>
<tr>
<td>Barbiturates</td>
<td>reds, red birds, phennies, tooies, yellows, yellow jackets</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>candy, downers, sleeping pills, tranks</td>
</tr>
<tr>
<td>Flunitrazepam (Rohypnol)</td>
<td>forgel-me pill, Mexican Valium, R2, Roche, roofies, rofinol, rope, rophies</td>
</tr>
<tr>
<td>GHB</td>
<td>G. Georgia home boy, grievous bodily harm, liquid Ecstasy</td>
</tr>
<tr>
<td>Methaqualone</td>
<td>ludes, mandrex, quad, quay</td>
</tr>
<tr>
<td>Dissociative anesthetics</td>
<td>cat Valiums, K, Special K, vitamin K</td>
</tr>
<tr>
<td>PCP</td>
<td>angel dust, boat, hog, love boat, peace pill</td>
</tr>
<tr>
<td>Hallucinogens</td>
<td></td>
</tr>
<tr>
<td>LSD</td>
<td>acid, blotter, boomers, cubes, microdot, yellow sunshine, fry(ing)</td>
</tr>
<tr>
<td>MDMA + LSD</td>
<td>candy flipping</td>
</tr>
<tr>
<td>Opioids and morphine derivates</td>
<td></td>
</tr>
<tr>
<td>Codeine</td>
<td>captain cody, cody, schoolboy, doors and fours, loads, pancakes and syrup</td>
</tr>
</tbody>
</table>
Fentanyl
Heroin
Morphine
Opium
Stimulants
Amphetaemine
Cocaine
MDMA
Methamphetamine
Methylphenidate
Others
Anabolic steroids
Inhalants
Acetaminophen (Tylenol):
'broids, juice, Deca
Therapy Manuals for Drug Addiction: NIDA's Therapy Manuals series presents clear, helpful information to aid drug treatment practitioners in providing the best
Assess and support cardiovascular status.
Ethchlorvynol (Placidyl): Lethal levels require hemodialysis or charcoal perfusion.
Barbiturates: Consider whether the barbiturate is long- or short-acting.
Glutethimide (Doriden): Alkaline lavage of the stomach and charcoal can be used to impede absorption of the drug. Dialysis and hemoperfusion, when indicated,
Monitor urinary output through a urinary catheter in comatose patients.
Monitor oxygen tension with pulse oximetry.
Short-acting: Use charcoal hemoperfusion for severe overdoses.
JIF, MPH, R-ball, Skippy, the smart drug, vitamin R
Establish and maintain a clear airway.
Benzodiazepines: Give flumazenil, 0.2 mg, over 30 seconds. Another 0.3 mg can be given over 30 seconds if there is no response after the first 30 seconds. If
Forced diuresis: This measure is helpful mainly for drugs that are excreted unchanged in the urine, especially for aspirin and barbiturate overdoses. It is
Research Report Series: NIDA's Research Reports simplify the science of research findings for the educated lay public, legislators, educational groups, and
Narcotics: Naloxone can reverse the respiratory and CNS depressive action of the opiates. Be prepared to give additional doses as necessary. The starting
bennies, black beauties, crosses, hearts, LA turnaround, speed, truck drivers, uppers, tweak
monitor vital signs frequently, including temperature and respiratory rate.
Long-acting: Use forced diuresis, alkalinization of the urine, charcoal hemoperfusion, or hemodialysis.
Hemodialysis: This is used to treat patients with severe intoxication, clinical instability, or coexistent hepatic or renal failure, or when the patient has ingested a
M, miss emma, monkey, white stuff
Removal of Toxins Already Absorbed
1. Forced diuresis: This measure is helpful mainly for drugs that are excreted unchanged in the urine, especially for aspirin and barbiturate overdoses. It is
essential to monitor volume status, electrolyte values, and urine output closely when proceeding with this treatment. Rhabdomyolysis is occasionally observed
with ingestions of amphetamine, MDMA, or PCP and requires aggressive management of fluids and electrolytes.
2. Alkalization of the urine: This measure is beneficial in the treatment of aspirin and phenobarbital overdoses.
3. Hemodialysis: This is used to treat patients with severe intoxication, clinical instability, or coexistent hepatic or renal failure, or when the patient has ingested a
potentially lethal dose and the drug is diffusible across dialysis membranes. Dialysis may help in the treatment of severe overdoses of lithium, amphetamines,
aspirin, long-acting barbiturates, or alcohol.
Specific Measures
1. Acetaminophen (Tylenol): N-Acetylcysteine (Mucomyst) has been shown to be effective when given within 24 hours after ingestion.
2. Amphetamines: Lorazepam (Alivan) or haloperidol (Haldol) is useful for agitation. Severe hypertension can be treated with nitroprusside; avoid b-blockers.
(Hemodialysis has been used in severe overdose.)
3. Barbiturates: Consider whether the barbiturate is long- or short-acting.
   a. Long-acting: Use forced diuresis, alkalization of the urine, charcoal hemoperfusion, or hemodialysis.
4. Short-acting: Use charcoal hemoperfusion for severe overdoses.
5. Ethchlorvynol (Placidyl): Lethal levels require hemodialysis or charcoal perfusion.
6. Glutethimide (Doriden): Alkaline lavage of the stomach and charcoal can be used to impede absorption of the drug. Dialysis and hemoperfusion, when indicated,
can improve clearance.
7. Methaqualone (Quaalude): Treatment is mainly supportive. When indicated, charcoal hemoperfusion can be used.
8. Narcotics: Naloxone can reverse the respiratory and CNS depressive action of the opiates. Be prepared to give additional doses as necessary. The starting
dose is 2 mg. More may be needed for an overdose, and less may be necessary to avoid precipitating withdrawal symptoms in a known addict.
9. Phencyclidines: Dystonic reactions can be reversed with diphenhydramine (Benadryl), 25 to 50 mg given intravenously. Treatment of overdoses should include
lavage and forced diuresis.
10. Phencyclidines: Dystonic reactions can be reversed with diphenhydramine (Benadryl), 25 to 50 mg given intravenously. Treatment of overdoses should include
lavage and forced diuresis.
11. Phencyclidines: Dystonic reactions can be reversed with diphenhydramine (Benadryl), 25 to 50 mg given intravenously. Treatment of overdoses should include
lavage and forced diuresis.
12. Tricyclic antidepressants, including Amitriptyline (Elavil, Triavil), imipramine (Tofranil), and doxepin (Sinequan): Gastric emptying is clearly of benefit within the
first 1 to 2 hours, and probably later because of delayed gastric emptying caused by anticholinergic effects. This should be followed by the use of activated
charcoal. The mainstay of treatment is alkalization of the blood with sodium bicarbonate. A dose of 1 to 2 mmol/kg is given intravenously for significant cardiac
conduction delay or ventricular dysrhythmias. Physostigmine should be avoided. In significant ingestions, early agitation may proceed rapidly to coma; elective
early intubation is prudent in these cases.
13. Lithium: Treatment includes gastric lavage, sodium as intravenously administered normal saline solution, urine alkalization, and, in severe cases,
hemodialysis.
14. Benzodiazipines: Give flumazenil, 0.2 mg, over 30 seconds. Another 0.3 mg can be given over 30 seconds if there is no response after the first 30 seconds. If
there is no response after the second 30 seconds, give 0.5 for 30 seconds at 1-minute intervals, up to a total dose of 3 mg.

WEB SITES
http://www.nida.nih.gov/TB/Clinical/ClinicalToolbox.html . The NIDA has extensive resources for providers on treatment. These can all be obtained at this Web site:
1. Therapy Manuals for Drug Addiction: NIDA's Therapy Manuals series presents clear, helpful information to aid drug treatment practitioners in providing the best
possible care. The therapies presented in the manuals exemplify the best of what is currently known about treating drug addiction. The first three manuals in the series are:
   Manual 3: An Individual Drug Counseling Approach to Treat Cocaine Addiction: The Collaborative Cocaine Treatment Study Model
2. Research Report Series: NIDA's Research Reports simplify the science and research findings of the educated lay public, legislators, educational groups, and
practitioners. The series is updated periodically to reflect current knowledge on drugs of national interest. The Toolkit contains six Research Reports:

Anabolic Steroid Abuse
Cocaine Abuse and Addiction
Methamphetamine Abuse (available in English or Spanish)
Nicotine Addiction
Inhalant Abuse
Heroin Abuse and Addiction
3. Approaches to Drug Abuse Counseling: This book gives detailed descriptions of 12 counseling approaches currently being used in the United States. It includes contributions from the University of Pennsylvania, Hazeldon Foundation, 12-step counselors at the Betty Ford Clinic, and other respected treatment programs. Target audiences are treatment researchers, clinicians, medical schools, colleges, and universities.
4. Principles of Drug Addiction Treatment: This 52-page booklet presents 13 principles of effective drug abuse treatment, answers frequently asked questions, describes categories of treatment programs, and outlines scientifically validated approaches to treating drug addiction.
5. NIDA Publications Catalog: The Institute's publications catalog, updated twice yearly, lists all available NIDA publications, posters, and audio/video products and provides information on ordering from a variety of sources.
6. Commonly Abused Drugs Chart: An 8.5- × 11-inch laminated chart lists the most commonly abused drugs with their commercial and slang names, Drug Enforcement Agency categories, routes of administration, and short- and long-term effects. Principles of drug addiction treatment are also listed.
7. Measuring and Improving Cost, Cost-Effectiveness, and Cost-Benefit for Substance Abuse Treatment Programs: This flyer describes a NIDA manual that takes the mystery out of cost accounting for treatment programs. The methodology presented in the manual is based on a cost-procedure-process-outcome analysis model that has been well researched and tested with substance abuse treatment programs.
8. The NIDA Community-Based Outreach Model: A Manual to Reduce the Risk of HIV and Other Blood-borne Infections in Drug Users: This brochure describes a NIDA manual that contains step-by-step guidance to help community planners, policymakers, programmers, and service providers conduct effective outreach programs and reduce the risk of HIV and other blood-borne infections among drug abusers. The NIDA Outreach Model is based on more than 15 years of studies in more than 50 communities demonstrating the effectiveness of community-based outreach strategies.

http://www.drugs.indiana.edu/druginfo/dotrules.html
http://www.nida.nih.gov/DrugsOfAbuse.html
http://www.whitehousedrugpolicy.gov/streetterms/

REFERENCES AND ADDITIONAL READINGS
Johnson MD, Herits TJ, St Dennis C. How to spot illicit drug abuse in your patients. Postgrad Med 1999;106:199.
During the adolescent years, adolescents and their families face a myriad of issues and concerns. As stated earlier in this book, what seems important to the adolescent may not be of concern to his or her parents, and vice versa. Often, the issues that concern adolescents are self-resolving, helped by friends or family, or are never brought to the physician's attention. When the physician is involved, he or she may be asked to answer questions such as, Am I normal? Is my adolescent normal? or What can I do about this problem? Occasionally, the issue becomes severe enough to create family disruption. And in the extreme, these problems may lead to acting-out behaviors such as truancy, juvenile delinquency, substance abuse, or suicide.

Just what is normal adolescent behavior? Chapter 2 dealt with many aspects of normal psychosocial development in the adolescent. This chapter emphasizes common psychosocial concerns to which parents and physicians should be especially sensitive. There are no clear cut answers to what is normal adolescent behavior. In an attempt to understand normal behavior and to build an alliance with the adolescent, it is often helpful for physicians to remember their own adolescence yet not rely purely on their own experiences to determine what is expected adolescent behavior. In assessing issues that trouble adolescents or their families, the health care provider must consider the following:

1. The severity of the problem: Is this behavior usual for the adolescent, or is there a marked change?
2. The chronicity of the problem: Has the problem been present for days, months, or years?
3. The adolescent's emotional development in regard to independence, body image, peers, school, and identity: Are the behaviors consistent with the developmental stage of the adolescent?
4. Daily functioning: Are the problems severe enough to interfere with the daily functioning of the adolescent in areas such as school and social activities?
5. Family functions: The health care provider should consider the adolescents' behavior within the social context of their immediate world, especially their relationship with their family or caregivers. It is helpful to understand the style of parenting, because research has determined that authoritative parenting—that which is warm, firm, involved, and consistent in establishing rules and limitations that are developmentally appropriate (Baumrind, 1991)—leads to increased adolescent competence and psychological well-being (Steinberg, in press). Understanding the severity of the adolescent's acting-out behavior within the interpersonal context of the teen and his or her parents helps the health care provider if it is determined that an intervention may be necessary.

Any concern of an adolescent or parent deserves assessment. Although some general and matter-of-fact topics such as daydreaming or pubertal gynecomastia can be handled by discussion and reassurance, other issues such as family conflicts, psychosomatic illnesses, or depression may require several or more sessions with the adolescent and family. When the problem involves severe or chronic disorders or high-risk violent or self-injurious behavior, referral is usually indicated.

Indications in considering a referral include the following:

1. Suicidal or self-injurious behavior
2. Mental disorder, such as a mood or anxiety disorder
3. Substance abuse
4. Psychotic or other severe psychiatric symptoms
5. Developmental delay or learning disabilities
6. Behavioral problems that either have been present since childhood or have acutely emerged
7. Problems that have persisted despite extensive interventions by the primary caregiver
8. Problems believed to be beyond the skills of the health care provider
9. A problem is present but the health care provider is unsure what it is (e.g., the adolescent with no friends who is socially withdrawn)
10. Severe life stressors or changes in the family, such as death, divorce, or suicide of a parent or sibling
11. School behavior and performance that has changed dramatically
12. Runaway behavior
13. Frequent fighting among peers and/or family
14. Chronic or acute illness

Types of behaviors that may indicate common adolescent behavior, a trouble sign, or a problem behavior are shown in Table 76.1.

![Table 76.1. Common adolescent behaviors, trouble signs, and problem behaviors](image)

## REFERENCES

When the health care provider decides that a referral is necessary, several considerations are important:

1. Motivation: Are the teen and the parents motivated to attend counseling sessions? Without such motivation, compliance is extremely poor.
2. Do the teen and family understand the reason for the referral?
3. Is the referral appropriate for the problem? Many options exist for referrals for psychosocial problems, including psychologists, psychiatrists, vocational counselors, youth programs (e.g., Big Brothers/Big Sisters, YMCA), and residential or vocational programs such as the Job Corps.

Several interventions may help in making the referral:

1. The health care provider should reassure the adolescent that the primary health care practitioner will continue to follow the adolescent and will be very much involved in his or her care.
2. The health care provider should explain that as part of the total evaluation and treatment of the adolescent's problem, a psychological or psychiatric evaluation...
is important. If, despite a negative medical evaluation, the adolescent or family feels strongly that the problem is organic, the practitioner can still explain that the psychological evaluation is important in the diagnostic workup. The adolescent and family should also be advised that even if the problem turns out to be organic, the counseling could still help the adolescent cope better with the symptoms.

3. The health care provider should explain his or her concerns to the adolescent and family. As part of this explanation, the health care practitioner could ask the adolescent whether he or she thinks that "things could be going better." If the adolescent answers yes, the practitioner can state that counseling is one way to help make things go better.

4. The practitioner should reassure the adolescent that the counseling is usually arranged for a limited time and that if counseling does not work out the adolescent or family can stop.

5. The adolescent should be aware that seeing a psychologist or psychiatrist does not mean that he or she is "crazy." Counseling should be described as an opportunity to help the adolescent feel better, to build coping skills, and to enhance family or interpersonal relations.

6. It is necessary for the physician and the parents to distinguish between the adolescent and his or her behavior. They must convey acceptance of the adolescent even if they believe the adolescent’s behavior to be negative or unhealthy.

CONCERNS OF ADOLESCENTS

Common concerns of adolescents include:

1. Parental conflicts: Rules (e.g., curfew, driving), privacy, expectations, and peer relationships
2. Peers: Interpersonal concerns regarding friendships, relationships, and sexuality
4. School: Popularity, academic pressures, teachers, and adjustment to a new school
5. Sibling/family conflicts
6. Social situations
7. Mild depression
8. Medical concerns: Menstrual disorders, short stature, acne, weight disorders, and pubertal gynecomastia
9. Psychosomatic problems: Headaches, stomach pains, and insomnia
10. Safety concerns: Violence in the environment, community, home, or school
11. Prospects for the future: Economic realities, pregnancy, and particularly human immunodeficiency virus (HIV)

CONCERNS OF PARENTS

Common concerns of parents with regard to their adolescent son or daughter include:

1. Adolescent acting-out behaviors: Mild acting-out behaviors are common in early and middle adolescence; marked acting-out behaviors may be an indication of an emotional or family dysfunction.
2. Risk-taking behaviors: Risk taking is a common part of the early and middle adolescent process. Life-threatening, risk-taking behaviors require family sessions for the purposes of educating, limit setting, and evaluation of any associated unmet needs of the adolescent.
3. Emotional lability: Assessment of the severity, including detailed description of the moods and changes, is required to determine whether a mood disorder is the underlying cause.
4. Drug and alcohol use: Evaluation of the type and degree of drug use is required.
5. Academic problems: Evaluation of the type and severity of the problem is required. Parents should be encouraged to follow-up with their child’s school for any available services that may be helpful.
6. Sexual activity: Parents should be allowed to express their concerns, but the need for confidentiality between youth and practitioner should be explained to the parents. Discussion of sexuality and sexual activity between teen and parent should be highly encouraged. Parents often have questions and concerns about limit setting, such as, What is adequate supervision at parties? Should I allow my son or daughter to spend time alone in the house or in a room with a girlfriend or boyfriend? and What degree and type of sexual activity is normal?
7. Eating disorders: An evaluation of weight loss or gain, attitude toward body image, eating habits, emotional health, family cohesion, and self-esteem should be undertaken.
8. Safety issues such as violence in the environment and driving safety (i.e., teen or other motorists driving under the influence): Having a new driver is a key stressor for parents and one that brings up many issues of limit setting and sharing of responsibilities.
9. Peer influences: Parents should be aware of the importance of peer influences and should monitor behaviors and activities while understanding that adolescents need to choose their own friends.
10. Psychosomatic problems: Medical evaluation should include an exploration of any sources of stress that the adolescent may be attempting to cope with psychosomatically.
11. “Wasting time” by the adolescent, especially daydreaming: Parents should be reassured that this is usually a normal part of adolescent development. However, parents should monitor to help redirect youth who may need more direction in their activities.

CONCLUSION

Despite the many problems and concerns that parents of adolescents struggle with, it is important to remember the many competencies and the energy, enthusiasm, and vivacity youth possess. Health care providers should encourage caregivers and parents to refocus on these positive aspects while encouraging follow-up with appropriate resources for help when needed. By being respectful, consistent, and caring, parents facilitate a positive transition through adolescence toward adulthood.

WEB SITES

http://www.ncfyl.com/support.htm: Supporting Your Adolescent: Tips for Parents, prepared by the National Clearinghouse on Families and Youth. The Clearinghouse has many helpful articles for parents needing help with their teenage children.

http://www.trpc.com/parenttalk/adoles.htm: Articles on parenting teens from the National Parenting Center, many by Kathleen McCoy and Charles Wibbelsman, M.D., from Teen Body Book.


REFERENCES AND ADDITIONAL READINGS


### Risk and Resilience

#### Epidemiology of Risk-Taking Behavior

<table>
<thead>
<tr>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morbidity</td>
</tr>
<tr>
<td>Factors involved in Risk-Taking Behavior</td>
</tr>
<tr>
<td>Biopsychosocial Factors</td>
</tr>
<tr>
<td>Incarcerated Youth and Juvenile Delinquency</td>
</tr>
</tbody>
</table>

#### Definitions

<table>
<thead>
<tr>
<th>Morbidity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
</tr>
</tbody>
</table>

#### Epidemiology

Types of Runaways

Reasons for Running Away

Suicide

Substance Abuse

Interparental

Web Sites

References and Additional Readings

---

Changes in society over the past 25 to 30 years have significantly influenced the adolescent years. The educational experience has been prolonged and the job market constricted. Adaptation to intrinsic psychological developmental triggers are now made in an environment of increasing drug use, sexual activity, and media stimulation and weakened family structure. Attempts by adolescents to cope with these pressures often result in social behaviors that are associated with inherent and inconstant degrees of risk to health. The consequences of these health risks may be immediate or long range.

In the United States it is estimated that:

- Every 31 seconds a teenager becomes pregnant.
- Every 1 to 2 minutes a teen gives birth.
- Every 78 seconds a teen attempts suicide.
- Every 20 minutes a teen is killed in a car accident.
- Every 90 minutes a teen is murdered and another commits suicide.

The major causes of death and disability among the approximately 40 million American youth age 10 to 19 years, who comprise 14% of the U.S. population, have essentially social and behavioral issues at their root—and parenthetically, the majority are preventable!

### RISK AND RESILIENCE

The concept of risk has been well established as a characteristic that detrimentally exposes young people to threats to their health and well-being. Not all youth exposed to similar risk situations respond in the same way. Where some do not sustain any damage, emotional or physical, others are compromised for the remainder of their lives. Some youth are said to be resilient in and fact may respond in a positive way to stress and adversity. As a characteristic, resilience is developmental and interactive with risk and stems from a mix of biology and early development (Rutter, 1987). Garvey (1991) describes resiliency as "the capacity to recover and maintain adaptive behavior after insult." Resilience involves a healthy set of behaviors and coping mechanisms that are integrated into decision making and elicited in response to a threatening situation. The youth responds flexibly and makes positive choices despite impoverishment of life experience. Factors involved in developing resilience include both internal factors, including the dispositional characteristics of the adolescent, such as intelligence, sense of humor, empathic abilities, and an internal locus of control, and external factors including family cohesion and warmth with the love and involvement of at least one parent.

This chapter focuses on risk-taking behavior among adolescents in general and on specific out-of-control, high-risk activities.

### EPIDEMIOLOGY OF RISK-TAKING BEHAVIOR

#### Mortality

In 1996–1997, about 19,000 adolescents died per year. Almost 14,000 deaths occurred from injuries and 5,000 from natural causes. The proportion of all deaths from injuries increased with age, from 47% among 10-year-olds to 81% among those 18 years of age. Motor vehicle traffic-related injuries and firearm-related injuries are the leading causes of injury death among 10- to 19-year-olds. In 1996–1997, they caused 55% of all deaths and 75% of all injury deaths. Motor vehicle accidents increase with age, with the greatest increase being between 15 and 16 years of age (see Chapter 5). Many of these events are related to drug or alcohol use. The mortality figures do not reflect the magnitude of morbidity and subsequent disability associated with these leading causes of injury.

#### Morbidity

It is estimated that 20% of U.S. teenagers have great difficulty making the transition from childhood to adulthood and that this difficulty is often reflected in their risk-taking behaviors. The frequency of these morbidities correlates with the teen's biobehavioral risk profile. The latter is directly dependent on the frequency and number of risk behaviors that the teenager uses to resolve psychological and social developmental needs. Frequent subsequent problems include the following.

1. **Pregnancy:** In the United States more than 900,000 teens become pregnant each year (MacKay et al., 2000). In 1996, the pregnancy rate was 98.7 pregnancies per 1,000 female adolescents age 15 to 19 years, a decrease of 15% since 1991. In 1997–1998, there were approximately 493,600 births to adolescents 13 to 19 years of age. Teenage pregnancies are associated with higher rates of complications, particularly low birth weight and infant mortality, and especially when the mother is very young. These complications may be related to the lack of regular prenatal care. Factors increasing pregnancy and parenting risks include poverty, low intellect, lower status of employment and wages, reliance on public assistance, poor literacy and work skills, substance abuse, emotional or sexual abuse, and increased number of children in the family of origin (i.e., many siblings and possibly early pregnancies in the index adolescent's female siblings). Fifty-one percent of adolescents use no contraception during first intercourse, and 20% of adolescent pregnancies occur within 1 month after first intercourse.

2. **Sexual activity:** The 1999 Youth Risk Behavior Survey found that approximately half (49.9%) of all high school students had had sexual intercourse during their lifetime. Female students in grades 11 and 12 (53.8% and 65.8%, respectively) were significantly more likely than female students in grades 9 and 10 (32.5% and 42.6%, respectively) to have had sexual intercourse. Male students in 12th grade (63.9%) were significantly more likely than male students in grades 9 and 11 (44.5% and 51.4%, respectively) to report this behavior. A total of 6.3% of students initiated sexual intercourse before age 13 years (nonabusive), including 12.2% of male and 4.4% of female students. In addition, 16.2% of all students had had sexual intercourse with four or more partners. Fifty-eight percent of currently sexually active adolescents reported condom use during their last sexual intercourse. Sexually transmitted diseases (STDs) are the most commonly reported infectious diseases among sexually active adolescents. Chlamydia and, to a lesser extent, gonorrhea are epidemic in this age group, with adolescents having the highest prevalence of any age group nationally, if prevalence is expressed only for those who are sexually active. Although the overall prevalence of human immunodeficiency virus (HIV) infection is relatively low among adolescents, adolescents in some minority and racial groups are disproportionately affected by HIV and AIDS.
Substance abuse: Estimates for problem alcohol use among senior high school students run as high as 30%. In 1999, about one half of all high school students (48% of girls and 52% of boys) reported alcohol use during the previous 30 days. Binge drinking (consumption of five or more drinks on one occasion) was reported by 28% of female students and 35% of male students during the same 30-day period. Use of marijuana, the most commonly reported illicit drug used among high school students, was reported by 47% of high school students (MacKee et al., 2000). Almost one third of adolescents by 12th grade had illicitly used drugs other than marijuana.

Runaway behavior: More than 1 million teens run away each year (Deisher and Farrow, 1986), and an estimated 10% to 25% of these adolescents become long-term street youth. Two federal studies found the numbers of runaway youths to range between 351,000 and 635,000 in 1975 and to be approximately 456,700 in 1988 (Rimpau et al., 1998). These youth often survive through illegal activities such as survival sex, burglary, or drug dealing. Approximately 28% of street youth and 10% of shelter youth reported having participated in survival sex. Participation was associated with age, days away from home, victimization, criminal behaviors, substance use, suicide attempts, STDs, and pregnancy.

Suicide: The age-adjusted death rate for suicide, the eighth leading cause of death, has been edging downward during the 1990s. The age-adjusted suicide rate was 10.4 deaths per 100,000 in 1998, compared with 11.5 in 1990. On the other hand, suicide ideation or attempting suicide is a powerful indicator of mental and emotional health. In 1999, 25% of girls and 14% of boys adolescents in grades 9 through 12 reported seriously considering or attempting suicide.

Although the majority of adolescents complete high school, those students who drop out of school have fewer opportunities to succeed in the work force or to assume a fully functional place in society. High-school dropouts have lower earnings, experienced more unemployment, and are more likely to receive welfare or be in prison. Using the indicator of event dropout rate, which measures the proportion of students who drop out each year and therefore do not successfully complete high school, 4.2% of students age 15 to 19 years who were in high school the previous year were not enrolled again. The event dropout rate increases with age. The cumulative effect of several hundred thousand adolescents leaving school each year translates into several million young adults outside of school and not earning a high school credential. Socioeconomic status is strongly associated with the decision to stay in school. Students from low-income families dropped out of high school at a rate more than 3 times greater than that of teenagers from middle-income families and 4 times greater than that of teens from high-income families. Members of nonwhite races, whether as a reflection of socioeconomic status or as an independent variable, are disproportionately represented among dropouts.

Crime: In the 1999 Youth Health Risk Behavior Surveillance (CDC, 2000), 17% of students had carried a weapon one or more times during the past month (28.6% of males and 6% of females); 4.9% of students had carried a gun within the past month (9% of males and 0.8% of females). Forty-four percent of males and 27.3% of females reported having been in at least one fight during the previous year. Approximately 5% of students reported missing school on 1 or more days during the past month because they felt unsafe at school or when traveling to or from school.

FACTORS INVOLVED IN RISK-TAKING BEHAVIOR

Childhood and adolescence are continuous and contiguous events in the life cycle. The manner in which the developmental challenges of adolescence are expressed is dependent on, if not largely determined by, personality traits and other characteristics established in childhood. The physical, psychological, and social maturational forces of development combine to determine behavior at any moment. During adolescence these behaviors may be perceived by those close to the teenagers as a problem because they may constitute a health risk. Viewed developmentally, however, these behaviors serve a purpose (i.e., that of a developmental task accomplishment). Often the adolescent does not perceive risk-taking behavior as a problem but, rather, as a solution. This paradox helps explain the behavior and also the difficulty of managing youth who engage in high-risk behaviors. What health professionals see as a problem, youth often see as a solution. People in general do not give up their solutions easily.

General characteristics of risk-taking behaviors in adolescents include the following:

1. Many behaviors that affect health, both positively and negatively, throughout an individual's life, are first tried out during the teenage years (e.g., cigarette smoking, sexual activity, exercise and physical conditioning, dietary changes, study habits).
2. The risk that any behavior has on health may be immediate (e.g., drinking and driving), delayed (e.g., pregnancy and education), or remote (e.g., smoking and lung cancer). The more immediate the consequence of behavior on health, the greater the likelihood of effecting change through intervention.
3. Consequences of risk behaviors may be universal and invariant (e.g., risk from crack), related to specific factors or cofactors (e.g., environment, gender, situation), or related to the intensity of involvement (e.g., dieting and anorexia nervosa).
4. Factors that significantly influence health-related behaviors are usually acquired or consolidated during adolescence (e.g., values, beliefs, attitudes, motivations, self-concept, general lifestyle).
5. Problem behaviors that contribute to risk tend to occur in combinations or clusters (e.g., smoking, drinking, interpersonal violence, suicidal ideation, school dropout, family discord, and drug use).
6. Risk at any developmental period reflects the number of risk factors present during that period and the cumulative effects of risk factors occurring earlier in life. The effects may be not only cumulative but also compounded and may lead to other risk behaviors (e.g., the effect of long-term alcohol or drug use on driving or suicidal ideation). High-risk adolescents usually have multiple social and psychological handicaps that amplify the severity of the consequences and limit the options for problem solving and task accomplishment.

Biopsychosocial Factors

Many factors have been suggested as contributing to problem behaviors among youth in the United States. Although biological maturational forces have remained relatively constant, the timing of puberty and the social environment in which it occurs has dramatically changed over the past decade. This has put increased pressure on the individual for adaptation to these new norms that define adolescence. These factors include the following:

1. Menarche occurs earlier (12.5 years), marriage has been delayed (average age, 26 years), and values have changed regarding premarital sexual intercourse. Incongruence between biological development and psychosocially preparedness enhances the potential for high-risk behaviors or dysfunctional personal responses to stress, such as early initiation of sexual activity in an attempt to reduce stress.
2. The U.S. population has become more urbanized, with little purposeful and meaningful work for youth.
3. The American family has increased mobility, with a subsequent need for teens to reestablish social relations at a time when social skills are often poorly developed.
4. Breakdown of the family results in an increased number of single and working parents, lack of an extended family, and the interposition of the media as an arbiter of family values.
5. The foundation of the adolescent experience, the educational process, has become more prolonged, to prepare the individual for a high-tech society. This has resulted in an increased risk for mainstream adolescents to drop out.
6. A shift has occurred in how society views its young, from being an economic asset to being an economic liability.
7. Western cultures tend to expose rather than protect adolescents from environmental influences (e.g., drugs and alcohol, automobiles, violent behaviors).
8. Changes during adolescence are rapid, and pressures for adaptation are great.
9. Immature processing of emotions: There is the suggestion that young adolescents continue to process emotions and future planning in the amygdala, similar to children, instead of in the frontal lobes. This can lead to physically mature teens’ handling information similar to younger children, which may result in seriously wrong decisions regarding long-term consequences of their behaviors.

Certain youth are predisposed to having difficulty with the transition from childhood to adulthood, including:

1. Youth reared in poverty
2. Youth who have been physically, sexually, or emotionally abused as children
3. Youth living with significant family pathology, parental mental illness, or substance abuse
4. Youth with educational handicaps
5. Youths with a chronic illness
6. Youth with a chronic illness

It is important to realize that the majority of these young people mature successfully through adolescence without apparent long-term problems. The health professional may be on the lookout for problems and offer help when appropriate but should not automatically label these teens as being at high risk.

In summary, high-risk and out-of-control behaviors require prompt evaluation and attention. Included is a wide spectrum of behaviors, including runaway behavior, truancy, theft, vandalism, substance abuse, sexual promiscuity, and suicide. Loss of parental control must be assessed along with what has been tried to regain control. The health professional must evaluate what are the greatest influences on the teen's present behavior and how those influences are related to developmental
Prevalence: Each year, more than 590,000 children are incarcerated in public and private juvenile facilities, including jails, detention centers, camps, and other controlled settings. Between 1990 and 1997, the number of children in public or private detention, correctional and shelter facilities increased from 387,900 to 595,000. In 1997, males accounted for 74% of juvenile arrests and 84% of juvenile arrests for violent crimes. Males are more likely to be arrested for violent crimes while females are more likely to be arrested for status offenses or for other non-violent offenses.

Sex: In 1997, males accounted for 74% of juvenile arrests and 84% of juvenile arrests for violent crimes. Females are more likely to be arrested for status offenses or for other non-violent offenses.

Characteristics

Medical precursors: Although a number of medical precursors to delinquent and violent behavior have been reported, the overall contribution of these factors is unknown. It is important to realize that an association may be valid but the number of cases rare.

Lead exposure: Increased blood lead concentrations have been reported to occur more commonly among detained delinquent youths. However, more research is needed to understand the long-range effects of these drugs will become evident as exposed children mature into their teenage years.

Fetal alcohol syndrome and exposure to illicit drugs: Some individuals with severe prenatal alcohol exposure may exhibit difficulty understanding the consequences of their actions. As a result, they may repeatedly engage in behavior that is forbidden and therefore become offenders. Likewise, some children exposed to cocaine and other psychotropic drugs may experience cognitive problems during childhood and adolescence. Full understanding of the long-range effects of these drugs must be understood as exposed children mature into their teenage years.

d. Medical precursors: Although a number of medical precursors to delinquent and violent behavior have been reported, the overall contribution of these factors is unknown. It is important to realize that an association may be valid but the number of cases rare.

Head trauma: Head trauma resulting in brain injury may be more common among delinquent teens. However, hyperactivity is also more common in delinquent youth and may cause some of the head injury episodes.

XYY: Klinefelter syndrome may be associated with offending behaviors such as fire-setting in a few boys, but the majority of these children do not run afoul of the law.

Incarcerated youth and juvenile delinquency

Definitions

A juvenile delinquent is a person younger than 17 or 18 years of age (depending on the state) who commits any criminal offense as defined by state or local laws. These individuals are subject to the regulations of the juvenile or family court, with a goal of rehabilitation and not punishment. Many states have excluded from the juvenile court jurisdiction such offenses as murder and assault with a deadly weapon and placed them under the jurisdiction of the adult criminal court.

A status offender is a juvenile younger than 17 or 18 years of age who is regularly disobedient to his or her parents or guardians and is beyond their disciplinary control or has run away from home or is unlawfully absent from school. The offense that was committed would not be illegal if carried out by an adult. Examples include truancy, runaway behavior, and curfew violation. These adolescents are often referred to as persons, children, juveniles, or minors in need of supervision (PINS, CHINS, JINS, or MINs, respectively). In some states, juvenile delinquents and status offenders are still grouped together. Increasingly, states and local agencies are separating these two groups, but an effective system to deal with status offenders is lacking in most states. Many of these young people are referred to mental health or social service agencies by the court.

A youthful offender is an individual 17 to 21 years of age who commits an illegal act. These individuals are tried in the criminal court system but may be separately housed away from adults while serving their sentence.

Young people may become incarcerated or removed from their homes and placed in foster care–like settings for numerous reasons, including illegal activity, status offenses, or the need for protection and guardianship. The placement of youth, particularly in adult facilities, puts them at risk for abuse and for coming in contact with more experienced and “hardened” criminals.

Epidemiology

1. Prevalence: Each year, more than 590,000 children are incarcerated in public and private juvenile facilities, including jails, detention centers, camps, and ranches. Another 90,000 are placed in adult jails each year. According to the U.S. Department of Justice, in 1997 about 23% of all reported arrests for crimes were of youth younger than 18 years of age; about 32% were younger than 21 years, and almost 6% were younger than 15 years. The percentages of arrests for violent crimes in 1997, were 5% for youth younger than 15 years of age, 17% for those younger than 18 years, and 30.7% for those younger than 21 years. The most frequent crimes included theft, motor vehicle theft, burglary, robbery, and aggravated assault (Table 77.1). Over the past 10 years, the number of arrests for juvenile crime has increased by approximately 35%, with a significant increase in violent crime. However, in the 1990s there was a decrease in juvenile arrest rates. For example, when serious crime is measured as the number of arrests per 100 persons in an age range, youth younger than 18 years old had an index volume of 11.6 per 100 persons in 1980 and 9.8 per 100 persons in 1996, a drop of 15%. In contrast, adults 30 to 39 years old showed a 36% rise in the index, going from 6.3 to 8.8 per 100 persons in the same period.

2. Characteristics

a. Sex: In 1997, males accounted for 74% of juvenile arrests and 84% of juvenile arrests for violent crimes. Females are more likely to be arrested for prostitution or running away. During the 1990s, most of the attention on juvenile delinquency concentrated on boys, but more recently the incidence of female delinquency has escalated. Over the past 10 years, the rate of arrest of females has increased six times more than that of males. Although female delinquency in the 1950s and 1960s centered mainly on sexual misconduct, acting out, or prostitution, today more girls are involved in armed robbery, gang activity, drug trafficking, burglary, weapons possession, and aggravated assault, as well as prostitution.

b. Race: As reported by the federal government, members of minority races, primarily blacks and Hispanics, accounted for 26% of juvenile arrests in 1997. Minorities, especially African-Americans and Hispanics, are disproportionately both the victims and the perpetrators of crime in the United States. The arrest rate leading to incarceration is increasing rapidly among Hispanic youth. Black youth accounted for 44% of juvenile arrests for violent crimes in 1997. Over the few years preceding 1997, there was little change in the disproportionate number of minority youth who were incarcerated, and 63% of all juveniles in residential placement were minorities.

c. Age: The peak age for juvenile arrests is 15 to 16 years. Eighteen years is the peak age for arrest for violent crimes (homicide, rape, and assault) (Table 77.2).

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Total</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>12-14</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15-16</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>17-18</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>19-21</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 77.2. Juveniles in public or private detention, correctional and shelter facilities by age and sex, United States on October 29, 1997.

<table>
<thead>
<tr>
<th>Race</th>
<th>Total</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Black</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 77.1. Juveniles in public or private detention, correctional and shelter facilities by offense, United States, on October 29, 1997.
work is needed to establish that the association is real.

- Frontal or temporal lobe epilepsy: This form of epilepsy involves complex neurological behavioral and psychiatric symptoms that are usually, but not always, seen in adolescents with developmental disorders. Rarely, there may be explosive or undirected aggression. Nasopharyngeal and/or anterior-temporal leads may be necessary to demonstrate the seizure focus on an electroencephalogram.
- Learning disability and/or attention deficit disorder: Poor academic performance is found in the majority of delinquent youth. The underlying reasons for this may include attention deficit disorder or other learning disorders, lack of parental supervision, peer pressure, poor schools, and low socioeconomic status.

e. Social and environmental factors

- Low socioeconomic status
- Lack of employment
- Sense of failure and low self-esteem
- Family conflicts
- School difficulties
- Peer-group involvement with delinquent adolescents
- Gang involvement
- Disorganization within the home and/or community environment
- Lack of a sense of belonging
- Lack of appropriate role models
- Lack of at least one caring adult
- Family history of alcoholism, criminal behavior, or psychiatric conditions
- History of physical or sexual abuse (in some cases, physical abuse may cause brain damage)

f. Seriously delinquent adolescents: Those youth with a higher prevalence of violent or sexually assaultive behaviors have a higher prevalence of violent behavior in childhood, a history of perinatal trauma, and more frequent head and facial trauma. Psychopathology, mostly characterized as conduct disorder, is common.

g. Incarcerated delinquents: Such individuals are reported to have had a higher prevalence of perinatal difficulties, child abuse, and history of severe head or face injury. Major depression and suicide attempts and frequent risk-taking behaviors are common in this group.

h. Recurrence: A subgroup of adolescents accounts for the majority of juvenile crime. In one study, 54% of juvenile delinquents were repeaters and accounted for 85% of crimes committed, and a subgroup of 6.3% committed 52% of the crimes (Wolfgang et al., 1972).

Legal Rights

1. Judicial rights: Adolescents usually are processed through a juvenile court without a jury trial. However, they have the right to legal counsel, the right to notice of charges, the right to remain silent, the right to confront their accuser, and the right to proof of guilt beyond a reasonable doubt. At the end of the proceeding, the judge will sustain the petition of delinquency if the youth is believed to be guilty of the offense.

2. Treatment rights: In the past 15 years, many laws have been enacted that govern the care of adolescents while in detention. These laws cover specific issues such as staffing requirements and guidelines for the use of psychiatric medication. There is a growing trend in this country to try more and younger juveniles as adults and then incarcerate them in adult prisons. In many cases, little rehabilitation is available in the adult setting. As of 1998, there were 76 death row inmates who committed their crime before the age of 18 years, and 12 such persons had already been executed.

Health Problems

A comprehensive review of health and medical issues of institutionalized youth is beyond the scope of this book. However, the health care professional should keep in mind that approximately 1 million adolescents live away from home, and about one half of these are in institutions for juvenile offenders. Between 40% and 80% of these adolescents have medical problems that may include the following.

1. Problems inherent to adolescents living in poverty
   a. Unmet nutritional needs
   b. Problems common to adolescents in general, including headaches, chest and abdominal pains, asthma, acne, scoliosis, weight control problems, peptic ulcers, minor trauma, short stature, delayed puberty, gynecological problems, cancers and leukemia, myopia, and hearing loss.
   c. Preexisting conditions that have been undetected due to poor access to medical care, including hernias, undescended testes, urethral strictures (congenital or acquired), tuberculosis in endemic areas, hepatitis, and congenital heart disease.

2. Problems related to delinquent behaviors and lifestyle
   a. Injuries: Four to eight times more common in institutionalized youth
   b. Substance abuse and drug withdrawal symptoms
   c. STDs, pregnancy, pelvic inflammatory disease, and occasionally HIV infection
   d. Retained bullets with increased risk of lead toxicity
   e. Gunshot wounds and auto accidents resulting in paraplegia, brain injury, bowel injury, and obstruction.

3. Health problems associated with delinquency (e.g., learning disabilities attention deficit disorders): Some researchers postulate a subpopulation of adolescents, in whom learning disabilities precede the onset of delinquency, who undergo a downward spiral of school failure, frustration, anger, and more failure, leading to lowered self-esteem, truancy, and social isolation.

4. Health problems attributable to the social and physical environment
   a. Suicide
   b. Institutional violence (gang violence)
   c. Depression

Delinquent youth rarely malinger. Obscure symptoms resulting in a confusing clinical picture usually result from an unusual presentation of a common disease or the presence of an unusual disease.

Providing medical services to detained youth can be very rewarding. Most institutionalized children have long histories of neglect and abuse. They respond well to kindness and understanding. Medical personnel should remember that they are caregivers and youth advocates rather than correctional staff.

Morris et al. (1995) reviewed the health risk behaviors of youth in juvenile correctional facilities. They found that risky behaviors began early and reached a plateau at 15 or 16 years of age. Male and female youth reported comparable rates of drinking, binge drinking, and illicit drug use. Native American youth began drinking at an earlier age, had more binge drinking and more illegal drug use, and had the most fight-related behavior. By 12 years of age, 62% of those in the study reported a history of sexual intercourse, and 89% were sexually active by age 14. The mean age at onset of sexual intercourse was 12 years. Fighting was common, with 25% reporting fight-related injuries in the past year. Almost one half of the group were in a gang. Suicide had been contemplated by 22%. STDs were common, and fewer than half of the group had used a condom at last intercourse.

Clearly, in light of these data, incarcerated youth need to undergo health and psychiatric screening as part of the intake procedures. In addition, short-term health and mental health care facilities need to be available. Guidelines for health care in juvenile detention institutions are available through state boards of correction, from the National Commission on Correctional Health Care (NCCHC), or from the American Correctional Association (ACA).

There are a substantial number of problems facing juvenile correctional facilities, including overcrowding, poorly trained staff, decaying facilities, inadequate medical and psychiatric care, and poor educational resources. These problems tend to persist because of a lack of public scrutiny and disenfranchisement of poor minority youth.

RUNAWAY BEHAVIOR

Definition
Runaway behavior is defined as an unauthorized absence from home.

**Epidemiology**

1. Incidence: Approximately 500,000 to 1 million adolescents run away each year (Carper, 1979). In 1997, the federal government reported 136,350 runaways. A Department of Health and Human Services report estimated that in 1983 between 733,000 and 1,300,000 youths in the United States could be classified as either runaways or homeless (Russell, 1995). A report issued by the U.S. General Accounting Office found a lower number based on a survey of intake workers at federally funded youth shelters. This survey estimated that in 1987 between 52,000 and 170,000 unaccompanied youths age 16 years or younger were homeless. In a CDC study (Ringwall et al., 1998), 7.6% of the youths questioned reported that they had spent at least 1 night in a youth or adult shelter (3.3%), a public place (2.2%), an abandoned building (1.0%), outside (2.2%), underground (0.4%), or with a stranger (1.1%). Boys were more likely to report having experienced a homeless episode.

2. Age: The mean age is 15 years, and almost all runaways are between 14 and 17 years old (Carper, 1979). In 1997, a total of 15,700 children younger than 13 years of age were reported by the U.S. Department of Justice to have run away. 48% of these children were girls.

3. Race: A majority of reported runaways are white suburban adolescents (Carper, 1979).

4. Length of time away from home: less than 3 days, 72%; between 4 and 14 days, 15%; longer than 14 days, 13%.

5. Return behavior: return home on their own, 50%; return home through parental or peer involvement, 30%; return home through police intervention, 14%; never return home, 6%.

**Types of Runaways**

1. Abortive: No actual runaway behavior—just a fantasy
2. Crisis: A short stay away from home, usually less than 3 days, secondary to an acute problem
3. Casual: The streetwise adolescent with frequent runaway episodes
4. Return behavior: return home on their own, 50%; return home through parental or peer involvement, 30%; return home through police intervention, 14%; never return home, 6%.

**Reasons for Running Away**

Many reasons exist for runaway behavior, including lack of communication between parents and the adolescent, school failure, overly strict or overly permissive parents, discovery of sexual identity discordant with parental values, experimentation, escape from a hopeless situation, being thrown out of the house, and the simultaneous crises of adolescence, parental middle-age crisis, and elderly grandparents. Other reasons include depression, revenge, and imitation of peers. Not infrequently, incestuous family incidents and other episodes of physical or sexual abuse are the precipitants for running away.

For those adolescents who become homeless, the situation is aggravated by decreased access to food, shelter, medical services, and social supports. A common characteristic of homeless youth is the lack of a mainstream social network. These youth therefore often create their own social networks within their runaway environment.

Runaway or homeless youth are at increased risk for many health problems, including STDS, suicidal ideation, pregnancy, minor trauma, skin infections, malnutrition, substance abuse, and HIV infection. Allen et al. (1994) reported HIV prevalence rates among homeless youth of 0% to 7.3% (median, 2.3%). Rotheram-Borus (1993) reported a rate of suicide attempts in runaway youth of 37%, with 44% of the attempters having made an attempt within the previous month. Girls were significantly more likely than boys to have attempted suicide and to be depressed. Runaways with a history of attempted suicide were significantly more likely to be currently suicidal and depressed.

**SUICIDE**

This topic is discussed in Chapter 80.

**SUBSTANCE ABUSE**

This topic is discussed in Chapter 69, Chapter 70, Chapter 71, Chapter 72, Chapter 73, Chapter 74 and Chapter 75.

**INTERVENTIONS**

For the primary care physician, the contact point with adolescents who are engaging in high-risk behavior is often the presentation of a medical problem. Rather than merely treating the medical problem, the physician needs to gather more background information to elicit the context in which the medical complaint has evolved. A brief psychosocial or lifestyle interview must be conducted before or during the medical examination. One method is the HEADSS Adolescent Risk Profile (Home, Eating activities, Affect, Drugs, Sex [activity, orientation, and sexual abuse], and Suicide) discussed in Chapter 3. The HEADSS evaluation not only assesses risk but also provides an opportunity to educate the adolescent with regard to practices or behaviors that may influence health. The assessment should include the following:

1. Medical evaluation
2. Psychosocial evaluation (HEADSS)
3. Family assessment
4. Vocational assessment
5. School assessment

Important considerations include the following:

1. **Identifying the youth's needs**: Although high-risk youth present with many serious problems that the care provider identifies as paramount in the hierarchy of interventions, the adolescent also has an agenda that must be determined and validated. Failure to meet young patients' perceived needs often results in their failure to "buy into" the professional's plan of care. The adolescent comes to the provider for help, and it is important to provide that help before and during any other interventions that the provider thinks are important.

2. **High-risk youth with multiple problems**: are best dealt with by a multidisciplinary team functioning in an interdisciplinary manner. Without allied health professionals, the physician must have a comprehensive listing of local resources. Effective referral, particularly for high-risk youth, is best accomplished through a telephone call to a specific contact person, who should be identified while the adolescent is still in the office.

3. **Basic needs such as food, shelter, and safety** must be addressed before major psychotherapeutic interventions are considered.

4. **Every effort should be made to draw on the adolescent's own resources or options for change** (i.e., find alternative solutions). Interventions must be both feasible and practical (i.e., within the realm of possibility for that particular teen and capable of serving the appropriate developmental function).

5. **Family involvement**, when indicated, may optimize the intervention strategy, but if such intervention is not done skillfully, the adolescent's problems may simply be compounded. The ability to educate a family for change is inversely proportional to the degree of dysfunction within the family.

6. **Risk profiles may be modified by direct or indirect interventions**. An example of a direct intervention would be a stop-smoking education program; an indirect method would involve increasing a health-enhancing behavior, such as jogging or running to discourage smoking.

7. **Characteristics intrinsic to health professionals that enhance their ability as vehicles for change** include:
   a. Ability to develop trust through establishment of a confidential relationship
   b. Willingness to see the youth's viewpoints as real
   c. Ability to listen
   d. Unconditional positive regard for the adolescent in his or her struggle
   e. Knowledge of self

8. **The opportunity to change a system** (individual or family) is greatest when the system is unbalanced or in transition. Staff availability during a crisis may be more effective than traditionally scheduled counseling or psychotherapy sessions.
REFERENCES AND ADDITIONAL READINGS


Shanok SS, Lewis DO. Medical histories of female delinquents. *Arch Gen Psychiatry* 1973;29:96.


Violence is a pervasive problem in American society. It is of particular significance for the adolescent, who more than anyone else is likely to be the victim. Violence takes many forms: homicide and assault, sexual assault, battering in intimate relationships, child abuse, and hate-crime violence. Suicide also may be considered a violent act turned toward oneself. Violent behavior is a complex phenomenon that is stimulated by multiple factors including poverty, racism, alcohol and drug use, and early childhood exposure to violence, including media violence. The consequences of violent behavior are made vastly more lethal with the presence of a firearm, particularly a handgun. Violence results in death, disability, emotional trauma, and tremendous financial cost for our society. Its presence affects all of us, both as citizens and health care providers, and confronts health care providers with particular challenges. Young perpetrators of violence may have their lives destroyed and wasted in the criminal justice system. Public attitudes about violence have recently shifted from considering it entirely a criminal justice matter to appreciating the important public health aspects. This chapter outlines the epidemiology, etiology, risk factors, and potential prevention strategies.

Several characteristics of adolescents make them vulnerable to involvement in violence. Adolescence is characterized by increasingly close identification with peers, a sense of invincibility, and risk taking and impetuousity. Adolescent thinking tends to be concrete, particularly in the younger teen, with an inability to appreciate long-term consequences. The young person may be susceptible to the dichotomous, simplistic moral code often found in gangs emphasizing loyalty to one's group and rejection of one's "enemies" or rivals. For many young people who grow up in homes with family violence, behaviors may mirror adult behaviors. Availability of firearms, particularly handguns, in many homes and on the streets, turns impulsive acts, which would otherwise be trivial, into lethal and tragic events.

**EPIEMIOLOGY**

1. Homicide rates: Reasonably good statistics are available for homicide victimization throughout the United States and are a barometer of violent crime, which can be more precisely measured than any other parameter.
   a. U.S. homicide rates: The United States has the highest homicide rate in the world among industrialized countries. The United States is the only industrialized country to have a homicide rate among young men (age 16–24 years) of more than 5 per 100,000; many countries have a rate less than 1 per 100,000. The United States has seen a significant drop in homicide rates since 1993 (Table 78.1).

   **TABLE 78.1. Adolescent homicide rates and absolute numbers 1989–1999**

<table>
<thead>
<tr>
<th>Year</th>
<th>Rate per 100,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>1989</td>
<td>5.5</td>
</tr>
<tr>
<td>1990</td>
<td>5.0</td>
</tr>
<tr>
<td>1991</td>
<td>4.5</td>
</tr>
<tr>
<td>1992</td>
<td>4.0</td>
</tr>
<tr>
<td>1993</td>
<td>3.5</td>
</tr>
<tr>
<td>1994</td>
<td>3.0</td>
</tr>
<tr>
<td>1995</td>
<td>2.5</td>
</tr>
<tr>
<td>1996</td>
<td>2.0</td>
</tr>
<tr>
<td>1997</td>
<td>1.5</td>
</tr>
<tr>
<td>1998</td>
<td>1.0</td>
</tr>
</tbody>
</table>

   Of particular significance, the homicide rate for African-American adolescents age 18–24 years, the highest risk group for death from homicide, dropped from 183.4 per 100,000 to 102.6 per 100,000. This represents a significant downward trend in homicide rates after 10 years of increasing rates. Even so, more than 50% of all homicides in the industrialized world take place in the United States. The homicide rate in the United States is 16 times that of 25 other industrialized countries combined (Centers for Disease Control and Prevention [CDC], 1997). During the 10 years from 1989 to 1999, 58,594 youths age 18–24 years died by homicide in the United States, more than half of these deaths, or 30,285, were African-American males.

2. Violent crime rate trends: After a decade-long rise in violent crime, which peaked in 1993, there has been a steady decline in all categories of violent crime. The rate of victimization by juveniles has dropped 36% in 1999 compared with the historic peak in 1994 (Snyder, 2000). From 1994 to 1999, arrest rates for violent crime for juveniles age 15–17 years declined 39%; for youths age 18–24 years, arrest rates declined by 19%. It should be remembered that youths frequently are in groups when crimes are committed and that multiple individuals may be arrested for single events. Arrest rate, then, gives an inflated impression of the incidence of assaultive events. Remarkably, the juvenile arrest rate for serious violent crimes has dropped 30% since 1994.

3. Gender
   a. Homicide victims: Teenage males outnumber females as victims of homicide by a factor of more than 6:1. Young males are more likely to be victims of violent crimes of all categories, except sexual assault and intimate partner violence.
   b. Adolescent homicide offenders: 94% percent of those younger than 18 years who are convicted of murder are males.
   c. The reasons for the male preponderance, both as victims and perpetrators of homicides, are controversial. Probable factors include cultural values that reward aggressive behavior of children, and the absence of nurturing and nonviolent male role models for many adolescents.
   d. Sexual assault victims: Female adolescents have the highest risk of any age group for being subjected to sexual assault. Most sexual assault victims are victimized before age 18 years. Because of the difficulty in obtaining reliable data, the incidence of adolescent sexual assault is not known. However, according to a recent CDC study, about 9% of women and 1.9% of men report being sexually assaulted before age 18 years (Tjaden and Thoennes, 2000).

4. Ethnicity: There is wide variation of homicide victimization rates among ethnic groups in the United States. African-Americans have the highest homicide victimization rate by far, and for African-American males and females age 15–34 years, homicide is the leading cause of death.

The overall national homicide victimization rate is 4.5 per 100,000; for males, it is 7.6 per 100,000. For young white males (ages 20–24 years), the rate is 11 per 100,000. However, for the highest-risk group, young male African-Americans (ages 20–24 years), the homicide victimization rate is 117 per 100,000. It is, however, an improvement from the peak year of 1992 when the homicide rate for young male African-Americans exceeded 150 per 100,000, and in urban centers such as Los Angeles and Washington, DC, it was well over 200 per 100,000 per year. These figures reveal mortality rates experienced by combat soldiers in the Vietnam War. National rates for Hispanic adolescents are less well known but appear to be lower, with a rate of 30.5 in 1989–1991, and are subject to wide geographical variation. In Los Angeles, young Hispanic males have a homicide rate of 74 per 100,000. Homicide is the third leading cause of death of white males and females in the 15- to 24-year-old age group. Asian minority groups have the lowest homicide victimization rates. In 1998, 47% of murder victims were African-American, 49% were white, and 2% were Asians, Pacific Islanders, and Native Americans. Separate statistics on Hispanic individuals were not available, and generally these were included in the category of white.
Ethnic discrepancies exist for nonlethal violent crime victimization as well. Forty-two per 1,000 African-Americans and 32 per 1,000 whites reported experiencing violent crimes in 1999. Native Americans experienced violent crime at more than twice the national average.

5. Age: In 1999, 1,800 juveniles were murdered; 1,000 of them were age 13–17 years, 80% were male, 20% were female, and 81% were killed with a firearm. The Department of Justice reports that children age 12–17 years were twice as likely as adults to be victims of serious violent crime and three times as likely to be victims of simple assault (Synder, 1999). Crimes against juveniles continue to be seriously underreported.

6. Juvenile crimes: Arrests for violent crimes by juveniles increased from 1980, peaking in 1993, and have been declining since then. The year 1999, the fifth consecutive year of decline, resulted in a reduction of arrests for serious violent crime (murder, forcible rape, robbery, and aggravated assault), 36% less than in 1994. The juvenile arrest rate for homicide fell 68%, reaching the lowest level since the 1980s. In 1999, juveniles were involved in 9% of murder arrests, involving 1,400 young people, one third the number arrested in 1993. However, convictions were obtained for only 6% of all murders, reflecting the fact that juveniles are more likely to be arrested in groups than as adults. Juveniles were involved in fewer than one per six arrests (12.4%) for a violent crime (Synder, 1999).

7. Geography: Youth homicide victimization is predominately a problem of large metropolitan counties, which on the whole have rates about five times those of non-metropolitan counties. Five states (California, Michigan, Missouri, Florida, and New York) and Washington, DC, account for most homicides of African-American youth. However, violence is not only an inner-city problem of African-Americans and Latin males. Poverty and residence in a low-income neighborhood are stronger predictors of violence in adolescents than race or ethnicity.

8. Relationship of offender to victim: The most common misconception is that intentional violence is a premeditated event that randomly affects people unknown to the assailant. The opposite is true, with most violent encounters being impulsive acts occurring among friends and acquaintances and within families. Among males of all ethnic groups, the most common relationship between offender and victim is that of a friend or acquaintance. In about 25% of youth homicides, the victim is the initiator of violence. For adolescent female victims, the most common perpetrator is a boyfriend, mirroring the situation for female adults, for whom the most common perpetrator is a family member or intimate partner. Ninety percent of female homicide victims are murdered by mates. Youth homicide overwhelmingly takes place between members of the same ethnic groups. In cases in which the perpetrator is known, about 93% of homicides of young African-American males are committed by other young African-American males. Among whites, about 85% of murders are committed by other white youths. In large urban centers, there has been a phenomenon of drive-by shooting. These events are largely gang related and appear to be motivated by a desire for retribution for a perceived wrong. However, victims are frequently unrelated to the perceived problems. The presumption that young victims of violence are themselves perpetrators is usually unjustified.

9. Schools: The horrifying and dramatic events in Columbine, Colorado, on April 20, 1999, in which 12 adolescents and an adult were killed, 23 wounded, and the 2 young perpetrators committed suicide received widespread media attention. Many people were left with the impression that high schools were dangerous places for young people, and that homicides on high school campuses were common. Despite the Columbine events, this is untrue. The events at Columbine were aberrant. Homicide numbers on school campuses have remained relatively stable over the last several decades, numbering 25–40 deaths per year nationwide; about 10%–20% of these homicides are of adults by other adults and do not involve adolescents. For perspective, about twice the number of Americans are killed by lightning each year as are killed on school campuses. When one considers the proportion of time that high school students spend in school, schools emerge as the safest environment in which young people can participate; more than 99% of violent student deaths occur off school grounds. For example, about 2,000–3,000 children and adolescents die every year in their homes at the hands of their parents (U.S. Advisory Board on Child Abuse and Neglect, 1995).

10. Role of firearms: In 1998, 3,792 children and adolescents younger than age 20 years experienced firearm-related deaths; a decline of 35% since 1994. Among 15–24-year-olds, there were 7,420 firearm-related deaths, including 4,484 homicides, 2,510 suicides, and 260 accidents. A firearm was used in 82.6% of homicides and 76% of completed suicides (CDC, 2000a). Figure 78.1 shows firearm deaths in adolescents and young adults.

FIG. 78.1. Firearm deaths among adolescents 15–24 years, 1998. (From Centers for Disease Control and Prevention, 2000, with permission.)

As of 1991, firearm-related deaths equaled or exceeded automobile accident deaths in seven states (California, Louisiana, Maryland, Nevada, New York, Texas, and Virginia), and the District of Columbia. In every urban center and for every ethnic group, the number of firearm suicides exceeds nonsuicide homicides. In urban areas, firearm homicide victimization rates are highest for male African-Americans and lowest for female whites. In addition to the mortality problem, for every young person killed with a firearm, there is an additional individual who is maimed and left permanently disabled, mainly from brain, spinal cord, and other neurological injuries. There are thousands of victims who survive firearm injuries but suffer lesser injuries.

An estimated 200 million firearms are in civilian hands in the United States, and about 60 million of these are handguns. About 43% of homes have one or more handguns; at least 30% of gun owners with children keep one or more loaded guns in the home. Consequently, about 9 million adolescents have access to hand guns in homes. When a teen owns his or her own gun, the teen who owns the same gun is him or her as well as the most common victim being a friend. The victim is essentially never an intruder. When there is a handgun in a home, a household member or friend is roughly 43 times more likely to be the victim of the firearm than an intruder. A gun stored in the home is associated with a 4- to 5-fold increased risk of completed suicide (Kellerman et al., 2000). All of the events that have involved multiple homicides on campuses and in communities by youth have one thing in common: The young perpetrators had easy access to firearms, on some occasions automatic firearms.

11. Weapon carrying: Several studies, including the Youth Risk Behavior Survey (YRBS) of the CDC, have indicated that surprising numbers of male adolescents carry weapons periodically. In the 1999 YRBS, 21% of male adolescent alternative students disclosed carrying a firearm in the last 30 days (CDC, 2000b). Nationally, 17.3% of students carried a weapon (e.g., a gun, knife, or club) on more than 1 of the 30 days preceding the 1999 YRBS of high school students, and rates were significantly greater for male students (28.6% versus 6.0%).

Most youths who carry guns do not do so for criminal, drug, or gang related ends (Sheley, 1999). Status enhancement appears to motivate some young people, but studies of juvenile motivation to carry firearms consistently point to fear; youths carry weapons because they believe their social worlds are dangerous places and that they need protection. Is there a basis for this perception? According to the National Crime Victimization Survey, in 1998 among 12- to 19-year-olds, 1 per 150 was the victim of a robbery, 1 in 13 was a victim of a violent crime, 1 in 16 was the victim of an assault, 1 in 76 the victim of aggravated assault (Criminal Victimization in the U.S., 2001). The YRBS found that 67% of male adolescent alternative school students stated that they had been in one or more physical fights during the previous 12 months. Despite the fact that most teens who carry guns do so for a sense of security, the reality is that this act puts them and their peers at greatly increased risk. The principal effect of having a gun is to worsen the outcomes of violent encounters: Fistfights or assaults result in deaths, retaliation for perceived slights may result in a death, attempted rapes and robberies are completed, and suicidal gestures are completed. The single most important factor in all sorts of firearm-related injuries is the accessibility of firearms themselves.

Preventing gun violence: Preventive events leading to assault include a desire for retaliation or retribution for previous perceived verbal or physical insult, escalation of showing-off contests, and jealousy. Homicides by adolescents are usually impetuous acts that are instantly regretted. Most youth homicides take place between friends and acquaintances and are not gang related. Adolescent homicide can almost be defined as “a fistfight with a gun in the fist.” Nationally, about
4% of youth homicides are gang related. However, in inner-city environments, in regions where gangs are prevalent, gang violence may account for as much as 30%–40% or more of young homicide victims.

13. Other related factors

a. Alcohol and drug use: Half or more of violent encounters among adolescents involve drug or alcohol use. This may be directly through disinhibition by the intoxicants or indirectly through involvement in the drug trade.

b. Media violence: More than 3,500 studies now confirm the association between higher levels of viewing violence and increased acceptance of aggressive attitudes and increased aggressive behavior. The key findings of research related to the impact of the media on violent behavior include the following:
   1. The average American child, by the age of 18 years, will have viewed 200,000 acts of violence, including 40,000 murders.
   2. Children form attitudes about violence at a young age.
   3. Preschoolers watching 2 hours of cartoons daily will be exposed to 10,000 acts of violence annually. Cartoons frequently show violence as the response of first resort, usually celebrated and justified, and without significant consequence, frequently the bad guys have foreign accents; these portrayals help form early values and perceptions.
   4. Children exposed to media violence are more likely to behave aggressively.
   5. Watching media violence causes desensitization, particularly among young viewers (Strasburger and Grossman, 2001).

Decreasing early childhood exposure to violent television and film is an integral component of effective violence prevention.

c. Child abuse: Experiencing child abuse is a well-documented risk factor for later participation in violent behavior. An interesting longitudinal study designed to examine long-term effects of abuse and neglect found that both physical abuse and neglect (but not sexual abuse) increased the likelihood of arrest as a juvenile by more than 50%, arrest as an adult by 38%, and arrest for a violent crime by 38%, compared with a matched comparison group (Widom, 1992).

Child abuse prevention is a critical component of violence prevention.

d. Domestic violence: Witnessing violence in the family environment as a young child, in particular spousal battery, has in a number of studies been found to correlate with later violent behavior, both in intimate relationships and in society at large. Subjecting children to intimate partner violence of parents is a form of emotional abuse of children and in many states may be reported to Child Protective Services.

14. Social factors

a. Poverty, unemployment, sense of hopelessness about the future
b. Racism, a sense of being excluded from the justice system
c. Poor schools and recreational opportunities
d. Obstacles to transition to adult roles, particularly access to employment

Intimate Partner Violence

Intimate partner violence among adolescents is an area that has been studied only over the last 10 years or so; most research focused on adult women. Violence against women, either sexual assault (see Chapter 82) or physical assault, is primarily a problem of intimate partner violence. Sixty-four percent of women who reported being raped, physically assaulted, and/or stalked since age 18 years were victimized by a current or former husband, cohabiting partner, boyfriend, or date (Tjaden and Thoennes, 2000). The risk of injury increases among female rape and physical assault victims when their assailant is a current or former intimate partner (Tjaden and Thoennes, 2000).

For women age 15 to 44 years, the U.S. Surgeon General has found that domestic violence is the leading cause of injury, more common than automobile accidents, muggings, and rape combined (Department of Health Services). Women age 16 to 24 years experience the highest rate of intimate partner violence (Bureau of Justice Statistics, 2001). Homicides related to domestic abuse have been declining. From 1976 to 1999, about one third of female murder victims were killed by an intimate partner, and 4% of male murder victims were killed by an intimate partner. Since 1976, the number of men murdered by intimate partners dropped by 69%.

The number of women killed by intimate partners was stable for two decades and declined after 1993. Among intimate partners that were murdered, two thirds were murdered with a handgun (Bureau of Justice Statistics, 2001). There has been a particularly significant decline in domestic homicides for African-Americans: Black females killed by intimate partners dropped 53%; black males, by 76%; and white males, by 55%. Children and adolescents may witness intimate partner violence among their parents; in California, this is now reportable under the umbrella of child abuse statutes. Reported incidents indicate that about 85% of victims of nonlethal intimate partner violence are female (Bureau of Justice Statistics, 1998). However, survey studies, not based on reports, that have been conducted seem to indicate that males are victims about as frequently as females (Malik et al., 1997), but that the injuries incurred by females tend to be more severe.

Data on intimate partner violence among middle school and high school teens are sparse. Intimate partner violence among teenagers is usually foreshadowed by controlling behaviors such as a male partner telling a girl

1. What she can and cannot wear
2. Which friends she can go out with
3. To stay home and wait for phone calls
4. Irrational, jealous accusations
5. Stalking behavior
6. Threatening physical violence for not complying with demands

Much of intimate partner violence among adolescents can be characterized as “mutual combat”; that is, it takes place among youths who are in an enmeshed, volatile, highly stressed relationship, frequently struggling with multiple other issues including conflicts with the family of origin, social isolation, substance abuse, homelessness, and survival needs.

Why Teens Stay in Abusive Relationships

In one study, teens gave the following reasons for staying in abusive relationships (Autphenne et al., 1998):

1. Fear of being further abused or even killed
2. Fear that no one else would love them
3. Fear that they may never find anyone else
4. Belief that the person will change
5. Partner threatens suicide
6. Not knowing where to go for help

Battered women’s shelters tend not to be available for teen victims, leaving young people with very limited options (Autphenne et al., 1998). Emerging from a study of intimate partner violence among adolescents were recommendations to develop services to address this issue. These include the following:

1. Shelters for battered teens
2. A teen relationship advice hotline
3. Teen abuser counseling
4. Peer support groups
5. Individual counseling

Assault by Caretaker

Children and adolescents have commonly experienced an assault by an adult caretaker. In the year 2000 National Violence Against Women Study conducted by the CDC and the National Institute of Justice, 40% of surveyed women and 54% of surveyed men disclosed that they were assaulted by an adult caregiver as a child. It is difficult to study violence against children by parents and caregivers because it is commonly socially construed as discipline, rather than violence in the United States (National Research Council, 1993). It is clear from the data that boys are at significantly greater risk than girls of being physically assaulted by caregivers. Despite the high prevalence of assault under these circumstances (most of which were described as hitting, slapping, or being hit with an object), fewer reported serious assaults or injuries and a negligible number reported caregiver use of a knife or a gun.

Assessment of Risk
To implement interventions which decrease the risk of violence, it is recommended that health care providers assess the risk of the youth's involvement with violence, including taking a thorough history of the teen's involvement with violence as an aggressor, a victim, a witness to violence in the community, a nonviolent problem solver, or a participant in gender role-related violence. In assessing risk, as with other situations, one must be cognizant of the developmental stage of the youth. Open-ended, nonthreatening, nonjudgmental questions should be used, such as the following:

Many young people I talk to have been affected by community violence, how have you been affected?
Do you feel safe in the community where you live and go to school?
Have you ever been in a serious fight?
Do you know anyone who has been seriously injured or killed by violence? How many? Were any of them close friends? Did you witness any of these events?
Have you ever been threatened with a weapon? Shot at?
Do you have friends who carry guns?

**PREVENTION AND INTERVENTION**

Recently, there has been a proliferation of violence prevention programs; however, evaluations of efficacy are exceedingly difficult and fraught with problems. Programs tend to be funded for relatively short periods and limited in scope, so longitudinal effects on participants and broader societal measures of violent incidents are not valid measures. Promising approaches begin as early in life as possible, are sustained over time, and enhance nurturant and nonviolent parenting methods.

**Primary Prevention Interventions**

Primary prevention strategies are approaches either directed at the entire population or focused on selected populations at greatest risk. Any serious strategy of violence prevention must include efforts directed at young children, when basic values and approaches to frustration and conflict are learned. Particular issues to be addressed include familial violence, corporal punishment, child abuse, and early exposure to media violence, which are known to correlate with later violent behavior of children and adolescents. Apparently effective strategies include the following:

1. Identification of young, stressed, and particularly socially isolated parents, and providing them with home visitation and early intervention parenting training programs
2. Increasing financial stability of impoverished families at risk, particularly families headed by single parents
3. Identification and referral of pregnant and parenting teenagers and their partners to teen parenting and support groups
4. Preschool programs that address intellectual, emotional, and social needs of young children and encourage the development of nonviolent conflict-resolution skills
5. Reduction of early childhood exposure to media violence, including cartoon violence
6. Engaging teens, particularly young teens, in supervised recreational activities
7. Improving the quality of the school environment, and development of safe after-school programs with extensive activities for youth
8. Provision of safe, supervised routes ("safe corridors") to and from school for youths in troubled neighborhoods
9. Increased access to after-school programs
10. Prevention of school truancy and dropout
11. Employment programs, particularly for young people who are out of school

In addition, curricula for conflict resolution have been developed for use in secondary schools. Specific curricula approaches that appear to be effective are as follows:

1. Alternative solution generation
2. Self-esteem enhancement
3. Peer negotiation skills
4. Problem-solving skills training
5. Anger management

Effective primary prevention programs must be developmentally appropriate and comprehensive in approach (particularly those involving teenagers) and must include multiple components, reinforcing nonviolent behaviors in various contexts such as the family, school, peer groups, and the media. These approaches attempt to provide access to ongoing relationships with nonviolent, caring adult mentors, particularly for those teens from stressed or single-parent families. Through reducing risk factors, children and adolescents are empowered to resist effects of detrimental life circumstances.

**Firearms**

Fundamental to a public health approach to prevention is a change in environmental risk factors. Access to firearms is the principal environmental risk factor for lethal violence. Removal of firearms from the environment of adolescents through legislation, strict enforcement of existing laws, and removal of firearms from the home environment is essential in the prevention of the grave consequences of violent behavior. It should be recognized that a serious consideration of adolescent emotional developmental characteristics must lead one to the conclusion that educational interventions alone are unlikely to be successful with many children and adolescents (American Academy of Pediatrics, 2000).

**Recommendations**

1. Parents of adolescents and children should be encouraged to remove firearms from their homes. This is consistent with the recommendations of the American Academy of Pediatrics (1994). Attempts at interventions short of removal have not been shown to reduce mortality. Parents who keep loaded firearms at home should be informed that this is extremely dangerous for their children, and they may be held legally culpable for any adverse consequences. Parents must be made aware that if they keep a gun at home, the most likely victim is their teenage son and that firearms at home are far more likely to be used to shoot a friend or a family member than an intruder. Additionally, parents may inquire about the presence of loaded firearms in the homes of their children's friends and require that they be eliminated before children can play in the area.
2. Locked containers: If parents are unwilling to remove firearms from the home, teenagers have manual dexterity equal to that of adults and these measures may have a limited impact on the adolescent's ability to obtain and use a firearm if he or she is determined to do so.
3. Safety classes: Because accidental discharges make up few firearm injuries, safety classes in use of firearms have never been shown to reduce the risk associated with firearm ownership.
4. Stricter laws: Most states have laws that make it an offense for a minor to be in possession of a firearm under most circumstances. These laws must be enforced. Because most teens obtain access to guns through adults, laws restricting adult access to firearms may also decrease teen access.
5. Handgun bans: The American Academy of Pediatrics (1994) and many other medical and health organizations recommend that handguns be banned. Bans on handguns and restrictions on handgun manufacturers may, over time, reduce the number of handguns in circulation. Preliminary studies in California indicate that most firearms used in homicides were purchased within 2 years of use in a crime. Reductions in sales may have a more rapid impact on reducing public access than is generally thought.

**Secondary Prevention Interventions**

Secondary interventions may be directed at teens who have been identified after risk behaviors have become apparent. These interventions support adolescents identified as at risk in making a successful transition through school and into employment; they help nurture relationships with supportive adults (Elliot and Delbert, 1994). They may include the following:

1. Enhancement of the school environment with smaller-size classes and supervised after-school activities
2. Supporting successful transition to adult roles through access to job training, apprenticeship, and job placement
3. Providing caring, nonviolent adult mentors
4. Integrating adolescents into activities with nondisturbed peers
Health practitioners who are affiliated with inner-city hospitals may be in a pivotal position to identify adolescents who have survived gunshot wounds or other assaults and initiate secondary intervention programs. The “patch them up and get them out” approach essentially sends identified very high-risk teens back into the same dangerous environment either to be further victimized or to seek retribution and perpetuate a cycle of violence.

It must be remembered that adolescents and young adults (age 11 to 24 years) are the most likely age group to be victims of violent crimes, which can initiate a vicious cycle of crime and retaliation. It is important then to educate them on how to avoid becoming victims, including the victims of other adolescents. This may be through avoiding particularly unsafe environments, developing after-school activities, and avoiding hanging out with youth with guns. Under some circumstances, it may require families to move out of communities if their child is specifically targeted.

Although the causes of juvenile violence are not completely understood and programs designed to prevent delinquency have not been thoroughly evaluated, successful approaches to intervention appear to have the following characteristics:

1. They are appropriately supportive of children and adolescents and their families.
2. They are intensive (i.e., they involve the commitment of considerable time, personnel, and effort).
3. They are broad based; that is, they intervene in a number of the systems, including family, school, and peer, in which the child or adolescent is involved and use multiple services including educational, health, and social as appropriate for the individual child or adolescent.

### Tertiary Intervention

Tertiary intervention takes place after a teen has become embroiled in violent activities and may occur largely through the juvenile justice system. When the juvenile justice system was created about 100 years ago, it was intended to be a “kind and just parent,” acknowledging that children were inherently different from adults, less culpable for their acts, more amenable to rehabilitation and that a community-based, comprehensive approach was the most effective way to achieve rehabilitation. By 1915, almost all states had a juvenile court and the model spread internationally. The original goals of the juvenile court were to shield children from adults, protect the privacy of children, and allow adolescents to enter the workforce without a police record. During the 1990s, despite the fact that crime rates had been dropping significantly, these goals were rapidly eroded. Many states passed legislation making sentences more punitive, facilitating transfers of juveniles to adult court, and corroding protections of confidentiality. In effect, these measures blur the distinctions between adult and juvenile offenders (National Academy Press et al., 2001). These policies rely less and less on rehabilitation and increasingly attempt to manage juveniles through the adult criminal justice system. More than 90% of children involved in the juvenile justice system are nonviolent offenders, most of which involve property or substance offenses such as theft, burglary, and drugs. On any given day, more than 90,000 children are in juvenile detention or correctional facilities; in addition, more than an estimated 9,000 adolescents younger than 18 years are in adult jails (Snyder and Sickmund, 1999). This is a cause for concern, because children held in adult jails are eight times more likely than those held in juvenile facilities to commit suicide, five times more likely to be sexually assaulted, and twice as likely to be beaten by prison staff (Forst et al., 1989).

The effectiveness of punishment on antisocial behavior is of significant debate, and there is no clear evidence that punishment either improves behaviors or reduces the recidivism rate. Research that exists tends to indicate that incarceration efforts of the judicial system tend to actually worsen the outcomes for young people. Evidence for the effectiveness of incarceration in reducing later illegal activity does not exist. Incarcerated adolescents have a 50% to 70% chance of being arrested within 2 years of release. Juvenile justice policies are frequently not designed based on prevention research but in a legislative response to particular aberrant and well-publicized events. For example, boot camps have been widely adopted as a model for treatment of incarcerated teens, with no evidence of effectiveness at all; in fact, studies indicate that teens who have participated in boot camps have a 75% recidivism rate, even worse than incarceration. In addition, recent investigations into some of the 50 boot camps operating around the country have revealed widespread abuse and neglect (Children's Defense Fund, 2000).

The disproportionate incarceration of minority adolescents, particularly Latino and African-American teens, has been a source of grave concern for many years. Research indicates that this overrepresentation is a product of actions occurring through the entire juvenile justice system, from the decision to make the initial arrest, the decision to hold a youth in detention, the decision to refer a case to juvenile court, the prosecutor's decision to prosecute a case, to the actual judicial decision and the subsequent penalty (Building Blocks for Youth, 2000). At every step of the process, minority adolescents are more likely to be treated in a way that inflates the charges and magnifies their chances of incarceration, including the incarceration of minority adolescents as adults, than are white teens for the same offenses (Males and Macallair, 1999). Minority adolescents are 8.3 times more likely than their white counterparts to be sentenced by an adult court to imprisonment in a California Youth Authority facility. The juvenile justice system has a budget of about $10 billion nationally; most is used for incarceration.

Family-focused, community-based, supervised programs involving offending teens have markedly lower recidivism rates. There is much room for continued research and modification of public policy regarding our approach as a society to young people who are apprehended for illegal activities (Mendel, 2000). Parenthetically, health care for teens in juvenile confinement is a serious concern because incarcerated teens have a greater than average number of health problems that may worsen during confinement, and only 1% of eligible juvenile justice facilities have been accredited as meeting existing voluntary standards for providing health care.

### WEB SITES


### Federal Resource Sites

- [http://www.gcpc.state.il.us/](http://www.gcpc.state.il.us/), Gang Crime Prevention Center.

### REFERENCES AND ADDITIONAL READINGS


Rosenberg ML. Academic medical centers have a major role in preventing violence. Acad Med 1993;68:268.


Depression is a common and significant problem during the adolescent developmental period. Depression is a condition in which the person experiences a state of general unhappiness, a lack of satisfaction with most aspects of life, a pessimistic view, and a loss of interest and energy. Depressive disorders are common, often chronic and intermittent with strong familial predispositions and often persisting into adulthood.

Mood disorders must be viewed in the context of a continuum during the life cycle. The Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV) (American Psychiatric Association, 1995) describes the symptom presentation as similar for children, adolescents, and adults. However, it is well recognized that the early adolescent presents normal developmental issues significantly different from those of the late adolescent, and this holds true for the manifestations of psychopathology. Therefore, presentation of depression during early adolescence may more closely resemble childhood symptomatology, whereas depression during later adolescence may more closely resemble adult symptomatology. Symptoms such as irritability, somatic complaints, anxiety, and social withdrawal are more common in younger adolescents, whereas psychomotor retardation with impairment in functioning, sleep and appetite disturbances, suicidal ideation and attempts, anger and acting-out behaviors, and psychotic and delusional states are more commonly seen in older adolescents. Regardless of age, many depressed or emotionally distressed patients initially present to primary care settings with various physical complaints that are usually unsubstantiated by physical or laboratory examination findings.

**Epidemiology**

The reported occurrence of depressive disorders in adolescents varies depending on which age group is being studied. For example, the incidence is lower in 10- to 14-year-olds and higher in 18- to 24-year-olds. Also, the numbers will vary depending on whether cross-sectional or longitudinal data are used. What is important to note is that depression is not uncommon during adolescence and the practitioner is bound to encounter depressed adolescent patients.

1. In normative, nonclinical samples, approximately half of all teenagers reported feeling depressed at the time of the sample or within the previous 6 months.
2. In surveys of adolescents seen for routine medical care, up to two thirds reported feeling depressed at the time of the medical visit or within the immediate past few weeks.
3. In the 1999 Youth Risk Behavior Surveillance (CDC, 2000), 28.3% of high school students reported feeling sad or hopeless, 19.3% seriously considered attempting suicide, 14.5% made a suicide plan and 8.3% attempted suicide.
4. Adolescents meeting DSM-IV criteria for a depressive disorder, which ranges from 1% for bipolar disorders, 3%–8% for dysthymic disorder (DD), and 5%–9% for major depressive disorders (MDDs).

At any one time then, 8%–20% of adolescents will be suffering from one of the depressive disorders. A compounding factor is that up to 40% of adolescents who present with a major depressive episode also have another comorbid Axis I diagnosis such as substance abuse, attention deficit hyperactivity disorder (ADHD), and/or conduct disorder/oppositional defiant disorder.

5. The gender ratio appears to be similar in children but increases to a female to male ratio of 2:1 in adolescents.

**Risk Factors**

Depression, like any other medical condition, is best diagnosed and treated from a biopsychosocial perspective. Although every risk factor places the adolescent at an ever increasing risk for depression, the interaction of various risk factors incrementally places the adolescent at greater and greater risk.

**Genetics** Adolescents with one parent who is depressed are three times as likely to experience a depressive episode, and conversely an adolescent who is depressed will have a depressed mother in one half to three quarters of all cases. Parents of depressed adolescents also demonstrate high rates of other disorders including substance abuse, personality disorders, and anxiety disorders.

**Family Factors** Studies indicate that families of depressed adolescents show more conflict and communication problems, less expression of affect and support, and more child maltreatment. These factors seem to have a greater risk loading effect for adolescent depression than parental depression itself.

**Exposure to Negative Life Events** Clinical and community samples show significantly more negative life events in depressed adolescents, including loss of a family member through death or divorce, the breakup of a romantic relationship, school or work problems, geographical moves or school changes, and physical, sexual, or substance abuse. Lower socioeconomic status also presents as a significant risk factor.

**Coexisting Psychiatric and Medical Conditions** The history of a previous depressive episode or anxiety disorder increases the adolescent's risk for future depression. Adolescents with ADHD, learning disabilities, and mild mental retardation are at increased risk, as are those with eating disorders and substance abuse. Patients with chronic, intermittent medical conditions such as asthma or inflammatory bowel disease often experience a sense of futility and hopelessness predisposing them to an increased risk of depression. Acute disfigurement or loss of bodily function, such as paraplegia, also increases the risk for depression.

**Personality Factors** Adolescents who have negative self-attributes such as feelings of unattractiveness, feelings of being not accepted or rejected, and feelings of being unintelligent or unlikable usually experience low self-esteem and poor self-worth, all of which contribute to depression in adolescents. Other psychodynamic factors that place the adolescent at risk may be a sense of a lack of control, particularly internal control, thereby overaccentuating their own dependency needs, which interfere with the normal developmental striving for autonomy and independence.

**Suicide** Suicidal ideation and attempts are the most serious manifestations of adolescent depression but also represent a very serious risk factor in depression. Unfortunately, the suicide rate in adolescents has skyrocketed over the past four decades and now represents 12% of the total mortality during adolescence. Any suicidal thought, gesture, or attempt demands careful and thorough clinical attention and often mental health interventions. Suicidal gestures often represent the adolescents' desperate attempt to communicate their depression and despondent feelings to family, friends, and school staff.

**Neurobiological Factors**
1. Possible reduction in absolute brain and cerebrospinal fluid serotonin levels.
2. Functional brain imaging (positron-emission tomography, single-photon emission computed tomography, and functional magnetic resonance imaging) shows decreased neuronal activity in the left prefrontal cortex and limbic areas.

The adolescent years are generally viewed as a period of exploration and experimentation on the journey toward adulthood. It is believed to be a time of blossoming and maturing, a time of moving toward independence, a time of relative abandon and carefree joy. Yet the cinema, popular literature, and contemporary life in the schools and communities often reveal a darker, more troubled, more depressing side for some adolescents. How then is the busy practitioner to decide if a teenage patient is experiencing “normal” depression after a romantic breakup or after being rejected from his or her college of choice, or after being grounded secondary to misbehavior or if the depth and breadth of the depression is clinically significant and demanding of treatment. In general, the normally depressed adolescent has a short-lived course of depression that does not interfere with normal socialization, does not result in falling grades, and does not lead to substance use and abuse.

DIAGNOSIS

DSM-III (American Psychiatric Association, 1980) put to rest a controversy regarding whether children and adolescents actually experience depression or a manifestation of sadness that is masked in some other form such as somatization. Since DSM-III, all of the criteria for depression in adults also apply to children and adolescents. DSM-IV classifies three types of mood disorders:

1. Depressive disorders, including major depressive disorders (MDD), dysthymic disorders (DD), and depressive disorders not otherwise specified (DD NOS)
2. Bipolar disorders, bipolar I disorder, bipolar II disorder, cyclothymic disorder, and bipolar disorder not otherwise specified
3. Mood disorder due to a medical condition and substance abuse mood disorder.

Signs and Symptoms

Major Depression At least five of the following symptoms are present for 2 weeks and represent a change from previous functioning. At least one of the symptoms is either depressed mood or loss of interest or of pleasure.

1. Depressed or irritable mood most of the day, nearly every day
2. Markedly diminished interest or pleasure in all or most activities of the day nearly every day
3. Significant weight loss or weight gain when not dieting or decrease or increase in appetite
4. Insomnia or hypersomnia nearly every day
5. Psychomotor agitation or retardation nearly every day
6. Fatigue or loss of energy nearly every day
7. Feelings of worthlessness or excessive or inappropriate guilt nearly every day
8. Diminished ability to think or concentrate nearly every day
9. Recurrent thoughts of death, suicidal ideation, or suicide attempts

Dysthymic Disorder This is mainly a chronic disturbance of mood, involving primarily a depressed or irritable mood for most days for at least 1 year (in adolescents). Dysthymia differs from major depression in that dysthymia is usually associated with milder symptoms for a longer period. A major depression is usually associated with discrete episodes of more severe depression that can be distinguished from the person's usual functioning. Criteria for dysthymia in adolescents include the following:

1. Poor appetite or overeating
2. Insomnia or hypersomnia
3. Fatigue
4. Low self-esteem
5. Poor concentration
6. Feelings of helplessness

All of the depressive disorders may have a seasonal component; that is, an existing depression may become more severe during the winter months, particularly in the northern areas of the United States. A discrete seasonal affective disorder does exist, manifesting only during the winter months and generally abating in early spring. Typical symptoms include decreased activity, excessive sleep, particular craving of carbohydrates, particularly chocolates, weight gain, and decreased libido.

Bipolar Disorders Bipolar disorders are frequently first manifested during the adolescent years. The depressive elements are similar to the signs and symptoms of the other depressive disorders with the very marked exception of one or more manic episodes. These manic episodes are characterized by periods of intense elation and energy, hyperactivity, sleeplessness, grandiosity, pressured speech, spending sprees, and hypersexuality. Manic episodes occur spontaneously as part of the natural history of the disorder but may also be precipitated during the treatment of a depression by the administration of an antidepressant medication, either a tricyclic compound or a newer serotonin reuptake inhibitor.

Diagnosis and Assessment

The diagnosis of depression in adolescents is primarily based on clinical signs and symptoms as outlined in the DSM-IV criteria. The data to substantiate the diagnosis are obtained during the clinical interview with the adolescent and through separate or conjoint interviews with the parents or caretakers. Diagnosis can be aided by the use of standardized checklists and questionnaires such as the Beck Depression Inventory and the Children's Depression Inventory.

Laboratory Tests

Laboratory tests have not been particularly helpful in making the diagnosis of depression in adolescents. Although thyroid disease is not common in adolescents without accompanying physical signs and symptoms, routine thyroid function studies are usually part of every workup for depressed adolescents. Routine urinalysis, complete blood cell count, and erythrocyte sedimentation rate would also be included in the workup to rule out any underlying asymptomatic physical condition. Other tests such as the dexamethasone suppression test, growth hormone stimulation test, and sleep electroencephalograms (EEGs) have been shown to be nonspecific and therefore are not used.

TREATMENT

All of the depressive disorders are amenable to treatment. Studies indicate that a combination of counseling, disease education, and medication offers the greatest likelihood of success.

The management of adolescents with depression by the primary care clinician is dependent on the severity of the illness (suicidal, manic), the availability of time and the interest and comfort of the clinician, and the availability of psychiatric resources in the community.

Assuming the primary care clinician is prepared to manage the depressed adolescent, a three-pronged approach should be considered, which includes the following:

- Patient and family education
- Counseling for the patient and family
- Medication

1. Education: Essential in all cases
   a. The patient and family should first be helped to understand the biological-familial transmission of depressive disorders.
b. Awareness: Next, everyone should be aware of the clinical signs and symptoms of depression to monitor the progress of treatment and to be alert to possible recurrence so immediate treatment may be initiated.

c. Treatment options: Lastly, the patient and family should understand the various treatment options and modalities and the rationale for each, as well as the predictable treatment response to each.

Printed materials for the American Academy of Pediatrics and the American Academy of Child and Adolescent Psychiatry can be made available and various Internet Web sites are available for support and education (see the "Web Sites" section of this chapter).

2. Counseling: Counseling, although primarily directed toward the depressed adolescent, must involve the parents to ensure optimal treatment success. Parental counseling is usually focused on helping them with their own sense of guilt, frustration, and perhaps depression. Often, helping parents differentiate depression from normal adolescent behaviors and setting appropriate limits can be very helpful. Counseling the adolescent requires time and availability. In general, supportive counseling, which implies a helpful, empathetic, listening approach to bolster self-esteem and foster positive behaviors, can be carried out by the primary care clinician. More sophisticated behavioral, cognitive, and insight-oriented counseling generally requires more specialized and advanced counseling training and usually warrants referral to a mental health specialist.

3. Medication: Medication can be an important modality in the three-pronged approach to treatment. The use of medications is dictated by the severity of the presenting symptoms, the parents' acceptance of medication as a treatment modality, and the adolescent's willingness to take the medication for the prescribed period. Although the scientific literature describes equivocal responses to antidepressant medication in adolescents, clinical practice trends indicate successful outcomes with the use of medications in the treatment of adolescent depression.

Classes of Medications

**Serotonin Reuptake Inhibitors** The most common and effective agents are the selective serotonin reuptake inhibitors (SSRIs) such as fluoxetine (Prozac), sertraline (Zoloft), paroxetine (Paxil), and fluvoxamine (Luvox). These medications work by blocking the reuptake of serotonin in presynaptic neurons. Doses for older adolescents parallel those of adults, whereas younger adolescents are generally started at lower doses and titrated upward more slowly. The advantages of the SSRIs are as follows:

- Minimal binding to H1, so less sedation and weight gain
- Minimal binding to a1-receptors, so less orthostatic hypotension
- Less binding to muscarinic cholinergic receptors, so less dry mouth, blurred vision, and constipation
- Do not potentiate effects of alcohol or sedative-hypnotic agents
- Once-daily dosing
- Less dose titration required

Thus, overall these medications are well tolerated and safe, with a much lower risk in overdose situations. However, there are also some disadvantages to consider:

- Inhibition of cytochrome P-450 enzyme system, which can lead to possible drug-drug interactions
- Sexual dysfunction including impotency and loss of libido can occur, which can reduce compliance
- Possible gastrointestinal side effects
- Disinhibition
- Precipitation of a hypomanic-manic episode may also occur

**Specific Drugs and Doses**

Common SSRI medications and doses are listed in Table 79.1.

<table>
<thead>
<tr>
<th>Common SSRI medications and other antidepressants medications: doses and side effects</th>
</tr>
</thead>
</table>

TABLE 79.1. Common SSRI medications and other antidepressants medications: doses and side effects

These SSRI medications are also commonly prescribed for obsessive-compulsive disorders, phobias, and anxiety disorders.

Other antidepressants used in adolescents and young adults are also summarized in Table 79.1 and discussed here.

**Bupropion (Wellbutrin).**

Mechanism of action An aminoketone that appears to have weak inhibition of dopamine uptake, less so for norepinephrine uptake, and little effect on serotonin reuptake.

Advantages

- Minimal affinity for H1, a1, and muscarinic receptors
- Low risk in overdose situations
- Does not potentiate effects of alcohol or sedative-hypnotic agents
- No significant cytochrome P-450 drug-drug interactions
- Least likely to cause sexual dysfunction

Disadvantages

- Short half-life requires multiple dosing
- Higher risk of seizures with doses >450 mg

**Venlafaxine (Effexor).**

Mechanism of action A phenylethylamine that blocks reuptake of both norepinephrine and serotonin in presynaptic neurons.

Advantages

- Minimal affinity for H1, a1, and muscarinic receptors
Close coordination between primary care provider and prescribing clinician (if not the same individual): Because these medications may interact with other medications, this coordination can be very important.

Side effects: Be aware of potential side effects, which may not be evident for 4–6 weeks.

Onset of action: Both the SSRIs and the TCAs generally give rapid improvement for anxiety symptoms and sleep disturbances, but the antidepressant effect may not be evident for 4–6 weeks.

Duration of use: In general, most clinicians recommend that a successful pharmacological treatment be maintained for at least 6 months and then be revaluated for continuation of treatment.

Table 79.1
Start at a low dose, and go slow with increases in doses.


Advantages

- Minimal affinity for H₁, a₁, and muscarinic receptors
- Low risk in overdose situations
- Does not potentiate effects of alcohol or sedative-hypnotic agents
- Smaller rates of sexual dysfunction and perhaps no higher than placebo

Nefazodone (Serzone)

Mechanism of action: A phenylethylamine that blocks reuptake of serotonin like SSRIs but also acts as potent antagonist of H₁, a₁ receptors.

Advantages

- Minimal affinity for H₁, a₁, and muscarinic receptors
- Low risk in overdose situations
- Does not potentiate effects of alcohol or sedative-hypnotic agents
- Smaller rates of sexual dysfunction and perhaps no higher than placebo

Disadvantages

- Short half-life requires multiple doses (extended release is once daily)
- Can have dose-dependent increase in blood pressure

Tricyclic Antidepressants: Tricyclic antidepressants (TCAs) are equally effective as the SSRIs in treating adolescent depression, but the potential serious side effects of cardiotoxicity (lengthening of the PR interval and QRS complex) and the troublesome dryness of the mouth and constipation tend to relegate this class of medications to a second choice, following the SSRIs.

Monoamine Oxidase Inhibitors: The monoamine oxidase inhibitors are infrequently used in the treatment of adolescent depression, because of the very serious, potentially life-threatening possibility of a hypertensive crisis for those adolescents who refuse to adhere to a strict tyramine-free diet (i.e., a pizza-free life).

Mood Stabilizers: Mood stabilizers such as lithium, carbamazepine (Tegretol), valproic acid (Depakote), and gabapentin (Neurontin) have all been used in adolescents with bipolar disorder, organic mood disorders, and as an adjunct to the SSRIs and TCAs in the treatment of major depressive disorders. In general, the primary care clinician should seek out mental health consultation, if available, when such augmentation is considered.

Phototherapy: Phototherapy is recommended specifically for adolescents with seasonal affective disorder. Special light boxes, which use lamps in the 2,500 to 10,000 Lux spectrum, are used one or two times a day for 15 to 45 minutes and are reported to provide relief of depression in 40% to 70% of patients. If light box treatment is unsuccessful, treatment with the addition of an SSRI is recommended.

Important Prescribing Issues

1. Onset of action: Both the SSRIs and the TCAs generally give rapid improvement for anxiety symptoms and sleep disturbances, but the antidepressant effect may not be evident for 4–6 weeks.
2. Start at a low dose, and go slow with increases in doses.
3. Close coordination between primary care provider and prescribing clinician (if not the same individual): Because these medications may interact with other medications, this coordination can be very important.
4. Laboratory testing for blood levels needs to be available for medications requiring close monitoring such as lithium.
5. Side effects: Be aware of potential side effects (Table 79.1).
6. Duration of use: In general, most clinicians recommend that a successful pharmacological treatment be maintained for at least 6 months and then be reassessed. Rate of recurrence of depression is 50% after first episode, 70% after second, and 90% after third.

CONCLUSION

Depression during adolescence occurs in up to 20% of the population at any given time. Adolescents present with the same symptomology as adults but often demonstrate anger and rebellion as the presenting signs. Adolescents also manifest somatic symptoms as an outward presentation of depression. The diagnosis can be made using the DSM criteria. Adolescent depression is amenable to treatment using education, counseling, and/or medication.

WEB SITES

For Teenagers And Parents


For Health Professionals

http://www.fda.gov/ohrms/dockets/ac/00/slides/3639s2c/sld001.htm. Slide presentation on suicide and adolescent depression from the Food and Drug Administration.

REFERENCES AND ADDITIONAL READINGS


Although adolescence is a relatively healthy age, the 15- to 24-year-old age group is the only age group in which the mortality rate has increased during much of the past few decades and did not meet the targeted decreases in the past decade as established by the Public Health Service. From 1950 to 1998, the suicide rate for adolescents age 15 to 24 years increased by 250%. However, on a positive side, the suicide rate for adolescents has fallen since 1994. Although suicide is the eighth leading cause of death for all Americans, it is the third leading cause of death in this age group, following unintentional injuries and homicide. In addition, many teens seriously consider suicide without an attempt. For all age groups, the age-adjusted suicide rate declined slowly in the 1990s, 10.4 per 100,000 in 1998 compared with 11.5 in 1990. In 1997, more adolescents and young adults died from suicide than from cancer, heart disease, acquired immunodeficiency syndrome, birth defects, stroke, pneumonia and influenza, and chronic lung disease combined. The gender ratio for completed suicides is about 6:1 (males:females). Although accurate data on attempted suicides are not available, researchers estimate that there are a minimum of 8 to 25 attempted suicides to one completion, and data show that the attempt ratio is higher in females than males.

Suicidal behaviors may be conceptualized as the adolescent’s ultimate yet inadequate coping behavior. For the adolescent, a suicide attempt may represent an attempt to escape pain or to obtain relief. For the family, suicide imposes grief at the loss, rage at the act of suicide, and guilt for having failed to prevent an untimely death. For the health care professional, a suicide attempt presents a crisis that he or she may feel totally inadequate to handle based on prior training. This chapter discusses the dynamics of adolescent suicide and suicide attempts, including epidemiology, risk profile, etiology, warning symptoms, evaluation, and treatment.

**EPIDEMIOLOGY**

1. Suicide rates: Efforts to estimate attempted and successful suicides are confounded by the fact that many suicide attempts are recorded as accidents. In 1997, 13% of all deaths in the 15–24-year-old age group were attributed to suicide. The Centers for Disease Control and Prevention (CDC) reported 4,186 suicides among people age 15–24 years in the United States that year. Forty-three percent (1,802 cases) were adolescents age 15–19 years, and 57% (2,384 cases) were among those age 20–24 years (303 suicides were reported for those age 10–14 years).

   a. Male suicide rates in the United States are indicated in Table 80.1.

<table>
<thead>
<tr>
<th>Year</th>
<th>10–14</th>
<th>15–19</th>
<th>20–24</th>
</tr>
</thead>
<tbody>
<tr>
<td>1990</td>
<td>0.2</td>
<td>2.2</td>
<td>2.9</td>
</tr>
<tr>
<td>1995</td>
<td>0.9</td>
<td>4.0</td>
<td>5.3</td>
</tr>
<tr>
<td>1990</td>
<td>0.9</td>
<td>3.8</td>
<td>2.1</td>
</tr>
<tr>
<td>1975</td>
<td>1.0</td>
<td>3.4</td>
<td>2.5</td>
</tr>
<tr>
<td>1975</td>
<td>1.0</td>
<td>2.3</td>
<td>1.9</td>
</tr>
<tr>
<td>1990</td>
<td>0.1</td>
<td>1.9</td>
<td>2.3</td>
</tr>
<tr>
<td>1990</td>
<td>1.1</td>
<td>5.9</td>
<td>5.3</td>
</tr>
<tr>
<td>1990</td>
<td>0.9</td>
<td>1.9</td>
<td>2.3</td>
</tr>
</tbody>
</table>


   **TABLE 80.1. Male suicide rate in the United States (per 1,000,000)**

   b. Female suicide rates in the United States are indicated in Table 80.2.

<table>
<thead>
<tr>
<th>Year</th>
<th>10–14</th>
<th>15–19</th>
<th>20–24</th>
</tr>
</thead>
<tbody>
<tr>
<td>1990</td>
<td>0.1</td>
<td>1.9</td>
<td>2.3</td>
</tr>
<tr>
<td>1995</td>
<td>0.2</td>
<td>1.8</td>
<td>2.1</td>
</tr>
<tr>
<td>1990</td>
<td>0.2</td>
<td>2.0</td>
<td>2.7</td>
</tr>
<tr>
<td>1995</td>
<td>0.4</td>
<td>2.0</td>
<td>2.6</td>
</tr>
<tr>
<td>1990</td>
<td>0.4</td>
<td>1.9</td>
<td>2.3</td>
</tr>
<tr>
<td>1990</td>
<td>0.6</td>
<td>3.4</td>
<td>4.1</td>
</tr>
<tr>
<td>1990</td>
<td>0.1</td>
<td>2.3</td>
<td>2.7</td>
</tr>
</tbody>
</table>


   **TABLE 80.2. Female suicide rate in the United States (per 1,000,000)**

   c. Trends in suicide rates for 10–24-year-olds by 5-year age groups from 1979 to 1998 are indicated in Fig. 80.1.

   **FIG. 80.1. Suicide rates for all races and both genders, 1979–1998, by year and age. (From Centers for Disease Control and Prevention, CDC Wonder, with permission.)**
TABLE 80.3. Behavior related to attempted suicide among high school students during 12 months preceding survey, 1999

Since 1950, suicide rates have increased four to five times for male adolescents age 15–24 years and almost doubled for female adolescents of the same age group. Between 1990 and 1998, suicide rates declined 19.7% in 15–19-year-old adolescents from 11.07 to 8.89 per 100,000 and 10% in 20–24-year-olds from 15.11 to 13.57 per 100,000. From 1981 to 1992, the suicide rate has increased most rapidly among male African-Americans age 10–19 years, going up 175% from 2.99 to 8.23 per 100,000. Between 1992 and 1998, the rate fell by 26.5% for this group.

2. Attempts: Estimates of the number of suicidal attempts to completed suicides in adolescents range greatly from study to study. Conservative studies estimate ratios of 8:1 to 25:1, whereas others approximate 50:1 to 200:1. Based on the 1997 figure of 4,186 suicides, estimates of attempts are 33,000–800,000 per year. Rates of second attempts vary from 6%–16% within 1 year.

3. Sex: Males outnumber females in completed suicides by 6:1, whereas it is estimated that females outnumber males in attempts. Nationwide, among all age groups, while males accounted for 72% of all suicides in 1997 and white males and white females accounted for >90% of all suicides. The gender difference in the rate of completed suicides is attributed to the difference in suicide methods. Males tend to use firearms, a method that is more fatal and prevents higher rates of rescue, whereas girls most often ingest poisons, which in the United States results in better rescue opportunities.

4. Race: Suicide rates are higher in white adolescents than African-American or Hispanic adolescents. From 1980 to the early 1990s, suicidal behaviors among all adolescents increased; however, rates for African-American adolescents increased at a higher rate, having more than doubled during that time, dramatically shifting the gap between the races. Since the early 1990s, suicide rates have been falling in adolescents. The suicide rate among Native American male adolescents is higher in comparison to the overall rate. In 1999, Hispanic adolescents report more suicide rates than any other ethnic group.

5. Family history: A family history of suicidal behaviors presents a greater psychological risk for all the surviving family members. A history of suicide attempts or suicide among first- or second-degree relatives increases risk for adolescent suicide by three times. Other family influences include a history of violence and family disruption and rapid sociocultural changes.

6. Age: As outlined in Table 80.1 and Table 80.2, suicide is uncommon in adolescents younger than 14 years, with the rates rising dramatically thereafter. The largest increase in suicide rates since 1970 has been in 15–19-year-old male adolescents.

7. Psychiatric comorbidity: Rich et al. (1986) summarized their findings in a study of suicides in San Diego County, with the statement that “psychiatric illness is a necessary (but insufficient) condition for suicide.” A review of the literature indicates that a history/diagnosis of a depressive disorder and the expression of hopelessness is associated with suicidal ideation and attempts. Probable or definite personality disorders were more common in adolescent suicide victims than in control subjects, particularly cluster B (impulsive-dramatic) and C (avoidant-dependent) disorders. Other factors contributing to suicidal attempts include aggressiveness and antisocial behaviors (Goodwin et al., 1989). In addition, substance abuse or dependence can be an important contributor in the escalation of suicidal thoughts.

8. Marital status: In the general population, suicide rates are lower for married individuals, but the reverse is true in the 15–19-year-old population, in which the rates of suicide for married individuals are increased 1.5–1.7 times over those for unmarried individuals.

9. Season: Rates are increased in the spring and fall.

10. Geographical: Rates are higher in the western United States than in other regions of the country and lower in the eastern and midwestern states. For adolescents and young adults age 10–24 years, the 1998 rates ranged from a low of 4.12 per 100,000 in Delaware to 28.71 in Alaska.

11. Method used for completed suicides

a. Firearms and explosives: Firearms are the most common method of adolescent suicide. This is the case for both males and females and younger and older adolescents. The use of firearms is more common in male suicides, whereas firework suicides have increased significantly in female adolescents. More than 60% of adolescent suicides in 1998 (age 15–24 years) were firearms-related suicides. The CDC has attributed almost all of the increase in the suicide rate since the 1980s to firearm-related suicides.

b. Hanging accounted for 25.4% of adolescent suicides in 1998.

c. Poisonings: In 1998, poison was used in 4.1% of adolescent suicides.

12. Others: A small percentage of suicides are accomplished through gas poisoning, cutting and piercing with a sharp instrument, or jumping from high places.

13. Suicide at college: Most studies indicate that suicide rates in college students are no higher than that in the general population for the same age group. The incidence of suicide in college students appears to be approximately 1.01 per 100,000 per year (see Chapter 85). Approximately 10% of college students have contemplated suicide in the past year, about 5%–6% have seriously made a plan and about 1.5% have made an attempt.

RISK FACTORS IN THE SUICIDAL ADOLESCENT

Although there are no assessment tools that can predict which adolescent will attempt suicide, risk factors are cited in the literature that should increase the index of suspicion for a potentially suicidal patient. These factors may also be of value in evaluating the future risk of an adolescent who has attempted suicide.

1. Prior suicide attempts: Approximately one third of teenage suicide victims have made a previous suicide attempt. A male teen who attempted suicide in the past is more than 30 times more likely to complete a suicide than a male who never attempted before. A female teen with a history of a suicide attempt presents with three times the risk. Other aspects of previous attempts are as follows:

a. A clear intention to repeat.

b. Agent used in a past attempt: Jumping and shooting are of higher risk than ingestion or cutting.

c. Location and chance of rescue: The risk is higher with an adolescent who has attempted suicide in a remote site with no probability of discovery.

2. A history of co-occurring mental and substance abuse disorders: Most young people who complete suicide have a diagnosable mental disorder, a substance abuse disorder, or both. Most teens who complete suicide suffer from depression, experiences higher levels of hopelessness, helplessness, or low self-esteem than their nonsuicidal peers. Cavaolia and Lavender (1999) studied the relationship between adolescent suicide behavior and substance abuse. Adolescents who abuse psychoactive substances experience greater psychological distress (“such as from obsessive-compulsive symptoms, depression, interpersonal sensitivity, hostility, phobic and generalized anxiety, and somatic complaints”) and appear to be at higher risk for suicidal behavior.

3. History of suicide in the family: A high percentage of suicides and attempted suicides have had close family members attempt or complete suicide.

4. Family history of mental and substance abuse disorders

5. Stressful life event or loss: Psychosocial problems and stressors are often cited by adolescents as reasons for attempting suicide. It is important to recognize that the degree of stress the teen experiences is subjective and reflects a personal level of vulnerability (such as when the teen is experiencing a loss of a significant person or relationship, a conflict with parents or peers, or problems at school).

6. History of a broken family or family discord including low levels of communication with parents

7. History of prior abuse: Riggs et al. (1990) reported a five times greater risk of suicide in adolescents with a prior history of physical abuse and a threefold increase of suicide in those teens with a history of sexual abuse.

8. Physical illness
9. Gay or bisexual adolescents: Research shows that gay and bisexual adolescents experience high rates of depression and are three times more likely than their peers to attempt suicide.

10. Poor school performance and experiencing learning disabilities

11. Recent behavioral changes and reporting feelings of anger, rejection, social isolation, or expendability

12. Presence of firearms in the house: The most common location of teen suicides by firearms is at their homes. The risk is directly related to the accessibility and the numbers of guns at home. Brent et al. (1993b) found that the presence of firearms may be associated with adolescent suicide even in the absence of clear psychiatric illness.

PROCESS OF THE ADOLESCENT SUICIDE ATTEMPT

Although the history of each suicidal adolescent is different, many such adolescents exhibit a behavior pattern that can be broken down into four components:

1. Long-standing history of problems: Suicide is a disease of deficiency, a deficiency of early social connections that a developing teen uses later as the basis for conflict resolution and problem-solving skills. Many adolescents who attempt suicide exhibit a long history of deficiency or problems that create an underlying vulnerability. These problems include parents or relatives who have attempted suicide; one or both natural parents absent from the home; unwanted stepparents; divorce in the family; history of family conflicts; parents with alcohol problems; history of foster placements; or marked residential mobility.

2. Escalation phase: In many adolescents who have attempted suicide, the vulnerability created during childhood increases during adolescence. This period of escalating problems is characterized by frequent family conflicts, because the family fails to deal adequately with the adolescent developmental process. The adolescent often begins to feel isolated from his or her family and other social structures. Significant physical or mental illness in the family and loss of the family unit may also exacerbate the adolescent's vulnerability.

3. Progressive social isolation: Failure of available adaptive techniques for coping with old and new problems often leaves the suicidal adolescent feeling progressively socially isolated. This is often associated with a significant failure of communication with parents. The adolescent seems to have lost or never developed the capability to express his or her feelings with words. Although these adolescents are often depressed, the depression may not be manifested in the typical adult behaviors of depressed affect, weight loss, and so forth. In fact, adolescent depression may manifest itself through oppositional or evasive behaviors such as reduced school attendance and performance, substance abuse, delinquency, runaway behavior, early onset of sexual activity or sexual promiscuity, and more.

4. Final stage: The suicide attempt is often preceded by a precipitating event that caps this long process of increasing despair. Precipitating events often include loss of a girlfriend or boyfriend, pregnancy, school problems, death of a friend or relative, or a family fight.

PRODROMAL SIGNS

Several signs in the adolescent should alert family, friends, or the health care provider to the potential for suicide. These prodromal signs include sadness, hopelessness, emptiness, lack of energy, insomnia, eating problems, loss of interest in social life and school, boredom, loneliness, irritability, truancy, substance abuse, or a change in social behavior. Other signs include accident proneness, giving away of prized possessions, and statements such as, "My family (or the world) would be better off without me."

ASSESSMENT OF THE SUICIDAL ADOLESCENT

All adolescents identified to be at risk for suicide need help. However, most suicidal adolescents are not likely to initiate help-seeking behaviors. Medical, as well as mental health providers, must take an active step in screening adolescents with significant risk factors for suicide. Any adolescent with a well-thought-out plan that includes intent, plan for place and time, and access to lethal means should be considered high risk. Even adolescents presenting with low or medium risk must be screened to assess past and present suicide-related factors. Based on the screening, the degree of protection and intervention necessary to prevent suicide can then be determined.

1. Medical therapy: The first priority is to treat any life-threatening medical complication of the suicide attempt.

2. Physical protection: The suicidal adolescent should be provided immediate physical protection so that a reattempt does not occur. Depending on the degree of risk and the resources available, an adolescent should be hospitalized or left at home with instructions to family members on how to ensure the youth's safety, and what helping resources to use.

3. Psychological intervention: As soon as the medical evaluation and therapy are completed, the adolescent requires calming down and reassurance that he or she is safe. At this time, an initial evaluation should be performed. This evaluation should attempt to assess the following:

a. Predisposing conditions
   - Sex and age of adolescent
   - Underlying health status
   - History or evidence of prior suicide attempts and mental disorders including history of substance abuse
   - History of family, school, or peer problems
   - History of suicide attempts or substance abuse in family members
   - History of incest or abuse
   - History of accidents or prior self-destructive behavior
   - Recent experience of loss
   - Presence of firearms or drugs available in the home
   - Prior use of coping strategies
   - Available support systems including reaction by parents and others: Do the parents take the attempt seriously and are they supportive of seeking help?
   - What family or peer support system will the adolescent be returning to at home?

b. State of mind: This includes evaluating the adolescent's
   - Level of depression
   - Level of hopelessness, helplessness, and self-esteem
   - Feelings of expendability (e.g., that the adolescent is not important to the family and that to some extent the family would be "better off" without the adolescent)
   - Openness to further counseling
   - Level of panic and disorganization
   - Attitude about death

c. Suicide attempt: This includes evaluating the following:
   - Method: Lethality and current access to method
   - Timing: Sudden impulse versus well planned
   - Intent: No real intention versus strong intention to die
   - Desire to repeat
   - Circumstances surrounding the attempt: Possibility of rescue from attempt versus an attempt carried out in isolation

Features suggesting a high risk of a second suicide attempt include lethal method, attempt carried out in isolation or precautions taken to avoid discovery, elaborate plan, history of prior attempts, high desire to repeat, marked degree of hopelessness and helplessness, sense of expendability, lack of a strong support system, and lack of desire on adolescent's part to seek help. High-risk adolescents must remain in a safe and protected environment. The adolescent and the family must receive intense mental health services to manage the psychological needs of the adolescent. Discharge should be considered once the suicide risk has declined and the youth and family are able to use appropriate resources.

4. Disposition: Ideally all adolescents with a suicide attempt should have a mandatory short-term hospitalization to assess the adolescent and the family.

   a. Indications for longer hospitalization
      - Medical complications
      - Psychosis
      - Use of a lethal method with clear intent of suicide
      - An uncommunicative adolescent or one who communicates ambivalence regarding the will to live
      - Lack of family support

   If the adolescent shows a high lethality index, the adolescent needs to be kept in a safe and secure environment under one-to-one nursing supervision. If
the adolescent refuses voluntary admission, initiate procedures for involuntary hospitalization.

b. Conditions for managing a suicidal adolescent at home
- Depression is mild and fits into adolescent pattern of mood swings.
- Adolescent has a supportive family willing to help.
- No evidence of long-standing psychosis or severe depression.
- Adolescent clearly no longer feels suicidal and does not wish to die.
- Appropriate medical and psychosocial follow-up have been arranged.
- Case has been evaluated by a psychiatrist, psychologist, or another appropriately trained health care professional.

5. Follow-up: Every suicidal adolescent should have conscientious follow-up care by a psychiatrist, psychologist, or other mental health counselor. The continuation of collaboration of a medical doctor and mental health provider is an essential component of follow-up care. Weekly or more frequent visits should be scheduled initially. During this period, the adolescent's problems can be explored in more depth, with careful attention given to the areas of school, social and family problems, and existing support mechanisms.

6. Outpatient management of at-risk adolescents: The previously described assessment and interventions should be performed, with plans for close follow-up by the appropriate mental health counselor. A suicide prevention contract is also in order. This is a written or oral contract with the practitioner that the teen will not attempt suicide without contacting the practitioner or another identified resource. If suicidal ideation is significant or the suicide potential is judged to be high, then voluntary or involuntary hospitalization would be necessary. Parents should always be notified if a minor is considered at risk of suicide.

Suicide is a tragic but increasingly more common expression of alienation among adolescents. Every suicidal gesture and threat must be taken seriously and evaluated in detail. Rather than viewing a suicide attempt as an impulsive attempt to “get attention.” All adolescent suicidal ideation, gestures, or attempts must be seriously considered and attended to in a professional manner.

RECOMMENDATIONS FOR PRIMARY CARE PHYSICIANS

(Adapted from a policy statement by the American Academy of Pediatrics [April, 2000].)

1. Know the risk factors associated with adolescent suicide. Be prepared to serve as a resource to adolescents, parents, and other members of the community.
2. Routinely ask questions about depression and suicide.
3. Ask specific questions about the availability of firearms. Advise parents of suicidal teens to remove firearms and other potential methods from the house.
4. Recognize the medical and psychiatric needs of the suicidal adolescent and work closely with health care professionals and family members to best manage the suicidal adolescent.
5. Physicians should become familiar with local, state, and national resources concerned with youth suicide. Working relations should be established with colleagues specializing in adolescent suicide to manage the care and follow-up of adolescents at risk for suicide.

PREVENTION OF ADOLESCENT SUICIDE

The CDC has published suicide prevention guidelines. The suggested strategies include the following:

1. School gatekeeper training to help school staff identify and refer students at risk for suicide
2. Community gatekeeper training to teach community members (e.g., clergy, police, recreation staff) and clinical health care providers to identify and refer teens at risk for suicide
3. General suicide education for students to learn about suicide, its warning signs, and how to seek help for themselves or others
4. Screening programs to identify high-risk adolescents and young adults
5. Peer support programs in or outside of school to foster peer relationships and competency in social skills among high-risk adolescents and young adults
6. Crisis centers and hotlines
7. Restriction of access to lethal means such as handguns, drugs, and other common means of suicide
8. Intervention after a suicide to help prevent or contain suicide clusters and to help adolescents and young adults cope effectively with feelings of loss that follow the sudden death or suicide of a peer


WEB SITES

For Teenagers and Parents

http://www.suicidology.org/, Provides information on current research, prevention, and help for the suicidal person. A list of crisis centers and support groups is also included.
http://www.suicidehotlines.com/, Suicide Crisis Center provides a state-by-state listing of suicide-prevention resources.
http://www.aap.org/visit/suicidenfo.htm, Information on suicide from the American Academy of Pediatrics and fact sheets for parents and caregivers on teen depression and preventing youth suicide.
http://www.safeyouth.org/, National Youth Violence Prevention Resource Center includes hot topics on youth suicide
http://www.nimh.nih.gov/publicat/harmaway.cfm, National Institute of Mental Health In Harm’s Way: Suicide in America.

For Health Professionals

http://www.cdc.gov/ncipc/ncipchm.htm, CDC, the National Center for Injury Prevention and Control.
http://www.spanusa.org/, Suicide Prevention Advocacy Network.

REFERENCES AND ADDITIONAL READINGS

School problems, including school phobia, truancy, dropout, academic performance problems, attention deficit hyperactivity disorder (ADHD), and learning disabilities, represent common concerns for adolescents and their families. The adolescent's primary care physician can play a critical role in the evaluation and management of such problems by:

1. Evaluating the adolescent for biomedical disorders such as hearing and vision dysfunction, ADHD, learning disorders, subtle mental retardation, and seizure disorders.
2. Screening the adolescent for emotional disorders such as depression, anxiety, and family conflict and initiating referrals as necessary.
3. Assessing the impact of chronic illness (or its treatment) on the adolescent and his or her family.
4. Assessing the impact of family, school, or community factors on academic performance.
5. Initiating and coordinating appropriate referrals for the psychological and psychometric testing necessary to determine the presence of learning disabilities, ADHD, and related problems.
6. Demystifying learning disabilities, ADHD, and related problems, educating the adolescent and the family about such disabilities, and encouraging the adolescent to develop appropriate attitudes for coping effectively with these disabilities.
7. Educating the patient and the family about the legal obligations of the public schools to meet the educational needs of youngsters with disabilities.
8. Cooperating with the public schools in determining the eligibility for special education services, which requires physician certification.
9. Contributing to the development and coordination of an overall school-based intervention plan and serving as an advocate for the adolescent.
10. Providing short-term counseling for milder school and home-related problems and anticipatory guidance to prevent the development of additional complications (e.g., adjustment reactions and parent-teen conflict).
11. Providing medical therapy for anxiety and affective disorders, as well as for ADHD.
12. Serving as a case manager with whom the adolescent can periodically “check in” to monitor the overall progress of a coordinated set of medical, school, and psychological services.

**SCHOOL PHOBIA**

School phobia is defined as a persistent and irrational fear of going to school. The problem usually arises either because the adolescent cannot cope with the pressures and challenges at school or as a result of other stresses, typically in the family. Common stress factors include the following:

1. Fear of undressing in a group
2. Fear of confrontations with teachers or students
3. Fear of poor grades
4. Fear of being picked first or last for a team or school project
5. Fear of participation in athletics
6. Family dysfunction
7. Fear that peers will criticize (openly or otherwise) their physical appearance
8. Fear of not having enough money
9. Fear of sexual expression
10. Fear of inadequate vocational or academic preparation
11. Fear of individuating or separating from parents

The health care provider must explore with the adolescent his or her fears and reasons for disliking school. Depending on the home situation, the practitioner may recommend more parental involvement and an immediate return to school, or in overrestrictive families, the physician may wish to lessen parental involvement by working out a contract regarding school attendance between the physician and the adolescent. Psychological referral may be advisable, depending on the severity and type of underlying problem (e.g., family dysfunction or clinical phobia). Because anxiety disorders, such as social phobia or generalized anxiety disorder, are a common cause of school phobia, medications for anxiety disorders can be useful as part of the overall management plan. The serotonin selective reuptake inhibitors (SSRIs) have been shown to be useful for these disorders and are generally very well tolerated. Paroxetine (Paxil, usual doses of 10 to 40 mg every day), fluoxetine (Prozac, usual doses of 10 to 40 mg every day), and sertraline (Zoloft, usual doses of 50 to 150 mg every day) are most often used. Buspirone (BuSpar, usual doses of 10 to 20 mg three times a day) may also be effective.

**SCHOOL TRUANCY AND DROPOUT**

Although the adolescent with school phobia has some fear of attending school, the adolescent who is truant or who drops out of school is making a conscious decision to miss school. It is clear that school failure is one of the common precursors to truancy and school dropout. And most importantly, school dropout often precedes high-risk social behaviors such as involvement in gangs and violence, running away, sexual promiscuity, and excessive drug or alcohol use. For the clinician who sees adolescent patients, these facts are critical in reinforcing the importance of an educational history that includes academic performance and goals, as well as low motivation toward school and skipping classes. School dropout is a major problem, particularly among lower socioeconomic classes, and can reach as high as 50% in certain school districts, particularly among male students. Data from college admissions reveal a significant gender difference, with males accounting...
for approximately 43% of students at colleges and universities at all levels. In addition to the risk behaviors seen in dropouts, they have higher rates of unemployment and lower incomes than those of high school graduates.

As mentioned, one of the primary causes of truancy and dropout is poor academic performance, and all of its causes, (see the next section). In addition, truancy and dropout may be caused by substance abuse, pregnancy, marriage, or the need to work to support family members.

It is critical to address the primary causes of truancy and dropout. For those at risk for dropping out (e.g., those with early school failure, truancy, high-risk behaviors, poor “fit” within a school system), it will be necessary to work with the adolescent and the family to identify any primary learning disabilities, ADHD, or related conditions, to establish appropriate goals for academic achievement and define an appropriate placement. In addition, the clinician will need to assess the motivation of the adolescent and family for academic performance, their short- and long-term goals, conflicts at home or at school, relationships with peers and teachers, and medical causes of academic difficulties. This information is necessary to develop a plan to improve performance or resolve barriers to continuing involvement in school. A behavioral plan of rewards and punishments is often needed to reestablish parental control and motivate the adolescent to attend school and complete homework. The adolescent should be involved in the development of this type of plan to attempt to optimize compliance. It is critical to identify and support the academic or extracurricular strengths of an adolescent. Educational options may include work-study programs, vocational programs, independent study programs, early graduation, or adult education programs. Follow-up is essential to determine if the initial plan is working and what further steps need to be taken.

It should be kept in mind that some of the world’s most famous people had difficulties in traditional school settings, so there may be room for optimism (particularly for those who have above-average intelligence). However, the fact remains that most school dropouts have a tough road ahead of them in our present economic milieu.

**ACADEMIC PERFORMANCE PROBLEMS**

Adolescents who are having difficulty with academic performance constitute a significant group of patients seen in the outpatient setting. During middle school and high school, there is an increased need to organize materials, develop appropriate study habits, and use abstract thought processes. Therefore, it is not uncommon for academic problems to arise during these years and in fact may be the presenting issue for an office visit. In addition, there will be a number of students who have never done well in school and now that they are adolescents may have poor academic performance complicated by other health risk behaviors. An interview with a parent or guardian is crucial in uncovering academic performance problems, because the adolescent may be less concerned with a drop in grades.

Poor academic performance can be due to a wide variety of causes related to factors within the individual adolescent, the school, the family, and the community. However, it is also common to have multiple factors that coexist and thus make the evaluation and management more complex. The specific causes of poor academic performance are not always clear. For example, it is commonly believed that substance abuse and membership in a gang are likely causes of school failure. However, academic failure may actually precede some of these health risk behaviors, as students gravitate toward other youth who are also failing at school. Motivation toward academic performance is a critical factor that often requires intensive interventions.

**Defining and Identifying the Problem**

The identification of academic performance problems is a critical step in the evaluation of every adolescent (see Chapter 4 on health screening). This is particularly crucial because school performance may be an important marker of other health risk behaviors. Therefore, the adolescent's physician should inquire about grades and absences at all routine office visits.

If a potential problem is identified, it is important to clearly define the problem.

1. What is the specific problem?
   a. Has there been a drop in grades, behavior problems, inconsistent performance, emotional issues, or underachievement for the presumed level of intelligence?
   b. Who “owns” the problem?
      a. Does the adolescent have concerns about his or her progress?
      b. Are parents concerned with “average” work that may not allow for matriculation into certain colleges?
      c. Have the teachers identified particular issues that should be resolved?

It is necessary to obtain information from the patient, the family, and the school to understand the nature of the problem and to begin an evaluation.

**Causes of Poor Academic Performance**

1. **Biomedical causes**
   a. Hearing or vision problems: Such problems are unlikely to be the primary cause for an adolescent but may contribute to the overall picture.
   b. Mental impairment or low intellectual ability: Subtle forms of mental impairment may not have been picked up earlier. For example, patients with fragile X syndrome (or female carriers of this syndrome), Klinefelter syndrome, Turner syndrome, XXX chromosome syndrome (females only), tuberous sclerosis, neurofibromatosis, or the fetal alcohol syndrome may not have been formerly diagnosed. Some teenagers may not have mental “retardation,” but they may score in the borderline range of intellectual ability (an intelligent quotient [IQ] of 70–79). Youngsters with borderline intellectual ability often cannot meet the demands of a regular education curriculum and are considered slow learners. They typically need additional help, but unfortunately do not usually qualify for special education.
   c. Chronic illness: Patients with severe asthma, cystic fibrosis, diabetes mellitus, sickle cell anemia, juvenile rheumatoid arthritis, epilepsy, congenital heart diseases, or other disorders may have had insufficient absences to cause academic problems. In addition, the side effects of medications may impair cognitive function.
   d. Neurological disorders: Certain seizure disorders such as simple generalized or partial complex seizures may be subtle enough to be missed. Borderline forms of cerebral palsy may also present difficulties in early diagnosis. Rarely, progressive neurological diseases such as Wilson disease or subacute sclerosing panencephalitis may present as cognitive impairment.
   2. **ADHD**: Adolescents may not have been diagnosed as a child, whereas others may have been diagnosed but never treated. In particular, females with attention deficit disorder without hyperactivity are often not diagnosed.
   3. **Learning disabilities**: Specific learning disabilities are common (occuring in approximately 3%–5% of students) usually related to specific problems in reading, spelling, mathematics, or written expression.
   4. **Psychological and behavioral causes**: An adolescent's school performance may be affected by depression, substance abuse, anxiety disorders, conduct disorder, or physical, sexual, or emotional abuse.
   5. **Family issues**: Various family problems may affect academic performance, including parental depression, drug or alcohol abuse, and divorce; conflict within the family (parent-teen or parent-parent); or mismatches between parent-adolescent-school expectations for achievement.
   6. **School and peer relationships**: Adolescents who have poor peer relationships or interact with a peer group that does not value academic achievement may present with academic problems. The school may not be able to meet the needs of certain students (e.g., the bright and bored, those with special needs, those who learn in different ways, or those who do not value the educational experience).
   7. **Cultural or environmental factors**: Adolescents who have had a lack of opportunity to achieve adequately, received poor teaching, or had cultural or environmental disadvantages that interfere with appropriate education may also present with academic performance problems. Children from ethnic or cultural backgrounds different from that of the prevailing school norm in which English is not the primary language may also experience difficulty with a standard curriculum. The practitioner should attempt to distinguish such cultural or environmental factors from all of the other previously mentioned causes of academic performance problems.

**Evaluation**

**History** The history is the most important and often the most challenging part of the evaluation to complete. It is necessary to develop rapport with the adolescent to let him or her know that your interest is to help him achieve his educational goals, rather than to “take the side of the parents or the school.”

1. **Interview with the parents**
   a. Developmental history
• Pregnancy history (use of drugs, alcohol, medications)
• Perinatal history (prematurity, birth history, sepsis, asphyxia)
• Developmental milestones (for delays in language acquisition, communications skills, and other discrete areas)
• Speech, vision, or hearing problems

b. Medical history
• Chronic illnesses such as asthma, otitis media
• Neurological disorders such as head injuries, neurological symptoms
• Hospitalizations
• Family history of neurological or psychological disorders, ADHD or learning disabilities (a family history of resistance to thyroid hormone is strongly associated with ADHD)

c. Behavioral history
• Peer and family relationships
• Suspected drug or alcohol use
• Psychological symptoms
• Antisocial behaviors
• Symptoms of ADHD (inattention, impulsivity, restlessness)

d. School history (attempt to get similar information from the school)
• History of prior problems
• Behaviors reported in school
• Specific problems (i.e., which classes, which hours, which teachers, missing assignments, missing homework, poor test scores)
• Perceived motivation and goals
• Grades, attendance, suspensions
• Parents’ educational level and their expectations for their adolescent
• Prior attempts to improve the situation
• Prior educational or IQ testing

2. Interview with the adolescent

a. School history
• The perspective of the adolescent on the problem or lack thereof
• Assess motivation and goals
• Likes and dislikes about school
• Specific problem areas in school: This area is important to assess both motivation and for specific deficits that may be indicative of a learning disorder or ADHD. Ask about difficulties in specific classes (to screen for learning disorders in math, reading, language skills), difficulties with specific teachers unrelated to course content, capability and willingness to do homework, difficulty with tests (what kind of tests pose particular problems), overall workload, and difficulty of the assignments.
• Factors that prevent academic achievement
• Future plans for employment
• Specific strengths: This is a critical area to identify. If an adolescent has one strong area, you can often build self-esteem by encouraging development in that area while using it as a “hook” to keep the adolescent motivated to stay in school.

b. Medical and behavioral history
• Symptoms of acute or chronic illness
• Drug and alcohol use
• Peer support and influences
• Family conflicts or problems with parents
• Psychological symptoms (particularly anxiety and depression)

3. School records or telephone interviews with teachers are helpful to obtain the school’s perspective and to identify the interventions that have been attempted.

Physical Examination

1. Height, weight, and head circumference
2. General inspection

a. For nutritional status
b. For minor anomalies (e.g., short palpebral fissures, epicanthal folds, thin upper lip of fetal alcohol syndrome, clinodactyly, wide-set eyes, epicanthal folds of XXX syndrome)
3. Ears, nose, and throat: For otitis, thyroid enlargement
4. Genital: For sexual maturity rating, testicular size (large testes in fragile X syndrome, small testes in Klinefelter syndrome)
5. Neurological: Neurological examination is indicated when a neurological problem is suspected. This may include testing of cranial nerves, muscle strength and tone, gait, coordination, involuntary movements (particularly looking for tics) and reflexes, and sensory examination. Some recommend testing for “soft” neurological signs. These may include reflex asymmetry, strabismus, hyperkinesia, coordination difficulties, poor fine visual-motor coordination, confused laterality, choreiform movements, overflow and mirror movements, and extinction to double simultaneous tactile stimulation. Five percent of healthy children display one or two “soft” signs.

Testing

1. Audiometric testing
2. Visual acuity testing
3. Cognitive ability testing: General intellectual ability test such as the Wechsler Intelligence Scale for Children III for up to age 16 years and the Wechsler Adult Intelligence Scale, third edition for older than 16 years
4. Achievement testing; Woodcock-Johnson Psychoeducational Battery; Wechsler Individual Achievement Test II; Kaufman Test of Educational Achievement
5. Learning disability analysis: Compare IQ and achievement test results, looking for significant discrepancies between average IQ and below-average achievement (usually discrepancies of at least 2 standard deviations). Occasionally, further educational testing of specific reading, mathematics, writing, and language skills must be done after determining that there is a significant discrepancy.
6. Neuropsychological testing: Testing is indicated if there is either an unusual pattern of functioning on IQ or achievement tests that defy a traditional learning disability explanation or if there are indications of neurological problems.
7. ADHD screening: See next section.
8. Psychopathology screening: May ask parent or youth to complete a standardized self-report measure that broadly screens for psychopathology such as the Child Behavior Checklist (CBCL) or the Behavior Assessment System for Children monitor. T scores higher than 70 would suggest the need for a follow-up clinical interview.
9. Family problems screening: May ask the adolescent or parent to complete a self-report screening measure of family conflict such as the Conflict Behavior Questionnaire.
10. Adolescents with low or borderline IQ scores should be screened for chromosomal anomalies, such as the fragile X syndrome.

ATTENTION DEFICIT HYPERACTIVITY DISORDER

ADHD is a developmental disorder affecting approximately 5% of children and adolescents, characterized by developmentally inappropriate degrees of inattention, impulsivity, and hyperactivity. It arises in early childhood, is relatively chronic and pervasive in nature, and is not accounted for on the basis of gross neurological, sensory, language, or motor impairment, mental retardation, or severe emotional disturbance. As a result of these core symptoms, adolescents with ADHD have difficulty getting their schoolwork done, organizing their personal lives, resolving disputes, communicating with their parents, following rules established by adult authority figures, and maintaining good peer relationships. Eventually, such cumulative life failure may thwart them from accomplishing the developmental tasks of adolescence, including independence seeking, identity formation, mature same- and opposite-sex interpersonal relationships, and vocational planning. As a result, many such adolescents develop low self-esteem and depressed affect.

Contemporary follow-up studies have suggested that ADHD is truly a life span disorder; more than 80% of ADHD children continue to manifest the full clinical
syndrome in adolescence, and more than 50% continue to manifest the full clinical syndrome in adulthood. In adolescence, paying attention and controlling impulses remain the greatest problems, whereas motoric hyperactivity usually diminishes and/or transforms into mental restlessness. Those adolescents with ADHD alone (i.e., without oppositional defiant disorder or conduct disorder) may exhibit comorbid difficulties such as learning disorders, low self-esteem, depression, or other emotional problems (see below), whereas those with ADHD plus oppositional defiant disorder, conduct disorder, or bipolar disorder are more likely to develop problems with truancy, dropout, substance abuse, and severe family conflict.

Etiology

Although the exact cause of ADHD remains unknown, mounting evidence from neurochemical, brain imaging, genetic, and family studies converges to suggest that in most cases, ADHD is an inherited condition with a biochemical basis involving deficits in the availability of neurotransmitters to the frontal-orbital circuits of the neurobehavioral regulatory systems of the brain. For example, a mutation in the dopamine 2 receptor gene is found much more frequently in those with ADHD (as well as in those with Tourette syndrome, alcoholism, and posttraumatic stress disorder) than in controls. Recent brain imaging studies show differences between individuals with ADHD and controls in the structure of the basal ganglia and parts of the corpus callosum. Family genetic studies show clustering of ADHD, as well as anxiety, affective disorders, and substance use disorders. In short, ADHD is a biologically handicapping condition that cannot be “cured,” and the goal of treatment is to maximize the quality of the adolescent's daily life and facilitate completion of the developmental tasks of adolescence through flexible combinations of medical, psychosocial, and educational interventions.

Diagnostic Criteria

The Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV) includes a list of nine inattention criteria and a list of nine hyperactivity/impulsivity criteria. Subtypes of ADHD are based on various combinations of these lists (1A and 1B), together with criteria 3 through 5.

1. Either inattention (a) or hyperactivity/impulsivity (b)
   a. Inattention: At least six of the following symptoms of inattention have persisted for at least 6 months to a degree that is maladaptive and inconsistent with developmental level
      - Often fails to give close attention to details or makes careless mistakes in schoolwork, work, or other activities
      - Often has difficulty sustaining attention in tasks or play activities
      - Often does not seem to listen when spoken to directly
      - Often does not follow through on instructions and fails to finish schoolwork, chores, or duties in the workplace (not due to oppositional behavior or failure to understand instructions)
      - Often has difficulty organizing tasks and activities
      - Often avoids, dislikes, or is reluctant to engage in tasks that require sustained mental effort (such as schoolwork or homework)
      - Often loses things necessary for tasks or activities (e.g., tools, school assignments, pencils, books, tools)
      - Is often easily distracted by extraneous stimuli
      - Is often forgetful in daily activities
   b. Hyperactivity/impulsivity: At least six of the following symptoms of hyperactivity/impulsivity have persisted for at least 6 months to a degree that is maladaptive and inconsistent with developmental level
      - Hyperactivity
        - Often fidgets with hands or feet or squirms in seat
        - Often leaves seat in classroom or in other situations in which remaining seated is expected
        - Often runs about or climbs excessively in situations in which it is inappropriate (in adolescents or adults, may be limited to subjective feelings of restlessness)
        - Often has difficulty playing or engaging in leisure activities quietly
        - Is often “on the go” or often acts as if “driven by a motor”
        - Often talks excessively
      - Impulsivity
        - Often blurts out answers before questions have been completed
        - Often has difficulty awaiting turn
        - Often interrupts or intrudes on others (e.g., butts into conversations or games)

2. Some symptoms that caused impairment were present since age 6 or 7 years.

3. Some impairment from the symptoms is present in two or more settings (e.g., at school, work, and at home).

4. There must be clear evidence of clinically significant impairment in social, academic, or occupational functioning.

5. The symptoms do not occur exclusively during the course of a pervasive developmental disorder, schizophrenia, or other psychotic disorder and are not better accounted for by another mental disorder (e.g., mood disorder, anxiety disorder, dissociative disorder, or a personality disorder).

6. DSM IV subtypes
   a. 314.01. ADHD, combined type: If both criteria 1a and 1b are met for the past 6 months.
   b. 314.00. ADHD, predominantly inattentive type: If criterion 1a is met but criterion 1b is not met for the past 6 months.
   c. 314.01. ADHD, predominantly hyperactive/impulsive type: If criterion 1b is met but criterion 1a is not met for the past 6 months.
   d. 314.09. ADHD, not otherwise specified: If prominent symptoms of inattention or hyperactivity/impulsivity are present that do not meet criteria for ADHD.

The DSM-IV criteria capture the core ADHD symptoms of inattention, impulsivity, and restlessness. Practitioners should keep in mind that with adolescents, attention is a broad construct including difficulties activating or getting started with tasks, sustaining concentration, sustaining effort, remaining organized, and making transitions. In addition, it is becoming increasingly evident that impulsivity and restlessness are really parts of a single, broader dimension of impaired delayed responding or behavioral disinhibition.

Although used for purposes of standardization, there are a number of problems with the DSM-IV approach to diagnosis: (a) The DSM-IV is developmentally insensitive in that the same number of symptoms are required for a positive diagnosis at all ages; research has suggested that fewer symptoms should be required in older adolescents (five out of nine) and adults (four out of nine); (b) the DSM-IV assumes that ADHD is a categorical diagnosis, (e.g., you either have it or you don’t); research clearly indicates that inattention and behavioral inhibition are dimensional, not categorical; and adolescents may have different degrees of difficulties in these areas; the practitioner is referred to the Diagnostic and Statistical Manual for Primary Care—Child and Adolescent Version for an approach to addressing this problem; and (c) the DSM-IV Item set was developed with school-age boys in mind and does not adequately capture the phenomenology of ADHD in adolescents, particularly adolescent girls, readers interested in a detailed discussion of ADHD in middle and high school girls should consult Understanding Girls with ADHD (Nadeau et al., 1999).

Associated Features or Comorbidity

1. Oppositional defiant disorder: A pattern of negativistic, hostile, and defiant behavior lasting at least 6 months, involving loss of temper, frequent arguments with adults, refusing to comply with requests, deliberately annoying others, being angry and vindictive, and blaming others for one's mistakes (Fischer et al., 1993).

2. Conduct disorder: A repetitive pattern of antisocial behavior violating others' basic rights or societal norms, involving physical aggression, threats, use of weapons, cruelty to people or animals, destruction of property, deceitfulness and theft, repeated running away from home, frequent truancy, or sexual assault. Forty-three percent of teens with ADHD have a conduct disorder (Fischer et al., 1993). There is sometimes a progression from oppositional defiant disorder to conduct disorder, and persistent conduct disorder is termed antisocial personality disorder in adulthood.

3. Learning disabilities or academic achievement problems: A significant discrepancy between averages in above-average intellectual ability and below-average academic achievement in reading, math, spelling, handwriting, or language, thought to reflect a processing deficit. Between 19% and 26% of children with ADHD have learning disabilities in at least one area. Even though most adolescents with ADHD do not have learning disabilities, they do consistently show academic achievement problems, with scores on Standardized Achievement Tests lower than those of matched controls, and a greater likelihood of grade retentions, school dropout, or expulsions.

4. Mood and anxiety disorders: Many adolescents with ADHD are somewhat depressed because of their school and home problems. As a result, their self-esteem suffers. Twenty-five percent to 75% of referred adolescents with ADHD and 15% to 19% of community samples have one or more of the following types of mood disorders: major depressive disorder, dysthymic disorder, or bipolar disorder. Adolescents with ADHD and bipolar disorder are particularly challenging to treat. Twenty-seven percent to 30% of referred adolescents with ADHD and 7% to 26% of community samples have one or more of the following anxiety disorders:
generalized anxiety disorder, panic disorder, obsessive-compulsive disorder, social phobia, or posttraumatic stress disorder.

5. Substance abuse: Adolescents with ADHD show more cigarette and alcohol use than matched controls, with these findings accounted for primarily by the subgroup with comorbidity for conduct disorder. Marijuana is emerging as the most commonly used illicit drug among adolescents with ADHD.

6. Driving behavior: Adolescents with ADHD show less sound driving skills or habits than matched control groups, with greater likelihood of accidents, more bodily injuries associated with crashes, and more traffic citations, particularly for speeding. The subgroup with comorbid oppositional defiant disorder or conduct disorder are at the highest risk for such deficient driving skills or habits.

7. Family relations: Adolescents with ADHD and their parents display more negative, controlling interactions, fewer positive, facilitative interactions, and more conflicts than matched controls. Mothers of adolescents with ADHD report more personal psychological distress than mothers of matched controls. The adolescents themselves underestimate the degree of family conflict, compared with their mothers.

8. High-risk sexual behaviors: A recent follow-up study found that adolescents with ADHD have an earlier age at first sexual intercourse, more sexual partners, less use of birth control, more sexually transmitted diseases, a greater frequency of testing for human immunodeficiency virus, and more teen pregnancies that their non-ADHD peers (Barkley, 1988b).

Epidemiology

1. Prevalence: 5%-6% of children between ages 4 and 16 years. Using Barkley's follow-up finding that 83% met ADHD criteria in adolescence, one could estimate that 4%-5% of adolescents have ADHD.

2. Sex: Male to female ratio is 6:1 in clinic samples and 3:1 in community samples.

3. Age: The problem typically starts in early grade school, with an increased prevalence of school and home-based problems in adolescence. Because the transitions to middle and high school entail increased organizational demands, many brighter youngsters or less hyperactive youngsters with ADHD may first become educationally impaired by attention problems in adolescence, resulting in diagnosis and treatment. For 50%-60% of adolescents with ADHD, there will be residual impairments into adulthood.

Making a Diagnosis of ADHD: Clinical Guidelines

1. Inclusion criteria: Does the adolescent meet the DSM-IV inclusion criteria for ADHD? Because of performance inconsistency, information from parents, adolescents, and teachers is required to answer this question. Interview the parents and the adolescent concerning the DSM-IV criteria, and collect rating scales from them. Many physicians prefer to rely upon an in-depth clinical interview performed by an experienced psychologist.

2. Differential diagnosis: If the adolescent meets the DSM-IV inclusion criteria, can alternative syndromes that resemble ADHD be ruled out? Refer for psychopharmacology learning disability, and conduct (or refer for) a thorough interview to explore other psychiatric syndromes. Inquire about the major life stressors in the adolescent's history, and examine the temporal covariation between the ADHD symptoms and the major life stressors (e.g., if the onset of the inattentive symptoms are in temporal proximity to a major life stressor, the stressor might explain the symptoms).

3. Rating scales: It is useful to give the parents, adolescents, and teachers a copy of the DSM-IV criteria and ask them to rate the presence on a four-point Likert scale. The most recent normative data are from a large national sample of adolescents used to renorm the TRF in 1991.

4. Parents, Teachers, and Rating Scales: Composite, well-validated measures assessing attention problems, as well as a broad array of other forms of psychopathology and social competence. Easily computer scored. Look for T scores higher than 60 on attention scales. Available from The Psychological Corporation, 555 Academic Court, San Antonio, TX 78204-2498; 800-228-0752.

5. Conners' Abbreviated Parent Questionnaire revised short and long forms: Use either the 80-item long form or the 27-item short form, which come as a set. For the short form, there are five subscales: TDAH, ADHD symptoms, hyperactivity, inattention, and conduct problems. The short form displays adequate reliability and validity and includes a demographic supplement and CONners' Addendum.

6. Differential diagnosis: If the adolescent meets the DSM-IV criteria, can alternative syndromes that resemble ADHD be ruled out? Refer for psychopharmacology learning disability, and conduct (or refer for) a thorough interview to explore other psychiatric syndromes. Inquire about the major life stressors in the adolescent's history, and examine the temporal covariation between the ADHD symptoms and the major life stressors (e.g., if the onset of the inattentive symptoms are in temporal proximity to a major life stressor, the stressor might explain the symptoms).

7. Rating scales: It is useful to give the parents, adolescents, and teachers a copy of the DSM-IV criteria and ask them to rate the presence on a four-point Likert scale. The most recent normative data are from a large national sample of adolescents used to renorm the TRF in 1991.

8. Brown Attention-Activation Disorder Scale (BAADS): A 40-item self-report measure assessing attention problems, as well as a broad array of other forms of psychopathology and social competence. Easily computer scored. Look for T scores higher than 60 on attention scales. Available from The Psychological Corporation, 555 Academic Court, San Antonio, TX 78204-2498; 800-228-0752.

9. Brown Attention-Activation Disorder Scale: A 40-item self-report measure assessing five components of a broad attention-activation construct:
   - Activating and organizing to work
   - Sustaining attention and concentration
   - Managing affective interference
   - Using working memory and accessing recall

T scores give an indication of how much impairment an adolescent is reporting relative to a nonclinical population. This promising measure has been recently normed. (Available from The Psychological Corporation, 555 Academic Court, San Antonio, TX 78204-2498; 800-228-0752.)

e. Continuous performance tests (CPTs): CPTs measure attention and distractibility for research and clinical settings. Respondents are required through the use of a computer program to press a button whenever a specific letter or number appears. The tests are presented in gamelike formats and take between 10 and 30 minutes. In preliminary studies, CPTs have been shown to be specific but not particularly sensitive (i.e., positives are usually correct but up to 33% false-negatives occur). They can be a useful adjunctive measure to obtain in office settings and can be useful in monitoring drug treatment but should not be the sole methods for the diagnosis or monitoring of drugs. Two CPTs to consider are the Gordon diagnostic system (available from Cordon Systems, PO Box 746, DEWitt, NY 13214; 315-446-4845) and the Conners' CPT (available from Multi-Health Systems, 998 Niagara Falls Boulevard, North Tonawanda, NY 14120; 800-456-3003).

4. Integration from ratings and interview: Make a differential diagnosis and clearly present it to the family and the adolescent.

LEARNING DISABILITIES

Public schools define learning disabilities in accordance with the Individuals with Disabilities Education Act (IDEA), the recertified version of PL94-142. Specific learning disabilities consist of disorders in one or more of the basic psychological processes involved in understanding or in using language, spoken or written, which may include, but are not limited to, such skills as listening, thinking, speaking, reading, writing, spelling, or doing mathematical calculations.

A cybernetic or information processing model can help us understand how an individual adolescent's learning disability in reading, writing, mathematics, or language is a complex interplay of four stages of cognitive processing:

1. Input: Input disabilities include visual perception problems, auditory perception problems, and sensory integration problems.

2. Integration: Integrative disabilities involve understanding information, sequencing, abstracting, and organizing.

3. Memory: Memory difficulties may involve short- or long-term memory.

4. Output: Output disabilities may involve language or writing problems and motor disabilities.

Educators commonly summarize such information processing disabilities in terms of reading, mathematics, writing, and language disorders. They commonly take the presence of a significant discrepancy between actual achievement and expected achievement for a given adolescent's intellectual ability as evidence of a learning disability. Practically, a discrepancy of 2 standard deviations between scores on an IQ test and scores on an achievement test is often presumptive evidence of a learning disability. For example, an individual with a full-scale IQ score of 100 with a reading achievement test score of 78 would qualify (assuming these tests have a mean of 100 with a standard deviation of 10).

Reading Disorders

Reading involves (a) decoding (the act of transcribing a printed word back into speech) and (b) comprehension (the act of interpreting the message or meaning of the text). With dyslexia, the most common reading disorder, the adolescent's decoding skills are impaired, but comprehension is intact. Common clinical indicators of decoding difficulties include guessing at words, having trouble with sound-letter combinations, and making spelling errors involving mispronunciations of words. In
addition, dyslexic teens may have trouble sequencing speech into words, syllables, and phonemes, and rearranging sounds into spoken words. If decoding is intact, but comprehension is impaired, this relatively rare reading disability is called hyperlexia. The hyperlexic adolescent can read any text but not understand what has been read; they often also have oral language disabilities.

Math Disorders
The terms dyscalculia and acalculia are often applied to teenagers with impairment in the ability to do arithmetic computations or develop number and spatial concepts, resulting in math achievement far below that expected for grade and intellectual level. Such youngsters have trouble learning to use number words and facts and difficulty applying math to common life problems. One subgroup of dyscalculic adolescents also has pervasive learning disorders in reading and spelling. However, Rourke (1989) has further identified a second group with low math achievement and poor spatial skills who have average to superior reading achievement and verbal abilities. IQ testing reveals that these adolescents consistently show high verbal and low performance ability; neuropsychological testing confirms that their verbal abilities are intact, but their spatial abilities are deficient. Rourke has labeled such a pattern a “nonverbal learning disability” and extensively studied its assessment, prognosis, and treatment.

Writing Disorder
The term writing disorder refers to difficulty with spelling and other linguistic aspects of writing, such as composing and punctuating sentences and organizing cohesive paragraphs. It does not refer to difficulties with handwriting. Because writing disorders often coexist with reading disorders, dyslexic adolescents should also always be evaluated for a possible writing disorder. The adolescent with a writing disorder is capable of formulating complex thoughts but because of difficulties with spelling is unable to express them in writing at the level expected for his or her intellectual ability. Paragraphs will be poorly organized; sentences will be short with abrupt endings; and expository writing will read more like a list of answers to test questions than a fluent essay. Writing disorders become particularly debilitating in high school and college, when there are increased demands for written expression.

Management of Learning and Achievement Problems

Legal Responsibilities of the Public Schools
Children with disabilities are guaranteed a free and appropriate education by three federal laws:

1. IDEA: IDEA is the basic special education act that outlines that schools are obligated to conduct multidisciplinary evaluations for adolescents suspected of having a handicapping condition, and if the handicap is confirmed, provide special education interventions. These interventions are encoded in an Individualized Education Program written at a team meeting including the parents. This law outlines specific types of disabilities such as learning disabilities, emotional impairment, mental impairment, and other health impairments. Since 1997, the other health impairment category has been revised to cover children with both ADHD and educational handicaps. IDEA has a funding stream associated with it at the local, state, and federal levels.

2. Section 504 of the Rehabilitation of the Handicapped Law: Section 504 is a civil rights law that outlaws discrimination against handicapped individuals in federally funded programs in education and the workplace and requires schools to make reasonable accommodations to educate handicapped individuals. Any condition that interferes with a major life function such as learning may be considered such a handicap; ADHD has recently been interpreted as a handicap under Section 504. Children suspected of having a handicap must be evaluated, and if the handicap is confirmed, reasonable accommodations are typically made first in regular education. Section 504 has no funding stream associated with it.

3. Americans with Disabilities Act: This law basically extends the protections of Section 504 to college students, adults, and the private sector, and therefore may apply to older adolescents who are working.

Also specific state laws and local policies within school districts elaborate on the federal laws. Most state education departments provide free manuals to professionals and parents explaining special education procedures. Primary care physicians should become familiar with these laws, inform parents about them, and encourage parents of adolescents suspected of having handicapping conditions to make written requests for school-based evaluations and interventions. Although an exhaustive account of educational interventions is not possible in this chapter, we summarize a few of the most common accommodations helpful to adolescents with ADHD and learning disabilities.

ACCOMMODATIONS
Failure to complete or hand in assignments on time is a major deficit of ADHD and learning disabled teenagers. Accommodations for adolescents with ADHD include the following:

1. Modifying lesson presentation: This will make it easier for the inattentive youngster to remain on task and complete assignments. It often involves breaking lessons into short segments, frequently monitoring on-task behavior, redirecting the adolescent to the task if the adolescent’s attention wanders, and providing frequent positive feedback for successful task completion. When a paper is due in 1 month, for example, the teacher might construct intermediate steps to monitor the adolescent: (a) hand in a reference list, (b) hand in notes, and (c) hand in a draft in a free period.

2. Adjusting testing procedures: Adjusting testing procedures by permitting extended time to complete examinations, providing a quiet environment, or administering oral tests.

3. Organizational assistance: This may take the form of note-taking training, assignment sheets, a second set of textbooks at home, checks to make sure students have the materials they need to complete assignments, and monitoring of hand-in assignments.

4. Computers: Students with writing disorders often benefit from an early emphasis on computers, using word processors in school to complete assignments and weekend assignments.

5. Weekly home or school progress reports: Coordination of weekly home or school progress reports, with home-based incentives for positive teacher ratings, motivates task completion and cements teacher-parent communication.

Special Education
A continuum of alternative placements for students certified as learning disabled or otherwise health impaired includes resource rooms, separate schools, resource-oriented placements, and even home-bound instruction. Placement is usually in the least restrictive environment to best prepare the disabled individual to live in a society with nondisabled individuals. Instructional procedures for reading, mathematics, and writing disabilities rely heavily on contemporary cognitive and developmental psychology and emphasize selecting alternative teaching methods that help the learner bypass his or her area of disability.

MANAGEMENT OF ATTENTION DEFICIT HYPERACTIVITY DISORDER
Management of ADHD requires a comprehensive plan that includes the adolescent in the decision-making process. A treatment plan that allows the adolescent to participate in setting goals and developing strategies is more likely to succeed. Many adolescents with ADHD have had significant conflicts with their parents, and often the treatment plan includes negotiation of those conflicts to help the parents and adolescent work toward common goals. These conflicts may relate to the parents’ inability to accept the condition or their anger at the child for their own insecurities. As described earlier in this chapter, many adolescents with ADHD have comorbid conditions, which should be considered in the treatment plan.

The principles of management of ADHD include education, medication, home interventions, counseling, school interventions (see previous discussion), and advocacy.

Education
Education about ADHD should be provided for the adolescents, for the parents and family, often for the school, and even for the friends of the adolescent. A wide array of useful pamphlets, books, and videos are available from the ADD Warehouse (800-233-9273). However, it is critical to take some time to explain some of the basics in person to ensure that the teenager has a clear understanding of the condition. This begins with the process of informing the adolescent and the parents of the diagnosis. It is common for adolescents to have some resistance to this diagnosis, as it may be regarded as a "psychological problem" that makes them feel different from their peers. It is important to explain to the parents and the parents’ friends for the condition can be deflected by describing the genetic origin and neurochemical nature of the disorder, which may make ADHD seem more acceptable to the family and adolescent. The authors usually inform patients that ADHD is real, it is due to a mild chemical imbalance in the brain, it is a relatively common and inherited condition, it is not due to psychological causes.
and does not mean the patient is “crazy.” It has nothing to do with intelligence, and it is treatable.

Adolescents must know that there is hope for improved academic performance. This is important, because adolescents with ADHD often have low self-esteem due to their poor grades, frequently hearing “they could do better if they only tried,” and seeing reports of “not living up to potential.” If physicians take a small amount of time at each visit to offer some education about ADHD to the adolescent, they will find that the adolescent is more likely to accept the diagnosis and begin to understand why he or she may act in certain ways. This is the first step in the development of insight, which can play a crucial role in allowing the adolescent to consciously alter his or her behaviors. A useful analogy in explaining ADHD is that of poor eyesight. Poor eyesight is hereditary and not someone’s “fault.” It causes one to have difficulty “focusing” and therefore may cause problems in school and in overall functioning. Simple interventions, such as wearing glasses, can help one see clearly and improve academic and overall performance. ADHD is an inherited “biochemical” condition that causes difficulty in focusing and organizing. Medical and behavioral interventions can help the person function better. If adolescents understand this line of reasoning, they will have an easier time in accepting the diagnosis and therapy. In addition, they may be less likely to feel some of the stigma that may be attached to the diagnosis.

Medication

Medication (Table 81.1) should not generally be the only treatment received by the adolescent, but it is frequently the cornerstone of treatment for ADHD, because when it is successful, it appears to correct the underlying disorder in the brain. Because about three quarters of adolescents respond to medical therapy, a medication trial should be undertaken for almost all adolescents diagnosed with ADHD. Results from the large Multimodal Treatment Trial of ADHD (MTA) show that medication therapy was the single most effective intervention and intensive and closely monitored medical therapy was more effective than the usual provision of stimulant medications in the community (The MTA Cooperative Group, 1999).

Immediate-release methylphenidate (Ritalin) has been the most commonly prescribed stimulant for ADHD. However, the development and acceptance of longer acting stimulants has led to increased flexibility in providing individual patients with a medication regimen that meets their needs. Shorter acting medications have the potential for the following disadvantages: (a) need for more frequent and “during school” doses and (b) increased likelihood of “wearing off” and “rebound” symptoms, such as irritability and fatigue. It should be recognized that ADHD affects the whole fabric of an adolescent’s life including their sports performance, their relationship with friends and family, their risk for injury (from their potential inattentive or impulsive actions while bicycling, skateboarding, rollerblading, boating, or driving), and their decisions about lifestyle risks (e.g., impulsive use of drugs or alcohol). Therefore, as they mature, it makes sense to negotiate a treatment plan that considers coverage by medication throughout the day and on weekends. This is particularly important for those adolescents who experience irritability when the dose “wears off.” Therefore, most patients with ADHD in the authors’ practice are now using one of the longer acting medications, such as dextroamphetamine spanosulfe capsules (Dexedrine), combination dextroamphetamine and amphetamine (Adderall or Adderall XR), or methylphenidate in a timed-release capsule (Concerta, Metadate, or Ritalin LA). Tolerance to stimulants rarely develops after the first month or two on medication, and drug “holidays” are not usually required (with the exception of those few adolescents who show decreases in their growth velocity).

Side Effects of Stimulants

Serious side effects (and the relative contraindications to use) include the following:

1. Elevated blood pressure
2. Arrhythmias (particularly when used in association with alcohol, caffeine, or sympathomimetics such as decongestants)
3. Development of psychosis or tics

Patients who develop tics may have underlying Tourette syndrome (a comorbid feature of ADHD in 2% to 5%), and these patients should be managed in conjunction with a neurologist. When systematic observation for tics is undertaken, they are observed more frequently but usually resolve with a decrease in dosage or discontinuation of the medication.

Minor side effects of stimulants include the following:

1. Weight loss (usually mild)
2. Headaches
3. Abdominal pain
4. Dizziness
5. Dry eyes or mouth
6. Sweating
7. Irritability
8. Insomnia: Insomnia may occur if the medication is taken too late in the evening, although many patients seem to have an easier time falling asleep while taking stimulants.

When a dosage trial is undertaken, persistent symptoms of nervousness or jitteriness and feeling “paced out” or “overfocused” are indications that the dose is too high. Suppression of growth is rarely a problem in adolescents (particularly those receiving lower doses) but should be monitored. It has been shown that ultimate height is not compromised. Some patients develop symptoms of irritability and acting out when the dose of stimulant is wearing off (particularly common with short-acting stimulants). These patients should be given doses at shorter intervals or be switched to a longer acting preparation.

Abuse of stimulants, although considerably less common than abuse of alcohol, tobacco, and marijuana, has increased among adolescents in the past 5 years. Abuse of prescription stimulants has also increased and 2% to 3% of high school seniors have taken methylphenidate without a doctor’s prescription. In our experience, abuse of methylphenidate is much more common among adolescents without ADHD than those with ADHD. Adolescents who are treated with stimulants should be warned of the legal and ethical consequences of providing these agents to other adolescents.

Immediate-release Methylphenidate

Doses. Methylphenidate should be started at low doses before titrating up to the optimal dose. The dose range is usually 5 to 30 mg per dose, given at intervals of approximately 4 hours (a typical titration method is to start with 5 mg and increase by 5-mg doses at weekly intervals to 20-mg doses, checking weekly by telephone.
for positive effects and side effects). The onset of action is about 30 minutes. Doses are usually given in the morning, at lunchtime, and after school. A new preparation soon to be approved by the FDA is the d-isomer of methylphenidate and will require approximately half of the usual dose to be effective.

**Long-acting Stimulant Medications**

Longer acting stimulant medications include sustained-release methylphenidate (Ritalin-SR), dextroamphetamine suspensions (with pemoline [Cylert]), combinations of dextroamphetamine and amphetamine (Adderal and Adderall XR), and methylphenidate in a timed-release capsule (Concerta, Metadate, and Ritalin LA).

**Sustained-release Methylphenidate (Ritalin-SR)**

Sustained-release methylphenidate can be useful, because its duration of action is about 6 to 8 hours and can be given once or twice daily. However, it only comes in a 20-mg preparation and is often not as effective as the short-acting tablet. Therefore, it is not commonly used as a single agent. However, it can be helpful for patients who require lower stimulant doses or those who experience too many 'ups and downs' with the short-acting methylphenidate. A good strategy in these situations is to use both short-acting and sustained-release methylphenidate together as one would use regular and lente insulin. A common regimen for this would be sustained-release 20-mg plus 10- to 20-mg short-acting methylphenidate three times a day.

**Dextroamphetamine (Spansules)**

Dextroamphetamine is a much more effective long-acting preparation and is also tolerated quite well. It comes in 5-, 10-, and 15-mg Spansules. The duration of action is usually about 8 hours, so it is generally given before school and after school. The usual doses are 10 to 20 mg twice daily, with some patients requiring doses up to 30 mg twice daily.

**Combination Dextroamphetamine and Amphetamine (Adderal and Adderall XR)**

Adderal is another long-acting stimulant for the clinician to consider. There is good evidence of its effectiveness and it is very well tolerated. Most adolescents can be dosed before and after school, but some will require a noontime dose as well. Commonly used doses are 10 to 20 mg two or three times a day, with some patients requiring up to 30 or 40 mg per dose. A new long-acting version entitled Adderall XR is effective for 10–12 hours with a single morning dose of 10 to 30 mg. Occasionally higher doses are necessary, up to 40 to 60 mg.

**Timed-release Methylphenidate Capsule (Concerta, Metadate, Ritalin LA)**

Concerta consists of methylphenidate capsules packaged using a medication delivery system similar to that used in the long-acting medications for hypertension and diabetes mellitus. The capsule contains an outer coating of methylphenidate that is released quickly and a minute hole in the capsule that allows the active ingredient to be released at a constant rate for up to 12 hours. Preliminary studies show good efficacy in the treatment of ADHD and most patients do not need a dose during school hours. Concerta is available in 18- and 36-mg capsules, with most patients requiring 36 to 108 mg per dose.

Metadate consists of beads of methylphenidate with two different release patterns; 30% of the beads are immediately released and absorbed, while the other 70% are released slowly over 8–10 hours. Doses of 20 to 80 mg per day in the morning are usually required.

Ritalin LA consists of methylphenidate beads in a 1:1 ratio of immediate and slow release forms. Half of the dose is released immediately and the rest is released approximately four hours later to provide 8 hours of medication effect. Morning doses of 20 to 60 mg are used.

**Tricyclic Antidepressants**

Tricyclic antidepressants are generally considered second-line agents in the medical treatment of ADHD but have been shown to be effective in approximately three quarters of patients. They may be the medication of choice for patients who do not tolerate stimulants (generally each of the stimulants should be tried before making this determination), for those who have coexistent enuresis or in whom a tic disorder has developed. Imipramine (Tofranil), desipramine (Norpramil), and nortriptyline (Pamelor) have been used successfully. A trial of 4 to 6 weeks at adequate doses should be attempted (blood levels are useful to confirm this because children often metabolize tricyclic medications faster than adults), and electrocardiogram monitoring should be done initially to look for cardiac toxicity (heart rate >130 bpm, PR interval >0.20 seconds, QRS duration >0.12 seconds, QT interval >0.45 seconds). Relative contraindications include a history of cardiac arrhythmias, heart disease, syncope, or family history of sudden death. Side effects include drowsiness, dry mouth, constipation, nausea, sweating, tremor, and postural hypotension. Rarely, neurological side effects such as seizures, an acute organic brain syndrome, and hypomania can occur. The daily dose of imipramine and desipramine is approximately 3 to 5 mg/kg of body weight (and 1.5 to 2.0 mg of nortriptyline per kilogram of body weight). Toxicity is more likely to occur at the higher dose ranges.

**Other Antidepressants**

Few studies have been completed with the newer antidepressants, such as fluoxetine (Prozac), and the other serotonin reuptake inhibitors, venlafaxine (Effexor), and desvenlafaxine (Nustim). In general, these agents have not been useful for the ADHD symptoms per se but can be very effective adjunctive treatments for coexistent anxiety and/or depressive symptoms. They are generally tolerated very well and can be used in combination with the stimulants. Atomoxetine (Strattera) is a specific norepinephrine reuptake inhibitor that is expected to be approved by the FDA for treatment of ADHD. In pilot studies, it has been shown to have similar efficacy to methylphenidate and, in the future, may provide an effective non-stimulant treatment for ADHD.

**Clonidine**

Clonidine (Catapres) is a central-acting α2-agonist that has been used for ADHD but has not been shown to be effective. However, it can be useful in the evening to help with insomnia and for patients with coexistent tic disorders. Some clinicians also use clonidine to treat extreme hyperactivity and aggressiveness. Carbamazepine (Tegretol) and mirtazapine (Remeron) have also been tried for such adolescents. Clonidine comes in tablets of 0.1 mg, 0.2 mg, and 0.3 mg, as well as skin patches with similar strengths. The tablets are taken two to three times a day (or at night only for insomnia) starting with 0.05 or 0.1 mg. The patch delivers the medication for 1 week (and can be divided to deliver smaller doses). A long-acting α2-agonist, guanfacine (Tenex), can be used in place of clonidine.

**Behavioral or Psychological Interventions**

In the large MTA study mentioned earlier, a comprehensive behavioral intervention alone was compared with medication alone, a combination of behavioral intervention and medication, and standard community care (MTA Cooperative Group, 1999). Medication was generally found to be more effective in reducing ADHD symptoms than behavioral intervention, and there were few differences in effectiveness between the combined condition and medication alone on ADHD symptoms. However, when it came to other domains of functioning, such as oppositional/aggressive symptoms, internalizing symptoms, teacher-rated social skills, parent-child relations, and reading achievement, there was evidence that the combined treatment was superior to community care while medication alone was not. Although many more analyses of this study are planned, it is clear at this point that behavioral interventions, when combined with medication, add an important dimension to the treatment of ADHD symptoms. In interpreting these results, the clinician must keep in mind that the study was limited to school-age children, not adolescents. No comparable study has yet been done with adolescents.

As noted earlier, the MTA study suggests the need to include behavioral interventions to have an impact on various issues other than ADHD symptoms (such as conduct disorder, oppositional defiant disorder, poor self-esteem, family conflict, depression, anxiety disorders, and the use or abuse of alcohol and other drugs) that require attention. When the initial evaluation reveals a significant substance use disorder, the clinician should refer the adolescent for a substance abuse workup or treatment before undertaking any additional intervention. There has been concern that stimulant medications may increase the risk of substance abuse. However, recent data appear to suggest that patients receiving stimulant therapy are less likely to use drugs and alcohol (Biederman et al., 1999). Therefore, clinicians must weigh the risks and benefits of medical therapy for an individual patient. The presence of oppositional behavior, family conflict, peer relationship difficulties, depression, or anxiety is an indication to refer the family for behavioral or psychological interventions. The most common behavioral or psychological interventions include family therapy, individual therapy, and social skills training. It is often useful for families with adolescents who are newly diagnosed with ADHD to have a burst of 10 to 15 sessions of behavioral or psychological intervention, followed by less frequent checkups. If new problems surface during a follow-up checkup, another burst of therapy may be scheduled. Individual therapy is usually helpful in building self-esteem and reducing anxiety but does not reliably result in behavioral changes in the classroom or at home.

Behavioral family system therapy is the treatment of choice for the home-based problems and conflicts between teenagers with ADHD and their parents. Early in treatment, the therapist divides the family issues into two categories: (a) nonnegotiable issues (basic rules for living in a family, such as no violence, drugs, or alcohol) and (b) negotiable issues (all other independence-related conflicts that may be subject to negotiation and compromise). Strategic structural intervention techniques are used to reinforce parental authority around the nonnegotiable issues (i.e., the therapist teaches the parents how to establish and consistently follow behavioral changes in the home while the ADHD symptoms are being treated with stimulant medication).
contracts for these basic rules). External authorities such as the juvenile justice system or mental health inpatient system are used to back up parents when they no longer have the ability to exert any control over the adolescents.

In the case of issues that can be negotiated between parents and adolescents, problem-solving communication training is used to teach parents and adolescents to work out mutually acceptable compromise solutions. The therapist instructs, models, and coaches the family to learn and practice the steps of problem solving: (a) clearly define the problem in a nonaccusatory fashion; (b) brainstorm a list of alternative solutions; (c) systematically evaluate the positive or negative impacts of each solution, culminating in a mutually acceptable compromise solution; and (d) plan the details for implementing the solution. The family resolves a number of significant conflicts with the therapist present as a coach and then is given successively more complex assignments to apply problem-solving skills at home in weekly family meetings.

As the family begins to practice problem-solving skills in the sessions and at home, the therapist targets negative communication patterns, again coaching families to replace accusatory, defensive language with more productive, goal-oriented language. In a recent study, Barkley et al. (1993) compared the effectiveness of problem-solving communication training, parent contingency management, and structural family therapy for ameliorating conflict between adolescents with ADHD and their parents. They found that all three treatments proved equally effective, but only 25% to 33% of the families reported clinically significant change (compared with much higher rates in children), indicating we have a long way to go in improving such treatment programs.

As part of an overall family intervention, it is also useful to teach parents the effective use of behavior modification techniques. A manual has been written to guide the clinician in teaching parents contingency management techniques and integrating these techniques with problem-solving communication training (Barkley et al., 1999). These techniques are crucial for parents of adolescents with ADHD to help them teach their children to stay motivated to complete homework assignments and household chores. Setting up explicit rewards for appropriate activities and punishments for proscribed activities is a cornerstone of behavioral management. Clinicians can help parents with home interventions by offering advice on how to carry out simple behavioral contracts.

**SUMMARY**

In summary, clinicians can best help adolescents with ADHD and learning disabilities by encouraging them, believing that they can succeed, helping them to understand their disorder and how it affects them, mediating conflict between them and their parents, finding the optimal medication regimen (if appropriate), and helping them obtain the services they require through their school system.

**WEB SITES**

- [http://www.chadd.org/](http://www.chadd.org/) Official Web site for the support group, Children and Adults with ADHD.
- [http://www.addvance.com/](http://www.addvance.com/). Commercial Web site and magazine for girls and women with ADHD.

**For Health Professionals**


**OTHER RESOURCES**

- C.H.A.D.D. National, 489 N.W. 70th Avenue, Suite 101, Plantation, FL 33317; 954-587-3700; 800-233-4050: Information about support groups for parents of children and adults with ADHD.
- Clearinghouse on Disability Information, Office of Special Education and Rehabilitative Services, U.S. Department of Education, Room 3132, Switzer Building, 3130 C Street, S.W., Washington, DC 20202-2524; 202-205-6241. Specializes in providing responses to questions about funding, federal legislation, and federal programs that serve persons with disabilities on national, state, and local levels.
- International Dyslexia Association, 8600 LaSalle Road, Chester Building, Suite 382, Baltimore, MD 21286-2044; 410-296-0232, 800-ABCD-123.
- Learning Disabilities Association of America, 4156 Library Road, Pittsburgh, PA 15234; 412-341-1515.
- National Information Center for Children and Youth with Disabilities, P.O. Box 1492, Washington, DC 20013; 800-695-0285: Services to assist those involved in helping children including referrals and patient education.

**REFERENCES AND ADDITIONAL READINGS**


RAPE

Rape is defined as sexual intercourse involving force or the threat of force without a person's consent or as sexual intercourse involving a person incapable of giving consent due to mental illness, intoxication, and so forth. Rape is defined in the Uniform Crime Reporting Program as "carnal knowledge of a female forcibly and against her will"; therefore, data reported nationally reflect sexual assaults against women only. The act of being raped is one of the most devastating encounters a person can experience. The assault dramatically changes the victim's view of the world. The victim, more often a female, is the object of a hostile, dehumanizing attack that may have long-lasting effects on the victim's self-worth and identity. This is particularly true for the adolescent who is still dealing with the issues of separation, independence, and the development of sexual identity. Rape as a first or early sexual experience may cause confusion between sex and rape and may jeopardize future sexual adjustment. Attempted sexual assaults may be deeply traumatizing for young people as well.

Rape is a serious medical and psychological emergency. Only a physician willing to devote the time and support needed should examine the rape victim. It bears emphasizing here that the future psychological impact of the rape will likely depend more on the care and attitudes of the treatment team, police, and family than on the physical act of rape itself.

Three main categories of rape vary in relationship to the perpetrator:

1. Stranger rape: Stranger rape is the most traumatizing and most likely to be associated with other injuries, use of a weapon, or threat to life. This is the least common category, but the most highly associated with grave medical and psychological consequences.

2. Acquaintance rape: Acquaintance rape may be extremely confusing to the young woman and although less likely to be associated with serious physical injury, may be associated with a great deal of self-blame and guilt. Date rape is one category of acquaintance rape to which teenagers are most vulnerable. This is estimated to be the most common type of sexual assault, although the extent of date rape is underestimated due to the reluctance to report these incidents to law enforcement officials.

3. Statutory rape: Statutory rape is a legal category that encompasses unlawful sexual activity between a minor girl younger than age 18 years and a man older than 18 years. The sexual activity is unlawful only because of the age or status of those involved. Rape in this instance is something of a misnomer because no assault or lack of consent is implied. In most states, it is not reportable.

Legal Issues

State codes vary in requirements of physicians reporting responsibilities. In general, rape cases occurring within 72 hours in which evidence is gathered or medical treatment provided must be reported. It is important for practitioners to become familiar with local laws. Usually in cases of rape, the patient may limit his or her consent to a confidential report that includes only the victim's name, address, type of crime, and extent of injuries. The victim usually has the option to consent to the treatment provided must be reported. It is important for practitioners to become familiar with local laws. Usually in cases of rape, the patient may limit his or her consent to a confidential report that includes only the victim's name, address, type of crime, and extent of injuries. The victim usually has the option to consent to the collection of evidence, in which case a full report and specimens are released to the police.

The physician's legal responsibility is limited to examination, treatment, and reporting of the case. It is not the physician's responsibility to determine whether an assault occurred; that is a legal decision. The physician can help legal authorities most by keeping accurate and thorough medical records.

Epidemiology of Forcible Rape

1. Incidence

   a. In 1999, 64 forcible rapes per 100,000 females were reported, or a total of >89,000 forcible rapes (Federal Bureau of Investigation [FBI], 1999). This represents a 4% decline from 1998 and a 13% decline from 1990.

   b. Rates of sexual assault among females age 12 years and older peaked in 1979 at about 3 per 1,000 and have tended to drift downward since. Rates from 1996 to 1999 have not changed, hovering at 0.9 per 1,000 (U.S. Department of Justice, 2000). However, females age 16–19 years, the highest risk group for sexual assault, experienced a sexual assault rate of 12.4 per 1,000.

   c. In the 1999 Centers for Disease Control and Prevention (CDC) National Health Risk Behavior Surveillance, 12.5% of females and 5.2% of males reported that they had been forced to have sexual intercourse.

   d. In the National Adolescent Student Health Survey (American School Health Association et al., 1989), 12% of eighth and tenth graders reported that someone raped or tried to rape them outside of a school. Eighteen percent reported that during the past year, someone tried to force them to have sex against their wishes.

   e. In a new report from the U.S. Department of Justice, "Full Report of the Prevalence, Incidence and Consequences of Violence Against Women," 17.6% of surveyed women stated they had been the victim of a completed or attempted rape at some time in their lives. Notably, of those with a history of rape, 21.6% were younger than 12 years when they were first raped, 32.4% were age 12–17 years, that is 9% of women reported being a victim of sexual assault before the age of 18 years. Adolescence then is the highest-risk period of life for experiencing sexual assault. Rape is truly a "tragedy of youth."

   f. Other injuries incurred during rape: About 31% of women who are sexually assaulted incur a physical injury (aside from the rape itself). Women are most likely to incur an injury if the perpetrator threatened to harm or kill them or someone close to them, if the perpetrator used a weapon, if the perpetrator used drugs or alcohol at the time of the rape, or if they were raped by a current or former intimate partner.

   g. Gender distribution: Rape is legally defined in gender-neutral terms. However, most child and adolescent victims are girls by a factor of at least five, and most women and men who are raped are raped by men (Tjaden and Thoennes, 2000).

2. Use of medical services: About one third of women older than 18 years who had been raped reported using medical services at some time after the assault (Tjaden and Thoennes, 2000).
Relationship between victimization as a minor and subsequent victimization: In the National Violence Against Women study, 18.1% of women who reported being raped before age 18 years also reported being raped as an adult, compared with 8.7% of women who did not report being raped before age 18 years. Women who were raped as minors were twice as likely to report being raped as an adult (Tjaden and Thoennes, 2000).

Reportability: Unreported cases range from an estimated 39% to as high as 90% of all rapes in the United States. Reasons for not reporting include fear of stigmatization by family and friends, fear of being blamed, desire to protect perpetrator (if he is friend, boyfriend, or family member), and fear of retaliation by perpetrator or perpetrator's friends.

Arrests: In 1999, 49% of forcible rapes were cleared by an arrest. Juveniles younger than 18 years were involved in 12% of clearances of forcible rape nationally (FBI, 1999). In 1999, 28,820 persons were arrested for forcible rape; 44% were younger than 25 years; and 61% were categorized as white.

Convictions: Two thirds of those arrested and booked for rape are prosecuted, and 47% of those prosecuted are found guilty. Thus, for every 100 reported cases of rape, there are 16 convictions. In 1991, 13.3% of the closed rape cases involved victims younger than 18 years.

Demographic characteristics

- **Age:**
  - **Rapist:** About 40% of sexual assailants are reported to be older than 30 years; about 25% are reported to be younger than 21 years; and 35% are reported to be between age 21 and 30 years.
  - **Victim:** Fifty percent of victims are younger than 18 years. Peak age for victimization is age 16–19 years.

- **Sex:**
  - **Rapist:** Nearly 99% of single victim sexual assailants are reported to be male (Greenfeld, 1997). In the National Violence Against Women survey, of those men and women who reported a rape before the age of 18 years, 99.2% of women and 89% of men reported a male assailant. About 10% of sexual assaults were reported to involve multiple perpetrators.
  - **Victim:** Ninety-six percent of victims are female, and 4% are male.

8. **Victim-offender relations:** In about one third of cases, the rapist is unknown to the victim (U.S. Department of Justice, 2000). About two thirds of the rapists are acquaintances of the victim. Almost seven in ten rape or sexual assault victims stated the offender was an intimate, other relative, a friend, or an acquaintance. The National Violence Against Women survey found that most children and adolescents are raped by someone they know; only 14.3% of women and 19.5% of men were raped by a stranger. Forty-six percent of women and 44% of men had been raped by an acquaintance, 39% of women and 30% of men were raped by a relative other than a spouse, and 15% of women were raped by a current or former intimate partner (Tjaden and Thoennes, 2000). Victims often underreport offenses in direct relationship to the degree of acquaintance with the rapist.

9. **Geography:** The South recorded the highest portion of forcible rapes, 39%, with a rate of about 70 per 100,000 women. Next are the Midwest at 25% (68/100,000), the West at 23% (66/100,000), and the Northeast at 13% (44/100,000) (FBI, 1999). Forcible rapes are somewhat more common in metropolitan areas. Over the last 10 years, all regions have reported a decreased rate of about 20%.

10. **Location:** About 60% of sexual assaults occur at home or at the home of an acquaintance.

11. **Other risk factors:** Irwin et al. (1995) reported that young women who had been raped in an urban community had a higher prevalence of a recent sexually transmitted disease (STDs) and have other human immunodeficiency virus (HIV) risk behaviors. Rape was not independently associated with HIV syphilis or herpes simplex virus 2 (HSV-2) infections.

12. **Temporal distribution:** The incidence of reported rapes is higher during the summer months and on weekends, and about two thirds of sexual assaults occur between 6 p.m. and 6 a.m. Sexual assaults are least frequent in December (FBI, 1999).

13. **Resistance:** Zoucha-Jansen and Coyne (1993) found that forcible verbal resistance, physical resistance, and fleeing were all associated with rape avoidance, whereas nonforceful verbal resistance and no resistance were associated with being raped. Injury rates were no higher in women who used forceful resistance.

14. **Use of drugs in rape:** Increasing reports of sexual assaults in which drugs or other substances have been used to sedate the victims are of great concern. The emotional effects of substance-related rapes are compounded by the partial or complete lack of memory accompanying the experience. Many of these rapes go unreported, and many of the reported rape cases go unprosecuted due to lack of evidence or ability to help law enforcement agencies identify the rapists. As the data on the drugs used (Rohypnol, gamma-hydroxybutyrate [GHB], and others) are collected and processed, more information on the epidemiology of such rapes will become available.

### Myths and Realities

**Myth**

- Rape is a sexual act.
- Rape is a nonviolent crime.
- Rapists are easy to spot.
- Most rapes are a “spur of the moment” act, occurring in a dark alley by a stranger.
- Rape only happens to young women.
- Men cannot be raped.
- Most rapes are interracial.
- It is impossible to really rape a nonconsenting female adult.

**Fact**

- Rape is a violent assault acted out sexually. It violates a victim's sense of integrity and control.
- Rape is a violent crime. Eighty-seven percent of rapists carry a weapon or threaten violence against the victim.
- Rapists look for vulnerable, unsupervised, young females. No person asks to be hurt or degraded.
- Most rapists appear normal. Most are young and married.
- Most rapes are planned; 50% are committed by an acquaintance. Fifty-seven percent occur in the victim's or rapist's house.
- Rape occurs at all ages and in both sexes. The age range reported is 4 months to 92 years.
- Men, particularly boys and male adolescents, are also subjected to rape.
- Most rapes involve persons of the same race or culture.
- It is possible to rape a nonconsenting female adult. An erect penis can penetrate any orifice, genital, or anal opening.

### Effects of Rape

Rape is a terrifying experience, with the threat of injury or death often present. Some of the reactions of adolescent rape victims are similar to those of adult victims, but there are important differences stemming from the developmental tasks facing adolescents. The major developmental tasks of adolescents include individuation and emancipation, intimacy, identity formation, and mastery, all of which may be affected by the experience of rape. A rape often disrupts the adolescent's sense of identity and the reactions of family members may inhibit the growing need for independence and autonomy. Adolescent rape victims must deal with the realization that the events may not be under their control, a fact that may delay successful emancipation. Identity formation and emancipation, intimacy, identity formation, and mastery, all of which may be affected by the experience of rape. The National Violence Against Women survey found that most children and adolescents are raped by someone they know; only 14.3% of women and 19.5% of men were raped by a stranger. Forty-six percent of women and 44% of men had been raped by an acquaintance, 39% of women and 30% of men were raped by a relative other than a spouse, and 15% of women were raped by a current or former intimate partner (Tjaden and Thoennes, 2000). Victims often underreport offenses in direct relationship to the degree of acquaintance with the rapist.

Several stages of emotional responses, called the **rape trauma syndrome** (Burgess and Holstrom, 1974), have been observed in rape victims:

1. **Acute reaction phase:** Begins during the assault itself and may last days to weeks after the assault.
   - a. There are two typical styles of reaction:
     - **Controlled:** Calm, composed, flat affect
     - **Expressed:** Visibly upset, angry, fearful, and anxious
   - b. The victim experiences disorientation characterized by shock, terror, and disruption of behavior and self-concept.
   - c. The victim experiences multiple fears: helplessness, and loss of control.
   - d. Depression and denial are used to minimize the effects of the assault.
   - e. Feelings of shame, self-blame, guilt, and humiliation are reported.
   - f. Depression, ranging from moderate to severe, is observed.
   - g. Anger, anxiety, and irritability are often reported.
   - h. Insomnia, anorexia, and vomiting are common.

2. **Outward adjustment/avoidance phase:** Lasts days to weeks
   - a. Survivor seems to adjust to normal life often becoming excessively preoccupied with activities.
   - b. Denial and suppression of anything associated with the assault are common.
   - c. Ongoing feelings of depression
   - d. Nightmares and flashbacks of the rape, as well as ongoing fears, are recognized by the survivor.
   - e. Mistreatment of men (by female victims) and friends is common.
f. Adolescents may withdraw from their peer group.
3. Integration and resolution phase: This phase begins when the survivor recognizes that the previous avoidance phase has not worked effectively and starts to process and integrate the rape experience.
   a. The survivor deals with the effects of the rape on his or her life.
   b. Feelings are processed (anger, depression, and guilt).
   c. Survivor gradually regains a sense of safety and trust.
   d. Slow integration of rape experience into the survivor's self-image.

When victims fail to reach the integration and resolution phase, they may continue to experience long-term effects of the rape via symptoms of Posttraumatic Stress Disorder and other lingering effects of depression and anxiety. It is important to recognize that adolescent victims can only resolve the rape experience in the developmental stage they are in at the time of the rape. Progression through later developmental stages may require additional processing as the adolescent may need to incorporate the rape experience into a more advanced age-appropriate coping style.

Common feelings after the rape include the following:
1. Fear
   a. Fear of being alone
   b. Fear of crowds
   c. Fear of the rapist returning
d. Global fear
e. Fear of men (by female victims)
f. Fear of others finding out
2. Guilt
   a. Guilt for "causing" the rape
   b. Guilt for not fighting back
c. Guilt "for being stupid and getting into that situation"
3. Shame
   a. Feeling dirty
   b. Feeling judged
4. Anger
   a. Anger at the rapist
   b. Anger at oneself
5. Depression
   a. Wanting to forget
   b. Guilt "for being stupid and getting into that situation"
   c. Feeling judged
   d. Feeling dirty
   e. Slow integration of rape experience into the survivor's self-image.

STD Risk

Reynolds et al. (2000) reviewed the epidemiology of STDs in sexual assault victims.

1. Neisseria gonorrhoeae: This was one of the most common STDs reported, with a prevalence between 0% and 26.3%.
2. Chlamydia trachomatis: Prevalence has ranged from 4% to 17% of sexual assault victims tested.
3. Syphilis: Ranged from 0% to 3%
4. HIV: HIV has only been reported in sexual assault patients in two studies; this was one of the two cases was a previous infection and neither could be directly linked to the assault.
5. Trichomoniasis: Another fairly prevalent infection found in sexual assault victims (0%–19%).
6. Human papillomavirus (HPV): Prevalence in sexual assault patients range from 0.6% to 2.3%. However, determining an incident-related viral infection is difficult because of the high baseline prevalence of HPV in the population.

Special Considerations for Adolescent Victims and Their Families

Data are scarce on particular concerns of adolescent rape victims. Table 82.1 outlines concerns of 122 sexually abused adolescents and their families, as reported in a study by Mann (1981). In this study, the impact of the rape was judged as severe in 80% of parents and only 37% of the adolescents. Although most teenagers expressed concern about bodily safety, guilt, and peer relations, parents were more often concerned with retaliation, sexual aspects, and future problems. Eighty percent of the adolescents in the study experienced problems with their parents after the rape, whereas only 20% of adolescents found their parents supportive and understanding. Twenty-five percent of adolescents felt their parents overreacted; 24% found their parents overprotective; and 24% felt rejected by their parents.

<table>
<thead>
<tr>
<th>Concern</th>
<th>Victims (%)</th>
<th>Parents (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fear of safety</td>
<td>33</td>
<td>30</td>
</tr>
<tr>
<td>Self-blame</td>
<td>30</td>
<td>17</td>
</tr>
<tr>
<td>Insults</td>
<td>48</td>
<td>57</td>
</tr>
<tr>
<td>Inability to trust</td>
<td>48</td>
<td>79</td>
</tr>
<tr>
<td>Any property to revenge</td>
<td>45</td>
<td>87</td>
</tr>
<tr>
<td>Physical abuse of the victim</td>
<td>34</td>
<td>92</td>
</tr>
<tr>
<td>Fear of parental reaction</td>
<td>21</td>
<td>86</td>
</tr>
<tr>
<td>Fear of future worth</td>
<td>5</td>
<td>41</td>
</tr>
</tbody>
</table>

TABLE 82.1. Concerns of 122 sexually abused adolescents and their families

Significant differences exist in the aftermath of rape, as experienced by adolescent victims and their parents. Adolescent rape victims must incorporate their recovery with the developmental tasks ahead of them. They are often lacking the developmental perspectives guiding their parents’ reactions. Adolescents often fear the loss of previously achieved independence and autonomy. This is particularly true if the adolescent was engaged in forbidden activities when the rape occurred. Both adolescents and their parents would benefit from an integrated system of care to address these issues.

Peipert and Domagalski (1994) compared adolescent rape victims with victims older than 20 years. Adolescent victims were more likely to be assaulted by an acquaintance or relative (77% versus 56%) and to delay medical evaluation. Cunningham et al. (1994) found that a history of physical abuse, sexual abuse, or rape is related to engaging in various HIV-risk behaviors, with an increase in these behaviors between adolescence and young adulthood.

In some cultural groups, teenage girls and their parents are concerned about what a sexual assault means regarding their state of virginity. In some cultural groups, this may have tremendous significance, and the young woman may be further victimized by being viewed as “spoiled goods” and have great anxiety about her ability
to marry. It is important to state that being victimized by sexual assault does not affect the state of virginity, and that rape is a violent act, not a sexual one.

Special Considerations for Mentally Retarded Victims

Furey (1994) examined sexual abuse in the mentally retarded population. Most of the victims were women (72%) who mostly had no problems communicating verbally and few secondary disabilities. Most of the perpetrators were men (88%) and included other individuals with mental retardation, paid staff, family members, and others. Most sexual abuse occurred in the victim’s residence, and in 92%, the victim knew the abuser.

Special Considerations for Male Victims

Male adolescents who have been sexually abused are probably the least reported and least studied group of abused victims. Most studies are weighted toward younger children or females. However, as reported by Deisher and Bidwell (1987), male sexual abuse is not uncommon and is significantly underreported. Males may be embarrassed by the homosexual aspect of an assault and by disclosure of such details. In addition, practitioners may fail to recognize and pursue this possibility because of their lack of awareness of this problem. In the 2000 National College Health Assessment, 12.4% of females and 5.2% of males described being touched against their will in the past year, whereas 6.7% of females and 2.4% of males reported either an attempted or a completed rape in the past year.

There are no precise epidemiological data regarding male sexual assault victims. A November 2000 study by the National Institute of Justice (NIJ) and the CDC found that 9% of women and 1.9% of men stated they were raped before age 18 years; about half of men who reported ever being raped were raped for the first time before age 12 years, about 23% were raped between the ages of 12 and 17 years. About 0.1% of men surveyed indicated that they had been raped in the previous 12 months. Extrapolating these findings, about 93,000 men are raped annually in the United States (Tjaden and Thoennes, 2000). In the 1999 CDC youth risk behavioral survey (2000), 5.2% of male 10th- to 12th-grade students indicated that they had been forced to have sexual intercourse. Finkelhor (1984) estimated that there is about one abused male for every two abused females. In large studies of sexual abuse, male victims have composed 8% to 14% of the total abused individuals. Spencer and Dunklee (1986) evaluated boys in the San Diego program and found that they composed 11% of abused children. In this study, 86% of the males had physical evidence of abuse. Fifty-three percent gave a history of anal penetration, 46% of fellatio, and 26% a history of the perpetrator ejaculating. Five percent had an STD. Another study of male victims by Anderson et al. (1981) reported the following types of abuse: 33% fondling, 42% orogenital contact, 31% anal-penile contact, 14% forced masturbation, and 4% other.

The offenders are usually known to the male victim, and 98% of the time, the perpetrators are male. In one study, 21% of the perpetrators were parental figures, 31% were acquaintances, 22% were others known to the victim, and 22% were strangers (Anderson et al., 1981). Most of the abuse occurred as a result of coercion by the perpetrators through their role as authority figures. Force was used in 8% of the cases if the perpetrator was a family member and in 28% of cases if the perpetrator was a nonfamily member. In an NIH-CDC study, about 20% of males reporting a sexual assault reported being raped by a stranger, 30% by a relative, and 44% by an acquaintance.

Two patterns of sexual abuse have been noted in males:

1. Abuse that is continuous in nature, beginning early in childhood and persisting into adolescence or stopping before adolescence, with acting-out behavior noted during adolescence.
2. Episodic abuse beginning in adolescence: This type is less frequently seen in family settings and often begins after a youth has run away from home. Adolescents are often reluctant to report such behavior.

Male adolescents who have been abused are often recognized in one of four settings: the criminal justice system, the mental health system, emergency medical care settings, and in retrospective studies of middle-class college populations. However, abused male adolescents can also be diagnosed in the course of providing outpatient services if the practitioner is able to recognize the subgroups that are at particular risk for abuse and the signs of abuse.

Subgroups

1. Street youth: Boyer (1986) reported that 75% of female adolescent prostitutes and 63% of male adolescent prostitutes had been sexually abused.
2. Homosexual male adolescents: Many homosexual male adolescents are often forced out of their homes at an early age when their orientation becomes known or are subjected to stigma associated with homosexuality subverting their self-esteem. This may result in damaging and abusive lifestyles and relationships.
3. Youth with a parental history of physical or sexual abuse.

Struckman-Johnson and Struckman-Johnson (1994) reported on forced sexual contact since the age of 16 years among a predominantly heterosexual group of college students. They found that 34% reported coercive sexual contact—24% from women, 4% from men, and 6% from both. In 12%, the sexual contact was forced through physical restraint, physical intimidation, threat of harm, or harm. In 77% of the incidents, that contact was initiated by an acquaintance.

Possible signs of abuse are discussed later in this chapter.

Medical Evaluation and Treatment

1. Timing and Location: The examination for a rape within the last 72 hours should only be undertaken when appropriate collection materials for a forensic examination, a "rape kit," are available. The patient may require to be transferred to a local emergency medical department, preferably one with a Rape Crisis Center. In the event that the young person declines transfer to an appropriate site for forensic examination, a speculum examination should not be undertaken before 72 hours have passed to allow the victim to change her mind and allow a forensic examination. A speculum examination will call into question the accuracy of evidence that may later be collected. The examination is best conducted by a physician comfortable with adolescents. STD prophylactic treatment and emergency contraception may be provided without a speculum examination if required.
2. Obtain details of the assault, other recent sexual experiences, and a history of previous STDs.
3. Perform a complete physical examination with attention to bruises, scars, and abrasions.
4. Perform a thorough examination of genitals, perineum, anus, rectum, and pharynx, explaining rationale for each step.
5. Take photographs of any area of trauma.
6. Obtain Venereal Disease Research Laboratory (VDRL) tests and cultures for gonorrhea and Chlamydia at all appropriate sites. Do not use nonculture techniques for Chlamydia or gonorrhea, because they have inadequate specificity for forensic use. Discuss possible testing for HIV, including appropriate pretest counseling. VDRL tests should be repeated after 1 month.
7. Other legally mandated tests for evidence collection may include foreign hair collection, clothing, blood from victim for typing, filter-paper disk with saliva from victim, and swabs from perianal, anal verge, and rectal canal for presence of acid phosphatase. Appropriate specimens for DNA testing should be obtained. The "chain of evidence" must be maintained when collecting forensic specimens by strictly following rape kit protocols or evidence will not be of value in criminal prosecution.
8. Treat acute injuries and administer tetanus, and STD prophylaxis—particularly for chlamydia and gonorrhea—should be administered. Emergency contraception should be provided if appropriate. Evidence of trauma has been found in about 20%–37% of adolescent male victims. In victims of long-term abuse, the trauma may be less obvious.
9. Provide information sheet or manual: The availability of a survivor manual or booklet is helpful to victims. The Los Angeles County Survivor Manual has a special section for male victims (Fig. 82.1).
10. Provide counseling follow-up.

Management of Rape Victim

General Approach The following are important considerations for the practitioner to keep in mind:

1. Need of privacy: The medical history should be taken and the examination performed in a quiet private area of the facility.
2. Need of an experienced practitioner: The interview and examination should preferably be conducted by a physician experienced in caring for rape victims.
3. Presence of a companion: A sympathetic friend or family member should be allowed to stay with the victim if he or she so desires. A companion can be extremely important to help the young person negotiate through interactions with the police and judicial system. If a friend or family member is not available, many communities have support agencies that can provide a trained person.
4. Need of emotional support: Crisis intervention begins when the rape victim enters the health facility. The treating physician should do the following:
   a. Endeavor to consider possible preexisting emotional problems in the victim.
   b. Allow the victim time to express his or her feelings.
   c. Urge the victim to get immediate emotional support through rape crisis centers, rape hotlines, and psychosocial follow-up. In addition, when possible, a friend or family member should accompany the victim home.
   d. Discuss with the victim the possibility of nightmares, psychosexual disturbances, or depression. The victim should understand that such problems are "normal" and natural and that help is available. It is also important to eradicate myths the teenager may have about rape.
5. Reporting: After taking the history, the practitioner should inform the victim that rape is a reportable crime by law (true in most areas; the practitioner should check local laws). The victim usually has the right to consent to examination and treatment without collection of evidence. It is recommended that the victim be encouraged to allow collection of legal evidence; this is mandatory if legal charges are contemplated.
6. Police: The police department should not be present in the examination room.
7. Issue of control: It is important for the physician to help the victim regain a sense of control over his or her body by encouraging the victim to make as many decisions during the examination as possible. During the examination, it is crucial that the victim be told that he or she is in control of what will be done. The victim has the right to refuse examination or treatment and can stop the examination at any time.

History The history should include the following:

1. Length of time between alleged assault and the examination
2. The manner of the alleged assault: Inquire whether the perpetrator used a condom; inquire about injuries sustained at the time of attack.
3. Date of last menses
4. Use of oral contraceptive or intrauterine device
5. Date and time of last voluntary coitus
6. Any significant actions after alleged assault, such as showering or douching.
7. Parity.

Examples of medical report forms for suspected sexual assault and suspected child sexual abuse are included as Fig. 82.2 and Fig. 82.3, respectively.

FIG. 82.1. "I am a male survivor" information sheet for male victims of sexual assault. (From Survivor. Los Angeles Commission on Assaults against Women, 543 North Fairfax Avenue, Los Angeles, CA 90036; 1985, with permission.)

FIG. 82.2. Example of medical form for suspected sexual assault. (From State of California, Office of Criminal Justice Planning, with permission.)

FIG. 82.3. Example of medical report form for suspected child sexual abuse. (From State of California, Office of Criminal Justice Planning, with permission.)

Examination

1. Recommended techniques for the examining physician
   a. Explain in detail what you will be doing and why; obtain consent for the examination.
b. Reassure the adolescent victim that he or she will be in control.
c. Keep personal contact with the adolescent, both through verbal and eye contact.
d. For the internal examination of a female, use a warmed speculum, without lubrication.
e. Proceed slowly, allowing the victim to relax.
f. During the examination, remark on the normal findings, so the victim can feel that he or she is still normal.

2. Physical findings
a. General appearance, emotional state, and behavior should be recorded.
b. Condition of patient's clothing should be observed and mentioned.
c. All areas of the body should be explored for signs of trauma. Look closely at the neck and upper arms, where bruises resulting from forced restraint are apt to appear.
d. Check for abdominal crepitus; this may signify vaginal or rectal laceration with intraabdominal bleeding.
e. Notice and record any areas of the body containing foreign material. Keep all such material for evidence. Do not write "no evidence of rape"; this can eliminate a case from court. Instead, if there is no evidence of trauma, write "no evidence of trauma."

3. Pelvic examination: Only after a thorough examination of the entire body is performed should the pelvic or rectal examination be performed. A primary responsibility of the physician is to avoid further trauma to the patient in performing this part of the examination. Be sure to ask the victim if he or she has ever had a pelvic or rectal examination.

a. External genitalia: Note and record signs of blood secretions and sites of hematoma, abrasions, and lacerations. Application of toluidine blue will make local injuries more apparent. In females, note the state of the hymen. In cases of prepubertal sexual trauma, a normal general and external genital examination excludes internal injuries, and a vaginal examination is not required. However, if there is pain, bleeding, a history of vaginal or rectal penetration, or sign of injury, internal, pelvic, and rectal examinations must be performed. General anesthesia may be required, particularly in the prepubertal female.

b. Vaginal and rectal examination: The examination should be performed with water-lubricated instruments. In females, note any injury to the vagina and cervix. In prepubertal females, digital or speculum examinations are rarely indicated unless there is active bleeding, in which case general anesthesia should be considered.

Collection of Specimens

The following list of specimens should be collected and properly labeled, including contents, site of collection, patient's name, physician's name, and the date. All specimens should be placed in separate sealed containers such as envelopes, culture tubes, or blood specimen tubes.

Other than photographs of areas of acute or chronic trauma, the following collections are for cases in which the adolescent has been sexually assaulted in the past 72 hours.

1. Clothing: The patient's clothing should be wrapped and handled as little as possible. Each article of clothing should be wrapped separately, if possible.

2. Debris: Any foreign matter, dried stains, vegetation, dirt, gravel, or loose hair should be placed in a labeled specimen container. To minimize loss, debris should be placed into a sheet of paper, which is then folded. The folded sheet is then placed in an evidence envelope.

3. Pubic combings
   a. Place clean paper under the patient's buttocks.
   b. Comb pubic hair toward paper to collect loose hairs.
   c. Fold paper and place inside a labeled envelope.

4. Dried secretions: Collect swabs of dried secretions on body.
   a. Slightly moisten a swap with distilled water.
   b. Swab each dried secretion with a separate swap (e.g., dried blood, dried semen, or bite mark).
   c. Smear the specimen onto a microscopic slide. Let it air-dry; initial and date the slide; and place slide into a slide holder.
   d. Insert swab into a tube and discard cap to allow the swab to air-dry. Tape the swab to the tube.
   e. Clearly label each swab and slide.

5. Collection from vagina and, if indicated, rectum and pharynx
   a. Swab site with nylon swab.
   b. Smear onto two slides: Air-dry one slide for blood typing. Examine the other slide for sperm presence and motility and then air-dry.
   c. Place slides in slide holder and initial and date the slides.
   d. Insert swab into a tube and discard cap to allow swab to air-dry. Tape swab to tube.
   e. Vaginal aspirate: Use 3 mL of sterile water for a vaginal lavage. Aspirate vagina and place contents into a test tube. Secure cap and initial test tube.
   f. Place all swabs, slides, and aspirate in collection envelope.

6. Control samples
   a. Blood: Use one purple-topped tube (serves as a control in blood typing) and one gray-topped tube (if drugs were suspected to be involved).
   b. Saliva: Collect on a piece of clean gauze or let patient spit on filter paper. Let dry in labeled envelope.
   c. Hair: Pubic, scalp hair, and hair from one or two other sites should be pulled or cut and placed in separate labeled containers.

7. With patient's permission, have photographs taken of any areas of trauma.

8. Reasons for slides, swabs, and aspirates: All these specimens are used to examine for presence of motile or nonmotile sperm. Slides are examined first by the criminology laboratory, then swabs, and then aspirates. Besides examining the slides and aspirate for the presence of motile or nonmotile sperm, an acid phosphatase test is performed on the swabs.

9. Chain of evidence: As findings are of importance in criminal prosecution, strict adherence to rape kit protocols is essential.

Laboratory Tests

1. Cultures: Gonococcal cultures should be obtained from the endocervix, rectum, and pharynx, as appropriate, whereas chlamydial cultures should be obtained from the endocervix and rectum. Do not use nonculture techniques of detection, because they have inadequate specificity for criminal prosecution. Amplified DNA techniques can be used as adjunct tests, but because of traditional court reliance on culture results, these should still be obtained as evidence.

2. Gram stain of any genital or anal discharge should be obtained.

3. Wet mount of vaginal secretions of female victim should be prepared and examined for evidence of Trichomonas or cervicitis.

4. Hepatitis B surface antigen and antibody in male victims should be checked.

5. A syphilis serological examination should be obtained as a baseline test and should be repeated within 6–8 weeks.

6. A purple-topped tube should be used for control blood typing.

7. A urine or serum pregnancy test should be performed.

8. A complete blood cell count and urinalysis are recommended by some authorities.

9. Other serological testing: The practitioner may wish to discuss HIV and hepatitis B testing at this time or at a later date. This should be fully discussed with the victim.

10. An extra urine sample should be collected for possible future testing.

Ferri and Sandercock (1998) review the sensitivity of forensic tests in rape cases.

Therapy

1. Trauma: Treatment for significant trauma should precede collection of medicolegal information.

2. Tetanus toxoid is indicated for severe or penetrating trauma.

3. STD prophylaxis: Recommended to use empirically. Ceftriaxone (250 mg intramuscularly) or cefixime (400 mg orally) or ofloxacin (400 mg orally) (if older than 18 years) PLUS azithromycin (1 g orally single dose) or doxycycline (100 mg orally twice a day for 7 days).

4. HIV postexposure prophylaxis (PEP). Another consideration in rape victims is HIV postexposure prophylaxis (PEP). See Chapter 32 for more information and Web sites on PEP. PEP is probably best reserved for individuals at higher risk, i.e., those who had penetration by an assailant known to be HIV positive or at high risk for HIV infection (men who have sex with men, injection drug users). It is difficult to discuss PEP issues in the acutely traumatized victim. In a study in Canada, followthrough with PEP was very low except in high-risk exposure cases (Wiebe et al., 2000). Bamberger et al. (1999) also review PEP in sexual assault victims.

5. Prevention of pregnancy: The risk of pregnancy after a rape is approximately 1.5%–4% (10% if on the day of ovulation). If the adolescent does not have an intrauterine device or is not taking oral contraceptives, pregnancy prophylaxis should be discussed. Plan B has a very low incidence of nausea or other
problems associated with it and would be a first choice. As an alternative, ethynylestradiol (Preven) (50 µg) and levonorgestrel (0.25 mg; two tabs every 12 hours for two doses) may be offered with a mild antiemetic such as diphenhydramine. Ovral (50 µg ethynylestradiol, 0.5 mg norgestrel, two tablets every 12 hours for two doses), Lo Ovral (four tablets every 12 hours for two doses) or others as noted in the section on postcoital contraception could also be used. Benadryl (25 mg) may be given 20 minutes before ingesting estrogen-containing tablets for expected nausea. These have a 0%–1.6% failure rate; a second pregnancy test should be performed if menses does not occur in 30 days.

6. Sleep aids: These should be prescribed if indicated but should be given in small quantities.

7. Psychological supports: The adolescent should be provided with psychological support, including the telephone numbers of rape hotlines or crisis centers. A follow-up appointment should also be scheduled with a physician or counselor. As stated earlier, the victim should be released to a caring friend or family member. In many cities, rape crisis centers will send a supportive individual to the emergency department if notified.

8. Medical follow-up: An appointment with a physician should be scheduled as indicated or 14–21 days after the alleged assault. A third visit may be scheduled at 6–12 weeks to repeat initial serological studies, including tests for syphilis, hepatitis B, or HIV.

9. Written materials: Written materials regarding the rape experience should be given to the victim before leaving the hospital. A sample patient information sheet appears in Fig. 82.4. Preferably, a booklet such as Survivor by the Los Angeles Commission on Assaults Against Women (available at www.lacaw.org/home.html) can be given to the victim. This publication discusses victims’ rights, the rape experience, reporting rape, feelings about rape, and special reactions (the teenage victim, male victim, and the disabled victim). (Survivor is also available from Los Angeles City Attorney, Victim-Witness Assistance Program, 605 West Olympic Boulevard, Los Angeles, CA 90012; 213-955-9090.) Most states and urban centers have resources and organizations dedicated to providing support for sexual assault victims.

FIG. 82.4. Sample rape information sheet for patients.

Other resources of information include the following: Kempe Children’s Center (formerly known as the C. Henry Kempe National Center for Prevention and Treatment of Child Abuse and Neglect) 1825 Marion Street, Denver, CO 80218; 303-864-5252, fax 303-864-5302 Childhelp USA’s National Child Abuse Hotline PO Box 630, Hollywood, CA 90028 15757 North 78th Street, Scottsdale, AZ 85260; 800-4-A-CHILD National Center for Missing and Exploited Children 699 Prince Street, Alexandria, VA 22314; 800-843-5678 National Coalition Against Sexual Assault 125 N. Enola Drive, Enola, PA 17025; 717-728-9764 National Committee for Prevention of Child Abuse 332 South Michigan Avenue, suite 1600, Chicago, IL 60604; 312-663-3520, fax 312-939-8962

10. Areas to explore with the adolescent during the initial examination and follow-up
   a. Feelings during the assault
   b. Feelings and worries regarding the rape, medical examination, and the legal process
   c. Concerns regarding physical health, emotional reactions, sexuality, and unusual behaviors
   d. Feelings regarding the perpetrator, family, peers, school, and job
   e. Willingness to receive crisis intervention services (from professionals, paraprofessional, peers, religious, and other possible resources)

Prevention

Prevention programs that are emerging today aim at challenging widely held attitudes and behaviors that tend to justify rape. These programs are comprehensive, long term, and interactive and contain positive messages about relationships:

1. Address cultural beliefs about power, sexuality, and violence
2. Promote healthy relationship skills, such as helping
   a. Youth distinguish between appropriate and inappropriate interpersonal behavior
   b. Boys and men learn alternative, nonviolent ways to express masculinity
   c. Girls and women to assert themselves and their needs
3. Show boys and girls how to
   a. Support victims
   b. Respond to sexually aggressive behaviors when others display it to a third party in their presence
   c. Stress that boys and men, not girls and women, are primarily responsible for preventing sexual assault
   d. Stress that boys and men, as well as girls and women, can be victims of sexual assault

SEXUAL ABUSE AND INCEST

Although rape is a prevalent form of sexual abuse in all ages, incest is becoming increasingly recognized as a common form of sexual abuse in children and teenagers. Finkelhor (1984) defined sexual abuse as sexual contact with a child that occurs as a result of an exploitative behavior because of the existence of an age difference or a caregiving responsibility. Incest is defined as sexual intercourse between closely related persons: parent-child, siblings, or other blood relatives. It is the most hidden form of child abuse. Intrafamilial sexual abuse means sexual activity among persons in a family setting. Incest and intrafamilial sexual abuse is increasing when the adolescent realizes that these are not common occurrences and is able to seek help outside the family. Adolescents are more likely to be abused, either sexually, physically, or emotionally, than any other age group. Physicians can play an important role in detecting abuse and facilitating intervention. Sexual abuse in families regardless of how trivial the initial activity is tends to escalate over time and frequently becomes a chronic sexual exploitation of the child, who is unable to avoid the contact. Sexual abuse ranges from overt intercourse to oral genital contact to fondling to voyeurism.

Epidemiology

1. Prevalence or incidence
   a. The annual incidence of sexual abuse or incest in children and teenagers has been estimated at between 200 and 5,000 cases per 1 million population (Carper, 1979).
   b. Studies of prevalence of sexual abuse among children and teens are generally retrospective and have given variable results. Variables include the definition of sexual abuse, the population studied, and the response rate to the surveys. Results indicate that 2%–27% of women report at least one episode of unwanted sexualized touching. The ages at peak vulnerability were 1–13 years (Finkelhor, 1994). However, sexual abuse frequently does not come to attention outside of the family until the child enters adolescence.
   c. Although most offenders identified by Child Protective Services (CPS) are family members, CPS is frequently not notified when nonfamily members are
involved. Retrospective surveys of adults indicate that family members are involved in one third to one half of cases. When family members are involved, the most common offender is a stepfather or paramour of the mother. About one third of perpetrators are reportedly younger than 18 years (Finkelhor, 1994).

d. Sexual abuse rates appear to be fairly similar between ethnic groups and income levels.

2. Demographics

a. Twenty-eight percent of child abuse victims are between the ages of 12 and 17 years.

b. About 10%–30% of offenders are strangers, and about one third to one half are family members.

c. Sexual abuse may be a single event or repeated over years. Intrafamilial sexual abuse tends to become chronic and continue until interrupted.

d. Ninety-five percent of offenders are male.

e. The sexual abuse usually takes one of three forms (Lourie, 1977)

   • Abuse that is a continuation from childhood.

   • Abuse that continues from childhood but is manifested in a new or more severe form.

   • Abuse with threats or force is used and the child is unable to reveal what is happening.

f. Abuse form: Twenty percent to 35% involve oral or anal penetration. Fifty-eight percent of males were sodomized, compared with 13% of females.

g. Risk profile: Factors influencing outcome include the preexisting relationships of the child, the situation that evolves after the abuse is disclosed, the response or consistency and presence of a trusted parental figure, the relationship to the abuser, the developmental stage of the victim, and the nature and chronology of the abusive activity. Contemporary patterns of divorce, remarriage, and cohabitation bring many children and young people in contact with multiple adults with whom they may share no emotional bond. This may contribute to the increasing prevalence of sexual abuse. Parental alcoholism and substance abuse may also contribute to the evolution of an environment in which young people may be sexually victimized.

h. Barriers to disclosure include expected to be blamed (29%), embarrassment (25%), not wanting to upset anyone (24%), expected disbelief (23%), not bothered by abuse or denial (18%), wish to protect the abuser (14%), fear of abuser (11%), and wanting to obey adults (3%) (Anderson et al., 1993).

Dynamics

Finkelhor and Browne (1985) identified four trauma-causing dynamics in victims of sexual abuse:

1. Traumatic sexualization in a developmentally inappropriate and interpersonally dysfunctional fashion

2. Betrayal

3. Disempowerment, particularly when threats or force are used and the child or adolescent is unable to reveal what is happening

4. Stigmatizations when negative messages surrounding the abusive acts are internalized by the abused individual

Summit (1982) identified characteristics of families with incest in the child sexual abuse accommodation syndrome:

1. Secrecy: Children or teenagers rarely tell anyone, particularly when first molested; the victim typically feels too guilty or ashamed.

2. Helplessness: The victim feels obligated to and overpowered by the inherent authority. Threats are often used by the incestuous relative to keep the victim from discussing the abuse.

3. Entrapment and accommodation: The process of helplessness leads the victim to exaggerate his or her responsibility for the act. Self-esteem is lowered, and the victim takes on the responsibility for the act, as well as that of holding the family together.

4. Delayed, conflicting, and unconvincing disclosure: Most sexual abuse is never disclosed (Finkelhor, 1979). During adolescence, if disclosure occurs, it is often during a conflict or fight and is often dismissed by the family and others as an act of vengeance by the victim. Teenagers will often act out, turning to drugs, promiscuity, runaway behavior, self-injurious behaviors, or suicide as a way of coping.

5. Retraction of complaint: Often the victim will retract his or her story because of guilt or ambivalent feelings or fear of the consequences of disclosure (family breakup, possible foster placement).

Legal Issues

All physicians and medical providers are mandated reporters of sexual abuse of minors. Every state has mandatory reporting of a reasonable suspicion child abuse, including sexual abuse, to a designated authority. The abuse does not need to be proven before being reported. In the role of mandated reporters, professionals are afforded legal immunity for such reports. Failure to report can result in most cases in a civil or criminal penalty.

One area of potential confusion is the issue of consenting sexual contact between two minors or one minor and an adult. The practitioner should consult with local legal and medical authorities regarding laws for a particular state. However, every practitioner should consider the following in making a decision:

1. How young is the adolescent? Adolescents who are sexually active younger than 14 years have a significant risk for a history of current or prior sexual abuse. This history should be explored even if the current relationship is consensual and nonabusive.

2. What is the age difference between the minor and the adult? Sexual activity between a 12-year-old and a 25-year-old is much different than that between a 17-year-old and a 19-year-old.

3. Does the sexual activity of the younger teen reflect inadequate parental monitoring and supervision?

4. What is the nature of the relationship between the two individuals? Is force or the threat of force being used?

5. In cases of young people who have a history of familial sexual abuse but are older than 18 years, are younger siblings still at home and in jeopardy?

A second area of concern is the potential breaking of confidentiality when abuse is reported in cases when the teen or family does not wish the incident reported. Society has determined that the public’s right to protect the victim supersedes a patient’s right of privacy. This leads to greater reporting of abused individuals, but less physician-patient confidentiality.

Policy Issues

Sexual assault remains a major social and public health problem; female adolescents are the most common victims. Injury and even death is associated with threats made before and during sexual assaults and must be taken seriously. The U.S. Supreme Court has ruled in Davis vs. Monroe County Board of Education that school boards may be liable for damages if they fail to act on known harassment that is severe, pervasive, and objectively offensive. This creates an opportunity for schools and communities to expand their capacity to effectively reduce sexual violence against youth.

Diagnosis

The diagnosis of sexual or physical abuse should be considered in an adolescent in the following situations:

1. STD (including gonorrhea, syphilis, herpes, Trichomonas, and condylomata) in a prepubertal adolescent or any adolescent with no history of sexual intercourse.

2. Recurrent somatic complaints, particularly involving the gastrointestinal, genitourinary, or pelvic areas.

3. Behavior indicators

   a. Significant change in mood, onset of withdrawal from usual family, school, and social activities

   b. Running away from home

   c. Suicidal and self-injurious gestures

   d. Rapid escalation of alcohol and/or drug abuse

   e. Onset of promiscuous sexual activity

   f. Early adolescent pregnancy

   g. Onset of sexual activity before age 13 years

   h. Sexualized play in the prepubescent child

As listed in Chapter 3, the HEADSS inventory is a helpful device to collect important psychosocial information regarding adolescents. In our experience at Children’s Hospital Los Angeles, adolescents who experience a significant problem in one of these areas are at risk for having a history of current or past abuse. In any teen with a problem in one of these areas, it is important to explore the possibility of abuse. The physician must make the adolescent aware that if abuse is disclosed, the professional is legally obligated to report this to a child protective agency. To introduce the terms of the concept of limited confidentiality, the physician may say
“Generally, what you say in here stays in here, but there are some exceptions. Namely, if you tell me that you want to hurt yourself or someone else, or that you were sexually or physically abused, I may need to inform your parents, the appropriate agencies, or both.” The practitioner can ask for such information with a question such as “We have seen many teens your age who have been touched in an area or at a time when they did not want to be. Has this ever happened to you?” Or “Some of the teens with whom I have worked who have tried to hurt themselves (or whatever the problem behavior is) have told me that they have been touched in an area where they did not want to be or have been beaten by a relative or parent. Has this ever happened to you?”

Evaluation
Evaluation of the sexually abused adolescent is similar to that described earlier in this chapter for the management of the rape victim. However, evidence collection such as swabs for semen analysis and collection of clothing and debris would only be performed if sexual contact had occurred in the past 72 hours. In the prepubertal adolescent, an internal pelvic examination should not be performed unless indicated by the presence of a foreign body or by trauma, in which case general anesthesia may be indicated.

WEB SITES
http://www.ndacan.cornell.edu/ National Data Archive on Child Abuse and Neglect.
http://www.atsa.com/ Association for the treatment of Sexual Abusers.
http://www.youthlaw.org/ National Center for Youth Law.
http://www.lacasaw.org/home.html Los Angeles Commission on Assaults Against Women.

REFERENCES AND ADDITIONAL READINGS
Dunn SF, Gilchrist VJ. Sexual assault. Prim Care 1993;20:359.


The prevalence of chronic conditions in adolescents has increased dramatically over the past 50 years, particularly in the last two decades of the 20th century, as more children with conditions such as congenital heart disease, cystic fibrosis, and even congenital human immunodeficiency virus infection (HIV), survive into their teens and beyond (Table 83.1). Despite the availability of excellent biomedical treatment for most common chronic diseases, optimal management of illness in adolescents is not limited to biomedical prescription alone. Developmental, psychosocial, and family factors all feature prominently in the ongoing care of adolescents with chronic diseases. Chronic conditions, by definition, have no cure and therefore must be endured and managed on a daily basis. Having such a condition is a continuing source of stress for the adolescent and his or her family and can contribute to maladaptive coping and dysfunction. On the other hand, the experience of successfully managing a chronic illness also may foster accelerated maturation and enormous strength in adolescents and their families. Helping adolescents manage the chronic illness well and reach their full developmental potential can be very rewarding for the clinician.

**Table 83.1. Prevalence of selected chronic conditions in adolescents age 10–17 years**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma</td>
<td>11.5%</td>
</tr>
<tr>
<td>Allergy</td>
<td>10.9%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>10.8%</td>
</tr>
<tr>
<td>Arrhythmia</td>
<td>9.4%</td>
</tr>
<tr>
<td>Attention deficit disorder (ADD)</td>
<td>7.8%</td>
</tr>
<tr>
<td>Obesity</td>
<td>7.4%</td>
</tr>
<tr>
<td>Epilepsy</td>
<td>5.1%</td>
</tr>
<tr>
<td>Mental illness</td>
<td>4.1%</td>
</tr>
<tr>
<td>Other chronic conditions</td>
<td>2.0%</td>
</tr>
</tbody>
</table>

The chapter emphasizes developmental and behavioral issues in management of chronically ill or hospitalized adolescents. It is beyond the scope of this book to discuss all the specific chronic conditions that can affect adolescents. The references at the end of this chapter address a number of the major chronic illnesses in this age group.

**Definition and Prevalence**

Stein et al. (1993, 1997) developed a noncategorical, or generic, approach to defining and measuring chronic health conditions in children, rather than using a list of diagnoses. Three definitional concepts provide the framework, all of which must be present for a child or adolescent to be classified as having a chronic health condition:

1. Disorder on a biological, psychological, or cognitive basis
2. Duration or expected duration of at least 12 months
3. Consequences of the disorder
   a. Functional limitations compared with healthy peers in the same age group
   b. Reliance on compensatory mechanisms or assistance, such as medications, special diet, medical technology, assistive device, or personal assistance
   c. Need for medical care or related services, psychological services, or educational services over and above the usual for the child's age

Applying this definition and using data from the 1994 National Health Interview Survey Disability Supplement for children age 0 through 17 years, Stein and Silver (1999) estimated that 10.3 million children (14.8%) had chronic conditions. Using a different but similar definition of “children with special health care needs” and the same data set, Newacheck et al. (1998) found that 12.6 million children (18%) had special health care needs. Both sets of analyses found that children with chronic health conditions or special health care needs were disproportionately older, male, poor, and socially disadvantaged.

Approximately 2 million adolescents have a chronic health condition that results in limitation of daily activities or disability. This accounts for about 6% of those age 10 to 18 years in the United States (Newacheck, 1989, 1991). Asthma and other chronic respiratory tract conditions and musculoskeletal disorders account for most of the physical disabilities. Mental health disorders, including developmental, behavioral, and emotional problems, also are a leading cause of disability in this age group.

**Interaction of Adolescent Development and Chronic Illness**

Early adolescence is a period of accelerated physical growth and pubertal development, and in middle and later adolescence, acceleration in cognitive and psychosocial development predominates. The interaction of chronic illness with these different developmental streams is complex and bidirectional; the illness may affect the development and/or the development may affect the illness. For example, some chronic diseases such as cystic fibrosis or sickle cell disease can cause delayed puberty, but for other chronic diseases such as diabetes mellitus, normal puberty can cause exacerbation of the disease. Similarly, disabling chronic conditions that impede peer interaction such as spina bifida can delay psychosocial development; conversely, normal psychosocial development that includes increasing independence from parents with experimentation and risk taking can lead to poor medication adherence and exacerbation of illnesses such as asthma or chronic renal failure.

Specific psychosocial areas, notably achieving independence and family relationships, have been found to be most vulnerable to dysfunction in adolescents with chronic health conditions. Wolman et al. (1994) examined emotional health in adolescents with and without a chronic illness. They found that although adolescents with chronic conditions do less well than adolescents without chronic conditions, the illness is not the most influential factor in emotional well-being. Family
The overwhelming medical requirements of caring for an adolescent with a chronic illness can interrupt the movement toward middle adolescence: This age may be the most devastating time for a chronic illness to strike. During this phase, the adolescent is intensely involved with visibility late adolescence: Chronic illness starting in late adolescence usually causes less upheaval. At this stage, the teenager should have already gained uncertainty course communication physiological functioning expected survival emotional/social sensory functioning limitation of age-appropriate activities deformity such as prominent ears, which is merely an exaggeration of normal, is not as likely to elicit support and may explain the poorer mental health in that to be as well as or better adjusted than nondisfigured peers, whereas those with prominent ears were less well adjusted. To explain this counterintuitive finding, the adjustment in children with facial port-wine stains compared with adjustment in children with prominent ears. The children with disfiguring facial birthmarks were found

Using this approach, clinicians can target adolescents with multiple risk factors, in addition to the chronic illness, for enhanced intervention to prevent dysfunction.

Specific Developmental Risks

Independence Dependence The overwhelming medical requirements of caring for an adolescent with a chronic illness can interrupt the movement toward independence that usually occurs during early and middle adolescence. Because chronic illness thus prolongs dependence on parents and others, including physicians, the adolescent may become compliant and childish or noncompliant and rebellious.

Body Image As stated in earlier chapters, adolescents are highly concerned with and self-conscious about their developing bodies. Delayed puberty or visible malformations may create an inferior self-image. This abnormal body image may lead to the following:

- Lowered self-esteem
- Segregation from peers
- Increased absences from school and other activities
- Increased anxieties over sexual function and sexual relations
- Eating disorders
- Depression, anger, or both

Peer Group Chronic illness may limit teenagers’ activities, not only because of physical, mental, or sensory disabilities but also even without overt disability, because of illness-related fatigue, frequent medical appointments, and hospitalizations. Chronically ill adolescents may be rejected by peers or have fantasies of such rejection. These problems may lead to social segregation and a fear of peer involvement.

Identity The adolescent with a chronic illness often has difficulties consolidating a mature identity. Concerns with future vocation, financial resources, separation from parents, marriage, and reproduction may all lead to an identity crisis.

Modifying Factors

Age at Onset The stage of development during which the chronic illness appears may have considerable bearing on the psychological impact of the illness on the adolescent.

1. Preadolescence: Chronic illness or disability that originates at birth or in early childhood may lead early on to altered parental expectations. Lowered parental perception of potential of the developing adolescent may foster reduced self-expectations by the teen. These misconceptions have major implications for the setting and achievement of future goals for the adolescent.

2. Early adolescence: Because the early adolescent has yet to separate from his or her parents, there may be little struggle for independence or the parents may become overprotective and resist normal and reasonable independence overtures by their child. Chronic illness diagnosed in early adolescence may be particularly likely to provoke deep concerns about body integrity and image. Such concerns can set the stage for dysfunctional coping, and if not resolved, eating disorders may develop later on. Gross et al. (2000) assessed the prevalence of eating disorder symptoms in a sample of young women with physical disabilities and found that 6% had a sufficient number of symptoms to suggest clinical disorder. Eating disorders also are reported with some frequency in adolescents with diabetes mellitus and inflammatory bowel disease, diseases that often have their onset in early adolescence.

3. Middle adolescence: This age may be the most devastating time for a chronic illness to strike. During this phase, the adolescent is intensely involved with separation, peers, and sexual development. A chronic illness may thwart the adolescent's progress in these areas, in addition to conflicting with the high energy levels and feelings of omnipotence typical of middle adolescence. Poor adherence to medical therapy is a frequent problem during this period, as is depression, sexual acting out, and substance use.

4. Late adolescence: Chronic illness starting in late adolescence usually causes less upheaval. At this stage, the teenager should have already gained self-confidence and a secure identity. Concerns are focused on how the disease may disrupt vocational and educational plans, as well as future serious relationships, parenthood, and the prospects for living independently.

Nature of the Illness Perrin et al. (1993) list 12 dimensions, other than age at onset, for describing chronic illness that potentially may have an impact on the adolescent's adjustment:

1. Duration
2. Limitation of age-appropriate activities
3. Visibility
4. Expected survival
5. Mobility
6. Physiological functioning
7. Cognition
8. Emotional/social
9. Sensory functioning
10. Communication
11. Course
12. Uncertainty

For example, a highly visible disease such as psoriasis may cause more emotional disruption than a life-threatening malignancy such as Hodgkin disease. However, as is true for all of these dimensions, there is a complex relationship between visible deformities and adjustment. Sheerin et al. (1995) evaluated psychosocial adjustment in children with facial port-wine stains compared with adjustment in children with prominent ears. The children with disfiguring facial birthmarks were found to be as well as or better adjusted than nondisfigured peers, whereas those with prominent ears were less well adjusted. To explain this counterintuitive finding, the authors suggest that having a clearly abnormal disfigurement, such as a port-wine stain, elicits uniformity of both opinion and support from family, whereas having a deformity such as prominent ears, which is merely an exaggeration of normal, is not as likely to elicit support and may explain the poorer mental health in that
An exacerbating and remitting course of illness with the accompanying uncertainty and lack of control over when the symptoms will strike seems to be more likely to be associated with emotional problems. In reviewing studies among children and adolescents with chronic medical problems, Bennett (1994) found that certain disorders with these characteristics (i.e., asthma, recurrent abdominal pain, and sickle cell anemia) are associated with a greater risk for depression than other disorders that are more predictable (i.e., cancer, cystic fibrosis, and diabetes mellitus). Ivey et al. (1994) studied young adults (mean age, 21.9 years) with chronic illness and found that hearing and speech problems, unpredictability of symptoms, and restricted activity days were illness characteristics that had significant adverse effects on mental health status. Diseases that interfere with cognition, sensory function, or communication are particularly likely to be associated with poor adjustment. Howe et al. (1993) found that adolescents with brain-based conditions had more behavioral problems, less autonomous functioning, and poorer school achievement than those without brain dysfunction.

**Number of Chronic Conditions** In an analysis of the National Health Interview Survey, children and adolescents who had multiple conditions of a chronic nature, even if few in number, had increased morbidity across various measures (Newacheck and Stoddard, 1994).

### COPING WITH CHRONIC ILLNESS

To cope with difficulties and frustrations of chronic illness, the adolescent usually adopts one or more of the following coping mechanisms:

- **Insightful acceptance:** Unusual in adolescents, particularly during early and middle adolescence.
- **Denial:** A common coping strategy used by adolescents. Some forms of denial may be adaptive and helpful, but more often, this strategy leads to poor adherence behaviors such as missed appointments and forgotten medications.
- **Regression:** Also common in chronically ill adolescents. With regression, the teenager becomes more dependent on parents and other adults and exhibits increasingly childlike behavior.
- **Projection:** This coping mechanism allows feelings of rage, frustration, or guilt to be transferred onto parents or health care providers. Projection is often observed on adolescent inpatient units, where anger is transferred to the staff.
- **Displacement:** A similar coping mechanism to projection, but the anger is usually transferred to an object or an activity. Displacement is observed frequently on adolescent units and is typified by behavior such as throwing of objects.
- **Acting out:** Similar to displacement but less constructive. In frustration, the adolescent exhibits out-of-control behavior, necessitating disciplinary management.
- **Compensation:** A highly useful coping strategy in which the patient alters usual activities in response to the restrictions of the disease. For example, an adolescent who formerly achieved self-esteem through dancing switches to performing music for fulfillment.
- **Intellectualization:** This coping mechanism separates the realities of the disease from the emotional impacts. Teenagers who become highly involved in the technical aspects of their disease are using intellectualization. Although intellectualization can be positive, there needs to be some period during which the adolescent acknowledges his or her emotional concerns.

Over time, the adolescent with a chronic illness or disability likely uses many of the listed coping mechanisms, often using different mechanisms to cope with different situations. Most adolescents who come from psychologically healthy and supportive families can cope amazingly well with a multitude of stressors and are able to use these situations as emotional growth experiences. It is not uncommon to observe regressed behavior in an adolescent during a period of acute distress, with a rapid regain of maturational status almost immediately afterward (e.g., when a bone marrow aspiration needle is removed).

With maturation and experience in dealing with chronic illness and its treatment, many adolescents are able to use cognitive reframing of situations to render them less threatening and stressful. Such adolescents also develop an array of coping strategies that have worked for them and learn to reuse those successful strategies instead of continuing to try unsuccessful ones. Exposure to multiple stresses of a similar nature permits stress inoculation and the ability to respond more rapidly and often more appropriately to familiar challenges.

For those adolescents who cannot consistently meet the challenges of chronic illness, breakdown of coping may be manifested behaviorally by poor adherence to treatment recommendations, increased risk-taking behaviors, or overall withdrawal from developmental tasks as a manifestation of depression.

### RISK BEHAVIORS

Risk taking, particularly in the areas of sexuality and substance use, contributes substantially to morbidity in healthy adolescents. When this behavior interacts with chronic illness, however, health consequences often are exacerbated. It is ironic that risk taking among chronically ill teenagers is probably directly related to improved management, which most often results in normal or near-normal growth, pubertal development, and fertility; better nutritional status; normal energy levels; and age-appropriate opportunities for social interaction that can, and often do, include risk-taking behaviors.

### Sexuality

For adolescents with a chronic illness, the health risks of sexual activity may be exacerbated by the illness itself, the medications used to treat it, or by a maladaptive emotional response to illness. Many clinicians fail to address sexually related issues with chronically ill adolescents. However, studies show that many adolescents with chronic illnesses are sexually active and most have concerns about their sexual attractiveness, normalcy of their reproductive system, and sexual response, fertility, safety of contraception use, and genetic aspects of their disease.

**Prevalence of Sexual Activity** Table 83.2 shows prevalence of sexual activity among chronically ill adolescents. Suris et al. (1996) conducted a statewide survey of Minnesota high school students and showed that for both boys and girls, there was no difference in age at first intercourse between those with chronic illness and those without, and no effect of visibility of illness on age at first intercourse. In a study of inner-city adolescents with various chronic diseases (e.g., asthma, diabetes mellitus, cancer, sickle cell disease, and others) and their healthy friends age 14 through 17 years, Alderman and Lauby (1995) found that approximately one third of both the chronically ill group and the healthy group were sexually active, with a mean age at first intercourse in the 13th year. However, these investigators also found that the interaction between gender and sexual debut was significantly different: boys without chronic illness initiated intercourse at a younger age (12.9 years) than boys with illness (13.4 years), and the reverse was true for girls, those with chronic illness initiated intercourse at a younger age (13.8 years) than their healthy friends (15.3 years). Britto et al. (1998) surveyed adolescents with cystic fibrosis and sickle cell disease from five pediatric tertiary care centers in North Carolina and compared their sexual behavior with that of controls matched for age, race, and gender. Fewer teens with cystic fibrosis (28.3%) and sickle cell disease (51.3%) than matched controls (46.4% and 76.4%, respectively) reported being sexually active. Also, the age at first intercourse for girls was older in those with chronic illness compared with matched controls, 15.7 versus 14.6 years and 14.8 versus 13.9 years for those with cystic fibrosis and sickle cell disease, respectively. The same was true for boys, only the ages at first intercourse were approximately 1 year younger in all groups.

**TABLE 83.2.** Prevalence of sexual activity among chronically ill adolescents
As this North Carolina study shows, sexual debut may be delayed in adolescents with illnesses that delay puberty such as cystic fibrosis and sickle cell disease. Onset of sexual activity may also be delayed for adolescents with mobility limitations and brain-based conditions that result in fewer opportunities for peer interaction. Sexual assault also is a salient issue, particularly for cognitively impaired adolescent girls who are uniquely vulnerable to exploitation.

Fertility Some chronic conditions are associated with impaired fertility related to the disease itself or to the treatment. For example, males with cystic fibrosis are sterile, but females are fertile and many have children. In a large study of survivors of childhood cancer, Byrne et al. (1987) demonstrated that compared with sibling controls, radiation therapy below the diaphragm had the greatest adverse effect on fertility in females. It is important to remember, however, that most chronic illnesses do not impair fertility, and particularly for sexually active girls, effective contraception is extremely important. Girls with chronic illness should be counseled about the necessity of carefully planning pregnancies to minimize teratogenicity from medications and treatments and to ensure the best outcome for mother and fetus. Chapter 43 reviews contraceptive options in teens with various chronic illnesses and Table 83.3 outlines contraceptive options for selected chronic diseases.

### Table 83.3. Choice of contraceptives for girls with selected chronic conditions

| Sexually Transmitted Disease | Girls who are immunosuppressed either from the disease (e.g., HIV) or the treatment (e.g., renal transplant, lupus) are at risk for a prolonged and more complicated course if infected with a sexually transmitted disease. These girls should receive detailed instruction and frequent reinforcement regarding barrier contraceptive use. Genital infection with human papillomavirus is particularly virulent in girls who are immunocompromised, and they are at increased risk of developing cervical cancer. |

Substance Use

Substance use by adolescents with chronic illness can contribute significantly to morbidity and mortality. Alcohol, illicit drugs, or over-the-counter herbal preparations may interact with prescribed medications to cause deleterious effects. Certain specific chronic conditions, notably heart disease, put affected adolescents at particular risk of death from even one-time use of stimulants such as cocaine, amphetamines, or "Ecstasy." Prevalence of Substance Use Westbrook et al. (1991) compared substance use in three different groups of adolescents age 13 to 19 years. The groups included 34 patients with idiopathic epilepsy, 32 with various chronic diseases other than epilepsy, and 50 with no chronic illness. Fewer adolescents with epilepsy were daily smokers (3%) than adolescents who had other chronic diseases (19%) or were healthy (30%). Approximately 15% of the teens in each group reported drinking alcohol once a week or more, and 20% in each group reported that they used marijuana, with less than half using it once a week or more. The study by Britto et al. (1998) in North Carolina also found that fewer teens with cystic fibrosis versus matched controls smoked regularly (2.6% versus 29.6%) were binge drinkers (18.0% versus 35.3%) or tried marijuana (9.7% versus 29.4%), respectively.

Although the proportion of adolescents with chronic illness using substances may be less than that of their healthy peers, the absolute numbers are still quite high and the risk of complications are greater. Screening by history for substance use and anticipatory guidance and counseling regarding specific substances and their effect on the adolescent's illness are mandatory.

### MANAGEMENT OF CHRONIC ILLNESS IN THE ADOLESCENT

#### General Principles

Optimal care of the adolescent's medical condition is of primary importance. However, high-quality treatment often cannot be achieved without consideration and exploration of the adolescent's mental health, developmental progress, and family relationships. Simply prescribing treatment is not enough. The adolescent must cooperate with the health care team, believe that adhering to a complex regimen is better than the alternative, and have family support and assistance in carrying out the treatment plan. Helpful principles for management include the following:

1. Educate: Inform the adolescent of the nature of the disease and the limitations of treatment. The educational process should be directed at both patient and family and should use language that is easy to understand.
2. Respond to emotion: Listen carefully, give permission, and allow time for the adolescent and the family to express feelings, fears, and hopes.
3. Involve the family: Family support and guidance are crucial. Families must be coached to avoid the "overs": overprotection, overanxiety, and overattention.
4. Involve the patient: The more an adolescent is involved with his or her own care, the greater the chance for compliance and a sense of self-control.
5. Use a multidisciplinary team: Many health care professionals usually are necessary to optimally manage adolescents with chronic illness, including physicians, psychologists, social workers, nurses, occupational therapists, physical therapists, and nutritionists. Respect for the skills of these individuals, as well as communication in interdisciplinary conferences, can improve the care of the adolescent.
6. Provide continuity of care. The chronically ill adolescent needs an advocate whom he or she can trust. At least one member of the health care team, preferably a primary care clinician, should maintain a long-standing relationship with the patient and family. This clinician's role is to coordinate care among various specialty disciplines, monitor adolescent development, provide anticipatory guidance, and treat intercurrent illnesses.
7. Provide comprehensive ambulatory service: Such services would include psychological, social work, educational, speech and hearing, and other special services. It may be difficult for families to obtain insurance reimbursement for such necessary services, although they are cost-effective. Liptak et al. (1998) showed that comprehensive ambulatory service decreased number of inpatient hospitalizations, length of stay, hospital costs, and readmissions for chronically ill children.
8. Referral to peer and disease support groups: Participation in such groups allows for increased expression of concerns and anxieties by both patients and families and sharing of information among families with similar problems. A number of support group agencies are listed at the end of this chapter.
9. Consider self-help techniques: Training the adolescent in various cognitive-behavioral techniques to manage stress and pain can enhance feelings of self-control and reduce disease- and treatment-related stress. Examples of these strategies include hypnosis, relaxation and distraction techniques, guided imagery, and thought stopping.
10. Limit setting: If compliance or behavior is a problem, limits must be set and the entire health care team and the parents must agree and enforce the limits. Avoidance of splitting and pitting one member of the team against another is crucial.
11. Inpatient care: When necessary, inpatient hospital care is best handled in an environment conducive to the developmental needs of the adolescent.

The Hospitalized Adolescent

In the course of their illness, most chronically ill adolescents will be hospitalized. There is considerable advantage in placing all adolescent patients on one inpatient unit regardless of diagnosis. Using the noncategorical approach to illness helps to clarify the fact that despite different medical diseases, adolescents' needs are much more similar than they are different. An adolescent inpatient unit provides an environment and staff oriented toward the developmental needs of the patients.
Environment and Setting

1. Separate unit: Allows for adolescents to interact and for a staff expert in adolescents' needs to be involved in their care.
2. Single- or double-bedded rooms: Miller et al. (1998) found that adolescents are approximately equally divided regarding whether they prefer a single room or having a roommate when hospitalized. Roommates can provide support, companionship, and entertainment during the adolescent's stay.
3. Recreation room: The adolescent unit should include a recreation room that provides various activities to enhance interaction, encourage peer involvement, and alleviate boredom. In the context of playing a game, the recreational therapist may be the first to discover a chronically ill adolescent's fears or anxieties. The activity program can also play an important role in pain management for those ill adolescents who require such intervention.
4. School room: Every effort should be made to continue an adolescent's schooling to the extent possible during a hospitalization. Having a teacher on staff is an asset.
5. Interested staff: Caring for adolescents consumes much time and energy, so the staff should be chosen from among those who enjoy working with adolescents.
6. Relevant rules and regulations: Rules should be flexible, sensitive, and explicit in regard to the adolescent unit. Such rules can include patient and staff responsibilities, and regulations regarding guests, television viewing, bedtime, the recreation room, and quiet times. Figure 83.1 lists a sample set of rules for an adolescent unit, along with a listing of patient rights and responsibilities.

![Image](https://example.com/image.png)

**FIG. 83.1.** Sample orientation sheet for an adolescent ward used at the Children's Hospital of Los Angeles.

7. Snacks: Adolescents are often hungry at times other than mealtimes, so some allowance should be made to provide snacks.

Staffing

1. The staff should be chosen on the basis of interest in working with and ability to work with adolescents.
2. The staff should include physicians, nurses, a psychologist, a social worker, a recreational therapist, a teacher, and a consultant nutritionist.
3. Staff meetings should include both continuing medical education and interdisciplinary case conferences.

In summary, a well-staffed adolescent inpatient service can provide chronically ill teenagers with an environment that increases their independence, respects their privacy, and enhances their knowledge of their particular illness while reinforcing behavior that encourages their continued growth and development.

RESOURCES

Agencies

**General** U.S. Department of Health and Human Services

Administration on Developmental Disabilities

200 Independence Avenue SW, room 329D
Washington, DC 20201
202-690-5504

Clearinghouse on Disability Information

202-205-8241

Department of Education

Office of Special Education and Rehabilitation Services

Office of Special Education Programs

Rehabilitation Services Administration

National Institute on Disability and Rehabilitation Research

330 C Street SW
Washington, DC 20202
202-205-8241

Girl Scouts of the U.S.A

Focus on Ability: Serving Girls With Special Needs

Scouting for Handicapped Girls Program

212-852-8000

March of Dimes Birth Defects Foundation

1275 Mamaroneck Avenue
White Plains, NY 10605
914-428-7100

National Center for Youth with Disabilities

University of Minnesota

Box 721
420 Delaware Street SE
Minneapolis, MN 55455
800-333-6293

(National Information Center for Children and Youth with Disabilities

PO Box 1492
Washington, DC 20013
800-695-0285

National Organization on Disability
American Cancer Society
1599 Clifton Road NE
Atlanta, GA 30329
800-ACS-2345
http://www.cancer.org/
(Supports education and research in cancer prevention, diagnosis, and treatment.)

American Diabetes Association
1701 North Beauregard Street
Alexandria, VA 22311
800-232-3472
http://www.diabetes.org/

American Foundation for the Blind
11 Penn Plaza
New York, NY 10001
800-232-5463
http://www.afb.org/

American Heart Association
7272 Greenville Avenue
Dallas, TX 75231-4596
800-242-8721
http://www.americanheart.org/
(Supports research and education to reduce death rates and disability from heart disease. Has a children and heart disease Web page with teen lounge; see www.americanheart.org/children/index.html.)

Arthritis Foundation—American Juvenile Arthritis Organization
1314 Spring Street
Atlanta, GA 30309
800-283-7800
http://www.arthritis.org/
(A resource for educational material about the diagnosis and treatment of arthritis. Web site has a special area for teens.)

Association for Retarded Citizens
500 East Border Street, suite 300
PO Box 1047
Arlington, TX 76010
800-433-5255

Asthma and Allergy Foundation of America
1125 15th Street NW, suite 502
Washington, DC 20005
800-227-8462
http://www.aafa.org/
(Provides information on support services and resource materials on asthma and allergy. Web site has a special section for children and teens.)

Autism Society of America
7910 Woodmount Avenue, suite 650
Bethesda, MD 20814
800-328-8476
http://www.autism-society.org/

Candlelighters Childhood Cancer Foundation
3510 Warner Street
Kensington, MD 20895
800-366-2223;
http://www.candlelighters.org/

Children and Adults With Attention Deficit Disorders (CHADD)
499 Northwest 70th Avenue, suite 109
Plantation, FL 33317
800-233-4050
http://www.chadd.org/

Children's Craniofacial Association
PO Box 571097
Dallas, TX 75357
800-353-3643
http://www.ccakids.com/

Crohn's and Collitis Foundation of America
386 Park Avenue South, 17th floor
New York, NY 10016-8804
800-932-2423
http://www.ccfa.org/  
(Information to patients and their families on inflammatory bowel disease.)

Cystic Fibrosis Foundation  
6931 Arlington Road  
Bethesda, MD 20814  
800-344-4823  
http://www.cff.org/  
(Provides educational material to patients, parents, and health care providers.)

Disabled Sports USA  
451 Hungerford Drive, no. 100  
Rockville, MD 20850  
800-966-4647  
http://www.dsusafw.org/  
(Web site for the far west chapter)  
(Sponsors various sports and recreational activities through a network of community-based chapters.)

Epilepsy Foundation of America  
4351 Garden City Drive  
Landover, MD 20785-2267  
800-332-1000  
http://wwwefa.org/  
(Provides educational material and resources to patients and their families.)

Independent Living Research Utilization  
Research and Training Center on Independent Living at The Institute of Rehabilitation and Research  
2323 South Shepherd, suite 1000  
Houston, TX 77019  
713-520-0232  
(Provides resources on sexuality and the disabled person.)

Learning Disabilities Association of America  
4156 Library Road  
Pittsburgh, PA 15234-1349  
412-341-1515  
http://www.ldanatl.org/  

Leukemia and Lymphoma Society  
600 3rd Avenue, 4th floor  
New York, NY 10016  
800-954-4572  
http://www.leukemia-lymphoma.org/  
(Sponsors programs of research, patient help, education, and community service.)

Lupus Foundation of America  
1300 Piccard Drive, suite 200  
Rockville, MD 20850-4303  
800-558-0121  
http://www.lupus.org/  

Muscular Dystrophy Association-USA  
National Headquarters  
3300 East Sunrise Drive  
Tucson, AZ 85718-3208  
800-572-1717  
http://www.mdausa.org/  

National Alopecia Areata Foundation  
710 C Street, suite 11  
San Rafael, CA 94901  
415-456-4644  
(Provides information on hair loss and support for people with alopecia areata.)

National Association of the Deaf  
814 Thayer Avenue  
Silver Spring, MD 20910  
301-587-1788  
http://www.nad.policy.net/  

National Chronic Fatigue Syndrome Association  
3521 Broadway, suite 222  
Kansas City, MO 64111  
816-931-4777  
(Organized to educate the public and health professionals about the nature of chronic fatigue syndrome.)

National Children's Cancer Society  
1015 Locust Street, suite 600  
St. Louis, MO 63101  
800-532-6459  
(Provides financial support for medical care of children with cancer.)

National Down Syndrome Society  
666 Broadway, 8th floor  
New York NY 10012-2317  
212-460-9330  
http://www.ndss.org/  

National Headache Foundation  
5252 North Western Avenue  
Chicago, IL 60625  
800-843-2256  
(Committed to research, education, and service for the headache sufferer.)

National Head Injury Foundation  
1776 Massachusetts Avenue NW, suite 100  
Washington, DC 20036-1904
800-444-6443  
(Acts as an advocate for head-injured patients and provides support for their families.)

National Kidney Foundation  
30 East 33rd Street, 11th floor  
New York, NY 10016  
800-622-9010  
http://www.kidney.org/  
(Resource for information on kidney and urinary tract disease and organ donation.)

National Mental Health Association  
1021 Prince Street  
Alexandria, VA 22314-2971  
800-969-6642  
http://www.nmha.org/  
(Advocacy group concerned with all aspects of mental health and mental illnesses.)

National Multiple Sclerosis Society  
733 3rd Avenue, 6th floor  
New York, NY 10017  
800-344-4867  
http://www.nmss.org/  
(A primary resource for information about multiple sclerosis research, diagnosis, and treatments.)

National Neurofibromatosis Foundation  
95 Pine Street, 16th floor  
New York, NY 10005  
800-323-7938  

National Organization for Rare Disorders  
PO Box 8923  
New Fairfield, CT 06812-1783  
800-999-6673  

National Rehabilitation Information Center  
http://www.naric.com/  

National Scoliosis Foundation  
72 Mount Auburn Street  
Watertown, MA 02172  
617-926-0397  

National Spinal Cord Injury Association  
545 Concord Avenue, suite 29  
Cambridge, MA 02138  
800-962-9629 (hotline only)  

Sickle Cell Disease Association of America  
200 Corporate Pointe, suite 495  
Culver City, CA 90203-7633  
800-421-8453  
http://sickcelldisease.org/  

Spina Bifida Association of America  
4590 MacArthur Boulevard NW, no. 250  
Washington, DC 20007-4226  
800-621-3141  

United Cerebral Palsy Association  
1660 L Street, suite 700  
Washington, DC 20036  
800-872-5827  
http://www.ucpa.org/  

Health-related Web Sites  
http://www.itstyoursexlife.com/. Developed by the Kaiser Foundation; aimed at the older teen; very straightforward sex information.  
http://www.health4teens.org/. Excellent alcohol, eating disorder, sex, smoking, sexually transmitted disease, and stress information; easy to read, catchy, encouraging, teen-friendly site.  
http://www.tchin.org/. Children's health information network; heart disease information and resources.  
http://www.chronicillnet.org/. Information source dedicated to chronic illness, particularly acquired immunodeficiency syndrome, cancer, autoimmune diseases, heart disease, chronic fatigue syndrome, and neurological diseases.

REFERENCES AND ADDITIONAL READINGS  
References for Specific Conditions

Asthma


Cancer


Levin S. The role of adolescents in decisions concerning their cancer therapy. Cancer 1993;71:3342.


Cystic Fibrosis


Diabetes Mellitus


**Sickle Cell Anemia**


**Spina Bifida**


Consumer use of herbal medicines has increased over the last several years at a remarkable pace. Herbal sales during the first quarter of 1998 increased by more than 100% compared with the previous year. Sales of herbal products have increased yearly by about 5%–6% until recently when sales have stabilized. Much has been written in the medical literature regarding the use of such treatments. Despite concerns among the medical community, consumer use remains popular and in many cases is not discussed with the physician.

Given the overwhelming popularity of herbal treatments in the general population, basic clinical guidelines are necessary for the health care provider to ensure patient safety and to assist the clinician in making rational decisions, particularly when confronted with limited data. Attempts have previously been made to formulate basic ground rules when dealing with herbal treatments. Although basic in nature, these concepts represent an initial attempt to assist the clinician when dealing with bioactive compounds such as herbal remedies (Table 84.1).

<table>
<thead>
<tr>
<th>TABLE 84.1. Ground rules for use of herbal remedies in the clinical setting</th>
</tr>
</thead>
</table>

**IMPORTANT ISSUES FOR THE CLINICIAN**

**Knowledge**

It is imperative that clinicians be knowledgeable regarding herbal treatments. Without such accurate knowledge, it will become difficult for the clinician to appropriately answer questions the teen or parents might have.

**Fostering Open Discussion**

If the clinician allows the teen or the parent to feel comfortable discussing herbal treatments in the office, the teen or parent is less likely to rely on erroneous and false information gleaned from friends, family, and the Internet. By creating an environment that fosters open and candid discussions regarding alternative medicine and other issues related to their health, the clinician fosters his or her patients to feel free to discuss uncomfortable issues that may arise from time to time. These same tenants also apply to teens, young adults, and parents who may wish to use herbal remedies. Clearly, if clinicians embrace this approach, rather than taking a negative or hostile attitude, patients will benefit and receive accurate information.

**Accurate Clinical Research Data**

Clinical data are often lacking for many herbal products. Because herbal treatments are considered dietary supplements and not drugs, premarket testing and studies on safety and efficacy are not required. On a positive note, more and more studies of herbal treatments using sound investigational methodology are appearing in respected peer-reviewed journals. This will undoubtedly assist in making informed and rational decisions regarding the use of herbal treatments.

**Medical-legal Issues**

The combination of lack of sufficient medical research and the wishes of the patient to utilize alternative medications may present a quandary for the practitioner. Not only is there concern for patient safety, but medical legal issues may also arise if a clinician recommends an herbal treatment in place of an established form of therapy considered to be standard of care. In many cases however, it is not the clinician that wishes to utilize such a treatment but in fact the patient. The provider must then decide what to recommend to a patient wishing to use an herbal remedy. One option is to plead ignorance and to dismiss the wishes of the patient outright. This however may lead to patient dissatisfaction and in fact may foster the use of herbal treatments without the knowledge of the health care provider, a frequent outcome of such interactions. Eisenberg (1997) has written on advising patients who seek alternative medicine. He advises that patients and clinicians must be aware that because of the lack of adequate information on efficacy and toxicity, advice about herbal product use remains imperfect and a matter of judgment. Advice based on available knowledge should be given in such a fashion that is congruent with the patient’s personal needs and in the physician’s best judgment. Responsible use of herbal treatments both by the patient and with assistance from a health care professional requires knowledge of these treatments regarding dosage, contraindications, side effects, potential drug-herb interactions, and proper indications.
Although certainly not indicated for use in acute settings, herbal remedies will undoubtedly add to the existing armamentarium of therapeutic options available to the clinician. This, coupled with significant patient demand, will not only improve care but also promote and foster a positive dialogue between patient and provider, strengthening the doctor-patient relationship.

Adequate Medical History

Given that many patients may be taking herbal products or supplements and given that many herbal treatments have the potential to interact with standard pharmaceutical agents, resulting in untoward consequences, dialogue with patients regarding use should be part of every office visit and initial history and physical.

All patients seen in the office must be queried regarding the use not only of botanicals but of all forms of alternative or complementary medicine. This ensures that patients will not have a significant drug-herb interaction and allows the health care provider to assess whether all supplements taken are actually necessary and if some may be stopped. This dialogue also functions to improve communication between the provider and patient and has the impact of fostering a "user-friendly" office visit. Many patients feel that disclosure of such treatments to the physician will result in scorn and possibly even ridicule. This is simply unacceptable behavior on the part of the provider, given the many data on a number of herbal remedies. In addition, harmful drug-herb interactions may be missed if the physician out-of-hand condemns their use or claims ignorance. All health care providers actively involved in patient care must be knowledgeable regarding use by their patients, specific side effects, toxicity, and potential interactions. During these discussions, patients should also be made aware of the fact that just because something is natural, there is no guarantee of safety.

Herb-Drug Interactions and Toxicity

As has been noted, herb-drug interactions do occur. Table 84.2 lists a number of herb-drug interactions of which the physician should be aware. One of the more significant of these involves those agents that have antiplatelet activity. In addition, recent case reports and studies indicate serious interactions regarding St. John's wort and cyclosporine, oral contraceptives, and antiretroviral agents including indinavir (Table 84.3). A number of herbs when combined with coumadin or nonsteroidal antiinflammatory drugs have been documented to lead to bleeding difficulties. Certainly, patients undergoing surgery should be counseled on the risks of these agents preoperatively, and discontinuation at least 2 weeks before surgery should in general be the rule until more concrete data are available to ensure safety. At a minimum, frequent measurements of the prothrombin time and/or the international normalized ratio may be necessary to avoid complications.

Herbal remedies have been known to cause toxicity to various organ systems including the following:

1. Liver: The organ that appears to be the most common target of serious herbal toxicity is the liver (Table 84.3). Two common types of liver insult include hepatitis or venoocclusive disease. Chaparral, for example, has been implicated in acute hepatitis, causing subacute hepatocellular necrosis leading to cholestatic hepatitis and eventually liver failure requiring transplantation. Additionally, germander has also been implicated in causing hepatotoxicity with a marked increase in serum aminotransferase levels and fatalities have occurred. Several Chinese herbal treatments have also been found to cause liver toxicity including Jin Bu Huan noted to contain the alkaloid levo-tetrahydropalmatine. This herbal remedy contains structural similarities to hepatotoxic pyrrolizidine alkaloids previously documented to cause liver damage. This liver toxicity has been noted in other remedies containing pyrrolizidine alkaloids known to cause hepatic venoocclusive disease leading to portal hypertension. Clinically, exposure to this compound may lead to hepatomegaly and ascorcy caused by hepatic central vein dilatation and fibrosis. Several case reports have documented this association with various herbal treatments. In addition, it appears that infants and young children are particularly susceptible to this effect. In utero exposure has been linked with hepatic venoocclusive disease and death in a newborn infant.

<table>
<thead>
<tr>
<th>Germanender</th>
<th>Chaparral</th>
<th>Jin Bu Huan</th>
<th>Mistakes</th>
<th>Sabatiae</th>
<th>Camphor</th>
<th>Coleus</th>
<th>Lithos</th>
<th>Plectech</th>
</tr>
</thead>
</table>

![Table 84.2](Image 72x826 to 272x968)

2. Cardiotoxicity and nephrotoxicity: Other organ systems have also been documented to suffer damage from ingestion of toxic herbal remedies. Of note, cardiotoxicity and nephrotoxicity are documented in the literature. Cardiotoxicity has been associated with ingestion of herbal products containing aconite alkaloids. It is felt that these agents activate sodium channels and have widespread effects on the excitable membranes of cardiac, neural, and muscle tissue. Enhancement of transmembrane inward currents induce afterdepolarizations with triggered automaticity. In case reports, this has led to fatal arrhythmias and even death. In general, although herbal remedies do possess the potential for harm, the widespread use among the population to date has not led to large numbers of injuries or harm, albeit that underreporting of herbal acute drug reactions may occur frequently. With common sense and more importantly knowledge of potential side effects and toxic herbal products, the physician may integrate herbal remedies into practice safely. We believe that with careful dialogue and follow-up, herbal remedies have the potential to add a great deal to the existing treatment options available for patients. Of course, further study and long-term trials are needed to further assess safety and efficacy.

Dosing Issues and Active Compounds

In traditional medicine, clinicians have become accustomed to using pharmaceutical agents that by definition possess the same strength and high quality. This is not always the case with herbal medicine. Because herbs represent complex entities containing hundreds of constituents, it is difficult to find one particular component representing the active agent. In many cases, particular herbal treatments have been studied with a focus on individual extracts and chemical entities. For instance, one Ginkgo biloba extract in particular (Egb 761) has been extensively studied. For this reason, patients should be counseled on the use of particular extracts if most clinical studies have been done using that extract. Manufacturers may or may not produce herbal products using extracts that have been the subject of scientific validation.
study, so they should not be used.

Whether there is benefit to standardizing an herbal treatment to one identifiable component is a matter of current debate. According to some, the worthy goal of standardization—that is, to achieve a consistent level of the main therapeutically effective active plant constituent—remains remote. Efforts to achieve this will require much more on-the-ground research, bioactivity assessment, and correlation with clinical end points. The standardization of phytomedicines serves primarily as a precaution for the quality of medicinal plant extracts.

The dosage and length of treatment of various herbal remedies represents another difficulty for the physician. As with any pharmaceutical agent, as dosage is increased, an increase in the risk of side effects may occur. It is therefore wise to recommend using the lowest dosages of herbal treatments initially to see whether a desired benefit may be obtained. As with other standard medications, idiosyncratic reactions may occur. In addition, many herbal therapies have not been studied for long periods. It is therefore prudent for the clinician to ascertain whether it is necessary to continue with use of an herbal treatment. One example is the use of Echinacea and its potential for harm if used long term. Similar to treating a patient for mild hypertension, for example, it is prudent to start with lower dosages and monitor for a response before initiating even higher dosages.

### Long-term Usage

Use of herbal remedies for extended periods presents a dilemma for the practicing clinician. Unfortunately, most studies involving herbal treatments do not evaluate long-term effects. As has been mentioned, certain inherent risks are present. These include herbal remedies containing tannins. These compounds have been documented to increase the risk of certain oropharyngeal cancers with long-term exposure. Additionally, several herbs have been theoretically thought to possess carcinogenic components that over time may be problematic. It is therefore our opinion that in general, herbal remedies should only be used on a limited basis until more data are available regarding long-term safety. Those patients wishing to remain on herbal remedies should be monitored periodically for signs of toxicity and potential adverse effects. Periodic measurements of liver function tests and renal function may be prudent. Ultimately, all patients should be advised not to take herbal treatments long term without the supervision of a physician.

### Contamination

Another issue that should be discussed with patients using or contemplating use of herbal treatments involves the fact that in many instances, a lack of quality control and regulation has resulted in contamination and misidentification of plant species (Table 84.4). For this reason, patients should be advised to use products from reputable manufacturers. This has become somewhat easier given that several large manufacturers of pharmaceuticals are now marketing their own lines of herbal treatments. This can only help to improve the quality of herbal treatments given the long-standing history and knowledge regarding proper manufacture and quality control. There are those, however, who view these changes with cynicism and consider these products nothing more than new plant-derived pharmaceutical compounds. This is a matter of debate. Certainly more federal regulation is needed perhaps similar to agencies in Europe (e.g., German Commission E) to ensure the safe manufacturing of herbal medicines. Possibly a new class of scientifically studied agents that are not required to undergo the rigors of current Food and Drug Administration (FDA) approval will aid this problem.

| Table 84.4. Documented contaminants/adulterants found in herbal remedies: not all inclusive |

<table>
<thead>
<tr>
<th>Aluminum</th>
<th>Indomethacin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arsenic</td>
<td>Lead</td>
</tr>
<tr>
<td>Aspirin</td>
<td>Mercury</td>
</tr>
<tr>
<td>Cobalt</td>
<td>Theophylline</td>
</tr>
<tr>
<td>Coffein</td>
<td>Thapsigargin</td>
</tr>
<tr>
<td>Contaminated Zinc</td>
<td></td>
</tr>
<tr>
<td>Datepoin</td>
<td></td>
</tr>
</tbody>
</table>


### Use in Pregnancy and Lactation

With regard to the use of herbal treatments in pregnancy and lactation, no women contemplating pregnancy, currently pregnant, or nursing should use herbal remedies, given several issues mentioned earlier and due to a lack of safety studies. In one study, St. John's wort, as well as several other herbal treatments, was implicated in decreasing fertility. Although having several methodological problems, this study does raise questions regarding the use of herbal treatments in patients endeavoring to have children.

### Herbalist Consultation

Patients wishing to use herbal remedies may wish to seek the advice of an herbalist or traditional Chinese medicine practitioner. If the clinician feels uncomfortable making specific recommendations regarding herbal treatments, a referral to a reputable practitioner may be indicated. Unfortunately, current lack of regulations may make referral to a reputable practitioner difficult and the clinician may be left relying solely on "word of mouth." This is clearly not a satisfactory situation, and the clinician may potentially be held liable if a bad outcome results from such a referral. Once again, it behooves the physician to become knowledgeable enough regarding herbal treatments that sound advice may be given to patients who wish to undergo this form of therapy.

### COMMON HERBAL REMEDIES IN THE ADOLESCENT POPULATION

In the adolescent patient population, it is quite common to find the use of herbal remedies for a number of conditions. These generally include those for weight loss, depression and anxiety, upper respiratory tract infections, and those to aid in performance of sports. Many younger patients find that the stimulating herbal Ma Huang (which contains ephedrine) increases energy and stamina. Several of these are covered in detail to help the provider counsel his or her patients regarding the pros and cons of use.

### Psychoactive Herbal Remedies

**St. John's Wort**

* Uses: St. John's wort has historically been used for wound healing and depression. St. John's wort has a multifactorial effect on the body, leading to its antidepressant activity.

* Mechanism of action: Several studies have implicated a serotonin reuptake inhibition as the primary mechanism of action; however, several other studies have noted monoamine oxidase inhibition in vitro and other mechanisms of action postulated have included catechol- O-methyltransferase activity along with modulation of serotonin secretion and norepinephrine uptake.

* Clinical studies: Several studies have compared St. John's wort with tricyclic antidepressants (TCAs) and noted that St. John's wort was superior to placebo and as effective as low doses of TCAs. These studies have for the most part involved patients with mild depression. Recently, several studies have compared St. John's wort with selective serotonin reuptake inhibitors (SSRIs) finding comparable efficacy when using high doses of St. John's wort compared with lower doses of standard SSRIs.
Side effects: St. John's wort has been noted to have a low incidence of side effects. When present, the most common include gastrointestinal (GI) symptoms, dizziness, and confusion. In rare cases, phototoxicity may occur with ingestion of high doses, which resolves with discontinuation of the herb.

Drug interactions: Recently, a number of case reports have noted a significant interaction with cyclosporine, oral anticoagulants, oral contraceptives, and certain antiretroviral agents including indinavir. It is felt that these interactions may be due to the ability of St. John's wort to induce the cytochrome P-450 metabolic pathway. The concomitant use of St. John's wort with standard antidepressants is also contraindicated due to the risk of serotonin syndrome, which may be precipitated. Due to a lack of safety data, use in pregnancy and lactation is contraindicated.

**Kava**

Uses: Kava has historically been used for its calming effects and has been an important cultural entity in the South Pacific, particularly in the Fiji Islands where it is used as a ceremonial drink. Most recently, it has been used as a natural alternative to sedatives and anxiolytics.

Mechanism of action: It is felt that kava works primarily by inhibition of g-aminobutyric acid (GABA) receptor binding.

Clinical studies: In a number of small studies, kava was found to reduce anxiety scores when compared with placebo and was as effective as standard anxiolytics.

Side effects: Kava when ingested in large doses can lead to “kava dermopathy,” which causes a yellowing of the skin with flaking. This resolves with discontinuation of the herb. Oversedation has been reported in patients taking kava with alcohol and standard anxiolytic medications. There are several reports of extrapyramidal-like dystonic reactions with use of kava.

Drug interactions: Combined use of sedatives and alcohol should be avoided.

Use in pregnancy and lactation is contraindicated.

**Valerian Root**

Uses: Valerian root has been used for centuries as a sedative agent and sleep aid. Recently, it has been mainly used as an aid for insomnia and jet lag. It also is used for migraine headaches, fatigue, and even intestinal cramps.

Mechanism of action: As with kava, it is felt that valerian root has effects on GABA receptors, leading to its sedative effects.

Clinical studies: Several human trials confirm a mild sedative effect. Few studies exist regarding the anxiolytic effects of valerian root in vivo.

Side effects: Side effects may include headache, excitability, uneasiness, and cardiac disturbances.

Drug interactions: Care should be exercised when combining valerian root with other sedative agents and alcohol.

Use in pregnancy and lactation is contraindicated.

**Chamomile**

Uses: Chamomile has been used historically for GI discomfort, peptic ulcer disease, pediatric colic, and mild anxiety.

Mechanism of action: It is felt that chamomile may act via binding to central benzodiazepine receptors.

Clinical studies: Several small human trials have noted chamomile to have hypnotic-sedative properties. However, none of these trials have been randomized or controlled.

Side effects: Chamomile is generally regarded as safe by the FDA as a spice, seasoning, or flavoring agent. Although several cases of significant allergic reactions to chamomile have been reported, no significant toxicity has been reported.

Drug interactions: No drug-herb interactions have been noted.

Use in pregnancy and lactation is contraindicated due to a lack of safety data.

**Herbs for Weight Loss**

**Ma Huang/Guarana**

Uses: The combination of Ma Huang and guarana is a popular formula in herbal weight-loss preparations.

Mechanism of action: This combination is based on the concept of thermogenesis, which has been noted to result in modest weight loss when combined with exercise and diet. Ma Huang (a source of ephedrine) and guarana (a source of caffeine) provide an herbal alternative to standard pharmaceutical weight-loss products. Ephedrine stimulates the metabolic rate via norepinephrine released from sympathetic nerve endings. This leads to both an anorectic effect and a thermogenic effect by increasing metabolism. The addition of caffeine to ephedrine appears to blunt the negative feedback control on the release of norepinephrine.

Clinical studies: Although a number of human trials support the concept of thermogenesis when combining ephedrine and caffeine, evidence suggests that 6 months of ephedrine/caffeine will result in the loss of approximately 7 pounds beyond a 1,000-kcal diet alone in a motivated obese patient.

Side effects: It is well known that Ma Huang and guarana have the potential to cause side effects that may be serious and have led to a number of reported deaths. Side effects may include increased blood pressure, palpitations, tachycardia, chest pain, coronary vasospasm, and even cardiomyopathy. Based on known side effects and minimal benefit, these products should not be recommended for use.

**Hydroxycitric Acid (Garcinia cambogia)**

Uses: Garcinia is marketed and touted as an herbal weight-loss product.

Mechanism of action: It is thought that hydroxycitric acid can increase fat oxidation by inhibiting citrate lyase, an enzyme that plays a crucial role in energy metabolism during de novo lipogenesis.

Clinical studies: Several clinical trials have shown no benefit to the use of this herbal over placebo.

Side effects: Side effects have been noted to be minor except at higher dosages leading to abdominal pain, vomiting and promotion of a laxative effect.

**Herbal Remedies for Sports Enhancement**
Although most supplements for athletic enhancement do not fall under the category of herbal remedies, there are several herbs that are popular among athletes.

**Yohimbe**

**Uses:** Yohimbe is derived from the bark of a West African tree *Pausinystalia yohimbe*. Historically, bark extract has been used as an aphrodisiac and when smoked can have hallucinogenic properties. Most recently, yohimbe has been touted as a body-building enhancer and as a “natural” Viagra.

**Mechanism of action:** Yohimbe is known to stimulate the release of norepinephrine, increasing cholinergic activity and decreasing adrenergic activity.

**Clinical studies:** Despite its widespread use, there are no objective data to support claims regarding its ability to stimulate muscle growth.

**Side effects:** Side effects may be numerous including agitation, tremors, insomnia, hypertension, tachycardia, nausea, and vomiting.

**Drug interactions:** Yohimbe should not be used in combination with tyrosine, antidepressants, sedatives, or amphetamines. Clonidine may reverse the effects of yohimbine.

**Ginseng (Panax Ginseng)**

**Uses:** Ginseng has been used for more than 2,000 years to strengthen both mental and physical capacity. Recently, ginseng has become popular as an “adaptogenic” (stress-protective) agent.

**Mechanism of action:** It is felt that ginseng may have effects on nitric oxide synthesis in endothelial tissue of lung, heart, and kidney. In addition, effects on serotonin and dopamine may also be responsible for its actions. Other effects may be related to activity on the hypothalamic-pituitary-adrenal system.

**Clinical studies:** Seven trials investigating ginseng’s effects on physical performance in young, active volunteers during cycle ergometer exercises have been noted. Four of these found no significant difference between placebo and ginseng. Three studies found a significant decrease in heart rate and an increase in maximal oxygen uptake in treated subjects.

**Side effects:** Adverse effects may include nervousness, insomnia, and GI disturbance associated with prolonged use. Ginseng use has led to mastalgia and vaginal bleeding in some female patients due to estrogen-like effects.

**Drug interactions:** Ginseng may interact with oral anticoagulants, antiplatelet agents, corticosteroids, and hypoglycemic agents.

**Miscellaneous Herbal Remedies**

**Echinacea**

**Uses:** Echinacea has been used for centuries by Native Americans for aches, colds, and as an analgesic. It has become extremely popular as a natural immune booster for the common cold.

**Mechanism of action:** It is felt that Echinacea works by protecting the integrity of the hyaluronic acid matrix and by stimulating the alternate complement pathway. It also promotes nonspecific T-cell activation by binding to T-cells and increasing interferon production.

**Clinical studies:** A number of clinical trials have found that Echinacea reduces the duration of cold symptoms compared with placebo. In addition, several studies have noted that Echinacea does not prevent the flu.

**Side effects:** Adverse effects are usually mild and may include skin rash, GI upset, and diarrhea. Echinacea should not be used in patients with autoimmune illnesses or in patients with human immunodeficiency virus.

**Drug interactions:** Echinacea should not be used in patients on immunosuppressant medications.

**Feverfew**

**Uses:** Feverfew currently has become a very popular herbal remedy for prevention and treatment of migraine headaches. Historically, it has been used for upper respiratory tract infections, melancholy, and GI distress.

**Mechanism of action:** It is felt that feverfew inhibits prostaglandin, thromboxane, and leukotriene synthesis. It also reduces serotonin release from thrombocytes and polymorphonuclear leukocytes. Its mechanism of action for preventing migraine headaches is unknown.

**Clinical studies:** Two randomized trials showed benefit in use of feverfew for prevention of migraine. However, these studies did not address acute treatment of migraines.

**Side effects:** Adverse effects include occasional mouth ulcerations, contact dermatitis, dizziness, diarrhea, and heartburn.

**Drug interactions:** Feverfew may interact with anticoagulants and antiplatelet agents due to its platelet aggregation inhibition.

**Garlic**

**Uses:** Garlic has long been used as a medicinal agent. It has been used to increase physical strength and has been used as a topical antiseptic. In recent years, it has been mainly used as a natural cholesterol lowering agent.

**Mechanism of action:** It is thought to be active via sulfur-containing substances in garlic and may inhibit 3-hydroxy-3-methylglutaryl coenzyme A reductase.

**Clinical studies:** A number of small studies have noted modest reduction in total cholesterol level when compared with placebo. Several studies have, however, noted no reduction. These studies have been somewhat controversial because they may have used preparations lacking the active ingredients in fresh garlic.

**Side effects:** Although generally considered safe, garlic may cause some GI distress, including gas symptoms and skin irritation.

**Drug interactions:** Garlic does possess some antiplatelet activity and therefore should not be used in patients on anticoagulant medication.

**Use in pregnancy is contraindicated.**
CONCLUSION

It is clear that herbal remedies have both the potential for interactions with standard pharmaceutical agents and inherent toxicities. These negative attributes however should be tempered with the fact that in most cases, herbal remedies are safe when used in the appropriate settings. As more clinical data become available, patients stand to gain from the use of herbal remedies, particularly in the setting of mild illness in which stronger standard pharmaceuticals may not be necessary. Studies of cost-effectiveness will hopefully justify the use of these remedies because they are easily obtained by patients and in most cases are less expensive than standard medications.

With time, a number of herbal remedies will hopefully stand the test of scientific study and will add to the clinician’s existing armamentarium of medicinal agents available for use in treatment. Certainly, these agents require careful scrutiny and analysis. Those found to be toxic and not effective should be discarded. Herbal remedies hopefully will add to the overall care of patients and will enhance the practice of medicine.

WEB SITES

http://www.herbs.org/, Herb Research Foundation.

REFERENCES AND ADDITIONAL READINGS

Blumenthal M. Herb sales down 3% in mass market retail stores—sales in natural food stores still growing, but at lower rate. HerbalGram 2000;49:68.


Overview of College Health Issues

Lawrence S. Neinstein and Betty Anne Johnson

Close to 15 million students are currently enrolled in the nation’s 3,700 colleges and universities. About 57% of these students are in the 18- to 24-year-old age group. This makes colleges and universities critical settings for reducing important health-risk behaviors among many young adults.

College health is an expanding field that provides health care to approximately 10 million adolescents, young adults, and adults in the United States. A wide variety of college health centers are in North America, ranging from part-time nurses providing triage and referral to comprehensive ambulatory health centers that provide extensive health and preventive services to thousands of students. Although the entire field of college health is beyond the scope of this book, this chapter provides an overview of the following:

- A philosophy of college health
- The demographics of college health centers and users
- Statistics regarding morbidity and mortality in this population
- Information for providers to consider when sending their patients off to college
- Information for parents to consider when sending their children off to college
- Appropriate Web resources for college students and health care providers

There are also many reasons that college health may be important to pediatricians and other health care professionals serving adolescents and young adults:

1. Precollege examinations and care during college: Physicians are often asked to perform precollege examinations and help with facilitating care during college years.
2. Health care providers may be in communication with college health center staff regarding health care needs of the student.
3. Employment opportunities.
4. Collaborations between programs: There are often collaboration opportunities between either individuals or adolescent medicine programs and clinics and college health centers.
5. Insurance partners: The health center may often collaborate as insurance provider with university health care systems.
6. Referral site for tertiary care/hospitalization: The college health center may be a referral source for hospitalized patients or secondary and tertiary care consultations.
7. Teaching/research opportunities: There may be significant opportunities for both teaching and research.

PHILOSOPHY OF CARE

College health developed over the past 150 years for numerous reasons:

- A support system to maintain the student’s health for academic studies
- Concern about public health and communicable disease within a compact campus community, particularly before the advent of vaccines and antibiotics
• The need for assisting with the specialized medical needs of a heavily adolescent and young adult population
• Protecting the confidentiality of health care issues for young adults as they establish a new relationship with parents
• The need for access to care for the many uninsured in the college population

However, college health should be more than just the provision of quality medical services on a college or university campus. The best of college health encompasses the ability to assess students’ physical, emotional, and social health in the context of their cultural and academic influences. This model includes significant interactions with the campus community and includes the best of health promotion and prevention. In addition, this model of care is usually provided by a multidisciplinary team that includes medical, nursing, counseling, health promotion, and ancillary services staff. The Carnegie Foundation outlined college health as the caring intersection between health and education. It is a community with a shared vision and common cause … college health is developmentally appropriate, educationally effective, medically expert, accessible, and convenient.

Similar to the best of adolescent health care, college health involves treating the medical conditions while assessing and intervening with students’ behavioral and health risks. It may involve preventing illness in students who never visit the health center. College health is also about instilling healthy lifestyles in all students on campus. The best of college health follows this multidisciplinary prevention and community model that includes high-quality medical care, attention to psychosocial needs, involvement with campus community, a developmental approach, and health prevention. The campus involvement often overlaps academic life, residential life, student affairs, and health care.

Qualities of a college health program include the following:

1. Provision of primary care, including medical and counseling services that are more accessible than community services, specifically designed for students and accessible to all
2. Provision of services based on data about the health needs and risk behaviors of the population and that change in response to that information
3. Provision of a health center that is student centered and caring
4. Involvement of a multidisciplinary team and approach
5. Significant involvement in the university campus life and mission, including academic affairs, student affairs, and residential life
6. Health prevention and promotion as a significant component
7. Welcoming the diversity of students on a college campus
8. Active encouragement of student participation as health center advisors
9. Teaching students to become wise health care consumers, knowledgeable about accessing services in the health care delivery system
10. The use of prepayment to help maximize access to preventive and treatment care without financial barriers

The American College Health Association’s Guidelines for a College Health Program states that:

Although institutions differ in size and scope of services, there are universal concepts that impact upon the provision of health promotion, health protection, disease prevention, and clinical care to college students. Current sociological trends, high-risk identification, public health issues, health care finance reform, and changes in preventive medicine have broad institutional implications. College health programs have a unique opportunity to help meet those new challenges.

ENROLLMENT

There are approximately 4000 institutions of higher education in the United States, with approximately 15.3 million students in fall 2000, rising to about 17 million by the year 2009. (National Center for Education Statistics, 1999, and the Chronicle of Higher Education, 2001).

Gender

Approximately 43.6% are male and 56.4% female.

Full Time Versus Part Time

Approximately 58.7% are full time and 41.3% are part time.

Age Distribution (Fall, 2000)

<table>
<thead>
<tr>
<th>Age</th>
<th>Millions</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>15–17 years</td>
<td>0.153</td>
<td>1.0</td>
</tr>
<tr>
<td>18–19 years</td>
<td>3.596</td>
<td>23.5</td>
</tr>
<tr>
<td>20–21 years</td>
<td>3.170</td>
<td>20.7</td>
</tr>
<tr>
<td>22–24 years</td>
<td>2.679</td>
<td>17.5</td>
</tr>
<tr>
<td>25–29 years</td>
<td>1.960</td>
<td>12.8</td>
</tr>
<tr>
<td>30–34 years</td>
<td>1.240</td>
<td>8.1</td>
</tr>
<tr>
<td>&gt;35 years</td>
<td>2.511</td>
<td>16.4</td>
</tr>
</tbody>
</table>

Overall, 62.7% of enrolled students are 24 years or younger.

Race/Ethnicity (1999)


<table>
<thead>
<tr>
<th>College Enrollment by Racial Group</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>69.3</td>
</tr>
<tr>
<td>Black</td>
<td>11.1</td>
</tr>
<tr>
<td>Hispanic</td>
<td>8.9</td>
</tr>
<tr>
<td>Asian</td>
<td>6.2</td>
</tr>
<tr>
<td>American Indian</td>
<td>1.0</td>
</tr>
<tr>
<td>Foreign</td>
<td>3.5</td>
</tr>
</tbody>
</table>

High school graduates (1998): 2,810,000

<table>
<thead>
<tr>
<th>Race</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>81.0%</td>
</tr>
<tr>
<td>Black</td>
<td>14.0%</td>
</tr>
<tr>
<td>Hispanic</td>
<td>11.2%</td>
</tr>
</tbody>
</table>

(More than 100% because some individuals overlapped two categories.)

High school graduates enrolled in college as percent of graduates.
Total graduates: 1,844,000 (65.6%)

<table>
<thead>
<tr>
<th>Race</th>
<th>1998</th>
<th>1978</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>65.8%</td>
<td>50.1%</td>
</tr>
<tr>
<td>Black</td>
<td>62.1%</td>
<td>45.7%</td>
</tr>
<tr>
<td>Hispanic</td>
<td>47.5%</td>
<td>42.9%</td>
</tr>
</tbody>
</table>

Types of Universities

(Chronicle of Higher Education, 2001)

2000 Data 4,048 universities and colleges

Four year (57.7% with majority being private)

- Public 4-year institutions: 612
- Private 4-year institutions nonprofit: 1,531
- Private 4-year institutions for-profit: 192

Two year (42.3% with majority being public)

- Public 2-year institutions: 1,069
- Private 2-year institutions nonprofit: 164
- Private 2-year institutions for-profit: 480

Number of Colleges by Enrollment, Fall 1999

<table>
<thead>
<tr>
<th>Enrollment Range</th>
<th>All</th>
<th>Public</th>
<th>Private</th>
</tr>
</thead>
<tbody>
<tr>
<td>Under 200</td>
<td>47918</td>
<td>461</td>
<td></td>
</tr>
<tr>
<td>200–499</td>
<td>58857</td>
<td>531</td>
<td></td>
</tr>
<tr>
<td>500–999</td>
<td>526103</td>
<td>423</td>
<td></td>
</tr>
<tr>
<td>1,000 to 2,499</td>
<td>893438</td>
<td>546</td>
<td></td>
</tr>
<tr>
<td>2,500 to 4,999</td>
<td>613398</td>
<td>215</td>
<td></td>
</tr>
<tr>
<td>5,000 to 9,999</td>
<td>454365</td>
<td>89</td>
<td></td>
</tr>
<tr>
<td>10,000 to 19,999</td>
<td>276239</td>
<td>37</td>
<td></td>
</tr>
<tr>
<td>20,000 to 29,999</td>
<td>92</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>30,000 or more</td>
<td>36</td>
<td>34</td>
<td>2</td>
</tr>
</tbody>
</table>

Level of Student

About 86% of enrolled students in 2000 were undergraduate students

Undergraduate: 12,894,000/14,979,000 = 86%
Postbaccalaureate: 2,085,000/14,979,000 = 14%
First professional:298,000
Graduate students:1,787,000

(Chronicle of Higher Education, 2001)

Changing Student Profile

1. The enrollment of students who are 25 years old and over increased from 4.9 million in 1987 to an estimated 6.1 million in 1995, an increase of 25 percent. While the proportion of students 25 years and over increased from 38.0% in 1987 to 43.8% in 1995, this percent dropped in 2000 to 37.3% (National Center for Education Statistics and Chronicle of Higher Education, 2001).

2. Women played a major role in the increase of enrollment between 1982 and 1995. The enrollment of women in college increased from 6.4 million in 1982 to 8.44 million in 2000, representing an average annual growth rate of 1.5%, for a 32% increase over the period (Chronicle of Higher Education 2001, and National Center for Education Statistics).

3. After several years of stagnation, the number of international college students coming to the United States was back up (5.1% in 1998). The number of international students has increased from 407,529 in 1990–1991 to 516,400 in 1999.

4. Approximately 25% of students do not have health insurance coverage and it is estimated that another 18%–24% have inadequate insurance. Nationally, non-insurance rates rises rapidly with level of student from about 12% as freshman to almost 30% as seniors.

5. Increasing numbers of college students are on financial aid (College Board).

6. Enrollment as a percent of all 18–24 year olds has increased between 1990 and 1998 from 35.2% to 40.6% for white, non-Hispanics, from 25.3% to 29.6% for African-Americans and from 16.2% to 20.4% for Hispanic students (National Center for Education Statistics).

By far the majority (80%) of college students attend campuses that have some organized arrangement for advancing their health (Patrick, 1988). Nationally, there are approximately 1,500–1,650 college health centers. There are about 10 million students making as many as 30 million visits per year at an approximate cost of $1.4 billion dollars. In addition, about 5%–25% of these students use the counseling center.

MORBIDITY AND MORTALITY

Data regarding morbidity and mortality are less available on college students than other populations. There are some overall data available from the youth risk behavior surveillance: National College Health Risk Behavior Survey (NCHRBS)—United States, 1995. These data have not been repeated. National data are also available on drug use from several studies, including Monitoring the Future Study (since 1975), Core Alcohol and Drug Survey (since 1989), the College Alcohol Study (Wechsler, 1993, 1997, 1999), and the Cooperative Institutional Research Program (CIRP) Freshman Survey.

Some overall trends found in the CIRP Freshman Survey have included the following:

- Tobacco use: Up since 1987, 20-year high
- Alcohol use: Decline in 1980s and 1990s
- Mental health: Perceived mental health dropped in past 10 years:
  - “Overwhelmed” 1985 (16%) 1995 (25.3%)
  - “Depressed” 1985 (8.2%) 1995 (9.7%)

Sexually Transmitted Infections

College populations are generally unnamed in overall reports on sexually transmitted infections (STIs). There are no random frequency studies that have been performed in this population. In general, national STI studies focus on adolescents and homeless and incarcerated youth. Students often do not recognize the risks and availability of treatment for most STIs.

Chlamydia

Although there are no randomized frequency studies on college campuses, the overall prevalence appears to be falling. One college health center reported a rate of
more than 9% in 1990, falling to just more than 3% by 1994.

1995 National College Health Risk Behavior Survey

The largest nationally representative data sample of health risks in college students comes from the Centers for Disease Control and Prevention (CDC) 1995 NCHRBS. This survey involved 74 two-year and 74 four-year institutions, including 4,609 undergraduate students. The questions were similar to those of the youth risk behavioral survey (YRBS) used in adolescents. The survey involved 96 questions in six areas: injuries, tobacco, alcohol/drugs, STIs and unintended pregnancy, dietary behaviors, and physical inactivity.

Demographics of Respondents

- 63.6% age 18–24 years
- 55.5% female
- 72.8% white, 10.3% black, 7.1% Hispanic
- 69.4% never married
- 50% work 1–39 hours and 22.9% >40 hours
- 68.2% full-time students
- 9.8% sorority or fraternity members

2000 Spring National College Health Assessment (NCHA)

Because the CDC has not continued the NCHRBS, the American College Health Association (ACHA) began conducting national surveys in the spring of 2000. The 2000 data set results (shown here) include 28 schools that chose randomly selected students (N = 16,024). Although students were randomized on these campuses, the overall included universities and colleges were not chosen on a random or selected basis. The schools included 1 two-year school and 27 four-year institutions. Twenty of the schools were public and eight private. In terms of size, eight were more than 20,000; ten were between 10,000 and 19,999; seven were between 5,000 and 9,999; and three were less than 5,000. The ethnicity of the students was 68.2% white, 7.5% African-American, 8.7% Hispanic, 10.6% Asian, 1% Indian, and 3.2% other. International students were 6.3% of responding students. The data used here are from prepublication data courtesy of the ACHA (Victor Leino, private communication).

1995 National College Health Risk Behavior Survey Summary

- Many college students were involved in activities that place them at health risks.
- Binge drinking: One third (34.5%) of college students reported episodic heavy drinking during the 30 days preceding the survey. In addition one third binge drink and drink and drive; 27.4% reported drinking alcohol and driving during the 30 days preceding the survey; and 30.5% of students who had gone boating or swimming during the 12 months preceding the survey had drunk alcohol while boating or swimming.
- Students in the Greek system had a much higher prevalence of drinking and alcohol-related problems.
- High-prevalence tobacco use with almost one third (29.0%) current cigarette smokers.
- High failure to protect against STIs and pregnancy. Only 29.6% of students who had sexual intercourse during the 3 months preceding the survey used a condom at last sexual intercourse.
- 20% were overweight.
- Female students in particular were at risk for eating disorders and history of being forced to have sexual intercourse (one in five [20.4%] female college students were forced to have sexual intercourse during their lifetime).
- Few students had engaged in vigorous (37.6%) or moderate (19.5%) physical activity at recommended levels.

The 2000 NCHA data included data supporting similar concerns.

Some national statistics are encouraging, including the following:

- The number of drinking and driving deaths is falling.
- Students are using condoms more frequently.
- STI rates are lower than they were 5 years ago.
- Violent crime rate is down; campuses safer than city streets.

INJURIES

Unintentional injuries

1995 NCHRBS

- 9.2% rarely or never used a seat belt (compared with 21.7% for high school seniors).
- 34% rarely or never wore motorcycle helmets (43.8% for high school).
- 27.4% drank alcohol and have driven a car in past 30 days (38.8% for high school).
- 30.5% drank alcohol while boating or swimming.

2000 NCHA data

- 5.1% rarely or never used a seat belt.
- 75.5% rarely or never wore bicycle helmets (of riders).
- 85% rarely or never wore helmets when inline skating (of skaters).
- 34% rarely or never wore motorcycle helmet (of riders).
- 30.3% drank alcohol and drove a car in past 30 days.

Intentional injuries

1995 NCHRBS

<table>
<thead>
<tr>
<th>Carried Weapon</th>
<th>Carried Gun</th>
<th>Fights/Forced to Have Intercourse</th>
</tr>
</thead>
<tbody>
<tr>
<td>8%</td>
<td>2.9%</td>
<td>10.2%/13.1%</td>
</tr>
</tbody>
</table>

2000 NCHA data

- 6.6% were involved in fights (11.7% in males and 3.2% in females).
- 5.0% were involved in attempted or completed rape (8.7% females, 2.4% males).

Suicide

1995 NCHRBS

<table>
<thead>
<tr>
<th>Gender/Age</th>
<th>Seriously Considered</th>
<th>Made Plan</th>
<th>Attempted Suicide</th>
</tr>
</thead>
</table>
Female 10.8% 6.3% 1.3%
Male 9.7% 7.2% 1.7%
18–24 years 11.4% 7.9% 1.7%
³25 years 8.3% 4.6% 1.0%

Although this is considerably lower than the high school adolescent population, in which almost 12% of female adolescents and 5.6% of boys have attempted suicide, the rates are still significant.

2000 NCHA data

<table>
<thead>
<tr>
<th>Suicidal Ideation</th>
<th>Suicide Attempt</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total 9.5%</td>
<td>1.5%</td>
</tr>
<tr>
<td>Female 10.0%</td>
<td>1.4%</td>
</tr>
<tr>
<td>Male 8.7%</td>
<td>1.6%</td>
</tr>
</tbody>
</table>

Of the group, 44.5% stated that they were depressed in the past year.

ALCOHOL, TOBACCO, AND OTHER DRUG USE

Monitoring the Future data for college students is available in Chapter 69 and also from Volume II of the National Survey Results on Drug Use, 1975–2000, Monitoring the Future (Johnston et al., 2001, http://www.monitoringthefuture.org/). This data examines both young adult high school graduates age 19–32 as well as college students. Trends noticed in the 2000 report include:

- American college students (2-year or 4-year) show annual usage rates similar to high school graduates their age including: any illicit drug, marijuana, inhalants, ecstasy (MDMA), and narcotics other than heroin. College students have lower rates than their age peers for: any illicit drug other than marijuana, hallucinogens, LSD, cocaine, crack cocaine, heroin, amphetamines, ice, barbiturates, and tranquilizers. College students have slightly higher use of hallucinogens other than LSD compared to their noncollege peers in 1999.
- In the first half of the 1990s, smoking rose some among college students and their same-age peers, although the increases were not as steep for either group as they were among high school seniors. But in 1998 and 1999, while smoking was declining among secondary school students at all grades, smoking increases significantly for college students. Between 1991 and 1999, the 30-day prevalence of cigarette smoking by college students rose from 23% to 31% and daily smoking rose from 14% to 19%. The year 2000 shows, for the first time in several years a decline in college student smoking.
- Alcohol use did not increase as use of other illicit drugs decreased among seniors from the late 1970s to the early 1990s. The opposite appears to be true. In the late 1990s, as illicit drug use leveled off in secondary schools and began a gradual decline, a similar trend was observed for alcohol.
- Cigarette smoking increased in college students beginning in 1995.
- Marijuana use (last year) in college students increased much more gradually (27% in 1991 to 34% in 2000) than in high school students in the 1990s and there was even less change in young adults who were not college students (24% in 1991 to 28% in 2000).
- Use of LSD among college students and young adults peaked in 1995 and declined in both groups through 2000.
- Between 1982 and 1992 amphetamine use declined among college students from 21% to 4%. Amphetamine use increased modestly among college students in the 1990s to 6.6% in 2000 (annual use) and the rates are about half those for 10th and 12th graders.
- MDMA (ecstasy) had a substantial increase in use in college students starting in 1995 and almost doubled in 2000 from 3.6% to 7.2% (annual use) and use of hallucinogens other than LSD compared to their noncollege peers in 1999.
- In general, the trends since 1980 in illicit substance use among American college students have paralleled those of their same peers of the same age not in college.

See Table 69.6 regarding trends in lifetime prevalence of various types of drugs among college students 1–4 years beyond high school and Figure 69.8 for trends in annual prevalence of use of alcohol, marijuana, and cocaine use by college students (from Monitoring the Future data).

Tobacco

1995 NCHRBS Tobacco use continues to be a major negative health behavior on college campuses.

<table>
<thead>
<tr>
<th>Gender/Age</th>
<th>Tobacco Lifetime Daily</th>
<th>Current Frequent (&gt;20–30 days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>33.4%</td>
<td>17.7%</td>
</tr>
<tr>
<td>Male</td>
<td>28.6%</td>
<td>14.9%</td>
</tr>
<tr>
<td>18–24 years</td>
<td>22.6%</td>
<td>13.5%</td>
</tr>
<tr>
<td>³25 years</td>
<td>47.0%</td>
<td>21.3%</td>
</tr>
</tbody>
</table>

2000 NCHA Data “Number of days of any cigarette use in past 30 days.”

<table>
<thead>
<tr>
<th>&gt;20 Days</th>
<th>1–19 Days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>11%</td>
</tr>
<tr>
<td>Female</td>
<td>11%</td>
</tr>
<tr>
<td>Male</td>
<td>15.5%</td>
</tr>
</tbody>
</table>

Interestingly, the perception of tobacco use rates of students was much higher.

“Typical student use at your school in past 30 days.”

Daily use (all respondents): 40.3%
Female respondents: 45.4%
Male respondents: 34.6%

Alcohol

1995 NCHRBS Data

<table>
<thead>
<tr>
<th>Alcohol/Episodic Heavy</th>
<th>Marijuana/Current</th>
</tr>
</thead>
<tbody>
<tr>
<td>College</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>27.0%</td>
</tr>
<tr>
<td>Male</td>
<td>43.6%</td>
</tr>
<tr>
<td>18–24 years</td>
<td>41.5%</td>
</tr>
<tr>
<td>³25 years</td>
<td>22.0%</td>
</tr>
</tbody>
</table>

2000 NCHA Data “How many days did you consume any alcohol in past 30 days?”

<table>
<thead>
<tr>
<th>10 Days</th>
<th>1–9 Days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>16.4%</td>
</tr>
<tr>
<td>Female</td>
<td>13.3%</td>
</tr>
<tr>
<td>Male</td>
<td>21.5%</td>
</tr>
</tbody>
</table>


**Student Perceptions**

“Typical student use of alcohol at your school in past 30 days.”

**Percent Responding Daily**

<table>
<thead>
<tr>
<th></th>
<th>Total respondents</th>
<th>Female respondents</th>
<th>Male respondents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Binge Drinking (Five Drinks or More at a Sitting in Past 2 Weeks)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Frequency</th>
<th>Total</th>
<th>Female</th>
<th>Male</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>62%</td>
<td>67.4%</td>
<td>52.4%</td>
</tr>
<tr>
<td>1–3 times</td>
<td>27.4%</td>
<td>25.5%</td>
<td>31.4%</td>
</tr>
<tr>
<td>4–6 times</td>
<td>8.2%</td>
<td>5.6%</td>
<td>12.1%</td>
</tr>
<tr>
<td>7–8 times</td>
<td>1.4%</td>
<td>0.8%</td>
<td>2.5%</td>
</tr>
<tr>
<td>&gt;=9 times</td>
<td>1.0%</td>
<td>0.5%</td>
<td>1.7%</td>
</tr>
</tbody>
</table>

**Consequences of Drinking in Past School Year**

- 13% had an injury to self.
- 3.3% injured another person.
- 28.7% did something they later regretted.
- 1.5% were involved in forced sexual activity by someone else.
- 12.5% were involved in unprotected sexual activity.

**College Students: Who Drinks?** Evidence suggests that the highest number of binge drinkers are in fraternities and sororities (Fig. 85.1).

**Marijuana Use**

**2000 NCHA**

“How many days did you use marijuana in past 30 days?”

<table>
<thead>
<tr>
<th></th>
<th>³10 Days</th>
<th>1–9 Days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>5.1%</td>
<td>9.8%</td>
</tr>
<tr>
<td>Female</td>
<td>3.8%</td>
<td>9.2%</td>
</tr>
<tr>
<td>Male</td>
<td>6.7%</td>
<td>10.9%</td>
</tr>
</tbody>
</table>

**Sexual Behaviors**
1995 NCHRBS College students:

<table>
<thead>
<tr>
<th></th>
<th>Ever Had Intercourse</th>
<th>%Six Partners</th>
<th>Condom Used at Last Sexual Intercourse</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>87.8%</td>
<td>31.8%</td>
<td>25.8%</td>
</tr>
<tr>
<td>Male</td>
<td>84.0%</td>
<td>37.8%</td>
<td>35.2%</td>
</tr>
<tr>
<td>18–24 years</td>
<td>79.5%</td>
<td>25.7%</td>
<td>37.7%</td>
</tr>
<tr>
<td>≥25 years</td>
<td>97.8%</td>
<td>49.6%</td>
<td>18.5%</td>
</tr>
</tbody>
</table>

For comparison, presented below are the 1995 YRBS data for high school students:

<table>
<thead>
<tr>
<th>Grade</th>
<th>Ever Had Intercourse</th>
<th>%Four Partners</th>
<th>Condom Used At Last Sexual Intercourse</th>
</tr>
</thead>
<tbody>
<tr>
<td>9th grade</td>
<td>36.9%</td>
<td>12.9%</td>
<td>62.9%</td>
</tr>
<tr>
<td>12th grade</td>
<td>66.4%</td>
<td>22.9%</td>
<td>49.5%</td>
</tr>
</tbody>
</table>

Of interest is the higher use of a condom at last sexual intercourse among high school students, compared with college students.

2000 NCHA Data

Prevalence of Intercourse and Condom Use at Last Sexual Intercourse

<table>
<thead>
<tr>
<th></th>
<th>Ever Had Vaginal Intercourse</th>
<th>Ever Had Anal Intercourse</th>
<th>Ever Had Oral Intercourse</th>
<th>Condom Used At Last Sexual Intercourse</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>71.3%</td>
<td>21.8%</td>
<td>75.2%</td>
<td>32.4%</td>
</tr>
<tr>
<td>Female</td>
<td>71.9%</td>
<td>20.5%</td>
<td>75.3%</td>
<td>31%</td>
</tr>
<tr>
<td>Male</td>
<td>69.7%</td>
<td>23.3%</td>
<td>75.2%</td>
<td>34.6%</td>
</tr>
</tbody>
</table>

Number of Partners (Vaginal, Oral, Anal Intercourse)

<table>
<thead>
<tr>
<th></th>
<th>None</th>
<th>1</th>
<th>2–5</th>
<th>%≥</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>27.6%</td>
<td>48.0%</td>
<td>21.1%</td>
<td>3.3%</td>
</tr>
<tr>
<td>Female</td>
<td>27.0%</td>
<td>51.4%</td>
<td>19.8%</td>
<td>1.8%</td>
</tr>
<tr>
<td>Male</td>
<td>28.5%</td>
<td>42.9%</td>
<td>23.1%</td>
<td>5.5%</td>
</tr>
</tbody>
</table>

Student Perceptions on Number of Partners “Typical student at your school has had sex (oral, anal, vaginal) with how many partners in past year?”

None: 2.7%
1–5: 88.1%
≥: 9.2%

Sex With Same or Both Sexes

Gay/Bi (Past Year)

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>2.4%</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>3.7%</td>
<td></td>
</tr>
</tbody>
</table>

Emergency Contraception Use and Unintended Pregnancies—Past Year

<table>
<thead>
<tr>
<th>Used Emergency Contraception</th>
<th>Unintended Pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>4.6%</td>
</tr>
<tr>
<td>Female</td>
<td>4.7%</td>
</tr>
<tr>
<td>Male</td>
<td>4.3%</td>
</tr>
</tbody>
</table>

Nonconsensual Intercourse

1995 NCHRBS

<table>
<thead>
<tr>
<th>Age</th>
<th>Female</th>
<th>Male</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>18–24 years</td>
<td>17.0%</td>
<td>3.6%</td>
<td>10.6%</td>
</tr>
<tr>
<td>≥25 years</td>
<td>25.5%</td>
<td>4.8%</td>
<td>17.5%</td>
</tr>
</tbody>
</table>

Forced nonconsensual intercourse occurring when older than 19 years:

<table>
<thead>
<tr>
<th>Age</th>
<th>Female</th>
<th>Male</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>19–24 years</td>
<td>2.4%</td>
<td>0.7%</td>
<td>1.6%</td>
</tr>
<tr>
<td>≥25 years</td>
<td>11.0%</td>
<td>1.1%</td>
<td>7.2%</td>
</tr>
</tbody>
</table>

2000 NCHA Data (Past School Year)

<table>
<thead>
<tr>
<th>Touched Against Will</th>
<th>Attempted/Completed Rape</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>5.0%</td>
</tr>
<tr>
<td>Female</td>
<td>6.7%</td>
</tr>
<tr>
<td>Male</td>
<td>2.4%</td>
</tr>
</tbody>
</table>

DIETARY BEHAVIORS

1995 NCHRBS

<table>
<thead>
<tr>
<th>Gender</th>
<th>Dieted to Lose</th>
<th>Exercised to Lose</th>
<th>Purged to Lose</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Overweight/Weight</td>
<td>Weight</td>
<td></td>
</tr>
<tr>
<td>College</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>20.2%</td>
<td>42.1%</td>
<td>62.6%</td>
</tr>
<tr>
<td>Male</td>
<td>29.9%</td>
<td>16.7%</td>
<td>42.3%</td>
</tr>
</tbody>
</table>

|        |                  |        |                  |
|        |                  |        | 4.2%             |
|        |                  |        | 0.8%             |
2000 NCHA Data

“In the past 30 days, to lose weight you...”

<table>
<thead>
<tr>
<th>Dieted</th>
<th>Exercised</th>
<th>Purged</th>
<th>Used Diet Pills</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>26.2%</td>
<td>49.7%</td>
<td>2%</td>
</tr>
<tr>
<td>Females</td>
<td>34.4%</td>
<td>58%</td>
<td>7.1%</td>
</tr>
<tr>
<td>Males</td>
<td>13.9%</td>
<td>37.9%</td>
<td>0.5%</td>
</tr>
</tbody>
</table>

PHYSICAL ACTIVITY BEHAVIORS

1995 NCHRBS

<table>
<thead>
<tr>
<th></th>
<th>Vigorous</th>
<th>Moderate</th>
</tr>
</thead>
<tbody>
<tr>
<td>College</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>43.7%</td>
<td>19.7%</td>
</tr>
<tr>
<td>Female</td>
<td>33.0%</td>
<td>19.3%</td>
</tr>
</tbody>
</table>

PREVENTATIVE HEALTH CARE

2000 NCHA Data

Hepatitis B vaccination 56%
Meningococcal vaccination 24%
Chickenpox vaccination 48%
Flu immunization last year 26.5%
Dental examination last year 77%
Testicular self-examination last month 27.2%
Self-breast examination last month 40.8%
Gynecological examination last year 60.9%
Cholesterol check in past 5 years 45.3%

HEALTH PROBLEMS

<table>
<thead>
<tr>
<th></th>
<th>Ever Had Last Year</th>
<th>Ever Diagnosed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Back pain</td>
<td>44.9%</td>
<td>21.2%</td>
</tr>
<tr>
<td>Sinus infection</td>
<td>26.5%</td>
<td>32.5%</td>
</tr>
<tr>
<td>Depression</td>
<td>16.4%</td>
<td>9.9%</td>
</tr>
<tr>
<td>Strep infection</td>
<td>14.5%</td>
<td>35%</td>
</tr>
<tr>
<td>Ear infection</td>
<td>10.5%</td>
<td>29.3%</td>
</tr>
<tr>
<td>Asthma</td>
<td>9.9%</td>
<td>15.1%</td>
</tr>
<tr>
<td>Bronchitis</td>
<td>9.2%</td>
<td>19.9%</td>
</tr>
<tr>
<td>Anxiety</td>
<td>6.8%</td>
<td>4.4%</td>
</tr>
<tr>
<td>Carpal tunnel</td>
<td>5.9%</td>
<td>4.8%</td>
</tr>
<tr>
<td>Fracture</td>
<td>5.1%</td>
<td>19.0%</td>
</tr>
<tr>
<td>Seasonal affective disorder</td>
<td>4.5%</td>
<td>1.5%</td>
</tr>
<tr>
<td>High blood pressure</td>
<td>3.4%</td>
<td>3.6%</td>
</tr>
<tr>
<td>Chronic fatigue</td>
<td>3.1%</td>
<td>1.2%</td>
</tr>
<tr>
<td>High cholesterol</td>
<td>3.1%</td>
<td>4.6%</td>
</tr>
<tr>
<td>Substance abuse</td>
<td>2.8%</td>
<td>1.6%</td>
</tr>
<tr>
<td>Mumps</td>
<td>2.1%</td>
<td>8.1%</td>
</tr>
<tr>
<td>Bulimia</td>
<td>1.8%</td>
<td>1.6%</td>
</tr>
<tr>
<td>Anorexia</td>
<td>1.4%</td>
<td>1.9%</td>
</tr>
<tr>
<td>Genital warts</td>
<td>1.4%</td>
<td>2.4%</td>
</tr>
<tr>
<td>Genital herpes</td>
<td>1.0%</td>
<td>1.2%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>0.9%</td>
<td>0.9%</td>
</tr>
<tr>
<td>Chlamydia</td>
<td>0.8%</td>
<td>2.0%</td>
</tr>
<tr>
<td>Pelvic inflammatory disease</td>
<td>0.7%</td>
<td>1.1%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Ever Had Last Year</th>
<th>Ever Diagnosed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gonorrhea</td>
<td>0.4%</td>
<td>0.7%</td>
</tr>
<tr>
<td>Hepatitis B or C</td>
<td>0.4%</td>
<td>0.8%</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>0.4%</td>
<td>1.1%</td>
</tr>
<tr>
<td>Human immunodeficiency virus</td>
<td>0.2%</td>
<td>0.3%</td>
</tr>
</tbody>
</table>

The second column may have some totals that are less than those in the first column, because the first column queried possible self-perceptions and the second queried about diagnosis.

HEALTH ACADEMIC CONSEQUENCES

Lower grade in class or dropped class secondary to the following problems (past year):

<table>
<thead>
<tr>
<th></th>
<th>Ever Had Last Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stress</td>
<td>8.5%</td>
</tr>
<tr>
<td>Depression</td>
<td>5.1%</td>
</tr>
<tr>
<td>Sleep problem</td>
<td>4.6%</td>
</tr>
<tr>
<td>Family concerns</td>
<td>3.9%</td>
</tr>
<tr>
<td>Flu/cold</td>
<td>2.7%</td>
</tr>
<tr>
<td>Alcohol</td>
<td>2.1%</td>
</tr>
<tr>
<td>Internet</td>
<td>2.1%</td>
</tr>
<tr>
<td>Injury</td>
<td>1.1%</td>
</tr>
<tr>
<td>Learning disorder</td>
<td>1.1%</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>0.9%</td>
</tr>
<tr>
<td>Drug use</td>
<td>0.9%</td>
</tr>
<tr>
<td>Chronic illness</td>
<td>0.7%</td>
</tr>
<tr>
<td>Eating disorder</td>
<td>0.5%</td>
</tr>
<tr>
<td>Sexual assault</td>
<td>0.4%</td>
</tr>
</tbody>
</table>

The second column may have some totals that are less than those in the first column, because the first column queried possible self-perceptions and the second queried about diagnosis.
### BELIEVABILITY AND SOURCE OF HEALTH INFORMATION OF COLLEGE STUDENTS

<table>
<thead>
<tr>
<th>Health Promotion and Prevention (HPPS)</th>
<th>Believe</th>
<th>Use as Source of Information</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>88.9%</td>
<td>47.3%</td>
</tr>
<tr>
<td>Medical staff</td>
<td>88.3%</td>
<td>54%</td>
</tr>
<tr>
<td>Leaflets</td>
<td>69.9%</td>
<td>63%</td>
</tr>
<tr>
<td>Parents</td>
<td>69.7%</td>
<td>71.2%</td>
</tr>
<tr>
<td>Faculty</td>
<td>59.5%</td>
<td>32.2%</td>
</tr>
<tr>
<td>Campus newspaper</td>
<td>48.3%</td>
<td>34%</td>
</tr>
<tr>
<td>Peer educators</td>
<td>43%</td>
<td>16.9%</td>
</tr>
<tr>
<td>Magazines</td>
<td>33.7%</td>
<td>60%</td>
</tr>
<tr>
<td>Residential advisors</td>
<td>33%</td>
<td>15.8%</td>
</tr>
<tr>
<td>Religious center</td>
<td>33.3%</td>
<td>14.2%</td>
</tr>
<tr>
<td>Friends</td>
<td>26%</td>
<td>60.5%</td>
</tr>
<tr>
<td>Internet</td>
<td>24.4%</td>
<td>46.3%</td>
</tr>
<tr>
<td>Television</td>
<td>21.7%</td>
<td>52.1%</td>
</tr>
</tbody>
</table>

It appears that health center staff have high believability by students but are used only by about 50% of students for their health information. At the same time, 60% of students use friends for their health information but only 26% believe them. Television and the Internet are also ranked low on believability but are used by about half of students.

### TYPES OF HEALTH PROBLEMS

Health problems facing college health centers include the following:

1. **Acute medical problems:** Primary care including minor infections (Epstein-Barr virus, genitourinary tract infections, upper respiratory tract infections, and acute gastroenteritis), musculoskeletal injuries, minor trauma, and skin problems. Occasionally, some of the infections become life threatening such as meningitis and tuberculosis. Reproductive issues are common, including the diagnosis and treatment of STIs, contraception, emergency contraception, routine gynecology and men's health care, unintended pregnancies.

2. **Chronic medical problems:** Many college health centers care for the multitude of college students with chronic medical conditions, including asthma, diabetes, seizure disorders, thyroid disorders, hypertension, hyperlipidemia, eating disorders, and malignancies. In addition, certain malignancies such as Hodgkin disease, melanoma, testicular neoplasms, leukemia, and primary bone cancer have incidence rates in this age group that are increased compared with those of other age groups.

3. **Mental health issues:** Many college students are under increased stress and the following are frequent on college campuses: stress-related symptoms, eating disorders, anxiety, depression, suicidality, chronic fatigue, and other disorders.

4. **Substance abuse:** Diagnosis and treatment

5. **Screening programs for STIs**

6. **Immunization programs**

7. **Tuberculosis screening**

8. **Routine screening for other health risks including smoking and hyperlipidemia**

9. **Campus-wide risk-reduction activities and health promotion including reducing unsafe sexual behaviors, alcohol use, and tobacco use**

### Trends

Some trends that appear to be occurring among college students include (data may not be available) the following:

- More students are entering college with chronic disease such as asthma, diabetes, physical disabilities, and mental health disorders.
- More students are traveling abroad.
- More students are interested in herbal and complementary medicine interventions.
- Fewer universities have overnight infirmaries to care for students not sick enough to be in a hospital.

### Challenges

With the many changes in the health care field, there are numerous challenges facing the college health center of the 21st century. Some of these include the following:

1. **Stability of finances:** In a 1991 survey of 400 colleges
   a. 85% funding prepaid (46% general fees and 39% a designated health fee)
   b. 5% service fees
   c. 10% grants and donations

   However, as funding becomes tighter on university campuses, health centers will need to continue to explore alternative, cost-effective funding mechanisms.

2. **Continued national accreditation of services**

3. **Continued integration into campus and academic life**

4. **Improved information technology:** Students comprise one of the largest groups with high-speed access to Internet information. They are also a group that expects communication via this modality. Health centers will need to adapt to these changes and use this technology for communication regarding appointments, laboratory results, medical care, and health education. In a review of electronic communication by college health centers with students Neinstein (2000) found that 64% of health centers used electronic communication with patients and 27% used e-mail to give out medical advice. Other uses included giving out laboratory test results, making appointments, and communicating insurance issues.

5. **Improved health facilities:** Many student health center facilities are old, outdated, and need replacement. This is often not a top priority on a college campus.

6. **Strong supplemental insurance policies:** Another critical issue among college students is coverage for health care, particularly beyond what a student health center can cover. Approximately 20%–33% of the 19–24-year-old age group are uninsured or underinsured. In addition, coverage may not extend outside the local area. It is critical that health centers explore adequate coverage opportunities for students and that students and their parents strongly consider insurance options during college years. Important questions to explore include the following:
   - What are the deductibles and copayments and what is the maximum lifetime coverage?
   - What coverage is provided when the student is out of school during winter and summer breaks?
   - Does the coverage include items such as contraception, immunizations, mental health, and substance abuse?

### THE PRECOLLEGE VISIT

#### Information for Providers to Consider when Sending Their Patients off to College

The precollege visit marks the beginning of the transition for the adolescent from health care that has largely been supervised by the parent to health care that is a personal responsibility. There are various concepts of what might be included in this visit. Stashwick (1997) describes a comprehensive visit as that intended to update the medical history, perform a complete physical examination, screen for health risk behaviors, update immunizations, and provide counseling and education. Time constraints and prematriculation health requirements of the university may alter the nature and focus of this visit.

**Prematriculation Requirements** Most universities require certain immunizations and tuberculosis screening, and others will have a health form that must be completed before the student arrives on the campus. The parental expectations for this visit then will be to have these prematriculation requirements met so the
college-bound student may register for classes.

**Health History** Health risk behaviors are important to consider before the adolescent leaves for college. Screening questions should cover the following:

- Eating disorders
- Tobacco use
- Alcohol and other potential substances of abuse including anabolic steroids
- Sexual behaviors
- Emotions that indicate depression or risk of suicide
- History of emotional, physical, or sexual abuse
- Learning or school problems
- Risk factors for tuberculosis

Given the time constraints of the visit, the provider may elect to do the screening history by questionnaire. The major drawback to this approach is that the adolescent will most likely be accompanied by a parent, and given the sensitivity of the questions that need to be asked, the adolescent may not feel comfortable responding openly. Alternative approaches include having the adolescent complete the questionnaire in an examination room or having the provider ask the questions directly once the parent has left the room.

An example of comprehensive screening questions on these topics can be found in the NCHA survey, which is posted on the ACHA Web site (at [http://www.acha.org/](http://www.acha.org/)). Table 85.1 gives examples of a simplified version of these questions. Another potential source for screening questions is the National Health and Nutrition Examination Survey created by the National Center for Health Statistics and available at the CDC Web site (at [http://www.cdc.gov/](http://www.cdc.gov/)). Figure 85.2 is a screening form given to students at the University of Southern California on the first visit.

### TABLE 85.1. Examples of screening questions

| Examination | If a complete physical examination has been completed in the past 3 years, the assessment during the precollege visit may be limited to determination of the height, weight, and blood pressure, as well as performance of a focused physical examination based on problems uncovered in the screening history. For the sexually active female, a pelvic examination with Papnicolaou (Pap) smear and testing for STIs is indicated. If the college-bound student presents for a preparticipation sports physical, a more comprehensive physical assessment is necessary and the reader is referred to excellent summaries on this topic (Smith, 1997). |

| The Body Mass Index | The body mass index (BMI) is helpful in assessing whether the adolescent is underweight or overweight. A simplified calculation of BMI, along with its classification has been published by the National Heart, Lung, and Blood Institute Obesity Education Initiative. To estimate BMI, multiply the adolescent's weight (in pounds) by 703 and divide by the height (in inches) squared. This approximate BMI can then be classified as in Table 85.2. Under-weight individuals may have anorexia nervosa and further screening should be performed. Weight-loss counseling should be provided for those individuals whose BMI is ≥25 kg/m². |

| TABLE 85.2. Classification for body mass index |

<table>
<thead>
<tr>
<th>Classification</th>
<th>Body mass index</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight</td>
<td>&lt;18.5 kg/m²</td>
</tr>
<tr>
<td>Normal weight</td>
<td>18.5 to 24.9 kg/m²</td>
</tr>
<tr>
<td>Overweight</td>
<td>25 to 29.9 kg/m²</td>
</tr>
<tr>
<td>Obesity (class 1)</td>
<td>30 to 34.9 kg/m²</td>
</tr>
<tr>
<td>Obesity (class 2)</td>
<td>35 to 39.9 kg/m²</td>
</tr>
<tr>
<td>Extreme obesity (class 3)</td>
<td>≥40 kg/m²</td>
</tr>
</tbody>
</table>


### TABLE 85.3A. Blood pressure levels for the 90th and 95th percentiles of blood pressure for girls age 16 and 17 years by percentiles of height
### TABLE 85.3B. Blood pressure levels for the 90th and 95th percentiles of blood pressure for boys age 16 and 17 years by percentiles of height

#### Diagnostic Testing

Diagnostic testing during the precollege visit is limited.

1. **Cholesterol** The Expert Panel on Blood Cholesterol Levels of Children and Adolescents recommends that adolescents whose parents have a serum cholesterol of more than 240 mg/dL and adolescents older than 19 years should be screened for total blood cholesterol level (nonfasting) at least once. If the parental cholesterol level is unknown or if the adolescent has other risk factors for future cardiovascular disease (e.g., smoking, hypertension, obesity, diabetes mellitus, excessive consumption of dietary saturated fats, and cholesterol), then ordering a screening serum cholesterol level (nonfasting) is also reasonable.

2. **STI Screening** Screening tests for chlamydia, gonorrhea, syphilis, and/or HIV should be based on risk factors. A Pap smear should be obtained annually on all sexually active females.

3. **Tuberculosis Screening** A skin test for tuberculosis should be placed only if there are risk factors for tuberculosis exposure (CDC, 2000). The major risk factor for exposure to tuberculosis in the college-bound population is birth in a tuberculosis-endemic country. The ACHA guidelines indicate that students should undergo tuberculin skin testing if they have arrived within the past 5 years from countries except those on the following list:

   - American region:
     - Canada
     - Jamaica
     - Saint Kitts and Nevis
     - Saint Lucia
     - United States of America
     - Virgin Islands (United States)

   - European region:
     - Belgium
     - Denmark
     - Finland
     - France
     - Germany
     - Greece
     - Iceland
     - Ireland
     - Italy
     - Liechtenstein
     - Luxembourg
     - Malta
     - Monaco
     - Netherlands
     - Norway
     - San Marino
     - Sweden
     - Switzerland
     - United Kingdom

   - Western Pacific region:
     - American Samoa
     - Australia
     - New Zealand

   Other risk factors for tuberculosis that would prompt a skin test include HIV infection, injection drug use, and clinical conditions such as diabetes, chronic renal failure, cancer, low body weight, gastrectomy, chronic malabsorption syndromes, prolonged corticosteroid therapy, or other immunosuppressive disorders. Also at risk are those who have lived in, worked in, or volunteered in high-risk congregate settings such as prisons, nursing homes, hospitals, residential facilities for patients with acquired immunodeficiency syndrome, or homeless shelters. Guidelines for interpretation of the skin test can be found in the CDC's core curriculum on tuberculosis, which is available at state health departments or at the CDC Web site (at [http://www.cdc.gov/](http://www.cdc.gov/)). Individuals with positive skin test results should have a chest radiograph. If the chest radiograph is negative and there are no contraindications to preventive therapy, isoniazid should be prescribed daily for 9 months.

4. **Immunizations** Most colleges and universities mandate proof of certain immunizations before arrival on campus. Although the ACHA (2000) gives guidelines for institutional prematriculation immunizations, the institution may vary these requirements as mandated by state law or otherwise. Therefore, to minimize disruption in the enrollment process, the health history form provided to the college-bound student by the college or university should be consulted. If proof of immunization cannot be obtained, then titers demonstrating immunity may often be substituted. An alternative is to reinmunize. Many colleges are now requiring or strongly recommending immunization against varicella and hepatitis B. These inoculations may be begun at the precollege visit and either completed before leaving for college or after arriving on campus.
Meningococcal Vaccination A new recommendation by the ACHA and the CDC's Advisory Committee on Immunization Practices (ACIP) is to provide information to students and parents about meningococcal disease and the meningococcal vaccine (ACIP, 2000). College freshmen living in dormitories or residence halls are at moderate increased risk of meningococcal disease (4.6 per 100,000) relative to other persons their age who are not attending college (1.4 per 100,000). Vaccination with the meningococcal polysaccharide vaccine will decrease the risk for meningococcal disease in these individuals but efficacy is less than 100% against serogroups C, Y, W-135, and A. It will confer no protection against serogroup B disease, and should an outbreak of meningococcal disease occur on campus, even those who have been vaccinated should seek medical attention. The vaccination costs about $75, insurance coverage is variable, and it should be repeated every 3 to 5 years during the years of risk.

Health Guidance

The remainder of the precollege visit should be devoted to the provision of health guidance information. Selected information, based on responses to the screening questionnaire, may be discussed during the office visit and additional information may be given out via handouts or brochures. The American Academy of Pediatrics publishes a brochure entitled “Health Care for College Students,” which covers recommendations for sleep, nutrition, exercise, responsible sexual activity including abstinence, responsible drinking including abstinence, common health problems, mental health, and safety on campus. The ACHA publishes a multitude of brochures on many of these topics as well.

For the adolescent with chronic medical conditions, an attempt should be made to arrange for transition of care, either to the health care providers in the college health service or to community providers near the college or university. The parent should sign a release of information (for the minor child) and a copy of the medical record, or an introductory letter summarizing the medical history should be sent to the new provider.

Information for Parents to Consider when Sending Their Children off to College

Available College Health Center Services and Costs

The college-bound student and parents should ask for information about the college health service. Campus health services vary from large, multispecialty centers providing all outpatient primary care, specialty, and diagnostic services to those that provide only rudimentary first aid. In general, however, college health services provide high-quality, low-cost accessible primary care and health education services. Parents and students should determine what services are available and what the student health fee (if any) covers.

After-hours Care

Information about provision of after-hours care and emergency services, pharmacy services, and the location of the referral hospital should be obtained and the information kept in an accessible location.

Health Insurance

Most colleges have no facilities such as infirmaries for overnight stays. Parents should ensure that the college-bound student has adequate health insurance to cover hospitalization and emergency, specialty, and diagnostic health services. It is estimated that currently 25% to 30% of college students are uninsured. An unexpected medical bill can interrupt or terminate a college career, and it is strongly recommended that students not go without adequate health insurance. Many campuses sponsor a group health insurance plan for students at reasonable rates. Parents should check the following:

1. Benefits: It is wise to explore the benefits of any and all plans to determine prescription drug policies, whether there are in-network providers in the college area, and the basics about out-of-network coverage, particularly as it concerns access to emergency care and hospitalization.
2. Insurance card: The student should be advised to carry a copy of his or her health insurance card at all times and have the name and phone number of the primary care provider.

Consent and Confidentiality

1. Minor Consent: If the college-bound student will be an unemancipated minor child on arrival on campus, the parent should sign a generic “consent for treatment” and forward this to the college health service. Many institutions provide this statement on their prematriculation health history form. The parent should be aware that certain disorders or conditions may be treated without parental consent, even if the student is an unemancipated minor. These may include diagnosis and treatment of STIs, contraception, pregnancy, and family planning, mental health or emotional disturbance, and/or substance abuse.
2. Alcohol Use: As of 1998, federal law permits, but does not require, colleges and universities to notify parents any time a student younger than 21 years violates drug or alcohol laws. Many institutions have since adopted a policy of mandatory parental notification if a student is found to be involved in risky or illegal behavior such as underage drinking, public drunkenness, drugs, or criminal activity. Because colleges and universities vary in their approach to this issue, the parent should become familiar with the policies on their child's campus.
3. Confidentiality: Once the student is age 18 years, he or she is considered an adult. At this point, the college health service will adopt a policy of strict confidentiality regarding medical records and medical information. Medical information will not be released to anyone (even the parent who is paying the tuition and fees) without the student’s written consent or a court order. This new approach to confidentiality often causes anguish and frustration on the part of the parent but is essential if the student is to engage openly in a professional relationship with the health care provider. Furthermore, confidentiality is essential if the college health service is to assist the student in assuming increasing responsibility for personal health care. Counseling services on campus will adopt the same policy of strict confidentiality.

Personal Health Information

The parent should ensure that the student is knowledgeable about his or her personal health information.

1. Medications: The student should have a list of all medications, dosages, and frequency of dosage and should be aware of why the medication was prescribed.
2. Allergies: The student should be aware of all allergies to medications, foods, and others, and should have some knowledge of the type of reaction (e.g., hives, rash, trouble breathing, and shock).
3. Family medical history: The student should be aware of important family medical history and should keep this current.
4. Prior health problems and records: If the student has a prior history of a chronic or significant medical or psychiatric condition, make sure a copy of these records is sent to the student health service or counseling service.

First Aid Supplies

Every student should have basic health care supplies and equipment to deal with minor illnesses and injuries.

1. First aid kit
   a. Bandages
   b. Antibiotic ointment
   c. Elastic wrap such as an Ace wrap
   d. Liquid soap
   e. 2 x 2 gauze pads
   f. Acetaminophen
   g. Ibuprofen
   h. Pepifo-Bismol
   i. Cough and cold medicine
   j. Sore throat lozenges or throat spray
   k. Allergy medicine
   l. Electronic thermometer
   m. Ice pack or chemical cold pack

Guidance Regarding Transition

Parents should be aware that entering college marks a transition for the student that reaches far beyond merely leaving home. Parents will no longer be personally responsible for attending to the health care needs of their son or daughter. Rather, the student begins the process of learning...
self-care and good health practices. Parents can assist with this process by "letting go" and allowing students to engage in their own decision making. The campus health service will assist with this transition, by one-on-one counseling and education within the clinic and through programmed health promotion activities on campus. Through these combined efforts, the student will transition toward a state of optimal health, physically, emotionally, socially, intellectually, and spiritually.

WEB SITES

**Health Resources**


www.98six.com/homepage.php. Web site with articles written by students, %recent graduates, doctors, health care professionals, and college %professors.


**Organizations**


http://www.acha.org/. ACHA home page, including position papers.


http://www.edc.org/hec/. The U.S. Department of Education established the center to provide nationwide support for campus alcohol and other drug-prevention efforts.

**Health Centers**


**REFERENCES AND ADDITIONAL READINGS**


Neinstein L. Presentation to University of Southern California, Board of Trustees, 1997.


Stashwick CA. The pre-college visit: make the most of it. Intern Med 1997;August.


Appendix I
Reference Materials on Adolescence

GENERAL ADOLESCENT MEDICINE


**PSYCHOSOCIAL CONCERNS**


Bauman L. The ten most troublesome teen-age problems and how to solve them. Secaucus, NJ: Carol, 1997.


ADOLESCENT GYNECOLOGY


BOOKS FOR TEENS AND PARENTS


Eagan AB. Why am I so miserable if these are the best years of my life? Philadelphia: JB Lippincott, 1976.


Gaffney CR. Dr. Gaffney's coaching guide for better parents and stronger kids. Wilsonville, OR: BookPartners, 1997.


Harris SO. When growing up hurts too much: a parent's guide to knowing when and how to choose a therapist with your teenager. Lexington, MA: Lexington Books, 1990.


JOURNALS

Adolescence
Libra Publishers, 391 Willets Road, Roslyn Heights, NY 11577 (Quarterly journal of current research in areas of social work and psychology.)

Adolescent and Pediatric Gynecology
Springer-Verlag, 175 Fifth Avenue, New York, NY 10010 (Official quarterly publication of the North American Society for Pediatric and Adolescent Gynecology.)

Archives of Pediatrics and Adolescent Medicine
American Medical Association

Journal of Adolescent Health
Elsevier Science Publishing Co., 655 Avenue of the Americas, New York, NY 10010

Journal of Adolescent Research
Sage Publications, Inc., 2455 Teller Road, Newbury Park, CA 91320, 805-499-0721 (Official publication of the Society for Research on Adolescence.)

Journal of American College Health
Heldref Publications, 4000 Albemarle Street, NW, Washington, DC 20016 (Journal dedicated to the exchange of information related to health care issues in community colleges, colleges, and universities.)

Journal of Youth and Adolescence
Plenum Publishing Corp., 233 Spring Street, New York, NY 10013 (Multidisciplinary quarterly research journal.)
Appendix II
Other Resources and Services

GENERAL RESOURCES AND SERVICES

The Center for Early Adolescence, School of Medicine, University of North Carolina at Chapel Hill, D-2 Carr Mill Town Center, Carrboro, NC 27510; 919-966-1148. (Offers bibliographies and booklets on many areas concerning young adolescents, such as community services, parenting, and sexuality.)

Available from the center:

- Understanding Early Adolescence: A Framework, by J. P. Hill
- Understanding Families With Young Adolescents, by L. D. Steinberg
- Schools for Young Adolescents: Adapting the Early Childhood Model, by S. Feeney

Resource Lists

- "Adolescent Literature"
- "Community Resources"
- "Early Adolescence"
- "Educating Young Adolescents"
- "Parenting"
- "Religion"
- "Sex Education"

ABORTION SERVICES

Check telephone listings under

- Clergy counseling service
- National Abortion Federation Hotline: 800-772-9100
- National Organization for Women
- Planned Parenthood

COUNSELING SERVICES

Check telephone listings under

- Family Services Association
- County department of health
- Counseling clinics
- Mental health clinics
- United Fund

HOTLINE SERVICES

Centers for Disease Control and Prevention (CDC)

- Acquired Immunodeficiency Syndrome (AIDS) Hotline: 800-342-2347 (24 hours, 7 days)
- Spanish: 800-344-7432 (8 a.m. to 2 a.m., Eastern time, 7 days)
- TTY: 800-243-7889 (Monday through Friday, 10 a.m. to 10 p.m., Eastern time)

Teens AIDS: 800-440-8336 (staffed by teens for teens; Fridays and Saturdays, 6 p.m. to midnight, Eastern time)
- Teens TAP (Teaching AIDS Prevention), an AIDS information line for teens (not a crisis line): 800-234-8336 (Monday through Friday, 4 p.m. to 6 p.m., Central Standard time)
- Gay and Lesbian Youth Hotline (not a crisis line): 800-347-8336 (Thursday through Saturday, 7 p.m. to 11:45 p.m., Eastern time)
- National Runaway Switchboard Hotline (for youth or parents: 800-621-4000 24) (24 hours)
- Adolescent Crisis Intervention and Counseling (the "nine" line): 800-999-9999 (24 hours, 7 days)
- Hit Home, a national youth crisis line for suicide, abuse, pregnancy, depression, counseling, and intervention: 800-448-4663 (24 hours, 7 days)
- National Child Abuse Hotline, for suspected child abuse reports and for referrals: 800-422-4453 (24 hours, 7 days)
- National Herpes Hotline: 919-361-8488 (Monday through Friday 9 a.m. to 7 p.m., Eastern time)
- STD Hotline: 800-227-8922 (Monday through Friday, 8 a.m. to 11 p.m., Eastern time)

Check local operator or directory for hotlines listed under

- Crisis counseling
- Counseling
- Drug abuse
- Rape
- Runaways
Suicide

Information also available from

National Clearinghouse for Mental Health Information, 5600 Fishers Lane Road, Rockville, MD 20857; 301-433-4515

See also "Adolescent Clinics" section later in this appendix

ALCOHOL AND DRUG PROBLEMS

Books

Schalter JA. Addiction is a choice. Chicago: Open Court, 2000.

Organizations

Al-Anon Family Group Headquarters

1600 Corporate Landing Parkway, Virginia Beach, VA 23454-5617; 8884AL-ANON

Alcohol and Drug Helpline

800-821-4357 (Provides referrals to local facilities where adolescents and adults can seek help for alcohol and drug problems.)

Alcohol Hotline

800-252-6465 (800-ALCOHOL)

Alcoholics Anonymous

PO Box 459, Grand Central Station, New York, NY 10163; 212-870-3400; or check local office

American Council on Alcoholism

800-527-5344 (Provides treatment referrals, counseling, and advice for alcoholics and their families and friends.)

Boys Clubs of America

771 First Avenue, New York, NY 10017; 212-557-7755

Cocaine Anonymous

National Referral Information line (not a hotline): 800-347-8998
World Service Office: 310-559-5833
National Cocaine Hotline: 800-262-2463 (800-COCAINE)

Narcotics Anonymous

PO Box 9999, Van Nuys, CA 91409; 818-773-9999; Fax: 818-700-0700
SEXUALITY

Books
Park JM, Card JJ, Muller KL. Just the facts: what science has found out about teenage sexuality and pregnancy in the U.S. San Jose: Sociometrics Corporation, 1998.

Organizations
AIDS Information Line, CDC, National Human Immunodeficiency Virus (HIV) and AIDS Hotline
800-342-AIDS

American Social Health Association
PO Box 13827, Research Triangle Park, NC 27709; 919-361-8400

Center for Population Options
1025 Vermont Avenue, NW, suite 210, Washington, DC 20005; 202-347-5700

International Planned Parenthood Federation, Western Hemisphere Regional Office
120 Wall Street, 9th floor, New York, NY 10005-3092; 212-248-6400

National Family Planning and Reproductive Health Association
1627 K Street, NW, 12th floor, Washington, DC 20006; 202-293-3114

National Sex and Drug Forums
330 Ellis Street, San Francisco, CA 94102

Planned Parenthood-World Population
810 7th Avenue, New York, NY 10019; 800-230-7526

Sex Information and Education Council of the United States (SIECUS) (main office)
130 West 42nd Street, suite 350, New York, NY 10036-7802; 212-819-9770

Society for Adolescent Medicine (SAM)
1916 Copper Oaks Circle, Blue Springs, MO 64015; 816-224-8010

Sex Education Resources
Manuals Contact the following organizations for up-to-date educational manuals:

- Planned Parenthood, national and local
- Family Planning Federation
- Local school district
- National Clearinghouse for Family Planning Information, Rockville, MD
- U.S. Department of Health and Human Services (U.S. Government Printing Office)

Other Resources

Odin Books

1522 West Broadway, Vancouver, BC V6J 1W8; 800-223-6346 (Education resource lists available on education curricula and reference lists on topics such as self-esteem, attention deficit disorder, depression, child abuse, eating disorders, and teen pregnancy.)

ETR Associates

PO Box 1830, Santa Cruz, CA 95061-1830; 831-438-4060 (Many pamphlets and books on AIDS, family life, sexual abuse, sexuality, drug abuse prevention, and reproductive health.)

POPLINE (POPulation information onLINE)

Johns Hopkins University, Population Information Program, 111 Market Place, suite 310, Baltimore, MD 21202-4024; 410-659-6300

Online service: National Library of Medicine, Bethesda, MD; 800-638-8480 (for user ID and password) (Citations and abstracts to the worldwide literature on population and family planning.)

Planned Parenthood-World Population

810 7th Avenue, New York, NY 10019; 800-230-7526 (Many pamphlets, books, and videotapes on reproductive health care; also available is Current Literature in Family Planning, a monthly review of literature in family planning.)

Teenage Pregnancy

Books


Adolescent Clinics

Alabama

Adolescent Health Clinic

Department of Pediatrics

University of Alabama

1600 5th Avenue South

Birmingham, AL

35233, 205-939-9230

Arizona

Adolescent Clinic

Department of Pediatrics

University of Arizona

1501 North Campbell Avenue

Tucson, AZ 85724-5073

520-694-7432

Adolescent and Young Adult Clinic

Phoenix Indian Medical Center (serves only Native Americans)

Primary Care Medical Center

4212 North 16th Street

Phoenix, AZ 85016
California
UCLA Adolescent Medicine Clinic
UCLA
200 Medical Plaza, suite 265
Los Angeles, CA 90095
310-825-5603
Other UCLA sites include:
UCLA Adolescent Medicine Clinic
UCLA
11303 Washington Boulevard
Los Angeles, CA 90066
310-391-7043
UCLA Adolescent Medicine Clinic
UCLA
15200 Sunset Boulevard
Pacific Palisades, CA 90272
310-459-7736
Adolescent Clinic
Children's Health Clinic
4460 East Huntington Boulevard
Fresno, CA 93702
559-459-5664
Youth and Young Adult Clinic
Packard Children's Hospital, Stanford University
Division of Adolescent Medicine
750 Welch Road, #325
Palo Alto, CA 94304
650-725-8293
Adolescent Clinic
University of California Medical Center
400 Parnassus Avenue, 2nd floor
San Francisco, CA 94143
415-353-2002
Adolescent Clinic
University of California San Francisco
3333 California Street, suite 245
San Francisco, CA 94119
415-353-2026
Adolescent Clinic
Harbor-University of California at Los Angeles Medical Center
1000 West Carson Street
Torrance, CA 90090
310-222-2321
Adolescent Clinic
University of California at San Diego Medical Center
4168 Front Street
San Diego, CA 92103
619-543-7672
Adolescent Clinic
Stanford University
750 Welch Road, suite 325
Palo Alto, CA 94304
650-725-8293
Adolescent Clinic
Children's Hospital Los Angeles
5000 Sunset Boulevard, 4th floor
Los Angeles, CA 90027
323-669-2153
Adolescent Clinic
Oakland Children's Hospital
747 52nd Street
Oakland, CA 94609
510-528-2885
Adolescent Clinic
San Francisco General Hospital
1001 Potrero Avenue
San Francisco, CA 94110
415-206-8376
Colorado
Adolescent Clinic
The Children's Hospital
1056 East 19th Avenue, B025
Denver, CO 80218
303-861-6133
Eating Disorder Program
The Children's Hospital
1056 East 19th Avenue, B025
Denver, CO 80218
303-861-6133
Connecticut
Adolescent Clinic
Yale New Haven Hospital
789 Howard Street
New Haven, CT 06510
203-785-4644
Adolescent Clinic
Bridgeport Hospital
287 Grant Street
Bridgeport, CT 06610
203-384-3064
Department of Child and Adolescent Psychiatry
Mt. Sinai Hospital
500 Blue Hills Avenue
Hartford, CT 06112
860-714-2948
Adolescent Medicine
Fair Haven Clinic
374 Grand Avenue
New Haven, CT 06513
203-777-7411
Adolescent Medicine
St. Francis Hospital
1000 Asylum Avenue
Hartford, CT 06105
860-714-4789

Delaware
Adolescent Clinic
Christiana Hospital
551 West 14th Street
Wilmington, DE 19899
302-428-2622

District of Columbia
Adolescent Clinic
Walter Reed Army Medical Center
Georgia Avenue and 16th Street
Washington, DC 20007-5001
202-782-6107
Adolescent Clinic
Walter Reed Army Medical Center
8901 Wisconsin Avenue
Bethesda, MD 20889
301-295-4902
Adolescent Clinic
Children's National Medical Center
111 Michigan Avenue, NW
Washington, DC 20010
202-884-2178
Adolescent Clinic
Howard University Hospital
2041 Georgia Avenue, NW
Washington, DC 20060
202-865-1401
Pediatrics
Georgetown University
Children's Medical Center
3800 Reservoir Road, NW
Washington, DC 20007
202-687-KIDS

Hawaii
Adolescent and Young Adult Clinic
Tripler Army Medical Center
1 Jarrett White Road
Tripler AMC, HI 96859
808-433-4165
Adolescent Clinic
Kapiolani Children's Medical Center
1319 Punahou Street
Honolulu, HI
808-983-8394

Illinois
Adolescent Clinic
Rush Presbyterian Hospital
1645 West Jackson Boulevard, #315
Chicago, IL 60612-3227
312-942-6067
Adolescent Clinic
Cook County Hospital
1900 West Polk Street, #112
Chicago, IL 60612
312-633-7438
Adolescent Clinic
Department of Pediatrics
Loyola University
2160 South First Avenue
Maywood, IL 60153
708-327-9119

Indiana
Adolescent Clinic
Riley Outpatient Parking Garage
575 North West Drive, #707
Indianapolis, IN 46202
317-913-8812
Wishard Hospital Adolescent Community Clinics
Wishard Primary Care
1002 Wishard Boulevard, 2nd floor
Indianapolis, IN 46202
317-692-2363
Blackburn Health Center
2700 Martin Luther King Drive
Indianapolis, IN 46208
317-931-4300

Cottage Corners Health Center
1434 South Shelby Street
Indianapolis, IN 46203
317-655-3200

Grassy Creek Health Center
9443 East 38th Street
Indianapolis, IN 46236
317-890-2100

North Arlington Health Center
2505 North Arlington Avenue
Indianapolis, IN 46218
317-554-5200

Bellflower Clinic
1101 West 10th Street
Indianapolis, IN 46202
317-221-8300

Methodist Hospital Adolescent Clinics
1633 North Capital Avenue, suite 680
Indianapolis, IN 46202
317-929-3798

ACTION Center
3500 North Lafayette Road, suite 518
Indianapolis, IN 46222
317-554-2810

Iowa
Adolescent Clinic
University of Iowa Hospitals and Clinics
200 Hawkins Drive
Iowa City, IA 52242
319-356-2229

Kansas
Eating Disorders Program
(Eating disorders evaluations and treatment only).
The Menninger Clinic
5800 SW 6th Street
PO Box 829
Topeka, KS 66601
785-350-5000

Adolescent Clinic
University of Kansas Medical Center
6600 West 95th Street
Shawnee Mission, KS 66212
913-588-5908

Kentucky
Adolescent Clinic
Kosair Children's Hospital
231 East Chestnut Street
Louisville, KY 40202
502-629-6000

Louisiana
Adolescent Medicine
Department of Pediatrics
SL 37, Tulane Medical Center
1430 Tulane Avenue
New Orleans, LA 70112
504-584-2568

Maine
Teen and Young Adult Clinic at the Family Practice Clinic
695 Union Street, suite 12
Bangor, ME 04401
207-973-7979

Maryland
Adolescent Clinic
Montgomery County Health Department
401 Hungerford Drive
Rockville, MD 26850
240-777-3400

Adolescent Clinic
University of Maryland Hospital
655 West Lombard Street, suite 311
Baltimore, MD 21201
410-328-6495

Massachusetts
Adolescent Clinic
New England Medical Center
750 Washington Street
PO Box 351
Boston, MA 02111
617-636-1332

Adolescent Clinic
Boston Medical Center  
850 Harrison Avenue  
Boston, MA 02118  
617-414-4086  
Adolescent/Young Adult Practice  
Children's Hospital  
333 Longwood Avenue, 5th floor  
Boston, MA 02115  
617-355-7181

Adolescent Clinic  
Milford-Whitinsville Regional Hospital  
Vittori Marsell Young Women's Health  
14 Prospect  
Milford, MA 01754  
508-482-5444

Pediatric Clinic  
University of Massachusetts Memorial Health Center  
Benedict Building, 2nd floor  
55 Lake Avenue North  
Worcester, MA 01655  
508-856-5624

Adolescent Clinic  
Family Health and Social Services (Community Health Center)  
26 Queen Street  
Worcester, MA 01610  
508-880-7700

Michigan  
Teenage and Young Adult Health Program  
University of Michigan  
Brianwood Health Specialists  
325 Brianwood Circle, Building 5  
Ann Arbor, MI 48108  
734-647-9000  
[www.med.umich.edu/ahp](http://www.med.umich.edu/ahp)

Adolescent Medicine Clinic  
Children's Hospital of Michigan  
3901 Beaubien Boulevard  
Detroit, MI 48201  
313-745-4045

Adolescent Clinic  
Hurley Children's Clinic  
806 Tuuri Place  
Flint, MI 48503  
810-257-9773

Adolescent Medicine Program  
Department of Pediatrics/Human Development  
Michigan State University, College of Human Medicine  
B-240 Life Sciences  
East Lansing, MI 48824  
517-353-5042

Adolescent Clinic  
University Hospital University of Michigan  
1500 East Medical Center Drive  
Ann Arbor, MI 48109  
734-647-5580  
Internal Medicine Program  
University Hospital University of Michigan  
1500 East Medical Center Drive  
Ann Arbor, MI 48109  
734-936-5582

Minnesota  
Adolescent Health  
University of Minnesota Hospital and Clinic  
McNamara Center, 200 Oak Street, SE, suite 260  
Minneapolis, MN 55455  
612-626-2820

Mississippi  
Teen Medicine Center  
University of Mississippi Medical Center  
Department of Pediatrics  
2500 North State Street  
Jackson, MS 39216  
601-984-2925

Missouri  
Adolescent Clinic  
Children's Mercy Hospital  
2928 Main  
Kansas City, MO 64128  
816-234-3050

Nebraska  
Youth Village  
Children's Memorial Hospital  
88200 Dodge Street  
Omaha, NE 68114  
402-955-5400  
Omaha Children's Clinic  
12808 Augusta Avenue  
Omaha, NE 68144
Nevada
Adolescent Medicine
University of Nevada School of Medicine
Department of Pediatrics
2040 West Charleston Boulevard, #402
Las Vegas, NV 89102
702-671-2231
Teen Clinic
Washoe County District Health Department
PO Box 11130
Reno, NV 89520
775-328-2400

New Hampshire
Pediatric and Adolescent Clinic
Dartmouth–Hitchcock Medical Center
1 Medical Center Drive
Lebanon, NH 03756
603-650-5473

New Jersey
Adolescent Clinic
Monmouth Medical Center
300 2nd Avenue
Long Branch, NJ 07740
732-923-6702
Adolescent Clinic
University Medical Group
(University of Medicine and Dentistry of NJ–Robert Wood Johnson Medical School)
125 Paterson Street
New Brunswick, NJ 08903
732-235-7896
Adolescent Clinic
Morristown Memorial Hospital
Children's Medical Center
200 South Street
Morristown, NJ 07962
973-889-6350
http://www.teenhealthfx.com/

New Mexico
Adolescent Clinic
University of New Mexico
Health Sciences Center & University Hospital
ACC 3rd floor
2211 Lomas NE
Albuquerque, NM 87106
505-272-5551

New York
Adolescent Clinic
North Shore University Hospital
865 Northern Boulevard, suite 103
Great Neck, NY 11021
516-622-5075
Adolescent Medicine/Teen Health Services
Rochester General Hospital
1425 Portland Avenue
Rochester NY 14621
716-338-4050
www.viahelth.org/rgh/Pediatrics/Teen.htm
Jordan Health Center Teen Center
42 Holland Street
Rochester, NY 14605
716-423-2846
Threshold Center for Alternative Youth Services
80 St. Paul Street, 4th floor
Rochester, NY 14604
716-454-7530
Adolescent Clinic
Mount Sinai Medical Center
312 East 94th Street
New York, NY 10029
212-423-3000
Adolescent Clinic
The Door
555 Broome Street
New York, NY 10013
212-941-9090
Adolescent Clinic
Children's Hospital
601 Elmwood Avenue
PO Box 690
Rochester, NY 14642
716-275-2964
Adolescent Oncology
Roswell Park Cancer Institute
Calton and Elm Street
Buffalo, NY 14263
716-845-2333
Montefiore Hospital and Medical Center
Division of Adolescent Medicine
111 East 210th Street
The Bronx, NY 10467
718-920-4321
Schneider Children's Hospital of Long Island
Division of Adolescent Medicine
270-05 76th Avenue
New Hyde Park, NY 11040
516-465-3270
Brookdale Hospital and Medical Center
Division of Adolescent Medicine
Linden Boulevard at Brookdale Plaza
Brooklyn, NY 11212
718-240-5045
Adolescent Clinic
Coney Island Hospital
2601 Ocean Parkway
room 901
Brooklyn, NY 11235
718-616-3919
Adolescent Clinic
North Shore University Hospital
300 Community Drive
Manhasset, NY 11030
516-622-5075

North Carolina
Pediatric Ambulatory Care Center
University of North Carolina
CB No. 7735
Mason Farm Road
Chapel Hill, NC 27599-7735
919-966-6666
Duke Medical Center
Department of Pediatrics
4020 North Roxbro Road
Durham, NC 27710
919-620-5374

Ohio
Teen Health Center
Children's Hospital Medical Center
Division of Adolescent Medicine
3333 Burnet Avenue
Cincinnati, OH 45229
513-559-4681
Adolescent Clinic
Children's Hospital
555 South 18th Street
Columbus, OH 43205
614-722-2450
Lakewood Hospital Teen Health Center
15644 Madison Avenue, #108
Lakewood, OH 44107
216-391-5338
Adolescent and Young Adult Health Services
2222 Cherry Street, suite 2600
Toledo, OH 43608
419-251-8010
Pediatric Clinic
Metro Health Metro Center
2500 Metro Health Drive, 1st floor
Cleveland, OH 44109
216-778-2222
Pediatric and Adolescent Clinic
University Internal & Pediatric Clinic
222 Piedmont
Cincinnati, OH 45219
513-584-1000

Oklahoma
Adolescent Medicine
Children's Hospital of Oklahoma
940 N.E. 13th Street
room 4419
Oklahoma City, OK 73104
405-271-6208

Oregon
Adolescent and Young Adult Clinic
Doernbecher Children's Hospital
Oregon Health Sciences University
3181 SW Sam Jackson Park Road
Portland, OR 97201-3098
503-418-5700
Outside In Health Clinic (serves homeless and high risk youth)
1236 SW Salmon
Portland, OR 97205
503-223-4121

Pennsylvania
Adolescent Health Center
Children's Hospital of Pittsburgh
3705 Fifth Avenue
Pittsburgh, PA 15213
412-692-6677
Adolescent Clinic
Children's Hospital
34th Street & Civic Center Boulevard
Philadelphia, PA 19104
215-590-3537

Rhode Island
Adolescent Medicine
Rhode Island Hospital
Department of Pediatrics
APC-585-A, 593 Eddy Street
Providence, RI 02902
401-444-4712

Texas
The Center for Adolescent Health
People's Community Clinic
2909 N IH 35
Austin, TX 78722
512-478-4939
Adolescent Clinic
Children's Hospital
1935 Motor Street
Dallas, TX 75235
214-648-3563
Adolescent Medicine
Kids Place
6410 Fannin Boulevard, #500
Houston, TX 77030
713-704-0755
Adolescent Clinic
University of Texas-Houston
PO Box 20708
Houston, TX 77225-0708
713-500-5755
Adolescent and Sports Medicine
Texas Children's Hospital
6621 Fannin Boulevard, #740
Houston, TX 77030
832-824-3660
Adolescent Clinic
University of Texas
301 University Boulevard
Galveston, TX 77555
409-772-3630

Utah
Pediatric Clinic
University of Utah Hospital
50 North Medical Drive
Salt Lake City, UT 84132
801-581-2321

Virginia
Adolescent Health
Medical College of Virginia
307 College Street
Richmond, VA 23219
804-828-9449
Pediatric Endocrinology and Adolescent Medicine
Children's Hospital of the King's Daughters
601 Children's Lane
Norfolk, VA 23507
757-668-7816

Washington
Adolescent Clinic
University of Washington
Division of Adolescent Medicine
1959 NE Pacific Street
PO Box 354410
Seattle, WA 98105
206-543-8705
Adolescent Medicine
University of Washington
4800 Sand Point Way, NE
Seattle, WA 98105
206-526-2028
The Adolescent Center
13451 SE 38th Street
Bellevue, WA 98006
425-562-0640
The Kent Teen Clinic
613 West Gowe Street
Kent, WA 98042
206-296-7450
The Teen Pregnancy and Parenting Clinic
200 15th Avenue East
MS (CWB-F112)
Seattle, WA 98112
206-326-2656
The Renton Teen Clinic
275 Bronson Way NE, (RNT)
Renton, WA 98056-4099
425-254-2710

West Virginia
Pediatrics
West Virginia University
Department of Pediatrics
PO Box 9214
Morgantown, WV 26506-9214
304-293-1225

Wisconsin
Pediatric and Teen Clinic
University of Wisconsin Hospital and Clinics
600 Highland Avenue
Madison, Wi 53792-4116
608-263-9000
Adolescent Clinic
Children's Hospital
1020 North 12th Street
Milwaukee, Wi 53233
414-277-8900
Pedicatrics and Adolescent Clinic
Marshfield Clinic
1000 North Oak Avenue
Marshfield, WI 54449
800-335-5251
Pediatric and Adolescent Department
Beaumont Clinic LTD
1821 South Webster Avenue
Green Bay, WI 54301
920-496-4700

Canada
Adolescent Clinic
British Columbia Children's Hospital
4480 Oak Street
Vancouver, BC V6H3V4
604-875-2130
Adolescent Clinic
St. Justine Hospital
3175 Chemin Cote Ste.-Catherine
Montreal, Quebec H3T1C5
514-345-4722
Adolescent/Teen Clinic
Hospital for Sick Children
555 University Avenue
Toronto, Ontario M5G1X8
416-813-6804
Adolescent Medicine/Gynecology Program
Montreal Children's Hospital
Gilman Pavilion
1040 Atwater Street
Montreal, Quebec H3Z1X3
514-934-4461
Child and Adolescent Services
Allan Memorial Institute
Royal Victoria Hospital
3666 McTavish Street
Montreal, Quebec H4A3M6
514-843-1619

Sleep Disorder Resources
Alabama
Banner Regional Sleep Disorder Program
Good Samaritan Medical Center
1111 East McDowell Road
Phoenix, AZ 85006
602-239-3990

California
North Valley Sleep Disorders Center
11550 Indian Hills Road, suite 291
Mission Hills, CA 91345
818-361-0996
Sleep Disorders Center
University of California
Irvin Medical Center
101 City Drive, Route 23
Orange, CA 92868
714-456-5105
Stanford Sleep Disorders Clinic
401 Quarry Road, suite 3301-A
Stanford, CA 94305
650-725-5917
UCLA Sleep Disorders Center
University of California
Los Angeles, 24-221 CHS
Box 957069
Los Angeles, CA 90095-7069
Florida
Sleep Disorders Clinic
Mount Sinai Medical Center
4300 Alton Road
Miami Beach, FL 33140
305-674-2613

Illinois
Sleep Disorders Center
Northwest Memorial Hospital
200 East Huron
Galter 7th floor
Chicago, IL 60611
312-928-8120
Sleep Disorders Center
Rush Presbyterian–St. Luke's Medical Center
1653 West Congress Parkway, room 218 Rawson
Chicago, IL 60612
312-942-5440
Sleep Disorders Center
University of Chicago (TS-301)
5841 South Maryland MC 2091
Chicago, IL 60637
773-702-1762

Louisiana
Tulane Sleep Disorders Center
1415 Tulane Avenue
Box HC17
New Orleans, LA 70112
504-584-1657

Maryland
The Johns Hopkins Sleep Disorders Center
Asthma and Allergy Building
room 4B-50
5501 Hopkins Bay View Circle
Baltimore, MD 21224
410-550-0571

Massachusetts
Center for Pediatric Sleep Disorders
The Children's Hospital
300 Longwood Avenue
Honeywell 2
Boston, MA 02115
617-355-6000/6663/6242
Sleep Clinic
Brigham and Women's Hospital
Department of Psychiatry
221 Longwood Avenue
Boston, MA 02115
617-732-6753
Sleep Disorders Clinic
Tufts-Newton Wellesley Hospital
2014 Washington Street
Newton, MA 02462
617-243-6624
Sleep Disorder Center
University of Massachusetts Memorial
119 Belmont Street
Worcester, MA 01605
508-334-8191

Michigan
Sleep Disorders Clinic
Clara Ford Pavilion
2799 West Grand Boulevard
Detroit, MI 48202
313-876-4417

Minnesota
Minnesota Regional Sleep Disorders Center
Hennepin County Medical Center
#867B, 701 Park Avenue South
South Minneapolis, MN 55415
612-347-6288

New Hampshire
Sleep Disorders Center
Dartmouth–Hitchcock Medical Center
1 Medical Center Drive
Lebanon, NH 03756
603-650-7534

New York
Sleep Disorders Center
University Hospital
MR 120A
State University of New York at Stony Brook
Stony Brook, NY 11794-7139
514-444-2916
Sleep-Wake Disorders Center
Montefiore Medical Center
111 East 210th Street
The Bronx, NY 10467
718-920-4841

Oklahoma
Sleep Disorders Center
Presbyterian Hospital and Medical Center
700 NE 13th Street
Oklahoma City, OK 73104
405-271-6312

Pennsylvania
Sleep Evaluation Center
Western Psychiatric Institute and Clinic
3811 O'Hara Street
Pittsburgh, PA 15213-2593
412-624-2246
Sleep Research and Treatment Center
Milton S. Hershey Medical Center
PO Box 850
Hershey, PA 17033
717-531-8520

Tennessee
Sleep Disorders Center
Baptist Memorial Hospital
899 Madison Avenue
Memphis, TN 38146
901-861-9001

Texas
Sleep Disorders and Research Medicine
Baylor College of Medicine & VA Medical Center
2002 Holcombe Boulevard, room 6C344
Houston, TX 77030
713-794-7563

Organizations Involved In Adolescent Health
American Academy of Child and Adolescent Psychiatry
3615 Wisconsin Avenue, NW
Washington, DC 20016
202-966-7300
www.aacap.org/
American Academy of Family Physicians (AAFP)
11400 Tomahawk Creek Parkway
Leawood, KS 66211-2672
913-906-6000
www.aafp.org/
American Academy of Pediatrics
141 Northwest Point Boulevard
Elk Grove Village, IL 60007-1098
847-434-4000
www.aap.org/
American College Health Association
PO Box 28937
Baltimore, MD 21240-8937
410-859-1500
http://www.acha.org/
American College of Obstetricians and Gynecologists
Division of Program Services, Department of Adolescent Health Care
409 12th Street, SW
Washington, DC 20090-6920
202-863-2579
www.acog.org/
American College of Physicians
190 N. Independence Mall West
Philadelphia, PA 19106-1572
215-351-2600; 800-523-1546 ext. 1546
www.acponline.org/
American College of Preventive Medicine
1660 L. Street NW, suite 200
Washington, DC 20036
202-466-2044
www.acpm.org/
American Dietetic Association
216 West Jackson Boulevard, suite 800
Chicago, IL 60606-6995
213-899-0040
www.eatright.org/
American Medical Association (AMA)
Department of Adolescent Health
515 North State Street
Chicago, IL 60610
312-464-5000
www.ama-assn.org/
American Nurses’ Association
Council on Maternal-Child Nursing
2420 Pershing Road
Academy for Sports Dentistry
University of Iowa Hospitals and Clinics,
Department of Otolaryngology
Iowa City, IA 52242
www.sportsdentistry.com/academy.htm

American Academy of Orthopaedic Surgeons
6300 North River Road
Rosemont, IL 60018
708-823-7186
www.aaos.org/

American Academy of Pediatrics
141 Northwest Point
Elk Grove Village, IL 60007-1096
847-434-4000
http://www.aap.org/

American College Health Association
PO Box 28937
Baltimore, MD 21240-8937
410-859-1500
http://www.acha.org/

American College of Sports Medicine
401 W. Michigan Street
Indianapolis, IN 46202-3233
317-637-9200
www.acsm.org/

American Council on Exercise
5820 Oberlin Drive, suite 102
San Diego, CA 92121-3787
858-535-8227, 800-825-3636
www.acefitness.org/

American Heart Association
7272 Greenville Avenue
Dallas, TX 75231-4596
800-242-8721
www.americanheart.org/

American Medical Association (AMA)
Department of Adolescent Health
515 North State Street
Chicago, IL 60610
312-464-5000
www.ama-assn.org/

American Medical Society for Sports Medicine
11639 Earnshaw
Overland Park, KS 66210
913-327-1491
www.amssm.org/index.html

National Athletic Trainers Association
2952 Stemmons Freeway
Dallas, TX 75247
214-637-6282
www.nata.org/

National Collegiate Athletic Association
6201 College Boulevard
Overland Park, KS 66211-2422
913-339-1906
www.ncaaa.org/

President's Council on Physical Fitness and Sports
701 Pennsylvania Avenue, NW, suite 250
Washington, DC 20004
202-272-3421
**How to subscribe to SAM and College listserv groups**

1. To subscribe, send a message to listserv@uconnvm.uconn.edu. The message should only say subscribe SAM-L “your name” (e.g., subscribe SAM-L “Mary Jones”) if you do, everyone on the listserv message will receive your reply. Instead, note the sender’s e-mail address, and send a new message using that address only.

2. To unsubscribe, send a message (using the e-mail address to which you sent a subscribe message) saying only unsubscribe SAM-L.

**Tips on health Web searching**

1. On the Internet, you can find a wealth of information about adolescent medicine and general medical topics. This information is going rapidly. This section reviews the following:

   a. **SAM ListServe (SAM-L):** The SAM, through the auspices of the University of Connecticut, offers a listserv. Through this listserv, SAM members and other health care professionals interested in adolescent medicine and adolescents health issues can share ideas.

   - To subscribe to the SAM-L, you must have access to the Internet and an understanding of the use of electronic mail. To subscribe to this free communication dependent on the volume of posts to a particular listserv. It is recommended that users learn how to use the “trash” icon quickly.
   - When you are on the listserv, you may receive several to 50 or more e-mails per day depending on the volume of posts to a particular listserv. It is recommended that users learn how to use the “trash” icon quickly.
   - To receive responses to these questions, as well as in all the posts that are listed. A listserv is a wonderful way to be able to get information and ask questions—clinical, educational, research, or administrative. However, when you are on the listserv, you may receive several to 50 or more e-mails per day depending on the volume of posts to a particular listserv. It is recommended that users learn how to use the “trash” icon quickly.
   - To post a comment, send the message to SHS@LISTSERV.UTK.EDU. The message should only say subscribe SHS NAME (name is your personal name, not a user or e-mail name) to unsubscribe, use the previously given address, but message is unsubscribe SHS NAME.
   - To receive a list of who’s on the site, send a message to the address only. The message should be subscribe SHS NAME.
   - To post a comment, send the message to SHS@UTK.EDU (this message will be sent to all subscribers) Command to leave the list: SIGNOFF SHS.
   - To temporarily leave the list: SET SHS NOMAIL.
   - To sign back on the list: SET SHS MAIL.
   - Send mail to SHS@LISTSERV.UTK.EDU.
   - Address for any commands: LISTSERV@LISTSERV.UTK.EDU.
   - Access Archives of list: http://listserv.utk.edu/archives/shs.html

2. **Best sites to get statistical and other information**

   - **Statistical Abstract of the United States**
     - National Center for Educational Statistics (trend information)

   - **Monitoring the Future Web site on Drug Usage**

   - **Statistical Resources**
     - Alan Guttmacher Institute
     - CDC
     - National Institutes of Health

   - **WEB SITES**

   On the Internet, you can find a wealth of information about adolescent medicine and general medical topics. This information is going rapidly. This section reviews the following:

   1. How to subscribe to SAM and College listserv groups
   2. Tips on health Web searching
   3. Best sites for browsing
   4. Best sites to get statistical and other information

   1. **How to subscribe to SAM and College listserv groups.** A listserv is a group of individuals interested in an area who can post questions and comments and receive responses to these questions, as well as in all the posts that are listed. A listserv is a wonderful way to be able to get information and ask questions—clinical, educational, research, or administrative. However, when you are on the listserv, you may receive several to 50 or more e-mails per day depending on the volume of posts to a particular listserv. It is recommended that users learn how to use the “trash” icon quickly.

   a. **SAM ListServe (SAM-L):** The SAM, through the auspices of the University of Connecticut, offers a listserv. Through this listserv, SAM members and other health care professionals interested in adolescent medicine and adolescents health issues can share ideas.

   - To subscribe to the SAM-L, you must have access to the Internet and an understanding of the use of electronic mail. To subscribe to this free communication mode, you perform the following steps:
     - Send a message to listserv@uconnvm.uconn.edu. The message should only say subscribe SAM-L “your name” (e.g., subscribe SAM-L “Mary Jones”)
     - When you want to post to the ListServe, e-mail to sam-l@uconnvm.uconn.edu (this is an “L” not the number 1 after “sam”)
     - When you receive a ListServe message and you want to provide an answer and/or share your thoughts with the sender, do not click on the Reply button; if you do, everyone on the ListServe message will receive your reply. Instead, note the sender’s e-mail address, and send a new message using that address only.
   b. **College Health listserv**

   - To subscribe, send message to LISTSERVE@UTK.EDU. The message should be subscribe SHS NAME (name is your personal name, not a user or e-mail name)

   - To unsubscribe, use the previously given address, but message is unsubscribe SHS NAME.

   - To receive a list of who’s on the site, send a message to the address, with entire message being REVIEW SHS.

   - To post a comment, send the message to SHS@UTK.EDU (this message will be sent to all subscribers).

   - Command to leave the list: SIGNOFF SHS.

   - To temporarily leave the list: SET SHS NOMAIL.

   - To sign back on the list: SET SHS MAIL.

   - Send mail to SHS@LISTSERV.UTK.EDU.

   - Address for any commands: LISTSERV@LISTSERV.UTK.EDU.

   - Access Archives of list: http://listserv.utk.edu/archives/shs.html

   2. **Tips on health Web searching.** One can gain a wealth of information and data quickly utilizing a concise approach to searching the Web.

   a. **Web searching:** Some of the best Web search tools include http://www.google.com/ and http://www.yahoo.com. Google uses an approach that combines finding the keywords and the utilization pattern of the Web sites by users. In practice, this means that in most cases, the most useful sites are found early in the search. In addition to putting down the keyword, it is useful to add a second key word that may help refine the search. For example, you can search on gonorrhea. In fact, with the google search, the top two sites are a CDC and an NIH site on gonorrhea. If you want CDC information, you could narrow this search by placing both gonorrhea and CDC in the search area. With a Web search tool, you are likely to find hundreds of “hits.” Each hit is
usually titled, has a brief description, and has the Web address. These can be very helpful to glance at quickly to help you narrow which "hits" to explore. In health sites, the addresses often lead to either government sites, academic centers, commercial health sites, commercial product sites (pharmaceutical companies and others), and private health care provider sites. Looking at the address can help you determine if you want to explore that site or not. There are some important questions to ask yourself about each site:

- Is the advice provided by qualified trained medical professionals?
- How old is the information? Often a site can look great, but the information was last updated 3 or 4 years ago.
- Who pays for the site? Is this a commercial for-profit site?
- Do you need to register or provide personal information? Make sure you read the privacy information before giving out such information.
- Where do these links go to (as outlined previously).

b. Health portals: There are also some specific health finders and portals that can help in finding health information. These include the following:

- Patient-oriented overall health sites
  - Drug use
  - Clinical guidelines
  - Reproductive health
  - Best sites to get statistical and other information: Another important use for searching is obtaining data on various areas such as trends in reproductive health, morbidity and mortality and overall risks
- Nutrition
  - Best sites for browsing: In addition to the sites already listed, there are many other excellent sites for browsing. Many of these are listed in individual chapters of this book. Some highlights include the following:

  a. Reproductive health
     - [www.intellhealth.com/](http://www.intellhealth.com/): Site from Aetna Healthcare and Johns Hopkins University Hospital featuring information on common health problems.
     - [www.mayoclinic.org/](http://www.mayoclinic.org/): Other site of basic information that's written for the public from Mayo Clinic.
     - [www.goaskalice.columbia.edu/about.html](http://www.goaskalice.columbia.edu/about.html): College student-oriented site on many topics with questions and answers.
     - [www.talkinginflatrends.org](http://www.talkinginflatrends.org): Site from Kaiser Family Foundation to facilitate communication between parents and teens.
  
  b. Clinical guidelines

  c. Health prevention and promotion

  d. Nutrition
     - [www.health.gov/othic/Pubs/clearinghouse.htm](http://www.health.gov/othic/Pubs/clearinghouse.htm): List and links to all government clearinghouses.

  e. Patient-oriented overall health sites
     - [http://www.emedicine.com](http://www.emedicine.com): Medical textbook online
     - [http://www.cdc.gov](http://www.cdc.gov): A wealth of information from the CDC that includes searchable health information, fact sheets, Morbidity Mortality Weekly Reports, supplements, statistics, travelers health updates, and much more
     - [www.health.gov/othic/Pubs/clearinghouse.htm](http://www.health.gov/othic/Pubs/clearinghouse.htm): List and links to all government clearinghouses.

  f. Best sites for browsing: In addition to the sites already listed, there are many other excellent sites for browsing. Many of these are listed in individual chapters of this book. Some highlights include the following:

    a. Reproductive health
       - [www.reproline.jhu.edu](http://www.reproline.jhu.edu): Reproductive Health Online affiliated with Johns Hopkins University, promoting information on reproductive health issues.
       - [www.teenpregnancy.org](http://www.teenpregnancy.org): Information from the National Campaign to Prevent Teen Pregnancy, with information and data on teenage pregnancy.
       - [www.teamknow.org](http://www.teamknow.org): Teen awareness site on STDs from the American Social Health Association.
       - [www.4wom shielding.](http://www.4wom shielding.): National Women’s Health Information Center.

    b. Clinical guidelines

    c. Health prevention and promotion

    d. Nutrition
       - [www.health.gov/othic/Pubs/clearinghouse.htm](http://www.health.gov/othic/Pubs/clearinghouse.htm): List and links to all government clearinghouses.

4. Best sites to get statistical and other information: Another important use for searching is obtaining data on various areas such as trends in reproductive health, drug use, morbidity and mortality. The following sites can be useful for this:

   a. Morbidity and mortality and overall risks
      - [http://wonder.cdc.gov/chltnt/Convert/data/AdHoc.html](http://wonder.cdc.gov/chltnt/Convert/data/AdHoc.html): CDC: CDC WONDER Searches and Queries on general population data.
      - [www.cpc.unc.edu/ad/health/](http://www.cpc.unc.edu/ad/health/): Data from the National Longitudinal Study of Adolescent Health.
      - [www.childstats.gov/](http://www.childstats.gov/): This Web site offers easy access to federal and state statistics and reports on children and their families, including population and family characteristics, economic security, health, behavior and social environment, and education.
      - [www.cdc.gov/nicic/ncipcmhm.htm](http://www.cdc.gov/nicic/ncipcmhm.htm): Statistics and searching tool from the National Center for Injury Prevention and Control. Click on either data or facts for information.
      - [www.cdc.gov/nccdphp](http://www.cdc.gov/nccdphp): Statistics and information on chronic diseases from the National Center for Chronic Disease Prevention and Health Promotion.

   b. Reproductive health
      - [www.socio.com/data_arc/daapp_0.htm](http://www.socio.com/data_arc/daapp_0.htm): The Data Archive on Adolescent Pregnancy and Pregnancy Prevention.

   c. Drug use

   d. Nutrition