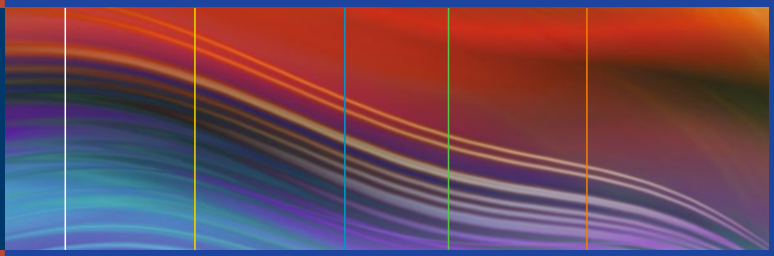
Mark A. Goldstein
Editor



The MassGeneral Hospital for Children Adolescent Medicine Handbook

Second Edition

Springer

The MassGeneral Hospital for Children Adolescent Medicine Handbook

Mark A. Goldstein
Editor

The MassGeneral Hospital for Children Adolescent Medicine Handbook

Second Edition

Springer

Editor
Mark A. Goldstein, MD
Division of Adolescent
and Young Adult Medicine
MassGeneral Hospital for Children
Harvard Medical School
Boston, MA, USA

ISBN 978-3-319-45777-2 ISBN 978-3-319-45778-9 (eBook)
DOI 10.1007/978-3-319-45778-9

Library of Congress Control Number: 2016955692

Printed on acid-free paper

This Springer imprint is published by Springer Nature
The registered company is Springer International Publishing AG
The registered company address is: Gewerbestrasse 11, 6330 Cham, Switzerland

Preface

Eight years ago, we decided to write a web-based handbook on adolescent medicine for the pediatric and medical residents at Massachusetts General Hospital as well as the Harvard Medical students who rotated through our service. Our decision was based in part on the numerous queries we received about adolescent medicine topics from the house staff. Subsequently the first edition of this handbook was printed, and it has been very well received nationally and internationally.

For the second edition, we have added new chapters as well as reviewed, revised, and updated the handbook and increased our contributors from 18 in the first edition to 33 in this edition. Our new chapters include an entry on hypertension in adolescents written by a pediatric nephrologist. In addition, a separate chapter on immunizations was developed, as there have been a number of changes in vaccine recommendations over the past several years. Members of the surgical service have authored a new chapter to review breast disorders. Because of increasing use of pre- and post-exposure prophylaxis medications for HIV, an infectious disease expert at Massachusetts General Hospital has written a new chapter on HIV in adolescents. Our final new chapter for this edition covers resilience and disease in adolescents, authored by the editor.

The handbook has three parts: general adolescent medicine, sexuality, and mental health. There is also an appendix with additional materials. References and additional readings are listed at the end of each chapter, and Web sites are interspersed among the content. Knowing that mental health and substance abuse competencies are goals recommended by the American Academy of

Pediatrics for primary care pediatricians, we have included an extensive section on each of these areas of learning. In addition, adolescents surface in the medical home asking for sexuality services, so we have included broad content for these important issues. We have made every effort to include practical materials useful for the primary care clinician realizing that these core areas of learning may not be addressed extensively in pediatric or internal medicine training programs.

Each of our outstanding authors represents expertise in pediatric or adult specialties. All authors have been trained at or are members of the staff of Massachusetts General Hospital. Except for neonatologists and geriatricians, any other medical or surgical specialist may see adolescents. While this handbook is aimed at clinicians who see a number of adolescents in their practices, it should be relevant to most clinicians.

Finally, to keep this edition a reasonable size, we have not intended that this handbook be a complete survey of all adolescent medicine topics. Rather, we have selected the content that we hope is relevant, practical, and user-friendly and cover those areas most often seen in the practice of adolescent medicine. We also have endeavored to develop a resource that addresses best practices in adolescent medicine where practice not only means the most appropriate approaches, diagnostic evaluations, and best treatments, but also the best ways to connect, communicate, and continue care with teenagers. After all, if the physician cannot develop a good relationship with an adolescent, the treatment and follow through will surely be compromised.

Boston, MA, USA
November 2016

Mark A. Goldstein, MD

Preface to the First Edition

Having been started in Boston by Dr. J. Roswell Gallagher in 1951, adolescent medicine is a relatively young specialty. Board certification was first offered in 1994. Many practitioners consider adolescent medicine to include ages 12–21 years, although exceptions are made at both ends of the age spectrum. Unique to this specialty is the emergence and completion of puberty, and all of the developmental tasks and events that may give rise to problems.

In adolescent medicine, there are strong links and interrelationships between developing physical bodies, emerging intellect, and social adaptations. As a result, the biopsychosocial aspects of each teen should be considered. For example, delayed puberty may affect academic achievement, and together these problems may lead to behavioral issues. During adolescence, the first manifestations of mental illness may occur, sexual awakening may lead to risk taking behaviors, and the growing need for independence arises affecting the adolescent's relationships with family, peers, schools, and other social institutions. Issues in any of these domains may result in interactions with the healthcare system. It is important to have resources to address these problems.

We have not intended that this handbook be a complete survey of adolescent medicine. Rather, we designed a text that we hope is practical and user-friendly. In addition, this is not a work consisting only of facts, diagrams, tables, charts, and pathways. Instead, it was our hope to develop a resource that addresses best practices in adolescent medicine where practice not only means the most appropriate approaches, diagnostic evaluations, and best treatments, but also the best ways to connect, communicate, and

continue care with teenagers. After all, if the physician cannot develop a good relationship with an adolescent, then treatment and follow through will surely be compromised.

This handbook has three parts: general adolescent medicine, sexuality, and mental health. There is also an appendix with additional materials. References and additional readings are listed at the end of each chapter. Knowing that mental health and substance abuse competencies are goals recommended by the American Academy of Pediatrics for primary care pediatricians, we have included an extensive section on these areas of learning. In addition, adolescents surface in the medical home asking for sexuality services, so we have included broad content for these important adolescent issues. We have made every effort to include practical materials useful for the primary care physician realizing that these core areas of learning may not be addressed extensively in pediatric or internal medicine training programs.

Except for neonatologists and geriatricians, adolescents may be seen by any other medical or surgical specialist. While this handbook is aimed at clinicians who see a number of adolescents in their practices, it should be relevant to most clinicians. Each of our outstanding physician authors represents expertise in pediatric or adult specialties and has taught or trained at Massachusetts General Hospital. Using their collective knowledge and wisdom, we have crafted a multispecialty approach to adolescent healthcare hoping to present a balance of the science and the art of adolescent medicine. Adolescence is time limited, and eventually adolescents will need to seek a new medical home. The last chapter addresses the issues inherent to care transition and offers a model for transfer of care to adult medicine.

September 2010 Mark A. Goldstein, MD

Acknowledgements

I wish to thank each of the contributors to this edition with special thanks to the resident authors, Drs. Rachel Alinsky, Michelle Chaney, Suni Jani, Philicia Moonsamy, Julia Shekunov, and Jiayin Xue, who managed to do the work of researching and writing despite their busy schedules. In addition, I wish to thank the faculty of the Division of Adolescent and Young Adult Medicine at Massachusetts General Hospital, Drs. Brigham, Gupta, Lemly, Murphy, Rosenblum, and Sadler, for their support and contributions to this edition.

In addition, I am eternally grateful to the late Dr. Robert Masland, Chief emeritus of the Division of Adolescent/Young Adult Medicine at Boston Children's Hospital, who introduced me to the care of adolescents and mentored me throughout my career. Modeling his care and concern for adolescents, Dr. Masland inspired me to complete a fellowship in adolescent medicine under his direction. Dr. Masland also guided my daughter Samantha Anne Goldstein Kamras M.D. from middle school through pediatric residency. I will always cherish his support.

Dr. Ronald E. Kleinman, Physician-in-Chief at the MassGeneral Hospital for Children, Chair of the Department of Pediatrics at Massachusetts General Hospital, and Charles Wilder Professor of Pediatrics at Harvard Medical School, supported this project from the beginning. Without his commitment, this handbook would not have been possible.

I also want to express my gratitude to Springer editors Lorraine Coffey and Caitlin Prim. Their assistance was invaluable and helped to make this project proceed smoothly.

And finally I want to thank my loving wife Myrna Chandler Goldstein for her support during the writing and editing of this edition. With her encouragement and assistance, I was able to devote the time and effort needed to complete this book.

Mark A. Goldstein, MD

Contents

Contributors

Rachel H. Alinsky, M.D. Departments of Medicine and Pediatrics, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

Ami B. Bhatt, M.D. Division of Cardiology, Adult Congenital Heart Disease Program, Department of Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

Kathryn S. Brigham, M.D. Division of Adolescent and Young Adult Medicine, MassGeneral Hospital for Children, Harvard Medical School, Boston, MA, USA

Michelle Chaney, M.D., M.Sc.P.H. Child and Adolescent Psychiatry Service, Department of Psychiatry, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

Tanishia Choice, M.D. Child and Adolescent Psychiatry Service, Department of Psychiatry, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

Laya Ekhlaspour, M.D. Division of Pediatric Endocrinology, MassGeneral Hospital for Children, Harvard Medical School, Boston, MA, USA

Lauren Fiechtner, M.D., M.P.H. Division of Pediatric Gastroenterology and Nutrition, MassGeneral Hospital for Children, Harvard Medical School, Boston, MA, USA

Laura D. Flannery, M.D. Division of Cardiology, Department of Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

Anna Cristina Garza-Mayers, B.A., Ph.D. Department of Medicine, Massachusetts General Hospital, Boston, MA, USA

Mark A. Goldstein, M.D. Division of Adolescent and Young Adult Medicine, MassGeneral Hospital for Children, Harvard Medical School, Boston, MA, USA

Nupur Gupta, M.D., M.P.H. Division of Adolescent and Young Adult Medicine, MassGeneral Hospital for Children, Harvard Medical School, Boston, MA, USA

Esther Jacobowitz Israel, M.D. Division of Pediatric Gastroenterology and Nutrition, MassGeneral Hospital for Children, Harvard Medical School, Boston, MA, USA

Peter Jackson, M.D. Department of Psychiatry, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

Suni Jani, M.D., M.P.H. Child and Adolescent Psychiatry Service, Department of Psychiatry, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

Jess L. Kaplan, M.D. Division of Pediatric Gastroenterology and Nutrition, MassGeneral Hospital for Children, Harvard Medical School, Boston, MA, USA

Michelle Katz, M.D., M.P.H. Division of Pediatric Endocrinology, MassGeneral Hospital for Children, Harvard Medical School, Boston, MA, USA

Cassandra M. Kelleher, M.D. Division of Pediatric Surgery, MassGeneral Hospital for Children

Department of Surgery, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

Jeffrey B. Kreher, M.D. Department of Orthopedics, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

Daniela Kroshinsky, M.D., M.P.H. Department of Dermatology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

Diana C. Lemly, M.D. Division of Adolescent and Young Adult Medicine, MassGeneral Hospital for Children, Harvard Medical School, Boston, MA, USA

Elizabeth Miller, M.D., Ph.D. Division of Adolescent and Young Adult Medicine, Children's Hospital of Pittsburgh of UPMC, Pittsburgh, PA, USA

Department of Pediatrics, University of Pittsburgh School of Medicine, Pittsburgh, PA, USA

Madhusmita Misra, M.D. Division of Pediatric Endocrinology, MassGeneral Hospital for Children, Harvard Medical School, Boston, MA, USA

Philicia Moonsamy, M.D. Department of Surgery, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

Mariette Murphy, M.D. Division of Adolescent and Young Adult Medicine, MassGeneral Hospital for Children, Harvard Medical School, Boston, MA, USA

Anne M. Neilan, M.D., M.P.H. Infectious Disease Unit, Department of Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

Jennifer Rosenblum, M.D. Division of Adolescent and Young Adult Medicine, MassGeneral Hospital for Children, Harvard Medical School, Boston, MA, USA

Karen Sadler, M.D. Division of Adolescent and Young Adult Medicine, MassGeneral Hospital for Children, Harvard Medical School, Boston, MA, USA

Amita Sharma, M.D. Division of Pediatric Nephrology, MassGeneral Hospital for Children, Harvard Medical School, Boston, MA, USA

Julia Shekunov, M.D. Child and Adolescent Psychiatry Service, Department of Psychiatry, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

Rajitha D. Venkatesh, M.D. Division of Pediatric Gastroenterology and Nutrition, MassGeneral Hospital for Children, Harvard Medical School, Boston, MA, USA

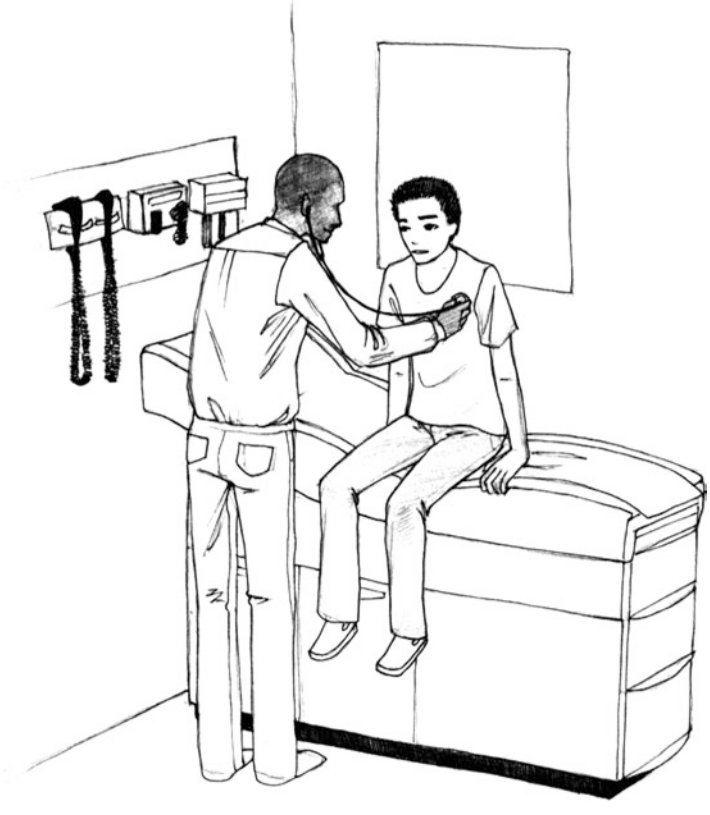
Timothy Wilens, M.D. Division of Child and Adolescent Psychiatry Service, Center for Addiction Medicine, Department of Psychiatry, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

Jiayin Xue, M.D., M.P.H. MassGeneral Hospital for Children, Harvard Medical School, Boston, MA, USA

Amy Yule, M.D. Child and Adolescent Psychiatry Service, Department of Psychiatry, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

Part I

General Adolescent Medicine



Adolescent Preventive Services

1

Jennifer Rosenblum and Jiayin Xue

The annual visit offers the opportunity to promote healthy behaviors, identify at-risk behavior, provide immunizations, and screen for health problems. The American Academy of Pediatrics (AAP) and the American Medical Association (AMA) provide a comprehensive set of recommendations that is designed to be delivered as a preventive services package during annual health visits between the ages of 11 and 21. These recommendations were developed in order to promote the developmental, psychosocial, and physical health of adolescents. The following is a summary of the recommendations based on the updated 2015 AAP *Periodicity Schedule* and the AMA *Guidelines for Adolescent Preventive Services* (GAPS), supplemented by recommendations from the National Heart, Lung, and Blood Institute (NHLBI) and the United States Preventive Task Force (USPSTF).

General Recommendations

- Conduct an annual visit from age 11 to 21 that includes a comprehensive physical exam, routine screenings, and age appropriate anticipatory guidance.
- Deliver preventive services that are developmentally appropriate and sensitive to individual and cultural differences.

M.A. Goldstein (ed.), *The MassGeneral Hospital for Children Adolescent Medicine Handbook*, DOI 10.1007/978-3-319-45778-9_1

- Establish office workflows that are conducive to maintaining the confidentiality of adolescents and that are adherent to state laws. Policies should be transparent to adolescents and their parents.

Measurements and Sensory Screens

- Weight and height should be measured annually. Body mass index (BMI) should be calculated based on weight and height measurements in order to screen for adolescents who have obesity or are underweight.
  - Adolescents with BMI ≥95th percentile have obesity and should have a comprehensive evaluation for weight-related complications.
  - Adolescents with BMI between 85th and 95th percentile are overweight and should have a comprehensive evaluation if:
    Their BMI has increased by 2 or more kg/m^2 during the last year.
    There is a family history of premature coronary artery disease, obesity, hypertension, or diabetes at first presentation.
    They express concerns about their weight
    They have elevated cholesterol or blood pressure
  - If weight loss >10 % of previous weight or BMI <5th percentile, assess for organic disease, anorexia nervosa, or bulimia nervosa.
- Screen annually for hypertension (SBP or DBP >95th %tile). See chapter on adolescent hypertension for details, and see appendix for blood pressure tables.
- Routine visual acuity screening every 2–3 years in early adolescent years, risk-based screening in late adolescent years.
- Routine hearing screen should be risk based in all adolescents.

Behavioral Assessments

- Consider using the HEEADSSS acronym to conduct annual comprehensive behavioral screen
  - Home environment

Ask about potential stressors at home, relationships, with family members.

- Education and employment
  Ask about learning or school problems.
  Ask about career goals or current employments.
- Eating
  Ask about body image and diet patterns.
  Assess for unhealthy behaviors that may contribute to obesity or being underweight.
- Activities
  Ask about extracurricular activities and hobbies.
- Drugs
  Ask about the use of alcohol, tobacco and tobacco-related products, and other substances of abuse including recreational drugs and performance enhancing agents.
  Consider using CRAFFT questions, which are more sensitive for adolescents than CAGE questions. Two or more positives suggest high risk of substance-use disorder.
    Have you ever ridden in a Car driven by someone who was high or had been using drugs or alcohol?
    Do you ever use alcohol or drugs to Relax, feel better about yourself, or fit in?
    Do you ever use alcohol/drugs while you are by yourself, Alone?
    Do you Forget things you did while using drugs or alcohol?
    Do your family or Friends ever tell you that you should cut down your drinking or drug use?
    Have you ever gotten into Trouble while using drugs or alcohol?
- Sexuality
  Ask about romantic partners and involvement in sexual activities
  Ask about contraceptive use
- Suicide/depression
  Annual screening for depression between ages 11 and 21 using Patient Health Questionnaire (PHQ)-2 or other screening tools.

- Safety from injury and violence
  Ask about experiences with bullying, injuries, firearms
  Ask about potential emotional, physical, relationship and sexual abuse

Physical Exam

- Complete an annual physical exam with thorough assessment of growth and development, with special attention to the cardiovascular and musculoskeletal systems during a sports pre-participation physical.
- Assess for the presence of cardiac murmurs and arrhythmias. Ask about chest pain and syncope during exercise as well as family history of early sudden death and serious cardiac events before the age of 55.
- AAP and the Pediatric Orthopaedic Society of North America recommend screening for the presence of scoliosis in girls twice, at 10 and 12 years of age, and once in boys at 13 or 14 years of age. Note that the USPSTF currently does not recommend routine scoliosis screening.
- Assess for the presence of acanthosis nigricans in overweight or obese patients.
- Assess for the development of secondary sexual characteristics using the Tanner scale. Always perform a full genitourinary exam to assess anatomy and evidence of sexually transmitted diseases.

Immunizations

- Adolescents should receive prophylactic immunizations according to guidelines published by the Center for Disease Control (CDC)/Advisory Committee on Immunization Practices (ACIP). These include vaccines for human papillomavirus, meningococcus, tetanus, diphtheria, pertussis, and any catch-up vaccines.
- For details, see chapter on adolescent immunizations.

Laboratory Testing

- Dyslipidemia (Table 1.1)
  - Universal screening for hyperlipidemia at least once between 9 and 11 years of age and between 17 and 21 years of age.
    Optimal (mg/dL): Total cholesterol (TC) <170, low-density lipoprotein cholesterol (LDL-C) <110, non-high-density lipoprotein cholesterol (non-HDL-C) <120, high density lipoprotein (HDL) >45, triglycerides (TG) <75 in 0–9 year olds, TG <90 in 10–19 year olds.
    Borderline (mg/dL): TC 170–199, LDL-C 110–129, non-HDL-C 120–144, HDL 40–45, TG 75–99 in 0–9 year olds, TG 90–129 in 10–19 year olds.
    Elevated (mg/dL): TC ≥200, LDL-C ≥130, non-HDL-C ≥145, HDL <40, TG ≥100 in 0–9 year olds, TG ≥130 in 10–19 year olds.
  - If Non-HDL >145 mg/dL, HDL<40 mg/dL on non-fasting lipid panel (non-FLP), then conduct fasting lipid panel (FLP). Or if LDL-C >130 mg/dL, non-HDL-C >145 mg/dL, HDL-C <40 mg/dL on FLP, repeat after 2 weeks but within 3 months.
  - Start with lifestyle modifications if abnormal values based on the average of two FLPs, and add pharmacological therapy if values do not improve in 6 months. A treatment algorithm is provided by the NHLBI Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents: Summary Report. [http://www.nhlbi.nih.gov/health-pro/guidelines/current/cardiovascular-health-pediatric-guidelines/summary#chap9]

Table 1.1 Dyslipidemia in adolescents ages 10–19. *Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents: Summary Report.* NHLBI

Category	Optimal	Borderline	High
TC	<170	170–199	>200
LDL-C	<110	110–129	>130
Non-HDL-C	<120	120–144	>145
HDL-C	>45	40–45	<40
TG	<90	90–129	>130

  - For TG ≥500 mg/dL or LDL-C ≥250 mg/dL, refer patient to a lipid specialist.
  - Universal screening is *not* recommended between age 12 and 16 years because of normal changes in lipid levels during puberty unless:
    First or second degree relatives with MI, angina, stroke, CABG/stent/angioplasty, sudden death at <55 years in males or <65 years in females.
    Parent with TC >240 or known dyslipidemia.
    Patient with CAD risk factors such as diabetes, hypertension, BMI >85th percentile or smokes cigarettes.
    Patient with one of the following moderate to high risk conditions:
      Diabetes mellitus, type 1 and type 2
      Chronic kidney disease, end-stage renal disease/post renal transplant, nephrotic syndrome
      Postorthotopic heart transplant
      Kawasaki disease with current or regressed aneurysms
      Chronic inflammatory disease
      Human immunodeficiency virus infection
- Sexually transmitted infections (STIs)
  - Gonorrhea: Yearly screen of all sexually active adolescents with nucleic acid amplification testing on urine sample (males or females, preferred method for males) or vaginal swabs (preferred method for females).
  - Chlamydia: Yearly screen of all sexually active adolescents with nucleic acid amplification testing on urine samples or vaginal swabs.
  - HIV: Screen should be offered to all adolescents between the ages of 16–18 at least once. Those who are sexually active, use IV drugs, or being tested for other STIs should be screened for HIV yearly.
  - Syphilis: RPR testing if they have lived in an endemic area, had other STDs, had more than one sexual partner in the last 6 months, have exchanged sex for drugs or money, or are males who have engaged in sex with other males

- Cervical dysplasia
  - Universal screening for all females starting at age 21 and every 3 years for cervical cancer by use of Pap test regardless of vaginal sexual intercourse history.
- Tuberculosis:
  - Screen if exposure to active TB, history of living in a homeless shelter, history of incarceration, history of living in an area with a high prevalence of TB, or working in a health care setting.
- Complete blood count:
  - Screen if history of menorrhagia or family history of hematologic disorders.

Anticipatory Guidance

- Provide anticipatory guidance to adolescents and parents at annual preventive visits for all patients between the ages of 11 and 21.
- Promote an understanding of normal physical, sexual, and psychosocial development, help recognize signs and symptoms of physical and emotional stress.
- Discuss healthy parenting behaviors, including those that promote healthy adolescent adjustment.
- Advise and provide guidance for a healthy diet and a physically active lifestyle.
- Encourage the avoidance of tobacco, alcohol, and other substances of abuse.
- Reduce unintended injuries by:
  - Promoting the use of safety devices such as seatbelts, helmets, and athletic protective devices.
  - Advising against the use of alcohol or other substances while using motor vehicles.
  - Advocating nonviolence in resolving interpersonal conflicts.
  - Discouraging the use of all weapons and firearms.

Sources

American Academy of Pediatrics. AAP updates schedule of screening and assessments for well-child visits. February 2014. https://www.aap.org/en-us/about-the-aap/aap-press-room/pages/AAP-Updates-Schedule-of-Screening-and-Assessments-for-Well-Child-Visits.aspx#sthash.s5ac1tZ6.dpuf.

Center for Disease Control and Prevention. Immunization schedules. January 2016. http://www.cdc.gov/vaccines/schedules/, http://www.cdc.gov/vaccines/who/teens/index.html.

Daniels SR, Greer FR, the Committee on Nutrition. Lipid screening and cardiovascular health in childhood. Pediatrics. 2008;122:198–208.

Feld LG, Corey H. Hypertension in childhood. Pediatr Rev. 2007;28:283–98.

Knishkowy B, Palti H. GAPS (AMA Guidelines for Adolescent Preventive Services): where are the gaps? Arch Pediatr Adolesc Med. 1997;151(2):123–8.

National Heart, Lung, and Blood Institute (NHLBI). Expert panel on integrated guidelines for cardiovascular health and risk reduction in children and adolescents: summary report. http://www.nhlbi.nih.gov/health-pro/guidelines/current/cardiovascular-health-pediatric-guidelines/summary#chap9.

U.S. Preventive Services Task Force. Final update summary: cervical cancer: screening. July 2015. http://www.uspreventiveservicestaskforce.org/Page/Document/UpdateSummaryFinal/cervical-cancer-screening.

Weinstein SL, Dolan LA, Cheng JCY, et al. Adolescent idiopathic scoliosis. Lancet. 2008;371:127–37.

The Adolescent Patient Interview: Adolescent Confidentiality and Consent

2

Mariette Murphy and Mark A. Goldstein

Interviewing an adolescent provides a transition from the pediatric encounter where the history is primarily provided by the parents, and the teen may or may not be able to provide his or her perspective. The adolescent is available for observation and some interaction, but the primary line of communication is with another adult, the parent. Interviewing the parent is often a good prelude to the adolescent interview, as the parent generally provides a more thorough family history, which may also be an important educational experience for the adolescent patient. The parental perspective and the observation of the interaction between parent and teen provide clinical information that helps to understand the family dynamic. But the stance is really to speak to both generations together, discussing confidential care, setting boundaries, and describing the contract upon which clinical care may be based. At that point, moving the parent to the waiting room is important to transition to the interview of the adolescent, which establishes the basis of the clinical relationship. The developmental aspects of early, middle, and late adolescence set the adolescent interview apart from the child and adult interview.

Approaching the adolescent from a clinical stance of neutrality is key. Nonjudgmental inquiry is essential to establishing the rapport that may develop into a supportive clinical relationship. Most adolescents enjoy talking about themselves

M.A. Goldstein (ed.), *The MassGeneral Hospital for Children Adolescent Medicine Handbook*, DOI 10.1007/978-3-319-45778-9_2

to a supportive and nonjudgmental listener. The clinician's role will also influence the investment and willingness of the adolescent to open up and speak honestly about what is going on in his or her life. If the clinician's role is to provide primary care that is ongoing, helpful, and available, an adolescent may be more likely to trust and invest in the relationship. If the clinician's role is evaluative or episodic, it may be more difficult to establish the trust that would enable honest disclosures. Assurances of confidentiality, particularly those established with the parent in the adolescent's presence, provide the basis for the development of a doctor–patient relationship that is open and honest. Being explicit about the limits of confidentiality, that is, harming oneself or others, is reassuring to the parents that their adolescent's safety is a priority.

In assisting an adolescent to tell his or her history, it is useful to open the interview with the context of the clinical relationship and the purpose of the visit. If the focus is on a particular medical complaint, a chronologic approach to the onset and development of symptoms allows the adolescent to tell the story as he or she has experienced it. Pulling back from the specifics and asking concrete questions, such as hospitalizations, operations, medications, and allergies, may trigger the history of particularly salient aspects of the medical history.

In the context of the past medical history, asking chronologic questions about the teen's development in the various domains of functioning often provides another structure for unfolding a history. In the physical domain, any periods of time of weight loss, abrupt weight or height gain may open up the adolescent's feelings about his/her rapidly changing body. Dating the onset of the development of secondary sexual characteristics and how the developmental pattern unfolded transitions into more private clinical material and sets the context for more sensitive historical questioning about sexual contact. The repeated pattern of questioning with onset, subsequent pattern, and last episode may be applied to each sensitive area and establishes a flow to the interview that defuses some of the intensity. For example, inquiring about the first menses and assisting the

adolescent's memory with memory joggers (e.g., what grade?) may help an adolescent return in her memory to that time and assists her in the forward progression of remembering the pattern of her menses such as monthly, skipping months, multiple menses within a month. The more recent history, such as the last menses, then becomes more reliable because there is an active use of memory. This same patterning can then be applied to sexual contact: actively remembering the first contact; subsequent partners and sexual practices; with most recent contact, partner, and practice tending to be more reliable. If there is no sexual contact, the open ended and chronologically factual approach tends to make it easier to share that and explore how the adolescent is thinking about sexuality, and when he/she may anticipate that sexuality may be part of his/her life. Answers may vary from not knowing, to waiting for marriage, to next month, but at least the chronologic flow has been established as part of the clinical relationship.

This same pattern of questioning may be applied to substances such as cigarettes, alcohol, and other drugs, and the neutral chronologically factually based questioning makes the pattern of use clearer, from experimentation, to use, to abuse. This approach to eliciting the history makes subsequent interventions and referrals easier as the adolescent may experience how the pattern of use leads to consequences that need intervention.

Applying this pattern of questioning to other domains such as school may also clarify areas of difficulty requiring intervention. Areas of strength and weakness may be explored as you progress through the chronologic facts of preschool, primary, middle, and high school from the adolescent's perspective and then checked with the parents when they rejoin at the end of the visit. Similarly, asking about how the family has changed over time and how the adolescent's relationship with family members is experienced now may yield valuable information about the family context as the adolescent is separating, individuating, and establishing more autonomy. The potential for the family to be supportive and to accommodate the assumption of more responsibility in tandem with the development of more autonomy may be explored as well

as the resistances to this transition. The other members of the family are engaged in their own developmental change, and this may at times cause tensions or withdrawal of supportive supervision, which may lead to vulnerability in the adolescent and derail healthy development.

More episodic or cross-sectional screening may be done using Home/Education/Activities/Drugs/Sex/Substances (HEADSS) or other screening tools, but the sensitivity of the material may not yield accurate information if the adolescent is not engaged in the flow of the clinical interview.

Screening for mental health issues should be performed using standardized tools such as the Pediatric Symptom Checklist or through applying this pattern of chronologic questioning to the domains of basic functions particularly eating, sleeping, and peer relationships. Disordered eating and sleep may be explored through 24-h recalls or patterns of eating as well as patterns of sleep that may change dramatically during adolescence. Behavioral issues with peers such as bullying, isolation, violence, peer pressure, or inability to articulate one's own perspective have developmental as well as psychological impact and early identification and intervention may have a major impact during this critical period of growth and development.

In summary, the adolescent interview should be approached from a nonjudgmental, neutral clinical stance to engage the adolescent in telling his or her history with an attentive, supportive listener within a context of confidentiality. Screenings may use a chronologic approach, which brings the adolescent to the beginning of any particular developmental domain or behavior and may elucidate the pattern of development of behaviors, which may facilitate early identification and intervention easier. Standardized screenings may also be employed such as the HEADSS, SIGECAPS, and Pediatric Symptom Checklist but may not elicit a full understanding of the development of problem behaviors.

After completion of the physical examination, the adolescent's privacy should be maintained while dressing or the clinician should leave the room. The clinician can then counsel the teen in private; afterward, the parent should be invited to return to the examining room for the summation and conclusion of the visit as well as to answer any questions.

Adolescent Confidentiality and Consent

Each state has its own laws in respect to a minor's ability to consent for health services. These services may include pregnancy-related care, contraceptive or family planning services as well as prevention, diagnosis, and treatment of sexually transmitted infections. Other services that may be available by a minor's consent include HIV/AIDS testing and treatment, drug or alcohol counseling and treatment, outpatient mental health services and examination, diagnosis, and treatment after a sexual assault. The reader is encouraged to seek out state-specific information (Please see Further Readings for suggested resources).

Fear of disclosure prevents some minors from seeking healthcare services. Confidentiality rests on the specific categories of minors who may consent to their own treatment. Those minors who are able to consent may also be responsible for payment of their treatment.

In general, the parent or legal guardian must consent to the nonemergency care of a child less than 18 years of age. Consent is not required for healthcare providers to render emergency treatment although the providers should make every effort to notify the parent or guardian and document such efforts in the patient's record.

Federal and Massachusetts's laws carve out exceptions that allow minor patients to consent for their own medical treatment without parental involvement (see Sects. Emancipated Minors, Mature Minor, and Minors Seeking Services for below).

Emancipated Minors

A minor is emancipated if at the time care is sought, he or she is:

1. Married, widowed, or divorced (can consent to abortion or sterilization).
2. A member of the armed forces.
3. Pregnant or believes herself to be pregnant.
4. Parent of a child.
5. Living separate and apart from his/her parent or legal guardian and managing his/her own financial affairs.

6. In addition, if the minor believes he or she to be suffering from or to have come into contact with any diseases defined by the Department of Public health as dangerous to the public health, except that in this instance, the minor may consent only to the diagnosis and treatment of the disease.

Usually, adolescents who fall into categories 1–6 cannot consent to abortion or sterilization. Additional documentation is required whenever a minor makes healthcare decisions. The physician must document which category is being relied on and why the physician believes the category applies.

Mature Minor

A physician or other practitioner can determine the following:

1. The minor is mature enough to make informed decisions and
2. It is in the minor's best interest to be treated without parental involvement. Additional documentation is required.

Both of the above factors must exist. An adolescent is not a mature minor simply because he or she has the maturity to consent, and it is convenient to accept the consent because a parent is not present. The provider has to affirmatively determine that involving the parents is not in the adolescent's best interests.

Minors Seeking Services for

1. Emergency contraception as a victim of a sexual assault.
2. Drug treatment: Drug-dependent minors 12 years and older seeking treatment for drug dependence must be found to be drug-dependent by two or more physicians. The minor may consent only to medical care related to the diagnosis and treatment.
3. Voluntary admission or outpatient treatment at a licensed mental health facility (if the patient is 16 years or older).
4. Family planning services through Department of Public Health Programs receiving federal funding under Title X. It should be

noted that for minors seeking family planning services outside of a family planning agency, the default is to treat the patient as a mature minor and provide such services confidentially including emergency contraception if requested unless the surrounding circumstances are such as to persuade otherwise.

Bear in mind that there are formal forensic cognitive psychology evaluations that can be done, but physician documentation requires the reasoning underlying the decision to allow minors to consent. The clinician is encouraged to consult with an attorney who is familiar with the laws of the particular state. In some emergency situations, a judge's order may be needed.

Sources

Cottrell LA, Nield LS, Perkins KC. Effective interviewing and counseling of the adolescent patient. Pediatr Ann. 2006;33:164–72.

English A, Shaw FE, McCauley MM, Fishbein DB, for the Working Group on Legislation, Vaccination, and Adolescent Health. Legal basis of consent for health care and vaccination for adolescents. Pediatrics. 2008;121:S85–87.

Goldenring J, Cohen E. Getting into adolescent heads. Contemp Pediatr. 1998;5:75–90.

Griffin C, Israel E, Lozowski D. Minor patients: access to health care, informed consent, and confidentiality. Massachusetts General Hospital Guidance 2016.

Pediatric Symptom Checklist. Child Psychiatry Service, Massachusetts General Hospital. http://www.massgeneral.org/psychiatry/services/psc_home.aspx.

Pubertal Development

3

Karen Sadler

Introduction

During all routine physical exams (and more frequently when indicated), health care workers should assess the development of secondary sexual characteristics. Along with growth trends, and, when necessary, X-rays to determine bone age and serum hormone levels, these changes reflect pubertal status. While there is value in comparing secondary sexual characteristics normatively, serial exams enable a longitudinal assessment of the timing and tempo of pubertal changes. The most widely used tool is the Tanner Staging system, described below. This chapter will conclude with information on secular trends in pubertal timing over the past two centuries.

Girls (Figs. 3.1 and 3.2)

Tanner Stage 1 (Prepubertal)

Height:	Increases at basal rate: 5–6 cm/year
Breast:	Papilla elevation only
Pubic Hair:	Villus hair only; no coarse, pigmented hair

M.A. Goldstein (ed.), *The MassGeneral Hospital for Children Adolescent Medicine Handbook*, DOI 10.1007/978-3-319-45778-9_3

Tanner Stage 2

Height:	Increases at accelerated rate: 7–8 cm/year
Breast:	Breast buds are palpable and areolae enlarge Age 10.9 years (8.9–12.9 years)
Pubic Hair:	Minimal coarse, pigmented hair mainly on labia Age 11.2 years (9.0–13.4 years)
Modifications based on increasingly earlier puberty	
Caucasian, Asian:	*Stage 2 changes may appear 1 year earlier*
African-American, Hispanic:	*Stage 2 changes may appear 2 years earlier*

Tanner Stage 3

Height:	Increases at peak rate: 8 cm/year (age 12.5)
Breast:	Elevation of breast contour; areolae enlarge Age 11.9 years (9.9–13.9 years)
Pubic Hair:	Dark, coarse, curly hair spreads over mons pubis Age 11.9 years (9.6–14.1 years)
Other changes:	Axillary hair develops (13.1 years) Acne vulgaris develops (13.2 years)

Tanner Stage 4

Height:	Increases at 7 cm/year
Breast:	Areolae forms secondary mound on the breast Age: 12.9 years (10.5–15.3 years)
Pubic Hair:	Hair of adult quality No spread to junction of medial thigh with perineum Age: 12.6 years (10.4–14.8 years)

Tanner Stage 5

Height:	No further height increases after age 16 years
Breast:	Adult breast contour Areola may recess to general contour of breast
Pubic hair:	Adult distribution of hair Pubic hair spreads to medial thigh Pubic hair does not extend up linea alba

Other Milestones

Adrenarche:	Age 6–8 years
Menarche:	Age 12.7 years (10.8–14.5 years) Delayed >1 year if low body fat (e.g., athlete, anorexia)

Growth in Girls

Peak height velocity:	11.5 years (9.7–13.3 years)
Basal growth:	Occurs up until Tanner Stage 2
Basal Growth rate:	5.0–6.0 cm/year
Pubertal growth	
Girls who mature with average timing: 8.3 (6.1–10.4) cm/year	
Girls who mature earlier: 9.0 (7.0–11.0) cm/year	
Girls who mature later: 7.5 (5.4–9.6) cm/year	

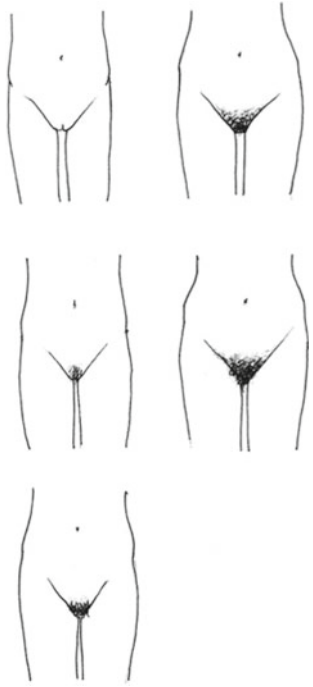


Fig. 3.1 Tanner stage pubic hair development

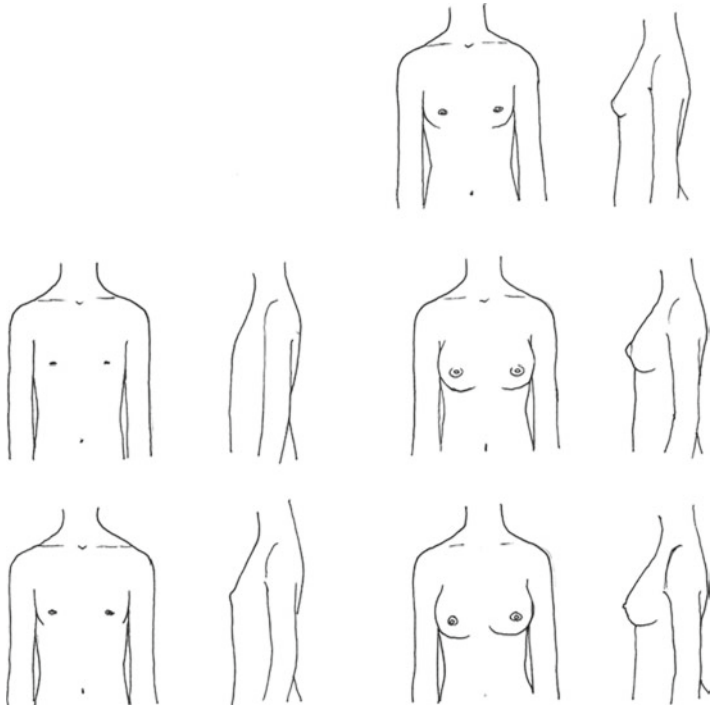


Fig. 3.2 Tanner stage breast development

Pearls

- Adiposity and ethnicity are independently associated with earlier puberty
- Mexican-American and non-Hispanic black children experience puberty earlier than Caucasians
- Determine thelarche in overweight girls by palpation to distinguish fat tissue from breast tissue.
- In normal-weight children: pubic hair in boys less than 10 years and in girls less than 8 years is abnormal.
- Girls who experience later menarche often take longer to establish regular periods.

- Girls who experience pubarche before thelarche are at higher risk of PCOS.

Boys (Fig. 3.3)

Tanner Stage 1 (Prepubertal)

Height:	Increases at basal rate: 5–6 cm/year
Testes:	Smaller than 4 ml or long axis <2.5 cm
Pubic Hair:	No coarse, pigmented hair
Penis:	No growth

Tanner Stage 2

Height:	Increases at basal rate: 5–6 cm/year
Testes:	Size 4 ml or long axis 2.5–3.2 cm
	Age 11.5 years (age 9.5–13.5 years)
Pubic Hair:	Minimal coarse, pigmented hair at base of penis
	Age 12.0 years (age 9.9–14.0 years)
Penis:	Earliest increased length and width
	Age 11.5 years (age 10.5–14.5 years)

Tanner Stage 3

Height:	Increases at accelerated rate: 7–8 cm/year
Testes:	Size 12 mL or long axis 3.6 cm
	Age 14.0 years (11.5–16.5 years)
Pubic Hair:	Coarse, dark curly hair spread over the pubis
	Age 13.1 years (11.2–15.0 years)
Penis:	Increased length and width
	Age 12.4 years (10.1–14.6 years)

Other changes:

Gynecomastia may occur (age 13.2 years) with increased estrogen
Voice breaks (age 13.5 years) with vocal cord changes
Muscle mass increases
Spermatogenesis

Tanner Stage 4

Height:	Increases at peak rate: 10 cm/year (age 13.8)
Pubic Hair:	Hair of adult quality
	Not spread to junction of medial thigh with perineum
	Age 13.9 years (12.0–15.8 years)
Penis:	Continued growth in length and width
	Age 13.2 years (11.2–15.3 years)
Testes:	Length 4.1–4.5 cm
Other changes:	
Axillary hair (age 14.0 years)	
Voice changes (age 14.1 years)	
Acne Vulgaris (age 14.3 years)	

Tanner Stage 5

Height:	No further height increases after age ~17 years
Pubic Hair:	Adult pubic hair distribution (15.3 years)
	Pubic hair spreads to medial thigh
	No hair spread to linea alba
Penis:	Mature genital size by 16.5 years
Testes:	Length >4.5 cm
Secondary sexual characteristics:	
Facial hair present on sides	
Mature male physique	
Gynecomastia resolves	

Growth in Boys

Peak height velocity:	Age 13.5 (11.7–15.3 years)
Basal growth occurs up until Tanner Stage 4	
Basal growth rate: 5.0–6.0 cm/year	
Pubertal growth	
Boys who mature with average timing: 9.5 (7.1–11.9) cm/year	
Boys who mature earlier: 10.3 (7.9–12.5) cm/year	
Boys who mature later: 8.5 (6.3–10.7) cm/year	

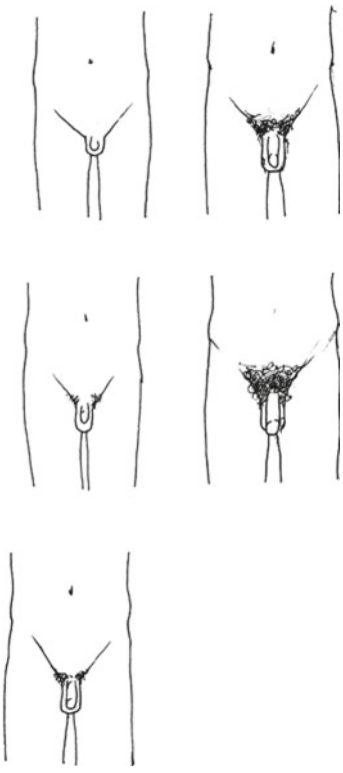


Fig. 3.3 Male tanner genital and pubic hair stages

Secular Trends in Pubertal Development

From the mid-1800s to the middle of last century, there was a trend towards earlier pubertal development as well as an increase in adult height. Since earlier onset of puberty also means earlier maturation of bones through epiphyseal closure, the gain in height is attained earlier in childhood. The age of menarche in the USA fell from 17 to 14 years in those ten decades, leveling off after 1960. Similarly, there has been a leveling of adult height. Traditionally, the factors thought to be responsible for these trends are improved nutrition and

health—the age of menarche is still declining in developing countries such as China, India, and Bulgaria and is also correlated within such countries with socioeconomic status. Body fat plays a role: body mass index after 3 years of age is linked to earlier maturation in girls, but negatively correlated with sexual maturity in boys. Currently being studied in this regard is the role of leptin. Adipose tissue is hormonally active, producing both sex steroids and leptin. It makes evolutionary sense that there be a peripheral metabolic signal that body mass and proportions can support the onset of puberty. In animal studies, leptin has been shown to be important in this regard, though whether it plays an active or permissive role is unknown, as are the exact mechanisms of action. Further, there may be a bidirectional effect between adiposity and pubertal onset: adipose tissue may store or generate hormones that promote pubertal changes, or pubertal changes may enhance adiposity. Research is ongoing in this important area.

Sources

Family practice notebook. Adolescent development. http://www.fpnotebook.com/Peds?Teen?AdlscntDvlpmnt.htm. Accessed 1/16.

Growth and puberty secular trends, environment and genetic factors. www.ncbi.nlm.nih.gov/books/NBK10786/?report=reader. Accessed 1/16.

Marshall WA, Tanner JM. Variations in pattern of pubertal changes in girls. Arch Dis Child. 1969;44:291–303.

Marshall WA, Tanner JM. Variations in the pattern of pubertal changes in boys. Arch Dis Child. 1970;45:13–23.

Rosen DS. Physiologic growth and development during adolescence. Pediatr Rev. 2004;25:194–200.

Normal Adolescent Development

4

Karen Sadler

Though adolescence may be a time of turbulence and conflict (the second "terrible twos"), 80 % of children pass through the teen years without a significant deterioration in their family relationships. The hardest times for parents and caregivers tend to be when great developmental leaps are taking place, and adolescence is one such time.

Psychosocial Development

Following the paradigm of Eric Erikson, the task of adolescence is to form an identity by:

(a) Striving for independence from parental control and attaining a measure of economic independence.
(b) Developing a value system.
(c) Becoming comfortable with one's identity and body.
(d) Building meaningful relationships.

Consequent Behaviors

Early Adolescence (11–14): Children begin to "break" from parents, preferring to spend less time with them, becoming "embarrassed" by them, demanding more privacy. They seek to

M.A. Goldstein (ed.), *The MassGeneral Hospital for Children Adolescent Medicine Handbook*, DOI 10.1007/978-3-319-45778-9_4

integrate into a peer group though that may take a few tries. They tend to be preoccupied by their bodies, especially those features they see as deviating from the norm.

Middle Adolescence (15–17): During this period, identification with peer group peaks. This fuels the continued drive for independence from parents, leading to battles over rules and limit-testing. Vulnerability to group norms and values may lead to risk-taking behavior.

Late Adolescence (18–21): Identity should be almost established, thus there is less vulnerability to group norms, more comfort with physical attributes, and a more stable self-image. Relationships are more reciprocal.

Cognitive Development

Early Adolescents: Expect concrete thinkers who are unable to appreciate the long-term consequences of their actions and who, when faced with a problem, have limited abilities to think through different hypothetical scenarios and to problem-solve. Communication skills are not mature: when faced with an emotionally charged issue, they may not be able to broach it with their caregivers. They may demonstrate the concept of "imaginary audience" and convince themselves everyone will see their physical imperfections or know their emotional issues.

Middle Adolescents: Around 16 years, most children develop the capacity for abstract thinking, which enables them to problem-solve more effectively. However, they apply this skill inconsistently, at the same time showing insight into difficult essay questions on exams and remarkable lack of insight into their own behaviors. Vacillation and inconsistency are seen. Feelings of invincibility engender risk-taking even with increased insight.

It is normal for teens to express opinions (strongly!), test limits, experiment with behaviors and identities, and to take risks.

Clinical tips:

1. Tailor your advice to the cognitive abilities of the teen: young teens need concrete, immediate analogies and rationales (smoking causes bad breath and black, infected lungs), while

older teens can understand more long-term thinking (and reduces life expectancy).
2. Help young/mid-teens problem-solve: think through different solutions together and discuss the pros/cons.
3. Be authoritative (you ARE a respected authority figure) but not judgmental.
4. Know the latest lingo, but use simple direct terms and descriptions.
5. Remember: they are listening, even if the sweatshirt hood is up and the earplugs are in. You remain a role model.
6. Always know the limits of confidentiality of each state in which you practice. You may be practicing within wide bounds of confidential care, but you remain a mandated reporter.
7. Know your resources: Planned Parenthood, Job Corps, social work, mental health providers, etc.
8. Important decisions are being made about sexuality, drug use/abuse, smoking, diet, exercise, and more. We cannot make their choices for them, but we can help them think them through and encourage safe, responsible behavior.
9. Expect "hot" thinking: neuronal development is not complete, and we all know that frontal lobe is still under construction. Teens can be emotional thinkers, lacking the ability to allow logic and consequences to fully factor into decisions. Talking through different ways to solve a problem can give them insight they may not otherwise have.
10. Don't take it (whatever it is) personally!

Physical Development (Table 4.1)

Three axes control growth:

1. Adrenal: activates around 8–9 years. DHEA, DHEA-S, and androstenedione are produced which control axillary sweating, body odor, and pubic hair.
2. HPA: GNRH → FSH, LH → gonadal stimulation → sex steroids → development of secondary sexual characteristics.
3. GHRH → Growth hormone → somatic growth.

Table 4.1 Physical development

Developmental period	Percent growth
Prenatal	30
0–1 Year	15
Until puberty	40
During puberty	15–18

Clinical tips:

1. The sequence and tempo of pubertal changes are just as, if not more, important than the time of onset.
2. After menarche, girls have on average, only 5 cm of growth left. Growth is complete 2–2½ years after menarche.
3. Girls increase percent body fat during puberty, boys decrease it. Girls end up with ~twice the percentage body fat as boys.
4. Approximately 20 % of girls experience pubarche (development of pubic hair) before thelarche (breast budding). This minority is at increased risk of hyperandrogenic conditions (PCOS).
5. Fifteen to 18 % of final height is attained during adolescence and weight gain during this period is 50 % of adult weight: providing knowledge about nutrients and discussing good dietary habits is an important part of anticipatory guidance.

Working with parents:

1. The extremes of parenting styles, authoritarian or permissive, are rarely effective. The authoritative approach is better. This includes reasonable limits and rules, but flexibility, active listening, and positive interactions.
2. Effective parenting combines love, warmth, acceptance, availability, and developmentally appropriate guidance, rules, expectations, and supervision. (If it sounds hard, that's because it is!)
3. Parents remain role models for their teens during adolescence. Teens are particularly sensitive to hypocrisy so parents need to model with actions as well as words.
4. Humor and an ability to choose battles are helpful.

5. In the long term, teens must pull away to discover and create themselves, and then renegotiate new, more adult relationships with their parents. Let it happen.

Gender and Sexual Identity Development

Gender identity: the sense of being male or female, usually established by age 3. Most 4-year-olds can understand that gender is constant. In early grade school, children pick up social "rules," including the culturally determined roles assigned to the different sexes, termed gender roles.

Sexual orientation: established in childhood and adolescence. This is the gender to which the individual is attracted to physically and emotionally.

The paradigm of seeing gender and sexuality as binary (one is either male or female) is being challenged by one that allows more fluidity over time, one in which identity exists on a continuum of "maleness" versus "femaleness." Hopefully, acceptance of this model will allow non-conforming preadolescents and adolescents to be seen as different, rather than deviant, as social nonacceptance in this developmental period can be very detrimental.

Transgender is a term that encompasses several groups: transsexual (those who desire to live as a member of the opposite sex), androgynous (of indeterminate sex), bigendered (identifying with both sexes or moving between the two), and gender-queer (those not subscribing to conventional gender distinctions). A transfemale was born a biological male; a transmale is/was a natal female.

Gender identity disorder, a DSM 5 diagnosis, emphasizes, along with gender dysphoria and cross-gender identification, the degree of distress, and/or disability an individual experiences.

Non-conforming youths are a very high-risk group: they suffer more violence and abuse and have higher rates of depression, suicidality, substance use and abuse, and STIs, including HIV.

The approach to the adolescent with a non-conforming identity should be, first and foremost, to encourage open communication. It is believed that less than 30 % of teens have "come out" to their providers. An attitude of acceptance rather than assignment should

be adopted, one that affirms the teen for whomever he or she chooses to be. Families who are supportive and accepting are tremendous buffers and mitigate many of the known morbidities. Treatment approaches range from the reversible (dressing as a member of the opposite sex), to partially reversible (puberty suppressing hormonal therapy) to irreversible (surgery). Pediatricians can be an invaluable resource, but must first be comfortable in this role. The discovery of gender and sexual identity is a journey, one that pediatricians can, in part, join and support. Additional resources are listed below.

Sources

Center for Excellence for Transgender Health. www.transhealth.ucsf.edu.
Gay and Lesbian Medical Association. www.glma.org.
Gender non-conforming youth: opportunities for better care and better outcomes. Michelle Fourcier, MD MPH Alpert School of Medicine, Brown University.
Hazen E, Schlozman S, Beresin E. Adolescent psychological development: a review. Pediatr Rev. 2008;29:161–8.
Ryan C, Futterman D. Lesbian and gay adolescents—identity development. Adolesc Med. 1997;211–23.
World Professional Association for Transgender Health. www.wpath.org.

Male Genitourinary Exam

5

Mark A. Goldstein

During adolescence, clinical examination of the male genitalia should be a part of the annual health supervision visit. The purposes of the genitourinary examination are to stage development, detect disease or anatomic issues, and answer questions that the boy may have on his development. In addition, some boys are assured by "normal" findings in the exam. A chaperone is generally unnecessary but could be offered to the patient. Usually, parents should be excused from observing the examination. Some boys prefer to be gowned; the gown should open to the front of the patient. The genital exam is best performed when the boy is standing and the area well illuminated. A brief description of the exam should be given beforehand. If applicable, it is best to have the patient himself roll back the foreskin. A rectal and prostate examination is generally not indicated unless the patient has symptoms that could be attributable to issues in these areas (see Fig. 5.1).

The genital examination should include a Tanner staging, testicular exams and evaluations for inguinal hernia, and sexually transmitted infections regardless of whether or not a patient reports that he is sexually active. It is appropriate also to check for unusual inguinal adenopathy.

Penile and testicular sizes: there is a large range of normal sizes that can depend on the patient's age and Tanner staging. Flaccid

M.A. Goldstein (ed.), *The MassGeneral Hospital for Children Adolescent Medicine Handbook*, DOI 10.1007/978-3-319-45778-9_5

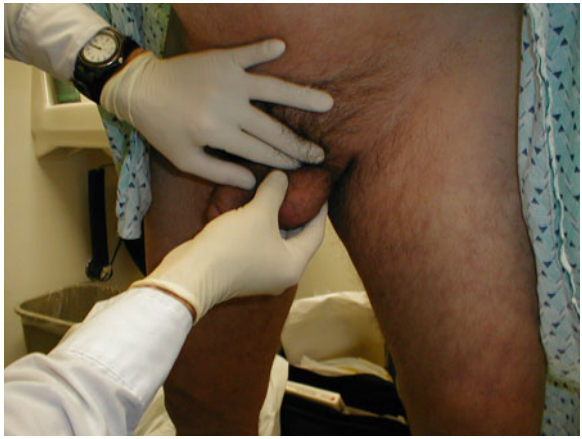


Fig. 5.1 Male genitourinary examination. Credit: Charlie Goldberg M.D., University of California San Diego School of Medicine

penile lengths between 5.5 and 10.5 cm are normal. Testicular length can range from 2.5 to 5 cm.

Some of the findings from the genitourinary exam include the following:

Pink Pearly Penile Papules (PPPP): these are observed in approximately 15 % of males; they are benign 1–2 mm lesions often located on the perimeter on the glans penis giving a cobblestone-like appearance. PPPP are not to be confused with genital warts or mollusca, and they do not require any treatment. The clinician should reassure the adolescent that PPPP are normal and that they require no treatment nor are they transmissible to others.

Meatal stenosis: a web of tissue along the posterior aspect of the urethra causing a narrowing of the orifice. This could produce some difficulties in micturition.

Tinea cruris: a fungal infection that could be seen in the intertriginous areas, inner thighs, and the scrotum characterized by a dry erythematous confluent sharply demarcated and slightly elevated rash.

Epidermal inclusion cysts: palpable skin colored nodules on the scrotum ranging in size from a few millimeters to several

centimeters. They may resolve spontaneously; if the patient has concerns, referral to dermatology is appropriate.

Phimosis: a condition where the foreskin in an uncircumcised male may not be fully retractable. Phimosis may be physiologic or pathologic or a combination of both. Uncircumcised infants have adhesions between the foreskin and the glans penis. Over time, these adhesions loosen and eventually most boys are easily able to retract the foreskin. However, some uncircumcised males enter puberty with a degree of physiologic phimosis. In addition, phimosis may result from repeated inflammation or injury on the prepuce causing a fibrotic ring, or the adolescent may acquire a disease resulting in secondary phimosis. Phimosis can interfere with hygiene, urination, and sexual relations. Although vitamin E or steroid cream may be helpful, the definitive treatment is a dorsal slit, removal of the fibrotic ring, circumcision, or treatment of the underlying disease (see Figs. 5.2 and 5.3).

Paraphimosis: this condition occurs when the foreskin is tight but still somewhat retractile. When the foreskin is pulled back and cannot be repositioned, then paraphimosis occurs. Most commonly seen in adolescents, it occurs during intercourse—sometimes

Fig. 5.2 Phimosis secondary to trauma. Credit: Charlie Goldberg M.D., University of California San Diego School of Medicine

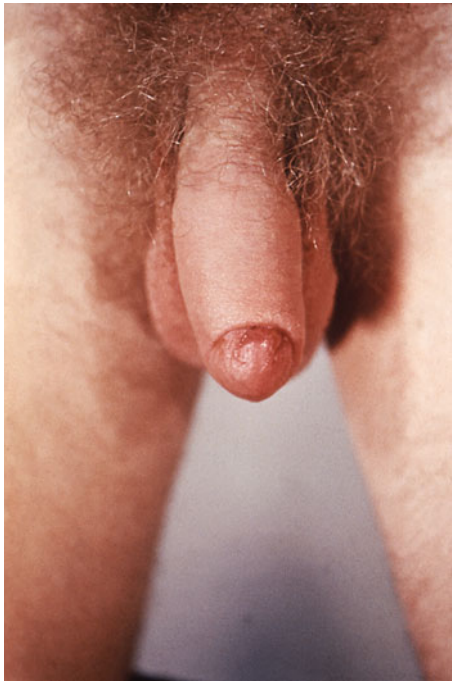


Fig. 5.3 Phimosis secondary to syphilis. Credit: U.S. Centers for Disease Control and Prevention/Susan Lindsley. http://phil.cdc.gov/phil/home.asp

during the first occasion. It is an emergent condition. Treatment includes reducing the swelling by ice packs or fluid evacuation. Under local anesthesia, the foreskin is then replaced into its normal position. Prevention includes a dorsal slit procedure or circumcision (see Figs. 5.4 and 5.5).

Varicocele: this condition consists of enlarged and often tortuous veins that are usually seen on the left side of the scrotum since the left gonadal vein is longer than the right. The left spermatic vein inserts at a right angle into the left renal vein and has a higher likelihood of incompetent valves. This leads to a higher potential for blood to back up and cause dilated spermatic veins. On the

Fig. 5.4 Paraphimosis before treatment. Credit: Charlie Goldberg M.D., University of California San Diego School of Medicine

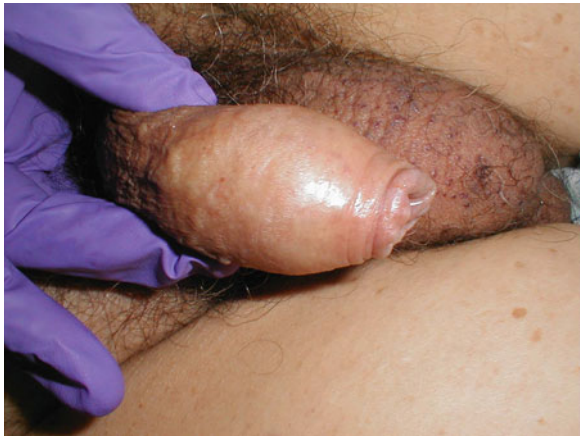


Fig. 5.5 Paraphimosis after treatment. Credit: Charlie Goldberg M.D., University of California San Diego School of Medicine

right side, the right spermatic vein enters the vena cava at an acute angle with backup less likely. Varicoceles present between age 10–15 years and are seen in about 15 % of adult males. Check to be certain a left-sided varicocele obliterates when the patient assumes

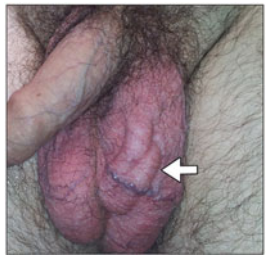


Fig. 5.6 Left-sided varicocele. Credit: Dr. Miguel Angel Arrabal-Polo, Department of Urology, San Cecilio University Hospital

a supine position. If not, then imaging studies including ultrasound should be considered to rule out venous obstruction in the abdomen from thrombosis or a mass lesion. Right-sided varicoceles should be evaluated with imaging studies to rule out a mass lesion or thrombosis. Varicoceles should be followed annually especially since larger varicoceles may be associated with discomfort and decreased sperm counts. Consultation with a urologist may be appropriate (see Fig. 5.6).

Balanitis: this is an infection of the glans penis usually seen in uncircumcised males and caused by Candida although bacterial superinfection may occur. A sex partner may also have the infection. A topical antifungal cream is the usual treatment. When the glans and the inner aspect of the foreskin are involved, it is termed balanoposthitis (see Fig. 5.7).

Hydrocele: this is a fluid collection between the parietal and visceral layers of the tunica vaginalis. In adolescents, hydroceles are usually painless, and they may change in size. Occasionally, hydroceles may develop in reaction to a testicular tumor, epididymitis, orchitis, trauma, or testicular torsion, so it is important to carefully examine the testicles. Hydroceles may transilluminate. If there is continuing concern about a secondary condition causing the hydrocele, then Doppler ultrasonography would be helpful. Elective surgery can be done for those hydroceles that are symptomatic or large (see Fig. 5.8).

Hernia: this usually presents as a bulge in the groin although it may appear as a scrotal mass. Valsalva maneuvers including cough or straining can make a hernia more apparent. A hernia usually

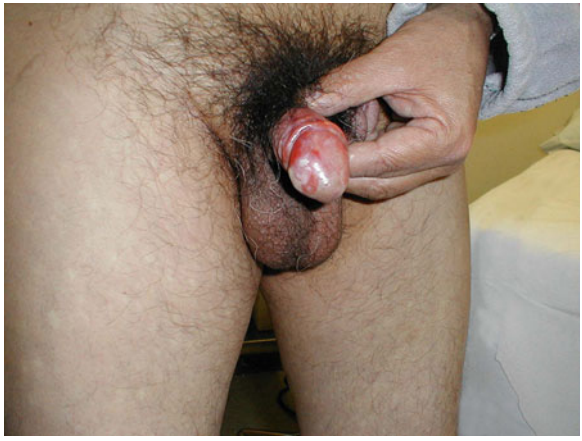


Fig. 5.7 Balanitis of glans. Credit: Charlie Goldberg M.D., University of California San Diego School of Medicine

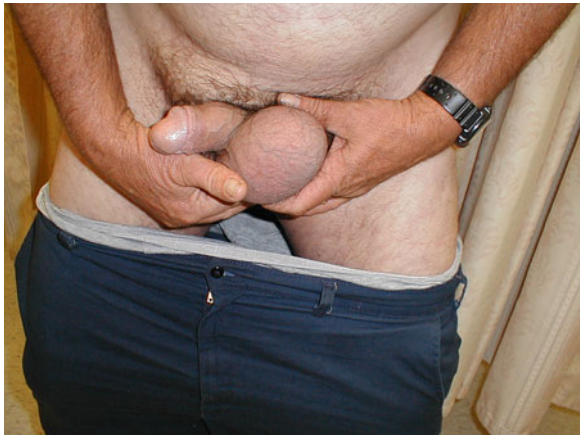


Fig. 5.8 Hydrocele. Credit: Charlie Goldberg M.D., University of California San Diego School of Medicine

disappears with the adolescent in the supine position. Unless incarcerated, the pain may be a dull ache; with incarceration, the pain is more severe. A hernia feels soft and smooth and often takes the shape of a sausage. Inguinal hernias are generally electively

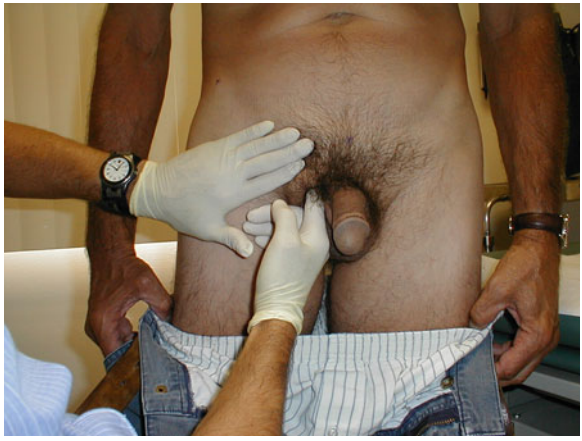


Fig. 5.9 Hernia exam. Credit: Charlie Goldberg M.D., University of California San Diego School of Medicine

repaired in adolescents; incarcerated hernias are a surgical emergency (see Figs. 5.9 and 5.10).

Spermatocele: this is a retention cyst of the rete testis, ductuli efferentes, or epididymis filled with fluid containing sperm. It rarely undergoes torsion. It is usually small, fluid-filled, and should transilluminate located above and anterior to the testis. Ultrasound is generally performed to evaluate for the chance of occult testicular malignancy. No treatment is usually needed.

Cryptorchidism: the absence of a testicle in an adolescent male is an important issue. Inquire as to the history of the absent testicle. Try to palpate it within the inguinal canal. If not palpable, then ultrasound may be helpful in localizing it. Patients with an undescended testicle in the adolescent age range need referral to a urologist as there is an increased risk for testicular malignancy,

Orchitis: this is enlargement of the testicle that can also involve the epididymis as well as the skin of the scrotum. Mumps, rubella, coxsackie, echovirus, and parvovirus infection can be a cause of orchitis in adolescents. Brucellosis has also been reported to cause orchitis. In addition, a careful testicular examination is needed to assess for tumor.

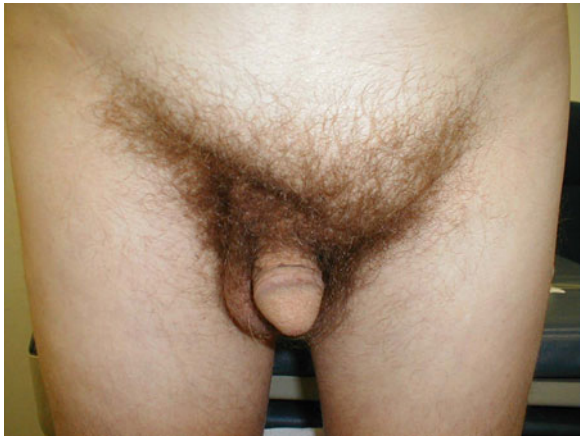


Fig. 5.10 Left inguinal hernia. Credit: Charlie Goldberg M.D., University of California San Diego School of Medicine

Testicular Torsion: torsion occurs from twisting of the spermatic cord that compromises blood supply to the testicle. There is usually a 4–8 h window before ischemic damage occurs; however, adolescents often present beyond that period. This condition is an urgent surgical emergency. Abnormal testicular fixation, "the bell-clapper" deformity, allows the testicle to twist especially as the testicle enlarges and becomes more vascular during early puberty. The classic presentation is severe unilateral scrotal pain often accompanied by nausea and vomiting. The affected testicle may be riding higher in the scrotum or have an abnormal transverse lie; the cremasteric reflex may be absent. The adolescent usually is in significant pain so a thorough testicular examination may not be possible. Immediate ultrasonography with color Doppler allows determination of blood flow is readily available and less time-consuming than radionuclide imaging of the scrotum. This test is highly reliable and does not expose the adolescent to radiation. A surgeon should be involved immediately.

Hidden or buried penis: this can occur if the patient has large adipose deposits surrounding the penis. The examiner can push back the pads to expose the penis. If there are issues with urination, the patient can be referred to urology.

Epididymitis: this disorder is usually characterized by scrotal pain and swelling that occurs over a period of days rather than hours. Generally, the epididymis is enlarged and tender as is the spermatic cord. There may be an associated hydrocele. Epididymitis may be caused by bacteria from urethritis or a urinary tract infection reaching the epididymis in a retrograde manner. A bacteriological diagnosis can be established by culturing urine or screening urine for chlamydia or gonorrhea. Men who have insertive anal sex may develop epididymitis caused by an enteric organism such as E. coli. Treatment is directed at the probable organism(s) and should be initiated before laboratory test results are available (see section on STI for appropriate treatment regimens). The sex partners of patients with confirmed infection with chlamydia or gonorrhea should be referred for treatment if his/her contact with the patient was within 60 days preceding the onset of his symptoms.

Testicular Tumor: tumors of the testicle are the most common cancers in adolescent and young adult males ages 15–34 years. The incidence may be as high as 5.4 cases per 100,000 males. It is highest in Caucasians, and males with a history of cryptorchidism have an increased risk for testicular cancer. Adolescents may complain of a dragging or heavy sensation to the testicle. Some teens develop gynecomastia when a tumor is secreting human chorionic gonadotropin. Others may have back or flank pain if there is metastatic disease. The normal testicle has the consistency of a hardboiled egg and its smooth surface; examination of a testicular tumor may reveal a firm or hard mass attached to the testicle that does not transilluminate. Testing should initially include a scrotal ultrasound (be sure to evaluate both testicles) which can discriminate between a malignant and nonmalignant process. If a tumor is suspected on the basis of ultrasound, then oncology and urology need to be involved immediately for staging and treatment.

Testicular Self Exam (TSE): TSE is an examination that may be taught to adolescents. This is most easily done during the annual examination. However at this time, the U.S. Preventive Services Task Force does not recommend routine screening for testicular cancer in asymptomatic males nor does the American Cancer Society recommend teaching patients testicular self-examination to detect cancer. Their concerns include the potential issues of false positive results, anxiety and adverse effects of diagnostic tests.

Nonetheless, examination of the male genitals including the testicles should be a regular part of the annual examination and when indicated during interval visits since the clinician is looking for other abnormalities or conditions. Patients and families should be educated about the importance of the male genitourinary exam. Some adolescents may not be aware of what is normal or abnormal in the genitourinary region, or they may be reluctant to bring concerns about an abnormality to the attention of a clinician. During the examination, the clinician can directly review with the adolescent any concerns he may have about the genitalia and perform a complete examination.

Sources

Blair RJ. Testicular and scrotal masses. Pediatr Rev. 2014;35:450–2.

Gatti JM, Murphy JP. Acute testicular disorders. Pediatr Rev. 2008;29:235–40.

Goldstein MA. Male puberty: physical psychological, and emotional issues. Adolesc Med. 2003;14:541–53.

Jenkins JT, O'Dwyer PJ. Inguinal hernias. BMJ. 2008;336:269–72.

U.S. Preventive Services Task Force. Screening for testicular cancer: U.S. Preventive Services Task Force reaffirmation recommendation statement. Ann Intern Med. 2011;154:483–86.

Wan J, Bloom DA. Genitourinary problems in adolescent males. Adolesc Med. 2003;14:717–31.

The Pelvic Examination and Pap Smear in Adolescents and Young Adults

6

Nupur Gupta

Cervical cancer takes many years to develop after exposure to the HPV virus and is rare in women below the age of 21 with the age adjusted incidence in 15–19-year-olds being 0.1 per 100,000. HPV infection, although common in sexually active adolescents, often resolves spontaneously in immunocompetent adolescents. Even if abnormal cells appear, they often resolve without any intervention. With research into the epidemiology of HPV infection and the advent of the HPV vaccine the American College of Obstetrics and Gynecology (ACOG) recommends that routine screening with Papanicolaou (Pap) smears in asymptomatic, immunocompetent women start only at 21 years of age and if normal be repeated every 3 years. A pelvic examination is thus often not required in adolescents who are sexually active as screening for sexually transmitted infections can be conducted in urine or by self-administered vaginal swabs.

Adolescents who are immunocompromised have HIV or have a history of exposure to diethylstilbestrol in utero should start Pap screening at the onset of sexual activity and may require more frequent screening. Those who at prior screening have had abnormal Pap smears should be screened as per guidelines below.

M.A. Goldstein (ed.), *The MassGeneral Hospital for Children Adolescent Medicine Handbook*, DOI 10.1007/978-3-319-45778-9_6

The Pelvic Examination

A pelvic examination was considered a rite of passage for adolescent females as they became sexually active. However with recent advances in screening for sexually transmitted infections (STIs) and research studies that have shown that Pap smears are unnecessary and can be harmful in young people, the age for a pelvic examination may be delayed.

These examinations are often dreaded by young women because of myths about the "pain" experienced during such examinations. Educating patients about how and why they are performed may help providers reduce this fear and make patients more comfortable with coming in for essential care.

Who Needs a Pelvic Examination?

1. Women 21 and older for the purpose of routine screening for cervical cancer by performance of Pap smears. Younger women may need a follow-up if they had a Pap smear prior to 21 and this was abnormal. In these cases, they will have follow-up as per ACOG recommendations.
2. Females considering an intrauterine device for contraception
3. Lower abdominal and/or pelvic pain
4. Vaginal discharge
5. Urinary symptoms in sexually active female
6. Irregular menstrual bleeding (may need)
7. Primary amenorrhea (may need)
8. Retained Tampon and/or foreign body
9. Pregnancy
10. Sexual Trauma or suspicion of abuse (If patient is comfortable and allows the examination)

How Should One Conduct a Pelvic Examination?

A. *Counseling patient*: Always counsel patient about the examination. Using pictures or showing them a speculum prior to the

examination often prepares them and reduces anxiety about the examination. Allowing the patient to touch the speculum is also helpful. Chaperones are recommended with male providers, but it may be helpful to ask the patient their preference even when the provider is a female.

Explain to the patient that there are three parts to the examination:

- The first involves inspection of the external genitalia to assess anatomy and the presence of abnormal lesions.
- The second is a speculum examination
- The third part to the examination is an internal examination in which the provider will insert gloved fingers to assess the size of the uterus, anatomical abnormalities, cervical motion, uterine or adnexal tenderness, or the presence of masses in the adnexae.

Also explain to them that if they experience pain during the examination they could ask to stop the examination at any time.

B. *Provider and Room Preparation:* The provider should prepare the swabs and screening tools prior to the examination. Being organized instills confidence in the patient that the provider is well prepared. The examination room should have running water, be warm, and preferably have a curtain to ensure privacy. There should be an examination table with stirrups.

Equipment:

1. Latex-free gloves
2. Gowns and draping material (cloth or disposable)
3. Speculum: Could be disposable plastic or steel speculum. Have both Pederson (7/8 in. wide) and Hoffman (0.5 in. wide) available to accommodate different sizes and virginal adolescents. The speculum should be at least 4 in. in length so as to allow the visualization of the cervix and thus pediatric speculums should not be used, as they are shorter.
4. Light attachment that inserts into the plastic speculum or an external light source.
5. STI screening test swabs: Gonorrhea (GC) and Chlamydia tests are usually those that check for antigen using a

nucleic acid amplification technique or NAATS. Cultures for GC and Chlamydia may be needed in cases where there is a resistant infection, patient is pregnant or a child with a suspicion for sexual abuse.

6. Swabs: Cotton, dacron, calcium alginate for genital, fungal cultures and for wet preparation.
7. Slides for a KOH and wet preparation and cover slips (this helps to determine the nature of the discharge and sometimes make diagnoses); Normal saline and 10 % potassium hydroxide solutions for making the slides; pH paper
8. Water-soluble lubricating jelly for a bimanual examination
9. For a Pap test: Endocervical brush or broom and ectocervical Spatula (liquid container if doing a liquid-based Pap; slide and fixative for other Pap tests)
10. Microscope (optional) if you have approval for point of care testing
11. Sanitary pads

C. *Patient preparation*: Prior to the examination have the patient empty her bladder and then change into a gown opening at the back. Once the patient is lying on the examination table (draped) with knees bent have her move down on the table until her buttocks are at the edge of the table. Then, help her insert her heels into the stirrups of the examination table. The patient may need to slither down a little more (until she is almost off the table) to get into lithotomy position. Once she is well positioned, ask her to abduct her hips a little so as to separate the knees and relax. Other positions may also be used especially if the patient has any musculoskeletal impairment.

D. Conducting the examination:

External examination: Inspect the external genitalia for Tanner staging and anatomical variations; clitoromegaly (width >10 mm) and hirsutism (pubic hair may extend onto the thigh and up the linea nigra) may suggest hyperandrogenism; erythema, marks of excoriation and any lesions including genital warts, vesicles suggestive of Herpes simplex or umblicated lesions representing Molluscum contagiosum. Evaluate the introitus and assess for hymenal abnormalities like a microper-

forate, imperforate, or cribriform hymen. An imperforate hymen warrants an emergent referral to a gynecologist. A small opening or the presence of a hymenal band may prevent insertion of a tampon and may make a pelvic examination (and sexual activity) difficult. After gently separating the labia inspect the vaginal epithelium to assess estrogen effect. A red, thin, beefy appearance is suggestive of hypoestrogenization (as seen in anorexia nervosa), and a pink moist mucosa indicates normal estrogen levels. A vaginal smear may be obtained to assess maturation index if needed, which is the proportion of superficial, intermediate, and parabasal cells. A higher percentage of superficial cells indicate greater effect of estrogen. Assess also for a vaginal septum that could be vertical or transverse and may indicate Mullerian abnormalities. Check for vaginal discharge or bleeding. Bartholin's glands present in the lower vestibule may also be enlarged or infected and cause swelling in the labia minora. Skene's glands are located lateral to the urethral opening and when infected may produce a discharge into the urethra when anterior pressure is applied on the vaginal wall.

Speculum Examination: Wetting the speculum with warm water and placing it on the thigh may help prepare the patient for the examination. Avoid pulling pubic hair or touching sensitive structures like the clitoris and the urethra. The labia should be gently separated and the speculum inserted laterally. While inserting make sure the speculum is closed and the tip directed 45° posteriorly; the other hand can put pressure on the introitus and gently pull it down to facilitate insertion. When the speculum is inserted completely to the hub, rotate it to the horizontal position and then open slowly till the cervix is visualized. Once the cervix is visible, click and lock if it is a plastic speculum and screw tight if a steel one. Open the speculum only to the extent that allows visualization.

The cervix should be examined for any lesions, friability, and discharge. Adolescents often have a large ectropion (junction between the squamous and columnar cells) that bleeds easily which may be a normal physiological finding or may indicate infection.

The Pap smear should be performed first followed by STI testing. Most institutions use an endocervical brush or broom that is to be inserted into the cervical os and rotated around ¼ to ½ turn to obtain the endocervical cells; the ectocervix can be sampled using a ectocervical spatula which is brushed along the ectocervix using the center of the os as a fulcrum while others use only a broom that does both. If using a liquid-based Pap medium like "Thin Prep" the brush or broom is then inserted into the liquid medium and thoroughly agitated and in some cases they can be broken off and detached into the medium. STI testing for both GC and Chlamydia using nucleic acid amplification technique (NAATS) is done with two swabs. The white swab is used to first clean the cervical os and then discarded, and the blue swab is used to do the testing. Once the appropriate testing is done, the speculum should be closed gently taking care not to pinch vaginal or cervical tissue and then slowly withdrawn. While doing so, an effort should be made to inspect the vaginal walls as well.

Bi-manual examination: For the last part of the pelvic examination, the clinician uses a water-soluble lubricant and inserts one or two gloved fingers of one hand gently into the vagina while applying a little bit of pressure over the lower abdomen with the other hand. A bimanual examination allows the provider to estimate the uterine size and also to assess cervical motion tenderness, elicited by moving the cervix anteriorly with the fingers. Ensure that what the adolescent is feeling is pain and not just discomfort because of the examination. Cervical motion tenderness usually indicates pelvic inflammatory disease. The nonpregnant uterus is usually small and firm while a pregnant uterus is soft and enlarged, usually about the size of an orange at 8 weeks of gestation. Moving the fingers laterally in the vaginal vault allows the clinician to evaluate the adnexa. Ovaries are usually very small and often hard to palpate in an adolescent. If the adnexa feels full, tender or a mass is palpated it raises concern for ovarian pathology including but not limited to an ovarian cyst, torsion, abscess, ectopic pregnancy or a tumor, and clinical correlation and imaging will help to elucidate the cause.

Special Populations

1. Vaginsmus: Patients who are very sensitive may have spasm of the lower third of the vaginal which will preclude an examination. The examination must be stopped and rescheduled.
2. Patients with disability: These patients may require special assistance depending on their disability. Different positions rather than a classic lithotomy position may be needed depending on the type of disability. Visually and hearing impaired adolescents may require more accommodations and an attendant or interpreter in the room at the time of the examination.
3. Patients with a history of trauma may find it especially difficult to undergo a pelvic examination because of post-traumatic stress disorder and may need extensive psychological support to prepare them for the examination.

Interpretation of Pap Smear Results

Pap smear results serve as screening tools to guide the clinician as to whether the patients require further testing like colposcopy or cervical biopsy. They are not diagnostic of cervical cancer but indicate whether there are cellular abnormalities that may predict histological changes. HPV testing is not usually indicated in women below the age of 30.

While reviewing the results it is important to pay attention to the following:

1. Adequacy of specimen: The specimen must have an adequate number of cells to be read accurately, with conventional Paps requiring at the least 8–12,000 and liquid specimens, 5000 squamous cells.
2. Adequate transformation zone and endocervical cells: This area is the highest risk for cervical neoplasia and thus it is important that this be represented in the Pap smear. (However, recommendations for management of these findings in patients 21–29 years have changed, see below)
3. Presence of blood or inflammation obscuring the cells: If 50–75 % of the specimen is obscured it is considered partially obscured; if more than 75 % of the cells are obscured because of these reasons, the specimen is considered inadequate.

4. Presence of infectious organisms: Occasionally, infectious organisms may be reported on the Pap smear but clinical correlation and confirmatory tests must be performed and treatment offered where appropriate. These include Candida, Bacterial vaginosis (clue cells), Trichomonas, Herpes simplex, Actinomyces (in older women with an IUD), and rarely Chlamydia.

Classification and Interpretation of Pap Smears

Classification is done using the Bethesda system (latest version 2014). Management is according to guidelines from the American Society for Colposcopy and Cervical Pathology. (ASCCP) and ACOG.

1. Negative for intraepithelial lesion or malignancy: Indicating that there are no epithelial cell abnormalities
2. Epithelial cell abnormalities:
   A. Squamous
   B. Glandular

A. Squamous cell abnormalities:
   I. Atypical Squamous cell which can either be of undetermined significance (ASCUS); or Atypical Squamous cell cannot exclude high-grade squamous intra epithelial lesion (ASC-H) when there is a mix of high-grade squamous intraepithelial lesions abnormalities.
   II. Low-grade Intraepithelial Lesion (LGSIL): Often associated with HPV infection and with a histological diagnosis of Cervical Intraepithelial Neoplasia (CIN) 1.
   III. High-grade Intraepithelial Lesion (HGSIL): Often associated with HPV infection and with a histological diagnosis of Cervical Intraepithelial Neoplasia (CIN) 2 or 3. Usually, the cytology will indicate if there is any evidence of invasive disease.
   IV. Squamous Cell Carcinoma

B. Glandular Cell abnormalities:
   I. Atypical glandular cells (AGC): These may be from the endocervix or endometrium or may not be clear from where they originate. These are often associated with high-grade glandular or squamous cells on histology.

II. Atypical glandular cells, favor neoplastic: These usually have a histology that suggests but is not definitive for adenocarcinoma
III. Endocervical Adenocarcinoma in situ
IV. Adenocarcinoma

Management of Abnormal Pap Smears: Women Aged 21–29

1. Insufficient cells: Repeat at 3 months.
   A. If abnormal then manage as per ASCCP guidelines
   B. If normal: Routine screening
2. Cytology Adequate but absent or insufficient endocervical cells (EC)/Transformation zone (TZ): Routine testing is recommended in women aged 21–29. *HPV testing should not be done and is unacceptable*
3. ASCUS : Reflex HPV testing may be done
   A. HPV negative: Routine screening in 3 years
   B. HPV positive or unknown: Repeat in 1 year
      I. If negative, ASCUS or LGSIL: Repeat in 1 year,
      II. If persists or worse, then colposcopy is indicated
      III. If normal, then return to routine screening
4. If ASC-H, AGC, HGSIL: Colposcopy
5. LGSIL: Repeat in 1 year
   A. I. If negative, ASCUS or LGSIL: Repeat in 1 year
      II. If persists or worse: Colposcopy.
      III. If normal: (i.e., negative for 2 years) then return to routine
   B. If ASC-H, AGC, HGSIL: Colposcopy
6. ASC-H or HGSIL: Colposcopy
7. All glandular cell abnormalities: Referral to gynecology for colposcopy or endometrial biopsy (rarely seen in women in this age group)

Sources

1. Bates CK, Carroll N, Potter J. The challenging pelvic examination. Gen Intern Med. 2011;26(6):651–7. doi:10.1007/s11606-010-1610-8. Published online 12 Jan 2011.

2. Braverman PK, Breech L, and the Committee on Adolescence (AAP). Clinical report—gynecologic examination for adolescents in the pediatric office setting. Pediatrics. 2010;126(3):583–90. www.pediatrics.org/cgi/doi. doi:10.1542/peds.2010-1564.
3. Massad LS et al. (2012 ASCCP Consensus Guidelines Conference) 2012 Updated consensus guidelines for the management of abnormal cervical cancer screening tests and cancer precursors. @2013, American Society for Colposcopy and Cervical Pathology. J Low Genit Tract Dis. 2013;17(5):S1YS27.
4. Practice Bulletin Number 157. Cervical cancer screening and prevention. Obstet Gynecol. 2016;127:185–7.

Adolescent Dermatology

7

Anna Cristina Garza-Mayers
and Daniela Kroshinsky

Acne

Acne is one of the most common skin conditions, affecting approximately 85 % of people at some point during their lives. The lesions consist of open and closed comedones ("blackheads" and "whiteheads"), papules, pustules, cysts, and/or nodules over the face, chest, and/or back. Treatment is geared toward the type of lesions and the presence or absence of scarring.

Comedonal acne responds best to topical retinoids such as tretinoin (Retin-A™), tazarotene (Tazorac™), or adapalene (Differin™) (Table 7.1). These medications increase skin turnover and make cells less "sticky" so they are less likely to clog pores. This is an important step, as the comedone is thought to be the precursor lesion to more inflammatory forms of acne. Efficacy and potential irritation are directly proportional, and these medications can be ranked in both as tazarotene > tretinoin > adapalene.

Topical retinoids should be used nightly, beginning with the lowest possible concentration and applied in small quantities. The easiest way to initiate use is with a pea-sized drop distributed evenly over the entire face beginning every other night for 2 weeks, then increasing to nightly as tolerated. Possible side effects include

M.A. Goldstein (ed.), *The MassGeneral Hospital for Children Adolescent Medicine Handbook*, DOI 10.1007/978-3-319-45778-9_7

Table 7.1 Acne therapy

Treatment	Options	
Topical antibiotics	Clindamycin 1 % pledget,[a] solution, lotion, or gel	
	Erythromycin 2 % solution, pledget[a], or gel	
Combination BP/ antibiotics[b]	Benzaclin™	5 % BP + 1 % clindamycin gel
	Duac™	5 % BP + 1.2 % clindamycin gel
	Benzamycin™	5 % BP + 3 % erythromycin gel
Antibiotic/retinoid[b]	Ziana™	Clindamycin 1.2 % + tretinoin 0.025 % gel
BP/retinoid[b]	Epiduo™	2.5 % BP + adapalene 0.1 %
Topical retinoids[b]	Tretinoin	0.025, 0.05, 0.1 % cream, gel
		0.04, 0.1 % microsphere gel[c]
	Tazarotene™ [c]	0.05, 0.1 % cream, gel
	Adapalene ™ [c]	0.1 % cream; 0.1, 0.3 % gel
Oral antibiotic	Minocycline 50 mg, 100 mg tab, cap	
	Doxycycline 50 mg, 100 mg tab, cap	
Oral contraceptives	FDA-approved for acne vulgaris	
	Estrostep™, Ortho Tri-Cyclen™, Yaz™	
	Clinical data to support use	
	Alesse™, Diane-35™, Yasmin™	

[a]May not be covered by insurance in MA, easiest for adolescent use ("wipe and go")
[b]May not covered by insurance in MA
[c]Least likely of options to be covered by insurance in MA

redness, dryness, and peeling. As the skin becomes tolerant to the medication, these will subside. The use of non-comedogenic (non-pore clogging) moisturizer can minimize this, but some adolescents will never be able to tolerate nightly use and should be encouraged to use the medication every other night or biweekly. Patients and parents should be counseled that 2–3 months of consistent use is necessary before any results are seen. After 2–3 months of successful (i.e., non-irritated) use, concentration may be increased to the next highest strength available for maximal efficacy. In addition to clearing comedones, this family of medications may help resolve post-inflammatory hyperpigmentation and mild scarring and may be useful in almost all types of acne.

Mildly inflammatory acne consists of few erythematous papules and/or pustules, usually accompanied by comedones. Topical erythromycin or clindamycin qam with a topical retinoid qhs is most effective though increased resistance to erythromycin is reported. Concomitant benzoyl peroxide (BP) use with topical antibiotics may help limit development of resistance but also increases irritation and dryness. In addition, topical BP can bleach clothing and linens. Use of an over-the-counter BP wash ranging from 4 to 10 %, with skin contact for 20–30 s may provide the same effect without the side effects.

For moderate-to-severe inflammatory acne, the topical retinoid should be continued and an oral antibiotic added. Minocycline or doxycycline 100 mg po bid is most effective. Use caution with doxycycline as significant photosensitivity may result in severe sunburns and patients should be warned of this. Major complaints with minocycline include headache and dizziness, which may be dose dependent in affected individuals. Patients should also be assessed regularly for blue-gray discoloration of old acne scars that can infrequently be associated with long-term minocycline use. Both medications should be taken after eating, despite package insert instructions, to minimize gastrointestinal upset. These medications should be maintained until very few lesions are appearing each month. At this point, a taper can be initiated. Tapering may vary, but it is recommended to decrease the oral medication from 100 mg bid to 50 mg qam and 100 mg qpm for 3–4 weeks then 50 mg bid for 3–4 weeks then discontinued. In general, minocycline is thought to be more effective than doxycycline due to improved sebaceous gland penetration and patients who fail doxycycline use may still respond well to minocycline instead.

Severe acne, typified by nodules, cysts, and significant scarring, tends to be unresponsive to the above regimens. Individuals with this type of acne should be referred for isotretinoin use, which requires registration in the iPLEDGE program and regular monitoring of pregnancy status, complete blood count, fasting lipid profile, and liver function tests. Isotretinoin remains the single most effective therapy for severe or scarring acne and when monitored appropriately, remains a safe therapeutic agent. Despite early concerns, recent studies indicate no increased risk of inflammatory

bowel disease or suicide. Patients with severe acne, especially young men with back involvement, should be asked about bone pain, myalgias, arthralgias, or fevers, as this may be a sign of more severe acne, acne fulminans, that will require both isotretinoin and prednisone use.

No matter what type of acne is present, affected adolescents should be followed initially 4–6 weeks after the first visit to assess for proper use of medications and possible side effects, as well as to provide reassurance. From that point on, subsequent follow-up may be spread out: 6 weeks later, then 2–3 months later, then 6 months later, then annually. Female patients should be asked about irregular menses and/or increased hair growth that may suggest polycystic ovary syndrome and should prompt a hormonal evaluation.

Tinea Pedis

Tinea pedis, or "athlete's foot," is the most common superficial fungal infection affecting adolescents. It is infrequently seen in children. There are three forms of this foot infection: intertriginous, moccasin-type, and inflammatory/vesicular. The intertriginous form typically presents as scaling, maceration, and inflammation in the toe web spaces. The moccasin-type of tinea pedis presents with erythema, scaling and hyperkeratosis of the soles of the feet, extending up the sides of the feet. The inflammatory variant of tinea pedis presents with inflammation, vesicles, and sometimes bullae. It represents an inflammatory reaction to the fungal organisms present. Occasionally, the inflammatory reaction can become generalized, producing papules or vesicles over the hands and/or torso.

Diagnosis may be confirmed with a potassium hydroxide (KOH) wet mount preparation that will demonstrate septated hyphae and/or a fungal culture taken from gentle scraping of the scale from the affected surfaces. Treatment of routine infections is with a topical antifungal such as econazole, terbinafine, or ciclopirox twice daily for 2–3 weeks. Severe infections may require oral therapy. Preventing infection or recurrence is

important. Humid or moist surfaces, such as the floors of the gym, pool decks or public showers are potential sources. It is important to keep feet dry and avoid occlusive or non-breathable shoes or socks. Antifungal powders or sprays and the use of footwear when walking on prone surfaces may be helpful to prevent reinfection. For those with sweaty feet, use of aluminum chloride 20 %, a prescription-strength antiperspirant, can be helpful to prevent recurrences. Aluminum chloride should be initially applied q3days, increasing to qd as needed to control the hyperhidrosis.

Tinea Cruris

Tinea cruris, or "jock itch," is a superficial fungal infection of the groin and/or upper thighs usually seen in adolescents and adults, typically male. It is most often seen in overweight individuals or persons involved in activities that produce sweating or chafing or who wear tight fitting clothing.

Clinically, the lesions present as well-demarcated, erythematous to hyperpigmented plaques with a raised border of scaling and relative central clearing. Tinea cruris is usually pruritic and bilateral and tends to spare the scrotum and labia majora. Involvement of these areas or the presence of satellite papules or pustules should suggest cutaneous candidiasis or inverse psoriasis. In chronic infections or if topical steroids have been applied, the margins, border, and scale may be more subtle, resulting in the loss of the characteristic "rings" and producing a "tinea incognito" picture. Chronic pruritus with scratching may produce lichenification. The diagnosis may be confirmed by potassium hydroxide (KOH) wet mount preparation that will demonstrate septated hyphae and/or fungal culture. The differential diagnosis for a rash in this distribution includes cutaneous candidiasis, intertrigo, inverse psoriasis, irritant contact dermatitis, allergic contact dermatitis, and erythrasma.

Treatment involves a topical antifungal agent for 3–4 weeks applied twice daily. Oral antifungal therapy may be necessary for extensive or inflammatory cases. Loose-fitting cotton undergarments and drying well after showers or perspiration may help to prevent recurrences. Prophylactic use of over-the-counter

antifungal powders may also be helpful though insufficient to treat an active infection and should not be used concomitantly with an antifungal cream as it will produce a paste-like substance that can be uncomfortable and cosmetically challenging. Concomitant tinea pedis should be treated to prevent re-seeding of the infection.

Tinea Versicolor

Tinea versicolor is a superficial fungal infection caused by the yeast forms of *Malassezia* fungi that create multiple circular and oval scaling macules, patches, and plaques, most often becoming confluent over the chest/back, proximal extremities, and sometimes the neck and face. The lesions tend to be pink or salmon colored in light skin types but can also present as hypo- or hyperpigmented areas. The organism produces azelaic acid which can bleach affected areas. Patients should be reassured that pigmentary discrepancies may persist for months despite adequate treatment and that this is not a sign of persistent or reinfection. Pigmentation will return spontaneously with time and additional treatment will not impact the course of repigmentation.

The causative organism is considered to be part of normal skin flora, but becomes clinically relevant during times of increased sweating and in adolescence with increased sebum production—both of which create a favorable environment for organism multiplication. The diagnosis may be confirmed by potassium hydroxide (KOH) wet mount preparation that will demonstrate "spaghetti and meatball" pattern of hyphae and spores. In darker skin types, confluent and reticulated papillomatosis (CARP), a benign dermatosis of unclear etiology should be considered when lesions fail to respond. These lesions tend to present with velvety hyperpigmented patches or plaques over the central torso that can mimic the lesional appearance of acanthosis nigricans.

For treatment of mild infections, selenium sulfide 2.5% or ketoconazole 2% shampoo may be applied daily for 10 min prior to rinsing for 1–2 weeks. Topical ketoconazole cream or lotion can be applied twice daily for 1–2 weeks as well. Severe cases, cases

involving hair-bearing regions, or recalcitrant cases can require oral therapy. Ketoconazole 400 mg PO followed by sweat-inducing activities 1 h later can be very effective, especially as this causes the medication to be secreted onto the skin where it is not rinsed for 10–12 h. This routine is repeated in 1 week to eliminate the hyphae resulting from the residual spores. Single dose fluconazole 400 mg PO × 1 followed by sweating is an alternate option. Use of the shampoo every other week or once a month may prevent recurrences in prone individuals.

Seborrheic Dermatitis

Seborrheic dermatitis is an inflammatory condition predominantly of the scalp (dandruff) and face, sometimes involving the chest, which can be chronic or relapsing and remitting in nature. It is characterized by erythematous plaques with waxy scale in sebaceous gland-rich areas, including the scalp, the retroauricular folds, the eyebrows, and the nasolabial folds.

Seborrheic dermatitis is usually a clinical diagnosis. Though it has been attributed to the fungus *Malassezia*, data are lacking to establish a clear pathogenic role and its etiology remains incompletely understood. It is possible that immune response to *Malassezia* colonization is to blame (Hay 2011). As such, first-line treatment of seborrheic dermatitis generally consists of topical antifungal agents, followed by topical corticosteroid use if these are ineffective. Daily shampooing with selenium sulfide, zinc-containing shampoo, or 2% ketoconazole may be used on the scalp. Use of such agents as a face wash or body wash may be used to treat the face and chest. The patient should be advised to apply the agent for 3–5 min before rinsing. If this is ineffective, or in cases with significant inflammation, a low potency corticosteroid such as hydrocortisone 2.5% cream for face used daily for 3–5 days and 0.01% fluocinolone acetonide (solution, foam or oil, depending on hair type and patient preference) used twice daily for up to 2 weeks can help resolve flares. Recalcitrant cases should be referred for dermatologic evaluation, particularly if other areas of the body are involved raising a concern for "sebopsoriasis," a term

used to describe the overlap of seborrheic dermatitis and psoriasis. The two can often look similar particularly on the scalp though it should be noted that psoriasis is not commonly diagnosed in adolescence.

Pityriasis Rosea

Pityriasis rosea, or PR, is a common scaling eruption of unclear etiology. Though it has been thought to be virally mediated, no specific cause has been identified and antiviral therapies are ineffective. It is reported in all age groups, with 75% of cases arising in individuals between 10 and 35 years of age.

Clinically, the eruption initially presents with a "herald patch"—the largest lesion that is first to arise, usually on the trunk, as a single papule that expands into a pink-erythematous oval patch or plaque with a raised border and scale that may be up to 10 cm in diameter. This lesion is followed 7–10 days later by the classic eruption of round to oval macules, patches, and plaques with fine central scale and a thicker ring of scale whose free edge faces inward (described as "collarette"). These lesions are arranged along the trunk in a "fir-tree" or "Christmas-tree" distribution (long axes of the oval lesions run parallel to the "branches" of the "tree" whose "trunk" is the spine). These lesions tend to arise on the trunk and proximal extremities, particularly the arms though face, palms, soles, and mucosa may be involved and an "inverse" or skin-fold variety exists, with a predilection for the axilla and groin. Palm and sole involvement should prompt consideration for secondary syphilis, and an RPR or syphilis antibody test can be checked if the clinical situation warrants. In a minority of cases, multiple herald patches may be found or can present concomitantly with the generalized eruption.

The eruption may be preceded by prodromal symptoms of fever, malaise, or arthralgias, and may be accompanied by pruritus. Patients should be reassured that the color will fade with time and does not represent a "resistant" case. Papular PR is another variant, most often seen in individuals of African descent. The herald patch is followed by the eruption of up to hundreds of small

maculopapules, some with a scaly border, over the same distribution as routine PR. Individuals affected by this variant are more likely to have scalp and facial lesions and more likely to report pruritus and post-inflammatory pigmentary alteration. The lesions are more likely to have abundant scale.

PR is a self-limited process and patients recover over 2–12 weeks though rarely as long as several months later. The eruption usually heals without scarring, but may leave pigmentary alteration in severe cases or in skin with darker pigmentation. Treatment should be geared toward control of pruritus and minimizing the scale if the patient is concerned by the appearance. Nonsedating antihistamines, such as loratadine, cetirizine, and fexofenadine may be used during the day with diphenhydramine or hydroxyzine qhs. Resistant pruritus may be treated with topical steroids though patients should be reminded that this will not alter the course. Hydrocortisone 2.5 % lotion bid for 1–2 weeks in mild cases or triamcinolone 0.1 % bid for 1–2 weeks may be helpful. Patients should be warned of the risk of cutaneous atrophy and striae formation if overused and caution should be maintained prior to providing a prescription for topical steroids that has refills. Scale may be improved with moisturizers, especially those containing lactic acid (6 % OTC Am-Lactin™ or 12 % Rx Lac-Hydrin lotions), used BID. Lac-Hydrin is often not covered by insurance in Massachusetts. Recalcitrant or severe cases may be referred for possible Narrow-Band Ultraviolet B Phototherapy TIW.

Sun Protection and Atypical Nevi

The negative effects of ultraviolet (UV) radiation from the sun are well established and include not only the risk of sunburn but also photoaging (wrinkles and pigment changes) and carcinogenesis. The risk of a diagnosis of skin cancer in adolescence is low. Nevertheless, exposure and risk are cumulative throughout one's life, with 80 % of sun exposure occurring prior to age 18 years. Counseling on sun protection is integral to disease prevention.

Patients should be counseled that sun exposure peaks between 10 am and 4 pm. When possible, particularly when long exposure

is predicted such as for athletic activity, photoprotective clothing including a hat should be used as well as sunscreen to all exposed skin. Exposure can occur even through car windows, thus daily sunscreen use is recommended for all skin types. A broad spectrum (UVA and UVB coverage) sunscreen with a Sun Protection Factor (SPF) of 45 or higher is recommended, preferably water resistant if worn for physical activity and with physical blockade such as zinc oxide. Sunscreen should be reapplied every few hours, with approximately two tablespoons applied to the entire body. SPF 30 sunscreen absorbs approximately 97 % of UVB radiation and by definition allows 30 times as much time in the sun before resulting in erythema in a given individual. On average, individuals using a quarter of the amount of sunscreen utilized in routine testing and studies have quoted an effective SPF of 9 in patients utilizing SPF 30. It is also important to note that SPF is not linear and that different individuals have a different minimal erythema dose (MED).

Adolescents in particular may be prone to risky behavior, such as sunbathing and indoor tanning. Recent legislation is working to ban indoor tanning in those less than 18 years of age. Adolescents should be counseled that tanning is a sign of photodamage, and indoor tanning is not safer than outdoor exposure. Any sunburn increases not only the risk of nevi (mole) development but also the lifetime risk of skin cancer.

Nevertheless, despite concern to the contrary, recent data demonstrate a decreasing incidence of melanoma in 2000–2010 in adolescents 15–19 years of age, with an incidence of approximately 17 per one million, representing 1–4 % of all melanoma. Adolescents with a history of melanoma in an immediate family member and/or a high density of nevi, particularly atypical nevi, may benefit from referral to a dermatologist. “Atypical,” or dysplastic, refers to clinical features shared with melanoma, though atypical nevi rarely develop into melanoma. Patients should be counseled on the importance of regular self skin examination, including the scalp and feet, and monitoring for the “ABCDEs” of atypia and melanoma: asymmetry, irregular borders, variations in colors (particularly if red, white or blue is present), diameter greater than 6 mm, and evolution in appearance over time. In most

cases, nevi can be monitored with the help of a primary care provider. Photography is often helpful. Attention should also be paid to a nevus that differs from the appearance of that generally found on the patient (the "ugly duckling"). Decisions on referral and follow-up interval are based on overall nevi density as well as the number of atypical nevi.

Sources

Alhusayen RO, Juurlink DN, Mamdani MM, Morrow RL, Shear NH, Dormuth CR. Isotretinoin use and the risk of inflammatory bowel disease: a population-based cohort study. J Invest Dermatol. 2013;133:907–12.

Campbell LB, Kreicher KL, Gittleman HR, Strodtbeck K, Barnholtz-Sloan J, Bordeaux JS. melanoma incidence in children and adolescents: decreasing trends in the United States. J Pediatr. 2015;166:1505–13.

Dennis LK, Vanbeek MJ, Beane Freeman LE, Smith BJ, Dawson DV, Coughlin JA. Sunburns and risk of cutaneous melanoma: does age matter? A comprehensive meta-analysis. Ann Epidemiol. 2008;18:614–27.

Hay RJ. *Malassezia*, dandruff and seborrhoeic dermatitis: an overview. Br J Dermatol. 2011;165 Suppl 2:2–8.

James WD. Acne. N Engl J Med. 2005;352:1463–72.

Ou-Yang H, Stanfield J, Cole C, Appa Y, Rigel D. High-SPF sunscreens (SPF ≥ 70) may provide ultraviolet protection above minimal recommended levels by adequately compensating for lower sunscreen user application amounts. J Am Acad Dermatol. 2012;67:1220–7.

Sundström A, Alfredsson L, Sjölin-Forsberg G, Gerdén B, Bergman U, Jokinen J. Association of suicide attempts with acne and treatment with isotretinoin: retrospective Swedish cohort study. BMJ. 2010;341:c5812.

Woo DK, Eide MJ. Tanning beds, skin cancer, and vitamin D: an examination of the scientific evidence and public health implications. Dermatol Ther. 2010;23:61–71.

Yan AC. Current concepts in acne management. Adolesc Med Clin. 2006;17:613–37.

Zaenglein AL, Thiboutot DM. Expert committee recommendations for acne management. Pediatrics. 2006;118:1188–99.

Obesity

8

Jennifer Rosenblum
and Rajitha D. Venkatesh

Background

Since 1980, the prevalence of obesity in adolescents has more than tripled with approximately 20 % of adolescents ages 12–19 in the United States currently with obesity, and over 1/3 with either overweight or obesity. There are racial disparities, with Hispanics and African-Americans being affected more than Caucasians. This epidemic is now recognized as a national crisis, with significant health consequences and financial burdens.

Definition

Obesity is determined by the body mass index (BMI), which is defined as weight (in kg) divided by height (in m^2). For children and adolescents, overweight is defined as BMI >85th percentile and obesity as ≥95th percentile for age. Severe obesity is considered to be ≧99th percentile.

M.A. Goldstein (ed.), *The MassGeneral Hospital for Children Adolescent Medicine Handbook*, DOI 10.1007/978-3-319-45778-9_8

Etiology

Obesity occurs due to an imbalance between energy intake and energy expenditure. The factors contributing to this imbalance include genetic, environmental, behavioral, and medical factors. The complex interaction between these factors as they contribute to obesity is unique for each individual.

Medical Evaluation

1. History: include age of onset of overweight and information about eating and exercise habits. Specifically, clinical providers should inquire about triggers of weight gain (excess appetite, emotional eating, medications), consumption of fast foods and sugar-sweetened beverages, meal patterns (skipping meals, grazing, binge or sneak eating), screen time, physical activity, mood, and prior weight loss attempts.
2. Physical exam: key findings include short stature, acanthosis nigricans, violaceous striae, hirsutism, goiter, hepatomegaly, micropenis, gynecomastia, abnormal gait, and enlarged dorsal and supraclavicular fat pads.
3. Identify medically treatable causes of obesity (Table 8.1)
4. Determine and treat obesity-related comorbidities (Table 8.2)

Table 8.1 Medically treatable causes of obesity

Drug-induced (>97 %)	(see Table 8.3)
Genetic syndromes (<1 %)	Albright hereditary osteodystrophy
	Alstrom-Hallgren syndrome
	Bardet-Biedl syndrome
	Beckwith-Wiederman syndrome
	Carpenter syndrome
	Cohen syndrome
	Prader-Willi syndrome
Single-gene disorders (<1 %)	Leptin deficiency (LEP)
	Leptin receptor deficiency (LEPR)
	Propiomelanocortin deficiency (POMC)
	Prohormone convertase 1 impairment (PCSK 1)
	Melanocortin receptor 4 deficiency (MC4R)

(continued)

Table 8.1 (continued)

Endocrine disorders (<1 %)	Cortisol Excess (corticosteroid medication, Cushing syndrome)
	Hypothyroidism
	Growth hormone deficiency
	Acquired hypothalamic lesions • Infection • Vascular malformation • Neoplasm • ROHHAD/ROHHADNET syndrome • Trauma

Table 8.2 Obesity-related comorbidities

Metabolic	Insulin resistance	Diabetes/impaired glucose tolerance
	Polycystic ovary syndrome (PCOS)	Metabolic Syndrome
	Diabetes	Sleep apnea
	Non-alcoholic fatty liver disease (NAFLD)	Migraines
	Dyslipidemia	Reproductive dysfunction
	Hypertension	Gallstones
	Thromboembolism	Kidney stones
	Proteinuria	Pancreatitis
Structural	Obstructive sleep apnea	Slipped capital femoral epiphysis (SCFE)
	Obesity hypoventilation syndrome	Tibia vara (Blount disease)
	Asthma	Fungal skin infections
	Back pain	Furunculosis/folliculitis
	Hip pain	Hidradenitis suppurativa
	Knee pain	Pseudotumor cerebri
Degenerative	Increased LV mass	Carotid intimal thickening
	Increased LA diameter	Coronary arterial fatty streaks/ plaques
	Endothelial dysfunction	Decreased arterial distensibility
Psychosocial (more common in females than males)	Depression/mood disorders	Eating disorders (Binge Eating Disorder)
	Anxiety disorders	Distorted body image
	Poor self-esteem	Discrimination and bullying by peers
	Alienation	Decreased achievement in education/jobs
	Stigmatization	

Table 8.3 Medications contributing to weight gain

Class	Meds causing weight gain	Possible alternatives
Anti-seizure	Carbamazepine, valproate, gabapentin	Topiramate, zonisamide, lamotrigine
Anti-depressant	Tricyclics (nortriptyline, amitriptyline, doxepin) SSRIs (paroxetine, escitalopram), mirtazapine, MAO-inhibitors, lithium	Buproprion (fluoxetine and sertraline are preferred SSRIs)
Anti-psychotic	Olanzapine, clozapine, quetiapine, risperidone	Ziprasidone, asenapine, aripiprazole
Anti-diabetic	Insulin, sulfonylureas, thiazolidinediones	Metformin, exenatide, pramlintide
Steroids	Corticosteroids Depo-Provera	NSAIDs Barrier methods, IUDs

5. Assess medications that may be contributing and adjust as needed (Table 8.3)
6. Perform a laboratory evaluation for causes and effects of obesity: fasting glucose and insulin, HgBA1C, liver panel, creatinine, fasting lipid panel, TSH, Vitamin D, free testosterone.
7. Determine the need for additional testing: sleep study, late night salivary cortisol, abdominal ultrasound, lower extremity X-rays, dilated ophthalmologic exam. (See Tables 8.1, 8.2, and 8.3)

Treatment

The mainstay of treatment for obesity for adolescents is behavioral modification. A smaller subset will benefit from adding weight loss medications, and the most severe cases may warrant weight loss surgery, if behavioral modification and medications prove insufficient.

1. Behavioral: Per American Academy of Pediatrics (AAP) guidelines, ideally interventions would involve family-based behavioral approaches. It is helpful to set discrete goals for behavioral change at each visit. Goals include regulating meal patterns (avoid meal-skipping), improving food choices, decreasing portion size, increasing physical activity, reducing emotional

eating, adequate sleep (8–10 h/night for teens), and addressing family dynamics that may be contributing to weight gain. Patients should be counseled to achieve a daily deficit of 500–1000 kilocalories (kcal), with the aim to lose 1–2 lb per week. Exercise should be increased gradually to achieve a goal of 1 h of physical activity daily 5–7 days per week.

2. Pharmacologic:
   (a) Approved medications for adolescents
      - **Orlistat**. The only medication currently approved in the United States for weight loss in adolescents is the lipase-inhibitor orlistat (Xenical™, Alli™, age 12 or older). Start 120 mg (Xenical™) or 60 mg (Alli™) with the highest fat-containing meal and increase by 1 pill every 3–7 days until taking 3×/day with meals or up to 1 h after. It causes malabsorption of vitamins A, D, E, K, and beta-carotene, so patients should take a daily multivitamin at least 2 h apart from orlistat. Gastrointestinal side effects are common and include diarrhea, oily stools, fecal urgency and leaking, flatulence, nausea, and abdominal cramps. Contraindications include pregnancy, cholestasis, and chronic malabsorption syndromes.
      - **Phentermine** (approved for use over age 16 years): Sympathomimetic drug; generally start 30 mg daily, 30–60 min before breakfast. If sensitive to medications or side effects, lower to 15 mg daily; maximum dose is 37.5 mg daily. It is approved for short-term treatment of obesity (3 months); however, many obesity experts prescribe it long term with continued monitoring as long as it is effective and well tolerated. Side effects include palpitations, tachycardia, hypertension, headache, jitteriness/nervousness, dizziness, insomnia, dry mouth, constipation, and diarrhea. Contraindications include pregnancy/breastfeeding, uncontrolled hypertension, hyperthyroidism, cardiovascular disease, and glaucoma.
      - **Dieythlpropion** (approved for use over age 16 years): Sympathomimetic drug with similar weight loss profile and adverse effects as phentermine, but is used much less commonly. Dosing is 25 mg three times daily with meals.

(b) Off-label medications commonly used for adolescents

- **Metformin** (use if insulin resistance): increases insulin sensitivity, which can decrease lipogenesis and increase lipolysis, thus promoting weight loss. Start 500 mg qPM with dinner for 2 weeks, then increase to 500 mg bid. Dose may be titrated as needed to maximum 1000 mg bid based on weight loss and insulin response. Check baseline liver and kidney function and monitor with each dose change, and then every 6–12 months once stable. Side effects include nausea, vomiting, abdominal cramping or pain, diarrhea, flatulence, dizziness, and a metallic taste. Contraindicated in the setting of renal/hepatic failure, metabolic or lactic acidosis, diabetic ketoacidosis, dehydration, sepsis, surgery, and/or IV contrast.
- **Topiramate** (use if migraines, seizures, and/or binge eating): may be used alone or in combination with phentermine. Anti-epileptic medication found to have side effect of weight loss; approved for treatment of migraines. It is not FDA approved as a single agent for obesity treatment. Generally, more effective in combination with phentermine for weight loss; approved for age 18 and over. Start 25 mg qhs and increase by 25 mg every 2–4 weeks to maximum 200 mg qhs. Check baseline basic metabolic panel, LFTs, and CBC and monitor with dose changes. Side effects include paresthesias, memory problems, fatigue, somnolence, dizziness, difficulty concentrating, depression, renal stones, acute angle glaucoma, metabolic acidosis, leukopenia, and hepatoxicity. Should not be used in pregnancy as it may cause teratogenic effects.
- **Buproprion**: useful adjunct for depression or smoking cessation. It may be dosed at 100 mg tid, SR 150 mg bid, or XL 300 mg daily. Side effects include dry mouth, insomnia, agitation, headache, nausea, dizziness, constipation, abdominal pain, and diarrhea. It is contraindicated in patients with seizure disorders, eating disorders, and alcoholism.

(c) Additional medications approved for age ≥18 and older

- Single Agent

  Lorcaserin (Belviq™): selective serotonin agonist and which reduces appetite; similar efficacy to orlistat. Start 10 mg twice daily; reevaluate for efficacy after 12 weeks, continue if weight loss ≥ 5 %. Side effects include fatigue, headache, back pain, upper respiratory infections, nasopharyngitis, dizziness, nausea/vomiting, and diarrhea/constipation. Contraindicated in pregnancy.

- Combination drugs

  Phentermine/Topiramate (Qsymia™): Begin phentermine 3.75 mg/topiramate 23 mg once daily for 14 days, then increase dose to phentermine 7.5 mg/topiramate 46 mg once daily for 12 weeks and evaluate weight loss. If 3 % of baseline body weight has not been lost, discontinue use or increase dose to phentermine 11.25 mg/topiramate 69 mg for 14 days, then phentermine 15 mg/topiramate 92 mg; discontinue if weight loss <5 % after 12 weeks on the maximum dose. Side effects include dry mouth, constipation, paresthesias, depression, anxiety, insomnia, dizziness, fatigue, headache, and back pain. Contraindicated during pregnancy due to teratogenic effects.

  Bupropion/Naltrexone (Contrave™): Begin naltrexone 8 mg ER/ buproprion 90 mg ER one tablet daily for 1 week, then 1 tablet 2×/day for 1 week, then 2 tablets in the morning and 1 tablet in the evening for 1 week, then 2 tablets twice daily by week 4. Reevaluate at 12 weeks; if <5 % weight loss, discontinue drug. Side effects include hypertension, tachycardia, suicidality, nausea/vomiting, constipation or diarrhea, headache, dizziness, insomnia, dry mouth. Contraindications include uncontrolled hypertension, seizure disorder, eating disorder, MAOi use, chronic opioid use, use of other bupropion-containing products, and pregnancy.

- Diabetes drugs (administered subcutaneously; not commonly used in adolescents.)
  Pramlintide (Amylin): synthetic analog of peptide hormone amylin; slows gastric emptying, reduces postprandial rises in blood glucose concentrations and improves HgbA1C.
  Exenatide: synthetic peptide acts as GLP-1 receptor agonist that stimulates glucose-dependent insulin secretion, inhibits gastric emptying.
  Liraglutide: long-acting GLP-1 analog that stimulates glucose-dependent insulin secretion, inhibits gastric emptying.
- Experimental:
  Leptin
  Peptide YY
  Oxyntomodulin
  Melanocortin-4 receptor agonists

3. Bariatric Surgery: Options include sleeve gastrectomy, gastric bypass surgery (RYGB), and adjustable gastric banding ("Lap Band"). Sleeve gastrectomy is becoming more commonly used than RYGB in adolescents as it is a less risky surgery and has a lower risk for micronutrient deficiencies, but there are less long-term data. Sleeve gastrectomy can be converted to RYGB in the future if weight is regained. Adjustable gastric banding is not FDA approved for < age 18 and thus remains investigational in this age range. Surgical indications for teens include BMI >35 with serious comorbidities (diabetes, severe steatohepatitis, pseudotumor cerebri, moderate to severe sleep apnea) or BMI >40 with less serious co-morbidities (such as hypertension, dyslipidemia, insulin resistance, glucose intolerance, impaired quality of life, mild nonalcoholic steatohepatitis NASH, and mild sleep apnea). Teens undergoing this surgery should have complete skeletal, sexual, and emotional maturity, be independently motivated, have a supportive family, and have failed previous organized conventional attempts at weight loss.

Sources

Baker S, Barlow S, Cochran W, et al. Overweight children and adolescents: a clinical report of the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition. J Pediatr Gastroenterol Nutr. 2005;40:533–43.

Barlow SE, Expert Committee. Expert committee recommendations regarding the prevention, assessment, and treatment of child and adolescent overweight and obesity: summary report. Pediatrics. 2007; 120 Suppl4:S164.

Center for Disease Control and Prevention. Childhood overweight and obesity. http://www.cdc.gov/obesity/data/childhood.html.

Dietz WH, Robinson TN. Overweight children and adolescents. N Engl J Med. 2005;352:2100–9.

Michalsky M, Reichard K, Inge T, et al. American Society for Metabolic and Bariatric Surgery pediatric committee best practice guidelines. Surg Obes Relat Dis. 2012;8(1):1–7.

Ogden CL, Carroll MD, Kit BK, et al. Prevalence of childhood and adult obesity in the United States, 2011-2012. JAMA. 2014;311(8):806–14.

Pratt JS, Lenders CM, Dionne EA, et al. Best practice updates for pediatric/adolescent weight loss surgery. Obesity. 2009;17(5):901–10.

Rosenblum J, Stein HK. Medical treatment of obesity. In: Farraye FA, Forse RA, editors. Bariatric surgery: a primer for your medical practice. Thorofare, NJ: SLACK Incorporated; 2006. p. 21–44.

Skinner AC, Skelton JA. Prevalence and trends in obesity and severe obesity among children in the United States, 1999-2012. JAMA Pediatr. 2014;168(6):561–6.

US Preventive Services Task Force, Barton M. Screening for obesity in children and adolescents: US Preventive Services Task Force recommendation statement. Pediatrics. 2010;125:361–7.

Yanovski SZ, Yanovski JA. Long-term drug treatment for obesity: a systematic and clinical review. JAMA. 2014;311(1):74–86.

9 Gastroenterology and Nutrition: Healthy Eating in Adolescence and Nutritional Supplements; Irritable Bowel Syndrome; Inflammatory Bowel Disease

Esther Jacobowitz Israel, Jess L. Kaplan, and Lauren Fiechtner

Nutrition/Nutrition Supplements

Healthy Eating in Adolescence

The 2015–2020 Dietary Guidelines release by the United States Department of Agriculture (USDA) emphasizes the components of healthy eating patterns for all ages. Adolescent and young adult eating habits are the furthest from the dietary guidelines than any other age group. A focus on healthy eating patterns in adolescence can lead to continued healthy practices as they transition into adulthood. A healthy eating pattern as defined by the USDA includes eating:

- A variety of vegetables
- Fruits (especially whole fruits)
- Grains (half of which are whole grains)
- Fat-free or low fat dairy including milk, yogurt, cheese, and/or fortified soy beverages
- A variety of protein foods (seafood, lean meats, poultry, eggs, legumes, nuts seeds, and soy products)
- Oils.

M.A. Goldstein (ed.), *The MassGeneral Hospital for Children Adolescent Medicine Handbook*, DOI 10.1007/978-3-319-45778-9_9

The guidelines suggest limiting saturated fats and trans fat as well as added sugar and sodium. Evidence has shown that these eating patterns lead to a decreased risk of cardiovascular disease and possibly type 2 diabetes, cancers, overweight, and obesity. Table 9.1 outlines dietary nutritional goals from the 2015–2020 dietary guidelines.

The guidelines recommend 8 ounces per week of a variety of seafood, which provides Vitamin D, Vitamin B12, omega-3 fatty acids, eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA). Research has suggested that eating patterns that include seafood are associated with reduced risk of cardiovascular disease and obesity. The guidelines focus on seafood choices that are higher in EPA and DHA but lower in mercury. Examples of these

Table 9.1 Daily nutritional goals for age-sex groups based on dietary reference intakes and dietary guidelines recommendations from USDA dietary guidelines for Americans 2015–2020

	Female 9–13 years	Male 9–13 years	Female 14–18 years	Male 14–18 years	Female 19–30 years	Male 19–30 years
Calorie level (s) assessed	1600	1800	1800	2200 2800 3200	2000	2400 2600 3000
Protein, g	34	34	46	52	46	56
Protein, % kcal	10–30	10–30	10–30	10–30	10–35	10–35
Carbohydrate, g	130	130	130	130	130	130
Carbohydrate, % kcal	45–65	45–65	45–65	45–65	45–65	45–65
Dietary Fiber, g	22.4	25.2	25.2	30.8	28	33.6
Added Sugars, % kcal	<10 %	<10 %	<10 %	<10 %	<10 %	<10 %
Total fat, % kcals	25–35	25–35	25–35	25–35	20–35	20–35
Saturated fat, % kcal	<10 %	<10 %	<10 %	<10 %	<10 %	<10 %
Minerals						
Calcium, mg	1300	1300	1300	1300	1000	1000
Iron, mg	8	8	15	11	18	8
Magnesium, mg	240	240	360	410	310	400
Phosphorus, mg	1250	1250	1250	1250	700	700
Potassium, mg	4500	4500	4700	4700	4700	4700

(continued)

Table 9.1 (continued)

	Female 9–13 years	Male 9–13 years	Female 14–18 years	Male 14–18 years	Female 19–30 years	Male 19–30 years
Sodium, mg	2200	2200	2300	2300	2300	2300
Zinc, mg	8	8	9	11	8	11
Copper, µg	700	700	890	890	900	900
Manganese, mg	1.6	1.9	1.6	2.2	1.8	2.3
Selenium, µg	40	40	55	55	55	55
Vitamins						
Vitamin A, mg (retinol activity equivalents)	600	600	700	900	700	900
Vitamin E, mg (alpha-tocopherol equivalent)	11	11	15	15	15	15
Vitamin D, IU	600	600	600	600	600	600
Vitamin C, mg	45	45	65	75	75	90
Thiamin, mg	0.9	0.9	1	1.2	1.1	1.2
Riboflavin, mg	0.9	0.9	1	1.3	1.1	1.3
Niacin, mg	12	12	14	16	14	16
Vitamin B6, mg	1	1	1.2	1.3	1.3	1.3
Vitamin B12, µg	1.8	1.8	2.4	2.4	2.4	2.4
Choline, mg	375	375	400	550	425	550
Vitamin K, µg	60	60	75	75	90	120
Folate, µg DFE	300	300	400	400	400	400

include salmon, anchovies, herring, shad, sardines, Pacific oysters, trout and Atlantic and Pacific mackerel. Not surprisingly, adolescents are consuming far less seafood then the recommended guidelines.

Despite the focus on healthy eating patterns, about 75 % of the population has a diet low in vegetables, fruits, dairy, and oils. Vegetable consumption is lowest among boys ages 9–13 and girls ages 14–18. Over 50 % of the population is exceeding grain and protein intake. Teenage males are far exceeding the recommended intake of meat, poultry, and eggs. Finally, most Americans exceed the recommendations for added sugars, saturated fats, and sodium and adolescents are no different. The average added sugars in adolescent

diets are between 16 and 18 % of total calories. The majority of these calories come from sugary beverages including soft drinks, fruit drinks, sweetened coffee, and sports and energy drinks.

How can we help shift adolescent diets to more healthful ones? Only half of adolescent females and young adult males consume three meals per day, but they have two or more snacks per day and more Americans are eating a higher percentage of their calories outside of the home. A recommendation for three meals and one snack as well as eating more foods at home rather than outside the home will help. But possibly, more importantly an increased focus on high fiber foods such as fruits, vegetables, and whole grains along with a reduction of proteins, high saturated fats, and sugar drinks could lead to most successful improvements in this age group.

Nutritional Supplements: Performance-Enhancing Drugs and Dietary Supplements

Performance-enhancing drugs and dietary supplements are a major concern to pediatricians; informed health care professionals can help by having knowledge about the proven benefits and health consequences of these substances.

The use of performance-enhancing drugs by adolescents has increased over the past decade in part driven by the decrease in age of participation in competitive sports, the increased popularity of competitive sports, the focus in the media on thinness in females and muscular bodies in males, pressure from coaches and parents, age-related risky behaviors, and the availability of the drugs.

Commonly used performance-enhancing drugs include: anabolic steroids, testosterone, steroid precursors, nutritional supplements (creatine, protein/amino acids, and β-hydroxy β-methybutyric acid), stimulants (ephedrine, caffeine/guarana), human growth hormone, blood doping, and diuretics.

- Anabolic-androgenic steroids are synthetic derivatives of testosterone that have been modified to maximize anabolic effects. It is estimated that about 3 % of adolescents had used anabolic-androgenic steroids in 2009. They promote increased nitrogen concentration in muscle, which promotes the anabolic state. They also

inhibit the binding of catabolic glucocorticoids which preserves muscle mass and prevents muscle breakdown. Anabolic-androgenic steroids increase fat-free mass and muscle strength. These drugs can be injected, taken orally or transdermally. Anabolic steroids are converted in the liver to testosterone. The typical course is given in 4–12 week cycles and the doses are in a pyramid sequence with the largest dose in the middle of the cycle. Adverse effects are numerous and include epiphyseal closure, acne, increased rate of tendon strains and rupture, hypertrophy of the clitoris in females and gynecomastia in males which is permanent and irreversible, impotence, prostate cancer, oligospermia, hepatoadenoma, hepatic carcinoma, peliosis hepatitis, aggression, decreased IgA, psychosis, and depression.

- Steroid precursors are sold over the counter and marketed as promoting increased endogenous testosterone and promoting lean body mass. Examples include: androstenedione, androstenediol, norandrostenedione, norandrostenediol, and dehydroepiandosterone (DHEA). Most are derived from DHEA. Despite marketing claims of increasing testosterone, multiple studies have shown increases in androstenedione and estradiol but little increase in testosterone. However, these substances still have many of the negative effects of anabolic steroids.
- The most popular nutritional supplement is creatine. One study noted that 5.6% of adolescents use creatine. Creatine is a nonessential amino acid that is made in the liver, pancreas, and kidneys and helps create ATP. It can be found in foods including meat, milk, and fish. The daily requirement is 2 g per day, but often athletes use 2–3 times as much. Although creatine has been shown to improve performance in short, high intensity exercises it has many adverse effects including weight gain, water retention, gastrointestinal cramping, fatigue, and diarrhea.
- Human growth hormone (hGH) is an endogenous hormone produced by the pituitary and has been used by athletes for performance enhancement since the 1970s. It is popular among athletes because it is hard to detect—because the appropriate blood test must be done within a small window of opportunity. It increases lean body mass and decreases fat mass. However, it has no or little effect on strength and athletic performance, and it may actually worsen exercise capacity by increasing exercise-induced lactate

levels. Adverse effects include diabetes, cardiomyopathy, hepatitis, and renal failure.
- Erythropoietin has recently gained notoriety. It leads to increased production of red blood cells, which increases oxygen delivery to muscles; however, the rise in hematocrit can create dehydration and increased blood viscosity, which in turn can lead to clots including strokes and pulmonary emboli.
- Adolescents use stimulants such as ephedrine and caffeine, and they are readily accessible. These substances reduce fatigue and improve neurocognitive and aerobic performance. Adverse effects of ephedrine include hypertension, weight loss, insomnia, headaches, arrhythmias, anxiety, strokes, and psychosis. It has also been linked to several athlete deaths. Caffeine and guarana, a plant extract sold in energy drinks have been used by 27 % of adolescent athletes in the USA. It only seems to be effective for prolonged sports containing short bursts like tennis and team sports.

Anticipatory guidance should include direct questions regarding the use of performance enhancing drugs of all youth regardless of involvement in sports. Educating adolescents about the dangers and adverse effects of these substances is important and promotion of healthy nutrition, and proper training may help decrease the prevalence of use.

Irritable Bowel Syndrome (IBS)

IBS is the most common functional bowel disorder in older children and adults. Prevalence may be as high as 10–15 % of adults in the USA/Europe and women are more affected than men (2:1).

Diagnostic Criteria (Rome III-Adult)

Recurrent abdominal pain or discomfort for >2 days/month in the last 3 months (with symptom onset at least 6 months prior to diagnosis) with at least two of the following:

1. Improvement with defecation
2. Onset associated with a change in stool frequency

Table 9.2 ALARM symptoms that make IBS less likely and should prompt search for organic pathology

Rectal bleeding	Greasy stools	Nocturnal stools
Unintentional weight loss	Unexplained fevers	Frequent canker sores
Arthralgias/arthritis	Persistent vomiting	Anemia
Thrombocytosis	Elevated ESR or CRP	High fecal calprotectin

3. Onset associated with a change in stool form

Four IBS subtypes: IBS-Constipation (IBS-C), IBS-Diarrhea (IBS-D), IBS-Mixed, IBS-no subtype

Symptoms

1. Chronic abdominal pain/discomfort
2. Altered bowel habits
   (a) Diarrhea: frequent loose stools, small to moderate volume, often with mucus, sensation of incomplete evacuation
   (b) Constipation: hard, pellet-like stools, straining, sensation of incomplete evacuation, often with normal or even diarrheal stool in between
3. Additional GI symptoms: GERD symptoms, dyspepsia, nausea, bloating, gassiness

IBS Symptoms can mimic those of certain organic disorders, which need to be considered (Inflammatory Bowel Disease, lactose malabsorption/intolerance, small intestinal bacterial overgrowth, celiac disease, non-celiac gluten sensitivity, chronic gastrointestinal infection).

Diagnosis: Clinical criteria with exclusion of organic disorders, especially if any ALARM signs/symptoms are present (Table 9.2).

Treatment

Treatment is directed towards symptom relief as the pathophysiology of the underlying process is not really known.

1. Diet modification: reducing gas containing foods (beans, brussel sprouts, onion, raw broccoli/cauliflower, ETOH, caffeine, sorbitol), lactose-free trial, gluten-free trial, high soluble fiber diet (in IBS-C). A low Fermentable Oligo-Di-Mono Saccharides and Polyols (FODMAP) diet may have the best evidence of any diet for controlling IBS symptoms but should be monitored closely by a dietician.
2. Pharmacotherapy

   IBS-C: Osmotic laxatives like polyethylene glycol and lactulose, Lubiprostone (Amitiza), Linaclotide (Linzess)

   IBS-D: Loperamide, bile acid sequestrants (cholestyramine), Rifaximin (Xifaxan)

   Abdominal pain: Anti-spasmodics (dicyclomine, hyoscyamine). Anti-depressants (TCAs-use with caution in IBS-C as it often leads to constipation), and SSRIs are both effective. There is less evidence in children that these are effective, and young people need very close monitoring for adverse reactions/side effects such as suicidal risk (Black Box Warning)
3. Additional treatments:

   Probiotic-data in IBS are mixed. Best evidence: *Bifidobacterium infantis* in adults and *Lactobacillus* GG in children but some studies show no benefit. Low risk for most patients.

   Psychotherapy, stress reduction, avoidance of known triggers, anxiolytic medications

Inflammatory Bowel Disease (IBD)

There are two major chronic idiopathic disorders—Crohn's disease and Chronic Ulcerative Colitis.

Common Symptoms

Ulcerative Colitis (UC): diarrhea, rectal bleeding, abdominal cramping, tenesmus, weight loss

Crohn's Disease (CD): abdominal pain, nausea, diarrhea (sometimes bloody), weight loss

Linear growth delay is common and can precede the onset of GI symptoms by 1–2 years

Extraintestinal manifestations of IBD: arthritis/arthralgia, aphthous stomatitis, erythema

Nodosum, pyoderma gangrenosum, osteopenia, primary sclerosing cholangitis

Autoimmune hepatitis, pancreatitis, iritis/uveitis, ankylosing spondylitis

Pubertal delay is also common

Perianal disease: skin tags, fissures, fistulae, abscess is common in CD (thorough external exam needed) and not seen in UC

Diagnosis: clinical, supported by lab and radiographic findings and confirmed by histologic evidence of chronic inflammation

- Abnormal lab findings (only present in 70 % of children with IBD): High ESR, High CRP, elevated WBC, thrombocytosis, anemia, hypoalbuminemia
  Fecal calprotectin is highly effective at differentiating between IBD and non-inflammatory conditions (outperforms CRP and ESR)
- Radiographic studies: MR/CT Enterography, Upper GI with small bowel follow through
- Endoscopy and ileocolonoscopy with mucosal biopsies
- Additional pearls: In patients presenting with diarrhea with or without blood, gastrointestinal infections should be ruled out prior to invasive testing: stool culture, ova and parasite exam and C.difficile testing)

Treatment: Goal is steroid free remission. TB testing required before immunosuppressive therapy

Induction of Remission

UC: 5-Aminosalicylates, prednisone, anti-TNFα agents (Infliximab, Adalimumab, Golimumab), Vedolizumab, Calcineuron Inhibitors (Tacrolimus/Cyclosporine)

CD: Exclusive Enteral Nutrition, prednisone, anti-TNFα agents (Infliximab, Adalimumab, Certolizumab), Vedolizumab

Maintenance of Remission

UC: 5-ASA, Thiopurines (6-MP and Azathioprine), anti-TNFα agents, Vedolizumab

CD: Thiopurines (6-MP and Azathioprine), Methotrexate, anti-TNFα agents, Vedolizumab

Adjunctive therapy: CD: Antibiotics (Metronidazole, Ciprofloxacin, Rifaximin), UC: Probiotics

Complications: bowel stricture/small bowel obstruction (CD), fistulizing disease (CD), growth failure (CD>UC), nutritional deficiencies (iron, Vitamin B12, Vitamin D, zinc), osteopenia/osteoporosis, pubertal delay, mood disorders, colon adenocarcinoma (UC>CD).

Health Maintenance in IBD

Monitor weight and linear growth. If growth delays, consider bone age X ray

For assessment of pubertal development, see Chap. 3 Tanner Staging

TB testing at diagnosis (and annually in patient on anti-TNFα agents)

DEXA bone density at baseline

Annual mid-winter 25-OH Vitamin D level: Ca and Vit D supplementation as needed

Vaccination status assessment: revaccination may be needed if there is no seroconversion

Influenza vaccine annually: no live vaccine for immunosuppressed patients

Psychosocial assessment: school, mood, friends, family

Sources

Benor S, Russell GH, Silver M, et al. Shortcomings of the inflammatory bowel disease Serology 7 panel. Pediatrics. 2010;125(6):1230–6.

Brenner DM, Moeller MJ, Chey WD, et al. The utility of probiotics in the treatment of irritable bowel syndrome: a systematic review. Am J Gastroenterol. 2009;104(4):1033–49.

Dandoy C, Gereige RS. Performance-enhancing drugs. Pediatr Rev. 2012;33(6):265–71; quiz 271–262.

Eaton DK, Kann L, Kinchen S, et al. Youth risk behavior surveillance—United States, 2009. MMWR Surveill Summ. 2010;59(5):1–142.

Elliott S. Erythropoiesis-stimulating agents and other methods to enhance oxygen transport. Br J Pharmacol. 2008;154(3):529–41.

Halmos EP, Power VA, Shepherd SJ, et al. A diet low in FODMAPs reduces symptoms of irritable bowel syndrome. Gastroenterology. 2014;146(1):67–75.

Henderson P, Anderson NH, Wilson DC. The diagnostic accuracy of fecal calprotectin during the investigation of suspected pediatric inflammatory bowel disease: a systematic review and meta-analysis. Am J Gastroenterol. 2014;109(5):637–45.

Liu H, Bravata DM, Olkin I, et al. Systematic review: the effects of growth hormone on athletic performance. Ann Intern Med. 2008;148(10):747–58.

Longstreth GF, Thompson WG, Chey WD, et al. Functional bowel disorders. Gastroenterology. 2006;130(5):1480–91.

Metzl JD, Small E, Levine SR, Gershel JC. Creatine use among young athletes. Pediatrics. 2001;108(2):421–5.

Powers ME. The safety and efficacy of anabolic steroid precursors: what is the scientific evidence? J Athl Train. 2002;37(3):300–5.

Rufo PA, Denson LA, Sylvester FA, et al. Health supervision in the management of children and adolescents with IBD: NASPGHAN recommendations. J Pediatr Gastroenterol Nutr. 2012;55(1):93–108.

U.S. Department of Health and Humans Services and U.S. Department of Agriculture. 2015-2020 Dietary guidelines for Americans. 8th ed. 2015. http://health.gov/dietaryguidelines/2015/guidelines/.

Sports Injuries in the Adolescent

10

Jeffrey B. Kreher

The number of children and adolescents participating in organized and recreational sports increases yearly. Adolescents are a heterogeneous population in regard to the musculoskeletal system and their sports injuries. Younger adolescents have open growth plates, or physes, while older adolescents have a majority of closed growth plates similar to an adult. In addition, the ability to generate more speed and force (i.e., load to the musculoskeletal system) advances in the committed adolescent athlete with devotion to supplemental strength and conditioning training. As a result, sports injuries are on the rise and will continue to be one of the most frequent presenting complaints in the Emergency Department and Adolescent Medicine Clinic. Injuries to the musculoskeletal system can be acute, subacute, or chronic in nature and nearly always present with pain as the primary symptom. Overuse and overtraining make up a majority of musculoskeletal pain complaints in the adolescent. Overuse nearly always presents as a subacute or chronic injury. Treatment requires rest from the offending agent and/or correction of the contributing mechanical element. Acute pain is more often due to trauma and requires radiographic investigation in the setting of debility. Locations of injuries are often related to the nature of the chosen sport with lower extremities predominating in running sports and upper extremity injuries found mostly in throwing athletes or upper extremity load bearing athletes like gymnasts and cheerleaders.

M.A. Goldstein (ed.), *The MassGeneral Hospital for Children Adolescent Medicine Handbook*, DOI 10.1007/978-3-319-45778-9_10

The differential of musculoskeletal pain is driven by the mechanism of injury and skeletal maturity of the patients. If a patient is skeletally immature, the differential of musculoskeletal pain should always begin with probable injury to the growth plate, or a physeal injury. Examination of the skeletally immature patient should include knowledge of apophyseal and epiphyseal locations. Apophyses are growth plates that do not contribute to the length of a bone and tend to be sites of tendon insertion (i.e., tibial tuberosity, inferior pole of the patella, calcaneus, base of the fifth metatarsal, medial epicondyle, lateral epicondyle, ischial tuberosity, anterior superior iliac spine, anterior inferior iliac spine). Epiphyses are growth plates found at the end of long bones (i.e., distal femur, proximal and distal tibia, proximal and distal fibula, proximal humerus, distal radius, distal ulna). If a patient is skeletally mature, the differential of musculoskeletal pain will include tendon and ligamentous injury, which are more common once physes close. A full survey of adolescent musculoskeletal conditions is beyond the scope of this chapter, but one will find more information in the references listed at the conclusion of the chapter. In short, the provider must consider injury to the bone, cartilage/joint, tendons, ligaments, or muscles in the athletic adolescent. In addition, a provider must consider referred pain from structures or joints proximal to pain location and contributions to local stress due to distal structures. Finally, the differential of musculoskeletal pain should include congenital, infectious, rheumatologic, and oncologic conditions. These entities may present after an apparent athletic injury.

Shoulder Pain

Dislocations and Instability

History

The shoulder joint is the most unstable joint in the human body. A joint is dislocated when subluxed and requiring external force to reestablish normal joint position. Subluxation of a joint is a

form of microinstability where joint contact is disrupted but returns spontaneously to a normal anatomical position. Subluxation is often reported as instability but may only present with shoulder pain.

Shoulder pain due to glenohumeral dislocation presents acutely while shoulder instability may present with acute, subacute, or chronic pain. Acute traumatic dislocations of the shoulder tend to be anterior (~95 % of the time). Often anterior dislocation is also slightly inferior and the result of a trauma with the shoulder abducted and externally rotated. Dislocation can also be posterior with a posterior force with the shoulder adducted such as football lineman or falling into a push-up position. Posterior dislocations may also be seen in the setting of seizures or electrical shock. Inferior only dislocations are very uncommon. Instability of the shoulder presents as pain with or without recurrent subluxation or recurrent dislocation. When atraumatic in onset, dislocation or subluxation of the shoulder is often due to hypermobility, or ligamentous laxity. Instability may be unidirectional or multidirectional. Whether the subluxations are voluntary or involuntary is an important historical element. Voluntary subluxation should be discouraged for future joint health.

Clinical Exam

A dislocated joint will present with decreased range of motion (ROM) and pain with ROM. Anterior dislocations show a palpable humeral head anteriorly and inferiorly with posterior dislocations notable for a prominent coracoid process anteriorly and posterior humeral head. The arm is slightly externally rotated with anterior dislocation and internally rotated with posterior dislocation. An instable joint may present with pain on range of motion and possible decreased ROM due to pain. With all shoulder dislocations, the distal neurovascular status should be investigated. The most common neurovascular injury is transient and to the axillary nerve, which provides sensation over the lateral deltoid. When obvious changes in landmarks from dislocation are not apparent, palpation of the proximal humerus may help reveal a fracture rather than dislocation.

Instability due to systemic hypermobility may be discovered using modified Beighton's criteria. However, a shoulder may be instable due to a prior traumatic dislocation. Anterior shoulder instability is tested by anterior apprehension test, or apprehension–relocation test. A positive test has pain and fear, or apprehension, in the "position of vulnerability" (arm at shoulder height, abducted to 90°, elbow flexed to 90° and externally rotated at the shoulder like the cocking motion of throwing overhand). The specificity of the test is increased when "relocation," or pressure anteriorly to the humeral head while supine, decreases the apprehension and one can externally rotate further. Multidirectional instability (MDI) shows positive anterior apprehension–relocation test along with apprehension on posterior translation (pushing on the elbow with 90° of shoulder forward flexion and 90° of elbow flexion) and a positive sulcus sign. Sulcus sign is positive with fear, or apprehension, and 2 cm or more with inferior distraction of the shoulder.

Imaging

Desired images are an AP view and scapular Y view at a minimum. Additional axillary view may be helpful at clinic presentation when searching for an anatomical cause for recurrent instability. Axillary view may be difficult if joint is dislocated. AP view with internal rotation may help show a Hill-Sachs defect, or compression fracture to the posterior humeral head in the setting of acute dislocation or recurrent instability/dislocation.

Imaging should be obtained before any reduction attempt in the skeletally immature patient with significant trauma or if there is suspicion of a proximal humerus fracture.

MRI is helpful for recurrent dislocation or instability not better with maximal conservative management. MR imaging with arthrogram is more specific and sensitive at finding anatomic defects requiring surgical correction.

Treatment

An acutely dislocated shoulder should be reduced at the first available moment. If unable to reduce quickly at the time of injury, the shoulder should be stabilized in a position of comfort and sent to

the Emergency Department for reduction. Sling immobilization after reduction can be used as needed for protection but beginning ROM (with arm circles and "wall walks") should be started when pain allows. ROM is started by leaning over and circling the hanging arm as pain allows followed by walking the hand up wall extended at the elbow with (1) forward flexion and (2) at 90° of abduction, or out to the side. Ice and analgesics should be added to decrease pain so ROM can be initiated. Physical therapy may be prescribed to decrease pain, increase ROM, and stabilize the joint through strengthening and increasing coordination of shoulder and scapular motions.

Traumatic dislocations have a high incidence of recurrence. Consider referral to an orthopedic surgeon for consideration of surgical correction if a collision or contact sport is desired and/or anatomical defect makes success with conservative measures unlikely.

Instability and/or subluxations of the shoulder are treated conservatively. Conservative management includes pain relief with ice and analgesics along with relative rest. In addition, referral to physical therapy will assist in stabilization of the joint by strengthening dynamic stabilizers of the shoulder and improving coordination of the shoulder and scapula. Surgical management of hypermobile and multidirectional instability is less successful, but should be considered in rare cases of severe debility and severe impairment in function.

Little League Shoulder

History

"Little League Shoulder" is a repetitive, overuse condition of the proximal humerus epiphysis, and therefore only seen in skeletally immature adolescents. Other terms include proximal humeral epiphysiolysis and a Salter–Harris type I fracture of the proximal humerus. The humeral epiphysis is stressed during the external rotation of throwing motion. Presenting pain is in the lateral shoulder and often localized to the proximal humeral epiphysis. The pain is worse in the late cocking and

early acceleration phases of throwing. Patients frequently are overhead throwers during peak height velocity phase of growth with a subacute presentation. Patients may report loss of velocity. The greatest risk factor is repeatedly throwing with a fatigued arm.

Clinical Exam

ROM is often full but may be painful. Resisted external rotation of the shoulder when not abducted is often painful. Palpation of the proximal humerus is painful. Occasionally, pain is present with resisted shoulder abduction.

Imaging

AP views of the shoulder in internal and external rotation along with a scapular Y view are often normal. However, occasionally one may appreciate obvious widening of the physis or fragmentation or sclerosis. MRI is rarely indicated but will show fluid signal around the physis.

Treatment

Little league shoulder is difficult to treat due to recurrence of pain with inadequate rest and recovery. Patients should be educated that the average return to full throwing is 3 months. Treatment includes rest from throwing and pain control. A return to throwing program should be slow and closely monitored after there is full resolution of pain, full ROM, full strength, and ability to soft throw without pain. Additional evaluation by a throwing coach or physical therapist specializing in throwing may be beneficial to assess mechanical causes.

Rotator Cuff Tendinopathy

History

Shoulder pain due to rotator cuff injury is rarely due to tendon tears in the adolescent population. Tendinopathy is pain in the tendons; in adolescents pain in the shoulder and rotator cuff is nearly always due to impingement. Patients present with

shoulder pain, which is difficult to localize but most often superiorly. Often overhead athletes will suffer repeated impingement of the tendons as they pass under the acromion, or coracoacromial arch. Pain is often in the overhead position, or "position of vulnerability" (described earlier), with decreased strength and ROM due to pain.

Clinical Exam

Exam may show pain with active ROM and strength testing of the rotator cuff muscles. Strength can be screened through resisted shoulder internal rotation (subscapularis) and external rotation (infraspinatus/teres minor) with elbows at side and flexed 90°. Strength and pain in the supraspinatus are tested with "empty can" testing. Rotator cuff tendinopathy will often show positive impingement signs, which include Hawkins' and Neer's impingement tests and "empty can" testing. Importantly, a positive impingement test is both painful and shows involuntary body movement to relieve the impingement. Hawkins' impingement test is done by forward flexing the shoulder to 90°, flexing the elbow 90°, and internally rotating the shoulder. Neer's impingement test is accomplished by placing downward force on the acromion while forward flexing the shoulder. "Empty can" testing is accomplished by holding figurative cans in hands out to the side, adducting the shoulders 15–20° from straight out, internally rotating shoulders (or dumping out the cans), and applying downward force on extended arms.

Imaging

Screening shoulder films of AP and scapular Y are often negative in rotator cuff tendinopathy. However, one may see a downsloping acromion leading to impingement or upward migration of humeral head due to rotator cuff weakness. If instability or a prior traumatic dislocation is suspected, an axillary view may be added to assess integrity of the glenoid. MRI is only indicated in uncertain diagnosis after lack of improvement with conservative care. MR imaging with arthrogram is more specific and sensitive at finding anatomic defects requiring surgical correction.

Treatment

Rotator cuff tendinopathy improves with conservative management in adolescents. Conservative management is often successful and includes pain relief with ice, pain relief with analgesics, and relative rest. In addition, referral to physical therapy will assist in decreasing pain and impingement by strengthening the rotator cuff muscles and improving coordination of the shoulder and scapula. In rare circumstances, subacromial/subdeltoid injection may be considered. Surgical management of rotator cuff tendinopathy is very rare in the younger population.

Elbow Pain

Little League Elbow

History

"Little League Elbow" can refer to many etiologies of pain about the elbow, but we will restrict discussion to the most common usage: medial epicondyle apophysitis in the skeletally immature or medial epicondylitis in the skeletally mature. The flexor-pronator mass originates on the medial epicondyle and is frequently a source of acute or chronic medial pain in the throwing athlete. Other potential sources of subacute or chronic elbow pain in adolescents include juvenile osteochondritis dessecans of the capitellum (lateral elbow), olecranon apophysitis (posterior elbow), ulnar collateral ligament injury (medial elbow), ulnar nerve injury (medial elbow and distally), or referred pain from shoulder or neck.

Clinical Exam

Pain is located in the medial elbow. Swelling over the medial epicondyle is more often present with acute avulsion fracture of the medial epicondyle. Tenderness to palpation is located medially on the epicondyle or into the flexor-pronator mass and present during or after throwing. There may be loss of full extension if chronic but any loss of full ROM must also raise concerns about intra-articular pathology. Pain will be present with resisted wrist flexion and/or pronation in both the skeletally mature and immature.

A Tinel's test posterior to the medial epicondyle over the ulnar nerve should be done looking for paresthesias in the ulnar distribution (fourth and fifth fingers).

Imaging

AP, oblique, and lateral views of the elbow are indicated to rule out joint effusion and other bony injuries such as osteochondritis dessecans. If the physis is still open medially, Little League Elbow may show widening and/or fragmentation, but imaging is often negative. Significant widening of the physis with acute onset or acute on chronic pain should raise concern for avulsion fracture. MRI is indicated with (1) lack of improvement with conservative care including rest or (2) mechanical symptoms such as locking, instability, or loss of motion not solely due to pain.

Treatment

Little League Elbow often improves with conservative management in adolescents. Conservative management includes pain relief with ice and analgesics along with relative rest. Rest from throwing for 6 or more weeks is often indicated. Cast immobilization for less than 4 weeks is indicated for avulsion fracture and the rare athlete that will not rest fully. Physical therapy may assist in decreasing pain and maintaining strength. Orthopedic surgical referral should be considered for a significant acute medial epicondyle avulsion fracture.

Knee Pain

Anterior Knee Pain

History

Anterior knee pain is one of the most frequent musculoskeletal complaints in adolescents. If growth plates are still open, one must consider Osgood–Schlatter disease (tibial tubercle apophysitis) or Sinding-Larsen–Johansson syndrome (apophyseal stress to inferior pole of the patella). Pain is often located anteriorly but may also be medial and/or lateral. Pain is increased with activity and

relieved with rest. Anterior knee pain due to patellar maltracking, or patellofemoral syndrome, is often worse with stairs or arising after prolonged sitting (aka "theater sign"). Acute knee pain may be a contusion, patellar subluxation, patellar dislocation, fracture, or other condition, but these conditions more commonly present acutely and with an effusion. Adolescents with chronic anterior knee pain due to patellar maltracking may report an acute onset but rarely is there a concurrent effusion. Finally, there should be an absence of other mechanical symptoms such as locking and instability. True locking of the knee is sudden while walking usually and may bring a patient to the ground. Locking is prolonged and requires repeated conscious attempts to reestablish full ROM. True instability of the knee is not "giving out" due to pain of stairs but rather is related to translation of the femorotibial articulation with change in directions.

Clinical Exam

Acute injuries may or may not present with an effusion. A quick sensitive screening test to rule out clinically significant effusion is full and equal flexion of knees while prone. Acute injuries with effusion will be discussed below. Anterior knee pain without effusion may have localized soft tissue swelling (often at the site of maximal tenderness). Apophyseal stress injuries will show focal tenderness to palpation on the tibial tubercle or inferior pole of the patella. Patella tendon tenderness to palpation in the setting of a skeletally immature patient should immediate bring one to palpate the surrounding apophyses. Patellar tendinopathy, or jumper's knee, is rarely an isolated finding in skeletally immature athletes but common in skeletally mature adolescents who jump frequently.

Patellofemoral pain syndrome will often have pain to compression of the patella (positive patellar grind test) with or without medial and/or lateral facet tenderness to palpation. Patellofemoral pain may be due to patellar instability, which is evident by apprehension on lateral gliding of the patella with the knee extended (positive apprehension test) during prone examination. There may be either medial or lateral patellar facet tenderness to palpation due to patellar maltracking.

Imaging

AP, lateral, and sunrise views of the knee should be obtained in the setting of acute pain without effusion limiting function or chronic pain. AP view may show patellar lateral positioning or bipartite nature. Lateral view is helpful to assess for joint effusion, apophyses, and patella alta or baja. Sunrise, or Merchant, view will provide an evaluation of patellar tilt and patellofemoral articulation (including trochlear dysplasia). MRI of the knee is indicated for chronic pain not better with maximal conservative care or with concern for a surgical condition, but referral to a sports medicine specialist or an orthopedic surgeon prior to advanced imaging may be indicated.

Treatment

Anterior knee pain often improves with conservative management in adolescents. Conservative management includes pain relief with ice and analgesics along with relative rest. There are no long-term complications from Osgood–Schlatter disease and Sinding-Larsen–Johansson syndrome so rest, ice, and limitation to painfree activity are appropriate. If pain is (1) short lived after exertion, (2) without abnormal mechanics, or limp, and (3) not progressive, an adolescent may continue sports participation with apophyseal stress injuries. Patellar maltracking, or patellofemoral pain syndrome, improves with ice, relative rest, and physical therapy focused on quadriceps strengthening along with hip and pelvis stabilization to prevent dynamic valgus with single-legged weight bearing. If there is significant patellar instability, adolescents may respond to patellar taping (aka McConnell taping) or lateral patellar stabilization brace. Significant pes planus and/or pronation also contribute to increased stress and dynamic valgus at the knee and may respond to foot orthotics. Femoral anteversion, external tibial torsion (out toeing), and pes planus with pronation are termed “miserable malalignment.” Miserable malalignment may be the cause of conservative care failure. A sports medicine specialist or orthopedic surgical referral should be considered for pain with or without patellar instability not better with maximal conservative care.

Knee Pain with Effusion

History

Knee pain after a trauma with effusion is often due to a hemarthrosis. Pain is acute in onset and often with inability to continue weight bearing. Pain improves with no knee movement and no weight bearing. Knee hemarthrosis in the setting of acute trauma is due to: (1) patellar dislocation/subluxation, (2) anterior cruciate ligament (ACL) injury, (3) meniscal tears, or (4) fracture. In the skeletally immature, all four entities are possible but ACL injury is more often in the form of tibial spine avulsion fracture. The onset of swelling is more acute with patellar dislocation/subluxation, ACL rupture, and fracture. Meniscal tears and osteochondritis dessecans may have a more subacute onset of swelling. Many of the above causes of hemarthrosis are acute, but chronic post-exertional swelling may be an overuse fracture of subchondral bone called osteochondritis dessecans. In addition, patients may complain of joint locking due to a meniscal tear or a fracture fragment, or foreign body, getting stuck in the femorotibial articulation. Joint instability is possible with severe patellar instability or loss of ACL function and noted especially with change in direction, or cutting in sports.

Clinical Exam

If there is a significant effusion, there will be loss of knee ROM; however, loss of ROM may also be a sign of pain. One can also compare the soft tissue swelling immediately above the patella along with medially and laterally by inspection and/or palpation. Acute patellar subluxation or dislocation will have positive patellar grind and patellar apprehension (see description above in "Anterior Knee Pain" section). ACL rupture or tibial spine avulsion fracture will have a positive Lachman maneuver. A positive Lachman shows increased anterior translation of the tibia when knee is flexed 20° in comparison to the opposite side and with a loss of a firm end point, which is the ACL stopping anterior translation. To increase the sensitivity and specificity of the Lachman maneuver, ensure the patient is relaxed by: (1) performing the Lachman first on the uninjured side, (2) slightly externally rotate at the hip, and (3) have a loose grip on the femur before anteriorly

translating the tibia. In addition, it is paramount that one translates the tibia posteriorly before performing the Lachman so the anterior translation of the tibia is more appreciable. (If the ACL is ruptured, the tibia is positioned anteriorly in relation to the femoral condyles.) Examination for meniscal tears is not very sensitive or specific with joint line tenderness and/or McMurray testing. However, adult studies have found increased likelihood ratios with Thessaly testing. In an appropriate clinical setting (i.e., a twisting knee injury with effusion), a positive Thessaly test is focal pain at site of joint line tenderness when the patient is standing with knee flexed 20° and twisting at the pelvis. Most meniscal injuries are medial but when lateral they may be due to congenital discoid meniscus. Acute fractures will have focal tenderness to palpation, but often bony contusions can present like a fracture. Imaging will help rule out clinically relevant fractures.

Imaging

AP, lateral, notch, and sunrise views of the knee should be obtained in the setting of acute pain with effusion. AP view may show fracture of tibial spine, tibial plateau, or patella or lateral joint space widening for discoid meniscus. Lateral view is helpful to assess for joint effusion, anterior translation of tibia, tibial spine fracture, osteochondritis dessecans lesions, and patella alta or baja. Notch or tunnel view is useful to view the posterior aspects of the femoral condyles and location of most osteochondritis dessecans lesions. Sunrise, or Merchant, view assists in evaluating for patellar fracture and investigating patellofemoral articulation. MRI of the knee with effusion is indicated for (1) acute pain not better with initial acute management of effusion with non-weight bearing and rest and (2) concern for a surgical condition. One may consider referral to an orthopedic surgeon or a sports medicine specialist prior to MRI.

Treatment

Knee pain with effusion is treated acutely with non-weight bearing. Non-weight bearing status is achieved with crutches with or without a knee immobilizer. A knee immobilizer helps to decrease acute pain by limiting joint motion. Partial weight bearing with

crutches is encouraged only if pain is improving. For an adolescent with knee pain, effusion, and partial weight bearing, one may initiate treatment with crutches without immobilizer to avoid knee stiffness. Pain and swelling should be managed with Protection, Rest, Ice, Compression, and Elevation (above the level of the heart), also known as PRICE. Response to PRICE therapy should be reassessed in the next 1–2 weeks. If pain is not improving or the etiology is uncertain, a sports medicine specialist or orthopedic surgeon referral should be considered. Any fracture should be referred to sports medicine or orthopedics.

Shin Pain

History

Pain in the anterior leg, or shins, is a common complaint in adolescent athletes. The etiology is often either medial tibia stress syndrome (also known as shin splints), tibia stress reaction/fracture, or chronic exertional compartment syndrome. All conditions commonly present with shin pain. However, medial tibial stress syndrome (MTSS) classically presents with pain on running that initially was short lived with ability to complete the run. Without appropriate rest from running, pain from MTSS may progress in intensity and duration. Pain may even progress to pain with simple ambulation. Pain due to tibia stress reaction/fracture has a similar history of progressive pain but lacking the initial ability to "warm up" the pain so remainder of the run is pain free. Both conditions often are seen after a period of increased volume and/or intensity of running. Chronic exertional compartment syndrome (CECS) will often present with predictable timing of pain onset that resolves with rest only to return with the same timing, or earlier, with repeated attempt at running. Pain of CECS is progressive if running is not discontinued and may be associated with paresthesias or weakness due to neurovascular compromise. CECS is found in the setting of increased compartment pressures and compression of muscle fibers and/or neurovascular structures in the bound compartments of the lower leg. It is exertional and does not

represent an acute compartment syndrome, which is an orthopedic emergency. With CECS one may report a preceding history of lower extremity hypertrophy due to additional strengthening. Additional symptoms may include distal paresthesias and/or weakness including foot drop.

Clinical Exam

Physical examination of MTSS is often positive for posteromedial tibial cortex tenderness to palpation with no pain on resisted ankle or knee ROM. Tenderness to palpation is diffuse and often more in the middle to distal thirds of the tibia. In contrast, the tenderness to palpation of a tibia stress reaction/fracture is often very focal. Additionally, pain from a tibia stress reaction or stress fracture may be positive on heel strike, single-legged hop, and/or distal application of a tuning fork. Examination for CECS is often negative with no tenderness to palpation or pain on resisted ROM. If examined after exercise to the point of symptoms, an athlete with CECS might have tense muscles but no focal tenderness to palpation.

Imaging

AP and lateral views of the tibia and fibula are indicated. Often findings will be negative in MTSS and CECS. A stress fracture of the tibia and less commonly the fibula may show a subtle periosteal reaction at the site of maximal tenderness, but this is rarely seen close to the reported onset of symptoms. When symptoms do not improve with rest and there are negative X-rays, MRI is indicated. MTSS may show diffuse periosteal edema. Stress reactions will show increased fluid signal without a hypointense fracture line. Stress fractures will show increased fluid signal on both sides of a hypointense fracture line. MRI of CECS will be negative.

Treatment

Treatment of MTSS and stress reaction/fractures is rest from the offending stressors (i.e., running and/or jumping). Athletes should be encouraged to cross-train in any manner that is pain free. For example, an athlete may maintain cardiopulmonary fitness cross-training. If pain free, the adolescent athlete may progressively

increase loads to the lower extremities through the following steps: (1) deep water pool running, then (2) stationary cycling without resistance, or running in a lap lane, then (3) stationary cycling with resistance, or elliptical, then (4) treadmill running, and finally (5) return to road or track running. Stress reaction/fractures that do not improve with relative rest should be treated with a pneumatic compression boot or cast immobilization. Additionally, one should consider orthotic management if running biomechanics may have contributed to MTSS or stress reaction/fracture.

If CECS is suspected, diagnosis can be confirmed by referral for compartment testing by a sports medicine specialist or orthopedic surgeon. Compartment pressures are obtained pre-exercise and then after the onset of symptoms. If CECS is confirmed, treatment includes full rest and/or fasciotomy by an orthopedic surgeon.

Ankle Pain

History

Ankle pain is a very frequent musculoskeletal complaint in adolescents. Exact location of pain is the most important clue from history. Ankle anatomy is partitioned into lateral, medial, anterior, and posterior compartments. Pain is often located laterally and less commonly medial, anterior, or posterior. Pain from sports injuries is increased with activity and relieved with rest. When acute, the mechanism of injury often correlates with the location: inversion injuries stress the lateral structures and eversion injuries stress the medial structures. Injury to the ankle often has either intra-articular or extra-articular swelling. A sense of instability is common with locking of the ankle remaining infrequent.

Lateral ankle pain is the most frequent complaint and common with an acute inversion injury. If growth plates are still open, one must consider distal fibula Salter–Harris I fracture or Iselin's disease (base of the fifth metatarsal apophyseal stress injury). In a skeletally mature adolescent, lateral pain is most likely an ankle sprain, or tear of static stabilizing ligaments. Additionally, there is a possible bony, non-physeal fracture in the skeletally mature athlete.

Posterior ankle pain is most often an overuse condition. In addition, Sever's disease, or calcaneal apophyseal stress injury, is nearly always the cause of heel, or posterior, pain in an athletic skeletally immature adolescent. Skeletally mature adolescent athletes may have posterior pain due to Achilles tendinopathy. Anterior ankle pain is similarly an overuse condition often due to ankle instability especially in gymnasts and tumblers.

Sports injuries to the medial ankle may be acute, subacute, or chronic. Most often medial pain is related to the navicular bone, posterior tibial tendon, or underlying robust medial deltoid ligaments. Occasionally, medial foot pain may be related to pes planus with or without pronation but this does not represent a sports injury.

Clinical Exam

Ankle exam can be simplified into four parts: (1) range of motion, (2) point of maximal tenderness, (3) resisted range of motion, and (4) stability testing with anterior drawer test. Decreased ankle ROM may be due to swelling within the joint or pain. In contrast, localized extra-articular swelling will not affect ankle ROM. Discovering the point of maximal tenderness is important to localizing the pain generator and etiology of pain. Landmarks that are important to palpate include lateral malleolus/distal fibula physis; medial malleolus/distal tibia physis; posterior calcaneus; base of the fifth metatarsal, navicular, lateral ligament complex (anterior talofibular ligament (ATFL), calcaneofibular ligament (CFL), and posterior talofibular ligament); and medial ligament complex. The most important landmark, and most commonly injured structure in the skeletally mature adolescent, is the ATFL. The ATFL is the first ligament to be disrupted in an ankle sprain. Holding the plantar flexed midfoot in one's palm and placing the thumb diagonally to the fibula, one locates the ATFL. All metatarsals should also be palpated for younger patients that have difficulty localizing the pain and for possible stress fractures. In addition, there may occasionally be a "high ankle sprain" which is a disruption of the connection between the distal tibia and fibula with stress forces progressing proximally. Anterior tenderness proximal to the joint line and/or pain at the joint with a tibia–fibula squeeze test most often indicates a syndesmotic injury with a severe acute ankle

injury. Resisted ROM from neutral will stress the tendons and their bony insertions, or physes if present for possible tendinopathy or physeal injury. For example, medial navicular prominence with pain on resisted inversion often signals stress to the posterior tibial tendon and possible accessory navicular bone connected to the navicular through injury-sensitized cartilage. Finally, anterior drawer testing is accomplished by firmly grabbing the calcaneus posteriorly and talus anteriorly, distracting, and anteriorly translating the foot. Increased translation compared to the uninjured side is a sign of instability. Instability of the ankle by anterior drawer testing is often due to ligamentous laxity due to injury or generalized hypermobility.

Imaging

AP, mortise, and lateral views of the ankle should be obtained in the setting of acute pain or subacute pain. AP view may show soft tissue swelling over the medial or lateral malleoli and non-physeal fractures. Both AP and mortise views may show loss of a normal but small tibia and fibular overlap in high ankle sprains. In addition, the mortise view may show osteochondritis dessecans lesions to the talar dome, which are possible with ankle overuse. Lateral view is helpful to assess for joint effusion, fractures, and calcaneal and fifth metatarsal apophyses. MRI of the ankle is indicated for chronic pain not better with maximal conservative care or with concern for a surgical condition, but referral to a sports medicine specialist or an orthopedic surgeon prior to advanced imaging may be indicated.

Treatment

Like many sports injuries in adolescence, ankle pain often improves with conservative management. Conservative management includes pain relief with ice and analgesics along with relative rest. Similar to Osgood–Schlatter disease and Sinding-Larsen–Johansson disease, there are no long-term complications from Sever's disease and Iselin's disease. Rest, ice, and limitation to painfree activity are appropriate treatment.

Acute sports injuries of the ankle should be managed with Protection, Rest, Ice, Compression, and Elevation (above the level

of the heart), also known as PRICE. Protection for ankle pain with debility includes non-weight bearing or partial weight bearing. Non-weight bearing status is achieved with crutches with or without immobilization. Partial weight bearing with crutches is encouraged only if pain is improving. Ankle immobilization can be achieved by cast or walking boot. Both forms of immobilization decrease acute pain by limiting joint motion. Cast immobilization is for fractures and more severe pain. Walking boot immobilization is beneficial if the debility is mild to moderate and expected to improve in a short period. Walking boot immobilization may allow for an early start with physical therapy and return to sport. The response to PRICE therapy should be reassessed in the next 1–2 weeks. If pain is not improving or the etiology is uncertain, a sports medicine specialist or orthopedic surgeon referral should be considered. Fractures are often referred to sports medicine specialist or orthopedics.

Commonly, ankle pain is subacute or chronic due to overuse and/or ankle instability. Overuse is treated with rest till pain free and a functional return back to sport under the care of the provider, physical therapist, or athletic trainer. Pain from ankle instability improves with ice, relative rest, and physical therapy. Physical therapy is focused on ankle stabilization through strengthening of the dynamic stabilizers and improving proprioception that is hindered for 2–3 months post ankle injury. If there is significant ankle instability, adolescents may respond to lace-up ankle stabilization brace. Significant pes planus and/or pronation also contribute to overuse of ankle stabilizers and may respond to foot orthotics. A sports medicine specialist or orthopedic surgeon referral should be considered for pain with or without ankle instability not better with maximal conservative care.

Sport-Related Concussion

History

Sport-related concussion (SRC) is a clinical diagnosis and makes up nearly 10 % of all high school injuries. Unfortunately, there are many different definitions but the most recent international

symposium on SRC defines it as "a complex pathophysiological process affecting the brain, induced by traumatic biomechanical forces." Five major features of SRC include: (1) a force transmitted to the head through direct contact to head or body, (2) short-lived neurologic dysfunction that resolves spontaneously, (3) functional disturbance of brain rather than a structural injury, (4) loss of consciousness may or may not be present but symptoms sequentially resolve with a very small percentage of cases with prolonged and persistent symptoms, and (5) negative standard structural neuroimaging. There is no validated grading system of SRC. Signs and symptoms are varied and divided into physical, cognitive, emotional, and sleep categories. Headache is the most common symptom. Loss of consciousness is an infrequent finding in SRC occurring less than 10 % of cases. Retrograde/antegrade amnesia, loss of consciousness greater than 30 s, and mental fogginess are more commonly seen in slower recoveries from SRC. Postconcussion seizure activity is uncommon and mandates evaluation at a medical facility, but it does not indicate a more significant injury if self-resolution occurs. Patients with SRC may have a delayed onset of symptoms hours after the injury. Often symptoms are measured and followed by a Postconcussion Symptom Score, but it must be recognized that many of the symptoms of SRC overlap with various medical conditions such as headache disorders, learning disabilities, mood disorders, and attention deficit hyperactivity disorder. It should be stressed that a majority of patients are symptom free by 10 days. Occasionally, symptoms may last weeks or months.

Clinical Exam

With acute injury during sport, a health care provider must attend to airway, breathing, and circulation while stabilizing the cervical spine. If airway, breathing and circulation (ABC) assessment is intact and cervical spine is cleared, an athlete should have symptoms assessed and a neurologic examination including cognition and vestibulocular function is assessed. Examination should be done on the sidelines by a health care provider with SRC expertise but also repeated by the primary care provider in the clinic. There are many standardized tools to use on the sidelines or in the clinic.

The most recent international symposium produced a scripted assessment title the Sports Concussion Assessment Tool 3 (SCAT3). Computerized neuropsychological testing may be used if baseline results were obtained and available. A specialist in SRC may also obtain computerized neuropsychological testing without baseline when indicated. However, computerized neuropsychological testing is not always necessary and not proven to alter outcome or management of SRC.

Imaging

There is no need for imaging with standard SRC. However, concern for cervical spine injury, skull fracture, or intracranial hemorrhage (i.e., subdural, epidural, intracerebral, or subarachnoid) should include advanced imaging with CT scan or MR imaging. Potential indications for advanced imaging include the following: severe headache, seizure, focal neurological exam findings, altered mental status (drowsiness, impaired orientation, mood status changes such as irritability), slurred speech, and neck pain.

Treatment

Treatment of SRC is varied and without evidence-based guidelines. However, no athlete with suspected SRC should be allowed to return to sport (1) on the same day of injury and (2) prior to evaluation by a health care provider with training in SRC management. Initial management should focus on symptom relief and avoidance of symptom triggers. Management should include relative physical activity and cognitive rest. Physical rest includes no excessive physical activity until symptom free. Cognitive rest may include accommodations from school. School accommodations can take the form of informal accommodations, 504 Plans, or Individualized Education Plans and often include aspects of the following: ability to remove self to school nurse with increased symptoms, decreased attendance and starting with less cognitively taxing classes, use of a scribe, extra time for testing and/or assignments, sunglass use in bright environments, avoidance of loud environments (such as hallways or cafeterias), and excusal from nonessential assignments. Occasionally, formal neuropsychological testing is indicated to investigate comorbid or resultant

conditions such as learning disorders, mood disorders, or attention disorders among others. Once an athlete has returned to baseline, or pre-injury symptom status, a health care provider should stress him/her with examination before clearance for a stepwise return to play. The progression back to sport follows a standardized progression through the following stages: no activity, light aerobic activity, sport-specific exercise, noncontact training drills, full-contact practice, and finally return to full game play. With any symptoms during the standardized progression, an athlete should decrease activity to a symptom-free level prior to progressing through the stages again. An athlete with SRC should not be cleared for return until symptom free at rest and with exertion. A certified athletic trainer often can provide the guidance and observation through the functional progression back to sport. Education of the athlete, family, coach, and school is paramount to recovery. Retirement from collision/contact sports may be indicated in athletes with multiple concussions (occurring with increased frequency or with lower levels of impact) or with very prolonged symptoms.

Sources

Armstrong A, Hubbard M, editors. Essentials of musculoskeletal care. 5th ed. Rosemont: American Academy of Orthopedic Surgeons; 2015.

Halstead ME, Walter KD, AAP Council on Sports Medicine and Fitness. Clinical report—sport-related concussion in children and adolescents. Pediatrics. 2010;126:597–615.

Harris S, Anderson S, editors. Care of the young athlete. 2nd ed. Elk Grove Village: American Academy of Pediatrics; 2010.

Sarwark J, LaBella C, editors. Pediatric orthopedics and sports injury: a quick reference guide. 2nd ed. Elk Grove Village: American Academy of Pediatrics; 2014.

Cardiac Issues in Adolescence

11

Laura D. Flannery and Ami B. Bhatt

Arrhythmias

Palpitations are a frequent complaint in adolescence leading to medical evaluation. The most common etiologies of palpitations are sinus arrhythmia (phasic variations with respiration, often accentuated in athletes and suppressed during illness), premature atrial contractions (more common at younger ages), premature ventricular contractions (more common in adolescence, generally benign when single and uniform, and lessen in frequency with exercise), and sinus tachycardia. Sinus arrhythmias and premature contractions in isolation do not necessitate further evaluation; however, sinus tachycardia warrants a history (pain, fever, medication, drugs, alcohol use, anxiety) and basic laboratories (TSH, CBC) if the history and physical are unrevealing.

Sustained palpitations, abrupt onset/offset, associated chest discomfort, syncope, shortness of breath, or irregular rhythm suggests arrhythmias that should be referred to a cardiologist for further evaluation. Documentation of an episode on electrocardiogram (ECG) is ideal but can be difficult to capture.

Supraventricular tachycardia (SVT) is the most common sustained arrhythmia in adolescence. It may occur as an isolated event or may signal the beginning of recurrent episodes. If the SVT is

M.A. Goldstein (ed.), *The MassGeneral Hospital for Children Adolescent Medicine Handbook*, DOI 10.1007/978-3-319-45778-9_11

caught on ECG or telemetry, the mechanism of origination and termination, presence of preexcitation, axis and width of the QRS complex, presence or absence of p waves and their appearance and axis, and rate of tachycardia can all help distinguish the mechanism of SVT.

The mechanism of SVT is often reentry although enhanced automaticity (rapid firing of a single atrial focus) comprises 10 % of cases. Reentrant rhythms may occur within the AV node (AV nodal reentrant tachycardia) or, more commonly in adolescents, via an extranodal accessory pathway such as the bundle of Kent (AV reentrant tachycardia). Patients with accessory pathways often have Wolff–Parkinson–White (WPW) preexcitation on ECG, as manifested by delta waves. Initial treatment of SVT should include enhancing vagal tone via a Valsalva maneuver, cold stimulus to the face to elicit the diving reflex, or adenosine in a controlled environment such as the emergency department. Adenosine may result in slowing of the rate by creating AV block which reveals the underlying rhythm or may terminate the rhythm. In cases of resistant or unstable SVT, direct current cardioversion is the treatment of choice.

Any cardiac rhythm which is irregular, wide, causes syncope, is resistant to treatment, or hemodynamically unstable should be referred to a cardiologist. An arrhythmia in a patient with structural heart disease or an adolescent with a family history of sudden cardiac death should be referred to a cardiologist as well. Further evaluation may include Holter monitor, echocardiogram, or exercise testing. Advanced imaging, electrophysiological studies, or drug provocation tests may be undertaken when specific diagnoses are suspected.

Syncope

Syncope is a common symptom in adolescents. The vast majority of cases are the result of benign vasovagal (neurocardiogenic) syncope. Other noncardiac causes include orthostasis, hypoglycemia, dehydration, seizure, or psychiatric. There are many potential cardiac etiologies, which include but are not limited to structural

disease (left heart obstructive lesions, valvular disease, cardiac tumor or mass), arrhythmias, myocarditis, pulmonary hypertension, or coronary artery anomalies.

Initial evaluation includes a detailed history consisting of the patient's recollection of the event and associated symptoms as well as a witness' description of the event. History should be performed both with the adolescent and guardian present as well as with the adolescent alone to elicit relevant history. Narrowing of peripheral vision, dizziness, or a pre-syncopal sensation preceded by an emotional situation or prolonged standing in a hot environment is strongly suggestive of a vasovagal etiology. Associated aura, incontinence, or a postictal state may point to a neurologic cause, whereas palpitations, chest tightness, shortness of breath, sudden collapse without warning, or exercise-associated syncope are more concerning for a cardiac etiology. Adolescents with eating disorders, history of substance use, or history of congenital heart disease deserve special attention. The clinician should also elicit a family history of cardiac disease, whether structural, arrhythmic, or sudden cardiac death. It is often helpful to better elucidate a family history of sudden cardiac death by asking if there were any unexpected deaths from car crashes or drowning incidents.

The physical examination should include orthostatic heart rate and blood pressure, and auscultation should include the use of dynamic maneuvers to elicit outflow tract obstruction. An ECG should be obtained to determine underlying rhythm, duration of intervals (PR, QRS, and QT), heart block, preexcitation, chamber enlargement, Brugada pattern, or repolarization and ST/T wave abnormalities. Any electrolyte abnormalities may lead to a diagnosis of eating disorders, diuretic/laxative abuse, or other drug effects.

A thorough history, physical exam, and ECG will identify the vast majority of adolescents with significant cardiac disease. A cardiologist should be consulted for any abnormalities. Advanced ECG interpretation, echocardiogram, exercise testing, tilt testing, Holter monitoring, genetic testing, or advanced imaging may aid in determining the patients with underlying cardiac etiology.

Chest Pain

Only one percent of chest pain in the adolescent is cardiac in origin. Potential, but rare cardiac etiologies of chest pain include: pericarditis/myocarditis, hypertrophic cardiomyopathy, anomalous coronary artery, coronary vasospasm, myocardial bridging, cocaine, Kawasaki disease, or aortic stenosis. A thorough history and examination should provide reassurance. Attention to the musculoskeletal, gastrointestinal, and pulmonary systems may provide a noncardiac diagnosis, as well as an assessment of anxiety and mental health (see Table 11.1). Findings that raise suspicion for a cardiac etiology include positional or exertional chest pain, chest pain associated with syncope or palpitations, or a positive family history of congenital heart disease. It is reasonable to perform an ECG on adolescents with chest pain unless the story is overwhelmingly convincing for a noncardiac etiology. A concerning personal history or family history, abnormal physical exam, or abnormal electrocardiogram should prompt a referral to cardiology for potential echocardiogram or Holter monitoring.

In adolescents with known Marfan syndrome or connective tissue disease, aortic dissection is an important cause of chest pain. Adolescents in the growth phase may dilate their aorta rapidly. Evaluation should include four extremity blood pressures, auscultation for diastolic murmur of aortic regurgitation, and a chest X-ray for widened mediastinum or imaging for aortic dissection if suspicion is high. It is important to recognize undiagnosed connective tissue diseases where the physical exam reveals pectus excavatum or carinatum, arachnodactyly, flat feet, high-arched palate, lens dislocation, striae or recurrent hernias, or if there is a relevant family history.

Postural Orthostatic Tachycardia Syndrome (POTS)

Postural orthostatic tachycardia syndrome (POTS) is a disabling disease of orthostatic intolerance that often first presents in adolescence, with a strong female predominance of 5:1. POTS is diagnosed when a patient has orthostatic symptoms from standing

Table 11.1 Causes of chest pain in adolescents

System	Etiology
Cardiac (1 %)	Pericarditis/myocarditis
	Hypertrophic cardiomyopathy
	Anomalous coronary artery
	Coronary vasospasm
	Myocardial bridging
	Cocaine
	Kawasaki disease
	Aortic stenosis
Musculoskeletal (most common, 37 %)	Costochondritis
	Trauma
	Overuse/exercise
	Herpes zoster
	Breast-related
Pulmonary (7 %)	Pneumonia
	Pleurisy
	Asthma
	Spontaneous pneumothorax
	Pulmonary embolism
	Sickle cell acute chest syndrome
Gastrointestinal (3 %)	GERD
	Peptic ulcer
	Esophagitis
	Esophageal foreign body/food
	Esophageal spasm
	Esophageal rupture
	Cholecystitis
	Perihepatitis
	Pancreatitis
Psychiatric (1 %)	Anxiety

(dizziness, nausea, vision changes) associated with an increase in heart rate greater than 30 beats per minute within 10 min of standing. Orthostatic hypotension is not seen in POTS, and POTS is a diagnosis of exclusion after alternative explanations for the symptomatology have been exhausted. Tilt table testing is often used to further validate the diagnosis. Patients with POTS often report

chronic fatigue, poor concentration, and intolerance to even mild exercise associated with activities of daily living, often in greater magnitud than in patients with autonomic dysfunction due to clinically detectable neuropathies. Deconditioning from limitations due to POTS often exacerbates and confounds the disease. Treatment for POTS includes a high salt diet, increased fluid intake (oral and sometimes even through long-term parenteral access), and medical therapy such as midodrine, fludrocortisone, and beta blockade. Biobehavioral strategies such as postural training, regular exercise, and healthy sleep habits are crucial aspects of treatment. A multidisciplinary team and involvement of cognitive-behavioral therapy to help with symptom management is helpful. Despite the initial crippling nature of this syndrome, the vast majority of adolescents with POTS report resolved or improved symptoms within 5 years of initial diagnosis.

Structural Heart Disease

Adolescents with congenital heart disease, hypertrophic cardiomyopathy, Marfan syndrome and related connective tissue disorders, and bicuspid aortic valve should be referred to a cardiologist. Specialty care with cardiologists trained in adolescent and adult congenital heart disease will enable patients to receive appropriate care and transition to becoming an independent adult with knowledge of their heart disease, understanding of the importance of routine follow-up, and the ability to traverse the complicated path of chronic disease in our health care system.

Preparticipation Sports Screening

Most states require preparticipation screening for adolescents participating in organized sports. The goal of these evaluations is to detect silent heart disease that could lead to sudden unexpected death. The vast majority of sudden death in adolescent athletes is indeed due to a cardiovascular abnormality, with hypertrophic cardiomyopathy being the most common cause. Unfortunately,

Table 11.2 AHA recommendations) for pre-participation screening of athletes

The 12-element American Heart Association recommendations for pre-participation cardiovascular screening of competitive athletes
Personal history
Exertional chest pain or discomfort
Unexplained syncope or near-syncope
History of heart murmur
Elevated blood pressure
Family history
Unexpected sudden death under the age of 50 in >1 relative
Disability from heart disease under the age of 50 in >1 relative
History of cardiomyopathies, long QT syndrome, channelopathies, Marfan
Syndrome, or arrhythmias
Physical examination
Heart murmur
Femoral pulses
Physical stigmata of Marfan syndrome
Blood pressure, preferably in both arms

very few athletes who have had sudden unexpected death had preceding symptoms or signs that indicated underlying pathology, and pre-participation medical evaluations were unrevealing for the majority of these patients. As a result, there have been no cost-effective guidelines to date that effectively detect underlying cardiac pathophysiology. The American Heart Association (AHA) has put forth guidelines for preparticipation screening of athletes which focuses on personal history, family history, and physical exam findings (Table 11.2) to guide further evaluation. A screening ECG in asymptomatic patients is discouraged.

Cardiovascular Health

Any text with regard to cardiac issues bears mention of the obesity epidemic which affects all the population, including adolescents. Adolescents who are overweight or obese have increased risk of developing atherosclerotic cardiovascular disease, hypertension,

and left ventricular dysfunction. Prevention as well as aggressive therapies aimed at weight reduction should be persued in overweight or obese adolescents. A discussion of risk of future disease may serve as a motivational platform.

Sources

Bhatia R, Kizilbash SJ, Ahrens SP, et al. Outcomes of adolescent-onset postural orthostatic tachycardia syndrome. J Pediatr. 2016 Mar;12 [Epub ahead of print].

DiVasta AD, Alexander ME. Fainting freshmen and sinking sophomores: cardiovascular issues of the adolescent. Curr Opin Pediatr. 2004;16:350–6.

Grubb BP. Neurocardiogenic syncope. N Engl J Med. 2005;352:1004–10.

Lewis DA, Dhala A. Syncope in the pediatric patient. The cardiologist's perspective. Pediatr Clin N Am. 1999;46:205–19.

Maron BJ. Sudden death in young athletes. N Engl J Med. 2003;349:1064–75.

Maron BJ, Thompson PD, Ackerman MJ, et al. Recommendations and considerations related to preparticipation screening for cardiovascular abnormalities in competitive athletes: 2007 update. Circulation. 2007;115:1643–55.

Nishimura RA, Holmes Jr DR. Hypertrophic obstructive cardiomyopathy. N Engl J Med. 2004;350:1320–7.

Saleeb SF, Li WY, Warren SZ, et al. Effectiveness of screening for life-threatening chest pain in children. Pediatrics. 2011;128(5):e1062–8.

Tainer NS, Carboni MP. Chest pain in the adolescent and young adult. Cardiol Rev. 2000;8:49–56.

Warnes CA, Williams RG, Bashore TM, et al. ACC/AHA 2008 guidelines for the management of adults with congenital heart disease. J Am Coll Cardiol. 2008;52:e143–263.

Washington R. Sports cardiology in the adolescent athlete: concerns for the pediatrician. Pediatr Ann. 2007;36:698–702.

Hypertension in Adolescents

12

Amita Sharma

Introduction

Blood pressure (BP) is the force exerted by blood against unit area of the vessel wall. BP is a continuous variable with no absolute dividing line between normal and abnormal values. An arbitrary definition of normal adult BP (120/80) is based on adverse events outcome data. BP is considerably lower in children than adults and almost steadily increases throughout the first two decades of life. During preschool years, blood pressure tracks and correlates with BP in childhood and adolescence. This pattern persists from adolescence to adult life supporting the view that essential hypertension begins in childhood and may contribute to premature atherosclerosis and early development of cardiovascular disease (CVD).

Among children older than 10 years of age, primary hypertension is far more likely than secondary hypertension, particularly if the patient is obese or overweight, has a family history of hypertension, or both. Statistically, 5 % of children should be hypertensive on first visit but the real prevalence is about 1 % as blood pressure normalizes on subsequent visits due to accommodation and regression to mean. The prevalence of essential hypertension is increasing among adolescents par with increasing obesity. Discussion of hypertensive urgency and emergency is beyond the scope of this chapter.

M.A. Goldstein (ed.), *The MassGeneral Hospital for Children Adolescent Medicine Handbook*, DOI 10.1007/978-3-319-45778-9_12

Diagnosis

Hypertension is defined in children based upon normative distribution of BP in healthy children unlike adults. US norms were determined on the basis of data on more than 60,000 children by NHBPEP (National High Blood Pressure Education Program Working Group), through age 1–17 years. Working group tables list 50th, 90th, 95th, and 99th percentiles for systolic and diastolic blood pressures ***measured by manual sphygmomanometer*** for children who are at the 5th, 10th, 25th, 50th, 75th, 90th, and 95th percentiles for height for *different sex*. These tables are complex and might lead to underdiagnosis of hypertension, especially in a busy primary care practice. Simplified versions of these tables though not validated are in place to help clinicians identify children and adolescents at risk. International standards for non-overweight children and adolescents aged 6–17 years are available but lack of clinical outcome data and variability of index population limit widespread use.

Evaluation of blood pressure is now an established feature of a complete well-child visit >3 years of age as per American Academy of Pediatrics (AAP) guidelines. Appropriate cuff is necessary to ensure accurate measurements. The width of the bladder of the BP cuff should be about 40 % of arm circumference midway between the olecranon and the acromion. The length should encircle 80–100 % of the circumference of the upper arm in same position. Use of an inappropriately small cuff may falsely elevate BP reading. The systolic and diastolic BPs are of equal importance, if there is disparity, the higher value determines the category.

Definition

Normal BP is defined as both systolic (SBP) and diastolic BP DBP < 90th percentile (See Table 12.1). Hypertension (HTN) is defined as either SBP *and/or* DBP ≥95th percentile measured on three or more separate occasions. The degree of HTN is further subdivided into two stages based on severity. Stage 1 HTN is

Table 12.1 Definition of hypertension

	Both SBP and DBP <90th centile of age, height, and sex-specific percentiles
Prehypertension	SBP *and/or* DBP ≥90th percentile but <95th percentile **or** if BP exceeds 120/80 mmHg (even if <90th percentile for age, gender, and height)
Hypertension	SBP *and/or* DBP ≥95th percentile measured on three or more separate occasions
	Stage 1: SBP *and/or* DBP between 95th percentile and 5 mmHg + 99th percentile
	Stage 2: SBP *and/or* DBP ≥5 mmHg + 99th percentile

defined as either SBP *and/or* DBP between the 95th percentile and 5 mmHg above the 99th percentile. Stage 2 HTN is defined as either SBP *and/or* DBP ≥99th percentile plus 5 mmHg. There is also a subset of patients at risk of developing sustained hypertension also known as prehypertensive state. This stage is defined as either SBP *and/or* DBP ≥90th percentile but <95th percentile **or** if BP exceeds 120/80 mmHg (even if <90th percentile for age, gender, and height).

Routinely, BP is measured using oscillometric devices that measure oscillations in the arterial wall and then derive systolic and diastolic blood pressure levels with use of proprietary algorithms. When compared with BP measurements obtained by auscultation, these readings are generally 10 mmHg higher. As programs used are company-owned trade secrets, therefore data cannot be verified or standardized independently. Readings obtained at the nursing station by oscillometric method thus need to be validated by auscultation in the examination room by the physician. Periodic BP measurements in the clinic are not reliable and reproducible. To circumvent these following modalities are being used.

Home or school blood pressure monitoring is a convenient, inexpensive technique to monitor BP in an environment familiar to the patients with great reproducibility. Use of the arm cuff is preferred. The instrument should be validated during an office visit. It overcomes digit preference and observer bias associated with clinic measurement.

In recent years, ambulatory BP monitoring (ABPM) has been an important additional tool in identifying hypertension and monitoring the effect of treatment particularly in older children and adolescents. ABPM uses a portable automated oscillometric device that records multiple BP measurements over a specific time period usually 24 h at fixed intervals. The device is worn on a belt in a pouch and cuff is placed on the nondominant arm. Diaries are given to the family to record activities and wake/sleep times. Information from the device is downloaded to a computer and then analyzed, usually manufacturer-specific software. ABPM thus provides a truer picture of BP trends and better correlation with cardiac outcomes. ABPM identifies white coat hypertension (WCH), masked hypertension (MH), and nocturnal HTN (non-dippers). ABPM data includes mean arterial pressure, BP load, and percent dipping. Hypertension is defined as elevated mean systolic BP >95th percentile and/or an elevated BP load >30 %. BP normally dips 10–20 % during sleep at night (due to loss of sympathetic tone). This nocturnal dipping is conserved in primary hypertension but is lost in most cases of secondary hypertension. Loss of nocturnal dipping is an important predictor of mortality and end organ damage independent of absolute BP levels.

White coat hypertension (WCH) is suggested by documented hypertension during an office visit, but normal BP on ABPM. Masked hypertension is the reverse of WCH and is suggested by normal office blood pressure but elevated BP on ABPM. Masked hypertension is less common (7.6 %) than WCH, but is a stronger precursor of sustained hypertension and left ventricular hypertrophy than WCH. WCH is a prehypertensive state with about 7 % of prehypertensive patients converting to sustained hypertension each year.

Physiology

BP is fundamentally viewed as a function of cardiac output (CO) and systemic vascular resistance (SVR). Cardiac output is a function of stroke volume and heart rate which are determined

by preload and sympathetic nervous system (SNS), respectively. Pressure natriuresis, the increase in sodium and water excretion that occurs when BP increases, is the predominant mechanism which allows kidneys to regulate BP. The renin-angiotensin-aldosterone system (RAAS) plays a key role in this feedback control system by direct effects on SVR and volume regulation. Excess activation of RAAS, reduction in real mass, or impaired regulation of renal blood flow hypertension results in disruption of pressure natriuresis resulting in hypertension. Except for renin, all components of a local vascular wall RAAS are present in normal vessels and their activity is dynamically regulated.

Most children (>10 years) and adolescents with primary hypertension have prehypertension or stage 1 hypertension. Primary hypertension, a diagnosis of exclusion, is a multifactorial and heterogeneous disorder. Multiple gene polymorphisms, low birth weight (LBW), and obesity are a few predisposing factors. Low birth weight causes hypertension as a consequence of reduced nephron number and associated compensatory glomerular hyperfiltration, intraglomerular hypertension, glomerulosclerosis causing a shift in pressure-natriuresis curve. Two major hormonal abnormalities in obesity-related hypertension are hyperinsulinemia and increased leptin levels. These abnormalities cause obesity-related hypertension through altered pressure natriuresis, activation of RAAS, increased sympathetic overflow, altered vascular reactivity, oxidative stress, and inflammation. Increased perirenal fat deposition causes capsular compression and renovascular changes.

In addition to the link with hypertension, obesity is strongly associated with type 2 diabetes, dyslipidemia, obstructive sleep apnea, left ventricular hypertrophy, orthopedic problems, and psychological disorders, and these comorbidities often complicate the lives of children with hypertension. Also, over time uncontrolled hypertension leads to hyperfiltration injury and increased glomerular TGFβ1 expression leading to microalbuminuria, glomerular sclerosis, and nephron loss, further exacerbating the trend towards sodium retention and hypertension. The African-American population is at higher risk to develop hypertension and hypertensive-related renal disease due to mutations in apolipoprotein L1 (APO-L1) gene.

Evaluation

The goal for the initial evaluation for hypertensive adolescents is to define the etiology and assess for the presence and severity of end organ damage. The evaluation should include detailed birth history inclusive of gestation age and umbilical artery catheterization, patient's medical history (i.e., urinary tract infections, CAKUT anomalies), prescribed medications (i.e., steroids, CNS stimulants for ADHD), family history (i.e., stroke, premature CVD), dyslipidemia, age at presentation of hypertension, and risk factors, including diet, sleep patterns, and activity levels. Clinicians should ask for use of other agents which can increase blood pressure (e.g., caffeine, power drinks), as well as about substance abuse and smoking.

Blood pressure should be measured in the upper and lower extremities to screen for coarctation, and also, measurements should be obtained while the patient is seated and while he or she is in recumbent and standing positions, to rule out postural changes in blood pressure.

All patients with diagnosed hypertension and prehypertension if associated with other risk factors (i.e., obesity, dyslipidemia), end organ damage (i.e., left ventricular hypertrophy), or other diseases with high atherosclerosis risk (i.e., diabetes, CKD) are recommended to undergo a *phase 1* evaluation.

Phase 1 evaluation involves basic laboratory tests (measurement of serum blood urea nitrogen, creatinine, electrolytes; glucose, complete blood count, calcium) and urinalysis. We also check thyroid function and vitamin D levels. Renal ultrasonography is obtained to assess renal scarring, disparate kidney size, and congenital anomalies. A fasting lipid panel and fasting blood glucose is indicated for overweight children with prehypertension, all patients with stage 1 hypertension, and more so in children with chronic kidney disease, family history of hypertension, and cardiovascular disease.

An echocardiogram should be obtained to identify adolescents with left ventricular hypertrophy (LVH) which, if present, would be an indication to initiate or intensify antihypertensive therapy. Like phase I laboratory studies, cardiac ECHO should also be

Table 12.2 Evaluation schema for hypertension

	Evaluation		Follow-up for end organ damage
Stage of hypertension	Phase 1	Phase 2	
Prehypertension with obesity	X		Cardiac ECHO once a year
Stage 1 hypertension	X		Cardiac ECHO once a year
Stage 1 HTN with end organ damage		x	Cardiac ECHO 6 monthly
Stage 2 hypertension	X	x	Cardiac ECHO 6 monthly

performed in prehypertensive adolescents with obesity, dyslipidemia, diabetes mellitus, and chronic kidney disease.

Phase 2 evaluation is indicated for mostly Stage 1 with end organ damage like LVH, and stage 2 hypertension. Plasma renin activity (PRA) or/and levels of plasma aldosterone; plasma and urinary steroid levels; and plasma and urinary catecholamines are likely to be of high yield in stage 2 hypertension as major secondary causes are renal and adrenal pathology. Renovascular hypertension (RVHT) should be suspected in patients with marked hypertension, elevated renin activity and those with history of neonatal umbilical artery catheterization, or in neurofibromatosis type I. There is no standard order of investigations, a range of imaging techniques exists, and local availability and expertise play a considerable role. We advise Doppler ultrasound as a first-line investigation. Due to lower exposure to radiation, MRA might be preferred over CT as a second-line investigation. Digital subtraction angiography (DSA), though invasive, is the "gold standard." Plasma-free metanephrines are the best screening test for pheochromocytoma with a high sensitivity (99%) (See Table 12.2).

Management

Once hypertension is confirmed and diagnostic procedures initiated, the assessment of end organ damage (i.e., LVH, retinal arteriopathy, microalbuminuria) should be started and continued at

regular intervals depending on initial findings and the degree of hypertension.

Treatment is usually a combination of non-pharmacologic and pharmacologic strategies, but many details go into the decision-making process.

Non-pharmacologic Therapy

If the evaluation suggests that the patient has primary hypertension (Stage 1 and asymptomatic), non-pharmacologic therapy is generally the first approach. Several non-pharmacologic measures have been demonstrated to be successful in lowering BP in adults and children. These include weight loss, regular exercise, restriction of sedentary activity, stress reduction, and dietary modification including salt restriction. The inclusion of family participation appears to be useful, if not essential, particularly if the child needs to lose weight.

DASH (Dietary Approaches to Stop Hypertension) in hypertensive teens decreases systolic BP in a nonlinear manner with most pronounced effect in persons consuming high-sodium diets. However, effecting these changes in a sustained manner is often difficult. Also, these dietary influences on BP, although present when large populations are studied, may not apply at the individual level. This is because a few patients are salt sensitive and others are not.

It is uncertain how much exercise should be recommended and how best to manage participation. Adherence to an exercise regimen appears to be improved with frequent visits to and feedback from a clinician, physical-fitness counselor, or nutritionist, as well as with the use of ancillary devices such as pedometers. Dynamic exercises (i.e., bicycling and running) are preferred over isometric exercises (i.e., push-ups and weight lifting) as the latter result in an acute rise in BP. The American Academy of Pediatrics (AAP) recommends unrestricted sports participation for prehypertensive, stage I hypertension without target organ damage and well-controlled Stage 2 hypertension.

Acute stress has been shown to increase BP in experimental settings, most likely via SNS activation. In addition, an individual's reaction to stress may lead to other changes in their environment that are themselves related to BP, such as obesity from increased caloric intake.

Pharmacologic Therapy

Pharmacologic therapy is started immediately for stage 2 hypertension and symptomatic hypertension (i.e., headaches, chest pain). Also, stage 1 hypertension with end organ damage and comorbid conditions (i.e., chronic kidney disease) which persists despite a trial of 4–6 months of non-pharmacologic therapy requires antihypertensive drugs. Antihypertensive treatment has a potential to reverse LVH. Also, strict BP control decreases proteinuria and CKD progression.

The number of antihypertensive agents that have Food and Drug Administration (FDA) approved pediatric labeling has increased markedly since the passage of the FDA modernization Act of 1997 and Best Pharmaceuticals for Children Act (2002) which led to approval and labeling of many antihypertensive drugs for pediatric use. There is no consensus regarding the best initial therapy for hypertension in children and adolescents; comparative trials are lacking in the pediatric population. A survey of pediatric nephrologists indicated that 47 % considered ACE to be first-line therapy, 37 % calcium channel blockers, 15.3 % chose diuretics, and 6.6 % chose beta-blockers (some chose more than one medication as a first-line agent).

Knowledge of the side effects and underlying pathophysiology guides decision-making. For example, if hypertension is associated with proteinuria, chronic kidney disease or diabetes angiotensin converting enzyme inhibitors (ACEIs) are preferred. However, ACEIs are contraindicated in a sexually active adolescent female at risk of becoming pregnant because of teratogenic potential. Similarly, non selective β blockers should be avoided in asthma, diabetes, and in an athlete as these agents may cause fatigue whereas they might be the drugs of choice if there are associated

migraine headaches. The general practice is to titrate the dose of the chosen agent to achieve therapeutic effect while monitoring for side effects.

Target BP goal is less than 95th percentile if there is no evidence of end organ damage, comorbid risk factors, or diseases associated with CVD. Target goal is lowered to below the 90th percentile in their presence. Gradual discontinuation of therapy is a possibility in children with mild initial primary hypertension controlled on a single drug with sustained maintenance on non-pharmacologic therapy.

Conclusions

Approximately 25 % of adult population in the United States has hypertension. Although the prevalence is far lower in children and adolescents at about 1 %, increasing evidence indicates that essential hypertension begins in the first two decades of life. It is a sign often without symptoms, thus is missed frequently. Addition of percentiles in an electronic health record (EHR) may improve recognition of hypertension during busy primary care visits. Early life interventions with even small decrements in numbers can have substantial effect on hypertension-related morbidity and mortality. Knowledge about hypertension among adolescents remains unsatisfactory and random. Attention should be paid to strengthen "health" as a personal value and to build young people's sense of personal competence for creation and implementation of healthy behavior.

Sources

ESCAPE Trial Group, Wühl E, Trivelli A, et al. Strict blood-pressure control and progression of renal failure in children. N Engl J Med. 2009;361:1639.

Flynn JT, Daniels SR, Hayman LL, et al. Update: ambulatory blood pressure monitoring in children and adolescents a scientific statement from the American Heart Association. Hypertension. 2014;63:1116–35.

Hansen ML, Gunn PW, Kaelber DC. Underdiagnosis of hypertension in children and adolescents. JAMA. 2007;298:874.

Keller G, Zimmer G, Mall G, et al. Nephron number in patients with primary hypertension. N Engl J Med. 2003;348:101.

Lauer RM, Clarke WR. Childhood risk factors for high adult blood pressure: the Muscatine Study. Pediatrics. 1989;84:633.

National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents. The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. Pediatrics. 2004;114:555.

Immunizations

13

Karen Sadler

Immunizations

AAP	American Academy of Pediatrics
ACIP	Advisory Committee on Immunization Practices
DTaP	Diphtheria toxoid, tetanus toxoid and acellular pertussis
DTP	Diphtheria toxoid, tetanus toxoid and whole cell pertussis vaccine
HIB	Hemophilus influenza B
HPV	Human papilloma virus
IPV	Inactivated polio vaccine
LAIV	Live, attenuated influenza vaccine
MMR	Measles, mumps rubella vaccine
PCV 13	13-valent pneumococcal conjugate vaccine
Tdap	Tetanus toxoid, reduced diphtheria toxoid and acellular pertussis
VZV	Varicella zoster vaccine

Vaccinations are, quite simply, one of the world's most successful public and individual health interventions. Along with safer water and a cleaner environment, they are responsible for the drastic reduction in mortality from infectious diseases over the past

M.A. Goldstein (ed.), *The MassGeneral Hospital for Children Adolescent Medicine Handbook*, DOI 10.1007/978-3-319-45778-9_13

century. The consent to vaccinate is both for individual benefit and a social good: rates of vaccination must usually be 95 % or better to create "herd immunity," which protects the vulnerable few who cannot be vaccinated. Currently, the anti-vaccine sentiment in this country is running high, in part due to their remarkable success, which has enabled a generation of parents to have no experience with the devastation that vaccine-preventable illnesses can cause. The current AAP recommendation for vaccine-hesitant parents is to work with them, trying to convince them to vaccinate their children, through patience and objective information.

There are two types of vaccination: passive and active. Passive vaccination involves the administration of immunoglobulin against a specific agent. It is used mainly in the acute setting after an exposure when there is no time for active vaccines to create protection, or in those who cannot respond to an active vaccine. Examples are VZIG (varicella immune globulin), the rabies vaccine, HBIG (Hepatitis B immune globulin), tetanus immune globulin, and gamma globulin given to travellers.

However, most childhood vaccines are active immunizations. An antigen is presented to the body, which then creates protective antibodies and immune memory. These antigens are sometimes live, attenuated virus particles (MMR, VZV, intranasal influenza), sometimes conjugated to an unrelated, but highly immunogenic antigen (HIB, PCV13), sometimes single but often combined (DTaP-IPV-HepB, MMRV). Most require more than one presentation before optimal protection is attained, with an interval between doses called a "lag period." Overall, contraindications are few and usually involve a known allergy to components of the vaccine (egg anaphylaxis for influenza or yeast for HPV) or immune-compromise. Furthermore, while there will always be concerns about the negative consequences of vaccines, they are remarkably safe: yellow fever and oral polio aside, the risk of a serious side effect to a vaccine is 1–2 in one million.

For reference, in the Appendix is the 2016 US vaccine schedule. While dense, it is a comprehensive and convenient point of care resource.

By age 13 years, a fully vaccinated child on the standard schedule will have received 5 DTaP, 4 IPV, 3 rotavirus vaccines, 4 HIB, 4 PCV13, 3 Hepatitis B, 2 Hepatitis A, 2 VZV, 2 MMR, and up to

14 influenza vaccines. The preadolescent and adolescent years are a time to consolidate and refresh memory with boosters to pertussis and influenza, as well as to immunize against meningococcal disease (if not already done) and HPV.

What follows is an expanded discussion of the major adolescent vaccines.

Human Papillomavirus: HPV is an ancient virus, with more than 200 serotypes affecting all vertebrate species. More than 40 subtypes affect humans. They are classified by their tropism for either skin or mucus membranes (of the oropharynx and genital regions), and further by their oncologic potential. The burden of HPV is tremendous. It is one of the most common STIs, infecting more than 40 % of sexually active adolescent females within months of the onset of sexual activity. Furthermore, new infections can be acquired throughout the life span. While the great majority are asymptomatic and clear spontaneously (90 % within 2 years in infection), 99 % of cervical cancers contain HPV DNA. Thus, they are seen as a necessary, but not sufficient cause of cervical cancer, with other known risk factors being immune-compromise and cigarette smoking. They also contribute to the development of warts, anogenital dysplasia, and head and neck cancers. While lower risk, types 6 and 11 can cause genital warts and low-grade cervical changes. Diseases are type-specific (see Table 13.1)

There are three HPV-related vaccines approved by the FDA.

Cervarix, (GlaxoSmithKline) containing types 16 and 18, was approved in 2009 for use in girls aged 9–26 years, but is used more widely in other countries. New data have been published that one

Table 13.1 Percent of cancers associated with HPV

Malignancy	% HPV associated	Most common types
Cervical cancers	>90 %	~70 % by 16 and 18
Vaginal cancers	~70 %	Largely by 16
Vulvar cancers	~70 %	Largely by 16
Anal cancers	>90 %	95 % by 16
Penile cancers	~60 %	Largely by 16
Oropharyngeal cancers	~70 %	>50 % by 16

Sources: www.cancer.gov and www.CDC.gov

or two doses of this 3-dose series may be just as effective as three doses, potentially enabling expanded and lower cost coverage.

Gardasil (Merck & Co.) is a quadrivalent vaccine containing HPV types 6, 11, 16, and 18. It was approved for use in females aged 9–26 years in 2006, and for males aged 9–21 (or up to 26 if high risk) in 2010. Current CDC recommendations are to begin the 3-dose series at 11–12, though it can be administered to those as young as 9 years. As of 2016, it is now advised to begin this series at 9 years in those with a history of trauma or sexual abuse. A history of sexual activity or prior abnormal cytology should not preclude this series, as it may still protect against strains to which the body is naïve.

Gardasil 9 (Merck & Co.) is an expanded vaccine approved in December 2014. In addition to those strains in the quadrivalent vaccine, it adds 5 more to include the 9 serotypes known to cause ~90 % of cervical, vulvar, vaginal, and anal cancers. It received approval for girls aged 9–26 and boys aged 9–15.

Despite its proven efficacy, the US rates of HPV immunization are far below the HealthyPeople 2020 goal of 80 % coverage. In 2014, ~40 % of girls and only ~22 % of boys aged 13–17 had completed the 3-series vaccine. It is estimated that, over a lifetime, 58,000 cancers would be prevented if current rates matched the goal of 80 %. Pediatric practitioners may be able to improve this rate: one study showed that, if the vaccine was offered as routine by a provider *without qualification*, parental acceptance increased from ~20 to 94 %.

Neisseria meningitidis: Disease caused by this organism is both rare (800–1500 cases/year in the USA) and potentially devastating. Clinically, it presents as meningitis, bacteremia, and/or pneumonia. Of 13 serotypes, 5 are important: A (now rare), B, C, Y, and W-135. Serogroup B causes 50 % of disease in infants (the age group most commonly affected), with C,Y, and W-135 being traditionally more prevalent in those 11 years and older. In 2014, college outbreaks of meningitis from group B led to the introduction in the USA of the first vaccine against this type.

Of the six vaccines on the market, one is a polysaccharide vaccine against A,C,Y, and W-135 (Menomune). It elicits immunity for

only ~3 years in children, does not reduce nasal carriage rates, and is not effective in those under 2. It is advised for those over 56 years, or those travelling to a high-risk region or during an outbreak.

There are three conjugate polyvalent vaccines on the market: Hib-MenCY (MenHibRix,), MenACWY-D (Menactra), and MenACWY-CRM (Menveo). MenHibRix is a vaccine for infants and children aged 6 weeks to 18 months. Children under 18 years with high-risk conditions (functional asplenia, complement component deficiencies) are advised to receive one of these vaccines (between 2 and 4 doses, depending upon the age of the child and the particular vaccine). All children should receive either Menactra or Menveo between 11 and 12 years, with a booster at 16 years. If vaccinated before 16, one booster at 16 is advised. If immunized at 16 or older, a second vaccine is not required. The recommendation to immunize also extends to those aged 19–55 years if at higher risk, which includes certain travellers, those in the military, microbiologists, and college freshman living in dorms.

In late 2014 and early 2015, the FDA approved two monovalent vaccines that target serotype B, in response to outbreaks from this strain on college campuses. Bexsero is a 2-dose series; Trumenba is three doses. Current CDC recommendations are as follows:

> *"Young adults aged 16 through 23 years (preferred age range is 16 through 18 years) may be vaccinated with either a 2-dose series of Bexsero or a 3-dose series of Trumenba vaccine to provide short-term protection against most strains of serogroup B meningococcal disease. The two MenB vaccines are not interchangeable; the same vaccine product must be used for all doses."*

This is a category B recommendation: at the discretion of the clinician based upon risk determined by current outbreaks and susceptibility.

Influenza: The battle to contain influenza requires constant vigilance for circulating strains and an annual vaccine campaign. Disease in humans is caused by strains A and B. Influenza A is subtyped by two surface antigens, hemagglutinin and neuroaminidase, which are also the targets of the vaccine. In 2008, the AAP and ACIP began advising that all children aged 6 months and older receive yearly influenza vaccines. There are two types of products

available. Inactivated influenza vaccine, injected intramuscularly, can be given to those over 6 months of age. In those less than 3 years, 0.25 mL is the recommended dose, whereas it is 0.5 mL in all others. Children under 9 years who have not yet been vaccinated are presumed to be influenza naïve, and given two doses, at least 4 weeks apart. Those who have received at least two prior doses or those over 9 years receive only one seasonal vaccine. Vaccine efficacy is variable from year to year, determined, in part, by the match between circulating strains and the antigens in the vaccine. For those under 6 months, cocooning is advised (the effort to vaccinate those in close contact with the infant), and inactivated vaccine is advised for all pregnant women.

The second type of vaccine is a live, attenuated product. In the 2015–2016 season, a quadrivalent formulation replaced all live, and most inactivated vaccine, containing 2 A strains and 2 B strains. The live, attenuated influenza vaccine (LAIV) is, in many ways, a superior product. It is given intranasally, inducing mucosal IgA antibodies. It is both more effective and longer lasting, and has been shown to protect against influenza-related otitis media. It is only approved, however, for those older than 2 years. It cannot be given to those with serious egg allergies, those on aspirin therapy, during pregnancy, or in those with immune-compromise.

Pertussis, known colloquially as whooping cough or the 100-day cough, causes a respiratory disease that ranges from asymptomatic to severe, the latter especially in young infants. After a catarrhal phase, a prolonged phase with a paroxysmal cough ensues, lasting up to 12 weeks. Before a vaccine was introduced in the 1940s, case rates often exceeded 100,000/year in the USA. By the 1980s, this rate had fallen to 10,000/year but has been steadily climbing since, reaching 32,000 reported cases in 2014. There are multiple reasons for the resurgence. In response to concerns about the side effects of the whole cell vaccine, (DPT), an acellular product (DTaP) was introduced in the 1990s. In 2005, two vaccines without the full complement of diphtheria antigen, (Tdap) and targeted to adolescents came on the market. Initial immunogenicity trials between Tdap and DTP demonstrated equivalency, but it is now known that Tdap and DTaP are neither as long lasting as the original vaccine (immunity wanes after 3–5 years versus 7–10 years) nor as

effective (as antibody to pertactin affords important protection, and some current pertussis strains are pertactin-deficient). In addition, since vaccinated individuals can still transmit this bacteria, despite being asymptomatic, herd immunity must be high. Vaccine refusal makes this effort particularly difficult.

Current recommendations are to "cocoon" infants too young to be immunized by immunizing close contacts, and to administer Tdap to all pregnant women, preferably in the third trimester. Children between 11 and 12 years should receive a Tdap booster (regardless of the timing of their last DTaP) All persons between 19 and 64 should receive at least one Tdap, with a Td booster given every 10 years, or sooner if acute tetanus protection is indicated. The two Tdap vaccines on the US market are Boostrix and Adacel.

Other vaccines, as they pertain to adolescents: All children under 19 should receive the Hepatitis B vaccine series, usually a 3-dose series of a pediatric formulation, though a 2-dose series for 11–15-year-olds can be used with the higher dose (adult formulation) of Recombivax HB (Merck & Co.). Adult formulations are used for those 20 years and older. In adulthood, this vaccine is advised for those with risk factors (see Appendix). Hepatitis A is now a universally recommended vaccine for children 6 through 23 months. For older children and adolescents it is advised in a 2-dose series separated by 6 months if indicated (potential travel exposure, men who have sex with men, illicit drug users, or those receiving clotting factors). A single dose of Hemophilus B vaccine is advised for those over 5 years who are unimmunized and have HIV or functional asplenia. Similarly, vaccination against pneumococcal disease, with the 13-valent recombinant vaccine, the 23-valent polysaccharide vaccine, or both, is targeted in the adolescent and adult population to those at particular risk (see CDC chart footnotes in appendix). All children older than 5 years and through adulthood should receive (with few exceptions and if not naturally immune) two doses of the live virus vaccine MMR at least 4 weeks apart, and be immunized against varicella with two doses at least 4 weeks apart (though preferably 3 months apart if between 7 and 12 years). Though active immunization against polio with inactivated polio vaccine (IPV, the only preparation

used in the USA) is not advised for those over 18 years, children under 18 are immunized with IPV if not adequately immunized by 4 years.

Although children receive most of their active vaccines when in their youngest years, adolescence is also a time to assure continued protection against vaccine-preventable diseases.

Sources

Belshe R, Alexander K, Marshall G, Dixon T. Immunization updates. 2015;1(1):3–22.

Brigham K, Goldstein M. Adolescent immunizations. Pediatr Rev. 2009;30(2):47–56.

Cooper Nellist C, editor. 2015 Pediatric vaccines (supplement). Pediatric News Fall. Frontline Medical Communications Inc.; 2015.

Part II

Sexuality, Gynecology, and Abnormal Growth and Development

Amenorrhea

14

Kathryn S. Brigham

In order to understand menstrual irregularities, one must be familiar with the normal menstrual cycle. Convention is that the first day of menses is termed day 0 of the menstrual cycle, and normal menses can last from day 0 through days 3–7. The first half of the menstrual cycle is the follicular phase, and while this can vary in length, it is stereotypically the first 14 days. During this phase, follicle stimulating hormone (FSH) released by the pituitary leads to development of a follicle in the ovary. Toward the end of the follicular phase, estradiol produced by the ovary causes growth of the endometrial lining and increases luteinizing hormone (LH) production by the pituitary. A surge of LH leads to ovulation, which occurs midway through the cycle, usually between days 10–14. After ovulation is the luteal phase (days 14–28), in which the theca cells of the ovary form a corpus luteum, producing progesterone and estrogen, leading to further endometrial maturation. If fertilization does not occur, the corpus luteum involutes, leading to declining levels of estrogen and progesterone, which ultimately leads to sloughing of the endometrial lining and onset of menses. In adolescents, normal menstrual cycles are anywhere from every 21 to 35 days.

Amenorrhea in the adolescent can be either primary or secondary. Primary amenorrhea is the absence of a menstrual period by age 15 or lack of menarche within 3 years of the onset of breast

M.A. Goldstein (ed.), *The MassGeneral Hospital for Children Adolescent Medicine Handbook*, DOI 10.1007/978-3-319-45778-9_14

development. Failure to develop any secondary sexual characteristics by age 13 is also considered abnormal and should be investigated. In the United States, median age of menarche is 12.4 years and 95 % of girls will have achieved menarche by the age of 14.1 years. Secondary amenorrhea is defined by absence of menses for duration of 3 months after prior menses.

Etiologies

While there is overlap in causes of primary and secondary amenorrhea, differentiating primary from secondary amenorrhea may guide your thinking (see Table 14.1). The causes of amenorrhea can be divided into central endocrinopathies, ovarian disorders, other endocrinologic disorders, structural abnormalities of the reproductive tract, as well as a few other etiologies. The etiology of amenorrhea can usually be determined with a careful history and physical, review of growth charts, as well as the judicious use of laboratory studies and in some cases imaging studies.

The most common central causes of amenorrhea in an adolescent or young adult include constitutional delay, chronic illness, and functional hypothalamic amenorrhea. Eating disorders, stress, the female athlete triad, and strenuous exercise should be recognized as important causes of functional hypothalamic amenorrhea. The female athlete triad, defined as low energy availability (with or without disordered eating), menstrual dysfunction, and low bone mineral density, has garnered much attention over recent years. Studies have shown a higher percentage of menstrual dysfunction in athletes. Given the high prevalence of eating disorders in this age group, they should be screened for in every adolescent and young woman with menstrual disorders (see Chap. 25). Inadequate estrogen levels occur in women with low body weight, and menstruation will not likely occur at weights less than 90 % ideal BMI. Bulimia also affects the hypothalamus, which may lead to menstrual irregularities despite having adequate weight or estrogen status.

Table 14.1 Causes of amenorrhea

	Primary and/or secondary amenorrhea	Primary amenorrhea	Secondary amenorrhea
Central (low to normal FSH)	Functional hypothalamic amenorrhea	Constitutional delay	
	Chronic illness	Congenital hypopituitarism	
	Pituitary infarction	Prader–Willi syndrome	
	Hemochromatosis (pituitary infiltration)	Kallman syndrome	
	Pituitary tumors		
	Hypothalamic tumors		
	Radiation		
	Surgery		
	Chemotherapy		
	Laurence Moon Bardet Biedl syndrome		
Ovarian (high FSH)	Pelvic radiation	Turner syndrome[a]	Autoimmune oophoritis[b]
	Chemotherapy	Single gene mutations	
	Galactosemia		
Other endocrine disorders	Hyperprolactinemia		Nonclassical Congenital Adrenal Hyperplasia[b]
	Thyroid disorders		PCOS[b]
	Cushing's disease		
	Addison's disease		
	Adrenal tumors		
Structural	Surgery affecting reproductive organs	Uterine agenesis	Uterine synechiae (Asherman syndrome)[b]
		Cervical agenesis	
		Vaginal agenesis (Mayer–Rokitansky–Küster–Hauser syndrome)	
		Transverse vaginal septum	
		Imperforate hymen	
Other	Pregnancy	Androgen insensitivity and other intersex disorders	Hormonal contraception[b]
	Antipsychotics		

[a]Could cause secondary amenorrhea, but typically causes primary amenorrhea
[b]Could cause primary amenorrhea, but typically causes secondary amenorrhea

Less common central etiologies of amenorrhea include additional conditions leading to pituitary or hypothalamic dysfunction. These can be congenital, such as in congenital hypopituitarism; iatrogenic from radiation, surgery, chemotherapy; or secondary to other medical conditions, such as tumors, infarction, infiltration from hemochromatosis, Laurence Moon Bardet Biedl Syndrome, or Prader–Willi Syndrome. If a patient has poor sense of smell, it is also worth considering Kallman syndrome, which is congenital gonadotropin-releasing hormone deficiency and anosmia.

Premature ovarian insufficiency (POI) may occur before or after menarche and occurs in 1 % of females under 40 years old and 0.1 % of females under the age of 30 years. Often premature ovarian insufficiency occurs slowly over years and 50 % of patients may have intermittent ovarian function with 20 % ovulating spontaneously. Etiologies of POI include autoimmune oophoritis, Turner's syndrome, galactosemia, and damage to the ovaries either from chemotherapy or pelvic radiation. Patients with POI should be screened for additional autoimmune disorders.

Polycystic Ovarian Syndrome (PCOS) is the most common endocrinopathy in female adolescents. There are multiple sets of diagnostic criteria for PCOS, but typically patients with PCOS have a combination oligomenorrhea, clinical or biochemical evidence of hyperandrogenism, and enlarged and/or polycystic ovaries on pelvic ultrasound (see Chap. 18 for more details). Nonclassical congenital adrenal hyperplasia (CAH) can present similarly to PCOS. In addition, thyroid disorders, Cushing's disease, Addison's disease, adrenal tumors, and elevated prolactin levels can cause primary or secondary amenorrhea.

In the adolescent with primary amenorrhea, structural abnormalities should be considered; the evaluation should include assessment of the genitalia and ascertaining the presence of a vagina, uterus, and ovaries. Mayer–Rokitansky–Küster–Hauser Syndrome (MRKH), also referred to as vaginal agenesis, is characterized by congenital absence of the vagina and varying degrees of uterine development. Patients with androgen insensitivity have an outwardly female phenotype but have a blind vaginal pouch, presence of testes, no uterus, and XY karyotype. A transverse vaginal septum or imperforate hymen can cause an outflow tract obstruction, leading to primary amenorrhea. Surgery can

cause uterine synechiae, or uterine adhesions, leading to amenorrhea; this is relatively rare in adolescents, but worth considering in patients with prior history of surgical procedures or more rarely a serious infection at the time of or following a pregnancy termination.

Medications, such as antipsychotics and hormonal contraception, can also lead to amenorrhea. Finally, pregnancy must be on the differential for every adolescent with amenorrhea, even in the patient who denies any sexual activity.

Evaluation

As with most medical disorders, a detailed history and physical may provide clues as to the etiology, as well as guide any additional workup (see Table 14.2). For primary amenorrhea, timing of thelarche and adrenarche can provide information about endogenous estrogen and androgen production, respectively. A history of cyclic lower abdominal pain could be suggestive of an outflow tract obstruction. A complete review of systems is crucial, as there may be signs of endocrinologic disorders, such as fatigue and constipation with hypothyroidism or headaches or galactorrhea with pituitary tumors. In addition, a detailed history may pick up potentially undiagnosed chronic illnesses that have led to amenorrhea. For secondary amenorrhea, it is worth asking about age of menarche and typical length of cycle and menses. Complaints of acne, hirsutism, or hair loss are common in patients with PCOS and nonclassical CAH. A detailed past medical and surgical history is crucial to evaluate if chronic illnesses and resultant treatments may have led to functional hypothalamic amenorrhea or have caused damage to any of the reproductive or endocrinologic pathways needed for regular menstruation. Medications should be evaluated as possible etiology, particularly chemotherapy, antipsychotics, or hormonal contraception, of which parents may not be aware.

A detailed family history should be obtained. If parents and siblings went through puberty later than their peers, constitutional delay should be considered as an etiology. Studies suggest that PCOS can be inherited, so a family history of PCOS in female

Table 14.2 Initial approach to amenorrhea

History	General history as taken with all patients
	Menstrual history: age of menarche, date of last menstrual period, days between menses, duration of menses, amount of flow, cramping
	Age of menarche, thelarche, adrenarche
	Review of systems, especially headaches, vision changes, weight changes, acne, hirsutism, fatigue, galactorrhea, bowel changes
	Family history, including timing of puberty of family members
	Medications, particularly antipsychotics
	Social history, especially eating and nutrition habits, exercise, and sexual activity
Physical	Vital signs, growth chart review, including BMI and percentiles
	Skin: Hirsutism, acne, acanthosis nigricans, striae
	Breasts: Tanner staging, galactorrhea
	External genital exam: pubic hair, clitoromegaly (>5 mm), hymen patency
	Internal genital exam: vaginal mucosa color, insert cotton swab for length
Studies	Urine HCG for every patient
	FSH, TSH, and prolactin for most patients
	Hypothalamic amenorrhea: estradiol level, progesterone withdrawal challenge
	Androgen excess: LH, FSH, DHEAS, SHBG, testosterone (total and free), and possibly a morning 17-OH progesterone
	Stigmata of Turner Syndrome, structural abnormalities, ambiguous genitalia, or significant growth or pubertal delay: karyotype
	Chronic illness: basic chemistries, cbc, inflammatory markers, markers of celiac disease
	Pelvic ultrasound; identified structural abnormalities should be followed up with a pelvic MRI
	Consider bone age in patients with short stature or growth delay
	Adrenal MRI in patients with markedly elevated DHEAS
	Brain MRI only in cases in which the workup has not suggested any other etiology

relatives or metabolic syndrome in any relative would raise PCOS higher on the differential.

A social history should be obtained in a confidential manner in order to ask about prior sexual history as part of evaluation for pregnancy. In addition, it is worth assessing any concerning dietary

or exercise habits that would be suggestive of an eating disorder or the female athlete triad.

The physical exam should begin with a review of the vital signs and growth charts, including BMI. A low BMI or significant decrease in BMI percentile could be suggestive of an eating disorder, female athlete triad, or other chronic illness, while a high BMI may be more suggestive of PCOS. If a patient is markedly shorter than expected given parents' heights, Turner Syndrome should be considered. The patient should be fully undressed and in a gown. A thorough skin exam should be done looking for hirsutism, acne, and acanthosis nigricans, suggestive of PCOS or late onset CAH. Violaceous striae can be present in Cushing's syndrome. The thyroid should be palpated to look for signs of thyroid disorders.

Breast exam should be performed for Tanner staging, as well as assessing for galactorrhea, which can be found with hyperprolactinemia and hypothyroidism. Consider Turner Syndrome if there is lack of breast development or widely spaced nipples. Tanner staging for pubic hair and an external genital exam should also be performed. Complete androgen insensitivity can present with development of breasts but little to no axillary or pubic hair. Partial androgen insensitivity may present with typical pubic hair development and clitoromegaly (glans wider than 5 mm). Clitoromegaly can also be seen with nonclassical congenital adrenal hyperplasia. The hymen should be examined to make sure it's patent; a bluish bulging hymen suggests the presence of hematocolpos seen with an imperforate hymen.

A full pelvic exam is typically not required, and may not be tolerated in virginal patients. The majority of patients can tolerate a small saline moistened swab inserted into the vagina to assess vaginal length; typical vaginal length is 7–8 cm, so significantly shortened vaginas should prompt for evaluation of vaginal agenesis. The color of the vaginal mucosa can provide a clue as to the estrogen status of the patient, as prepubertal vaginal mucosa is a beefy red color, while more estrogenized vaginal mucosa is typically moist with a more pinkish hue.

The workup can generally be guided by the history and physical (see Fig. 14.1). A urine HCG should be checked on every patient. Generally FSH, TSH, and prolactin are obtained as part of the

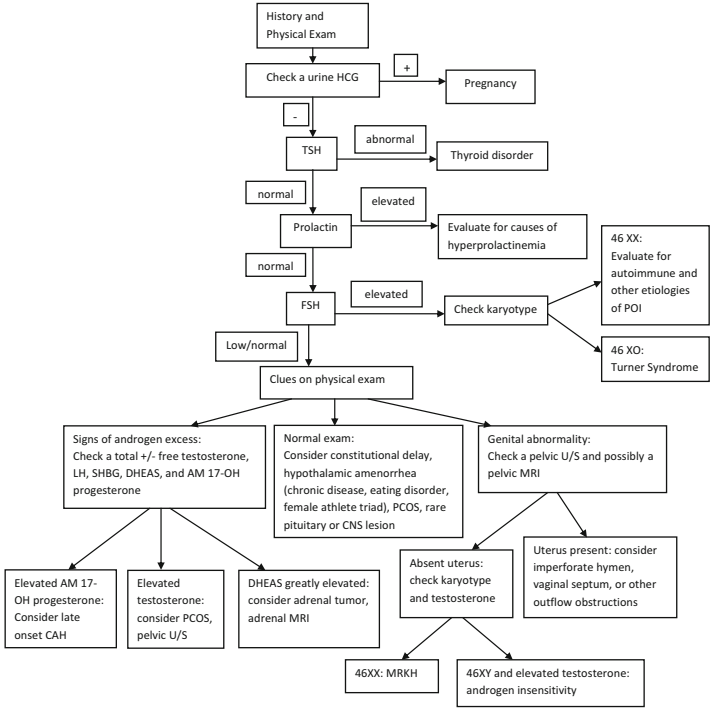


Fig. 14.1 Stepwise evaluation of amenorrhea (Adapted from Emans 2005 and Golden and Carlson 2008)

initial evaluation of amenorrhea to evaluate for premature ovarian insufficiency (POI), thyroid disorders, and elevated prolactin. If FSH is high, then ovarian insufficiency is present and a typically karyotype is obtained next. If the karyotype is normal, etiologies of ovarian insufficiency could be autoimmune, iatrogenic (radiation, chemotherapy), specific single gene mutations, or more rarely galactosemia. A 45,XO or 45,XO/46,XX mosaic karyotype reflects Turner syndrome.

In addition, if hypothalamic amenorrhea is suggested by history or growth charts, estradiol could also be checked, and the combination of low or inappropriately normal FSH in the setting of a low estradiol is highly suggestive of hypothalamic amenorrhea. Estrogen status can also be assessed by progesterone withdrawal

challenge. Progesterone is given in the form of Provera™ 10 mg or Prometrium® 200 mg orally daily for 10 days. If adequate levels of estrogen are present (generally >40 pg/ml), a withdrawal bleed will typically occur within 3–4 days after completing the challenge, but may happen up to a week after completion. If estradiol levels are low, such as with eating disorders, female athlete challenge, or chronic illness, then a withdrawal bleed will not occur because the endometrial lining is not under the influence of adequate estrogen levels.

If there are signs of hyperandrogenism, the workup would also include an LH, dehydroepiandrosterone sulfate (DHEAS), sex hormone binding globulin (SHBG), free and total testosterone, and potentially a morning (7–8 am) 17-OH progesterone. Briefly, the hallmark of PCOS is elevated testosterone levels, but unfortunately not all labs have reliable testosterone assays. The free testosterone should be calculated by the lab as a product of the SHBG. The provider can calculate a free androgen index by multiplying the total testosterone level in ng/dL by 3.47 and then divide by the SHBG in nmol/L; a normal free androgen index for females is 1.2–4.0. SHBG levels are low in PCOS, which leads to an elevated free testosterone level. An elevated LH to FSH ratio (≥2.5:1) can be suggestive of PCOS although it is not one of the diagnostic criteria. Please see Chap. 18 for more information on the diagnostic criteria for PCOS. DHEAS is a marker of adrenal androgen production but it is often elevated in PCOS. If DHEAS is markedly elevated, an adrenal tumor and nonclassical CAH should be included in the differential. A morning 17-OH progesterone should be obtained to evaluate for nonclassical CAH; if this is not checked first thing in the morning, a normal reported result could actually be a false negative.

Chromosomal analysis should also be included in those with ambiguous genitalia, blind vaginal pouch, or absence of axillary or pubic hair. In females with normal breast development but absent uterus or vaginal pouch, then a testosterone level and karyotype must be obtained. Testosterone elevated to a male level and a 46, XY karyotype is evidence of testicular feminization or androgen insensitivity. In this case, the androgen receptors are insensitive to testosterone, leading to a lack of pubic and axillary hair. There will be normal breast development, but the uterus and ovaries will be absent.

Finally, basic chemistries, cbc, inflammatory markers, and serum markers of celiac disease can be useful to determine if a chronic illness is thought to be the cause of amenorrhea.

Selective use of imaging studies can also be helpful. In primary amenorrhea, a pelvic ultrasound is the first step to assess for structural abnormalities; however, it is important that this is performed at an institution that has pediatric radiologists, as the prepubertal uterus can sometimes be missed by ultrasonographers and radiologists unaccustomed to premenarchal patients. An ultrasound can also be useful for evaluation of PCOS, as multiple small ovarian follicles or enlarged ovarian volume can be found in PCOS. If there is an outflow tract abnormality, ultrasound will show an echogenic midline mass with internal echoes due to fluid and debris.

If there are structural abnormalities, an ultrasound can be followed up by a pelvic MRI for additional detail. MRKH syndrome is diagnosed in the female who has normal ovaries, normal hormonal pattern, normal development of breast and pubic hair and 46XX karyotype but with primary amenorrhea and an absent cervix, uterus and upper 2/3 of the vagina. Renal ultrasound should be obtained due to the increased incidence of renal anomalies in these patients.

Additional studies may be ordered in certain circumstances. In patients with short stature, growth delay, or suspected constitutional delay, a bone age can also give useful information. If the DHEAS is markedly elevated, an adrenal MRI should be obtained to evaluate for a virilizing adrenal tumor. Finally, if the history, exam, and workup are not suggestive of any particular etiology, an MRI of the brain can be considered to assess for a tumor.

Treatment

Treatment needs to target the underlying cause of the amenorrhea. In the case of chronic illness, hyperprolactinemia, thyroid disorder, Cushing's Disease, and Addison's disease, treating the underlying disorder will often resolve the amenorrhea. If the cause of the amenorrhea is from a medication, then the risks and benefits of this medication must be weighed.

If low weight from an eating disorder is the etiology of hypothalamic amenorrhea, weight restoration should be the goal, which ultimately leads to restoration of menses. In the female athlete triad, the best treatment is to decrease exercise and increase caloric intake for an overall net decrease in energy expenditure. While a combined birth control pill will produce a regular period, it will mask the underlying condition and unfortunately will not reverse the long-term damage to bone mineralization. Constitutional delay will naturally resolve without any intervention.

If a patient has PCOS or nonclassical congenital adrenal hyperplasia, the treatment is typically a combined hormonal contraceptive method or periodic courses of progesterone in order to induce a withdrawal bleed. This is necessary in order to prevent endometrial hyperplasia, putting the individual at risk for endometrial cancer. See Chap. 18 for more details.

Patients with premature ovarian insufficiency are at risk for sequelae from estrogen deficiency, including diminished sexual function, hot flashes, low bone mineral density, and endothelial dysfunction leading to increased cardiovascular morbidity and mortality. For these reasons, unless there is an absolute contraindication to estrogen, estrogen therapy should be given until menopause. Often estrogen is given as a transdermal patch, which is more physiologic than a combined oral contraceptive pill. Oral microgenized estradiol is another alternative. Since a small percentage of individuals with POI spontaneously ovulate, it is important to counsel that these forms of estrogen do not work as contraception. In addition, patients with a uterus should also receive regular courses of progesterone to induce a withdrawal bleed to reduce their risk of endometrial hyperplasia.

If a structural anomaly is identified, such as a vaginal septum or imperforate hymen, the individual should be seen by a gynecologist for definitive surgical treatment. If the patient has MRKH or androgen insensitivity, options to create a functional vagina include self-dilatation or vaginoplasty. In addition, patients with androgen insensitivity require surgical removal of undescended testicles, given the increased risk of testicular cancer. Hormone therapy with transdermal estrogen is given following the gonadectomy.

Sources

Edozien L. Mind over matter: psychological factors and the menstrual cycle. Curr Opin Obstet Gynecol. 2006;18:452–6.

Emans SJ. Amenorrhea in the adolescent. In: Emans SJ, Laufer MR, Goldstein DP, editors. Pediatric and adolescent gynecology. 5th ed. Philadelphia, PA: Lippincort Williams & Wilkins; 2005. p. 214–70.

Gamboa S. Clinical inquiries: what's the best way to manage athletes with amenorrhea? J Fam Pract. 2008;57:749–50.

Golden N, Carlson JL. The pathophysiology of amenorrhea in the adolescent. Ann NY Acad Sci. 2008;1135:163–78.

Goodman L. The female athlete and menstrual function. Curr Opin Obstet Gynecol. 2005;17:466–70.

Gordon C. Amenorrhea. In: Neinstein LS, editor. Adolescent health care. Philadelphia: Lippincott Williams and Wilkins; 2002. p. 973–95.

Gray SH. Menstrual disorders. Peds Rev. 2013;34:6–18.

Meskhi A, Seif MW. Premature ovarian failure. Curr Opin Obstet Gynecol. 2006;18:418–26.

Nelson LM. Primary ovarian insufficiency. N Engl J Med. 2009;360:606–14.

Abnormal Vaginal Bleeding

15

Kathryn S. Brigham

It is not unusual for young women who recently achieved menarche to report irregular or heavy vaginal bleeding. The physiology of the normal menstrual cycle has been reviewed in Chap. 14. Due to immaturity of the hypothalamic–pituitary–ovarian axis controlling the menstrual cycle, it is common for girls to have irregular menstrual cycles in the first 2 years after menarche. As a result of this maturation defect, many cycles are anovulatory. In an anovulatory cycle, follicle stimulating hormone (FSH) induces ovarian estrogen secretion, stimulating the endometrial lining to proliferate. Normally, a mid cycle luteinizing hormone (LH) surge induces ovulation, but when the axis is not mature, there is neither an LH surge nor ovulation. As a result, there is no corpus luteum to produce progesterone to stabilize the endometrial lining, cause vasoconstriction, and myometrial contractility. In addition, the negative feedback response by the hypothalamic–pituitary system to estrogen may not be fully developed, leading to unopposed endometrial proliferation. Ultimately, the thickened endometrial lining outgrows its blood supply, producing focal necrosis and partial shedding, which leads to irregular, prolonged, and potentially heavy bleeding.

Although dysfunctional uterine bleeding (DUB) due to immaturity of the hypothalamic–pituitary–ovarian axis may frequently be the explanation for irregular or heavy menstrual periods, DUB is a diagnosis of exclusion so it is important to consider other

M.A. Goldstein (ed.), *The MassGeneral Hospital for Children Adolescent Medicine Handbook*, DOI 10.1007/978-3-319-45778-9_15

systemic (Table 15.1) and gynecologic causes (Table 15.2) of the bleeding. Pregnancy should be considered in all cases. In addition, heavy menstrual bleeding in adolescents can be the initial presentation of a previously undiagnosed bleeding disorder. Studies have shown that adolescents presenting with heavier than usual menses from the onset of menarche have a higher rate of bleeding disorders than the general population, particularly von Willebrand disease. Another common cause of irregular heavy bleeding is polycystic ovary syndrome (see Chap. 18 for additional details).

A thorough history, including a detailed review of systems and complete physical examination, is needed. The history should detail the menstrual cycle, including age at menarche, the pattern of bleeding, frequency and length of the menstrual periods, the presence or absence of cramping and mid-cycle pain, and number of pads or tampons utilized on a daily basis. Many adolescents overestimate blood loss, so it is important to ask them if the tampons or pads are fully soaked through before they are changed to

Table 15.1 Systemic causes of vaginal bleeding

System/cause	Disease/agent
Hematologic	Platelet disorders (e.g., thrombocytopenia)
	Coagulopathy (e.g., von Willebrand's disease or hemophilia)
	Hematologic malignancies
Endocrine	Anovulatory cycles (e.g., immature hypothalamic–pituitary–ovarian axis)
	Polycystic ovary syndrome
	Hyperprolactinemia
	Hypothyroidism
	Ovarian/adrenal tumors
	Excess adrenal androgen production
General	Chronic illness (e.g., lupus, diabetes mellitus, renal disease)
	Henoch–Schönlein purpura
	Hereditary disease, e.g., Osler-Weber-Rendu
Medication	Anticoagulants and platelet inhibitors
	Oral contraceptives
	Antipsychotics
	NSAIDs
	Chemotherapy
	Androgens

Table 15.2 Gynecological causes of abnormal vaginal bleeding

Anatomical region	Disorder
External genitalia	Trauma (patient may erroneously believe that the blood is vaginal)
Hymen	Trauma
Vagina	Trauma
	Foreign body
	Malignancy
	Ulceration
	Hemangioma
	Congenital vaginal abnormalities
Cervix	Trauma
	Cervicitis and sexually transmitted infections
	Cervical polyp
	Malignancy
Uterus	Pregnancy
	IUD
	Endometritis
	Pelvic inflammatory disease
	Congenital uterine abnormalities
Ovaries	Ectopic pregnancy
	Tumor

get a sense of how heavy the bleeding is. It can also be helpful to inquire as to whether they bleed through their pads onto their underwear and pajamas while asleep. Many adolescents struggle to recall an accurate menstrual history, so keeping a menstrual calendar or using a menstrual tracking app, such as Period Tracker, can be a helpful tool prospectively. In addition, the adolescent should be asked about the use of tampons, condoms, or other foreign objects in the vagina. It is also important to inquire about a family history of bleeding disorders or endocrinopathies.

A confidential sexual history should be obtained. This history should include any prior history of sexually transmitted infections or pregnancies, any new sexual partners, and the use of hormonal contraception. It is also important to inquire about nonconsensual sexual contact. Regardless of the sexual history given by young adolescents, a pregnancy test is required to rule out pregnancy.

The physical examination should start with a complete set of vital signs, height, weight, and BMI. The examination should include a general physical exam, specifically looking for evidence of bleeding, palpation of the thyroid, as well as looking for signs of hyperandrogenism, such as acne and hirsutism. The decision to do a pelvic examination is done on a case-by-case basis, but should be encouraged in those patients who have severe bleeding. Younger adolescents may not tolerate a speculum examination, so one could start with an external genital examination to evaluate for Tanner development stage, enlarged clitoris (suggestive of androgen excess), and trauma. If possible, a speculum and bimanual examination should be done to further evaluate the source of bleeding and any genital abnormalities.

Diagnostic Testing

The history and physical examination will help to guide the laboratory evaluation. However, every patient needs to have a pregnancy test. In addition, a complete blood count, platelet count, and differential are usually warranted. In more severe bleeding, prothrombin time, PTT, a von Willebrand panel, and a blood blank sample are also appropriate. Appropriate hormonal testing for PCOS, thyroid function, diabetes, and other endocrine tests may be done depending on the clinician's index of suspicion. Be aware that anovulatory menses may also occur with eating disorders and the female athlete triad. It is worth noting that the results of von Willebrand testing, LH, FSH, testosterone, and sex hormone-binding globulin are quickly altered in the presence of hormonal therapy, so if these are desired, they should be obtained prior to starting any hormonal therapies. In addition, testing for Chlamydia and Gonorrhea with a NAAT should be performed in those with a history of sexual activity.

The provider should consider obtaining a transabdominal pelvic ultrasound if the patient does not tolerate a pelvic exam or the bleeding is prolonged despite appropriate treatment. In addition, an ultrasound should be obtained if a pelvic mass or uterine anomaly is suspected. Most young girls tolerate a pelvic ultrasound as long as it is transabdominal and not transvaginal.

Management

If trauma, neoplasm, pregnancy, endocrinopathy, or an infectious etiology is noted as the cause of the abnormal vaginal bleeding, then that underlying issue should be promptly addressed. If the patient appears to have dysfunctional uterine bleeding, then management will depend on the severity of the bleeding, the patient's clinical status, and laboratory results.

Mild DUB: For mild DUB without anemia, the patient may be observed and given iron supplementation. Studies have shown that NSAIDs will reduce menstrual blood flow if they are started at the beginning of the menstrual flow and continued through the entire period. However, she may also be placed on a monophasic oral contraceptive pill that has a moderate amount of estrogen, such as a 30 μg ethinyl estradiol, with a potent progestin, such as Norgestrel 0.3 mg or Levonorgestrel 0.15 mg (examples include Lo-Ovral™, Nordette™, Levlen™, Levora™). Recent studies have also shown that levonorgestrel releasing IUDs can also be effective in decreasing bleeding.

Moderate DUB: If the adolescent has moderate bleeding compounded with anemia, then the oral contraceptive pill (OCP) should be given every 12 h until bleeding ceases, then decreased to once a day. Frequent doses of estrogen containing pills can be quite emetogenic, so antinausea medication may be warranted while the patient is taking an OCP twice daily. The patient should be warned that occasionally there may be some bleeding during the transition from twice daily to once daily dosing, but this is usually relatively mild. Iron should be administered orally, and the patient should be maintained on the once-a-day OCP regimen, skipping the placebo pills, for 3–6 months or until the anemia has resolved. For patients who have a contraindication to estrogen or whose parents are opposed to a birth control pill, oral medroxyprogesterone or norethindrone acetate are options. However, this tends to be somewhat less effective than estrogen containing methods, as estrogen helps stabilize the endometrium.

Severe DUB: This is characterized by a hemoglobin of 8–10 g/dL or less, signaling moderate anemia and symptoms of severe

bleeding. Generally, the oral contraceptive is given every 6 h until the bleeding is controlled, then every 8 h for 3 days, then every 12 h for 14 days. The patient should then be placed on daily continuous oral contraceptive pills, skipping the placebo pills until the anemia has resolved. Hematocrit and hemoglobin should be monitored closely. If the patient has severe bleeding, and severe anemia (hemoglobin < 7 g/dL) or hemodynamic instability, then consider inpatient admission, transfusion, and hormonal treatment; a gynecological consultation is recommended. Antinausea medication will almost certainly be warranted. Intravenous estrogen should be avoided as it increases risk of clotting at the capillary level. Norethindrone acetate or medroxyprogesterone are again options for those in whom estrogen is contraindicated. If the bleeding cannot be stopped within 24 h, it is worth considering antifibrinolytic drugs such as aminocaproic acid or tranexamic acid. In the adolescent with DUB, very rarely is a dilatation and curettage necessary. The prognosis for DUB is excellent as most adolescents will develop appropriate ovulatory cycles within 3 years after menarche.

Sources

Gray SH, Emans SJ. Abnormal vaginal bleeding in adolescents. Pediatr Rev. 2007;28:175–82.

Hillard PJA. Menstruation in adolescents: what's normal, what's not. Ann NY Acad Sci. 2008;1135:29–35.

Rimsza ME. Dysfunctional uterine bleeding. Pediatr Rev. 2002;23:227–33.

Basics of Hormonal Contraception

16

Nupur Gupta

The United States (US) has the highest rate of teen pregnancy and births in the western industrialized world. Over the past two decades there has been a consistent fall in the teen pregnancy rate from 116.9 (1990) to 57.4 per 1000 (2010) teenage girls. Seventy-seven percent of these pregnancies are unintended and to unmarried teens and about 45 % of these end in miscarriages or planned terminations. Adolescents usually approach providers about 1 year after initiation of sexual activity to seek contraception. Barriers to care include lack of knowledge, confidentiality concerns, and fear of a pelvic examination. Preventive visits prior to initiation should address these issues and open up the conversation about sexual activity and contraception.

Contraceptive methods for adolescents can be divided into short-acting reversible methods and long-acting reversible contraception (LARC). The short-acting methods include those containing estrogen and progestin such as the combined oral contraceptive pill (COCP), the transdermal patch, and the vaginal ring; and those that contain only progestin—the progestin only pills (POPs) and progestin containing injectable contraception. LARC includes the intrauterine devices and the etonorgestrel implant.

M.A. Goldstein (ed.), *The MassGeneral Hospital for Children Adolescent Medicine Handbook*, DOI 10.1007/978-3-319-45778-9_16

The American Academy of Pediatrics (AAP) and American College of Obstetrics and Gynecology (ACOG) recommend that LARC be offered as a first choice to adolescents and young adults desiring contraception because of the low risk and high efficacy of these methods.

Initiation of Birth Control

Medical and Social History

Prior to starting adolescents on birth control, a good medical and social history should be obtained. This should include a:

- Menstrual history including age at menarche, date of last menstrual period (LMP), regularity and length of menses, cycle length, presence of cramps/back pain/mood changes/premenstrual symptoms.
- Personal history of thrombosis, migraine with aura or focal neurological deficits, or other chronic diseases such as diabetes and systemic lupus.
- Family history of first-degree relatives with thromboembolic phenomenon. If positive provider may need to avoid combined methods or do a basic workup to rule out prothrombotic disorders.
- A detailed sexual history should also be obtained including number of lifetime sexual partners, age of coitarche, history of sexually transmitted infections (STIs), pregnancies and terminations, and current relationships.
- Information on previous contraceptive methods used and side effects experienced

More detailed information can be obtained from the US medical eligibility criteria for contraceptive use (USMEC, 2010):

http://www.cdc.gov/reproductivehealth/unintendedpregnancy/usmec.htm

When to start hormonal contraception

1. First day start: start on the first day of the menstrual cycle.
2. Sunday Start: start method (usually for pill, patch, and ring) on the first Sunday after the onset of menses. This helps in remembering but also prevents menses from coming on a Sunday.
3. Quick start: patients may choose to start on the day of the visit.

If the patient is within 5 days of the start of her menses, then start method/insert LARC the same day; If the patient is more than 5 days from the start of menses, urine pregnancy test is negative, and no unprotected sex, then start/insert the same day; if the patient is more than 5 days from the start of menses, urine pregnancy test negative, and has had unprotected sex, then start/insert same day with the caveat that she should use a back up method for at least 7 days after starting the method of choice. Provider may also prescribe emergency contraception (EC) but still start/insert on the same day and patient should be advised to come back in 2 weeks for a pregnancy test.

Long-Acting Reversible Contraception (LARC)

Subdermal Contraceptive Implant

What Is It?

Contraceptive implants are devised for women who are seeking reliable and reversible methods of contraception, not requiring daily compliance, and who need protection from pregnancy for 1–5 years. Implanon® (Organon) and Nexplanon® (Merck) are the two subdermal implants currently available in the USA and provide contraception for 3 years. These consist of a single ethylene vinyl acetate rod, 4 cm in length and 2 mm in diameter, with a matrix that carries the active hormone, etonorgestrel. The matrix is covered by a thin membrane that allows the release of the hormone into the surrounding tissue and then into the circulation. The implants can be used in adolescents immediately postpartum and have not been known to affect breast feeding.

Mechanism of Action: The subdermal implant was designed to suppress ovulation for 3 years. However although ovulation is

inhibited, the levels of hormone do not suppress follicular activity so that estrogen levels remain almost normal. Thus there is less concern for effects on lipoproteins and bone mineral density (BMD). At lower concentrations, the progestin exerts its contraceptive action by causing thickening of the cervical mucus that prevents the penetration of sperm, and making the endometrium thin, and thus hostile to implantation.

Method of use: Insertion of these single rod systems is easy, with the devices being preloaded and disposable; removal often only requires a 2 mm skin incision and some finger pressure. Providers need some basic training for insertion.

Timing: Any time if provider can ensure that the patient is not pregnant (see Quick start).

Efficacy: Perfect Use: 0.05 % failure rate. Typical Use: 0.05 % failure rate.

Side Effects: Irregular bleeding (68 %) which usually diminishes with continued use. Many women regain regular bleeding patterns after 6–9 months of use; weight gain (20.7 %) with an increase of >10 % above baseline; acne (15.3 %); breast pain (9.1 %); headache (8.5 %); mood changes may also occur and are more commonly reported in teens (33 %) than in adults (17 %).

Return to Fertility: Almost immediate. Most women ovulate within 4 weeks.

Levonorgestrel-Releasing Intrauterine Contraceptive System (LNG IUS)

What Is It?

There are three levonorgestrel-releasing intrauterine systems (LNG IUS) now available in the USA: Mirena®LnG52/5 (Bayer Healthcare), Liletta® 52/3 (Allergan), and Skyla® 13.5/3 (Bayer Healthcare). The first two implants consist of a 32 mm T-shaped polyethylene frame with a cylinder wrapped around its stem. This cylinder contains 52 mg of LNG mixed with polydimethyl siloxane that allows the slow release of the hormone through the surface membrane. Skyla® has less LNG and is smaller in size. The FDA has

approved Mirena for 5 years and the other two for 3 years of contraceptive use. The devices are impregnated with barium sulfate, which allows easy visibility on x-ray and ultrasonography.

Mechanism of action: Levonorgestrel is released locally and exerts its contraceptive effect by thickening cervical mucus to reduce sperm penetration, inhibiting sperm motility and function, and causing endometrial atrophy. The hormone suppresses ovulation in only 25–50 % of users and similar to other intrauterine devices (IUDs), it also induces a foreign body reaction that causes localized inflammation and may be spermatotoxic.

Method of Use

Prior to Insertion

1. The size of the uterus must be assessed by a bimanual examination. The cavity should be 6–9 cm in length and unobstructed.
2. Visualization of the cervix is also recommended to ensure that there are no cervical abnormalities and no evidence of purulent cervicitis.

Insertion of the intrauterine device requires training, but is fairly straightforward. It is inserted with the help of an applicator. This involves a one-hand technique that allows continuous control of the uterine position of the device throughout the procedure.

Timing

The LNG IUS should be inserted within 7 days of commencement of menses, 4 or more weeks postpartum (if it can be determined that the woman is not pregnant), and immediately postabortion. If it is inserted more than 7 days after initiation of menses, then women must use a back up method for 7 days. Prophylactic antibiotics are not required.

Contraindications to Use

1. Diagnosed pelvic infection/Chlamydia or gonorrheal infection*
2. Mucopurulent cervicitis

3. Anatomic distortions of the uterine cavity
4. Abnormal uterine bleeding
5. Pregnancy

*The Centers for Disease Control and Prevention (CDC) recommends that even if patients are at high risk for STIS (25 years or younger and/or with multiple sexual partners) if they are asymptomatic then the IUD may be inserted with STI testing. If the tests are positive, then the STI should be treated without removal of the IUD. However providers must also evaluate prevalence of STIs in the population while making decisions.

Efficacy: Perfect Use: 0.1 % failure rate. Typical Use: 0.1 % failure rate.

Side effects: Bleeding disturbances (31.9 %), common in the first 1–4 months after insertion often followed by amenorrhea; abdominal pelvic pain (22.6 %); headaches (16.3 %); vaginal discharge (14.9 %); breast pain (8.5 %); benign ovarian cyst and associated conditions (7.5 %); acne (6.8 %); dysmenorrhea (6.4 %); and depressed mood (6.4 %). The chance of ectopic pregnancy is less than 1 per 1000 women years of use, slightly less than a copper containing device.

Return to Fertility: This is usually immediate after the removal of the device.

Short-Acting Reversible Contraception

The Oral Contraceptive Pill

What Is It?

The oral contraceptive pill (OCP) is one of the most common forms of birth control used by adolescents. There are two types of OCPs. The combined oral contraceptive pill (COCP) consists of a synthetic estrogen and progestin, and the progestin only pill (POP). The latter are not often used as they require teens to take the pill at almost the same time every day to ensure efficacy. In almost all COCPs, the estrogen used is ethinyl estradiol (EE). In some mestranol is used but this is converted rapidly in the body to EE. OCPs contain different amounts of EE ranging from 20 to 50 μg. The type

of progestin also varies in the COCPs and can be taken into account when prescribing the pill. There are three generations of progestins. The first-generation progestins or estranes are ethynodiol diacetate, norethindrone acetate, and norethindrone. Second-generation progestins or gonanes are norgestrel and levonorgestrel. Third-generation progestins or high potency gonanes include desogestrel and norgestimate. As one progresses from first to third generation, there is an increase in half-life and androgenic effects may vary.

Combined OCPs come in both monophasic and multiphasic packs. Monophasic pills have a constant amount of estrogen and progestin while the amount of hormones varies through the cycle in multiphasic pills. For adolescents one may start with either type, but preferably one that contains a low dose estrogen (20, 30, or 35 μg).

The POPs available in the USA contain Norethindrone 0.35 mg (Micronor® and generic versions).

Mechanism of Action

(a) Preventing ovulation by inhibiting the gonadotropin releasing hormone axis
(b) Thickening cervical mucus to prevent sperm penetration
(c) Possibly inhibiting capacitation of the sperm (ability of the sperm to penetrate the egg)
(d) Creating endometrial atrophy and changing the tubal transport mechanism

The POPs also suppress ovulation but their main mechanism of action is by the other three mechanisms. The pill can easily be changed according to individual side effects, but a trial of 3 months is recommended as it may take that long for an individual to become used to the pill and for the initial side effects to subside.

Method of Use: Both COCPs and POPs are taken orally. However the POPs have to be taken at almost exactly the same time every day to ensure efficacy. They also have to be taken continuously without allowing for any withdrawal bleeding as their efficacy depends on local action rather than suppression of ovulation.

Efficacy: COCPs: Perfect Use: 0.3 % failure rate, Typical Adult Use: 8 % failure rate, Adolescent Use: 5–15 % failure rate. Reasons

for reduced efficacy in adolescents include ineffective education and counseling about how to use the OCP and its side effects. They also may be ambivalent about contraception or forget to take the pill on a regular basis.

POPs: Much higher failure rate (as high as 50 %), as the progestin has a much shorter half-life and is dependent on the user taking it at exactly the same time every day.

Counseling About the OCP

- Initiation: can use any of the different "start" methods.
- Patients must be reminded to take their pills every day at about the same time. Tips to remember include keeping the pill with their toothbrush, using apps (My pill, My iPill, Ladypill reminder) to help them remember, or setting an alarm on their cell phones or computers. Taking the pill at night often reduces nausea.
- If the patient misses a pill or two, they may double up for up to 2 days. If they have missed three pills, it is better to stop, get a withdrawal bleed, and then start a new pack.
- COCs must be taken for 21–24 days (depending on the pill) and then there is a set of inert pills that allows patients to get a withdrawal bleed. POPs must be taken almost at the same time every day **without a break.**

Side Effects: may be related to the estrogen and the progestin components.

- Estrogen related include, but are not limited to, irregular menstrual bleeding, breast tenderness, fluid retention, nausea, increased appetite, headache, and hypertension.
- Progestin related include, but are not limited to, menstrual changes, bloating, mood changes, and increased appetite with weight gain, acne, hirsutism and rarely male pattern hair loss.
- Adolescents who use combined OCPS are at a three to four fold increased risk of venous thromboembolism as compared to non-users.

Return to Fertility: may vary but may be as much as 5 months after discontinuation of the COCP.

Who Should NOT Take Combined Oral Contraceptive Pills (COCPs)? (Absolute Contraindications)

- Patients with previous history of venous thromboembolism (VTE)
- Patients with known Factor V Leiden mutation (risk of clot increased 30-fold) or other thrombophilia condition (e.g., prothrombin mutation, Protein C or S deficiency)
- Smokers 35 years of age or older
- History of breast cancer
- Uncontrolled hypertension
- History of stroke
- History of migraine with neurologic symptoms (there is some controversy to this recommendation. This is a relative contraindication.)
- Undiagnosed uterine bleeding
- Liver disease

Within the first 21 days postpartum combined hormonal methods are contraindicated because of the increased risk of VTE; from 21 to 42 days if the adolescent has any other factors increasing her risk for VTE these methods are not to be used; beyond 42 days they may be used; POPs may be used even immediately postpartum. (Refer to US MEC see link:)

http://www.cdc.gov/reproductivehealth/unintendedpregnancy/usmec.htm

Non-contraceptive benefits of the combined OCP Although primarily prescribed for the purpose of contraception, both combined and progestin only methods can be beneficial in other disorders. These include menstrual cycle disorders including dysmenorrhea, menorrhagia, and premenstrual dysphoric disorder (PMDD); syndromes associated with symptoms of hyperandrogenism like polycystic ovarian syndrome; menstrual migraines where continuous cycling is helpful; dermatological disorders like acne; and endometriosis where continuous cycling may prevent the cyclical pain

Other Oral Contraceptives

Extended cycle regimes are available for those adolescents who desire less frequent menses or would benefit from extended cycles due to medical conditions like premenstrual dysphoric disorder (PMDD) or endometriosis. These can include OCPs that have 84 days of active hormone tablets followed by 7 inactive ones providing an extended cycle of 91 days. These give the user only 4 "menstrual" periods a year. They also reduce other side effects that occur because of hormone withdrawal like premenstrual symptoms, headaches and migraines, mood changes, and heavy or painful monthly bleeding. Another combination OCP supplies hormone throughout the year with a withdrawal bleed occurring only once a year and some formulations contain 24-day active and 4-day placebo regimen with a slightly reduced period of bleeding.

COCPs containing Drospirenone, a 17-α-spironolactone derivative that possesses diuretic and antiandrogenic activity, were developed for use in women with PCOS. However in 2012 the FDA warned of an increased risk of VTE by three to fourfold in those using these OCPs compared with other progestins. Also as this progestin has anti-mineralocorticoid activity, these OCPs should not be used in adolescents who are at risk for hyperkalemia such as those with renal, hepatic, or adrenal insufficiency or those on angiotensin-converting enzyme inhibitors, angiotensin II receptor antagonists, and nonsteroidal anti-inflammatory drugs.

Spearmint-flavored chewable OCPs are also available that are as effective as other contraceptive pills and often more acceptable to females who find it hard to swallow pills.

Transdermal Contraception

What Is It?

The transdermal contraception that is currently available is the contraceptive patch. This is a 20 cm^2 plastic patch that contains a combination of the progestin, norelgestromin (NGMN), and ethinyl estradiol. It consists of a thin, matrix-type system with three layers, the backing layer which is composed of a translucent, flexible polyester film, a middle drug adhesive layer that contains the active

components and a clear, polyester film that protects the adhesive layer during storage and is removed just before application.

Mechanism of Action: Similar to the COCP. The hormones are released from the adhesive layer, absorbed across the skin, and allow for a fairly constant level to be maintained.

Method of Use: A new patch is placed on the skin once a week for 3 weeks. The fourth week is patch-free which allows for a withdrawal bleed to occur. A single patch is said to release enough hormone to last 7 days and in effect actually prevents ovulation for up to 9 days.

Efficacy: Perfect Use: 0.3 % failure rate; Typical Use: 8 % failure rate.

Detachment rate: 3–5 % but in adolescents may be as high as 35 %. There has been evidence that patch is less efficacious in women heavier than 90 kg.

Counseling About Patch

- The patch can be applied to the buttocks, upper outer arm, lower abdomen, or upper torso (excluding the breasts). All sites have been shown to be equally effective.
- When a new patch is applied, the site should be changed.
- The site should also be free of creams, oils, and cosmetics.
- Regular activities including exercise, bathing, swimming, and use of a whirlpool or sauna do not usually result in detachment of the patch.
- If the patch becomes detached, it may be reapplied or a new patch must be applied immediately to maintain hormone levels and efficacy. The patch is then changed on the regular patch change day. However if the adolescent is unaware of the amount of time that has lapsed since the last patch became detached, she must use a new one and start the cycle again, and efficacy then cannot be guaranteed.
- Obese women interested in using the patch should be counseled about the potential for reduced efficacy.

Side Effects: Patch users experience a higher incidence of dysmenorrhea (22 %); breast symptoms (21 %) including breast

discomfort, engorgement, or pain; nausea (17 %); and dysmenorrhea (10 %) than COCP users. Also skin irritation or rash can occur at the site of application (17 %).

The patch is said to expose women to 60 % more total estrogen in their blood as compared to someone taking a 35 μg oral contraceptive pill that may increase the risk of adverse events especially VTE in users of the patch compared to those using the COCP.

Return to Fertility: Similar to COCP.

Vaginal Ring

What is it? The vaginal ring is a hormone containing silicone ring approximately 2 in. in diameter. The hormones, etonorgestrel (a progestin), and EE are implanted in the core of the ring.

Mechanism of Action: Similar to COCP. The hormones are released slowly and constantly into the vagina, and subsequently absorbed through the vaginal mucosa into the general circulation.

Method of Use: The ring is flexible and is inserted intravaginally by pressing the two sides together. A tampon applicator may also be used for this purpose. The user inserts the ring into the vagina usually on the last day of her menstrual period. The ring then remains in place all day and night and requires no further attention. It is removed 3 weeks later and a withdrawal bleed then ensues. A new ring is then reinserted 1 week later.

Efficacy: Perfect Use: 0.3 % failure rate. Typical Use: 8 % failure rate.

Counseling About the Ring

- Because the ring is self-inserted, it requires relative comfort with touching one's genitalia.
- If the ring falls out, it should be washed with cold water and then reinserted as soon as possible.
- If the ring is removed for more than 3 h in the first 2 weeks of use, back up methods should be used and the ring reinserted as soon as possible. If in the third week then either a new ring should be put in place and a new 3-week cycle started or it should be left out for 7 days so as to get a withdrawal bleed

and then a new cycle started. In either case back up methods should be instituted till the new ring has been in place for at least 7 days.

Side Effects: Nonspecific vaginitis (14 %); breakthrough bleeding comparable to COCP; headache (12 %); leukorrhea (6 %); nausea (5 %); vaginal discomfort (4 %). The most common causes for discontinuation were device-related events like expulsion; foreign body sensation; and coital-related events.

Return to Fertility: Similar to COCP.

Progestin-Only Injectable Contraception

What is it? Depot Medroxyprogesterone Acetate (Depo-Provera) (DMPA) is a progestin-only injectable contraceptive that provides 3 months of contraception and can be used by women in whom estrogen is contraindicated.

Mechanism of action: It acts by inhibiting ovulation, thickening the cervical mucus, and thinning the endometrium so that implantation is prevented. It also affects tubal motility thus impairing sperm migration.

Method of Use: It is injected deep intramuscular in the gluteal or deltoid muscle, every 3 months, in a dose of 150 mg. The vial should be shaken vigorously prior to administration to ensure that a uniform suspension is given.

Efficacy: Perfect Use: 0.3 % failure rate. Typical Use: 3 % failure rate.

Side Effects: Menstrual irregularities (irregular bleeding and amenorrhea, with about 50 % of women becoming amenorrheic by 1 year of use); weight gain (54 %); headache; mastalgia; hair loss; and change in libido.

Reduction in bone mineral density: There have also been concerns regarding DMPA usage and its effects on bone mineral density (BMD). Several prospective studies have shown that adolescents who use DMPA experience a relative loss of BMD as compared to those not using hormonal contraception. In November 2004, the FDA introduced a black box warning that stated that prolonged use

of the drug may result in significant loss of bone density, that the loss was greater the longer the drug was administered and that it may not be completely reversible. However since that time several longitudinal studies have shown that the loss of BMD is reversible. The WHO recommends that "the advantages of using DMPA generally outweigh the theoretical safety concerns regarding fracture risk. Since data are insufficient to determine if this is the case with long-term use among these age groups, the overall risk and benefits for continuing use of the method should be reconsidered over time with the individual user." The Society for Adolescent Health and Medicine (SAHM) recommends that DMPA may be offered to adolescents with proper counseling about the effects on BMD.

Return to fertility: Delayed, usually about 10 months.

Counseling About DMPA

- Patients should be counseled about the fact that they may have irregular menstrual bleeding on DMPA and occasionally amenorrhea. They should also know that most adolescents who use DMPA do become amenorrheic by their third shot (i.e., in 9 months).
- Counsel about weight gain and explain that it is seen in about half of users.
- Adolescents with a history of uncomplicated VTE may consider DMPA to be an acceptable contraceptive agent as per CDC and ACOG recommendations. Also may be safely used by others with chronic disease like epilepsy and sickle cell disease.
- Counsel about potential reduction in bone density and recommend adequate intake of calcium and vitamin D and regular weight-bearing exercise to help prevent these issues.

Discontinuation rates for Depo-Provera are exceedingly high with 33 % of adolescents not choosing to get a second injection at 3 months and 75 % discontinuing use by 12 months.

Subcutaneous DMPA formulation: Subcutaneous DMPA or DMPA-SC was approved by the US FDA in December 2004 under the name depo-subQ provera 104™. This contains 104 mg of MPA

compared to the intramuscular injection currently available. This is administered subcutaneously into the anterior thigh or abdomen, after shaking the vial well; it is also administered every 3 months, provides slower and more sustained absorption of the DMPA, and is just as efficacious as the intramuscular injection in preventing ovulation.

When Should It Be Given?

Initial: Within 7 days of the onset of the menstrual cycle or a quick start method.

Return injection: Patients should return in 13 weeks. A 2-week grace period is acceptable in women who have been coming regularly. A pregnancy test should be done prior to administration if returning >15 weeks from the last injection.

If patients are switching from one method to another, they should be advised in the following way:

(a) From COCs, contraceptive patch or ring: DMPA should be given 7 days prior to completion of current method or a back up method should be used if the injection is given more than 7 days after the onset of the menstrual cycle. If using an IUD, then DMPA should be given 7 days before the removal of the device. If given after, women should be counseled to use a back up method or abstinence in the last 7 days of IUD use or they may be given EC at the time of removal.

Emergency Contraception

What Is It?

Progestin Only Pills and COCPs

There are two types of emergency contraception (EC), the progestin only method, (levonorgestrel) and the combination pill, containing ethinyl estradiol and a progestin. (The copper-releasing IUD may also be used for the purpose of EC but is not approved in the USA for this purpose). Although EC is not an ideal form of contraception, it should be available to all adolescents who are exposed to the risk of pregnancy by virtue of having unprotected

intercourse. This should include failure of contraceptive methods and failure to use such methods such as broken condoms, delayed withdrawal, displaced diaphragms, incorrect usage of the contraceptive patch, ring or OCP and all instances of sexual assault.

Mechanism of Action: Levonorgestrel acts primarily by inhibiting ovulation with some effects on sperm motility and by thickening cervical mucus. The progestin only method acts only before fertilization and has no postfertilization action.

Method of Use: Levonorgestrel is available as a single tablet of 1.5 mg (Plan-B One step) and a pack of two tablets of 0.75 mg of LNG (Plan B), which are supposed to be taken 12 h apart. The single dose tablet is preferred and should be taken as soon after unprotected intercourse as possible, for up to 120 h. If only the two tablet pack is available, then the two tablets could also be taken together for greater efficacy. Ovrette, a progestin only pill containing norgestimate, may also be administered as EC. However, to achieve an equivalent dose of LNG in Plan B, 20 tablets of the OCP have to be administered twice at an interval of 12 h (total dose of 40 tablets). The "Yuzpe regime" involves the use of combined oral contraceptives (COCs) for the purpose of emergency contraception. Patients often have to take a large number of pills to achieve an effective dose for emergency contraception. Often this is associated with nausea and vomiting attributable to the estrogen content of the pills and an antiemetic may also need to be prescribed. Although the CDC medical eligibity criteria has certain contraindications to use of daily hormonal contraception for some women based on their medical history these same do not apply for the use of emergency contraception as it is thought that the benefits outweigh the risks.

Efficacy: Rate of pregnancy 1.1 % with LNG (Plan B) and 3.2 % in the Yuzpe group. The efficacy of Plan B declines from 98 % if taken within the first 12 h to 50 % if taken within 120 h of unprotected intercourse.

Side Effects

Progestin only pills (POPs): headache, fatigue, spotting, nausea, and dizziness reported in the first week after taking the EC.

Yuzpe Regime: estrogen-related symptoms are more common including nausea, vomiting, spotting, breast tenderness, and headache.

Patients are advised to come back to the clinic at 2–3 weeks if they do not get a withdrawal bleed. This form of EC does not require a pregnancy test as the hormones themselves are unlikely to affect the fetus.

Antiprogestins

Ulipristal is an antiprogestin agent that acts by attaching to the progestin receptor. It prevents ovulation even after the initial LH surge and thus is effective in preventing pregnancy even at 120 h after unprotected sex**.** It is available by prescription as "Ella®" in the USA. It is recommended that a pregnancy test be done prior to taking this medication as it is contraindicated in pregnancy.

Dose: 30 mg as soon as possible after unprotected sex. Can be given up till 120 h.

Efficacy: Pregnancy rate of 0.9–1.4 %.

Side Effects: Headache (18–19 %); abdominal pain (8–15 %); Nausea (12–13 %); Suppressed menstruation (9 %); Dysmenorrhea (7–13 %).

Counseling About the Hormonal Contraception

- Adolescents do not need a pelvic exam to initiate birth control.
- In the sexually active adolescent, screen for STIs; Pap smears begin at age 21 years and should be recommended but are not a prerequisite for initiation of contraception.
- A careful history and blood pressure is sufficient to decide if hormonal contraception can be safely initiated and should help adolescents make an informed decision as to which method is best for them.
- Condom use should be reinforced.

Initial follow-up should be 6 weeks after initiation to check for side effects and proper use of the OCP. Subsequent follow-ups should be every 6 months.

Sources

Contraception for Adolescents: American Academy of Pediatrics Policy statement. www.pediatrics.org/cgi/doi/10.1542/peds.2014-2299. Accessed 7 Apr 2016.

U.S. Medical Eligibility Criteria for Contraceptive Use, 2010. Centers for Disease Control and Prevention (CDC). MMWR Recomm Rep. 2010; 59(RR-4):1–86. [PubMed] [Full Text]. http://www.cdc.gov/reproductivehealth/unintendedpregnancy/usmec.htm.

U.S. Selected Practice Recommendations for Contraceptive Use, 2013: adapted from the World Health Organization selected practice recommendations for contraceptive use. 2nd ed. Division of Reproductive Health, National Center for Chronic Disease Prevention and Health Promotion. MMWR Recomm Rep. 2013; 62:1–60. [PubMed] [Full Text].

Understanding and using the U.S. Medical Eligibility Criteria for Contraceptive Use, 2010. Committee Opinion No. 505. American College of Obstetricians and Gynecologists. Obstet Gynecol. 2011;118:754–60. [PubMed] [Obstetrics & Gynecology].

Adolescent Pregnancy

17

Rachel H. Alinsky and Mark A. Goldstein

Adolescent Sexual Activity

Adolescent sexual activity and its consequences are topics most providers will encounter. According to the 2013 CDC Youth Risk Behavior Surveillance survey, approximately half (47 %) of US high school students have had sexual intercourse. There has been only a gradual decline in this rate over the past two decades, down from 54 % in 1991. This is a relevant topic for even younger adolescents, as 5 % of students first had sexual intercourse before the age of 13. While predictors of early sexual intercourse include early pubertal development, history of sexual abuse, poverty, lack of attentive/nurturing parents, lack of school or career goals, substance abuse, and poor school performance, an adolescent of any racial, socioeconomic, or geographical background can be affected. Many students partake in risky sexual behaviors that contribute to unintended pregnancy and sexually transmitted infections, including having multiple partners (15 % of sexually active students report 4 or more partners) or drinking alcohol or using drugs at the time of intercourse (22 % of sexually active students).

M.A. Goldstein (ed.), *The MassGeneral Hospital for Children Adolescent Medicine Handbook*, DOI 10.1007/978-3-319-45778-9_17

Contraception

Many adolescents use contraception either inconsistency or chose less effective methods due to lack of sex education, suboptimal access, or worries about confidentiality or side effects. While 86 % of sexually active high school students report that they (or their partners) had used a method to prevent pregnancy the last time they had sex, only 59 % of students had used a condom. Even less common, 25 % had used a form of birth control such as oral contraceptive pills (19 %); shot, patch, or ring (4.7 %); or long-acting reversible contraceptives ("LARCs") including IUDs and implants (1.6 %). Merely 8 % of sexually active high school students had used both a condom AND birth control.

Adolescent Pregnancy Epidemiology

Given the high percentage of adolescent sexual activity and infrequent use of effective forms of birth control, adolescent pregnancy continues to be a topic of concern. There are approximately 600,000–700,000 teen pregnancies annually in the USA, of which 4 out of 5 are unintended. Rates of teen pregnancy peaked in 1990 at 116 per 1000 adolescents and declined to 57 pregnancies per 1000 adolescents as of 2010. This represents a 50 % decline in adolescent pregnancy over the last two decades, due to relative increases in contraceptive use and decreases in sexual activity. However, the United States continues to have the highest rates of teen pregnancy in the developed world. Factors associated with an increased risk of teen pregnancy include age of sexual debut, lack of contraception during first sexual experience, age difference between partners, greater number of sexual partners, and mental illness.

As the teen pregnancy rate has declined, so too has the birth rate. The teenage birth rate peaked in 1991 at 62 per 1000 adolescents and decreased to 24 per 1000 by 2014 (for a total of 249,000 births). Of teenage pregnancies, approximately 60 % result in live births, with 25 % ending in abortion and 15 % in miscarriage.

Consent and Confidentiality

Confidential adolescent reproductive health care begins long before a positive pregnancy test. All teenagers should have their first reproductive health visit between the ages of 11–15, including private conversations between the provider and teen. This respect for privacy is based on the notion that minors may not seek the medical care they need if it were not confidential.

Minors' rights to consent to STI testing and treatment are protected in all 50 states; the confidentiality of this testing (prohibiting physicians from informing a minor's parents) is protected in more than half of states. Similarly, all but four states (ND, OH, RI, WI) have laws explicitly permitting minors to consent to contraceptive services. Conversely, a minor's right to consent to prenatal care, adoption, abortion, and the confidentiality of such care varies greatly across the country and is under continuous flux. Physicians should refer to their state governments, local medical boards, and attorneys for up to date legal guidance. In order to maintain an optimal relationship, providers should uphold their adolescent patients' privacy to the extent the law allows (allowing for breaches when there is concern for self-harm, harm to others, or abuse), while encouraging the patient to involve her parents and the father of the baby.

Symptoms and Diagnosis

Although some adolescents may present to medical providers with the suspicion of being pregnant, providers must have a low threshold for considering and testing for pregnancy for a variety of other chief complaints. As many adolescents have irregular menses, amenorrhea or irregular menses may not alarm them. More commonly, the symptoms of pregnancy that bring adolescents to medical care are nonspecific constitutional or gastrointestinal concerns, though symptoms of pregnancy can pertain to virtually any body system (Table 17.1).

Table 17.1 Symptoms of pregnancy

	First trimester	Second trimester
Constitutional	Fatigue	Weight gain
	Dizziness	Generalized itching
	Weight gain or loss	Body aches and pains
	Malaise	
	Mood swings	
Neurological	Headache	Carpal tunnel
Gastrointestinal	Abdominal pain, discomfort	Abdominal bloating, enlargement
	Nausea +/− vomiting	Constipation
	Heartburn	
	Constipation	
	Craving or distaste for certain foods	
Skin	–	Stretch marks
		Patches of darker skin
Genitourinary/ gynecological	Amenorrhea	Amenorrhea
	Irregular menses	Vaginal discharge
	Tender, swollen breasts	
	Urinary frequency	

For adolescent patients presenting with the above symptoms, it is important to take a complete sexual and menstrual history, including recent sexual activity, partners, and contraceptive methods. This can be used as an opportunity to counsel sexually active teens regarding risk reduction and the importance of always using dual-protection methods (birth control plus a condom). Providers should always engage an adolescent in counseling prior to the test, including asking what she would do if the pregnancy test is positive.

Pregnancy testing can begin with a urine qualitative human chorionic gonadotropin (HCG), which may be positive within the first 7–10 days after conception. Positive tests can be followed with a serum quantitative HCG to ensure adolescents are not further along than their history would imply (using Naegele's rule to calculate the estimated date of delivery based on LMP). Occasional false-negative results can happen if pregnancy testing is performed too early into the pregnancy. If a provider has a high

Table 17.2 Signs of pregnancy

Timing of uterine findings	
6+ weeks	Uterine artery pulsation palpable in vaginal fornix
	Uterine size equivalent to a small juice orange
6–8 weeks	Softening of cervix (Goodell Sign) and Uterus (Hegar Sign)
8–12 weeks	Blue/purple discoloration of vulva, vagina, cervix due to vascular congestion of mucous membranes (Chadwick Sign)
	Uterine size equivalent to a large navel orange
10–12 weeks	Fetal heart activity detectable by handheld Doppler
12 weeks	Uterine fundus palpable abdominally above symphysis pubis
	Uterine size equivalent to a grapefruit
16 weeks	Uterine fundus palpable midway between symphysis pubis and umbilicus
	Uterine size equivalent to a cantaloupe
20 weeks	Uterine fundus palpable at umbilicus
	Auscultation of fetal heart activity
20+ weeks	Length in cm from uterine fundus to symphysis pubis correlates with week of gestation
Timing of other findings	
6+ weeks	Breast fullness, tenderness to palpation, darkening of areolae
12–24 weeks	Linea Nigra: hyperpigmented vertical line through umbilicus to symphysis pubis
24+ weeks	Striae on abdomen, legs, breasts

suspicion for pregnancy and urine HCG is negative, this can be repeated in 1 week or a serum quantitative HCG can be checked as this more sensitive test is likely to be positive within 7 days of conception.

At the time of diagnosis, the primary provider should perform a complete physical exam, including pelvic examination of the cervix, uterus, and adnexa to evaluate for signs of pregnancy (Table 17.2), date the pregnancy, and obtain screening for chlamydia and gonorrhea. Additionally, an ultrasound should be performed to confirm dating. Pregnancies are assumed to be intrauterine in the absence of ectopic pregnancy risk factors (prior ectopic pregnancy, tubal pathology or surgeries, IUD use, PID), adnexal tenderness or mass, or vaginal bleeding. If there is concern for extrauterine pregnancy, an urgent transvaginal ultrasound should be performed and serum HCGs trended.

Prenatal Care

The Affordable Care Act offers many protections and supports for pregnant women. Pregnancy care and childbirth are considered essential health benefits, thus all qualified health insurance plans must cover them. Women can find information about what is available in their state by contacting their local health departments, or work with social service. Social workers may also be valuable resources in helping adolescents navigate the financial, educational, psychosocial, and family implications of teen pregnancy. The adolescent should be encouraged to inform her partner and her parents of the pregnancy and be supported in this difficult yet important process. Ideally the adolescent should involve her partner and parents in ongoing visits; however, it is also crucial for the clinician to have a confidential patient contact phone number.

When pregnancy is diagnosed in an adolescent, all pregnancy options should be offered and discussed including parenting, adoption, and termination. Pregnant adolescents should be referred for obstetric/prenatal care by 10 weeks of pregnancy, or to an organization such as Planned Parenthood if termination is desired. Until the establishment of obstetric care, pregnant adolescents should be seen weekly by their primary physician to monitor and optimize their physical, mental, and emotional health.

All pregnant women, including teenagers, should immediately start taking a prenatal multivitamin with folic acid. Patients' medication lists, including over the counter medications and supplements, should be assessed for potential teratogens and women counseled accordingly. All chronic medical conditions should be reviewed and optimized in pregnant teenagers, as many health conditions can adversely affect pregnancy, including asthma, depression, diabetes, eating disorders, seizure disorders, hypertension, HIV, obesity, and thyroid disease.

Prenatal Counseling and Anticipatory Guidance

Physicians should be ready to engage in discussions with their pregnant adolescents about health habits and behavioral changes necessary for a healthy pregnancy. It is important to counsel

pregnant teens regarding smoking cessation, as smoking while pregnant significantly increases the risk of miscarriage, stillbirth, premature birth, and low birth weight. Similarly, teenagers should be given advice to abstain from alcohol and drugs, and offered substance use disorder resources as needed.

Adolescents should be encouraged to continue to exercise and stay physically fit. Physicians should counsel patients regarding appropriate weight gain and nutritional requirements including folate, iron, calcium, and fluid intake. Food safety should be discussed, including avoidance of raw meats, unpasteurized milks and soft cheeses, fish with high mercury content, and raw sprouts. Given the increase in circulating blood volume, pregnant women need to increase their fluid intake; up to ten cups of fluids daily is recommended.

Adolescents should be advised to minimize exposure to infections that may cause pregnancy complications or congenital infections. In particular, cleaning cat litter boxes should be avoided to decrease the risk of toxoplasmosis. If women are planning international travel, they should consult the CDC Travelers Health website to learn about relevant infectious risks. Adolescents who continue to be sexually active during pregnancy should use barrier methods to prevent the transmission of STIs.

Complications

Pregnant teenagers have higher rates of pregnancy complications compared to older women, such as miscarriage/fetal death, high blood pressure, premature birth, stillbirth, and low birth weight. Physicians should be aware of complications such as ectopic pregnancy, pelvic inflammatory disease, and ovarian torsion. Any adolescent presenting with vaginal bleeding and pain, either known to be pregnant or with a missed menstrual period, should have an urgent pelvic examination and ultrasound to evaluate for ectopic pregnancy or other obstetrical complication. Physicians should also advise adolescents of and carefully monitor for medical problems that may arise during pregnancy such as anemia, depression, hypertension, hyperemesis gravidarum, diabetes, venous thromboembolism, and infections (including bacterial vaginosis, cytomegalovirus,

group B strep, hepatitis B, influenza, listeriosis, parvovirus b19, sexually transmitted infections, toxoplasmosis, urinary tract infections, and yeast infections).

Mental Health and Intimate Partner Violence

Providers should engage all pregnant adolescents in conversations regarding mental health and physical safety. Pregnant adolescents have higher rates of depression, suicidal ideation, and suicide completion; thus all patients should be screened for depression with appropriate treatment if screening is positive. Psychiatric referral may be helpful in weighing the relative risks and benefits of psychoactive medications during pregnancy for individual patients. Additionally, the risk of intimate partner violence is higher in pregnant adolescents compared to both their nonpregnant peers as well as pregnant adults. Specific risks pregnant adolescents may face include being forced by a partner to either continue or terminate a pregnancy against her wishes, threats or actualized injuries that may cause miscarriage, and even homicide. Providers should screen all patients for the various forms of intimate partner violence and offer appropriate resources and referrals. Physicians should refer to state laws regarding mandated reporting. See Chap. 26 for more information on relationship violence.

Follow-Up

Throughout an adolescent's pregnancy, her primary physician should remain in contact. Postpartum follow-up care should be arranged, as this time period can be associated with complications such as postpartum depression, thyroid disease, and difficulty losing pregnancy weight. Effective contraceptive methods should be discussed, as one fifth of teen mothers go on to have repeat births during adolescence. The socioeconomic impact of teen pregnancy is significant for not only the adolescent mother but the father and child as well. Adolescent mothers are less likely to graduate from high school and attend college, and more likely to live in poverty.

Teen fathers have lower rates of education, and higher rates of unemployment. The children are at higher risk of cognitive disorders, chronic health problems, incarceration, and becoming a teenage parent themselves.

Sources

American College of Obstetricians and Gynecologists. ACOG Committee opinion no. 554: reproductive and sexual coercion. Obstet Gynecol. 2013;121(2 Pt1):411–5.

Bastian LA, Piscitelli JT. Is this patient pregnant? Can you reliably rule in or rule out early pregnancy by clinical examination? JAMA. 1997;278(7):586–91.

Crochet JR, Bastian LA, Chireau MV. Does this woman have an ectopic pregnancy? The rational clinical examination systematic review. JAMA. 2013;3099:1722.

Guttmacher Institute. An overview of minors' consent law. State Policies in Brief, Feb 1, 2016. https://www.guttmacher.org/statecenter/spibs/spib_OMCL.pdf. Accessed 3 Feb 2016.

Hamilton BE, Martin JA, Osterman MJ, Curtin SC, Matthews TJ. Births: final data for 2014. Natl Vital Stat Rep. 2015;64(12):1–64.

Health coverage if you're pregnant or plan to get pregnant. U.S. Centers for Medicare & Medicaid Services, Healthcare.gov Web site. https://www.healthcare.gov/what-if-im-pregnant-or-plan-to-get-pregnant/. Archived 3 Feb 2016. Accessed 3 Feb 2016.

Kann L, Kinchen S, Shanklin SL et al. Centers for Disease Control and Prevention (CDC). Youth risk behavior surveillance—United States, 2013. MMWR Surveill Summ. 2014;63 Suppl 4:1–168. Erratum in: MMWR Morb Wkly Rep. 2014;63(26):576.

Kost K, Henshaw S. U.S. teenage pregnancies, births and abortions, 2010: national trends by age, race and ethnicity. Guttmacher Institute. 2014. http://www.guttmacher.org/pubs/USTPtrends10.pdf.

Lenders CM, McElrath TF, Scholl TO. Nutrition in adolescent pregnancy. Curr Opin Pediatr. 2000;12:291.

Lindahl V, Pearson JL, Colpe L. Prevalence of suicidality during pregnancy and the postpartum. Arch Womens Ment Health. 2005;8:77.

Pregnancy. Office on Women's Health, U.S. Department of Health and Human Services Web site. http://womenshealth.gov/pregnancy/index.html. Updated 27 Sep 2010. Accessed 3 Feb 2016.

Reproductive Health. Centers for Disease Control and Prevention Web site. http://www.cdc.gov/reproductivehealth/. Updated 3 Feb 2016. Accessed 3 Feb 2016.

Reproductive Health: Teen Pregnancy. Centers for Disease Control and Prevention Web site. http://www.cdc.gov/teenpregnancy/. Updated 11 Dec 2015. Accessed 3 Feb 2016.

Sedgh G, Finer LB, Bankole A, et al. Adolescent pregnancy, birth, and abortion rates across countries: levels and recent trends. J Adolesc Health. 2015;56(2):223–30.

Polycystic Ovary Syndrome

18

Jennifer Rosenblum and Laya Ekhlaspour

Background

Polycystic ovary syndrome (PCOS) is a spectrum of disease that is characterized by menstrual irregularity due to ovulatory dysfunction and hyperandrogenism. Presenting signs and symptoms are heterogeneous and may vary over time. It is associated with an increased risk of obesity, the metabolic syndrome, endometrial carcinoma, as well as infertility. The diagnosis of PCOS should be considered in any adolescent girl with hirsutism, severe acne, menstrual irregularity, or obesity.

Clinical Presentation

1. Hirsutism: Excessive terminal hair that usually appears in male pattern (in androgen-sensitive areas). Hirsutism can be graded by the semiquantitative Ferriman–Gallwey (FG) score, which assigns a score from 0 (no hair) to 4 (frankly virile) to nine body areas, the sum of which provides a hirsutism score. The cutoff value for abnormal score varies by ethnicity. Hirsutism is defined by FG score above the 95th percentile for the population, which is >8 in premenopausal adult white and black women, ≥9–10 in Mediterranean, Hispanic, and Middle Eastern

M.A. Goldstein (ed.), *The MassGeneral Hospital for Children Adolescent Medicine Handbook*, DOI 10.1007/978-3-319-45778-9_18

women, ≥ 2 for Han Chinese women, and ≥5 in Southern Chinese women. For more information on hirsutism as well as a visual of the FG scoring system, please visit http://www.hirsutism.com/hirsutism-biology/ferriman-gallwey-score.shtml.
2. Acne: Acne vulgaris should be considered as clinical evidence for hyperandrogenism if acne is persistent and poorly responsive to topical treatments.
3. Oligo-Anovulation: Average menstrual cycles shorter than 20 days or greater than 45 days in adolescents who are 2 or more years post-menarche suggest abnormal anovulation.
4. Metabolic manifestations: These are primarily mediated through insulin resistance and may be suggested by acanthosis nigricans on exam. They include obesity, the metabolic syndrome, sleep disordered breathing, and nonalcoholic fatty liver disease.

Definition

Stein and Leventhal originally described PCOS in 1935 in women with amenorrhea, hirsutism, obesity, and a characteristic polycystic appearance to their ovaries. There are no formal criteria established for adolescents with PCOS, who face unique challenges in diagnosis due to the normal occurrence of anovulation in the first 2 years after menarche, the difficulty of distinguishing between polycystic ovaries and the normal appearance of multifollicular ovaries in adolescence, and the lower detection of polycystic ovaries by transabdominal ultrasound compared to transvaginal ultrasound which is inappropriate to use in virginal adolescents. In adults, three sets of diagnostic criteria exist (see Table 18.1):

1. NIH (1990)—must have all three of the following:
   (a) Menstrual irregularity due to anovulation or oligo-ovulation
   (b) Hyperandrogenism, either clinical (hirsutism, severe acne, male pattern balding) or biochemical evidence (elevated serum androgens)

Table 18.1 Diagnostic criteria for PCOS

	Clinical or biochemical hyperandrogenism	Oligomenorrhea/ chronic anovulation	Polycystic ovaries
NIH,1990	Yes	Yes	No
Rotterdam, 2003	Yes	Yes	Yes
Rotterdam, 2012	Yes	Yes (present for at least 2 years)	Yes
Endocrine Society Clinical Practice Guidelines, 2013	Yes	Yes	Not in adolescents

(c) Exclusion of other causes of the above: congenital adrenal hyperplasia, androgen-secreting tumors, hyperprolactinemia, Cushing's syndrome, acromegaly, hypothyroidism, and drugs

2. Rotterdam (2003)—must have 2 out of 3 of the following:
   (a) Oligomenorrhea or amenorrhea
   (b) Unexplained hyperandrogenism, either clinical or biochemical evidence
   (c) Polycystic ovaries on ultrasonography

   The revised consensus in 2012 suggested that oligomenorrhea or amenorrhea should be present for at least 2 years after menarche.
3. The Endocrine Society Clinical Practice Guidelines (2013)
   (a) Clinical and/or biochemical evidence of hyperandrogenism
   (b) Persistent oligomenorrhea

Phenotypes here based on these criteria:

1. Phenotype 1 ("classic PCOS")
   (a) Clinical and/or biochemical evidence of hyperandrogenism
   (b) Evidence of oligo-anovulation
   (c) Ultrasonographic evidence of a polycystic ovary
2. Phenotype 2 (essential National Institutes of Health Criteria)
   (a) Clinical and/or biochemical evidence of hyperandrogenism
   (b) Evidence of oligo-anovulation

3. Phenotype 3 (“ovulatory PCOS”)
   (a) Clinical and/or biochemical evidence of hyperandrogenism
   (b) Ultrasonographic evidence of a polycystic ovary
4. Phenotype 4 (nonhyperandrogenic PCOS)
   (a) Evidence of oligo-anovulation
   (b) Ultrasonographic evidence of a polycystic ovary

To summarize, diagnostic criteria for PCOS in adolescents should include:

1. Abnormal uterine bleeding pattern
   (a) No menarche by age 15 years or by more than 2–3 years after thelarche
   (b) A menstrual cycle greater than 90 days even in the first year after menarche
   (c) Average menstrual cycles shorter than 20 days or greater than 45 days in post-menarche year 2 or more

   AND
2. Evidence of hyperandrogenism
   (a) Persistent testosterone elevation above adult norms in a reliable reference laboratory is the best evidence
   (b) Moderate–severe hirsutism is clinical evidence of hyperandrogenism
   (c) Moderate–severe inflammatory acne vulgaris is an indication to test for hyperandrogenemia

In addition, other etiologies of hyperandrogenism and anovulation should be excluded. These include virilizing tumors, late onset congenital adrenal hyperplasia, acromegaly, Cushing Syndrome, thyroid dysfunction, and hyperprolactinemia.

Etiology

PCOS is a result of excess ovarian androgens, although there is debate as to whether this is due to a primary steroidogenesis disorder in the ovaries (functional ovarian hyperandrogenism) and/or adrenals (functional adrenal hyperandrogenism), or secondary to

excessive LH secretion from the pituitary gland which causes the ovary to secrete androgens. The most recent studies suggest that PCOS is primarily caused by an intraovarian disorder of the regulation of steroidogenesis, often associated with functional adrenal hyperandrogenism. In addition, there is evidence that tissue-selective insulin-resistant hyperinsulinism may play a role in the steroidogenic dysregulation of PCOS. The development of PCOS likely involves a complex interaction between genetic traits and environmental factors (both intrauterine and postnatal).

Evaluation

1. Serum androgens: total testosterone, sex hormone binding globulin (SHBG), free testosterone, and DHEAS
2. Rule out other causes of hyperandrogenemia and irregular menses: early morning 17-OHP, TSH, FSH, and prolactin. A pelvic ultrasound should be obtained if there are clinical signs of a virilizing tumor such as clitoromegaly, pelvic mass, DHEAS >700 μg/dL, or total testosterone >200 ng/dL. Obtain IGF-1 if clinical signs of acromegaly. If clinical signs of Cushing's syndrome, evaluate further with 24-h urine cortisol, late-night salivary cortisol, or low-dose dexamethasone suppression test.
3. Assessment for associated conditions and risks: fasting lipid profile, HbA1C, fasting insulin, and 2-h oral glucose tolerance test (suggest repeating this every 2–3 years), ALT and AST (to screen for nonalcoholic steatohepatitis)

Treatment

1. Lifestyle modification

   Lifestyle modification including dietary intervention and exercise may improve hyperandrogenism and ovarian function, in addition to obesity and other comorbidities associated with PCOS.
2. Combined hormonal contraception is the first-line treatment to regulate menses and thus prevent endometrial hyperplasia, as

well as to improve hirsutism and acne. Hormonal replacement decreases ovarian androgen production via inhibiting pituitary gonadotropin secretion and decreases free testosterone concentration by increasing SHBG. Oral contraceptive pills (OCPs) are associated with an increased risk of venous thromboembolism (particularly in individuals with a Factor V Leiden deficiency/mutation). OCPs may have an effect on insulin sensitivity, glucose tolerance, and lipid metabolism. It is recommended to use an OCP that contains a progesterone with antiandrogenic (drospirenone—in Yaz™ or Yasmin™) or minimal androgenic activity (norgestimate—in Ortho-tri-Cyclen™ or Orthocyclen™, ethynodiol diacetate—in Demulen™ or Zovia™, and desogestrel—in Orthocept™, Apri™). Cyproterone acetate is a progestin with antiandrogenic activity that is available in Canada, Mexico, and Europe (Diane™) but is not available in the USA. Of note, there is an increased risk of thromboembolism with third and fourth generation progestins such as desogestrel, norgestimate, and drospirenone. OCPs should be used until the patient is 5 years postmenarchal or has lost a substantial amount of excess weight.

3. Progestins alone may be used cyclically to regulate menses, but this will not improve clinical symptoms of hyperandrogenism. Progesterone-only OCP is a good choice when there are contraindications to using estrogen-containing OCPs. Micronized progesterone (Prometrium™ 100–200 mg qhs) or medroxyprogesterone acetate (Provera™ 10 mg qhs) may be given for 7–10 days every 2–3 months.
4. Insulin-lowering agents may help to improve ovulation as well as reduce androgen levels, although are not as effective as OCPs in controlling menstrual irregularity and hirsutism. Metformin may be used as an adjunct to weight-loss efforts and should be considered in adolescents with PCOS who have obesity, hyperinsulinemia, or glucose intolerance. It increases the frequency of menses and ovulation by ~50 % and lowers testosterone by ~20 %. Usually one should start at 500 mg qpm with dinner and increase by 500 mg per week as tolerated to maximum dose of 2000 mg daily or divided bid. The most common side effect is gastrointestinal discomfort (diarrhea, nausea, or vomiting). Thiazolidinediones should not be used in adolescents

with PCOS given concerns of weight gain and rare hepatic toxicity (it is not approved in the pediatric population).

5. Antiandrogen therapy may be added to OCP therapy for the treatment of hirsutism. When given alone, it may cause menstrual irregularities as well as teratogenic feminization of the male fetus. Spironolactone (50–100 mg bid) is the recommended choice as it is the safest and most potent antiandrogen in the USA. However, it does not improve metabolic abnormalities.
6. Glucocorticoid therapy may be used to regulate menses when adrenal androgens are markedly elevated, but this does not result in consistent ovulation. There is controversy about the efficacy and safety of this treatment for PCOS. It does not appear to improve hirsutism or acne.
7. GnRH agonists (depot leuprolide—Lupron™) may be used to regulate menses in patients who do not tolerate OCPs and in whom progestins do not suffice. It should not be used in girls < age 16 due to concerns about bone mineral accrual.
8. Cosmetic treatments may be used for hirsutism. Inexpensive options include shaving, chemical depilatory agents, bleaching, and waxing. More expensive options include eflornithine hydrochloride cream (Vaniqa™), laser therapy, and electrolysis.

Sources

Barbieri RL, Ehrmann DA. Diagnosis of polycystic ovary syndrome in adults. www.uptodate.com.

Ehrmann DA. Polycystic ovary syndrome. N Engl J Med. 2005;352:1223–36.

Hecht Baldauff N, Arslanian S. Optimal management of polycystic ovary syndrome in adolescence. Arch Dis Child. 2015;100(11):1076–83.

Nestler JE. Metformin for the treatment of polycystic ovary syndrome. N Engl J Med. 2008;358:47–54.

Rosenfield RL. The diagnosis of polycystic ovary syndrome in adolescents. Pediatrics. 2015;136:1154–65.

Rosenfield RL. Treatment of polycystic ovary syndrome in adolescents. www.uptodate.com.

Rosenfield RL. Definition, clinical features and differential diagnosis of polycystic ovary syndrome in adolescents. www.uptodate.com.

Witchel SF, Oberfield S, Rosenfield RL, et al. The diagnosis of polycystic ovary syndrome during adolescence. Horm Res Paediatr. 2015;83:376–89.

Breast Disorders in Adolescence

19

Philicia Moonsamy
and Cassandra M. Kelleher

The Breast Exam

A brief description of the breast exam should be given to ensure patient comfort, either before or during the exam itself. The patient is first positioned sitting upright with her hands resting on her thighs with her shoulders and arms relaxed. Begin with general inspection for abnormalities such as asymmetry, skin changes including color, dimpling and scars, obvious masses and nipple abnormalities including inversion, discharge, or the presence of accessory nipples. Inspection should then be repeated after the patient is asked to raise her hands above her head. Next, each breast is palpated individually with the patient in the supine position and the ipsilateral arm raised above the patient's head with the elbow flexed. There are numerous techniques for palpation including the vertical strip method, the concentric circle method, or the spokes on a wheel method, all of which aim to systematically examine the breast without missing any areas of breast tissue. This can be challenging due to the predominance of glandular tissue in this age group. It is important to remember to palpate under the nipple and examine the axillary Tail of Spence. The patient should then be

M.A. Goldstein (ed.), *The MassGeneral Hospital for Children Adolescent Medicine Handbook*, DOI 10.1007/978-3-319-45778-9_19

palpated for axillary or supraclavicular lymphadenopathy. While examining the axilla, the weight of the ipisilateral arm should be fully supported by the examiner. Finally, the areola is compressed to assess for nipple discharge.

Self-Exam

The American College of Obstetricians and Gynecologists recommends against self-examination in low-risk patients aged 13–18 for the purpose of breast cancer screening. The United States Preventive Services Task Force (USPSTF) also recommends against teaching breast self-examination in all age groups. Given the extremely low incidence of breast cancer in adolescents and that performing regular self-examination has not been shown to decrease rates of breast cancer diagnosis and death, we recommend against advocating for breast self-examination in this age group. Unlike adults, the majority of breast lesions in adolescents are benign. Breast masses in this patient population cause significant distress to both the patient and their parents and therefore clear communication and reassurance is critical.

History

A complete gynecologic history should be obtained including age at onset of menstrual cycle and pregnancy history. The physician should inquire about when the mass was first discovered, changes in the size and texture over time, and its association with the menstrual cycle. Associated symptoms such as pain, skin changes, and nipple discharge should be elucidated. History of radiation, malignancy, previous breast masses, and family history of gynecologic cancer are also important.

Physical Exam

Physical exam should be performed as outlined at the beginning of this chapter. The size and location of palpable masses should be documented and monitored over time.

Imaging

Ultrasound is the first imaging study of choice and has two distinct advantages over mammography: (1) no ionizing radiation and (2) superior sensitivity in distinguishing lesions from the dense glandular tissue in the adolescent breast. Mammography should not be used to evaluate breast masses in adolescents. Seventy five percent of palpable masses went unidentified by mammography in women under 30 in one study because the fibroglandular tissue in the adolescent breast is radio-opaque and interferes with the identification of lesions with this modality. Magnetic resonance imaging (MRI) may be valuable in evaluating chest wall lesions or vascular malformations. The American Cancer Society recommends annual screening breast MRI for young women carrying the BRCA1/2 mutation beginning at age 25–30 years, or at the age of the youngest family member diagnosed with breast cancer. For adolescents with a history of chest radiation, yearly breast MRI should begin 8–10 years after thoracic radiation or between the ages of 25 and 30 years. Computed tomography (CT) has no role in evaluating the adolescent breast.

Benign Lesions

Benign lesions of the adolescent breast can be characterized as cystic, solid, inflammatory, and traumatic. The following sections outline the most common benign breast lesions in the adolescent population.

Fibrocystic Change

The exact etiology of fibrocystic change is unknown; however, it is thought to be a result of monthly fluctuations of estrogen and progesterone. Patients complain of painfully enlarged breast tissue 1 week before the onset of menses and report that their pain resolves during menstruation. This cycle repeats monthly with the menstrual cycle. On exam they have palpable cord-like thickenings and palpable nodules that are usually found in the upper outer quadrants of the breast and are not mobile from the underlying breast tissue (unlike fibroadenomas or cysts). The diagnosis is made with a thorough history and physical exam alone and further imaging is not indicated. It is helpful to ask the patient to keep a diary of their symptoms to be reviewed at a follow-up visit that can be used to temporally relate their symptoms to their menstrual cycle.

Treatment is focused on relieving mastalgia. Some physicians advocate for wearing a sports bra or supportive underwire bra. Ibuprofen is effective in treating pain and is safe for use in adolescents. If conservative treatment does not improve mastalgia, a low dose daily oral contraceptive such as 20mcg of ethinyl estradiol can be prescribed and has been shown to treat symptoms in 70–90 % of women. Finally, some studies suggest that caffeine worsens the symptoms thus leading physicians to traditionally recommend eliminating caffeine intake. However, more recent controlled studies have failed to demonstrate an association. Research investigating the efficacy of primrose oil and vitamin E in relieving mastalgia is inconclusive.

Cysts

These are most common in middle-aged women but can occur in adolescents. They are usually single, palpable, and can be painful if they have become infected. On ultrasound, a simple cyst has an anechoic structure with posterior acoustic enhancement and is avascular on Doppler. Simple cysts are benign and treatment is conservative with no further imaging or intervention. Occasionally they may require treatment with antibiotics or drainage if they become infected.

Inflammatory

Although breast abscesses are most common in lactating women, they can occur in adolescents. Predisposing factors in nonlactating adolescents include trauma, shaving or hair plucking, nipple piercing, obesity, underlying cysts, and ductal ectasia. Patients present with an erythematous, warm, fluctuant, tender mass. The most common pathogen is *Staphylococcus aureus* (32%), followed by *Streptococcus*, *Enterococcus*, *and S. pyogenes* (group A streptococcus). Treatment includes incision and drainage of the abscess with or without ultrasound guidance and culture of the fluid to inform appropriate antibiotic treatment. The patient should also be treated with 7–10 days of oral antibiotics such as clindamycin or trimethoprim-sulfamethoxazole in areas of increased MRSA incidence. The total duration of antibiotic treatment should be based on clinical response. Recurrent infections despite treatment may indicate underlying pathology such as a hemangioma or lymphangioma.

Traumatic

Trauma to the breast can result in a hematoma. A clear history of trauma and thorough physical exam for bruising makes the diagnosis. Treatment includes pain medications, ice packs for comfort, and a sports bra or elastic wrapping to tamponade the breast. Hematomas usually resolve over weeks to months but can result in fat necrosis. Fat necrosis can be mistaken for malignancy since it presents as a solid mass containing calcifications. Ultrasound characteristics of fat necrosis are varied. Surgical excision may be therapeutic for painful chronic areas of fat necrosis.

Fibroadenoma

The fibroadenoma is the most common benign breast tumor in female adolescents and accounts for over half of all breast masses. They are extremely rare in males because they arise from the proliferation of the connective tissue stroma surrounding breast lobules. The overall incidence in female adolescents is 2.2%. These usually present as a

single, slowly growing, painless mass with the mean age of diagnosis at 15–17 years. They are estrogen sensitive and can vary in size during the menstrual cycle. On physical exam the mass is rubbery, often nontender, well circumscribed, and freely mobile. They most often occur in the upper outer quadrant of the breast. Characteristic ultrasound findings are a well circumscribed, round, or oval homogenous hypoechoic mass that is hypovascular on Doppler.

Although these lesions rarely have malignant transformation in adults, they are not regarded as premalignant in the adolescent population. Therefore, patients with the typical history, physical exam, and sonographic findings can be followed with serial breast exams and ultrasound alone. If the patient desires a tissue diagnosis, a core-needle biopsy can be pursued since an open biopsy can result in a permanent deformity in the developing breast. Surgery is reserved for symptomatic fibroadenomas that cause breast pain or disfigurement. If the patient desires surgical removal because the diagnosis causes significant anxiety, it is advisable to observe for a few months before an excision is pursued since as many as 40–50 % will regress spontaneously. Fibroadenomas that are less than 3 cm can be removed with minimally invasive techniques such as vacuum-assisted percutaneous biopsy and cryotherapy. Endoscopic removal has also been described and prevents any scars on the breast. However, a small circumareolar incision with open excision is still the most frequent method of excision.

Giant Fibroadenoma

Also called juvenile fibroadenomas, these are classified as greater than 5 cm in diameter and are more common in African-Americans. They grow rapidly and distort the normal breast tissue. Giant fibroadenomas should always be removed surgically because they cannot be reliably distinguished from phyllodes tumors on exam or imaging.

Phyllodes Tumor

The phyllodes tumor is a primary tumor of the breast that is usually benign but has malignant potential. They are very rare; however, they are the most common primary breast malignancy in adolescents when

they are malignant. They were previously termed cystosarcoma phyllodes due to their cystic appearance and sarcoma-like characteristics including their propensity for hematogenous rather than lymphatic spread. Hence, they most commonly spread to the lung rather than the axillary lymph nodes. They initially present as a large (8–10 cm) painless, firm, mobile mass that stretches the overlying skin and making it shiny and taut. Patients may also have distended veins, erythema, ulcers, and nipple discharge on exam.

On ultrasound, the tumor has smooth, lobulated borders, appears hypoechoic, or heterogenous with posterior acoustic enhancement and without microcalcifications. A biopsy should be performed for diagnosis and a complete surgical excision with wide margins is indicated even for benign lesions. Positive margins can lead to local recurrence. Phyllodes tumors are histologically categorized into low, intermediate, and high grade and lower grade tumors are associated with lower rates of recurrence. Recurrence rates are lower in adolescents than in adults.

Malignant Lesions

Malignant lesions of the breast are extremely uncommon in adolescents. Metastatic disease is in fact more common than primary breast malignancy and is associated with advanced systemic disease. Rhabdomyosarcoma is the most common tumor known to metastasize to the breast in adolescence. Other tumors include hepatocellular carcinoma, neuroblastoma, lymphoma, leukemia, melanoma, and renal cell carcinoma. Ewing's sarcoma or rhabdomyosarcoma of the chest wall can also rarely involve the breast via contiguous growth or local metastasis.

The incidence of primary breast carcinoma in patients aged 15–19 is only 0.2 per 100,000 and is virtually zero in patients 14 years and younger. Risk factors specific to adolescents include previous radiation exposure to the chest (e.g. for the treatment of lymphoma) and a previous history of cancer. Although females carrying the BRCA1/2 mutation have an increased risk of developing cancer, there are currently no documented cases of BRCA-associated breast cancer in patients under 18 years of age. Patients present with a hard irregularly shaped mass that is fixed to the chest

wall. On physical exam, there may be overlying skin changes (peau d'orange), axillary or supraclavicular lymphadenopathy and nipple retraction or discharge. Ultrasound is indicated for diagnosis. Patients who are diagnosed with a breast malignancy should be referred to a multidisciplinary team of medical, radiation, and surgical oncologists for treatment.

Accessory Breast Tissue

Accessory breast tissue may contain some or all the components of the normal breast, including glandular tissue, areola, and nipple. Most patients have one small unilateral areola and nipple. When glandular breast tissue is present, it is referred to as polymastia. One percent of the general population has accessory breast tissue at birth, and there is no gender predominance. It often goes unrecognized until puberty when hormonal changes can result in increased pigmentation or tenderness.

Physical exam: Supernumerary nipples are usually unilateral and are found along the mammary lines in 95 %. The mammary lines extend from the axilla to the groin bilaterally. The most common site for a supernumerary nipple is just inferior to the normal breast. The most common site for polymastia is the lower axilla.

Treatment: Accessory breast tissue is considered to be a benign congenital anomaly of no clinical significance. Surgical removal is based on patient preference and can be indicated for cosmetically undesirable or symptomatic accessory breast tissue. There are rare case reports of patients who develop breast cancer in accessory breasts. However, ectopic breast tissue does not have an increased malignant potential compared with normal breast tissue.

Gynecomastia

Gynecomastia is defined as the excessive growth of glandular breast tissue in males. It is caused by an increase in the estrogen:androgen ratio. Physiologic pubertal gynecomastia is attributed to a delay in the maturation of androgen synthesis that leads to a period of unbalanced estrogen. Up to 60 % of boys will develop some degree

of physiologic breast enlargement during adolescence, with a peak incidence at 13–14 years. Most cases are self-limited and resolve within 2 years.

A common cause of gynecomastia is an increase in aromatization of androstenedione to estrone due to excess body fat in obese patients. Pathologic causes of gynecomastia can be divided into those that cause an increase in estrogen or a decrease in androgen, with the former being more common (see Table 19.1).

History: A detailed history alone can often lead to the underlying cause. Gynecomastia that progresses rapidly is more ominous, since physiologic gynecomastia is usually a slow process that progresses over years. Pain is a common presenting symptom of true physiologic gynecomastia but uncommonly associated with fatty pseudogynecomastia that is caused by excess adipose (not breast) tissue in the chest area. Patients with a history of milky nipple discharge should be

Table 19.1 Causes of gynecomastia

Increased estrogen	Increased aromatase activity
	Obesity
	Familial gynecomastia (autosomal dominant transmission of increased aromatase activity)
	Neoplasia
	Estrogen-secreting testicular tumor (tumor of the germ, Sertoli, or Leydig cell)
	Gonadotropin-secreting tumor (hepatoblastoma, fibrolamellar carcinoma)
	Adrenal tumor
	Congenital adrenal hyperplasia
	Hyperthyroidism
	Cirrhosis
	Exogenous estrogen
Decreased androgen	Primary hypogonadism
	Klinefelter syndrome
	Kallman syndrome
	Secondary hypogonadism
	Craniopharyngioma resection
	Prolactinoma/hyperprolactinemia
	Viral orchitis
	Defect in androgen biosynthesis
	Androgen insensitivity

worked up for causes of increased prolactin secretion. Patients who previously underwent testicular surgery may have developed gynecomastia as a result of primary testicular dysfunction.

The presence of gynecomastia before 9 years of age suggests an underlying malignancy until proven otherwise. Boys that present with isolated gynecomastia and have begun puberty within the normal age range of 9–14 years most likely have physiologic gynecomastia and can be observed. Patients who present with gynecomastia in the setting of late pubertal onset (after age 14) should be worked up for abnormalities in testosterone biosynthesis or gonadal dysfunction. Illicit drug use should be considered in all patients who present with gynecomastia after puberty. Many of these patients may also have a history of behavioral issues. All medications must be reviewed, since gynecomastia is a potential side effect of numerous drugs (See Table 19.2). Anabolic steroid use should be strongly considered in all male athletes.

Physical exam: The breast exam should be carried out in the same manner as previously described at the beginning of this chapter. Patients with physiologic pubertal gynecomastia should have breast tissue measuring less than 4 cm bilaterally. Examination of the male external genitalia is also important for pubertal staging. Both testes should be examined for masses and transilluminated. Small, firm undeveloped testes can be indicative of primary gonadal dysfunction (Klinefelter syndrome). A thorough overall physical exam can reveal important findings that are indicative of underlying disease processes (See Table 19.3).

Laboratory evaluation: Patients who have physical exam or history findings suggestive of underlying disease should be referred to an endocrinologist for workup. Hepatic and thyroid function studies should be obtained if indicated by the history and physical exam. Patients who appear to have hormonal abnormalities should undergo an initial 8 AM screening panel of luteinizing hormone (LH), follicle-stimulating hormone (FSH), testosterone, estradiol, beta-HCG, dehydroepiandrosterone (DHEA). Evaluation of the testosterone–estrogen imbalance in physiologic pubertal gynecomastia requires a 24-h screen and is usually unnecessary.

Imaging: Imaging studies are generally not indicated in the workup of gynecomastia. Ultrasound and fine needle biopsy may be required to rule out malignancy if a patient presents with hard

Table 19.2 Drugs associated with gynecomastia

Drugs: licit and illicit	Alcohol
	Marijuana
	Heroin
	Amphetamines
Hormones	Anabolic steroids
	Growth hormone
	Estrogen
	Human chorionic gonadotropin
Anti-infectives	Antituberculosis: Isoniazid, Ethionamide, Thiacetazone
	Antibacterials: Metronidazole
	Antivirals: HAART
	Antifungals: Ketoconazole
Cardiovascular	Diuretics: Furosemide, Spironolactone
	Calcium channel blockers: Nifedipine, Verapamil, Reserpine
	Angiotensin-converting enzyme inhibitors
	Amiodarone
Psychiatric	Risperidone
	Selective serotonin reuptake inhibitors
	Phenytoin
	Tricyclic antidepressants
	Clonidine
	Diazepam
	Phenothiazines
	Methadone
Chemotherapy	Methotrexate
	Alkylating agents
	Cyclophosphamide
	Vincristine
	Cisplatin
Other	Finasteride
	Histamine blockers: Cimetidine, Ranitidine
	Proton pump inhibitors: Omeprazole

Table 19.3 Physical findings in underlying disease associated with gynecomastia

Physical exam finding	Underlying pathology
Visual field defect or abnormal neurologic exam	Pituitary tumor or CNS disease
Enlarged liver or abnormal liver contour	Liver disease or hepatocellular carcinoma
Eunuchoid body habitus	Klinefelter syndrome

lymph nodes, skin dimpling, or bloody discharge. However, this is exceedingly rare in the adolescent population.

Treatment: Since most cases of gynecomastia during puberty are physiologic, close clinical follow up alone is usually appropriate. Up to 10 % of adolescent boys presenting with physiologic gynecomastia will have persistent symptoms into adulthood without underlying pathology or laboratory values. While gynecomastia may be clinically benign, it has been linked to negative social and psychological consequences including depression, anxiety, decreased self-esteem, and body dissatisfaction. There is no current consensus on the correct timing of elective mastectomy for these patients and this should be managed on a case-by-case basis. In the case of pathologic gynecomastia, treatment should focus on the underlying disease.

Sources

Bizzarri C, Bottaro G. Endocrine implications of neurofibromatosis 1 in childhood. Horm Res Paediatr. 2015;83:232–41.

Carel JC, Léger J. Clinical practice. Precocious puberty. N Engl J Med. 2008;358:2366–77.

Diamantopoulos S, Bao Y. Gynecomastia and premature thelarche: a guide for practitioners. Pediatr Rev. 2007;28:e57–68.

Gao Y, Saksena MA, Brachtel EF, terMeulen DC, Rafferty EA. How to approach breast lesions in children and adolescents. Eur J Radiol. 2015;84:1350–64.

Greydanus DR, Matytsina L, Gains M. Breast disorders in children and adolescents. Prim Care. 2006;33:455.

Lee N, Soltanian HT. Breast fibroadenomas in adolescents: current perspectives. Adolesc Health Med Ther. 2015;6:159–63.

Siu AL, U.S. Preventive Services Task Force. Screening for breast cancer: U.S. Preventive Task Force recommendation statement. Ann Intern Med. 2016;164:279–96.

Williams SM, Kaplan PA, Petersen JC, Lieberman RP. Mammography in women under age 30: is there a clinical benefit? Radiology. 1986;161:49–51.

Sexually Transmitted Infections (STI) in Adolescents

20

Anne M. Neilan

General Information

There are five major principles for prevention of STI:

1. Education and counseling of patients at risk for STI
2. Identification of asymptomatic patients with STI who are unlikely to seek treatment
3. Effective diagnosis and treatment of STI
4. Effective diagnosis and treatment of partners of patients with STI
5. Identification and immunization of patients at risk for vaccine preventable STI.

In all states, adolescents can consent to the confidential diagnosis and treatment of STI. In the majority of states, adolescents can consent to HIV counseling and testing.

The Guttmacher Institute tracks and analyzes federal and state policies regarding education on HIV and other STI and access to treatment for minors and other underserved groups. For updated information see: www.guttmacher.org.

The rates of STI are highest among adolescents compared to other age populations. Younger adolescents (<15 years) who are in detention facilities, injecting-drug users, a history of being in foster care,

M.A. Goldstein (ed.), *The MassGeneral Hospital for Children Adolescent Medicine Handbook*, DOI 10.1007/978-3-319-45778-9_20

those attending STI clinics, or males having sex with males are at an even higher risk for STI. Survey data from NHANES (National Health and Nutrition Examination Survey) indicate that more than 1 in 4 females between ages 14 and 19 years have laboratory evidence of an STI including HPV, Herpes type 2, Chlamydia, or Trichomoniasis.

Adolescents' Unique Susceptibility to STI

Biological Factors

Increased cervical ectopy, decreased cervical mucous, possible lower levels of secretory IgA, larger cervical transformation zone, increased trauma during intercourse, presence of other STI, douching, coitus during menses

Behavioral Factors

Use of substances during sex, multiple sexual partners, unprotected intercourse, early sexual initiation, coercive sex, having sex with partners who have had multiple partners, inconsistent use of condoms

Cognitive Factors

Lack of information about STI and symptoms, a sense of invulnerability

Other Factors

Lack of access to health care, shame, poverty, homelessness, sexual abuse

Special Adolescent Populations

Females: higher reported rates of STI, may suffer more complications including ectopic pregnancy, PID, infertility, and pelvic pain

Disadvantaged Youth: are generally at increased risk for STI
Race and Ethnicity: African Americans and Hispanics have higher STI prevalence rates in comparison to non-Hispanic whites.

Males who have sex with males: some are at higher risk for HIV and other STI. Routine testing for HIV and syphilis as well as immunization against Hepatitis A and B if documentation of immunity is not available is recommended. MSM with HIV should also be screened for HCV and can be considered in HIV-uninfected MSM. In addition, if the adolescent has had insertive intercourse within the past year, screen urethra for chlamydia and gonorrhea (urine or swab sample); if patient has had receptive anal intercourse within the past year, screen for rectal gonorrhea and chlamydia; if patient has had receptive oral intercourse, screen for oral gonorrhea.

Women who have sex with women (WSW): few data are available on the risks associated with sex between women. Most WSW report one or more lifetime male sexual partners. Digital vaginal or digital anal contacts especially with shared penetrative sex items may present a means for transmission of microorganisms. HPV transmission can occur with skin-to-skin or skin-to-mucosa contact. Pap tests should be performed consistent with national guidelines: begin at age 21 years even if no sexual intercourse has occurred. Although bacterial vaginosis (BV) is common among WSW, routine screening for BV is not currently recommended, nor is the treatment of partners of women with BV.

Transgender Men and Women: because of the diversity of transgender persons regarding surgical affirming procedures, hormone use, and their patterns of sexual behavior, providers must remain aware of symptoms consistent with common STIs and screen for asymptomatic STIs on the basis of behavioral history and sexual practices.

HIV prevalence may be as high as 27.7 % among all transgender women and 56.3 % among black transgender women (see Table 20.1)

History Taking

Use gender-neutral language such as partner rather than boyfriend or girlfriend. Avoid homosexual or heterosexual unless used first by the adolescent. Explain why a sexual history is important for the adolescent's health and inform the patient that these

Table 20.1 Screening recommendations for STI in lesbian, gay, and bisexual adolescents (Source: Centers for Disease Control-CDC)

STI	Males	Females
Gonorrhea: urethra/cervix	Yes	Yes
Pharynx	If indicated by history[a]	If indicated by history[a]
Anus	If indicated by history[b]	If indicated by history[b]
Chlamydia: urethra/cervix	Yes[c]	Yes[c]
Pharynx	No	No
Anus	If indicated by history[b]	If indicated by history[b]
Syphilis and HIV	Yes, Yes	Yes, Yes
Hepatitis A, B	Yes, Yes	No, Yes
BV	No	Yes
Trichomoniasis	No	Yes
HPV	No[d]	Yes

[a]History in the past year of receptive oral intercourse
[b]History in the past year of receptive anal intercourse
[c]History in the past year of insertive or receptive intercourse
[d]Consider with anal pap at age 30 (Wilkin, NEJM 2015)

discussions are confidential and will not be revealed to a parent (unless the life of the adolescent is threatened by an STI).

- "Have you had sex with men, women or both"?
- "In the past two months, with how many partners have you had sex"?
- "How many lifetime partners have you had"?
- "Do you use condoms during sex; if so, do you use condoms every time, sometimes, usually not"?
- "Have you ever had an STI"?
- "Have any of your partners told you that he/she has had an STI"?

Vaccine Preventable STI (Source: CDC)

Hepatitis A

Indications: should be offered to adolescents and young adults who have not previously received the HAV vaccine series. Men who

have sex with men; illegal injection and noninjection drug users; persons with chronic Hepatitis B or C or those with chronic liver disease; persons taking HIV preexposure prophylaxis (PrEP). Prevaccination serologic testing for susceptibility is not necessary and should not interfere with the initial vaccination; postvaccination serologic testing is not generally indicated (see Table 20.2).

Hepatitis B

Indications: vaccine is recommended for all unvaccinated adolescents. Prevaccination serologic testing may be done if immunization history is unclear. Antibody to hepatitis B core antigen (anti-HBc) is the test of choice. If positive, then test for Hepatitis B surface Antigen (HBsAg). If anti-HBc positive and HBsAg negative, then no follow-up or immunization is necessary. If HBsAg positive, then refer for medical follow up (see Table 20.3).

Table 20.2 Hepatitis A dosage schedule (Source: CDC)

Vaccine	Age (years)	Dose	Volume (mL)	Two dose schedule (months)
HAVRIX	1-18	720 (EL.U.)	0.5	0, 6–12
HAVRIX	>18	1440 (EL.U)	1.0	0, 6–12
VAQTA	1-18	25 (U)	0.5	0, 6–18
VAQTA	>18	50 (U)	1.0	0, 6–18

Table 20.3 Hepatitis B dosage schedule (Source: CDC)

Vaccine	Adolescents 11–19 years: three dose schedule (0, 1, 6 months)	Adolescents 11–15 years: two dose schedule (0, 4–6 months)	Adults 20 years or older: three dose schedule (0, 1, 6 months)
Recombivax HB	5 (μg) 0.5 mL	10 (μg) 1.0 mL	10 (μg) 1.0 mL
Energix B	10 (μg) 0.5 mL	Not available	20 (μg) 1.0 mL

Check CDC Website or AAP Redbook for dialysis patient vaccine recommendations

Table 20.4 Human papillomavirus vaccine dosage schedule (Source: CDC)

Vaccine	Dosage schedule
Gardasil™ (serotypes 6, 11, 16, 18)	0, 1–2, 6 months (males and females 9–26 years)
Cervarix™ (serotypes 16, 18)	0, 1–2, 6 months (females 10–25 years)
Gardasil 9™ (serotypes 6, 11, 16, 18, 31, 33, 45, 52, 58)	0, 1–2, 6 months (males and females 9–26 years)

Human Papillomavirus Vaccine

Indications: vaccine is recommended for all females age 9–26 years and males age 13–21 years (can be vaccinated up to age 26), recommended for MSM through age 26 years. Prevaccination serologic testing is not done (see Table 20.4).

Testing

HIV

- CDC recommends routine testing of all adolescents age 13 and older and at least one time in the health care setting; high-risk adolescents (see later) should be tested annually
- US Preventive Services Task Force (USPSTF) recommends routine HIV screening for adolescents aged 15 and older, and screening all high-risk adolescents;
- Massachusetts Department of Public Health endorses CDC and USPSTF guidelines
- Adolescents are able to and must provide oral consent (no requirement to document) in Massachusetts; extensive pretest counseling is not necessary; negative results may be telephoned or sent to the patient; positive results may be telephoned or preferably given in person. Having a referral plan at the time of notification is optimal. Check other states regulations for information on adolescent HIV testing consent. High-risk groups include unprotected intercourse with more than one partner, MSM, persons seeking treatment for STIs or with a prior his-

tory of STIs, past or present injection drug use, sex for money or drug situations, history of Hepatitis B or C, inmates, residents of homeless shelters, active TB
- A negative HIV test may not reflect recent exposures during the past 3 months
- Screening EIA cost is ~$1–2; positive EIA is repeated and confirmatory Western blot is checked if second EIA is positive
- Combined EIA and Western blot have sensitivity of >99.7 % and specificity of >99.9 %
- Rapid HIV Antibody Test available especially for source patients from needle-stick injury; 20 min for results
- Currently, there are two FDA-approved home HIV tests; no guidelines for use in adolescents

Syphilis

Routine screening of all individuals is not recommended

- Screening of high-risk individuals is recommended including MSM, sex workers, sex for drugs, syphilis contacts, persons with other STIs
- USPSTF recommends screening pregnant women and high-risk patients
- Massachusetts Health Quality Partners (MHPQ) recommends screening high-risk patients and pregnant women
- Screening algorithm varies by clinical laboratory
- Optimal testing frequency is not determined

Chlamydia

- The optimal screening frequency is not known but may be decided on the adolescent's risk factors
- Females may be tested with an endocervical swab or urine (not a clean catch), or anal swab (not FDA approved)
- Males may be tested with a urine or urethral swab or anal swab (not FDA approved)
- CDC recommends annual screening of sexually active adolescent females and screening of adolescent males in high-risk settings (correctional facilities, adolescent clinics, and STI clinics)

- USPSTF recommends routine screening of sexually active adolescent females
- MHQP recommends annual screening of sexually active adolescent male and females

Gonorrhea

- USPSTF recommends sexually active female adolescents be screened for gonorrhea
- MSM (see MSM guidelines)

Sexually Transmitted Infections

Office Testing

1. Wet mount: take a drop or two of fresh vaginal fluid preferably from the cul-de-sac and place it immediately on a slide; add one or two drops of normal saline and cover with a cover slip. Evaluate under low and medium power microscopy. Epithelial cells, white and red blood cells, and bacteria are commonly seen (Fig. 20.1)

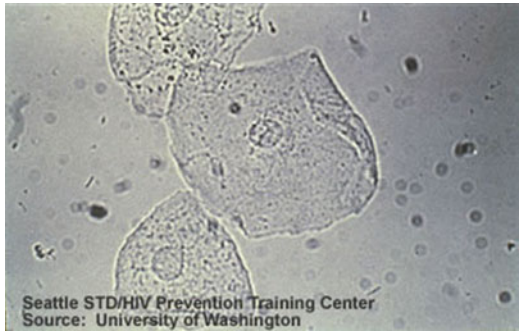


Fig. 20.1 Saline preparation of vaginal fluids. (Used with permission from Amy L. Radford, MSW/University of Washington STD Prevention Training Center)

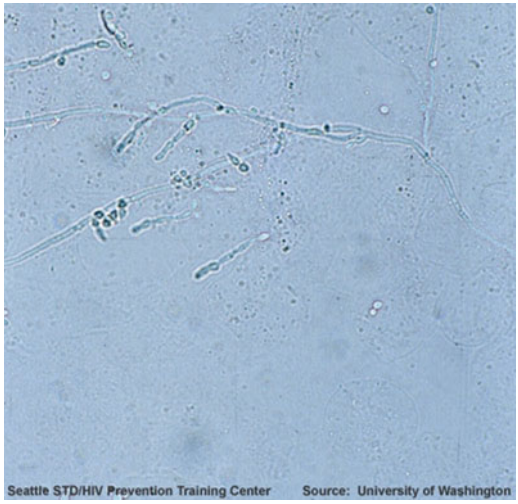


Fig. 20.2 Yeast (Used with permission from Amy L. Radford, MSW/ University of Washington STD Prevention Training Center)

2. KOH mount: take a drop or two of fresh vaginal fluid preferably from the cul-de-sac and place it immediately on a slide; add one or two drops of 10 % KOH and cover with a cover slip. Warm the underside of the slide gently with a match. Evaluate for fungal forms under low and medium power microscopy (Fig. 20.2)
3. pH paper is useful in testing vaginal pH for diagnosis of bacterial vaginosis

Sexually Transmitted Infections

Vaginitis

Bacterial Vaginosis

Symptoms: malodorous-fishy smell vaginal discharge; >50 % of women are asymptomatic

Signs: thin gray or white homogenous discharge coating the vaginal walls

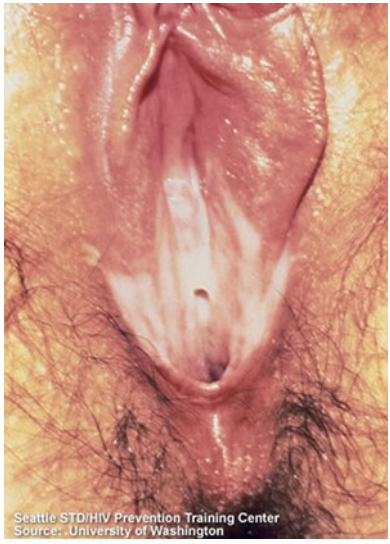


Fig. 20.3 Vaginal discharge in bacterial vaginosis (Used with permission from Amy L. Radford, MSW/University of Washington STD Prevention Training Center)

Diagnosis: Amsel criteria—3 out of 4: pH of vaginal fluid >4.5, a fishy odor to vaginal discharge before or after addition of 10 % KOH, and the gray or white vaginal discharge (Fig. 20.3)

There is also the presence of clue cells on microscopic examination. Clue cells, which are vaginal epithelial cells studded with coccobacilli should be seen in 20 % of the epithelial cells on a wet mount (Fig. 20.4)

Treatment: Metronidazole 500 mg orally two times a day for 7 days or Metronidazole gel 0.75 %, one full applicator (5 g) intravaginally once a day for 5 days or Clindamycin cream, 2 %, one full applicator (5 g) intravaginally at bedtime for 7 days

For alternative treatments and treatment of pregnant women check website:

http://www.cdc.gov/std/tg2015/bv.htm

Management of Sex Partners: none currently recommended

Follow up: not necessary if symptoms resolve

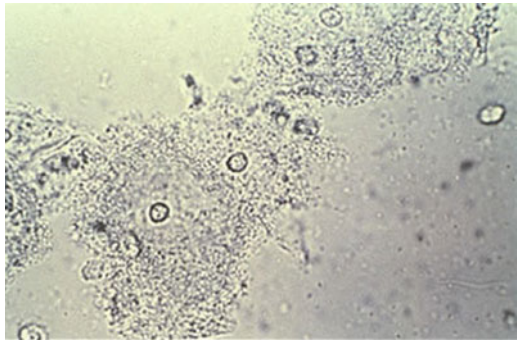


Fig. 20.4 Clue cells (Used with permission from Amy L. Radford, MSW/ University of Washington STD Prevention Training Center)

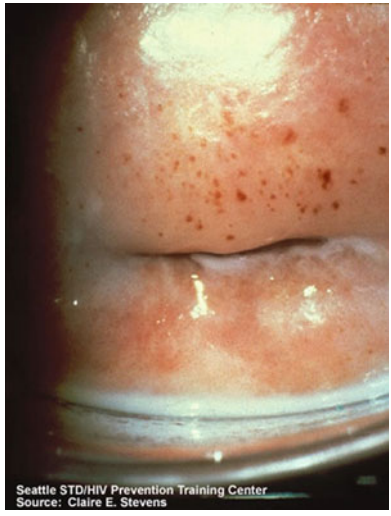


Fig. 20.5 Strawberry cervix (Used with permission from Amy L. Radford, MSW/University of Washington STD Prevention Training Center)

Trichomoniasis

Symptoms: diffuse, malodorous, yellow-green vaginal discharge with vulvar irritation; some women are asymptomatic

Signs: characteristic vaginal discharge with frothy appearance; strawberry cervix (Fig. 20.5)

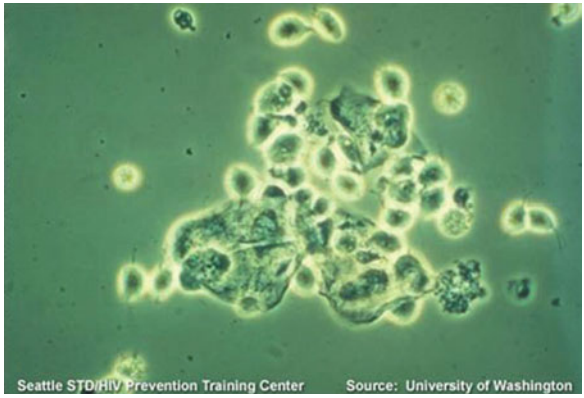


Fig. 20.6 *T. vaginalis* in wet mount preparation (Used with permission from Amy L. Radford, MSW/University of Washington STD Prevention Training Center)

Diagnosis: wet prep of vaginal secretions for presence of trichomonads (60–70 % sensitive); NAAT detects 3–5 × more infections than wet mount; OSOM Trichomonas Rapid Test also useful >83 % sensitivity and >97 % specificity males require culture of urethral swab, urine, or semen. Trich appear to be swimming in a wet mount with whipping motions of the flagellae (Fig. 20.6).

Treatment: Metronidazole 2 g orally in a single dose or Tinidazole 2 g orally in a single dose. For alternative treatment and further information check website:

http://www.cdc.gov/std/tg2015/trichomoniasis.htm

Management of Sex Partners: sex partners should be treated

Follow up: unnecessary if patient becomes asymptomatic. Check website if patient continues to be symptomatic

Vulvovaginal Candidiasis

Symptoms: vulvar pruritus, vaginal discharge, vaginal soreness, dysuria, dyspareunia

Signs: vulvar erythema, edema, excoriations or a thick cottage cheese-like vaginal discharge (Fig. 20.7).

Diagnosis: wet prep 10 % KOH examination of vaginal fluid is best looking for hyphae. Candida culture may also be performed.

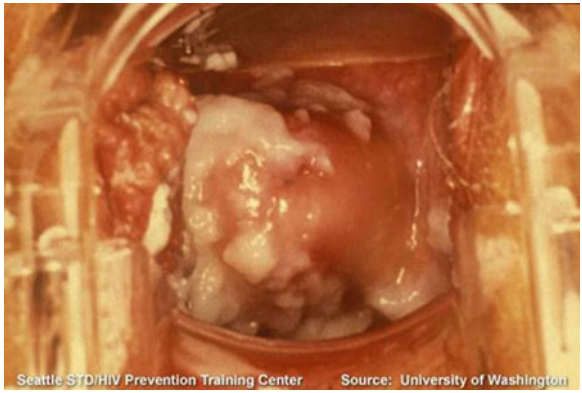


Fig. 20.7 Candida vaginal discharge (Used with permission from Amy L. Radford, MSW/University of Washington STD Prevention Training Center)

A positive wet prep may give the appearance of "meatballs and spaghetti."

Treatment: numerous regimens are available including Butoconazole 2 % cream 5 g intravaginally for 3 days or terconazole 80 mg vaginal suppository, one intravaginally for 3 days.

Note that alternatives to fluconazole are suggested during pregnancy; may raise risk of miscarriage.

For other treatments and further information check website: http://www.cdc.gov/std/tg2015/candidiasis.htm

Urethritis and Cervicitis

Symptoms: males with urethritis are often, but not always, symptomatic with pruritus, dysuria, or a urethral discharge.

Females with cervicitis may be asymptomatic, have vaginal discharge, or some intermenstrual vaginal bleeding

Signs: males may have a scant to copious clear, purulent, or mucopurulent urethral discharge; females may have mucopurulent cervicitis (Figs. 20.8, 20.9, and 20.10).

Diagnosis: in males, a gram stain of the urethral discharge that shows 5 or more WBC per oil field is consistent with urethritis (Fig. 20.11).

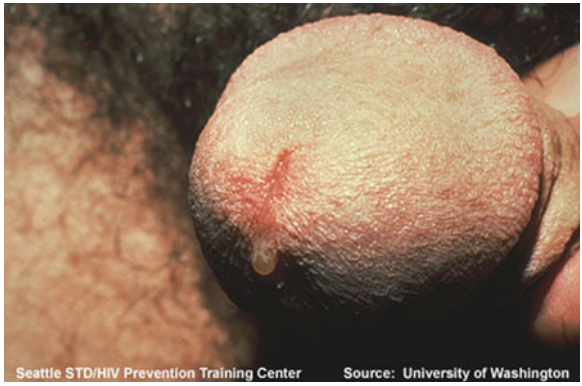


Fig. 20.8 Nongonococcal urethritis (Used with permission from Amy L. Radford, MSW/University of Washington STD Prevention Training Center)

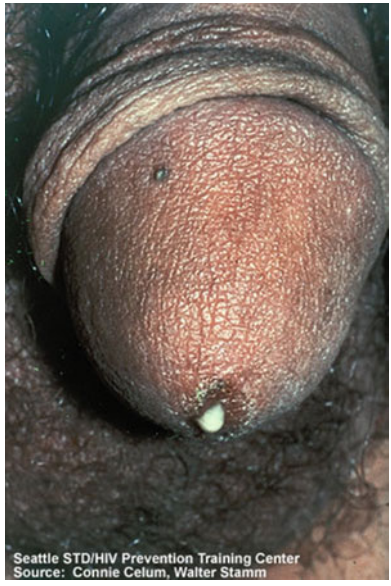


Fig. 20.9 Gonococcal urethritis (Used with permission from Amy L. Radford, MSW/University of Washington STD Prevention Training Center)

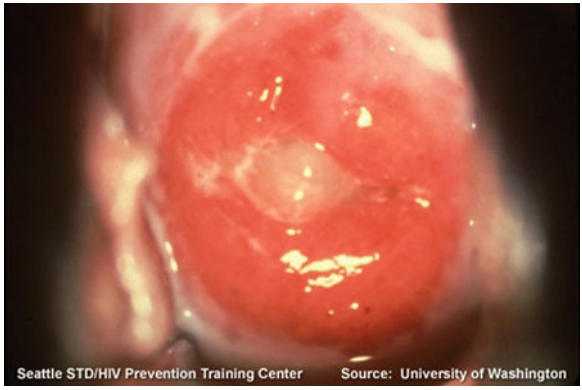


Fig. 20.10 Gonococcal cervicitis (Used with permission from Amy L. Radford, MSW/University of Washington STD Prevention Training Center)

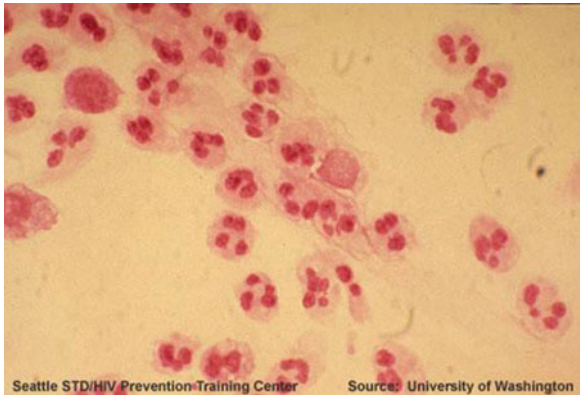


Fig. 20.11 Urethral gram stain as seen in nongonococcal urethritis (Used with permission from Amy L. Radford, MSW/University of Washington STD Prevention Training Center)

The presence of gram-negative intracellular diplococci establishes a gonococcal infection (Fig. 20.12).

Chlamydia and gonorrhea nucleic acid amplification testing (NAAT) should be sent on first catch urine (preferably) or urethral discharge.

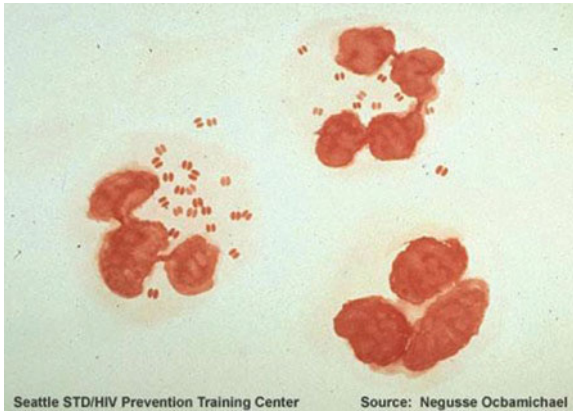


Fig. 20.12 Intracellular gram-negative diplococci (Used with permission from Amy L. Radford, MSW/University of Washington STD Prevention Training Center)

In females, the gram stain has little value in establishing a diagnosis. Cervical or urine specimen is best with cervical specimens preferred. NAAT is not approved by the FDA to test for rectal and oropharyngeal infections caused by *Chlamydia trachomatis* and *N. gonorrhoeae*; however, some laboratories have met CLIA regulatory requirements and established performance specifications for using NAAT with rectal and oropharyngeal swab specimens that can inform clinical management. In females, cervical (preferably) or urine specimens should be sent for NAAT to establish presence of gonorrhea or chlamydial infection. A wet prep of cervical secretions will help to evaluate for the presence of BV or trichomoniasis.

Treatment: a number of treatment options are available; use the CDC website:

http://www.cdc.gov/std/tg2015/urethritis-and-cervicitis.htm

Also note that directly observed dual therapy is now recommended for GC (first line ceftriaxone 250 mg IM + azithromycin 1 g) and that fluoroquinolones are not indicated for the treatment of gonorrhea due to resistant GC. Updated guidelines at: http://www.cdc.gov/std/tg2015/gonorrhea.htm

Generally, if a patient is diagnosed with gonorrhea, then treatment should be given for concurrent chlamydia infection.

Chlamydia infection may be diagnosed by testing urine with NAAT or obtaining a cervical swab or urethral swab in male patients. An NAAT test that is approved for vaginal swabs obtained by the patient or provider may also be done.

Treatment: a number of options are available including
Azithromycin 1 g orally in a single dose or
Doxycyline 100 mg two times a day for seven days

Addition treatment guidelines for chlamydia can be found at the following link:

http://www.cdc.gov/std/tg2015/chlamydia.htm

Partner treatment for chlamydia can be provided in some states. Please see the following link:

http://www.cdc.gov/std/ept/

Management of Sex Partners: patients with nongonococcal urethritis should refer all sexual partners from the past 60 days for treatment. Patients diagnosed with gonorrhea should refer all sexual partners from the past 60 days; if a patient last had intercourse more than 60 days before the symptoms began or diagnosis established, that partner should be referred for evaluation.

Follow up: generally follow up is not needed unless there is persistence of symptoms, pregnancy, or a question of medication compliance.

Pelvic Inflammatory Disease (PID)

Symptoms: PID is a spectrum of inflammatory disorders of the upper female genital tract. Thus, symptoms could be secondary to endometritis, salpingitis, tubo-ovarian abscess, and/or peritonitis. Symptoms could range from vaginal discharge, dyspareunia, abnormal vaginal bleeding, dysuria, nausea, vomiting, or pain.

Signs: abdominal tenderness with or without rebound. Pelvic examination may show vaginal discharge, mucopurulent cervicitis, uterine or adnexal tenderness, cervical motion tenderness or an adnexal mass (Fig. 20.13).

Diagnosis: PID is an imprecise diagnosis. Any sexually active female adolescent with pelvic or lower abdominal pain should be tested for PID if another etiology has not been established. In addition, one or more of the following should be present for empiric

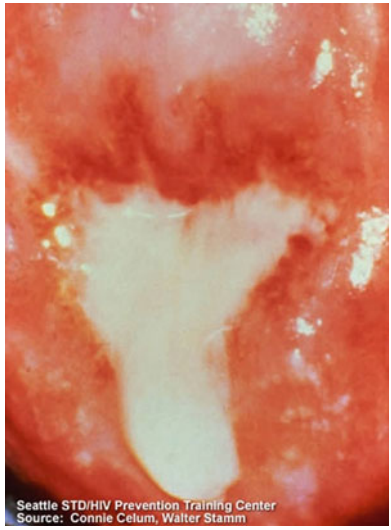


Fig. 20.13 Mucopurulent cervicitis (Used with permission from Amy L. Radford, MSW/University of Washington STD Prevention Training Center)

treatment of PID: cervical motion tenderness or uterine tenderness or adnexal tenderness.

Treatment: a decision should be made if the patient should be treated with oral medication or parenteral medication. In addition, all treatment regimens must be effective against gonorrhea and chlamydia. Hospitalization and parenteral treatment are based on one or more of these criteria: patient is severely ill with nausea, vomiting, or high fever; patient is pregnant; patient is unable or cannot tolerate outpatient oral medications; surgical emergency cannot be ruled out; patient does not respond to oral antimicrobials; patient has a tubo-ovarian abscess. This website has up-to-date information on the currently recommended treatment regimens for PID:

http://www.cdc.gov/std/tg2015/pid.htm

Management of Sex Partners: regardless of the etiology of the PID, male sex partners who had sexual contact with the patient within the 60 days prior to her developing symptoms should be

evaluated and treated empirically for chlamydia and gonorrhea. The patient is at high risk for reinfection if this is not done, and there is a strong likelihood that the male partner has an infection with chlamydia, gonorrhea, or both.

Follow up: regardless of treatment, patients should show clinical evidence of improvement within 72 hours of treatment initiation. If not, an examination should be done and therapeutic options considered. Some recommend rescreening for chlamydia and gonorrhea 4–6 weeks after completion of therapy if one or both of these agents were identified in the patient.

Genital Lesions

Papules

Molluscum Contagiosum

Symptoms: often asymptomatic, the lesions may appear on external genitalia and in the public region and upper legs; rarely pruritic

Signs: multiple raised, flesh colored or erythematous domed-shaped papules often umbilicated ranging in size from 1 to 5 mm; giant mollusca may be seen in HIV infected patients

Diagnosis: clinical appearance (Fig. 20.14)

Treatment: most lesions will disappear without treatment; cryotherapy with liquid nitrogen is effective. Apply liquid nitrogen to the lesion for 20 seconds. Curettage is also effective.

Scabies

Symptoms: pruritus especially at night

Signs: papular rash often on genital areas including penis and vulva, flexor areas of the wrists, interdigital folds, areolae, abdomen, buttocks, intergluteal cleft; nodules may appear in the axillae or groin; secondary infections due to scratching may be seen.

Diagnosis: scrape a lesion with a No. 15 scalpel blade after applying mineral oil and look for parts of the mite, eggs, feces under microscopy; some clinicians may diagnose based on clinical appearance (Fig. 20.15)

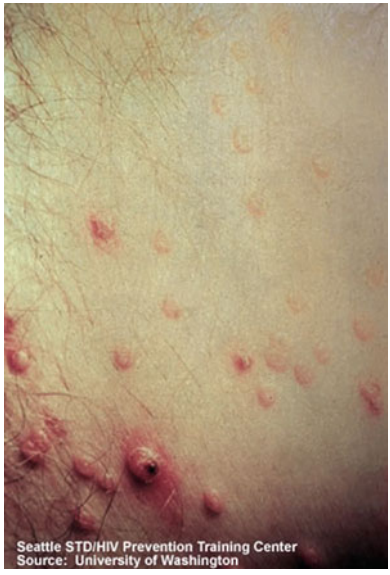


Fig. 20.14 Molluscum (Used with permission from Amy L. Radford, MSW/ University of Washington STD Prevention Training Center)

Treatment: Permethrin cream (5 %) applied to all areas of the body from neck down and washed off 8–14 h later. Itch may persist for two weeks. Decontaminate bedding and clothing by machine wash and dry or by dry cleaning.

Management of sex partners: contacts within the preceding month should be examined and treated.

Follow up: some recommend retreatment if the patient is still symptomatic after 1–2 weeks.

Vesicular and/or Ulcerative Lesions

Genital Herpes

Symptoms and signs: local symptoms may include a vesicular and/ or ulcerative genital rash, pain, dysuria, local swelling, pruritus, adenopathy. Systemic symptoms may include fever, malaise,

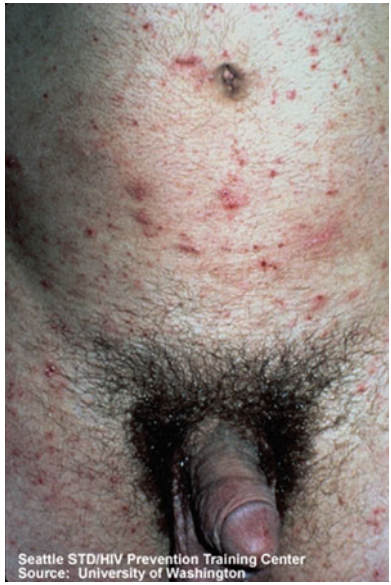


Fig. 20.15 Scabies (Used with permission from Amy L. Radford, MSW/ University of Washington STD Prevention Training Center)

headache, and myalgias especially in primary herpes infections (Fig. 20.16)

Diagnosis: for first time diagnosis, isolation of the virus in cell culture; PCR assays for HSV DNA are more sensitive. Further options are noted in the following link.

http://www.cdc.gov/std/tg2015/herpes.htm

Treatment: management is complicated depending on patient's level of illness and whether it is the primary episode or a recurrence. In addition, suppressive therapy is an available option. For first time infection acyclovir 400 mg orally three times a day for 7–10 days, or acyclovir 200 mg five times a day for 7–10 days or famciclovir 250 mg three times a day for 7–10 days or valacyclovir 1 g twice a day for 7–10 days. Adolescents may be more compliant with less frequent dosage schedules. See link for further information.

http://www.cdc.gov/std/tg2015/herpes.htm

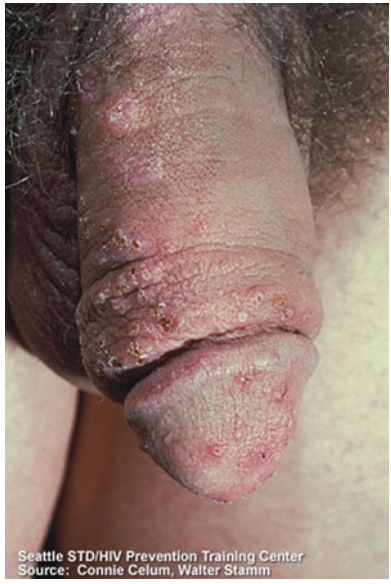


Fig. 20.16 Genital herpes lesions (Used with permission from Amy L. Radford, MSW/University of Washington STD Prevention Training Center)

Management of Sex Partners: symptomatic partners should be evaluated and treated; asymptomatic partners should be questioned and offered type-specific serologic testing for HSV infection.

Syphilis

Symptoms: primary syphilis presents with a painless chancre at the site of inoculation. Secondary syphilis is characterized by a generalized body rash that may also be located on mucous membranes. See link for more information and symptoms of tertiary syphilis.

Signs: the chancre has an indurated generally painless perimeter; the chancre may be solitary or possibly multiple at the inoculation site (Fig. 20.17).

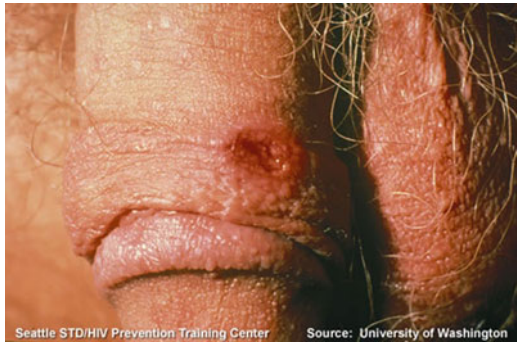


Fig. 20.17 Primary syphilis (Used with permission from Amy L. Radford, MSW/University of Washington STD Prevention Training Center)

Lesions of secondary syphilis may present as macules, papules, or pustules and be seen on palms and soles, or as mucous patches on the oral mucosa or lesions on other body areas. Some may have scale and multiple types of lesions may be present at any one time (Figs. 20.18 and 20.19).

Diagnosis: in primary syphilis, darkfield microscopy or direct fluorescent antibody tests from lesion exudates are definitive. Serological testing may be done first with a screening test: use of treponemal or nontreponemal antibody test (RPR or VDRL) varies by clinical laboratory.

Treatment: Penicillin G is the treatment of choice for all stages of syphilis. See link for details on treatment:

http://www.cdc.gov/std/tg2015/syphilis.htm

Management of Sex Partners: sexual partners within the 90 days prior to diagnosis of primary, secondary, or early latent syphilis may be infected even if seronegative and should be treated presumptively. Check link for details.

Chancroid

Symptoms: a tender papule that becomes pustular then a painful, friable ulcer.

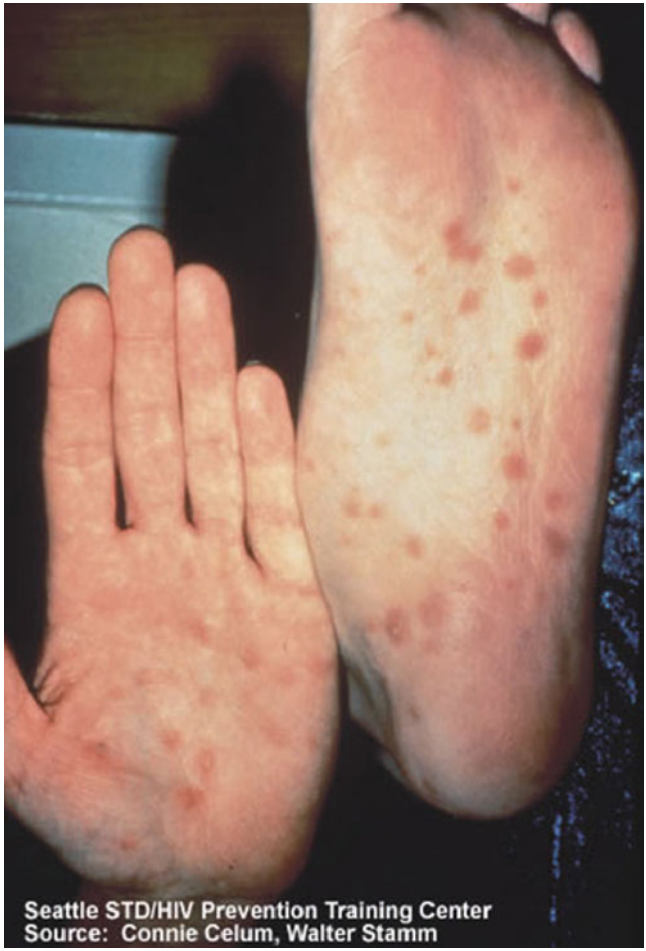


Fig. 20.18 Secondary syphilis (Used with permission from Amy L. Radford, MSW/University of Washington STD Prevention Training Center)

Signs: the ulcer is 1–20 mm in size, with a purulent exudate and a granulomatous base. In contrast to the chancre in syphilis, the edges are nonindurated and the chancre is painful (Fig. 20.20).

Diagnosis: rule out syphilis and HSV; culture (if available) for *H. ducreyi.*

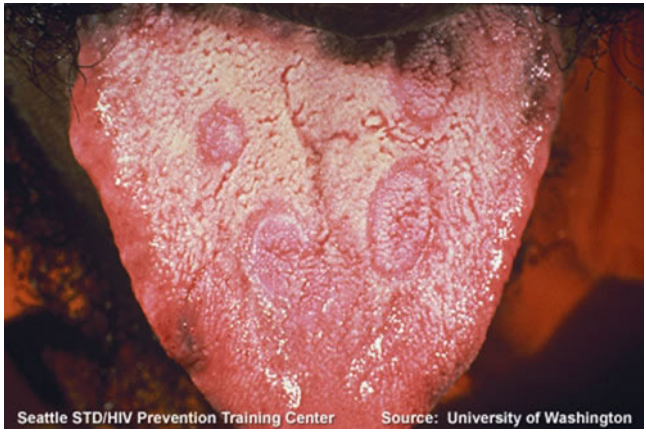


Fig. 20.19 Secondary syphilis (Used with permission from Amy L. Radford, MSW/University of Washington STD Prevention Training Center)

Treatment: Azithromycin 1 g orally in a single dose. See link for further treatment options and additional information. http://www.cdc.gov/std/tg2015

http://www.cdc.gov/std/tg2015/chancroid.htm

Follow up: patients should be reexamined 3–7 days after therapy begins. See link for further details

Management of Sex Partners: partners who have had sexual contact with the patient in the 10 days prior to the patient's onset of symptoms should be examined and treated regardless of symptoms.

Granuloma Inguinale (Donovanosis)

This illness is caused by Klebsiella granulomatis and occurs only rarely in the United States.

Symptoms: single or multiple subcutaneous nodules that progress to larger and more vascular ulcers with regional lymphadenopathy. Diagnosis rests on demonstration of Donovan bodies on a tissue sample. Treatment is doxycycline. See link for further information: http://www.cdc.gov/std/tg2015

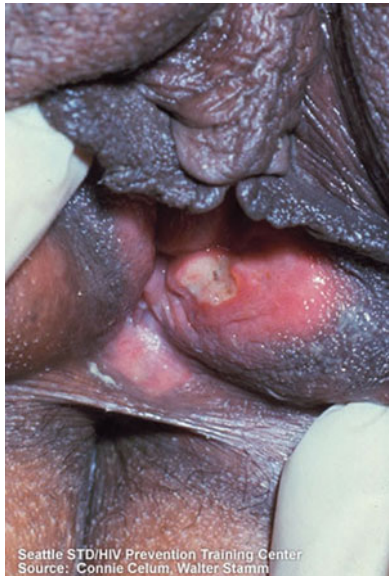


Fig. 20.20 Chancroid (Used with permission from Amy L. Radford, MSW/ University of Washington STD Prevention Training Center)

Lymphogranuloma Venereum

This is an invasive lymphatic infection beginning with an initial ulcerative lesion on the genitals. This is followed by tender, suppurative inguinal, and possibly femoral adenopathy. Rectal exposure in MSM or women having anal intercourse may present with proctocolitis. The causative agent is *Chlamydia trachomatis* serovars L1, L2, or L3. Definitive diagnosis is best made by isolating the organism. See link for further information and treatment recommendations at:

http://www.cdc.gov/std/tg2015/lgv.htm

Verrucous Lesions

Genital Warts

Symptoms: verrucous lesions in genital regions including cervix, vulva, vagina, pubic regions, penis, scrotum, anus

Signs: in large crops, there could be maceration or urethral/anal obstruction

Diagnosis: visual diagnosis is possible; hand lens may be helpful (Fig. 20.21)

Treatment: No one recommended treatment; depends on provider experience, patient preference, wart size, number and anatomic site, convenience, cost, and adverse effects. Cryotherapy is effective with two 30-s freeze–thaw treatments and follow up. Trichloroacetic acid (TCA) or Bichloroacetic acid (BCA) may be used.

Patients may apply podofilox 0.5 % solution or gel or imiquimod 5 % cream. For large numbers of warts lasers may be used. See link for further treatment options including cervical, anal, and urethral warts see link:

http://www.cdc.gov/std/tg2015/hpv.htm

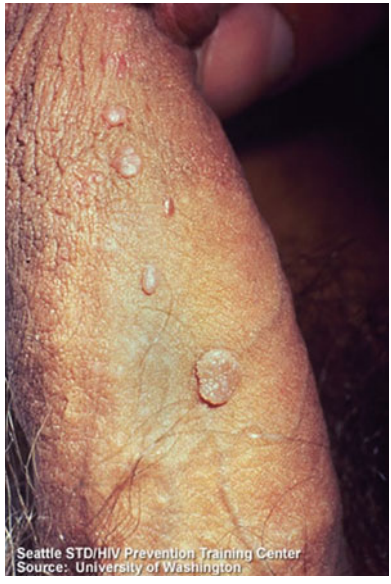


Fig. 20.21 Genital warts (Used with permission from Amy L. Radford, MSW/University of Washington STD Prevention Training Center)

Non Genital Lesions: Ectoparasites

Pubic Lice

Symptoms: itch in the pubic region
Signs: excoriations
Diagnosis: nits on pubic hair; live lice (Fig. 20.22)
Treatment: permethrin 1 % cream applied to affected areas and rinse off after 10 min. See link for further options: http://www.cdc.gov/std/tg2015/. Partners in the previous month should be treated.

Scabies (Mites)

See entry on papules and Fig. 20.22.
See following link for further information on ectoparasites: http://www.cdc.gov/std/tg2015/ectoparasitic.htm

Hepatitis A

Symptoms: malaise, fatigue, abdominal pain, jaundice, anorexia

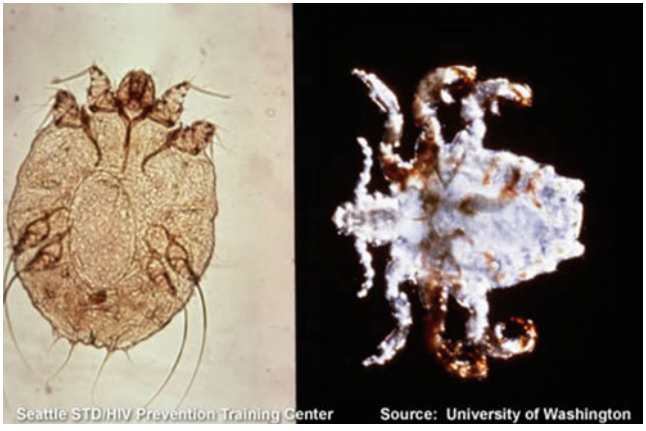


Fig. 20.22 Mite and Louse (Used with permission from Amy L. Radford, MSW/University of Washington STD Prevention Training Center)

Signs: icterus, tender liver edge
Diagnosis: elevated transaminases, IgM antibody to HAV
Treatment: supportive See link for further information:
http://www.cdc.gov/std/tg2015/hepatitis.htm#hepA

Hepatitis B

Symptoms: , fatigue, abdominal pain, jaundice, anorexia
Signs: icterus, tender liver edge
Diagnosis:
Early acute infection: + HBsAg,
Acute infection: + HBsAg, + total anti-HBc, +IgM anti-HBc
Acute resolving infection: + total anti-HBc, +IgM anti-HBc
Chronic infection: +HBsAg, +total anti-HBc
Treatment: supportive treatment for acute infection; patients with chronic HBV should be referred to a physician experienced in treatment protocols
See link for more information:
http://www.cdc.gov/std/tg2015/hepatitis.htm#hepB
Sexual transmission of Hepatitis C virus can occur, especially among MSM with HIV. For further information: http://www.cdc.gov/std/tg2015/emerging.htm#hepc

HIV

Adolescents are able to provide oral consent to HIV testing. Testing should be voluntary and available to all adolescents who seek evaluation and treatment for STIs. Testing algorithms vary depending on the clinical laboratory. Before adolescents with a positive HIV test are referred to a treatment facility, prevention counseling should be given. Consultation with an HIV treatment specialist should be immediate.

In conjunction with an HIV specialist, an initial evaluation of the HIV positive adolescent can include a detailed history and physical including a gynecological/genital examination. This should include information on sexual and substance abuse history, vaccinations, previous STIs, HIV symptoms, and other diagnoses. Screening

should be performed for gonorrhea, chlamydia (including anal, pharyngeal, and cervical as indicated by history), Pap, wet mount of vaginal secretions, CBC, chemistries, toxoplasmosis antibody, RPR, testing for Hepatitis C and immune serologies for Hepatitis A and B, urinalysis, chest x-ray, PPD, CD4 count, and HIV plasma viral load. Arrangements should be made for a psychosocial evaluation. Minors under age 18 should be encouraged to involve their parent(s) or guardian. See Chap. 21 for further information on HIV.

Epididymitis

See Chap. 5 Male Genitourinary Examination for description.
Treatment guidelines:
http://www.cdc.gov/std/tg2015/Epididymitis

Sources

Ahrens KR, Richardson LP, Courtney ME, McCarty C, Simoni J, Katon W. Laboratory-diagnosed sexually transmitted infections in former foster youth compared with peers. Pediatrics. 2010;126:e97–103.

American Academy of Pediatrics, Committee on Adolescence. Care of the adolescent sexual assault victim. Pediatrics. 2008;122:462–70.

Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2006. MMWR. 2006;55 (No. RR-11).

Ekcert LO. Acute vulvovaginitis. N Engl J Med. 2006;355:1244–52.

Forhan SE, Gottlieb SL, Sternberg MR, et al. Prevalence of sexually transmitted infections among female adolescents aged 14 to 19 in the United States. Pediatrics. 2009;124:1505–12.

Freeto JP, Jay MS. What's really going on down there? A practical approach to the adolescent who has gynecologic complaints. Pediatr Clin N Am. 2006;53:529–45.

Gupta R, Warren T, Wald A. Genital herpes. Lancet. 2007;370:2127–37.

National Network of STD/HIV Prevention Training Centers (NNPTC) and Centers for Disease Control and Prevention. NNPTC online case series. This is a web-based case series for clinicians who diagnose, treat, and manage patients with, or at risk for, STIs. http://www.stdhivtraining.net/nnptc/start.cfm.

Peipert JF. Genital chlamydial infections. N Engl J Med. 2003;349:2424–30.

Sexually transmitted infections. Adolesc Med. 2004;15:203–428.

HIV in Adolescents

21

Anne M. Neilan

Epidemiology

Both non-perinatally and perinatally HIV-infected youth do more poorly at each step of the HIV "continuum of care" (fewer diagnosed, linked to care, retained in care, and virally suppressed compared to adults).

- HIV incidence is rising among adolescents and young adults (AYA).
  - 50,000 new infections per year in the USA
    22–26 % occur in AYA 13–24 years.
- AYA are less likely to be aware they are HIV-infected.
  - 57,200 AYA 13–24 years are living with HIV.
    44 % are unaware of their status (compare to 13 % of 1.2 million persons in the USA being unaware).

Special populations:

- Perinatally HIV-infected youth.
  - 76 % of the approximately 10,000 perinatally HIV-infected youth in the USA are older than 13.
- Children in foster care and the homeless.
  - 16 times more likely to have HIV
  - 7x more likely to die from AIDS

M.A. Goldstein (ed.), *The MassGeneral Hospital for Children Adolescent Medicine Handbook*, DOI 10.1007/978-3-319-45778-9_21

- LGBTQ youth are 6–12 times more likely to become HIV-infected than other youth.
  - 20–40 % of all homeless youth in the USA are LGBTQ.
- Transgender women.
  - HIV prevalence may be as high as 27.7 % among all transgender women and 56.3 % among black transgender women.
- Men who have sex with men (MSM).
  - Rate of new infections increased by 43 % from 2003 to 2014
  - Young MSM of color disproportionately at-risk

HIV Testing

Whom to Test

1. Offer routine HIV screening to patients 13 years and older, regardless of risk factors if local prevalence of HIV is greater than 0.1 %.
2. Offer frequent HIV testing (every 3–6 months) for high-risk youth.

- Youth are not being tested.
  - 13–18-year-olds
  13 % had ever been tested in 2012.
  - 18–24-year-olds
  30 % had ever been tested in 2010.
- All persons with risk factors should be tested for HIV as outlined by the CDC.
- Are you a man who has had sex with another man?
- Have you had sex—anal or vaginal—with an HIV-positive partner?
- Have you had more than one sex partner since your last HIV test?
- Have you injected drugs and shared needles or works (for example, water or cotton) with others?
- Have you exchanged sex for drugs or money?
- Have you been diagnosed with or sought treatment for another sexually transmitted disease?
- Have you been diagnosed with or treated for hepatitis or tuberculosis (TB)?

- Have you had sex with someone who could answer yes to any of the above questions or someone whose sexual history you don't know?

You should be tested at least once a year if you keep doing any of these things. Sexually active gay and bisexual men may benefit from more frequent testing (for example, every 3–6 months).

- Guidelines on when to begin routine HIV screening vary
- *Age 18*
  - American Academy of Family Practitioners (2013)
- *At least once by age 16–18 years*
  - American Academy of Pediatrics (AAP) (2011)
- *Age 15*
  - United States Preventive Services Task Force (USPSTF) (2013)
- *Between age 13 and 15*
  - International Antiviral Society (2014) "agree with CDC and USPSTF"
- *Age 13*
  - CDC (2006)
  - American College of Physicians (2009)
  - American Congress of Obstetricians and Gynecologists (2014)
- *"Test at-risk, discuss screening with all adolescents"*
  - Society for Adolescent Health and Medicine

Indications for testing: Possible HIV exposure, individuals seeking STI screening, patients considering PrEP, males who have sex with males, intravenous drug users (IVDU), those who exchange sex for money, sex with partners who are HIV-infected, bisexual or inject drugs, sex with persons with unknown HIV status.

Which HIV Tests Are Recommended

- Use a fourth generation antigen/antibody combination HIV-1/2 immunoassay plus a confirmatory HIV-1/HIV-2 antibody differentiation immunoassay.
- If suspicion for acute HIV, additionally send HIV RNA (qualitative or quantitative).

Revised 2014 CDC HIV laboratory testing recommendations can be found here:

http://www.cdc.gov/hiv/pdf/guidelines_testing_recommended-labtestingalgorithm.pdf.

Recommendations

1. Offer routine HIV screening to patients 13 years and older, regardless of risk factors if local HIV prevalence is greater than 0.1 %.
2. Offer frequent HIV testing (every 3–6 months) for high-risk youth.

Symptoms of Early HIV

Fever, fatigue myalgia, most frequent. Mononucleosis-like syndrome common: non-tender adenopathy, sore throat (no exudate), generalized maculopapular rash; nausea, diarrhea, anorexia, and weight loss; headache (retro-orbital, pain with eye movement); rarely opportunistic infection (candidiasis most comment). Ten to sixty percent of acute HIV is asymptomatic.

Care for HIV-Infected Youth

Manage in coordination with HIV-trained provider.

Location of care (pediatric, adolescent, adult) clinic and availability of youth-friendly services likely affects outcomes.

African-Americans aged 18–24 have the lowest level of viral suppression (18.3 %).

Adolescents and young adults may face unique challenges to adherence compared to adults and required age-appropriate interventions:

- Denial and fear of their HIV infection
- Misinformation
- Distrust of the medical establishment
- Fear and lack of belief in the effectiveness of medications
- Low self-esteem
- Unstructured and chaotic lifestyles
- Mood disorders and other mental illness
- Lack of familial and social support
- Absence of or inconsistent access to care or health insurance
- Risk of inadvertent parental disclosure of the youth's HIV infection status if parental health insurance is used

Patients with higher viral load are at risk of accruing resistant mutations and transmitting resistant virus.

Transition of Care for HIV-Infected Youth

See AAP Committee on Pediatric AIDS.

http://pediatrics.aappublications.org/collection/committee-pediatric-aids.

Four key steps in the transition process:

- Written policy, circulated to all participants.
- Patient participation in development of the plan (pre-transfer visit suggested).
- Transfer letter, portable medical record summary, emergency care plan.
- Post-transfer communication between referring team and adult provider.
- See Chap. 29 for more information on transition of care.

Prevention of HIV

Counsel adolescents to use condoms correctly, take medicines to prevent or treat HIV, choose less risky sexual behaviors, get tested for other STIs, limit the number of sex partners, or abstain from sexual relations.

For further information on tailored prevention advice based on gender and sex partners, see www.cdc/hivrisk.

Provisional guidelines for anal sex with female condoms can be found:

http://www.aidsmap.com/Female-condoms-for-anal-sex/page/1746303/.

Preexposure Prophylaxis (PrEP)

- Antiretroviral medications for HIV-uninfected people at high risk for acquiring HIV
- 2014 CDC Guidelines for PrEP for those >18 years CDC
  - http://www.cdc.gov/hiv/pdf/prepguidelines2014.pdf
  - Eligible patients: HIV-uninfected and "high-risk:"

HIV-infected sexual partner

Men who have sex with men; sex without condom or any STI in the past 6 months.

Heterosexual male or female; no regular condom use and sex with IDU or MSM partner.

Injection drug users especially shared equipment in the past 6 months.

Preexposure Prophylaxis (PrEP): Recommendations for <18 Years Old

- Local laws, regulations, and policies may apply.
- Weigh carefully:
  - Lack of data on safety and effectiveness
  - Possibility of bone or other toxicities among youth who are still growing
  - Potential benefit of providing PrEP for an individual adolescent at substantial risk of HIV acquisition

– US clinical trials ATN 110/113 studying PrEP in 15–22-year-olds forthcoming

Nonoccupational Postexposure Prophylaxis (nPEP)

Who are considered for nPEP

Risk of HIV acquisition varies by exposure: receptive anal intercourse (1 transmission/200 sex acts) > receptive vaginal intercourse > insertive anal intercourse > insertive vaginal intercourse > receptive oral sex (1 transmission/10,000 sex acts).

Consider nPEP for those who present for medical care within 72 h of exposure after:

Exposure to a source known to be HIV-infected or known to be in a high-risk category (e.g., MSM, sex worker, IVDU) AND receptive or insertive vaginal.

Guidance is limited for "unknown source" and should be taken on a "case by case" basis. We recommend consultation with a subspecialist when available.

CDC recommends consultation with infectious disease or HIV specialist if health care providers are unfamiliar with managing patient on antiretrovirals, if the exposure source indicates the possibility of antiretroviral resistance, in children, pregnancy, and persons with renal dysfunction. If consultation is not available, nPEP should be initiated promptly and revised if necessary after consultation.

Expert consultation can also be found at: PEPline at the National Clinician's Consultation Center at 888-448-4911

http://nccc.ucsf.edu/clinician-consultation/pep-post-exposure-prophylaxis/

2016 CDC guidelines can be found at:

http://www.cdc.gov/hiv/pdf/programresources/cdc-hiv-npep-guidelines.pdf (See Table 21.1).

Preferred regimen for otherwise healthy adolescents (Rx 28-day course): tenofovir disoproxil fumarate (tenofovir DF or TDF) (300 mg) with emtricitabine (200 mg) once daily plus raltegravir (RAL) 400 mg twice daily or dolutegravir (DTG) 50 mg daily.

Additional regimens and updated recommendations may be found at http://www.cdc.gov/hiv/pdf/programresources/cdc-hiv-npep-guidelines.pdf (See Table 21.1).

Table 21.1 nPEP guidelines

Initial nPEP evaluation

- Obtain history of potential exposure event
  - HIV and HBV status of exposed person and source person, if available
  - Timing of most recent potential exposure
  - Type of exposure event and risk for HIV acquisition
  - Make determination of nPEP is indicated
- If nPEP is indicated
- Conduct laboratory testing

  HIV blood test (rapid combined Ag/Ab test, if available)

  STIs, HBV, HCV, pregnancy, and chemistries, as indicated
- Prescribe 28-day nPEP course

  Educate patient about potential regimen-specific side effects and adverse events

  Counsel patient about medication adherence

  Provide patient with nPEP prescription *or* full 28-day nPEP course *or* nPEP starter pack and prescription
- When necessary, assist patients with obtaining nPEP medication through a medication assistance program for the prescribed regimen
- For all persons evaluated
  - Prescribe prophylaxis for STIs and HBV infection, if indicated
  - Provide counseling related to HIV prevention strategies, as appropriate
  - Document sexual assault findings and fulfill local reporting requirements
  - Conduct confidential reporting of newly diagnosed STIs and HIV infection to health department
  - Link HIV-infected persons to relevant medical and psychosocial support services

Follow-up evaluations for persons prescribed nPEP

- Conduct HIV and any other indicated laboratory testing
- Consider changing nPEP regimen if indicated by side effects or results of initial testing
- Provide additional counseling and support for medication adherence and HIV prevention, if indicated

Source: Centers for Disease Control

Ag/Ab antigen/antibody combination test, *HBV* hepatitis B virus, *HCV* hepatitis C virus, *HIV* human immunodeficiency virus, *nPEP* nonoccupational post-exposure prophylaxis, *STI* sexually transmitted infection

Baseline evaluation includes HIV Ag/Ab testing, Hep B surface antigen, Hep B surface antibody, Hep B core antibody, Hep C antibody, Syphilis testing, as well as testing for Gonorrhea, Chlamydia, pregnancy, serum creatinine, ALT, AST, HIV VL, and HIV genotypic resistance.

Follow-up testing occurs at 4–6 weeks, 3 months, and 6 months after exposure.

HIV status of the source should be determined whenever possible.

Special populations:

Persons provided nPEP after sexual assault or child sexual abuse should be examined and comanaged by professionals specifically trained in assessing and counseling patients and families during these circumstances.

Sources

Guidelines for the use of antiretroviral agents in HIV-1 infected adults and adolescents. 2014. www.AIDSinfo.nih.gov

HIV testing trends in the United States, 2000–2011. Centers for Disease Control and Prevention. 2013.

HIV Surveillance Supplemental Report 2015. Centers for Disease Control and Prevention. 2015.

Updated guidelines for antiretroviral postexposure prophylaxis after sexual, injection drug use, or other nonoccupational exposure to HIV-United States, 2016. Centers for Disease Control and Prevention. 2016.

Delayed Puberty, Short Stature, and Tall Stature

22

Michelle Katz and Madhusmita Misra

Normal Puberty

The onset of puberty is heralded by an increase in pulsatile GnRH secretion by the hypothalamus, which leads to increased secretion of LH and FSH by the pituitary and of testosterone and estrogen by the gonads. The normal age range for onset of puberty is 8–13 years in girls and 9–14 years in boys. This often corresponds to a bone age of 11 in girls or 12 in boys. The onset of puberty is characterized by breast budding in girls (thelarche or Tanner II breast development) or testicular size greater than 3 mL in boys, most easily measured with a Prader Orchidometer. The duration between the beginning of breast buds until menarche in girls is around 2 years, but is of longer duration in girls with a younger age of onset of puberty and of shorter duration in girls with later pubertal onset. The development of axillary and pubic hair, adult body odor, and acne may be related to increased secretion of androgens subsequent to maturation of the gonads (gonadarche), or adrenals (adrenarche), or both.

M.A. Goldstein (ed.), *The MassGeneral Hospital for Children Adolescent Medicine Handbook*, DOI 10.1007/978-3-319-45778-9_22

Delayed Puberty

This is defined as lack of breast development by 13 years of age in girls, or lack of testicular enlargement by 14 years of age in boys. This should be distinguished from delayed menarche which is the failure to reach menarche by age 15 or by 2–3 years after thelarche in girls, and distinguished from pubertal arrest where puberty begins but stalls before full pubertal maturation is reached. When evaluating delayed puberty, a family history of the timing of puberty in parents (and grandparents and siblings if available) can be very helpful. The growth curve should be carefully examined for evidence of prepubertal growth attenuation or a growth spurt. Girls tend to experience their pubertal growth spurt in early puberty while boys grow fastest in late puberty. Causes of delayed puberty are listed in Table 22.1.

Constitutional Delay

Constitutional delay of puberty is the most common cause of pubertal delay, especially in boys. Typically, adolescents will be short and have a bone age delayed more than 2 standard deviations from their chronological age. In general, children grow at a rate of 4–6 cm/year until about 12 years of age, following which height velocity decreases by 1 cm/year for every year that an adolescent does not go into puberty. Therefore, adolescents with constitutional delay may have a markedly diminished growth velocity. There are standardized curves of growth velocity for early, late, and typical maturers and plotting an adolescent's growth velocity on one of these growth charts may be helpful both in the evaluation of short stature and in explaining this condition to parents. There is often a family history of pubertal delay. LH, FSH, and testosterone will be at prepubertal levels. Despite short stature during adolescence, final adult height is preserved. Boys may opt to be treated with low dose testosterone for a short period of time (4–6 months) in an attempt to "jump start" puberty. This therapy does not change adult height but may lead to an earlier growth spurt.

Table 22.1 Causes of delayed puberty

Low LH and FSH	High LH and FSH
Constitutional delay	Genetic syndromes
	Turner syndrome
	Klinefelter syndrome
CNS pathology	Gonadal dysgenesis
Tumor, radiation therapy	Primary ovarian insufficiency
Granulomatous disease	
Langerhans cell histiocytosis	
Midline defects	
Vascular defects	
Severe head trauma	
Gonadotropin deficiency	"Late Effects" of childhood cancer
Kallman syndrome	Chemotherapy
Isolated deficiencies of LH or FSH	Radiation therapy
DAX1 mutation	
Others	
Syndromes	Disorders of steroid synthesis
Prader–Willi	LH/FSH resistance
Bardet–Biedl	Synthetic enzyme defects
Others	
Functional deficiency	Metabolic disease
Nutritional deficiency	
Eating disorders	
GI disease	
AIDS	
Chronic renal disease	
Endocrine causes	Rare syndromic associations
Hypothyroidism	
Cushing syndrome	
Hyperprolactinemia	
Poorly controlled diabetes mellitus	

Hypogonadotropic Hypogonadism (or Secondary Hypogonadism)

Hypogonadotropic hypogonadism is characterized by low LH and FSH secretion from the pituitary leading to lack of pubertal onset or progression. Intracranial processes such as tumors, irradiation,

infection, severe head trauma, or granulomas can all lead to hypogonadotropic hypogonadism and may be associated with other hormone deficiencies. Isolated hypogonadotropic hypogonadism with anosmia is Kallman Syndrome, an X-linked recessive or autosomal dominant disorder caused by the failed migration of GnRH neurons from the olfactory placode associated with aplasia or hypoplasia of the olfactory bulb. Additionally, systemic chronic disease such as chronic renal disease, malnutrition, or eating disorders can lead to hypogonadotropic hypogonadism. As in constitutional delay, LH, FSH, and testosterone levels will be in the prepubertal range. Clinical features and the leuprolide stimulation test aid in diagnosis. Diagnosis of hypogonadotropic hypogonadism in the absence of systemic illnesses should prompt evaluation of the other pituitary axes and a brain MRI.

Hypergonadotropic Hypogonadism (or Primary Hypogonadism)

Hypergonadotropic hypogonadism is caused by a primary dysfunction of the gonads and is associated with high levels of LH and FSH and low levels of testosterone or estrogen. Radiation to the gonads, chemotherapy, surgery such as orchidopexy for highly placed testes, and infections such as mumps can all lead to gonadal failure. In addition, gonadal dysgenesis can occur in both XX and XY individuals and cause primary gonadal failure. In short girls, Turner syndrome should always be considered (XO, XX/XO, and other mosaic karyotypes). Associated findings in Turner Syndrome include a low hairline, webbing of the neck, broad "shield" chest, dysplasia of the nails, widened carrying angle, and renal and left-sided heart abnormalities. Klinefelter's Syndrome (47 XXY karyotype) is associated with tall stature, learning problems, and small testicular size in adolescent boys. Primary ovarian failure, which can be autoimmune or idiopathic in nature, is a rare cause of pubertal delay or pubertal arrest and more commonly causes secondary amenorrhea.

In general the workup for pubertal delay should include a bone age, and morning (8 a.m.) serum LH, FSH, and testosterone or

estradiol. A leuprolide stimulation test, evaluation of the entire pituitary axis, a karyotype and an MRI are useful in some cases. It may be difficult to distinguish between constitutional delay and isolated hypogonadotropic hypogonadism and watchful waiting may be indicated to differentiate between the two conditions.

Short Stature

Short stature is defined as having a height more than 2 standard deviations below the mean for age and sex, whether the cause is physiologic or pathologic. In addition to a thorough history and physical exam, specific areas deserve additional focus. In the history, special attention to any signs or symptoms of systemic disease, the timing of puberty, or use of medications (especially corticosteroids) that may slow growth is warranted. Next, growth curves for both height and weight are invaluable. In general, an adolescent growing along his/her own curve below the fifth percentile is much less concerning that an adolescent whose growth velocity is not keeping pace with his peers and who is crossing percentile lines. Further, in a child with both deceleration in height and weight, endocrine causes typically demonstrate a deceleration in height before weight whereas nutritional causes of poor growth will demonstrate a decline in weight percentiles before a decline is evident in height percentiles. A history of familial heights is useful as height is inherited to a great degree. The mid-parental height is calculated by adding 5 in. to the maternal height and averaging this with the paternal height in boys and, subtracting 5 in. from the paternal height and averaging it with the maternal height in girls. Most children will be within 4 in. (2 S.D.s) of this height, and a predicted adult height (based on current height and bone age) falling outside this range should indicate a need for further evaluation. On physical exam, puberty should be staged since pubertal stage substantially influences growth velocity. Further, measurement of the arm span and upper to lower segment ratio (obtained by measuring from the pubic symphysis to the floor to get the lower segment and subtracting this from the total height for the upper segment) can be helpful in determining if there is disproportionate short stature

(such as with a skeletal dysplasia or spinal irradiation). A bone age, which is an x-ray of the left hand and wrist, is most commonly evaluated according to the standards of Greulich and Pyle (see Reference List) based upon the maturation of the epiphyses and can be useful in calculating a patient's predicted adult height. Laboratory evaluation for short stature can include evaluations for systemic disease such as blood counts, inflammatory markers, and a metabolic panel; thyroid studies; celiac studies; and measures of the growth hormone axis (IGF1 and/or IGFBP3).

Idiopathic Short Stature

Idiopathic Short Stature (ISS) is defined as an adult height prediction below 5′ 3″ for males or 4′ 11″ for females in an otherwise healthy child in the absence of pathological causes for short stature. This includes constitutional delay of growth and puberty (see above) and familial short stature. Familial short stature describes patients who have a family history of short stature and whose heights are appropriate for their parental heights. ISS, including familial short stature but not constitutional delay, is an FDA-approved indication for recombinant human (rh) Growth Hormone (GH) therapy. Therapy is expensive (in tens of thousands of dollars per year), gains are modest (about 2–3″ after years of therapy), and insurance rarely covers this indication. Children with idiopathic short stature are often brought to medical attention because of concerns of quality of life or societal bias against shortness. However, studies of these concerns are contradictory, and overall reassuring that shortness, in the absence of other medical conditions, is not a significant handicap.

Endocrine Causes

GH Deficiency, which may be isolated or associated with broader pituitary abnormalities or intracranial processes, may cause short stature. Children with GH Deficiency tend to have a cherubic appearance because they have increased fat mass and decreased

muscle mass. While growth hormone deficiency is the most common perturbation of the growth hormone axis, disorders of hormonal signaling from the hypothalamus down the entire growth hormone axis to IGF1 signaling have all been implicated in growth disorders. A deficiency of GH is also suspected in Prader–Willi syndrome. Treatment with rhGH leads to a dramatic increase in growth rate in children who are GH deficient. Other endocrine causes of short stature include hypothyroidism and hypercortisolism (Cushing's Syndrome). While growth may be preserved in children with mild hypothyroidism, children with Cushing's Syndrome almost always show attenuation in their growth rate. In both conditions, children have a dramatic plateauing of their growth curves and exhibit catch-up growth once the condition is adequately treated.

Intrinsic or Skeletal Causes

The SHOX gene located in the pseudoautosomal region of sex chromosomes appears to have a dose dependent effect on height, such that girls with Turner Syndrome are short and boys with Klinefelter Syndrome are tall. SHOX mutations cause short stature with or without other skeletal abnormalities such as the Madelung deformity of the wrist, and are an indication for rhGH therapy. Another intrinsic cause of short stature is a mutation in the FGFR3 gene causing hypochondroplasia or achondroplasia. Turner and Noonan Syndromes are both associated with intrinsic short stature and are indications for rhGH therapy.

Systemic Diseases: Short stature may also be secondary to systemic diseases such as renal tubular acidosis, inflammatory bowel disease, celiac disease, cystic fibrosis, malnutrition, or chronic anemias such as Sickle Cell Disease. Children who are small for gestational age and who do not have catch-up growth in the first few years of life leading to short stature also qualify for rhGH therapy.

For the evaluation of a child with short stature, a complete history and an accurate growth chart are invaluable. Measurements of height and comparison with arm span and upper:lower segment

ratios help to differentiate skeletal dysplasias from other causes of short stature. Screening labs for children presenting with short stature include levels of IGF-1, IGFBP3 (especially helpful in very young children, and also thin children who may have low IGF-1 levels from undernutrition), CBC, ESR, Complete Metabolic Panel, Celiac Screening, TSH, fT4 and, in the right clinical setting, prolactin, LH, FSH and estradiol or testosterone levels. A karyotype should be strongly considered in girls. A bone age is helpful for distinguishing between familial short stature and constitutional delay and can aid in predicting the final adult height. The bone age may also be delayed in GH or thyroid hormone deficiency. In the case of a low IGF-1 or IGFBP3, growth hormone testing with provocative stimuli is indicated. Protocols for provocative growth hormone testing vary by institution and many protocols have limited positive predictive value. Random GH levels independent from GH stimulation testing are of limited utility because of its pulsatile nature.

A failed GH stimulation test should prompt an MRI in order to exclude intracranial pathology before initiating rhGH therapy. GH is available by daily injection only and is generally continued until adolescents have completed most of their skeletal growth or until they wish to stop treatment. Risks associated with rhGH therapy include intracranial hypertension, insulin resistance and hyperglycemia, SCFE from the rapid growth, edema, and arthralgias. In adolescent boys who do not qualify for rhGH therapy, aromatase inhibitors, which prevent conversion of testosterone to estrogen, may be used to prevent bone age advancement, thus extending the time available for skeletal growth.

Tall Stature

Tall stature is a rare complaint in adolescents. Constitutional early maturers may have a period of being taller than their peers. Some girls with familial tall stature desire estrogen therapy to close their epiphyses. However, use of high dose estrogen is fraught with side effects and is controversial. In very rare instances, tall stature is secondary to a GH-secreting tumor. These patients often have particularly large hands and feet and a coarsening of their facial

features over time. Screening for a GH-secreting tumor can involve obtaining a random IGF-1 and GH level, followed by GH suppression testing with oral glucose and a brain MRI. Transsphenoidal surgery is considered first-line therapy for GH-secreting adenomas, although recent data suggest improved outcomes with initial use of somatostatin analogues.

Sources

Brook C, Brown R. Handbook of clinical pediatric endocrinology. Hoboken: Wiley-Blackwell; 2008.

Greulich WW, Pyle SI. Radiographic atlas of skeletal development of the hand and wrist. Stanford: Stanford University Press; 1959.

Harrington J, Palmert M. Definition, etiology, and evaluation of precocious puberty. In: Snyder P, Crowley W, Geffner M, editors. UpToDate. Waltham: UpToDate; 2016 (Accessed on September 9, 2016).

Rogol A. Diagnositic approach to children and adolescents with short stature. In: Geffner M, editor. UpToDate. Waltham: UpToDate; 2016 (Accessed on September 9, 2016).

Sperling M, editor. Pediatric endocrinology. 3rd ed. Philadelphia: Saunders; 2008.

Styne D. Pediatric endocrinology. Core handbooks in pediatrics. Philadelphia: Lippincott Williams and Wilkins; 2004.

Part III

Mental Health and Transition of Care

Adolescent Substance Use and Prevention

23

Peter Jackson, Amy Yule, and Timothy Wilens

Introduction

Adolescence is a period of crucial and relatively rapid physical, intellectual, emotional and social development. Adolescents experience normal developmental drives to seek and experience new stimuli and discover personal identity. During this period, brain regions that process reward develop more quickly than the frontal area of the brain in charge of executive functioning oversight such as emotional regulation and impulse control. This normal biological and psychological development represents a key period of increased risk for substance experimentation and use as well as the development of substance use disorders (SUDs). It is well known that the earlier an individual is first exposed to or begins to heavily use substances, the higher the likelihood of progressing to develop a SUD later in life. Early onset SUD also predicts increased severity and prolonged duration of SUD. Pediatricians and other primary care providers, often an adolescent's only point of contact with the healthcare system, have a key role in preventative guidance, screening and detection, and early intervention for problematic substance use.

M.A. Goldstein (ed.), *The MassGeneral Hospital for Children Adolescent Medicine Handbook*, DOI 10.1007/978-3-319-45778-9_23

Prevalence

According to Monitoring the Future (MTF) 1975–2015, the annual prevalence of 12th grade students using illicit drugs was 38 %. Tenth grade students' prevalence was 28 % and 8th grade students' was 15 %. With respect to the use of licit drugs (alcohol and tobacco), 17 % of 12th grade students, 11 % of 10th graders, and 5 % of 8th grade students reported heavy alcohol drinking ("binge drinking") in the past 2 weeks, defined as five alcoholic drinks in a row. Since a peak in the late 90s, there continues to be a steady decline in current tobacco smoking among high school students. The percent of students who smoked tobacco in the past 30 days was 3.6 % of 8th graders, 6.3 % of 10th graders, and 11.4 % of 12th graders, all of which are the lowest percentages since the beginning of the MTF study.

Though many may not have used regularly, statistics of any lifetime use should be kept in mind. As a general estimate, when all adolescents are combined, about one in six have used an illicit drug in the past 30 days, one in four in the past year and one in three have used an illicit drug in their lifetime. One fourth of teens have used alcohol in the past 30 days and almost half have used alcohol in their lifetime. Data from the National Comorbidity Study-Adolescent Supplement (NCS-A) show that about 11 % of adolescents meet criteria for a substance use disorder, with a steep increase in incidence after age 15 (Fig. 23.1).

Risk

Since SUDs know no social, cultural, economic, or geographic bounds, all adolescents should be screened and counseled about substance use. Awareness of risk and protective factors will assist the pediatrician's care for and counsel of preadolescents and adolescents.

Risk factors for adolescent substance abuse are delineated in Table 23.1. At an individual level, youth with psychopathology such as ADHD, mood or conduct disorders are at approximately twice the risk for developing a SUD—with emerging data suggesting

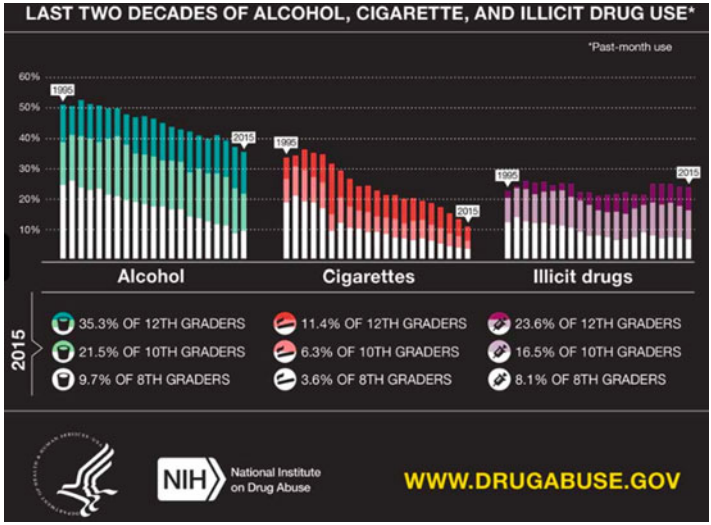


Fig. 23.1 Trends in adolescent alcohol, cigarette, and illicit drug use over the past two decades. (*Source*: National Institute on Drug Abuse, National Institutes of Health, U.S. Department of Health and Human Services. Date from: Monitoring the Future, www.monitoringthefuture.org)

Table 23.1 Risk factors for adolescent substance abuse (Adapted from Hazen et al., 2010)

Domain	Risk factors
Individual	Early aggressive behavior; male gender; untreated psychiatric illness especially ADHD, mood disorders, PTSD, and learning disorder; history of physical or sexual abuse, low self-esteem; academic underachievement; poor social skills; peer rejection
Family	Family history of substance abuse; poor parental or sibling modeling behaviors; chaotic home environment; poor parent–teen communication; high family conflict, or witnessing domestic violence; permissive or neglectful parenting style
Community	High prevalence of substance abuse in the community including availability of substances and tolerance of their use, lack of supportive relationships with other caring adults

ADHD attention deficit, hyperactivity disorder, *PTSD* post-traumatic stress disorder

that continuous treatment of these disorders can reduce the increased risk back to population levels. Children who are from communities with high availability and permissive attitudes towards substance use are also at increased risk for SUD. Counseling these groups as to the enhanced SUD risk and monitoring for cigarette smoking (an early sign of later SUD) or substance use is advised.

Conversely, a number of protective factors exist to reduce SUD risk (Table 23.2). Reminding parents as to the importance of parental modeling and monitoring, pro-social and pro-religious activities, and knowing a youth's peer group all help to mitigate later SUD. Since SUD may start as early as age 10–12 years, it is advised to begin these discussions in fifth grade (prior to middle school).

Risk Factors (Tables 23.1 and 23.2)

Healthcare providers can have an important role in recognizing, asking about, and educating parents and primary caregivers about potential warning signs of substance use. These are outlined in Table 23.3.

Table 23.2 Protective factors against adolescent substance abuse (Adapted from Hazen et al., 2010)

Domain	Factors
Individual	High impulse control and emotion regulation skills
Parents	Positive modeling behaviors; excellent communication skills; high level of emotional support combined with limit setting and consistent enforcement of rules (authoritative model); appropriate supervision
Peers	Non-substance using friends; presence of peers with authoritative parents
Community	Zero-tolerance policies; strong community attachment, low availability of substances
School	Extracurricular activities; sports; positive role modeling in teachers and coaches; educational programming

Table 23.3 Warning signs for the onset of substance use in adolescents

Behavioral	– Academic decline or school truancy
	– Decline in work performance
	– Cessation of extracurricular activities and hobbies
	– Sudden change in peer group
	– Stealing or borrowing more money
	– Sudden changes in appearance, preferred clothing style
	– Violating curfew, sneaking out of the house or other delinquent behavior
Emotional	– Dramatic changes in mood or behavior, including irritability and anger
	– Loss of motivation
	– Increased withdrawal and isolation
	– Periods of unusual hyperactivity
	– Appearing paranoid, anxious or fearful without explanation
Physical	– New onset of lack of attention to hygiene
	– Appearing fatigued or frequent complaining of being tired
	– Sudden changes in appetite or sleep pattern
	– Unexplained injuries/accidents/bruises
	– Bloodshot eyes or frequent nosebleeds
	– Unusual smells on body or clothing, including new heavy use of perfumes or incense

Screening and Brief Intervention

Substance use screening, accompanied by brief interventions, is one of the most essential roles of primary care providers and pediatricians in the prevention/detection of adolescent substance use since they often have a longitudinal relationship with adolescents that is associated with high trust and respect. Recent data show that the juvenile justice system is the most common source of referral to publicly funded substance treatment programs, providing ten times the amount of referrals compared to primary care providers and psychiatrists combined. This suggests a missed opportunity for referrals to be made prior to more severe psychosocial consequences of use.

Multiple nonproprietary tools for screening for substance use have been studied for use with adolescents and were developed to be accurate but quickly administered, given practical demands of a

busy primary care office setting. Among the most commonly used is the CRAFFT, included below. Other validated tools include the two question Alcohol Screening tool developed by the National Institute of Alcohol and Alcoholism (NIAAA), and more recently the Screening to Brief Intervention (S2BI) which includes a single screening question about frequency of past year use for seven different substance categories. It is important to note that all of the above mentioned tools include not only screening questions but recommendations for brief interventions to be done by the pediatric practitioner based on how the screening questions are answered.

The CRAFFT Screening Questions

Part A: During the past 12 months, did the adolescent:

1. Drink any alcohol (more than a few sips)
2. Smoke any marijuana or hashish
3. Use anything else to get high (including illegal drugs, OTC, and prescription drugs) and things that are sniffed or "huffed"

If the adolescent answered NO to ALL three questions, then ask B1 and then stop. If the teen answered yes to any of the three questions, ask B1 through B6.

Part B: During the past 12 months, did the adolescent:

1. Ride in a car driven by someone, including the adolescent who was "high" or had been using alcohol or drugs
2. Did the adolescent ever use alcohol or drugs to relax, feel better, or fit in
3. Did the adolescent ever use alcohol or drugs when alone
4. Did the adolescent ever forget things while using alcohol or drugs
5. Did the adolescent's family or friends ever tell him or her to cut down on drinking or drug use
6. Did the adolescent ever get into trouble while using alcohol or drugs

CRAFFT Interventions:

If the adolescent answers No to A1–3 and No to B1, then praise the teen.

If the adolescent answers No to A1–3 and Yes to B1, ask the teen to avoid riding with a driver using alcohol or drugs.

If the adolescent answers YES to one or more of A1–3, then B1–6 needs to be administered with each Yes answer to B1–6 receiving one point.
If there is a Yes only to B1, then ask the adolescent to avoid riding in a car with a driver who has used drugs or alcohol.
If the CRAFFT score is 0 or 1 using questions B2–B6, then counsel the teen to stop using substances and review how substance use may lead to undesirable outcomes in the social, academic, and health domains; follow up at the next visit.
If the CRAFFT score is 2 or more using questions B2–B6, then further assessment is indicated, including a brief assessment of substance use, follow up in primary care or referral to a treatment program.

Further assessment for substance use may include asking for more history about whether use has caused any problems for the teen, peer use, availability, screening for any other substances used, and if the adolescent has tried to quit and why. Based on the additional information, the pediatrician may decide that further evaluation by another professional is needed. If there appear to be no major problems and the adolescent believes that he/she can change, then arrange a follow-up visit to ascertain if the adolescent has stopped the use of substances.

Physical Exam and Review of Systems

Pediatricians, particularly those working in emergency settings, may be the first point of contact for a teen who is intoxicated. Table 23.4 includes a system-based list of possible signs and symptoms of acute substance ingestion/use.

Laboratory Testing

If an adolescent endorses substance use, objective toxicology testing can be helpful in the assessment for problematic substance use. Even when an adolescent acknowledges substance use, they may be reluctant to disclose the full extent of their substance use

Table 23.4 Symptoms and signs of adolescent substance abuse (adapted from Table 19.3, previous edition)

System	Symptom/sign	Substance
Vital signs	Hypertension	Cocaine, amphetamine, anabolic steroids, LSD, phencyclidine, Ecstasy, ketamine, bath salts
	Hypotension	Opiates, barbiturates
	Tachycardia	Marijuana, cocaine, LSD, amphetamine, ecstasy, ketamine, bath salts
	Hyperthermia	Cocaine, amphetamine, LSD, ecstasy
	Hypothermia	Heroin
Skin	Track marks, abscesses	Intravenous drugs
	Acne, stretch marks	Anabolic steroids
	Itchiness	Opiates
Eyes/nose	Injected conjunctivae	Marijuana
	Dilated pupils	Marijuana, cocaine, amphetamine, LSD, ketamine
	Constricted pupils	Heroin/opiates
	Nystagmus	Benzodiazepines, barbiturates
	Lacrimation	LSD
	Nasal irritation, mucosal erosion	Cocaine, glue sniffing
Heart	Arrhythmia	Heroin, cocaine, amphetamines
		Inhalants, PCP
GI	Constipation	Opiates
	Increased appetite	Marijuana
Neurologic	Hyperreflexia & hyporeflexia	Marijuana, cocaine, amphetamines, bath salts
	Ataxia	Amphetamines, alcohol, psilocybin, ketamine, inhalants
	Seizure	Cocaine, PCP
Mental status	Decreased libido	Anabolic steroids
	Rapid speech	Amphetamines, cocaine, bath salts
	Slurred speech	Alcohol, benzodiazepines, inhalants
	Drowsiness	Marijuana, benzodiazepines
	Hallucinations	LSD, psilocybin, amphetamines, ketamine, inhalants, synthetic marijuana
	Agitation	PCP, amphetamines
	Trance-like state	Salvia divinorum
	Paranoia	Amphetamines
	Rage	Ketamine, PCP
	Flashbacks	PCP, LSD
		Anabolic steroids, cocaine, psilocybin, ketamine

and toxicology testing can be helpful for detection of other substances of misuse or substances that may have been included in the substance that the teen was using that they were unaware of (e.g., laced).

Urine or oral fluid (saliva) samples are generally used for drug testing given a longer window for detection of substance use. Serum toxicology testing can be helpful for detection of substance use when an adolescent presents with an unclear mental status or is acutely intoxicated although it is a more invasive type of testing and is not useful for certain drugs such as cannabis use which is the most common illicit substance used. With all toxicology testing it is important to be aware of what substances are being tested for as well as the test's sensitivity and specificity for each substance tested. For example, unless specified many urine toxicology tests that test for opioids are unable to detect synthetic opioids such as oxycodone or fentanyl. Furthermore adolescents who are reluctant to change their substance use may attempt to adulterate urine toxicology samples through dilution and it is important to assess a urine toxicology sample for validity with a measure of the sample's concentration since an overly dilute sample may be invalid. If there is concern for adulteration or false positive or negative screening tests, it can be helpful to have a sample tested further with more expensive but more specific confirmatory testing through gas chromatography or mass spectrometry. Since oral fluid (saliva) testing obviates the adulteration of urine testing and tends to be more accepted by patients, it may be a more useful tool for toxicology testing in adolescents. Toxicology testing may also be useful for monitoring progress in treatment, such as with quantitative urine toxicology tests for marijuana (cannabis levels).

Determining Severity and Referral to Treatment

The American Academy of Pediatrics (AAP) has identified several stages of use. A pediatrician should be knowledgeable about the spectrum of substance use and appropriate forms of intervention for all stages.

Abstinence: No substance use. This is the period before an adolescent has ever used drugs or had more than a few sips of alcohol. Even in abstinence the pediatrician has an important role in applauding youth for their wise choices and educating parents and teens about risks involved with substance use. There should be clear and consistent reinforcement of a nonuse message.

Experimentation: The first couple of times a teen uses, often prompted by a desire to know how intoxication feels. In this case, pediatricians should promote patient strengths and encourage abstinence through brief, clear medical advice and educational counseling.

Limited Use: Usually occurs with friends on weekends, in lower risk situations and without related problems. Again, providers should promote patient strengths and further encourage cessation through brief, clear medical advice and educational counseling. In addition, pediatricians should thoroughly clarify which substances are being used and should educate about risks inherent even in infrequent use.

Problematic Use: Any use in a high-risk situation, such as when driving or babysitting. Use is associated with problems such as legal charges, school suspension, and fights. Substances may be used to relieve stress or depression. Intervention goals include those listed for limited use but in addition, close follow-up appointment or referral for brief intervention is suggested. At this stage, a provider should consider breaking confidentiality.

Use Disorder: The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V) identifies 11 criteria by which to gauge the severity of substance use. These include: craving, using more or longer than intended, unsuccessful attempts to cut down or quit, excessive time spent obtaining substances, failure to fulfill academic, work or family responsibilities because of substance use, continued use despite recurring problems, stopping or reducing important personal activities because of use (e.g., quitting an athletic team), recurrent substance use in hazardous situations, continued use despite acknowledgement of physical or psychological

problems associated with use, tolerance (diminished physical effect of the same dose or needing a higher dose to achieve desired effects), and withdrawal. A substance use disorder is considered mild if two or three of the criteria are met within the same year, and a moderate substance use disorder is present when 4–5 criteria are met. Intervention goals for a mild or moderate substance use disorder in addition to those mentioned above should include brief motivational enhancement through exploration of ambivalence. These adolescents should be referred for a comprehensive assessment and treatment in a subspecialty clinic. Providers should strongly consider breaking confidentiality and monitor for progression to severe use disorders.

Severe Use Disorder: Six or more of the above criteria indicate a severe substance use disorder. At this stage, pediatricians should make a referral to subspecialty treatment and work to enhance motivation to accept such a referral. Providers should strongly consider breaking confidentiality and parental involvement is strongly encouraged.

Additional red flags for which to consider breaking confidentiality with family and/or make a referral to treatment, regardless of stage of use:

- Any intravenous (IV) drug use
- Prescription medication misuse
- Cocaine, heroin, or methamphetamine use more than once
- CRAFFT score >2 in an adolescent 14 years or younger
- CRAFFT score of 5 or higher
- Daily or near daily use of any substance
- Alcohol-related blackouts
- Change in medical status resulting from substance use (e.g., passing out from use, any physical problem requiring medical attention)

Adolescents that have been identified as misusing substances should have a complete psychosocial history, physical examination, and mental status evaluation as there may be a dual psychiatric diagnosis along with the SUD. In fact, data suggests that nine

out of ten adolescents with a SUD have a comorbid psychiatric disorder (e.g., attention-deficit hyperactivity, mood, anxiety, and/or conduct disorders).

Licit Drugs

Tobacco

It is known that delaying an adolescent's use of tobacco until at least age 18 will significantly decrease the chance that the teen will become an established smoker. Most teens who try tobacco smoke their first cigarette between ages 14 and 15 and become regular users between 16 and 17 years. Most teens are in a trajectory from early users of tobacco to tobacco addiction when initially screened by the clinician.

Pediatricians should be comfortable with strategies to reduce tobacco use in adolescents (and their parents) by screening for tobacco use and intervening if tobacco use is detected. The following is a brief scheme with more details in the reference (Pbert et al.):

ASK: if the teen uses tobacco; if no, then congratulate and encourage abstinence; if yes, then
ADVISE: the teen to quit and offer the teen your help
ASSESS: will the teen make a quit attempt in the next 30 days—if no, then provide motivational intervention. If yes, then
ASSIST: in helping the teen to quit tobacco by helping to develop a quit plan, giving key advice to successful quitting and consider the use of pharmacologic treatment.
ARRANGE: for follow-up; that may include referring the teen to intensive services and reviewing the teen's progress in quitting.

Tobacco cessation methods consist of behavioral interventions, pharmacologic treatments, or a combination. The reference section has a citation and website (Fiore et al.) endorsed by the American Academy of Pediatrics for treatment of tobacco use and dependence. Successful behavioral programs have the following qualities: easy accessibility, adolescent friendly and adolescent specific, and provision of ongoing support to teens trying to quit tobacco.

Alcohol

Widely used by adolescents, alcohol is a rapidly absorbed CNS depressant. At mild levels, euphoria and disinhibition occur, at moderate levels there is sedation, ataxia, and slurred speech, and at high levels there may be coma, respiratory depression, and death. Motor vehicle accidents, violence, traumatic experiences, and other injuries may occur secondary to use. The best acute tests for alcohol intoxication are a breathalyzer or blood alcohol level. Adolescents who require medical care for intoxication need follow-up and referral for appropriate counseling.

Illicit Drugs

Marijuana

This is the most commonly used illicit drug in adolescence, generally by smoking and less commonly by vaporization of marijuana concentrates (oil, dabs, wax, shatter) or by ingestion of the whole plant matter. Effects include euphoria, time distortion, and memory issues. At higher levels, teens may encounter anxiety, panic, or hallucinations. There is no clear lethal potential from the drug itself, but injuries occur from the drug's effects on the user's behavior. Marijuana is detectable in the urine or saliva up to 2 weeks after an acute exposure and up to 6 weeks after heavy, chronic use. Quantitative urine monitoring is available to guide a clinician in estimating the amount and frequency of marijuana use and to monitor treatment. See below for a discussion on medical marijuana.

Prescription Drugs

Prescription drug misuse is second to marijuana as the most frequently misused class of agents by adolescents. For instance, prescription pain killers, followed by sedatives (benzodiazepines) and stimulants (e.g., mixed amphetamine salts) are used by approximately one in ten teens in the past year. Data indicate that three-quarters of teens locate prescription medications from friends or family (e.g., medicine cabinet, old prescriptions not being used or monitored). It is strongly advised that parents be

advised to turn back or dispose of all controlled substances no longer being used, and lock up any controlled substances they or their children are currently taking.

Opiates

These include the illicit drug heroin as well as prescription morphine, oxycodone, methadone, hydromorphone, and others—that can be obtained in an illicit manner. Opiates may be taken by a variety of routes. Effects include euphoria, sedation, diminished reflexes, analgesia, and somnolence. Overdose can cause cardiorespiratory arrest and death. Teens may start with prescription drugs but then because of lack of availability or cost, transition to using heroin. Heroin is detectable for 24 h in the urine; other opiates are detectable for 2–3 days. Some synthetic opiates are not detectable in the urine.

Depressants

Barbiturates and benzodiazepines may be very short, short, intermediate, or long acting in their effects. They produce sedation, drowsiness, fatigue, and euphoria and can depress the vital signs. Barbiturates are a common cause of fatal accidental overdose in young individuals; benzodiazepines are less lethal than barbiturates and more commonly misused. Both barbiturates and benzodiazepines are detectable in the blood and urine and both classes include a range of short acting to long acting agents which influences the time frame for positive urine screen. For barbiturates the range is 3–15 days and for benzodiazepines the range is 2–10 days.

Amphetamines (Speed)

This group includes licit medication such as (dextro)amphetamine, or methylphenidate and illicit substances such as crystal meth (methamphetamine). Amphetamines produce CNS stimulation with effects of euphoria, alertness, reduced fatigue, insomnia, panic, and occasionally hallucinations. Data suggest that young people who misuse stimulants often have other substance use disorders and/or neuropsychological deficits. In overdose, coma, circulatory collapse, arrhythmias, and stroke may occur. Crash may occur with a withdrawal syndrome seen also in cocaine. Amphetamines are detectable in the urine for up to 3 days.

Cocaine

The two chemical forms include the powdered, salt form which is snorted or injected intravenously and the water insoluble base ("freebase" or "crack"), which is smoked. Use leads to CNS and peripheral nervous system stimulation. Effects include anxiety, agitation, paranoia, delirium, and hallucinations. Cocaine is detectable in the urine for less than 24 h but the main metabolite, benzoylecgonine, is often screened for and will be positive for up to 5 days after use. Complications of cocaine use may include erosion of the nasal septum. Crack has shown a higher potential for addiction given a more immediate onset of effects.

Hallucinogens (e.g., LSD, Salvia, Mushrooms, PCP, Ketamine)

These drugs produce alterations in perception, dissociation, loss of time sense, depersonalization, body image changes, illusions, and hallucinations. Teen may present with restlessness, paranoia, and anxiety. LSD is detectable in the urine for less than a day but a metabolite can be tested for up to 5 days. PCP can be detected in urine for up to 8 days. Flashbacks may occur.

Inhalants

These drugs are more commonly used among young male adolescents often in group activities. Forms include model airplane glue, rubber cement, correction fluid, paint thinner, gasoline, butane, and aerosol propellants. Effects include euphoria, giddiness, impaired judgment, and drowsiness. Hallucinations and psychosis have been reported. Use of plastic bags or tents to enhance inhalation has produced fatalities. These drugs are not detectable in the urine or blood, but examination may show a rash on the face, odor to the teen's breath, or eye irritation.

Club Drugs

These include MDMA, ketamine, GHB, and rohypnol, which are termed "club drugs" because they are often used in social gatherings. MDMA (ecstasy) can produce euphoria, calm and an increase in perception and empathy. Ketamine (Special K) produces a disconnected feeling, pain relief, and visual hallucinations. Flashbacks may occur after long-term use. GHB (liquid ecstasy) produces

euphoria, relaxation, and drowsiness; it has the potential to suppress pulse, blood pressure, and respiration. It may be used by body builders to increase muscle mass; some have used it as a "date rape" drug. Rohypnol (roofies) is an illegal fast acting benzodiazepine that may lead to physical dependence; it has been used as a date rape drug.

Designer Drugs

These compounds are chemically synthesized with a goal to mimic the highs produced by other drugs but can have even more dangerous side effects and often evade detection on drug screens. Commonly marketed as "Spice" or "K2," synthetic marijuana can produce psychosis, stroke, heart attack, or kidney damage. "Bath Salts" (bloom, flakka, Ivory wave, vanilla sky, cloud nine), named for their physical resemblance to Epsom salts, contain a synthetic chemical related to the stimulant cathinone and seek to mimic the euphoria and energetic high produced by amphetamines or cocaine. These can lead to dangerous physiological excitation including hyperthermia, dehydration, muscle breakdown, and kidney failure as well as excited delirium. NBOMes is a synthetic hallucinogen meant to mimic the high of LSD but which has been associated with self-inflicted violence, paranoia, delirium, and seizures. As designer drugs are identified, made illegal, and added to drug screening panels, other synthesized compounds emerge with slight chemical alterations and with significant unknowns and associated risks.

Performance Enhancing Drugs

These substances are used to enhance performance or to improve body image. There are pharmacologic agents (such as methylphenidate) for studying, agents to reduce weight (such as diuretics, laxatives, or stimulants), nutritional supplements, blood doping, OTC agents to increase muscle mass (such as creatine) and human growth hormones and anabolic steroids. The use of performance enhancing drugs should be strongly discouraged in adolescents by pediatricians, parents, schools, and other sports organizations. Serious side effects may occur from their use especially with anabolic steroids, human growth hormone, laxatives, and diuretics (Table 23.5).

Table 23.5 Additional information on drugs commonly used by adolescents

Substance	Street names	Neurobiological effects	Signs and symptoms of intoxication	Withdrawal symptoms	Comments
Alcohol		Central CNS depressant via potentiation of GABA effect at GABA-A receptors	Euphoria and disinhibition at low levels, sedation, ataxia, and slurred speech at higher levels	Tremor, anxiety, insomnia, transient hallucinations; severe forms include seizure, autonomic instability, delirium	– Rates of use are additionally elevated among college enrollees – Advise about risk of even single episodes of binge drinking
Tobacco	Bidis, hookahs, snuff, chew	CNS stimulant via activation of nicotinic receptors	Elevated blood pressure, respiratory rate, and heart rate	Irritability, insomnia, inattention, increased appetite	– As cigarette smoking has steadily declined, e-cigarette use among adolescents is on the rise – Important to ask about chewing tobacco and not just smoking
Marijuana	Weed, hash, joint, bud, dope, reefer, grass, hemp	Main active ingredient, THC, binds to cannabinoid receptors throughout the brain (CB1>CB2)	Enhanced sensory perception and euphoria followed by drowsiness, increased appetite, slowed reaction time and impaired coordination; hallucinations, anxiety, panic, and psychosis at higher doses	Irritability, insomnia, decreased appetite, anxiety	– Possible loss of IQ points with early, repeated use – Most commonly used illicit drug by teens, nearly 50% of 12th graders have used it – Used in concentrated forms (hash or honey oil, wax or "budder," "shatter" which can deliver much higher amounts of THC per use

(continued)

Table 23.5 (continued)

Substance	Street names	Neurobiological effects	Signs and symptoms of intoxication	Withdrawal symptoms	Comments
Prescription stimulants	Speed, Uppers, MPH, The smart drug, black beauties	Central CNS stimulants	Alertness, increased energy, increased BP and pulse, hyperthermia	Depression, tiredness, sleep problems	– Most commonly misused drug is Adderall – Often associated with other SUD, academic decline
Prescription opioids	Many names depending on drug	Opioid agonists at the mu-opioid receptor	Euphoria, drowsiness, diminished reflexes respiratory depression	Body aches, restlessness, diarrhea, chills	– Most commonly used are Vicodin and OxyContin – Risk for progression to heroin use – Advise family members to dispose of old/unused prescriptions
Inhalants (aerosols, paint thinner, gasoline, permanent markers, glue, nitrous oxide)	Whippets, poppers, snappers, laughing gas	Generally, CNS depressants. Nitrates lead to vasodilation	Euphoria, giddiness, somnolence, confusion, disinhibition, slurred speech, dizziness	Nausea, loss of appetite, mood swings, sweating, tics	– More commonly used by younger adolescents – Facial rash or eye irritation
Synthetic cannabinoids	K2, spice, incense, black mamba, fire, skunk, yucatan, fake weed	Bind to cannabinoid receptors, often more strongly than THC	Tachycardia, agitation, confusion, anxiety, paranoia, increased blood pressure	Headache, depression, anxiety, irritability	– Persistent withdrawal symptoms not uncommon in users – Chemical composition of many products is unknown and they can produce unpredictable health effects

Cough medicine (Dextromethorphan or DXM) (codeine)	Triple C, robo, robotripping	Opioid-like actions	Euphoria, dissociation, slurred speech, increased BP and pulse	Unknown	– Consider effects of other ingredients as well, i.e., antihistamines
Prescription Tranquilizers/Sedative hypnotics	Candy, downers, tranks	Prominent GABA effects	Drowsiness, sedation, amnesia, impaired coordination and reaction time, confusion, respiratory depression	Headache, tension, anxiety, restlessness, numbness in hands and feet, hallucinations, seizures, delirium	– Withdrawal can be dangerous, detox/taper requires medical supervision – Some in this category, i.e., Rohypnol (flunitrazepam), are used as date rape drugs – Increased concern for overdose when used with alcohol
MDMA (Ecstasy)	Molly, Adam, Eve, Lover's speed, peace, uppers, "E"	Mixed serotonin and norepinephrine/ Dopamine effects, additional increase in serotonin release compared to amphetamines	Enhanced sensory perception, disinhibition, increased BP and pulse, bruxism, confusion, hyperthermia, dehydration	Fatigue, loss of appetite, depression, poor concentration	– Molly often contains more methamphetamine constituent – Other adulterants frequently found in tablets include cocaine, caffeine, ephedrine

(continued)

Table 23.5 (continued)

Substance	Street names	Neurobiological effects	Signs and symptoms of intoxication	Withdrawal symptoms	Comments
Hallucinogens – Classic: LSD, psilocybin, Peyote, DMT, ayahuasca – Dissociative Drugs: PCP Ketamine, DXM, Salvia	Acid, angel dust, vitamin K, shrooms	Prominent serotonergic properties, particularly in the prefrontal cortex. Dissociative drugs disrupt glutamate activity at NMDA receptors	Varied effects depending on drug used, visual, auditory and tactile hallucinations, nightmares, increased energy, tachycardia, psychosis	Varied effects depending on drug used, commonly includes headache, sweating	– Long-term effects can include persistent psychosis or perceptual disturbances
Heroin	Dope, junk, skunk, white horse, china white, brown sugar	Direct mu-opioid receptor agonist	Euphoria, constricted pupils, alternating wakefulness and drowsiness, clouded thinking, itching, slowed respiratory rate and heart rate	Restlessness, body aches, diarrhea, vomiting, chills, restless legs, insomnia	– Often preceded by prescription opioid use – Overdose antidote is intranasal naloxone – Buprenorphine and Naltrexone are approved treatments for older adolescents
Cocaine	Coke, crack, rock, blow, bump, snow, flake, charlie	Blockade of the dopamine transporter, preventing reuptake of dopamine into the presynaptic neuron	Increased energy, euphoria, enlarged pupils, hypertension, hyperthermia, headache, aggression, paranoia, psychosis	Fatigue, insomnia, restlessness, depression, increased appetite, vivid nightmares	– Risk of stroke, myocardial infarction or bowel infarction given vasoconstriction

CNS central nervous system, *GABA* gamma-aminobutyric acid, *THC* tetrahydrocannabidiol, *CB* cannabinoid, *BP* blood pressure, *NMDA* *N*-methyl-D-aspartate

Additional Recent Considerations

E-Cigarettes

Although there has been a decline in tobacco smoking, there has been a recent increase in the use of electronic cigarettes in adolescents. In 8th, 10th, and 12th graders, e-cigarettes are used more often (more than twice as often for 8th and 10th graders) than any other tobacco product, including cigarettes. Though most teens report only using flavoring, e-cigarettes are not regulated so those liquids might contain nicotine. The American Academy of Pediatrics issued a 2015 policy statement opposing any use of e-cigarettes for any purpose, pointing out the absence of supportive data that e-cigarettes can assist with smoking cessation. They encourage a ban on any internet sale of e-cigarettes, any sale to persons under age 21 and a ban on any flavoring in e-cigarettes or advertisement viewable by youth.

Medical Marijuana

In its most recent policy statement (2015), the American Academy of Pediatrics (AAP) reaffirmed its opposition to the legalization of marijuana for recreational purposes as well as opposition to any use of "medical marijuana" outside the regulatory process of the Food and Drug Administration. The AAP also supports the decriminalization of marijuana for adolescents and young adults and a change in schedule classification (from schedule I to schedule II) to support research and development of pharmaceutical cannabinoids.

Perceived risk is strongly impacted by efforts to legalize marijuana for both medicinal and recreational purposes. Nearly 70 % of high school seniors do not see regular marijuana use as harmful. Year after year, amount of use and perception and harm have been inversely proportional among adolescents. The potential benefits for life-limiting or debilitating conditions in pediatric groups appear to be more related to the action of cannabidiol (CBD, another active substrate of the plant; e.g., stimulants) rather than THC. Of concern, there are a number of studies that show persistent cognitive and brain functioning and structural changes in teens who beginning smoking marijuana heavily prior to age 16 years. Clearly more research is necessary.

Useful Clinical Resources

- National Institute on Drug Abuse. www.drugabuse.gov
- National institute on Alcohol Abuse and Alcoholism. www.niaaa.nih.gov
- Substance Abuse and Mental Health Services Administration. www.samhsa.gov
- www.monitoringthefuture.org

Sources

American Academy of Pediatrics, Committee on Substance Use and Prevention. Use of performance-enhancing substances. Pediatrics. 2005;115:1103–6.

American Academy of Pediatrics, Committee on Substance Use and Prevention. Substance use screening, brief intervention, and referral to treatment for pediatricians. Pediatrics. 2011;128(5):e1330–40.

American Academy of Pediatrics, Committee on Substance Use and Prevention. Testing for drugs of abuse in children and adolescents. Pediatrics. 2014;133:305–7.

American Academy of Pediatrics, Committee on Substance Use and Prevention. Adolescent drug testing policies in schools. Pediatrics. 2015;119(3):627.

Fiore MC, Jaen CR, Baker TB, et al. Treating tobacco use and dependence: 2008 update-clinical practice guideline. Rockville: Public Health Service, US Department of Health and Human Services; 2008. http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=hstat2.chapter.28163

Hawkins JD, Catalano RF, Miller JY. Risk and protective factors for alcohol and other drug problems in adolescence and early adulthood: implications for substance use prevention. Psychol Bull. 1992;112(1):64–105.

Hazen EP, Goldstein MA, Goldstein MC. Mental health disorders in adolescents: a guide for parents, teachers, and clinicians. Piscataway: Rutgers University Press; 2010.

Johnston LD, O'Malley PM, Miech RA, et al. Monitoring the future national survey results on drug use, 1975–2015: overview, key findings on adolescent drug use. Ann Arbor: Institute for Social Research, The University of Michigan; 2016.

Kilpatrick DG, Acierno R, Saunders B, et al. Risk factors for adolescent substance abuse and dependence: data from a national sample. J Consult Clin Psychol. 2000;68(1):19–30.

Klein JD, Camenga DR. Tobacco prevention and cessation in pediatric patients. Pediatr Rev. 2004;25:17–26.

Levy S, Weiss R, Sherriff L, et al. An electronic screen for triaging adolescent substance use by risk levels. JAMA Pediatr. 2014;168(9):822–8.

Massachusetts Department of Public Health Bureau of Substance Abuse Services. Provider guide: adolescent screening, brief intervention, and referral to treatment using the CRAFFT screening tool. Boston: Massachusetts Department of Public Health; 2009.

Merikangas K, He J, Burnstein M, et al. Lifetime prevalence of mental disorders in US adolescents: results from the national comorbidity study-adolescent supplement (NCS-A). J Am Acad Child Adolesc Psychiatry. 2010;49(10):980–9.

National Institute of Alcohol Abuse and Alcoholism. Alcohol screening and brief intervention for youth: a practitioner's guide. http://www.niaaa.nih.gov; 2015

Pbert L, Moolchan ET, Muramoto MD, et al. The state of office-base interventions for youth tobacco use. Pediatrics. 2003;111:e6650–60.

Toumbourou JW, Stockwell T, Neighbors C, et al. Interventions to reduce harm associated with adolescent substance use. Lancet. 2007;369:1391–401.

Adolescent Mental Health Disorders

24

Michelle Chaney, Suni Jani, Julia Shekunov, and Tanishia Choice

The occurrence of mental health disorders in adolescents is common with lifetime prevalence of any disorder being 46.3 % among 13–18 year olds. The most frequent diagnoses are ADHD followed by depression and other mood disorders. The majority of these conditions is mild to moderate in severity and can be managed in the outpatient setting. Despite the high frequency of mental health disorders in adolescents and their generally straightforward course, many such adolescents go without adequate treatment. One of the biggest factors inhibiting access to treatment is the limited number of child and adolescent psychiatrists. Recent estimates show that there are only 6449 active child psychiatrists involved in patient care and nearly seven million children and adolescents in need of mental health care. In contrast, there are 49,000 active pediatricians involved in patient care, often making pediatricians the "front line" for screening, diagnosing, and managing many of these children and adolescents. This chapter will review evaluation and management strategies of the three most common mental health disorders seen in adolescents in primary care. Appropriate treatment strategies of these disorders in primary care and criteria for referral to specialized mental health care treatment will also be discussed.

M.A. Goldstein (ed.), *The MassGeneral Hospital for Children Adolescent Medicine Handbook*, DOI 10.1007/978-3-319-45778-9_24

ADHD

Attention-deficit/hyperactivity disorder (ADHD) is one of the most common childhood psychiatric illnesses, often persisting through adolescence into adulthood. Medications are the mainstay of evidence-based treatment and can significantly improve symptoms and functioning. Nonpharmacological approaches including behavioral interventions can be important adjuncts to medications.

Prevalence

ADHD is estimated to affect 7–8 % of school-aged children in the United States. The majority (60–85 %) of children with ADHD will continue to meet criteria for the disorder as teenagers. Boys (ages 8–15 years) are estimated to have a 2.1 times greater prevalence of ADHD than girls. It is important to note that in clinical samples, there may be up to a 10:1 overrepresentation of boys to girls: boys more commonly have disruptive behavior and therefore are more likely to come to the attention of clinicians than girls, who more often have inattentive symptoms.

Evaluation

The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), defines ADHD as a cognitive and behavioral syndrome characterized by varying expressions of hyperactivity, impulsivity, and inattention that is functionally impairing in at least two settings (e.g., both in school and at home; with immediate and extended family members). There are three subtypes of ADHD: inattentive, hyperactive-impulsive, and combined inattentive and hyperactive-impulsive. To meet diagnostic criteria for the ADHD subtypes, children must have at least six symptoms from either the hyperactivity/impulsivity group or the inattention group of criteria (or six symptoms each

from both groups if ADHD, combined type), while adolescents and those over age 17 must have at least five symptoms. Onset of functionally impairing symptoms must occur before age 12 (this is a change from the DSM-IV in which age of onset was before age 7). Inattention is characterized by having trouble holding attention; being easily distracted; forgetful; making careless mistakes or failing to pay close attention to details; seeming to not listen; having trouble organizing tasks and activities; frequently losing things such as keys, glasses, or homework; avoiding or disliking tasks that require mental effort over a period of time; and not following through on instructions or tasks. Hyperactivity includes fidgeting, tapping, or squirming; talking excessively; being unable to stay in one's seat; and running around or climbing in inappropriate situations. Impulsivity may include interrupting or intruding on others, blurting out answers before a question has been completed, and being unable to wait for his or her turn. Adolescents (and adults) are less likely to exhibit overt hyperactive behaviors and are more likely to acknowledge feeling restless. Poor executive functioning often manifests as deficits in planning and organization (i.e., leaving homework at home; not starting a big project until close to due date) and goes hand in hand with the above mentioned core deficits in ADHD.

Evaluation of adolescents may be more difficult than assessing younger children for ADHD as adolescents are more likely to minimize problematic behaviors and their parents typically have fewer opportunities to closely observe their adolescent's behavior compared to younger children. In addition to asking the patient and parent about ADHD symptoms, it is helpful to use a standardized rating scale that is completed separately by parent(s), teacher(s), and the adolescent. Commonly used rating scales for ADHD include the Conner's Rating Scales (for parents, teachers, and adolescent self-report) and the Vanderbilt ADHD Diagnostic Parent and Teacher Scales. The Vanderbilt ADHD scales are freely available and include screening questions for all 18 symptoms of ADHD. A positive diagnostic screen includes 6/9 hyperactive-impulsive symptoms and/or 6/9

inattentive symptoms occurring often or very often. It is important to note that ADHD symptoms may be more explicit in situations requiring sustained mental effort or unstructured or boring environments. In these environments, the child is unable to regulate attention well enough to perform at a level that is typical for the child's age and development. In contexts where there is constant stimulation (such as watching TV or playing video games) or in environments where there are few distractions (i.e., small group settings, the doctor's office) ADHD symptoms may be less prominent.

Many adolescents are diagnosed with ADHD in childhood and as they grow older, dose adjustments or further optimization of their ADHD treatment may be needed. Adolescents without a prior diagnosis of ADHD should be carefully evaluated for symptoms beginning in their childhood that may have been missed at the time. It is not uncommon, however, for ADHD symptoms to present in later years with increasing demands in academic work coupled with decreased tolerance for poor organizational skills and disruptive behaviors. Important diagnoses to consider with ADHD include disruptive behavior disorders (oppositional defiant disorder, conduct disorder), mood and anxiety disorders, learning disabilities, borderline intellectual functioning, substance use disorders, and sleep disorders. All of these disorders can mimic ADHD, worsen ADHD, or be comorbid with ADHD. The Vanderbilt ADHD scales also screen for disruptive behavior disorders. Additional screening tools can be used if there is concern for anxiety and mood disorders or for substance use disorders (see relevant sections of this handbook for more information on those screening tools).

Neuropsychological testing can be obtained if there is concern for learning disabilities or borderline intellectual functioning. Estimates show that 31–45 % of children with ADHD having a learning disorder. An important role of the pediatrician can be to educate the patient and family about their right to request testing through the school and to serve as an advocate for the patient and family as they navigate the school system. This may sometimes entail writing a letter to the patient's school detailing the pediatrician's concerns about a possible learning disorder and recommending academic testing. Based on testing results, the school

will determine whether the child is eligible for an individualized education plan (IEP); a written contract detailing specific services, accommodations, goals, and measurable outcomes for the child. In some cases, a child will not qualify for an IEP but may be eligible for a 504 plan, which may include accommodations such as longer time on tests, classroom seating adjustments, and homework modifications. An IEP or 504 plan can be provided for a child with learning disabilities or with emotional disabilities such as ADHD, anxiety, or depression.

Management

Untreated ADHD can have far-reaching consequences beyond the adolescent and their family, given the widespread effects of stress on relationships, decreased functioning at school and later in life, decreased productivity at work, and overall increased health costs.

Management of ADHD should include psychoeducation about the disorder and treatment options as well as linkage with community supports and additional school resources if appropriate. Treatment options include both pharmacological and behavior therapies, although pharmacological interventions have consistently been found to be more effective than behavioral treatments alone. In certain clinical situations, however, behavior therapy alone could be pursued, for example, in younger children when the diagnosis of ADHD is uncertain, if there is disagreement between parents or between parents and teachers about the diagnosis of ADHD, or if parents reject medication treatment and the patient's symptoms are mild with minimal impairment in functioning. A number of behavioral programs have been developed, primarily providing parent guidance in 10–20 one hour sessions, with occasional booster sessions after completion of the sessions. There is little evidence to support other nonpharmacological interventions.

In adolescents, pharmacotherapy with stimulants is the mainstay of evidence-based ADHD treatment. The FDA has approved two groups of stimulants—methylphenidates and amphetamine-derived compounds—for the treatment of ADHD in the pediatric population (See Table 24.1). Both classes of stimulants have equal efficacy in treating ADHD and are available in branded and generic

Table 24.1 Medications for ADHD

Class/name	Duration	Dosing	Notes
Methylphenidates			
Short-acting		Max 2 mg/kg or 60 mg/day	
Ritalin	3–5 h	Start at 2.5 mg, increase by 5 mg/week	Crushable, Methylin available in liquid and chewable tabs
Methylin			
Focalin	4–6 h	Start at 5 mg, increase by 5 mg/week	D-isomer only; for conversion, use half the dose of other methylphenidates, e.g., Focalin 5 mg BID=Ritalin IR 10 mg BID
Intermediate acting		Max 2 mg/kg or 60 mg/day	
Ritalin SR	5–8 h	Start at 10 mg daily	Cannot crush
Metadate ER	5–8 h	Start at 10 mg daily	
Metadate CD	7–8 h	Start at 10 mg daily, increase by 10 mg	Capsule can be opened and sprinkled or dissolved; beads in a 30:70 ratio with 30 % released immediately and the rest 3 h later
Ritalin LA	8–10 h	Start at 20 mg daily; increase by 10 mg	Capsule with 1:1 ratio of immediate release to delayed release beads, can be opened and sprinkled or dissolved
Long acting			
Focalin XR	10–12 h	Start at 5–10 mg daily, can increase by 5–10 mg/week, max 1 mg/kg or 30 mg/day	Beads in 50:50 ratio, capsule can be opened and sprinkled or dissolved; for conversion note that Focalin XR 10 mg=Focalin 5 mg BID=Ritalin IR 10 mg BID
Daytrana	Up to 12 h (90 min to start working, remove after 9 h)	Start at 10 mg patch daily; can increase weekly, patch dose usually less than equivalent Ritalin dose as no first-pass metabolism. Max 30 mg/day	May have more frequent anorexia, insomnia, tics, mild skin reaction (rotate placement), or rare permanent skin color changes. Olive oil can help remove adhesive; if edema/erythema at site, consider tea tree oil; if itchy, consider nonsedating antihistamine

Concerta	10–12 h	Start 18 mg daily, can increase by 18 mg per week; max doe: 72 mg daily	Osmotic delivery releases drug slowly, must be swallowed whole. When cross tapering, use higher dose of Concerta as not all of drug is released from OROS sponge, e.g., Concerta 18 mg = Ritalin IR 15 mg total daily dose
Quillivant XR	Up to 12 h	Start 20 mg daily, titrate by 10–20 mg max dose: 60 mg daily	Liquid-only formulation (25 mg/5 mL)
Amphetamines			
Short acting			
Dexedrine	4–6 h	Start at 5 mg daily, increase by 10 mg/week	Available in tablets or liquid
Adderall	4–6 h	Start at 2.5 mg–5 mg daily, increase by 5 mg/week	Can be crushed
Long acting			
Dexedrine spansule	6–8 h	Start at 5 mg daily, increase by 5–10 mg/week	Can be sprinkled
Adderall XR	8–12 h	Start at 10 mg daily, increase by 5–10 mg/week	Beads with 50 % released immediately, 50 % in 4 h; can be sprinkled
Vyvanse	8–12 h	Start at 20–30 mg daily	Pro-drug and requires metabolic cleaving to release active drug; less abuse potential
Nonstimulants			
Atomoxetine (Strattera)	24-h	Start 0.5 mg/kg/day × 1 week then gradually increase. Max dose 1.4 mg/kg/day	Requires 2–6 weeks to see effect; can help with comorbid anxiety; FDA black box warning for suicidal thoughts

(continued)

Table 24.1 (continued)

Class/name	Duration	Dosing	Notes
Bupropion (Wellbutrin; off-label for ADHD)	24-h	Sustained release—start 100 mg daily; increase by 100 mg q1 week as needed; dosed BID; max dose 400 mg Extended release—start 150 mg daily and increase by 150 mg q3 weeks if needed; max dose 450 mg	Can treat comorbid depression (off-label use); contraindicated in seizure disorders and eating disorders; FDA black box warning for suicidal thoughts
Alpha-agonists	Taper when stopping to avoid rebound hypertension		
Clonidine	4-h immediate release; 12 h extended release	Catapres (immediate release)—start at 0.05 mg daily, increase by 0.05 mg q4–5 days to max 0.3 mg (divided TID-QID) Kapvay (extended release)—start at 0.1 mg hs, increase to 0.1 mg BID to max 0.2 mg BID	Sedating; may help tics; may lower blood pressure
Guanfacine	4–6 h immediate release; 24-h extended release	Immediate release: start at 0.5 mg daily, increase by 0.5 mg q4–5 days to max 4 mg divided BID Intuniv (extended release): start at 1 mg and increase by 1 mg weekly	Less sedating than clonidine; may help with aggression; may lower blood pressure

formulations. Before prescribing a stimulant, the American Heart Association (AHA) and the American Academy of Pediatrics (AAP) recommend careful physical examination and assessment of patient and family histories of sudden death, palpitations/arrhythmias, syncope, hypertrophic cardiomyopathy, long QT syndrome, and other cardiac disease. Any concern for underlying heart disease should prompt a cardiac workup prior to prescribing a stimulant. Routine electrocardiograms are not recommended by the AAP or the American Academy of Child and Adolescent Psychiatry (AACAP).

Factors in choosing a stimulant include a prescriber's experience and comfort with particular medications, insurance formulary considerations, consideration of efficacy and side effects in past medication trials, feasibility of dosing more than once a day, risk of diversion, and inability to tolerate swallowing pills. Starting with a longer acting formulation is generally the preferred strategy, although it is important to keep in mind that addition of a short-acting stimulant (typically in the same class) later in the day may be necessary as the initial dose of stimulant medication wears off. Initiation is typically at the lowest dose with steady titration (often at 1-week intervals) until an adequate response is achieved. It is usually best to maximize the morning dose of a long-acting formulation before adding a dose of short-acting stimulant in the afternoon for breakthrough symptoms.

Several formulations, in particular, are less likely to be successfully used recreationally and therefore come with less risk of drug diversion. These include transdermal methylphenidate (Daytrana), the inactive prodrug lisdexamfetamine (Vyvanse), which becomes active once hydrolyzed in the gastrointestinal tract, and osmotic release oral system (OROS) methylphenidate (Concerta). The OROS uses an osmotic pump mechanism to create an ascending profile of methylphenidate in the blood and is nearly impossible to be crushed or for methylphenidate to be extracted.

Common side effects of treatment with stimulants include delayed sleep onset, headaches, appetite suppression, abdominal discomfort, and behavioral rebound (the sudden and pronounced recurrence of ADHD symptoms as the medication is wearing off). Less common side effects include mood changes such as dysphoria,

irritability or anxiety, elevated blood pressure and heart rate, and very rarely, priapism. Transient motor tics may emerge with stimulant treatment and these often resolve once medication is stopped or as the dose wears off. Stimulants may uncover or exacerbate an underlying tic disorder (Tourette's Disorder often co-occurs with ADHD) and depending on severity of the tics, nonstimulant treatment options may be necessary. Families will often ask if stimulants can be held on weekends or over the summer. This is best determined on a case-by-case basis and keeping in mind that ADHD symptoms often extend beyond school and work, affecting family and social functioning. Outside of school, adolescents are often engaged in activities (such as driving, working, babysitting, etc.) where the consequences of inattention/distractibility or impulsivity can be serious.

In some cases, pharmacologic treatment with a nonstimulant medication may be necessary (see Table 24.1). Although the treatment response is typically less robust than with stimulants, medications such as atomoxetine (Strattera), bupropion (Wellbutrin; off-label use for ADHD), and alpha-2 agonists such as clonidine (Catapres, Kapvay) and guanfacine (Tenex, Intuniv) can be considered in failed trials of stimulant medications, if underlying physical conditions contraindicate stimulant use, if there is comorbid substance abuse or concern for diversion, or patient and family preference. Nonstimulants may be used as monotherapy or as adjuncts to stimulant medication in cases of partial response. Alpha-agonists may also be used to target insomnia related primarily to ADHD or as side effect of stimulant use. Atomoxetine may be helpful in cases of comorbid anxiety disorders, while bupropion may improve symptoms of comorbid depression (off label use for depression).

Referral to a child and adolescent psychiatrist may be indicated in patients who are refractory to treatment or demonstrate atypical response to treatment, or if the clinician suspects a comorbid condition such as a depression, anxiety, or bipolar disorder that complicates a patient's presentation and/or treatment. In such cases, a referral offers the opportunity to confirm or refine a diagnosis and to further optimize treatment.

Depressive Disorders

Depression is a debilitating disorder that is frequently unrecognized and undertreated. The challenging task of identifying depression falls disproportionately to primary care physicians, as most depressed adolescents present in primary rather than specialty care. Adolescent depression is associated with negative social, academic, and health outcomes including depression in adulthood, higher medical expenses, substance abuse, early pregnancy, and increased suicide risk.

Prevalence

In 2014, an estimated 2.8 million adolescents aged 12–17 in the United States had at least one major depressive episode in the preceding year, representing 11.4% of the U.S. population aged 12–17. While estimates of prevalence have varied, a recent survey found lifetime prevalence of depression and dysthymia increases from 8.4% for ages 13–14 to 15.4% for ages 17–18. These estimates appear to be stable across races/ethnic backgrounds but females are twice as likely to be affected as males.

Evaluation

The DSM-5 diagnostic criteria for major depressive disorder are the same in children and adolescents as in adults, although the presentation may differ. For example, it is common for the mood of depressed children and adolescents to be irritable rather than sad or down. In addition, the ability of children and adolescents to report depression symptoms may be limited and requires inference from observations (i.e., declining school performance, less interaction with peers/social activities, more self-critical, conduct issues) as well as obtaining collateral information from parents and teachers. In the Guidelines for Adolescent Preventive services (GAPS), the American Medical Association recommends that all

children be asked annually about signs of recurrent or severe depression or suicide risk and depression screening for adolescents who demonstrate signs or risk factors. Common screening tools include the Children's Depression Inventory (ages 7–17; proprietary tool), Patient Health Questionnaire-9 (ages 13–17; freely available tool), Center for Epidemiological Studies Depression Scale (ages 14 and older; freely available electronic survey), and the Beck Depression Inventory (ages 14 and older; proprietary tool). The website Guidelines for Adolescent Depression in Primary Care (GLAD-PC: II; www.glad-pc.org) also contains several screening tools.

For a major depressive episode, a person must have at least five of eight depressive symptoms present for a 2-week period that represents a change from previous functioning. At least one symptom is depressed/irritable mood or loss of interest or pleasure in activities. The other depressive symptoms may be recalled with the mnemonic "SIG: E CAPS" (a prescription for energy capsules). This represents the following diagnostic criteria: **S**leep (↓or ↑), **I**nterest (↓interest in or pleasure with activities), **G**uilt (↑ feelings of guilt/self-blame, hopelessness or worthlessness), **E**nergy (↓), **C**oncentration (↓), **A**ppetite (↓or ↑; changes in weight), **P**sychomotor changes (agitation or retardation/slowing), and **S**uicidal thoughts.

Depression should be considered when the chief complaint pertains to changes in overall functioning at home or school. School difficulties may be a manifestation of depression symptoms of decreased interest, decreased energy, decreased concentration, and/or feelings of hopelessness. Other common signs of depression in children and adolescents include: delays in going to/falling asleep, refusal to wake for school, feeling tired/ "lazy," loss of interest in activities, frequently feeling "bored," giving up favorite activities, self-critical (i.e., "no one likes me"; "everyone hates me"; "I'm stupid"), conduct problems, as well as new somatic complaints including stomach pains and headaches.

Symptom severity is very important to assess as it can determine appropriate treatment recommendations. According to the DSM-5, severity is based on the number of criterion symptoms, the severity of those symptoms, and the degree of functional

disability. "Mild" severity includes an individual with few symptoms in excess of those required to make the diagnosis, symptoms are distressing but manageable, and the symptoms result in overall minor impairment in functioning. "Severe" severity includes an individual with symptoms substantially in excess of that required to make the diagnosis, intensity is seriously distressing and unmanageable, and cause great interference with functioning. "Moderate" severity is more vaguely defined as somewhere between mild and severe.

A comprehensive safety assessment is critical when evaluating for depression. Asking questions about safety in multiple ways can be helpful. If possible, the adolescent should be interviewed individually as this enables the adolescent to share with the physician important information s/he may withhold with the parent in the room. Important questions to ask adolescents when assessing for safety include: asking if they have ever thought about ending their life, if they have ever wished to be dead, or if they have made any attempts to end their life. If a patient has suicidal thoughts, further questions should inquire about frequency of these thoughts, whether there is any plan, whether there is any intention and availability to carry out the plan, and other risk factors including previous self-harm, substance use, access to guns, and family history of depression and suicide. If a screening tool for depression is used, paying close attention to the suicide measures can be particularly important to ensure concerns about suicide do not get missed. The Columbia-Suicidal Severity Rating Scale can be used to specifically monitor suicidal ideation. If there is any concern about a patient's risk for suicide an urgent referral to an emergency room or mental health specialist is warranted.

It is important to ensure a depressive episode is not attributable to the physiological effects of a substance or to another medical condition. The most common substances that effect depressive symptoms include alcohol, cannabis, opiates, benzodiazepines, and withdrawal from cocaine or other illegal stimulants. Medical causes are varied but typical workup includes complete blood count (assessing for anemia and/or infection), thyroid function test (assessing for hypothyroidism), and toxicology screen as indicated by the patient's presentation and physical condition.

Management

The severity of depression symptoms is important for determining overall treatment recommendations. For mild depression, close monitoring, increasing supports at home and at school, and/or a trial of supportive counseling is generally recommended. There is disagreement between guidelines concerning essential components, timing, and duration of brief supportive counseling. GLAD-PC-II and The Best Evidence Statement (BESt) recommend up to eight sessions of supportive therapy as initial treatment of adolescents with mild depressive symptoms. The AACAP indicates that education, support, and management should accompany all phases of treatment and may be adequate for uncomplicated brief depression with mild functional impairment. For adolescents with moderate to severe depression or those who do not respond to supportive treatment, psychotherapy and/or medication is recommended. Major multisite medication and psychotherapy trials (including the Treatment for Adolescents with Depression Study) indicate the combination of medication and psychotherapy is most effective in reducing depression symptoms for moderate to severe depression.

The types of psychotherapy that have the most evidence for adolescent depression include cognitive-behavioral therapy (CBT) and interpersonal therapy (IPT). CBT has also been proven effective in treatment of childhood depression. Other forms of psychotherapy may have great benefit as well, however they have not undergone as rigorous study. CBT typically consists of techniques to increase coping skills, improve communication skills and peer relationships, correct negative thinking patterns, and regulate emotions. IPT generally focuses on adapting to changes in relationships including identifying interpersonal problem areas, improving interpersonal problem-solving skills, and modifying communication patterns.

SSRIs are considered first-line medication treatment for depression treatment. There are only two FDA approved SSRIs for treatment of depression in children and adolescents: Fluoxetine (Prozac) in children 8 years of age and older and escitalopram (Lexapro) in adolescents 12 years of age and older. Other SSRIs

that are commonly prescribed off-label to treat depression in adolescents include citalopram (Celexa) and sertraline (Zoloft). These medications have been studied in the pediatric population and sertraline has FDA approval for OCD (see anxiety disorder section). The Texas Children's Medication Algorithm on medication treatment of childhood depression suggests using fluoxetine, citalopram, or sertraline as first-line medications. Fluoxetine has the largest amount of positive data for treatment of adolescent depression. A Cochrane review found that fluoxetine was the only SSRI with consistent evidence (from three randomized trials) that is effective in decreasing depressive symptoms in adolescents. Fluoxetine also has the longest half-life among the SSRIs, which could be problematic if adverse effects arise. Paroxetine (Paxil) has had the largest number of studies with negative results in adolescents and in June 2003, the FDA recommended it no longer be used to treat depression in children and adolescents.

Other non-SSRI antidepressants are venlafaxine (Effexor), duloxetine (Cymbalta), bupropion (Wellbutrin), and mirtazapine (Remeron). There are fewer studies showing effectiveness of these agents for adolescent depression and they are generally not first-line treatments. Of this group, only duloxetine has an FDA approval in the pediatric population and this is for treatment of generalized anxiety disorder. These antidepressants are more likely to be used if comorbid diagnoses exist such as ADHD (bupropion) and neuropathic pain (duloxetine), or for their side effect profile such as sleep and appetite stimulation (mirtazapine). It is typical for clinicians to try at least two SSRI medications before switching to another class of antidepressants if depression symptoms remain after adequate treatment.

Treatment should begin at the lowest dosage (sometimes half the lowest dose if particularly concerned about side effects) and titrated according to the patient's response and adverse effects. It is recommended for treatment to continue for 6–12 months after patient achieves symptom remission and then to slowly wean the dose while monitoring for return of symptoms. Table 24.2 lists details of antidepressant dosing and titration scheduling.

Possible side effects to most antidepressants include nausea, loose stools (which can be beneficial in patients with chronic

Table 24.2 Depression and anxiety medications for adolescents

Medication	FDA indication	Starting dose, mg/day	Increments	Effective dose, mg	Maximum dose, mg
Fluoxetine	MDD and OCD; off-label for anxiety	5–10	5–10 mg q1–2 weeks	20	60
Escitalopram	MDD; off-label for anxiety	5	5 mg q3 weeks		20
Sertraline	OCD; off-label for anxiety and depression	25	12.5–25 q1 week	50	200
Duloxetine	GAD; off-label for depression	20	20 mg q2–4 weeks	20	60
Fluvoxamine	OCD; off-label for anxiety and depression	25	25 mg q1 week divided in BID dosing	50–100	200
Citalopram	None; off-label for anxiety and depression	5–10	5–10 mg q1–2 weeks	20	40
Bupropion	None; off-label for depression	XL preparation: 150	XL preparation: 150 mg q2–3 weeks	XL preparation: 150	XL preparation: 450
		SR preparation: 100	SR preparation: 100 mg q1–2 weeks divided BID	SR preparation: 100	SR preparation: 400

constipation), headaches, dizziness, vivid dreams, dry mouth, fine tremor, weight gain, and decreased libido. Except for decreased libido and weight gain, these often resolve a few days after the medication is started or the dose is titrated. Bupropion has a lower risk of weight gain and decreased libido. A rare side effect is serotonin syndrome (mental status changes, hyperthermia, hyperreflexia, and clonus) and this risk is increased when there is coadministration with other serotonergic medications (including supplements such as St. John's Wart and SAMe) or triptan medications. Any drastic changes in mood and behavior may represent a switch to mania; those with family history of bipolar disorder should be carefully monitored. Some adolescents experience increased activation (jitteriness, restlessness, increased energy) that is similar to mania but much less severe. Activation side effects may respond to lowering the dose but may necessitate discontinuing antidepressant treatment.

Physicians may be concerned with the possibility of making mood symptoms, particularly suicidal thoughts worse. The FDA issued a "black box warning" regarding the use of antidepressant medications in children and adolescents in 2003 due to concern for small, but statistically significant increase in suicidal ideation. Given the greater number of patients who benefit from SSRIs than who experience serious adverse effects, the lack of any completed suicides, and the decline in overall suicidality ratings, the risk/benefit ratio for SSRI use in pediatric depression is considered to be favorable with careful monitoring. The FDA stated, "Ideally, such observation would include at least weekly face-to-face contact with patients or their family members or caregivers during the first 4 weeks, then at biweekly visits for the next 4 weeks, then at 12 weeks, and as clinically indicated beyond 12 weeks." In clinical practice, many clinicians use telephone contact to help maintain the goal of close in office follow-up. The AACAP emphasizes that there are no data to suggest that the monitoring schedule proposed by the FDA or telephone calls have any impact on the risk of suicide. Documenting that suicidal ideation and the black box warning were discussed is important. The primary care provider needs to be informed about this risk, educate the patient and family, and develop an appropriate safety plan.

Referral to psychiatry for treatment should be considered if: patient is refractory to treatment (failed ≥2 antidepressants), patient has an atypical response to treatment, if the patient has been psychiatrically hospitalized for depression, if the patient has chronic suicidal thinking or is at high risk for suicide, and/or the clinician suspects bipolar disorder or another comorbid condition that complicates treatment.

Bipolar Disorder

It is important to consider bipolar disorder when evaluating a patient with overall mood changes. It was once thought that this disorder did not exist in children; however, evidence within the last few decades indicates this is no longer the case. Prevalence is hard to estimate in adolescents, but lifetime prevalence of bipolar disorder is about 1 %; disorders in the bipolar spectrum may affect 4–6 % of the population. At least half of all cases of bipolar disorder start before the age of 25 (20–30 % before age 20). Approximately 20 % of youths with diagnosis of major depressive disorder develop symptoms consistent with a manic state at a later age. It is well established as a familial disorder, with 5–10 % prevalence in first-degree relatives of adults and children with bipolar disorder, compared to 0.5–1.5 % prevalence in community samples.

While pediatric bipolar disorder may present with similar symptoms to the more clearly recognizable forms of mania seen in adults, the patterns of illness and symptom definition described in children and adolescents often vary from the classic description. How to best define and diagnose pediatric bipolar disorder is a debate in the field that requires continued research. Some researchers have found that children with chronic, severe irritability, and symptoms of ADHD may be misdiagnosed as having bipolar disorder. Out of this debate, a new diagnosis has been added to the DSM-5 called Disruptive Mood Dysregulation Disorder (DMDD), a syndrome of chronic irritability and temper outbursts. Children with DMMD are more at risk for developing depression or anxiety disorders than manic episodes as they age. If there is concern for bipolar disorder in a patient in primary care, referral to psychiatry for consultation and/or continued treatment should be done.

Anxiety Disorders

Anxiety is a normal and often anticipated part of childhood, particularly in response to numerous physical, emotional, and social changes that children experience as they grow. Anxiety that persists through new experiences but dissipates with gradual exposure and reassurance is a normal part of the child's growing emotional repertoire. An anxiety disorder is present when there is a persistent state of fear that stagnates a child's growing experiences, impairs exposure to new and necessary aspects of life as part of adaptability, results in refusal to engage in basic responsibilities and activities of daily living, and/or hampers social and educational relationships.

Prevalence

The lifetime prevalence of anxiety disorders among 13–18-year-old adolescents is in the range of 25 %, with 5 % of this population having a severe disorder. Risk factors for anxiety disorders depend in part on the specific disorder. General risk factors include gender, age, and the presence of preexisting medical conditions. Females have twice the risk for anxiety disorders compared to males except for obsessive–compulsive disorder (OCD) where the risk is equal for both genders. Social phobia and panic disorder typically first present in adolescence while phobias, OCD, and separation anxiety often first present in early childhood. More specific risk factors are the family history, interpersonal dynamics, traumatic events, and personality traits present in children. Anxiety disorders tend to run in families, genetically and through interactions within the household that result in parental fears having a profound impression on children. Exposure to traumatic events or witnessing parents reacting to trauma does not always result in anxiety disorders but can increase the risk of developing them. Interpersonally, children who are bullied or lack social connections have a higher propensity for anxiety disorders. With or without these external factors, children with personality traits that classify them as "shy" or "worriers" with an inability to tolerate uncertainty have a higher risk of developing anxiety disorders.

Evaluation

As a result of improved research and understanding of anxiety disorders, the DSM-V has divided the classically understood anxiety disorders into separate sections for Obsessive–Compulsive and Related Disorders, Trauma- and Stressor-Related Disorders, and Anxiety Disorders. These distinct categories emphasize the significantly varied presentations of anxiety disorders, but it does not disavow their interconnectedness throughout a child's lifespan. The most common anxiety disorders that might present in primary care are listed in Table 24.3.

Table 24.3 Anxiety disorder classification

Anxiety disorder	Description
Generalized Anxiety Disorder (GAD)	Excessive worry out of proportion to the situation and results in significant functional impairment. Characterized by: frequent worry about grades, family issues, relationships with peers, and/or performance in sports. May be seen as perfectionists who seek constant approval or reassurance from others
Panic disorder	Frequent panic attacks (sudden onset of fear, palpitations/chest pain, difficulty breathing, a sense of losing control over bodily functions and emotions, sense of impending doom) and intense, constant fear that panic attacks will recur
Separation anxiety disorder	Excessive anxiety, extreme homesickness, and misery from being away from home or when separated from parents or caregivers. May refuse to go to sleepovers, camp, or school. In adolescents they may frequently text/call parent for reassurance if separated from parent; may have parent speak for him/her at doctor's appointments
Social anxiety disorder	An extreme fear of social situations due to fear of being judged by peers, made fun of by peers, and/or making a fool of self in front of others
Specific phobia	An intense, irrational fear of a specific object or event. Examples are fear of insects, heights, blood/needles, etc.
School refusal	Refusing to go to school on a regular basis or has problems staying in school, likely because of a stressful life event, separation anxiety, or fears related to a peer or class work. May manifest as complaints of physical ailments or panic/anxiety that dissipates after the child is allowed to miss school

(continued)

Table 24.3 (continued)

Anxiety disorder	Description
Posttraumatic Stress Disorder (PTSD)	Manifests as sustained (≥1 month) symptoms of severe anxiety, irritability, nightmares, emotional numbing, and avoidance behaviors after experience a traumatic event, such as the death of a parent, physical violence, and severe injury
Obsessive–Compulsive Disorder (OCD)	Frequent, unwanted, and intrusive thoughts that may or may not be accompanied by frequent, compulsive rituals to relieve intrusive thoughts. If no rituals then it is called OCD, primarily obsessional. Examples: intense fear of germs/getting sick and with excessive hand washing; intrusive thought of something "not right" or wrong and with frequent checking/arranging/ordering behaviors

To evaluate symptoms of anxiety a good screening assessment is the SCARED (Screen for Child Anxiety Related Disorders) scale. The SCARED is a freely available screening tool and has both a parent form and a child/self-assessment form. The SCARED assesses anxiety symptoms of GAD, OCD, social anxiety, separation anxiety, panic disorder, somatic issues, and school avoidance. The use of this screening tool can help guide the clinician in a more focused clinical interview and the diagnosis of a specific anxiety disorder.

Anxiety disorders most commonly co-occur with depression, ADHD, and eating disorders. Depression and anxiety can independently present with agitation, insomnia, and poor concentration. When present together, there is an increased risk for substance abuse and suicide. For ADHD, concentration is often worse during times of high anxiety and ADHD treatments may worsen anxiety. The correlation of anxiety, particularly OCD, with eating disorders is likely due to bidirectional causality and susceptibility factors along with common biologic pathways of both types of disorders. Other conditions that can result from anxiety disorders include insomnia, bruxism, frequent nightmares, gastrointestinal symptoms, chronic headaches, and substance use disorders. Substance use often starts as a way to alleviate anxiety symptoms but may eventually develop into an addiction. Discussion of screening tools for depression, ADHD, and substance use can be found earlier and in other sections of this handbook.

It is important to remember that various medical conditions can present with symptoms similar to anxiety. A medical exam and corresponding tests should be done if indicated by the child's presentation and physical condition. Mitral valve prolapse, paroxysmal supraventricular tachycardia, asthma-related symptoms, hyperthyroidism, hypoglycemia, adrenal tumors, pulmonary emboli, medication side effects, caffeine or amphetamine intoxication, and alcohol withdrawal can all present with anxiety as a primary symptom.

Management

As with depression, anxiety disorders are treated with therapy, behavioral interventions, and medications. For mild to moderate anxiety disorders, therapy remains the primary treatment recommendation for children and adolescents. One of the most commonly known therapeutic options is Cognitive Behavioral Therapy (CBT), a treatment which aims to help children regain control of reactions to stressful stimuli through exposure, response prevention, and restructuring distorted thinking patterns that worsen anxiety. CBT and medication are each effective as singular treatments but studies have shown that a combination of CBT and medication can lead to greater improvement in moderate to severe anxiety disorders. Other types of therapy include group therapy and family therapy and these are often used in conjunction with CBT treatment. Family therapy often focuses on changing patterns in the home/family system that might exacerbate anxiety symptoms and helping to develop behavior plans (such as with school attendance) to help reduce the impact of anxiety on the child's functioning. Even with appropriate treatment of anxiety, recurrence is common and often necessitates "booster" therapy sessions.

Other therapy treatment options focus on the physiological aspects of anxiety. Breathing retraining techniques allow patients to practice measured, controlled breathing at the onset of anxiety/panic and this can help reduce the physical effects of anxiety. Biofeedback is another technique that makes patients aware of changes in pulse rate, skin temperatures, and muscle tone in order to recognize an anxiety state and to practice reducing their reactions to anxiety.

SSRI antidepressants are currently the recommended first-line medications in the pharmacotherapy of anxiety disorders in children. Duloxetine, a selective serotonin/norepinephrine reuptake inhibitor (SNRI), is FDA approved to treat generalized anxiety disorders in children age 7 years and older. Fluoxetine, fluvoxamine, and sertraline are SSRIs approved for the treatment of OCD in children age 8 years and older. Most of the SSRI medications are also used off-label to treat generalized anxiety disorder and social anxiety disorder. For PTSD in children and adolescents, the efficacy of SSRI medications is not well established and trauma-focused cognitive behavioral therapy remains the most effective treatment in this population. Refer to Table 24.2 for dosing strategies for SSRI/SNRI medications.

Benzodiazepines should be avoided due to risks of sedation, cognitive slowing, and physical dependence and abuse. If benzodiazepines are used, it is best to use longer acting benzodiazepines, such as clonazepam and lorazepam, and to avoid short-acting benzodiazepines such as alprazolam. Short-acting benzodiazepines have a higher risk for dependence and abuse. When benzodiazepines are used they should be used for severe symptoms of panic and for as short a time as possible with the goal of discontinuing once the adolescent is on therapeutic doses of an SSRI/SNRI medication.

Herbal remedies and dietary supplements do not need FDA approval to sell their products but are frequently manufactured as treatments for anxiety. There are no evidence-based studies to confirm the efficacy of Valerian, St. John's Wort, or passionflower for anxiety treatment. The herbal remedy kava has been associated with liver problems and should be discouraged. There is conflicting evidence that Omega-3 supplementation has mild benefit for depression and irritability in children but this effect has not been found for anxiety.

Much like the other disorders discussed in this chapter, referral to psychiatry should be considered in patients who are refractory to treatment, demonstrate atypical response to treatment, or if the clinician suspects a comorbid condition such as a depression, ADHD, or bipolar disorder that complicates treatment. Patients with OCD and PTSD often benefit from referral to a psychiatrist or therapist for specialized management.

Sources

American Academy of Child and Adolescent Psychiatry. Practice parameter for the assessment and treatment of children and adolescents with attention-deficit/hyperactivity disorder. J Am Acad Child Adolesc Psychiatry. 2007;46:894–921.

American Academy of Child and Adolescent Psychiatry. Bipolar disorder: parents' medication guide for bipolar disorder in children and adolescents. 2010. www.Parentsmedguide.org

American Academy of Pediatrics, Subcommittee on Attention-Deficit/Hyperactivity Disorder, Steering Committee on Quality Improvement and Management. ADHD: clinical practice guideline for the diagnosis, evaluation, and treatment of attention-deficit/hyperactivity disorder in children and adolescents. Pediatrics. 2011;128:1007–22.

American Psychiatric Association and American Academy of Child and Adolescent Psychiatry in consultation with a National Coalition of Concerned Parents, Providers, and Professional Associations. (2010). The use of medication in treating childhood and adolescent depression: information for patients and families. www.Parentsmedguide.org

American Psychiatric Association. Diagnostic and statistical manual of mental disorders: DSM-5. Washington, DC: American Psychiatric Association; 2013. 20 Oct 2015.

Beidel DC, Alfano CA. Child anxiety disorders: a guide to research and treatment. New York: Taylor & Francis; 2011.

Biederman J, Mick E, Faraone SV, Spencer T, Wilens TE, Wozniak J. Pediatric mania: a developmental subtype of bipolar disorder? Biol Psychiatry. 2000;48:458–66.

Birmaher B, Brent D, et al. Practice parameter for the assessment and treatment of children and adolescents with depressive disorders. J Am Acad Child Adolesc Psychiatry. 2007;46(11):1503–26.

Brotman MA, Schmajuk M, Rich BA, et al. Prevalence, clinical correlates, and longitudinal course of severe mood dysregulation in children. Biol Psychiatry. 2006;60:991–7.

Brown RT, Amler RW, Freeman WS, et al. Treatment of attention-deficit/hyperactivity disorder: overview of the evidence. Pediatrics. 2005;115:e749–57.

Cheung AH, Zuckerbrot RA, Jensen PS, et al. Guidelines for adolescent depression in primary care (GLAD-PC): II. Treatment and ongoing management. Pediatrics. 2007;120:e1313–26.

Cheung AH, Dewa CS, Levitt AJ, et al. Pediatric depressive disorders: management priorities in primary care. Curr Opin Pediatr. 2008;20:551–9.

Clark M, Jansen K, Cloy A. Treatment of childhood and adolescent depression. Am Fam Physician. 2012;85:442–8.

Costello EJ, Erkanli A, Angold A. Is there an epidemic of child or adolescent depression? J Child Psychol Psychiatry. 2006;47:1263–71.

Crawley SA, Caporino NE, Birmaher B, et al. Somatic complaints in anxious youth. Child Psychiatry Hum Dev. 2014;45:398–407.

Cummings C, Fristad M. Pediatric bipolar disorder: recognition in primary care. Curr Opin Pediatr. 2008;20:560–5.
Drake KL, Ginsburg G. Family factors in the development, treatment, and prevention of childhood anxiety disorders. Clin Child Fam Psychol Rev. 2012;15:144–62.
Dunsmore JC, Booker JA, Ollendick TH. Parental emotion coaching and child emotion regulation as protective factors for children with oppositional defiant disorder. Soc Dev. 2013;22:444–66.
DuPaul GJ, Gormley MJ, Laracy SD. Comorbidity of LD and ADHD: implications of DSM-5 for assessment and treatment. J Learn Disabil. 2013;46:43–51.
DuPaul GJ, Pinho TD, Pollack BL, et al. First-year college students with ADHD and/or LD: differences in engagement, positive core self-evaluation, school preparation, and college expectations. J Learn Disabil. 2015. pii: 0022219415617164 [Epub ahead of print].
Farchione TR, Birmaher B, Axelon D, et al. Aggression, hostility, and irritability in children at risk for bipolar disorder. Bipolar Disord. 2007;9:496–503.
Geller DA, March J. Practice parameter for the assessment and treatment of children and adolescents with obsessive-compulsive disorder. Focus. 2012;10:360–73.
Geoffroy MC, Boivin M, Arseneault L, et al. Associations between peer victimization and suicidal ideation and suicide attempt during adolescence: results from a prospective population-based birth cohort. J Am Acad Child Adolesc Psychiatry. 2016;55:99–105.
Goldenring JM, Rosen DS. Getting into adolescent heads: an essential update. Contemp Pediatr. 2004;21:64–90.
Hoge EA, Ivkovic A, Fricchione GL. Generalized anxiety disorder: diagnosis and treatment. BMJ. 2012;345:e7500.
Hughes CW, Emslie GJ, Crismon ML, et al. Texas children's medication algorithm project: update from Texas consensus conference panel on medication treatment of childhood major depressive disorder. J Am Acad Child Adolesc Psychiatry. 2007;46:667–86.
Kendall PC, editor. Child and adolescent therapy: cognitive-behavioral procedures. New York: Guilford Press; 2011.
Kim YS, Koh YJ, Leventhal B. School bullying and suicidal risk in Korean middle school students. Pediatrics. 2005;115:357–63.
Klein D, Myhre K, Ahrendt D. Bullying among adolescents: a challenge in primary care. Am Fam Physician. 2013;8:87–92.
Kodish I, Rockhill C, Ryan S, et al. Pharmacotherapy for anxiety disorders in children and adolescents. Pediatr Clin North Am. 2011;58:55–72.
Leenarts LE, Diehle J, Doreleijers TA, et al. Evidence-based treatments for children with trauma-related psychopathology as a result of childhood maltreatment: a systematic review. Eur Child Adolesc Psychiatry. 2013;22:269–83.
Lereya ST, Copeland WE, Costello EJ, et al. Adult mental health consequences of peer bullying and maltreatment in childhood: two cohorts in two countries. Lancet Psychiatry. 2015;2:524–31.

Lewandowski RE, Acri M, Hoagwood K, et al. Evidence for the management of adolescent depression. Pediatrics. 2013;132:e996–1009.
Maynard BR, Heyne D, Brendel KE, et al. Treatment for school refusal among children and adolescents: a systematic review and meta-analysis. Research on Social Work Practice. 2015. doi:10.1177/1049731515598619.
McClellan J, Kowatch R, Findling RL, Work Group on Quality Issues. Practice parameter for the assessment and treatment of children and adolescents with bipolar disorder. J Am Acad Child Adolesc Psychiatry. 2007;46:107–25.
McLean CP, Asnaani A, Litz BT, et al. Gender differences in anxiety disorders: prevalence, course of illness, comorbidity and burden of illness. J Psychiatr Res. 2011;45:1027–35.
Mendlowicz MV, Stein MB. Quality of life in individuals with anxiety disorders. Am J Psychiatry. 2000;157:669–82.
Merikangas KR, He J-P, Burstein M, et al. Lifetime prevalence of mental disorders in U.S. adolescents: results from the National Comorbidity Survey Replication—Adolescent Supplement (NCS-A). J Am Acad Child Adolesc Psychiatry. 2010;49:980–9.
Muris P, Ollendick TH. Children who are anxious in silence: a review on selective mutism, the new anxiety disorder in DSM-5. Clin Child Fam Psychol Rev. 2015;18:151–69.
Nansel TR, Overpeck M, Pilla RS, et al. Bullying behaviors among US youth: prevalence and association with psychosocial adjustment. JAMA. 2001;285:2094–100.
Perrin JM, Friedman RA, Knilans TK, Black Box Working Group; Section on Cardiology and Cardiac Surgery. Cardiovascular monitoring and stimulant drugs for attention-deficit/hyperactivity disorder. Pediatrics. 2008;122:451–3.
Pilkington K, Kirkwood G, Rampes H, et al. Homeopathy for anxiety and anxiety disorders: a systematic review of the research. Homeopathy. 2006;95:151–62.
Roza SJ, Hofstra MB, van der Ende J, et al. Stable prediction of mood and anxiety disorders based on behavioral and emotional problems in childhood: a 14-year follow-up during childhood, adolescence, and young adulthood. Am J Psychiatry. 2003;160:2116–21.
Scheeringa MS, Zeanah CH, Cohen JA. PTSD in children and adolescents: toward an empirically based algorithm. Depress Anxiety. 2011;28:770–82.
Schulte EE. Learning disorders: how pediatricians can help. Cleve Clin J Med. 2015;82(11 Suppl 1):S24–8.
Singh T. Pediatric bipolar disorder: diagnostic challenges in identifying symptoms and course of illness. Psychiatry. 2008;5:34–42.
Smoller JW, Tsuang MT. Panic and phobic anxiety: defining phenotypes for genetic studies. Am J Psychiatry. 1998;155:1152–62.
Southammakosane C, Schmitz K. Pediatric psychopharmacology for treatment of ADHD, depression, and anxiety. Pediatrics. 2015;136:351–9.

Stevens JR, Wilens TE, Stern, TA. Using stimulants for attention-deficit/hyperactivity disorder: clinical approaches and challenges. Prim Care Companion CNS Disord. 2013;15:PCC.12f01472.

Testa A, Giannuzzi R, Daini S, et al. Psychiatric emergencies (part III): psychiatric symptoms resulting from organic diseases. Eur Rev Med Pharmacol Sci. 2013;17 Suppl 1:86–99.

Van Meter AR, Burke C, Kowatch RA, et al. Ten-year updated meta-analysis of the clinical characteristics of pediatric mania and hypomania. Bipolar Disord. 2016;18:19–32.

von der Embse N, Barterian J, Segool N. Test anxiety interventions for children and adolescents: a systematic review of treatment studies from 2000–2010. Psychol Sch. 2013;50:57–71.

Williams JH, Veeh CA. Continued knowledge development for understanding bullying and school victimization. J Adolesc Health. 2012;51:3–5.

Wolitzky-Taylor K, Bobova L, Zinbarg RE, et al. Longitudinal investigation of the impact of anxiety and mood disorders in adolescence on subsequent substance use disorder onset and vice versa. Addict Behav. 2012;37:982–5.

Zuckerbrot RA, Cheung AH, Jensen PS, et al. Guidelines for adolescent depression in primary care (GLAD-PC): I. Identification, assessment, and initial management. Pediatrics. 2007;120:1299–312.

Eating Disorders

25

Karen Sadler

Eating disorders in adolescents and young adults are common, complex, evolving, and the most lethal mental health condition in pediatrics. Even when not deadly, they have profound negative effects on health, development, education, relationships, and emotional well-being. While many patients conform to the stereotype as high achieving, Caucasian, mid-adolescent females, the epidemiology is changing. Younger children, males, and non-Caucasians are increasingly represented. Expanding also are the 'paths' that lead to an eating disorder. A change in diet (whether as an effort to lose weight, avoid antigens, or eat in a 'healthier way') is but one entrance point; compulsive exercise, number counting on apps, fear of normal pubertal changes, and refusal to eat as a form of self-punishment are others.

The most common type of eating disorder was formally called Eating Disorder, Not Otherwise Specified [ED,NOS] but is now included in a DSM 5 category called Other Specified Feeding or Eating Disorder [OSFED]. It has a more varied presentation than the crisper diagnoses of bulimia or restrictive anorexia nervosa, but a similar rate of complications. Typically cited lifetime prevalence rates are 0.5–2 % for anorexia, 1–3 % for bulimia, and almost 5 % for ED, NOS/OSFED. Early detection and successful intervention can help mitigate the deadliness

M.A. Goldstein (ed.), *The MassGeneral Hospital for Children Adolescent Medicine Handbook*, DOI 10.1007/978-3-319-45778-9_25

and tremendous morbidity of eating disorders, thus prevention and early action are important.

It is not known what 'causes' an eating disorder, and the notion that there is one etiology is likely simplistic. There is a heritable component demonstrated in twin studies, but, more likely, the final common pathway of an eating disorder is a 'perfect storm,' a confluence of sociocultural, biologic, environmental, and developmental factors resulting in a multidimensional illness. As such, it is better understood, and approached, in a larger context. Healthcare providers are now facing 'second-generation' anorexia nervosa, affected children of parents who were themselves affected by this illness: the risk for these children increases by tenfold.

Making the Diagnosis

Eating fads are commonplace in American society, fueled by food producers who are eager to sell new products. 'Low fat' foods, low glycemic index products, and foods made with artificial sweeteners are just part of what has become a confusing food landscape. We eat in our cars and struggle to gather for communal meals. Antiobesity messages, while important, can have unintended consequences. Not surprisingly, it is easy in this society to lose a healthy relationship with food, and thus develop disordered eating. When is it an 'eating disorder'? As with many other psychiatric diagnosis, the degree of disability helps define the illness. Moreover, eating disorders are multidimensional: signs and symptoms are found in physical, emotional, and psychological realms, though not necessarily in equal measure.

Primary caretakers are often the first to become aware of a potential problem, though at times it may be a psychologist or gastroenterologist who arrives at the diagnosis. Often, a concerned parent first raises the issue, worried about missed menses, or dramatic changes in eating habits or personality. Other times, however, families remain remarkably unaware or in denial of alarming signs. Concern voiced by friends, teachers, or siblings should not be dismissed without further assessment.

A list of potentially concerning behaviors, symptoms, and signs are listed in Tables 25.1, 25.2, and 25.3, respectively.

The initial diagnostic approach should always include a review of growth parameters (preferentially longitudinal and well as normative data), a comprehensive history (including input from caretakers), a physical exam, and a limited laboratory evaluation.

Special mention should be made of children who, while not necessarily losing weight, are no longer gaining along their expected trajectory, children not progressing normally through

Table 25.1 Potential eating disorder behaviors

- Eating progressively less
- Eating only 'safe' foods
- Cutting food into very small pieces
- Playing with food on the plate, rather than eating it
- Reluctance to be weighed
- Claiming to be 'allergic' to many foods
- Compulsive activity
- Food rituals
- Measuring food
- Comparing body size to others
- Disappearing after meals (purging)
- Difficulty eating socially
- Refusing to eat out, or with family or friends
- Wearing baggy clothes and many layers
- Social isolation
- Cooking for others
- Anxiety in new food situations
- Insistence on preparing own meals
- Frequently weighing oneself
- Verbalizing an unrealistic body image

Table 25.2 Potential symptoms in anorexia nervosa and bulimia nervosa

Anorexia nervosa	Bulimia nervosa
Cold intolerance	Dizziness
Early satiety	Sore throat
Fatigue	Abdominal pain
Thinning hair	Facial swelling (parotids)
Overactivity	Personality changes
Constipation	Menstrual changes
Personality changes	
Amenorrhea	

Table 25.3 Potential physical signs in anorexia nervosa and bulimia nervosa

Anorexia nervosa	Bulimia nervosa
Low body weight	Dental erosion
Bradycardia	Weight fluctuations
EKG changes	Irregular menses
Orthostasis	Syncope
Lanugo	EKG changes
Halitosis	Hematemesis
Acrocyanosis	Russell's sign
Muscle wasting	Parotid enlargement
Leukopenia, lower platelets, RBC	Petechiae
Increased LFTs	Hypokalemia
Electrolyte abnormalities	
Osteopenia/osteoporosis	
Slowed cognition	
Brittle hair and nails	
Amenorrhea	

puberty, those with amenorrhea, and previously overweight children with precipitous weight loss. Weight should be compared to both the expected weight based on previous growth trajectories and an ideal body weight, based upon normative body mass index (BMI) data. One standard formula to calculate ideal body weight (IBW) uses the 50% BMI for age (based upon CDC growth charts) multiplied by height in meters squared for an IBW in kilograms. (For example, the mean BMI for a 16-year-old girl is 20.4. For a teen of this age whose height is 5 ft 5 in., or 1.65 m, the IBW would be $1.65 \times 1.65 \times 20.4$ or 55.5 kg).

Helpful questions to ask, both for diagnostic purposes and to assess severity include:

1. What was your highest and lowest weight? When?
2. What do you do for exercise? How much and how often?
3. Run me through a typical 'food day,' recalling all that you eat and drink.
4. What are your 'safe' (and 'unsafe') foods?
5. What would you like to weigh?

6. Would gaining weight upset you?
7. If you feel that you have eaten too much, how do you react? What do you do about it?
8. How much of the day do you spend thinking about, worrying about, avoiding and preparing food?
9. Do you avoid going out if it involves eating? How do you handle it?
10. Do you feel you are too heavy, too light?
11. How is your sleep? Energy level?
12. Do you menstruate? When was your last menstrual period?
13. Have you ever taken a diuretic or laxative?
14. Do you purge? How? How often?
15. Do you feel you have a problem with your eating? Do others?
16. Do you count calories? Use a food app?
17. What foods did you use to love, but now won't eat?

While not an exhaustive list, these questions can help ferret out food attitudes and problem behaviors.

Diagnostic Criteria

As eating disorders evolve, so do their definitions. Following are the DSM 5 criteria for Anorexia nervosa, Bulimia nervosa, OSFED, and Avoidant/Restrictive Food Intake Disorder:

Source: American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 5th ed. Washington (DC): American Psychiatric Press; 2013.

DSM 5 Criteria for Anorexia Nervosa

Significantly low body weight.

Intense fear of gaining weight or becoming fat.

Disturbance in the way in which one's body weight or shape is experienced, undue influence of body weight or shape on self-evaluation, or persistent lack of recognition of the seriousness of the current low body weight.

Subtypes

Restricting: only caloric restriction and exercise.

Binge Eating/Purging: Binge Eating and or purging also present.

DSM 5 Criteria for Bulimia Nervosa

(a) Recurrent episodes of binge eating:

Eating, in a discrete period of time, an amount of food that is definitely larger than most people would eat during a similar period of time and under similar circumstances.

A sense of lack of control over eating during the episode.

(b) Recurrent inappropriate compensatory behavior in order to prevent weight gain, such as self-induced vomiting; misuse of laxatives, diuretics, or other medications; fasting; or excessive exercise.

(c) At least once a week for 3 months.

(d) Self-evaluation is unduly influenced by body shape and weight.

When the revised fifth edition of the DSM was published in 2013, changes were made to the criteria for both diagnoses. This was done as an effort to include more patients in these categories (and fewer in the less specific categories) for better diagnostic accuracy and to promote more effective research. For anorexia, refusing to maintain an appropriate weight was substituted with wording that focused more on behavior than intent. The psychological component of disturbed body image was broadened to include lack of recognition of the seriousness of low weight as an alternative criterion. Amenorrhea was removed, opening this diagnosis to males, prepubertal females, and those on hormonal contraception who cannot accurately ascertain lack of natural menses. For bulimia, the frequency required was reduced from twice to once weekly for at least 3 months. Importantly, what was termed EDNOS was subsumed into a broader category of eating disorders called OSFED, and binge eating disorder was teased apart from bulimia nervosa. While still overeating at least weekly for 3 months with a feeling of loss of control and consequent distress, those with binge eating disorder do not display the compensatory behaviors seen in those with bulimia nervosa. A new category,

Avoidant/Restrictive Feeding or Eating Disorder was included as well, to describe those children whose nutritional and energy deficiencies stemmed from other motivators, such as textural sensitivity, fear of choking, or learned food avoidance from past negative experiences.

DSM 5 Criteria for Other Specified Feeding or Eating Disorder

1. *Atypical Anorexia Nervosa*: All criteria are met, except despite significant weight loss, the individual's weight is within or above the normal range.
2. *Binge Eating Disorder (BED)* (of low frequency and/or limited duration): All of the criteria for BED are met, except at a lower frequency and/or for less than 3 months.
3. *Bulimia Nervosa* (of low frequency and/or limited duration): All of the criteria for Bulimia Nervosa are met, except that the binge eating and inappropriate compensatory behavior occurs at a lower frequency and/or for less than 3 months.
4. *Purging Disorder*: Recurrent purging behavior to influence weight or shape in the absence of binge eating.
5. *Night Eating Syndrome*: Recurrent episodes of night eating. Eating after awakening from sleep or by excessive food consumption after the evening meal. The behavior is not better explained by environmental influences or social norms. The behavior causes significant distress/impairment. The behavior is not better explained by another mental health disorder (e.g., BED).

DSM 5 Criteria for Avoidant/Restrictive Food Intake Disorder

An Eating or Feeding disturbance as manifested by persistent failure to meet appropriate nutritional and/or energy needs associated with one (or more) of the following:

1. Significant loss of weight (or failure to achieve expected weight gain or faltering growth in children).
2. Significant nutritional deficiency.
3. Dependence on enteral feeding or oral nutritional supplements.

4. Marked interference with psychosocial functioning.

1. The behavior is not better explained by lack of available food or by an associated culturally sanctioned practice.
2. The behavior does not occur exclusively during the course of anorexia nervosa or bulimia nervosa, and there is no evidence of a disturbance in the way one's body weight or shape is experienced.
3. The eating disturbance is not attributed to a medical condition, or better explained by another mental health disorder. When it does occur in the presence of another condition/disorder, the behavior exceeds what is usually associated, and warrants additional clinical attention.

Differential Diagnosis and Medical Evaluation

Usually, a thorough history and physical exam narrow the diagnostic possibilities considerably, and laboratory workup can be limited. However, depending upon the presentation, a practitioner may need to exclude the following: celiac disease, inflammatory bowel disease, food allergies, gastrointestinal dysmotility, endocrinopathies such as hyperthyroidism or Addison Disease, malignancies, pregnancy, and/or diabetes.

Initial laboratory evaluation includes CBC, comprehensive metabolic panel, ESR, phosphorous, calcium and magnesium levels, pregnancy test, urinalysis, TSH, and EKG. Results both screen for other illnesses and gauge the degree of metabolic and cardiac derangement.

Management

After a diagnosis is made, the first consideration is always to assure medical stability. This is an illness with high morbidity as well as mortality, and one that can lead to rapid deterioration. Medical complications are numerous and affect almost every organ system (see Table 25.4).

Table 25.4 Medical complications of anorexia nervosa

Constitution/whole body
Cachexia and low body mass index
Arrested growth
Hypothermia
Cardiovascular
Myocardial atrophy
Mitral valve prolapse
Pericardial effusion
Bradycardia
Arrhythmia, which may cause sudden death
Electrocardiogram (ECG) changes
Long QT syndrome (QTc prolongation)
Increased PR interval
First-degree heart block
ST-T wave abnormalities
Hypotension
Acrocyanosis
Gynecologic and reproductive
Amenorrhea
Infertility
Pregnancy and neonatal complications
Endocrine
Osteoporosis and pathologic stress fractures
Euthyroid hypothyroxinemia
Hypercortisolemia
Hypoglycemia
Neurogenic diabetes insipidus
Gastrointestinal
Gastroparesis (delayed gastric emptying)
Constipation
Gastric dilatation
Increased colonic transit time
Hepatitis
Superior mesenteric artery syndrome
Renal and electrolytes
Decreased glomerular filtration rate
Renal calculi

(continued)

Table 25.4 (continued)

Impaired concentration of urine
Dehydration
Hypokalemia
Hypomagnesemia
Hypophosphatemia
Hypokalemic nephropathy
Hypovolemic nephropathy
Pulmonary
Pulmonary muscle wasting
Decreased pulmonary capacity
Respiratory failure
Spontaneous pneumothorax and pneumomediastinum
Enlargement of peripheral lung units without alveolar septa destruction
Hematologic
Anemia (normocytic, microcytic, or macrocytic)
Leukopenia
Thrombocytopenia
Neurologic
Cerebral atrophy (decreased gray and white matter)
Enlarged ventricles
Cognitive impairment
Peripheral neuropathy
Seizures
Dermatologic
Xerosis (dry skin)
Lanugo hair (fine, downy, dark hair)
Telogen effluvium (hair loss)
Carotenoderma (yellowing)
Scars from self-injurious behavior (cuts and burns)
Muscular
Muscle wasting
Vitamin deficiencies
Refeeding syndrome

Up To Date 2016: Graphic 67080 Version 3.0

Inpatient Management

At times, an acute care medical hospitalization is required before ongoing comprehensive treatment is established (or, in the case of deterioration, continued). Indications for hospitalization are listed as follows (see Table 25.5).

The goals of hospitalization are several. The most important are to halt medical deterioration and to begin to restore weight in a safe, supervised setting. This is done with a nutritional rehabilitation protocol that combines a controlled, graduated meal plan with vital sign and electrolyte monitoring and often includes a behavioral modification component. During a medical admission, input is also requested of psychiatrists, social workers, nutritionists, and other specialists as needed. Severely malnourished and/or underweight patients can develop refeeding syndrome, a potentially fatal situation. With increased energy and carbohydrate intake, insulin is released, which stimulates intracellular uptake of phosphate, potassium, and magnesium as well as shifts in fluid. The result can be severe hypophosphatemia, as well as lowered serum levels of magnesium, potassium, and thiamine. Calcium levels can also be affected. Metabolic rate is increased as positive energy balance is attained. The resultant stress on the cardiac system can lead to acute heart failure and arrhythmias. Confusion, seizures, and coma can also be seen. Phosphorous supplementation is often begun empirically for at risk patients, and electrolytes are monitored at least on a daily basis. Other inpatient goals are to assess for psychiatric comorbidities, assemble an outpatient team or secure admission to an eating

Table 25.5 Criteria for hospitalization

Anorexia nervosa	Bulimia nervosa
Less than 75 % IBW	Syncope
Refusal to eat	Serum potassium less than 3.2
Heart rate less that 50 during the day, less than 40 at night	Serum chloride less than 88
Systolic BP less than 80/50	Esophageal tears
Orthostatic BP changes >20 mmHg or pulse >20 BPM	Cardiac arrhythmias
Arrhythmias	Suicidality
Suicidality	Hematemesis
Failure of outpatient management	Failure of outpatient management

disorder program, and to inform and support the family. Psychiatric comorbidities are common, most notably depression, anxiety, substance use and obsessive compulsive disorder, and worsen the prognosis with this disorder.

Outpatient Management

Optimally, caring for a patient with an eating disorder outside of the hospital setting involves a multidisciplinary team consisting of a therapist, nutritionist, and medical provider, each with defined roles. Team communication and decision sharing is essential, as the road to recovery is long (2–5 years, on average) and often bumpy. In addition to monitoring weight, vital signs, and labs and participating in decisions pertaining to allowable exercise, schooling, and activities, medical providers should also check the bone density in women who have been amenorrheic for more than 6–12 months. With weight recovery, patients can be come hypermetabolic, requiring very high calorie diets, which are challenging to consume.

Prognosis

Patients in need of more structure or those who are not able to recover with an outpatient team are advised to participate in an eating disorder program. Graduated levels of care exist in most programs, ranging from intensive outpatient programs (usually evening commitments, 3–4 times per week) to partial day programs to residential options and finally to inpatient options, the highest level of medical and psychiatric supervision. These programs will combine the services of nutrition support, group therapy, individual therapy and variably psychotherapy, meditation, and tutoring.

Psychological Treatment Strategies

Several treatment modalities are used in the outpatient and program setting. No one approach will likely emerge as the sole treatment method, given the heterogeneity of patients and the factors that drive eating disordered behavior.

Individual (or interpersonal) psychotherapy (IPT) has the goal of uncovering etiologies with respect to personality and relationship dynamics, targeting interpersonal difficulties.

Cognitive behavioral therapy (CBT) is more symptom oriented. This therapy focuses more on distorted thoughts that cascade into maladaptive behaviors and provides strategies to control these proximal triggers.

Family-based therapy (FBT) takes a different tact. An example of FBT is the Maudsley Method. Developed in London, it has shown promise in multiple studies for anorexia nervosa. Rather than asking why an eating disorder has developed (or who, or what, is to blame), FBT engages family members as allies in the recovery process, with nutritional restoration being the first priority. FBT progresses through three phases. In Phase 1, caregivers are given essentially complete control over their child's intake: selecting, cooking, and plating meals. Fear foods are introduced to overcome anxieties and reluctance in this controlled setting. Therapists act more in the role of advisor. After a target weight has been achieved, Phase 2 begins, allowing gradual control of food autonomy to be regained by the patient. Phase 3 is a maintenance phase, geared toward providing the structure needed to prevent relapse and to continue full psychological and emotional recovery. This method takes, on average, 6–12 months.

For Bulimia, CBT remains the most common first-line approach.

Depending upon the needs of individual patients, other team members can include traditional family therapists, psychopharmacologists, and, more recently, private food coaches. Digital options include recovery apps, which record daily progress and can provide motivation and serve as a communication tool between team members.

The role for pharmacotherapy is limited. There is no evidence supporting the use of medication for the sole treatment of anorexia nervosa. Selective serotonin uptake inhibitors (SSRIs) have been shown to reduce binge/purge compulsions in bulimia nervosa, and fluoxetine has FDA approval for this indication in adults. Other atypical antidepressants and mood stabilizers are sometimes used to target specific symptoms (such as anxiety) or to address known concurrent psychiatric conditions.

Prognosis and Prevention

Full recovery (defined as the complete reversal of symptoms and damage to organs, achievement of optimal weight, and restoration of emotional and psychological function and well-being) takes years and is achieved by only ~50–60 % of patients. Another 1/3 function, but with residual symptoms or only partially, and a final ~20 % suffer a chronic course. Mortality is ~5 % with cardiac failure and suicide being the most common proximal causes of death. Factors associated with a worse prognosis are a long duration of illness, a lower minimum body weight, comorbid mental health diagnoses, and family dysfunction.

Children and adolescents who suffer from eating disorders pay a high price, physically, emotionally, and psychologically. Prevention efforts are essential and many studies are underway examining which efforts may have efficacy. Although this is an illness often managed by a specialist, primary caretakers play a key role in prevention, as well as early identification and aggressive intervention. Although there are certainly high-risk environments (involvement in weight conscious sports and activities, family characteristics, personality types) primary caretakers should remain vigilant for early signs of disordered eating in any child. Social media presents intervention opportunities, but also danger in that there are many sites and blogs promoting body dysmorphism and disordered eating. Pro-Ana and Pro-Mia are nicknames for eating disorders used on sites on the Internet. Searching these terms will bring up many sites, such as Anorexic Nation and 2Bthin. Providers should be aware of these messages and some of the sites. During health care encounters, health and wellness should be stressed as a goal, rather than the attainment of a certain weight, even with patients who are overweight. Screening tools are available for disordered eating. Two such are the Eating Attitudes Test (EAT) and the SCOFF Questionnaire. (Links are provided.)

Almost all providers of medical care will come across patients with eating disorders. Caring for these patients is often frustrating. Well-meant and logical advice is met with resistance and, sometimes, deception. It is important to remember that no one chooses to have an eating disorder and that patients are caught in the fear

and anxiety that comes with living with this illness. Patience, compassion, and a firm set of expectations and support from mental health and nutrition colleagues are helpful. Recovery is a long, but worthwhile, road.

Female Athlete Triad

The constellation of low energy availability with or without an eating disorder, hypothalamic amenorrhea, and osteoporosis in the female athlete has been recognized as a common occurrence and is termed the female athlete triad. Most of these athletes present with low body fat composition, which contributes to a hypoestrogenic state that leads to amenorrhea. As in patients with anorexia, estrogen deficiency along with hypogonadotropic hypogonadism contributes to reduction in bone mineralization. Excessive exercise also contributes to amenorrhea in causing hypogonadotropic hypogonadism. At times, the female athlete may be normal weighted but still present with low body fat and amenorrhea placing her at risk for osteopenia.

Two studies have looked at the occurrence of eating disorders in female athletes who present with low body weight and amenorrhea. In one study, 31 % of the female athletes in sports that promoted leanness met DSM IV criteria for eating disorders compared to the general population where 5.5 % had eating disorders. Another study found that 25 % of elite female athletes had clinical eating disorders compared to 9 % in the general population.

Diagnosis of the female athlete triad should begin with careful assessment of the female athlete's body weight, body fat, nutritional status, and menstrual history. Screening for eating disorders should also be performed. If low body weight or body fat composition is present along with primary or secondary amenorrhea, then a bone density scan should be obtained to screen for osteopenia or osteoporosis.

Treatment needs to address the issue that is underlying the disorder. If there is low energy availability, then caloric intake should be increased and exercise should be limited with the goal of positive energy balance and appropriate weight gain. If the patient has

disordered eating or an eating disorder, a team should be formed including a physician experienced in the management of an eating disorder, a nutritionist, and a therapist. Bone loss including osteopenia and osteoporosis should be managed with the help of an endocrinologist.

Sources

American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 5th ed. Washington, DC: American Psychiatric Press; 2013.
Campbell K, Peebles R. Eating disorders in children and adolescents: state of the art review. Pediatrics. 2014;134:582–92.
Goldstein MA, Dechant EJ, Beresin EV. Eating disorders. Pediatr Rev. 2011;32:508–21.
Hergenroeder AC, De Souza MG, Anding RH. The female athlete triad: energy deficiency, physiologic consequences, and treatment. Adolesc Med State Art Rev. 2015;26:116–42.
Nattiv A, Louchks AB, Manore MM, et al. The female athlete triad. Med Sci Sports Exerc. 2007;39:1867–82.
www.ceed.org.au/wp-content/uploads/2012/05/scoffqairehandout.pdf
www.clevelandclinicmeded.com
www.eat26.com
www.medainc.org
www.ncbi.nim.nih.gov/pmc/articles/PMC4096990
www.recoveryrecord.com

Adolescent Relationship Abuse in Clinical Settings: Opportunities for Prevention and Intervention

26

Elizabeth Miller

Approximately one in three adolescent girls in the United States is a victim of physical, emotional, or verbal abuse from a dating partner—a figure that far exceeds victimization rates for other types of violence affecting youth. Nationwide, nearly one in ten high-school students (8.9 %) has been hit, slapped, or physically hurt on purpose by a boyfriend or girlfriend. The negative health consequences for adolescents and young adults include pregnancy, sexually transmitted infections, substance abuse, depression, and suicidality.

Adolescent relationship abuse refers to physical, sexual, or emotional abuse within a dating or sexual relationship in which one or both partners is a minor. In addition to sexual and physical violence, for adolescents, abusive behaviors may include a range of controlling behaviors: monitoring cell phone usage, telling a partner what s/he can wear, controlling where s/he goes, manipulating contraceptive use (See Table 26.1).

M.A. Goldstein (ed.), *The MassGeneral Hospital for Children Adolescent Medicine Handbook*, DOI 10.1007/978-3-319-45778-9_26

Table 26.1 Diverse manifestations of power and control in adolescent relationships

Dimensions of abuse	Examples[a]
Emotional/ psychological	Name calling via text and social media; telling partner what s/he can wear; threatening to spread rumors; threatening to commit suicide if partner tries to leave relationship; smashing things; breaking partner's things
Social	Cell phone usage monitoring; preventing partner from going to school; calling or text messaging multiple times a day to monitor partner's whereabouts; getting angry if partner is talking to someone else
Financial	Controlling what partner can or cannot buy; refusing to pay for things that the abuser insisted the partner purchase
Sexual	Insisting on sexual acts; videotaping (by cell phone) sexual acts then threatening to put them on the Internet; preventing partner from using birth control; forcing partner to get pregnant; forcing partner to use drugs before sexual activity
Physical	Threatening to hit; threatening with a weapon; hurting the partner's pet

[a]These are examples of abuse in addition to physical and sexual violence (i.e., hitting, slapping, kicking, choking, forcing to engage in sex)

Unique Characteristics of Adolescent Relationship Abuse

Developmental Considerations

Depending on the adolescent's stage of social/emotional development, the young person may not recognize the warning signs of abuse, confusing the controlling behaviors and possessiveness as signs of 'true love.' Similarly, a young person may defer seeking care due to multiple barriers, including fear of breaches of confidentiality, lack of trust in adult care providers, and inability to access care. The health care provider should always consider the adolescent's developmental stage and discuss concrete and specific behaviors ("does s/he get mad at you if you don't respond to his/her calls right away?") rather than vague questions such as "Are you in an abusive relationship?"

Teens and Electronic Media

Instant messaging, social networking sites, cell phones, all help teens to connect in ways that were unfathomable even a decade ago; this electronic networking can become an arena for exploitation and abuse, including excessive texting, 'sexting' (transmitting nude images of oneself or one's partner), or constant cell phone monitoring. Discussion of risks associated with such electronic media with young patients and their parents is now requisite for health care providers. (See www.thatsnotcool.com for teens to learn about setting their own 'digital line.')

Role of Adult Caregivers

Adolescents are far less likely to disclose experiences of relationship abuse to adults than to their peers; those teens who are more disconnected from family, school, and their community are also the most vulnerable to abusive relationships. Adult caregivers (e.g., parents, teachers, health care providers) may dismiss warning signs of abuse among teens, assuming that teen relationships are less serious than adults. Family chaos and disruption (including family violence) are risk factors for adolescent relationship violence, underscoring that engaging parents/guardians in supporting youth experiencing violence also requires careful assessment of parental safety.

Minor Consent Laws and Confidentiality

A critical difference with adolescent relationship abuse in comparison to adult domestic violence is that at least one of the partners involved is a minor, which means clinicians must pay attention to minor consent, confidentiality, and reporting requirements. In addition, the health care provider is required to balance the safety of the minor while creating safe spaces that are confidential for teens to share experiences with their provider. Providers need to know their state's minor consent/confidentiality and

mandated reporting requirements for child abuse, neglect, and sexual abuse; knowledge of these reporting requirements and how to support a teen in the safest way possible requires consultation. It is important to develop connections with colleagues (e.g., social workers, domestic violence agencies, rape crisis centers) to discuss options. Reporting a case to an outside agency without carefully considering safety could place the young person at significantly greater risk for harm and even death.

Assessment for Relationship Abuse

Adolescents report disclosing problems and abuse in their relationships to friends far more often than to adults. Providers are encouraged to share information universally about relationship abuse to all of their adolescent patients in the context of their friendships, without pushing for disclosure. For example, "We make sure to talk about healthy and unhealthy relationships with all of our patients, because you may know someone for whom this information might be useful. Please know that this is a safe place to bring friends whom you are concerned about."

Experiences of relationship abuse cluster with other common adolescent behaviors. Adolescents experiencing family violence are more likely to experience an abusive relationship; in an attempt to escape the family context, they may become more dependent on a partner. They may also be depressed, using substances, or pregnant. This means that when addressing any other adolescent behavior relevant to a young person's health and well-being (whether it be smoking or school performance), the provider should consider the possibility of an abusive relationship as part of the differential diagnosis for their problem.

In addition to universal, consistent, and frequent inquiry about the quality of their relationships and relationship abuse, providers should be alert to particular warning signs and symptoms that may signal the possibility of an abusive relationship. In the presence of such signs and symptoms, providers should conduct a more thorough assessment, while not pushing for disclosure. Drawing on a young person's strengths and using motivational interviewing

Table 26.2 Examples of clinical symptoms and signs of potential relationship abuse

Domain/system	Clinical symptoms and signs
Social functioning	School failure, disengaged from school activities, lack of friends, lack of hobbies
Constitutional	Frequent headaches, sleep disorders, rapid weight gain or weight loss
Ears, nose, throat	Frequent ear pain (from being slapped); sore throats (forced oral sex; strangulation); palatal bruising (forced oral sex)
Reproductive and sexual health	Multiple requests for pregnancy or STI tests; inconsistent or no contraceptive use; frequent use of emergency contraception; pelvic pain; vaginal discharge; dysuria
Gastrointestinal	Nonspecific abdominal pains; constipation and rectal pain (forced anal sex); irritable bowel syndrome
Musculoskeletal	Joint or limb pains; neck pain and low back pain; scratches or bruising
Mental health	Poor sleep; sad or anxious mood; suicidal ideation; substance abuse; withdrawn; depressed affect

techniques, providers can offer education on what constitutes abusive behavior, identify potential behaviors that may be placing the teen at increased risk for abuse and violence, as well as ensure that the young person is aware of specific resources and supports available to support victims of violence (see Table 26.2).

Creating a Safe Environment for Possible Disclosure

A supportive and safe environment includes having posters, brochures, and messages in the clinical space that reflect a teen's reality. Posters with concrete examples of what love is and what love is not communicates that the clinic staff care about the health of their adolescents. Brochures that provide education about relationship abuse with questions for adolescents to consider lay the groundwork for a conversation with the provider. The materials used should be multicultural and reflect a diversity of relationships and gender expression.

(See www.futureswithoutviolence.org and www.loveisrespect.org for teen relevant materials.)

Beyond Screening and Disclosure: Universal Education and Brief Counseling

Every encounter with an adolescent in the health care setting is an opportunity to educate youth about the ways in which relationships can affect their health and how health care providers are prepared to support youth experiencing abuse and violence in their relationships, regardless of disclosure. That is, even if a practice uses a risk assessment tool (or similar screening tool) and the adolescent does not check 'yes' to relationship abuse exposure on the tool, the provider should still offer education and resources. The use of a palm-sized educational brochure about healthy relationships is one evidence-informed approach for conducting universal education and brief counseling (available at https://www.futureswithoutviolence.org/hangingout-or-hooking-up-2/).

Universalizing: "Many of our teen patients have shared with us how they have experienced things in their relationships that made them feel uncomfortable and even scared. We care about this a lot as health care providers, because unhealthy relationships can really affect your health. We now talk with all of our patients about their relationships because you and your health are really important to us. How are things going for you?"

Educational: "As unhealthy relationships have such an impact on the health of young people, we have been sharing this information with all of our patients, because it is likely you know someone who could use this information. We want you to know that this is a safe place for young people to share with us things they are concerned about."

Concrete: "Does this person ever tell you where you can go or who you can talk to? Or constantly checking up on you, or checking your cell phone?"

"Do they ever try to make you have sex when you don't want to?"

"Do you ever feel scared? Like do they ever totally lose it, throw things?"

Collaborative Model for Care

Given the complexities and nuances of caring for adolescents, providers must know local resources and specialists in partner and sexual violence to consult.

- Identify allies in mental health, social work, pediatrics, as well as other local community resources, including domestic violence and rape crisis centers, child protection services, and legal advocates familiar with youth law.
- Create an adolescent-friendly environment in the clinical setting, and enlist other clinic staff in helping to create this 'safe' space for teens that is respectful of a young person's strengths and growing independence. This includes signs and materials that affirm diverse backgrounds and signal openness to different gender and sexual identities (such as a rainbow flag).
- Ensure that all youth in the practice see information on relationship abuse and healthy relationships, and that they leave the clinic knowing that the clinic team cares about them and their well-being.

Sources

Decker M, Silverman J, Raj A. Dating violence and sexually transmitted disease/HIV testing and diagnosis among adolescent females. Pediatrics. 2005;116:272–6.

Dick RN, McCauley HL, Jones KA, et al. Cyber dating abuse among teens using school-based health centers. Pediatrics. 2014;134(6):e1560–7.

Exner-Cortens D, Eckenrode J, Rothman E. Longitudinal associations between teen dating violence victimization and adverse health outcomes. Pediatrics. 2013;131(1):71–8.

Futures Without Violence: Health Cares about IPV Tools. http://www.healthcaresaboutipv.org/

Miller E, Levenson RL. Hanging out or hooking up: clinical guidelines for responding to adolescent relationship abuse—an integrated approach to prevention and intervention. Futures Without Violence. 2012. http://www.futureswithoutviolence.org/userfiles/file/HealthCare/Hanging-Out-or-Hooking-Up_Low_Res_Cropped_FINAL.pdf

Miller E, Goldstein S, McCauley HL, et al. A school health center intervention for abusive adolescent relationships: a cluster RCT. Pediatrics. 2015;135(1):76–85.

Vagi KJ, O'Malley Olsen E, Basile KC, Vivolo-Kantor AM. Teen dating violence (physical and sexual) among US high school students: findings from the 2013 National Youth Risk Behavior Survey. JAMA Pediatr. 2015;169(5):474–82.

Bullying and Cyberbullying

27

Rachel H. Alinsky and Mark A. Goldstein

Overview and Definition

The American Academy of Pediatrics (AAP) defines bullying as "a form of aggression in which one or more children repeatedly and intentionally intimidate, harass, or physically harm a victim who is perceived as unable to defend herself or himself." Bullies try to exert control over their victims by scaring or humiliating them, usually when other peers are observing.

The prevalence of bullying is thought to peak in childhood and to decrease through adolescence, being nearly twice as common in 6th grade as in 12th grade. One in five youths has been bullied on school property, as the majority of face-to-face bullying takes place at or on the way to and from school. A survey of over fifteen thousand 6–10th graders in the USA found that nearly 30 % of students were involved in bullying on a regular basis, either as a perpetrator (13 %), a target (10.6 %), or both (termed "bully-victim," 6.3 %).

M.A. Goldstein (ed.), *The MassGeneral Hospital for Children Adolescent Medicine Handbook*, DOI 10.1007/978-3-319-45778-9_27

A fourth category of participant is the bystander—a role much discussed in bullying prevention and response literature given their potential power to intervene and change social norms.

Types of Bullying

There are several types of bullying, which can be broadly categorized as direct or indirect. Direct bullying involves overt behaviors by the bully to the victim, usually in a face-to-face setting. This includes both physical and verbal bullying. Physical bullying consists of assault such as hitting, tripping, or pushing, or property destruction. Verbal bullying entails speech designed to be hurtful or demeaning, including name calling, teasing, insulting remarks, and threats.

In contrast, indirect bullying is more covert and can be harder to identify. This type of bullying includes both social or relational bullying and cyberbullying. Social or relational bullying involves undermining the victim's social reputation, or jeopardizing the support, security, and closeness of their relationships. It often encompasses more people than simply the bully and victim, as the bully may involve other members of a social group. This happens via rumor spreading, telling others not to be friends with someone, purposeful exclusion from groups or activities, or embarrassing someone in public.

With the increase in adolescents' use of technology, cyberbullying has emerged as a major threat in the last two decades, affecting up to one quarter of adolescents. Cyberbullying entails the use of technology, electronics, or the Internet (texting, e-mail, instant messaging, social media, websites, and chat rooms) to send or post demeaning, threatening, or embarrassing information. Cyberbullying differs from typical bullying in that the audience is effectively limitless, perpetrators can be more anonymous, bullying displays are more permanent, and it is harder to be monitored by adults.

Characteristics of Victims and Bullies

Although any child or adolescent can be bullied, characteristics that make a child seem "different" than their peers carry a higher risk of victimization. Among those disproportionately bullied (Table 27.1) are youth with certain physical appearances, social skills and backgrounds, or special health care needs, which includes disabilities, mental health conditions, and chronic medical conditions. For example, approximately one in four children with food allergies has been teased, bullied, or harassed regarding their food allergies; half of such bullying was physical—entailing intentional contamination of food with allergen, being touched by an allergen, or having an allergen thrown or waved at them. Additionally, youths who belong to gender and sexual orientation minorities (those whose gender or sexual identity differ from cultural norms) are bullied, abused, and traumatized more frequently by peers both at school and at home by their caregivers and community.

Certain attributes make children and adolescents more likely to bully others. Youth with the following factors have a higher risk of

Table 27.1 Adolescents at risk of being bullied

	Specific characteristics
Physical appearance	Overweight, underweight, wearing glasses, racial minority
Social	Non-native speaker, new to a school, less popular, have fewer friends, quiet, seen as annoying, perceived as weak or unable to defend themselves, unable to afford what kids consider "cool"
Special health care needs	Disabilities (intellectual, physical, developmental, sensory) Mental health conditions (ADHD, autism, depression, anxiety, learning disorder) Chronic medical conditions (diabetes, epilepsy, allergies)
Gender or sexual orientation minorities	Gay, bisexual, transgender, or those who do not conform to standard gender roles

bullying perpetration: problems with aggression or following rules, poor impulse control, less parental involvement or harsh parenting, attitudes accepting of violence, poor self-esteem, easily peer-pressured, overly concerned about their popularity, and having friends who bully.

Signs and Symptoms of Bullying

Bullying can manifest in adolescents in a variety of ways, ranging from affecting their school performance and social participation, to more frequent psychiatric and somatic complaints (Table 27.2). Additionally, parents should monitor for signs of bullying perpetration, which can include involvement in frequent physical or verbal fights, having friends who bully others, increasing aggression, getting sent to principal's office or detention, unexplained extra money or new belonging, blaming others for their problems, not accepting responsibility for their actions, overly competitive or concerned with their reputation/popularity, attempts to hide or conceal cell phone/computer usage.

Table 27.2 Signs and symptoms of being bullied

	Specific signs and symptoms
School	Difficulty concentrating and/or completing schoolwork, declining grades, attempts to stay home from school
Social	Avoidance of certain social situations, activities, sports, clubs; loss of friends; threatening to hurt others
Property	Frequently losing items, damage to clothes or other personal items
Electronic	Becoming sad or upset after using the computer or cell phone, switching screens on the computer when an adult walks in
Somatic	Abdominal pain, nausea, anorexia, being very hungry after school, headaches, problems with sleep such as insomnia, nightmares, enuresis
Psychiatric	Feeling unhappy, sad, depressed, anxious; simply appearing more withdrawn or moody than usual; new substance use; suicidality
Physical	Unexplained bruises, cuts, or injuries; attempts to cover up or hide such injuries

Consequences of Bullying

Despite its prevalence, bullying should not be accepted as a normal developmental bump because longitudinal research has found that bullying results in significant immediate and enduring consequences for both the victim and the perpetrator (Table 27.3). The relationship between bullying and violence/weapon-carrying is even stronger in the USA compared to other countries.

Table 27.3 Consequences of bullying

	Victims	Bullies
Mood		
Poor self-esteem	X	X
Higher rates of depression	X	X
Higher rates of suicidal ideation and suicide attempts—especially with cyberbullying	X	X
School		
Declining school performance	X	X
Poor grades	X	X
Truancy	X	X
Lower levels of academic achievement	X	X
Violence		
Carrying weapons	X	X
Engaging in violent behavior	X	X
Involvement in fighting serious enough to cause injury	X	X
Conduct disorder		X
Long term		
Depression	X	X
PTSD (for gender minority youth)	X	
Economic hardship	X	X
Antisocial personality disorder		X
Delinquency, incarceration, conviction of a crime		X
Unemployment		X
Substance abuse		X
Abusive to partners		X
Less likely to be married/in stable adult relationship		X

Prevention

Bullying prevention starts in early childhood, thus pediatricians have a crucial role in providing appropriate counseling and anticipatory guidance. Pediatricians should encourage parents to strive to be good role models. They should promote parenting strategies that are emotionally supportive, and provide a structured home setting. Pediatricians should counsel families about resiliency, the factors and skills that enable children to adapt successfully to stress or trauma, such as bullying. Such protective or resilience factors include parental resilience, social connections, concrete/tangible help in times of need, parent knowledge of child development, and social and emotional competence of the child. Pediatricians should recognize, reaffirm, and encourage these resilience factors in their patients and explain to families how to foster a healthy childhood. And pediatricians should teach parents about the signs and symptoms of bullying and advise them to limit and monitor adolescents' screen time.

On a community level, pediatricians can advise schools and school districts to adopt comprehensive anti-bullying programs. Many school-based interventions to combat bullying have been developed; a systematic review of such interventions found that the most effective interventions were multidisciplinary and school wide. This involves creating and enforcing school-wide rules and sanctions, implementing classroom curriculum and conflict management training, educating teachers and school personnel, and providing individual counseling. Anti-bullying campaigns aim to make bullying less socially acceptable and mobilize bystanders, and change the overall culture of the school.

On a broader level, physicians may also advocate for legislative actions that promote resources to prevent bullying or develop programming to treat perpetrators and victims. A large cross-sectional study across the USA demonstrated lower rates of bullying in states with anti-bullying legislation. In particular, the most effective legislation defined the scope and circumstances of when schools can take action (i.e., including bullying by students off school property or online), described specific prohibited behaviors, and required school districts to develop and implement anti-bullying policies. Physicians can advocate for laws such as these via their local or state medical societies or via national organizations such as the AAP.

Screening for Bullying

Pediatricians should incorporate screening for bullying in all children and adolescents at routine health care maintenance visits. In addition, pediatricians should consider further evaluation for bullying in certain circumstances as described above, when they note the onset of psychosomatic or behavioral symptoms, academic or social problems, or substance use. While there is no particular accepted screening tool, it can be helpful for providers to open with normative statements then follow with specific questions. It is also important to directly ask about being a bullying perpetrator or bystander. For example, "Sometimes kids get picked on at school. Has your child heard of or seen instances of this? Does this happen to you/your child? Has your child picked on or bullied anyone else?" This strategy can also work well for children presenting with school avoidance or psychosomatic complaints, using language such as "A lot of teenagers who [avoid school, have frequent morning stomachaches, etc] have had problems with bullying. Have you ever felt scared to go to school because of bullying?"

Interventions

If a pediatrician identifies that a patient is a victim or perpetrator of bullying, intervention is required. Physicians should counsel families about the seriousness of bullying. Many bullying victims internalize the criticism they receive, and may feel ashamed, thus it is important to encourage the child by explaining they should not be treated in this way. They may be fearful of the backlash from disclosing the bullying, and being labeled a tattletale. Pediatricians and parents can help patients learn how to respond to bullying. For example, pediatricians should advise parents to keep records documenting the bullying, and to involve school personnel including counselors, teachers, administrators, and even the local or state Department of Education. The child and their parents should identify allies at their school whom they can trust, including school personnel and friends. Participation in organized activities (sports, teams, clubs) can be helpful in expanding an adolescent's social skills and social network, as well as provides more structured supervised time free of bullying.

These children should be screened for other psychiatric conditions, namely depression and anxiety, and those who screen positive should receive further psychiatric evaluation and therapy. Victims of bullying may benefit from referrals to learn more in-depth secondary prevention strategies such as how to defuse tense situations. Providers should maintain an accurate database of counseling and treatment resources available in their community. Pediatricians can both learn from and refer parents to the AAP for resources such as "Connected Kids: Safe, Strong, Secure" and HealthyChildren.org, the Centers for Disease Control's online bullying resources, and the government multiagency website StopBullying.gov. In circumstances involving weapons, serious injury or threats of such injury, or hate motivated violence, it may be necessary for pediatricians and/or parents to reach out to law enforcement for further assistance.

In addition to treating victims, it is equally important for pediatricians to identify bullying perpetrators and intervene. They should establish that this behavior is not acceptable, and action is required. Bullies should be screened for comorbid psychiatric conditions such as depression and conduct disorder, and treated for such. Parents should reach out to their school systems for assistance. Additionally, it may be helpful to refer families to therapy or parental education programs regarding creating structured home environments, and setting and enforcing consistent rules and limitations.

Sources

Committee on Injury, Violence, and Poison Prevention. Policy statement—role of the pediatrician in youth violence prevention. Pediatrics. 2009;124(1):393–402. doi:10.1542/peds.2009-0943. Epub 11 Jun 2009.

Featured topic: bullying research. Centers for Disease Control and Prevention, Injury Prevention & Control: Division of Violence Prevention Web site. http://www.cdc.gov/violenceprevention/youthviolence/bullyingresearch/. Updated 7 Oct 2015. Accessed 1 Feb 2016.

Hatzenbuehler ML, Schwab-Reese L, Ranapurwala SI, et al. Associations between antibullying policies and bullying in 25 states. JAMA Pediatr. 2015;169(10):e152411. doi:10.1001/jamapediatrics.2015.2411. Epub 5 Oct 2015.

Holt MK, et al. Bullying and suicidal ideation and behaviors: a meta-analysis. Pediatrics. 2015;135(2):e496–509.

Kann L, Kinchen S, Shanklin SL, et al.; Centers for Disease Control and Prevention (CDC). Youth risk behavior surveillance—United States, 2013. MMWR Surveill Summ. 2014;63(Suppl 4):1–168. Erratum in: MMWR Morb Wkly Rep. 2014 Jul 4;63(26):576.

Lieberman JA, Weiss C, Furlong TJ, et al. Bullying among pediatric patients with food allergy. Ann Allergy Asthma Immunol. 2010;105:282.

Nansel TR, Overpeck M, Pilla RS, et al. Bullying behaviors among US youth: prevalence and association with psychosocial adjustment. JAMA. 2001;285:2094.

Roberts AL, Rosario M, Slopen N, et al. Childhood gender nonconformity, bullying victimization, and depressive symptoms across adolescence and early adulthood: an 11-year longitudinal study. J Am Acad Child Adolesc Psychiatry. 2013;52:143.

Spivak H, Sege R, Flanigan E, Licenziato V, editors; American Academy of Pediatrics (2006). Connected kids: safe, strong, secure clinical guide. Elk Grove Village: American Academy of Pediatrics; 2006. http://www2.aap.org/connectedkids/clinicalguide.pdf

Stop bullying. U.S. Department of Health & Human Services, U.S. Department of Education, U.S. Department of Justice. http://www.stopbullying.gov/. Accessed 1 Feb 2016.

The resilience project: we can stop toxic stress. American Academy of Pediatrics Health Initiatives Web site. https://www.aap.org/en-us/advocacy-and-policy/aap-health-initiatives/resilience. Accessed 1 Feb 2016.

Van Geel M, Vedder P, Tanilon J. Relationship between peer victimization, cyberbullying, and suicide in children and adolescents: a meta-analysis. JAMA Pediatr. 2014;168:435.

Vreeman RC, Carroll AE. A systematic review of school-based interventions to prevent bullying. Arch Pediatr Adolesc Med. 2007;161:78.

Nature, Nurture, Adolescents, and Resilience

28

Mark A. Goldstein

What Is Resilience

Resilience is defined by an individual's ability to maintain or regain mental health despite adversity. Resilience is thought to be a dynamic process that some experts believe begins at the time of conception. Resilient individuals feel they are in control, manage strong emotions well, and can deal with stress in a positive way rather than negatively such as abusing substances. Resilient adolescents are healthier than those who lack resilience. Through complex interactions between children and their parents, siblings, relatives, schools, communities, and cultures, we may or may not acquire the ability to withstand and grow from tragedy, catastrophe, or even every day stress. Ongoing research has determined that there is a genetic and neurobiological basis for some forms of resilience.

M.A. Goldstein (ed.), *The MassGeneral Hospital for Children Adolescent Medicine Handbook*, DOI 10.1007/978-3-319-45778-9_28

Epidemiology of Mental Health Disorders in Adolescents

Researchers at the National Institute of Mental Health, Genetic Epidemiology Research Branch authored a report on the lifetime prevalence of mental health disorders in adolescents using the National Comorbidity Survey-Adolescent Supplement, which is a nationally representative face-to-face survey. The investigators were able to assess for DSM-IV mental health disorders using a structured interview of 10,123 adolescents ages 13–18 years in the continental United States. These data examined the lifetime prevalence of mental health disorders, and the findings are remarkable: anxiety disorder (31.9 %), behavioral disorders (19.1 %), mood disorders (14.3 %), and substance use disorders (11.4 %). The researchers found that 40 % of adolescents with one class of disorders also met criteria for another class of a lifetime disorder.

Studies on Infant Deprivation

In 1945 René Spitz, an Austrian born psychiatrist, published a seminal paper on "hospitalism" and its adverse consequences on the health of infants. Defining hospitalism as the effects of prolonged institutionalization in this age group, Spitz designed a study of infants in four situations. The study group included a nursery in a penal institution where delinquent pregnant girls were sequestered and cared for their children after birth, and a "foundling" home where care for the 45 infants was provided by six staffers. Apparently, parents did not provide care for the babies in the foundling home. One control group in the study consisted of infants of professional parents living in private homes, and the second control group included infants of working class parents living in private homes. In both control groups, parents delivered care to the children.

The results from the study were dramatic. Spitz assessed the development of each baby several times during the study year and assigned a number—the development quotient—after each examination. The higher the development quotient according to the

study, the better was the baby's development. The mean development quotient of infants in professional families for the first 4 months of life was 133 compared to 124 for the children in the foundling home. However, the average development quotient for children from 8 to 12 months in the foundling home had dropped to 72 compared to 131 in the professional home. Children in the prison nursery, who were cared for by their prisoner mothers, had a quotient of 105 while the working parents' children scored at 108. Spitz underscored the extraordinary significance of the mother–child relationship for the appropriate development of the infant in the first year. This important paper established the groundwork for a natural but extraordinarily tragic study of infant deprivation in the latter part of the twentieth century.

Institutional Rearing and Effects on the Developing Brain

Several research groups have evaluated children in respect to their development who were placed in Romanian orphanages as infants and stayed for extended periods of time. Many children in these orphanages had profound deprivation in respect to sensory, cognitive, linguistic, and psychosocial domains. Brain development after birth is guided by the interactions of genes and experience. It is thought that genes will set the early specification of circuits and structures; experiences will provide the fine-tuning necessary for mature function. Common to all babies should be an accessible caretaker, good nutrition, linguistic input, and sensory stimulation. These essential experiences were often less than satisfactory in Romanian orphanages. It is thought that a lack of such input can lead to underspecification and misfiring of neural circuits.

Long-term studies into the adolescence of Romanian orphanage adoptees have found four somewhat distinct behavior patterns termed quasi-autism, cognitive impairment, disinhibited attachment and inattention-over-activity. It is also theorized, beside the genes and postnatal environment, that prenatal exposures including malnutrition or maternal drug or alcohol use may work in combination on brain development and have effects for an extended period.

Adverse Childhood Experiences

Researchers believe that adverse or positive early childhood experiences can lead to "biological embedding." That is, by gene/environment interplay, an individual may be programed to react in a certain manner to internal or external stressors later in life. It is theorized that in a stressful environment, extreme or moderately extreme conditions such as lack of sensory input early in life can alter neural and physiological parameters.

The Adverse Childhood Experiences (ACE) Study found a relationship between childhood abuse and household dysfunction and the leading causes of death in adults. Adults who reported childhood exposure to physical, sexual, or psychological abuse, violence against their mothers or who lived with household members who were substance abusers, mentally ill or suicidal had a strong graded relationship between the breadth of exposure to these issues and multiple risk factors for several causes of death including chronic pulmonary, cardiac, and liver issues. The linkage between childhood ACE and chronic adult disease is thought to be certain behaviors including substance abuse, smoking, overeating, and sexual promiscuity. These behaviors may have an immediate pharmacologic or psychologic benefit on the adult with a history of early abuse or household dysfunction. It is important to consider that an adolescent smoking tobacco and thus exposing himself to a neuroregulatory substance, nicotine, may be self-medicating for a childhood ACE. Over the longer term, the chronic exposure to tobacco smoke could lead to disease including pulmonary or cardiac conditions.

In addition, studies of young women 18–25 years and free of mental and physical illness have demonstrated that the number of their ACEs was associated with an attenuated heart rate and cortisol response to stress. The investigators suggested that such altered reactivity could compromise future and necessary biological and psychological reaction to stress. Such patients could be at higher risk for depression, substance abuse, obesity, and burnout.

Genes × Environment and Depression

The response of an individual to environmental insults can be influenced in a gene-by-environmental interaction. Brain serotonin (5 HT) is involved in a broad range of functions including mood, sleep, and sexual activity. The serotonin transporter protein (5-HTT) transports serotonin from synaptic spaces into presynaptic neurons. A mutation associated with the serotonin transporter gene can result in changes of the serotonin transporter function. The serotonin transporter gene promoter has a polymorphism of the promoter region in the gene encoding 5-HTT; the short allele has less transcriptional activity and lower serotonin uptake than the long variant.

Researchers evaluated members of the Dunedin Multidisciplinary Health and Development Study, a representative cohort of 1037 children who were studied up to the age of 26 years. The members were divided into three groups based on whether they had two copies of the short allele of the 5-HTT gene, one short allele and one long allele or two long alleles. Individuals in this study cohort with one or two short alleles exhibited more depressive symptoms, depression and suicidality to stressful events compared to individuals with two copies of the long allele. The authors noted that in this situation the specific genetic makeup of the individual could moderate in a positive or negative way their response to stressful environmental insults.

Genes × Environment and PTSD

It is believed that exposure to trauma in early life is a risk factor for posttraumatic stress disorder (PTSD) in adulthood. It is theorized that adult PTSD is a continuation of the body's response to the early trauma. PTSD is thought of as a condition precipitated by a potentially life threatening situation. In a number of studies of the hypothalamic–pituitary–adrenal axis of patients with PTSD, the cortisol responses are blunted despite high corticotrophin releasing hormone levels.

Also, it is believed that prenatal and postnatal environmental events can induce developmental programming in the individual that can impact an individual's behavioral, psychological, neuroendocrine processes, and mental health into adulthood. Gene × environment interactions as well as the biological underpinnings of these interactions are areas of active investigation.

Promoting Resilience in Adolescents

Resilience is very likely to be influenced by genes and upbringing. But the acquisition of resilience is much more complicated; it is a trait that adolescents should acquire by complex biological, psychological, and social interactions and connections.

Bullying and dating violence likely impact adolescent resilience. These issues will be reviewed in this section. Substance abuse may be an indicator of a resilience issue. This topic is also discussed in this section. The family unit including parenting methods, quality of family life, personal violence, separation, and divorce will likely impact the adolescent's resilience. Poverty, race relations, and war are examples of areas where resilience could be impacted and appropriate interventions could be promoters. And of course the impact of neighborhoods, schools, religion, and government on adolescent resilience are domains that can promote or detract a teen's resilience. Promoting resilience therefore should occur on many levels from the global perspective to the family unit to the adolescent. Such interventions can and should occur at multiple levels for each adolescent.

For individuals with PTSD, cognitive behavioral therapy can assist the adolescent in reappraising the traumatic events in a more positive view. Medications may be developed that will enhance the adaptive function of the HPA axis and other stress response systems. And as the neural circuitry of resilience is understood, new interventions including behavioral modifications may be developed to enhance resilience.

Sources

Alves E, Fiedler A, Ghabriel N, et al. Early social environment affects the endogenous oxytocin system: a review and future directions. Front Endocrinol. 2015;6:32.

Caspi A, Sugden K, Moffitt T, et al. Influence of life stress on depression: moderation by a polymorphism in the 5-HTT gene. Science. 2003;301:386–9.

Comasco E, Gustafsson P, Sydsjo G, et al. Psychiatric symptoms in adolescents: FKBP5 genotype-early life adversity interaction effects. Eur Child Adolesc Psychiatry. 2015;24:1473–83.

Feder A, Nestler E, Charney D. Psychobiology and molecular genetics of resilience. Nat Rev Neurosci. 2009;10:446–51.

Felitti V, Anda R, Nordenberg D, et al. Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults. Am J Prev Med. 1998;14:245–58.

Fries A, Ziegler T, Kurian J, et al. Early experience in humans is associated with changes in neuropeptides critical for regulating social behavior. Proc Natl Acad Sci U S A. 2005;102:17237–40.

Herrman H, Stewart D, Diaz-Granados N, et al. What is resilience? Can J Psychiatry. 2011;56:258–64.

Karatsoreos I, McEwen B. Annual research review: the neurobiology and physiology of resilience and adaptation across the life course. J Child Psychol Psychiatry. 2013;54:337–47.

Merikangas K, He J, Burstein M, et al. Lifetime prevalence of mental disorders in US adolescents: results from the National Comorbidity Study-Adolescent Supplement (NCS-A). J Am Acad Child Adolesc Psychiatry. 2010;49:980–9.

Nelson C. A neurobiological perspective on early human deprivation. Child Dev Perspect. 2007;1:13–8.

Nelson C, Bos K, Gunmar M, et al. The neurobiological toll of early human deprivation. Monogr Soc Res Child Dev. 2011;76:127–46.

Rutter M. Annual research review: resilience-clinical implications. J Child Psychol Psychiatry. 2012;54:474–87.

Voelimin A, Winsaeler K, Hug E, et al. Blunted endocrine and cardiovascular: reactivity in young health women reporting a history of childhood adversity. Psychoneuroendocrinology. 2015;51:58–67.

Yehuda R, Flory J, Pratchett L, et al. Putative biological mechanisms for the association between early life adversity and the subsequent development of PTSD. Psychopharmacology. 2010;212:405–17.

Transition of Care

29

Rachel H. Alinsky and Diana C. Lemly

Transition from Adolescence to Adulthood

As adolescents reach adulthood, inevitably they must transition from pediatric to adult-oriented health care. Far too often, this passive process occurs when an adolescent ages out of his or her pediatrician's practice. During this period, a fifth of adolescents and young adults lose access to health insurance, and a quarter of them have gaps in their medical care. This transition is particularly challenging for the 20 % of youth with special health care needs, defined as those who have or are at increased risk for a chronic physical, developmental, behavioral, or emotional condition and who also require more than routine health and related services. Medical progress in the last several decades has improved the survival rates for children with chronic illnesses such that 90 % of such youth now survive and thrive into adulthood.

Transition medicine, as defined by the Society for Adolescent Health and Medicine, refers to the purposeful, planned movement of adolescents and young adults from child-centered to adult-oriented health care systems. The goal of health care transitions (HCT), according to a 2002 consensus statement by the American Academy of Pediatrics (AAP), American Academy of Family Physicians (AAFP), and American College of Physicians (ACP), is to "maximize lifelong functioning and potential through the

M.A. Goldstein (ed.), *The MassGeneral Hospital for Children Adolescent Medicine Handbook*, DOI 10.1007/978-3-319-45778-9_29

provision of high-quality, developmentally appropriate health care services that continue uninterrupted as the individual moves from adolescence to adulthood." In addition to preparing for medical transitions and transfer of care, providers should prepare and empower adolescents for transitions throughout all other aspects of their lives, including psychosocial, work, school, and independent living. While the timing of the actual "transfer" of medical care will vary between pediatricians, adolescent specialists, and med-peds or family medicine (where the health care provider may follow them longitudinally), all providers of health care services to adolescents should incorporate transition planning into their practice.

Best Practices: *Six Core Elements of Health Care Transition*

With the publication in June 2011 of "Supporting the Health Care Transition from Adolescence to Adulthood in the Medical Home," the AAP, AAFP, and ACP provided detailed practice-level guidance for supporting this health care transition. Out of this consensus, the National Health Care Transition Center (called "Got Transition") developed the Six Core Elements of Health Care Transition (see www.gottransition.org). They adapt these core elements for each type of provider, outlining concrete steps in the transition process for providers practicing pediatrics, adult internal medicine, or both (see Table 29.1 for Provider Transition Checklist and Timeline).

1. **Transition Policy**

   Create a transition policy to establish a consistent practice-wide approach and describe how transition planning is a part of lifelong preparation for a successful adult life. The policy should explicitly state the age and process by which youth shift from a pediatric to an adult model of care. It should be included in practice introductory materials and be reintroduced to youth and families around age 12 years.

Table 29.1 Provider transition checklist and timeline

Transition step	Ages 11–13	Ages 14–16	Ages 17–19	Ages 20–22
Transition readiness				
• Encourage the adolescent to assume increasing responsibility for his/her health care management	❑	❑	❑`	❑
• Meet privately with the adolescent for part of the visit	❑	❑	❑	❑
• Assure the adolescent understands his/her health condition and medications	❑	❑	❑	❑
• Assess the adolescent's and the family's readiness for transfer to an adult care provider		❑	❑	❑
• Address gaps in preparation, knowledge, and skills		❑	❑	❑
Transition planning				
• Address health care transition needs		❑	❑	❑
• Assess the need for guardianship/conservatorship; assess the adolescent's ability to make independent decisions		❑	❑	❑
• Create health care transition action plans, portable medical summary		❑	❑	❑
• Identify possible adult care providers			❑	❑
• Initiate communication with the adult provider			❑	❑
Transfer of care and transition completion				
• Send "Transition Package" and transfer letter			❑	❑
• Discuss nuances of care with the adult provider via direct communication			❑	❑
• Follow-up after the transfer			❑	❑

The timeline provided here can be modified as developmentally appropriate for your adolescent patient. Use your clinical judgment as to which items apply to your patient

(continued)

Table 29.1 (continued)

Reprinted from Lemly DC, Weitzman ER, O'Hare K. Advancing healthcare transitions in the medical home: tools for providers, families and adolescents with special healthcare needs. Curr Opin Pediatr. 2013; 25:439–46 with permission from Wolters Kluwer Health, Inc.
Modified from a document produced by the Institute for Community Inclusion at Boston Children's Hospital, as part of the Massachusetts Initiative for Youth with Disabilities, a project of the Massachusetts Department of Public Health, Supported in part by project #HOIMC00006 from the Maternal and Child Health Bureau (Title V, Social Security Act), Health Resources and Services Administration, Department of Health and Human Services.

2. **Transition Tracking and Monitoring**

   Identify transitioning youth and create a transition registry or database for the practice to track the preparation and progress of these patients. Some electronic health records can be used to identify and tag these patients.

3. **Transition Readiness**

   Assess an adolescent's strengths and weaknesses in order to guide the process of transition to adult health care. This involves identifying an adolescent's specific needs and goals in self-sufficiency and management. A number of tools are available to assess this transition readiness (see Table 29.2 for Provider Resources). One such validated form is the Transition Readiness Assessment Questionnaire (TRAQ), which has been shortened to a 20-item scale, organized into five main categories: managing your own medications; appointment keeping (accessing medical care and health insurance); tracking health issues (keeping a medical history); communicating with providers (talking with your doctor or nurse); and managing other transition activities (job or school, activities of daily living, personal safety).

4. **Transition Planning**

   Address the HCT needs and gaps in knowledge and readiness identified in step three. This involves creating a HCT action plan with the youth and family, as well as a portable medical summary and emergency care-plan if needed (see Table 29.3 for web sites that allow families and youth to create portable medical summaries and develop self-care skills). These forms should be given to the family, patient, and eventually to the adult provider. Families should be given information regarding

Table 29.2 Resources for providers

Resource	Web site
American Academy of Pediatrics Medical Home Modules: offers an education module for residents on Facilitating the Transition from Pediatric to Adult Care	www.aap.org/en-us/professional-resources/practice-support/medicalhome/Pages/Modules.aspx
Florida Health and Transitions Services (HATS) (Supported by the Florida Dept of Health, Children's Medical Services Network, Florida Developmental Disabilities Counsel, University of Florida): offers training modules and continuing education credits on Health Care Transitions, tools for transition, resources for youth and families	www.floridahats.org/
Got Transition? National Health Care Transition Center (supported by the US Maternal and Child Health Bureau/HRSA and the Center for Medical Home Improvement): broad source of information for providers, youth, families—including training materials and a comprehensive list of resources for transition planning and preparation	www.gottransition.org
National Alliance to Advance Adolescent Health: adolescent advocacy organization	www.thenationalalliance.org
Adolescent Health Transition Project (Supported by the University of Washington): resources for youth, families, providers	depts.washington.edu/healthtr

Used with permission from Got Transition: Center for Health Care Transition Improvement

Table 29.3 Resources for youth and families

Resource	Web site
Being a Healthy Adult: How to Advocate for Your Health and Health Care (Supported by Boggs Center on Developmental Disabilities at Robert Wood Johnson Medical School): guide to transition for youth with disabilities in English and Spanish	http://rwjms.rutgers.edu/boggscenter/products/documents/transitiontoadulthealthcare-en-complete.pdf
Center for Children with Special Needs (Supported by Seattle Children's Hospital): information on communication, planning future, keeping track of medical information	http://cshcn.org/teens
Florida Health and Transitions Services (HATS) For Youth and Families: skill building curricula and videos, care plans, medical summary forms	www.floridahats.org/?page_id=616
Got Transition? National Health Care Transition Center: FAQs, educational materials, tools	www.gottransition.org/youthfamilies/index.cfm
Healthy Children (from the American Academy of Pediatrics): parenting web site with information for specific age groups, including teens and young adults	https://healthychildren.org
Kids as Self-Advocates (KASA): leadership and advocacy organization run by youth with disabilities	www.fvkasa.org
National Center for Medical Home Implementation (supported by the American Academy of Pediatrics and the US Maternal and Child Health Bureau): guide to building a care notebook and medical history summary	https://medicalhomeinfo.aap.org/tools-resources/Pages/For-Families.aspx
Sick Kids Good 2 Go Transition Program (from the Hospital for Sick Kids, University of Toronto): transition tools including health passport, health apps, educational materials	www.sickkids.ca/Good2Go/For-Youth-and-Families/Index.html
Teens Health (Supported by Nemours Center for Children's Health Media): information on general teen health, chronic disease and conditions	www.kidshealth.org/teens

insurance planning, self-care management, and community resources. And for families whose youth have intellectual disabilities, it is important to plan early to address guardianship issues (see below).

5. **Transfer of Care**

   Ensure an appointment is set up with an adult provider. In advance of this appointment, there should be direct communication between the pediatric and adult providers (e-mail, phone, or in-person) regarding the patient's medical history, unique needs, and anticipatory guidance on potential complications that may arise in the transition period. The pediatric provider should send a transition package, not merely a copy of the patient's whole medical record, but rather this includes a transfer letter, portable medical summary, and supplemental documents as needed (i.e., guardianship or legal documents, condition fact sheets). For adolescents continuing with the same provider, at this point an adult approach-to-care should be implemented. Adolescents should be counseled on shared decision-making, privacy and consent, adherence to care, and preferred methods of communication.

6. **Transition Completion**

   Finally, the pediatric team remains a resource for the transferred patient and the adult team following care transfer. The pediatric team should make contact with the adult team 3–6 months post transfer to answer any unforeseen questions and ensure successful continuity of care.

Addressing Guardianship

The legal age of majority in most states is 18 years. Health Insurance Portability and Accountability Act (HIPAA) privacy rules apply—meaning that a clinician cannot release information about a patient over 18 without the patient's consent, regardless of the intellectual level or communication abilities of the patient. Therefore, parents should be informed that they cannot be given health information about their adult child without consent or legal guardianship. There are less restrictive forms of guardianship that

can support specific decision-making, while still allowing the youth to share in the process and participate as much as possible in the assent and consent of their care. But, like most aspects of the transition process, families and providers must plan ahead, as successful implementation of these important changes cannot happen overnight.

Barriers and Solutions

There are many barriers to successful transitions. Patients and families are often reluctant to leave their trusted pediatrician of many years. Additionally, they may feel uneasy about moving away from the comfortable pediatric model into an adult-centered model in which the youth takes on more autonomy. Accordingly, pediatricians should introduce the concept of transition planning at an early age and emphasize that it will be a long-term collaborative journey. Listening to and communicating carefully with the patient and family remain key parts of transition planning and have been found to be predictive of successful transitions. Transition practices must be flexible, and adapt to the unique needs of each individual, as some adolescents and their families may need more guidance in acquiring self-sufficiency and management skills.

Providers cite time constraints and the lack of reimbursement for transition services and care coordination as additional barriers to adequate transition planning. These issues can be mitigated by using coding strategies to increase reimbursement. Transition planning often happens within regularly scheduled office visits (checkups, chronic disease management), and thus providers can bill for their time using existing Current Procedural Terminology (CPT) codes for health maintenance visits (CPT 99394, 99395) or prolonged encounter with an established patient involving counseling for more than 50 % of the visit (99214, 99215). Even work such as phone calls, emails, and other coordination activities outside of discrete office visits can be billed using care plan oversight CPT codes (99374, 99375). In addition, training modules and resources have been developed to guide providers through the transition process (see Table 29.2).

Sources

American Academy of Pediatrics, American Academy of Family Physicians, American College of Physicians—American Society of Internal Medicine. A consensus statement on health care transitions for young adults with special health care needs. Pediatrics. 2002;110:1304–6.

American Academy of Pediatrics, American Academy of Family Physicians, American College of Physicians, Transitions Clinical Report Authority Group, Cooley WC, Sagerman PJ. Supporting health care transition from adolescence to adulthood in the medical home. Pediatrics. 2011;128:182–200.

Davis AM, Brown RF, Taylor J, et al. Transition care for children with special health care needs. Pediatrics. 2014;134:900–8.

Geenen SJ, Powers LE, Sells W. Understanding the role of health care providers during the transition of adolescents with disabilities and special health care needs. J Adolesc Health. 2003;32:225–33.

Lemly DC, Weitzman ER, O'Hare K. Advancing healthcare transitions in the medical home: tools for providers, families and adolescents with special healthcare needs. Curr Opin Pediatr. 2013;25:439–46.

McManus MA, Pollack LR, Cooley WC, et al. Current status of transition preparation among youth with special needs in the United States. Pediatrics. 2013;131:1090–7.

Perrin JM, Anderson LE, Van Cleave J. The rise in chronic conditions among infants, children, and youth can be met with continued health system innovations. Health Aff (Millwood). 2014;33:2099–105.

Rosen DS, Blum RW, Britto M, Society for Adolescent Medicine, et al. Transition to adult health care for adolescents and young adults with chronic conditions: position paper of the Society for Adolescent Medicine. J Adolesc Health. 2003;33:309–11.

Sawicki GS, Lukens-Bull K, Yin X, et al. Measuring the transition readiness of youth with special healthcare needs: validation of the TRAQ—Transition Readiness Assessment Questionnaire. J Pediatr Psychol. 2011;36:160–71.

Sharma N, O'Hare K, Antonelli RC, Sawicki GS. Transition care: future directions in education, health policy, and outcomes research. Acad Pediatr. 2014;14:120–7.

White PH, McManus MA, McAllister JW, et al. A primary care quality improvement approach to health care transition. Pediatr Ann. 2012;41:e1–7.

Appendix 30

Recommended Immunization Schedules for Persons Aged 0 Through 18 Years: United States, 2016

Recommended Immunization Schedules for Persons Aged 0 Through 18 Years
UNITED STATES, 2016

This schedule includes recommendations in effect as of January 1, 2016. Any dose not administered at the recommended age should be administered at a subsequent visit, when indicated and feasible. The use of a combination vaccine generally is preferred over separate injections of its equivalent component vaccines. Vaccination providers should consult the relevant Advisory Committee on Immunization Practices (ACIP) statement for detailed recommendations, available online at http://www.cdc.gov/vaccines/hcp/acip-recs/index.html. Clinically significant adverse events that follow vaccination should be reported to the Vaccine Adverse Event Reporting System (VAERS) online (http://www.vaers.hhs.gov) or by telephone (800-822-7967).

The Recommended Immunization Schedules for Persons Aged 0 Through 18 Years are approved by the

Advisory Committee on Immunization Practices
(http://www.cdc.gov/vaccines/acip)

American Academy of Pediatrics
(http://www.aap.org)

American Academy of Family Physicians
(http://www.aafp.org)

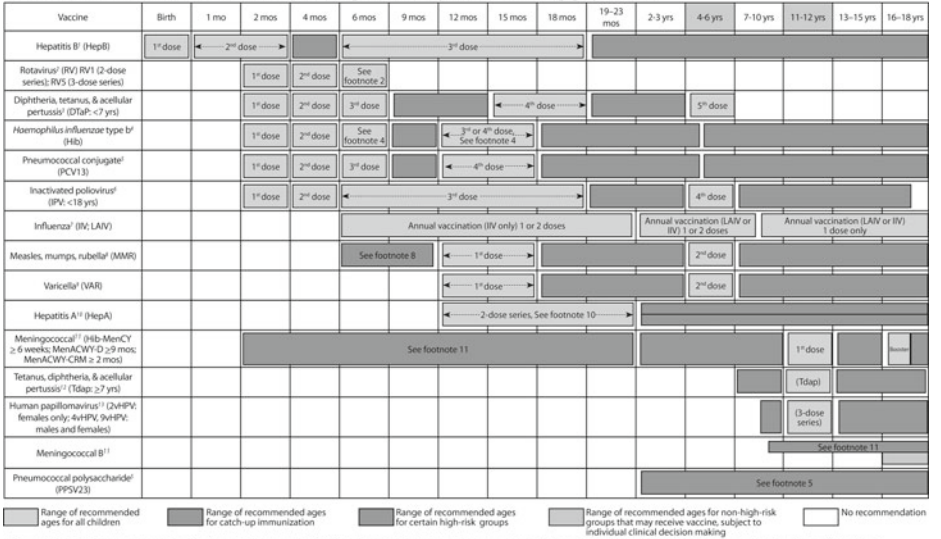
American College of Obstetricians and Gynecologists
(http://www.acog.org)

M.A. Goldstein (ed.), *The MassGeneral Hospital for Children Adolescent Medicine Handbook*, DOI 10.1007/978-3-319-45778-9_30

Figure 1. Recommended immunization schedule for persons aged 0 through 18 years – United States, 2016.

(FOR THOSE WHO FALL BEHIND OR START LATE, SEE THE CATCH-UP SCHEDULE [FIGURE 2]).

These recommendations must be read with the footnotes that follow. For those who fall behind or start late, provide catch-up vaccination at the earliest opportunity as indicated by the green bars in Figure 1. To determine minimum intervals between doses, see the catch-up schedule (Figure 2). School entry and adolescent vaccine age groups are shaded.



This schedule includes recommendations in effect as of January 1, 2016. Any dose not administered at the recommended age should be administered at a subsequent visit, when indicated and feasible. The use of a combination vaccine generally is preferred over separate injections of its equivalent component vaccines. Vaccination providers should consult the relevant Advisory Committee on Immunization Practices (ACIP) statement for detailed recommendations, available online at http://www.cdc.gov/vaccines/hcp/acip-recs/index.html. Clinically significant adverse events that follow vaccination should be reported to the Vaccine Adverse Event Reporting System (VAERS) online (http://www.vaers.hhs.gov) or by telephone (800-822-7967). Suspected cases of vaccine-preventable diseases should be reported to the state or local health department. Additional information, including precautions and contraindications for vaccination, is available from CDC online (http://www.cdc.gov/vaccines/recs/vac-admin/contraindications.htm) or by telephone (800-CDC-INFO [800-232-4636]).

This schedule is approved by the Advisory Committee on Immunization Practices (http://www.cdc.gov/vaccines/acip), the American Academy of Pediatrics (http://www.aap.org), the American Academy of Family Physicians (http://www.aafp.org), and the American College of Obstetricians and Gynecologists (http://www.acog.org).

NOTE: The above recommendations must be read along with the footnotes of this schedule.

FIGURE 2. Catch-up immunization schedule for persons aged 4 months through 18 years who start late or who are more than 1 month behind — United States, 2016.

The figure below provides catch-up schedules and minimum intervals between doses for children whose vaccinations have been delayed. A vaccine series does not need to be restarted, regardless of the time that has elapsed between doses. Use the section appropriate for the child's age. Always use this table in conjunction with Figure 1 and the footnotes that follow.

Vaccine	Minimum Age for Dose 1	Minimum Interval Between Doses			
		Dose 1 to Dose 2	Dose 2 to Dose 3	Dose 3 to Dose 4	Dose 4 to Dose 5
Children age 4 months through 6 years					
Hepatitis B[1]	Birth	4 weeks	8 weeks and at least 16 weeks after first dose. Minimum age for the final dose is 24 weeks.		
Rotavirus[2]	6 weeks	4 weeks	4 weeks[2]		
Diphtheria, tetanus, and acellular pertussis[3]	6 weeks	4 weeks	4 weeks	6 months	6 months[3]
Haemophilus influenzae type b[4]	6 weeks	4 weeks if first dose was administered before the 1st birthday. 8 weeks (as final dose) if first dose was administered at age 12 through 14 months. No further doses needed if first dose was administered at age 15 months or older.	4 weeks[4] if current age is younger than 12 months **and** first dose was administered at younger than age 7 months, **and** at least 1 previous dose was PRP-T (ActHib, Pentacel) or unknown. 8 weeks and age 12 through 59 months (as final dose for healthy children)[4] • If current age is younger than 12 months **and** first dose was administered at age 7 through 11 months (wait until at least 12 months old) OR • If current age is 12 through 59 months **and** first dose was administered before the 1st birthday, **and** second dose administered at younger than 15 months OR • If both doses were PRP-OMP (PedvaxHIB; Comvax) **and** were administered before the 1st birthday (wait until at least 12 months old). No further doses needed if previous dose was administered at age 15 months or older.	8 weeks (as final dose) This dose only necessary for children age 12 through 59 months who received 3 doses before the 1st birthday.	
Pneumococcal[5]	6 weeks	4 weeks if first dose administered before the 1st birthday. 8 weeks (as final dose for healthy children) if first dose was administered at the 1st birthday or after. No further doses needed for healthy children if first dose administered at age 24 months or older.	4 weeks if current age is younger than 12 months and previous dose given at <7months old. 8 weeks (as final dose for healthy children) if previous dose given between 7-11 months (wait until at least 12 months old); OR if current age is 12 months or older and at least 1 dose was given before age 12 months. No further doses needed for healthy children if previous dose administered at age 24 months or older.	8 weeks (as final dose) This dose only necessary for children aged 12 through 59 months who received 3 doses before age 12 months or for children at high risk who received 3 doses at any age.	
Inactivated poliovirus[7]	6 weeks	4 weeks[8]	4 weeks[8]	6 months[7] (minimum age 4 years for final dose).	
Measles, mumps, rubella[9]	12 months	4 weeks			
Varicella[9]	12 months	3 months			
Hepatitis A[10]	12 months	6 months			
Meningococcal[11] (Hib-MenCY ≥ 6 weeks, MenACWY-D ≥9 mos, MenACWY-CRM ≥ 2 mos)	6 weeks	8 weeks[11]	See footnote 11	See footnote 11	
Children and adolescents age 7 through 18 years					
Meningococcal[11] (Hib-MenCY ≥ 6 weeks, MenACWY-D ≥9 mos, MenACWY-CRM ≥ 2 mos)	Not Applicable (N/A)	8 weeks[11]			
Tetanus, diphtheria; tetanus, diphtheria, and acellular pertussis[12]	7 years[12]	4 weeks	4 weeks if first dose of DTaP/DT was administered before the 1st birthday. 6 months (as final dose) if first dose of DTaP/DT or Tdap/Td was administered at or after the 1st birthday.	6 months if first dose of DTaP/DT was administered before the 1st birthday.	
Human papillomavirus[13]	9 years	Routine dosing intervals are recommended.[13]			
Hepatitis A[10]	N/A	6 months			
Hepatitis B[1]	N/A	4 weeks	8 weeks **and** at least 16 weeks after first dose.		
Inactivated poliovirus[7]	N/A	4 weeks	4 weeks[8]	6 months[8]	
Meningococcal[11]	N/A	8 weeks[11]			
Measles, mumps, rubella[9]	N/A	4 weeks			
Varicella[9]	N/A	3 months if younger than age 13 years. 4 weeks if age 13 years or older.			

NOTE: The above recommendations must be read along with the footnotes of this schedule.

Footnotes — Recommended immunization schedule for persons aged 0 through 18 years—United States, 2016

For further guidance on the use of the vaccines mentioned below, see: http://www.cdc.gov/vaccines/hcp/acip-recs/index.html.
For vaccine recommendations for persons 19 years of age and older, see the Adult Immunization Schedule.

Additional information

- For contraindications and precautions to use of a vaccine and for additional information regarding that vaccine, vaccination providers should consult the relevant ACIP statement available online at http://www.cdc.gov/vaccines/hcp/acip-recs/index.html.
- For purposes of calculating intervals between doses, 4 weeks = 28 days. Intervals of 4 months or greater are determined by calendar months.
- Vaccine doses administered 4 days or less before the minimum interval are considered valid. Doses of any vaccine administered ≥5 days earlier than the minimum interval or minimum age should not be counted as valid doses and should be repeated as age-appropriate. The repeat dose should be spaced after the invalid dose by the recommended minimum interval. For further details, see *MMWR, General Recommendations on Immunization and Reports* / Vol. 60 / No. 2 / Table 1. *Recommended and minimum ages and intervals between vaccine doses* available online at http://www.cdc.gov/mmwr/pdf/rr/rr6002.pdf.
- Information on travel vaccine requirements and recommendations is available at http://wwwnc.cdc.gov/travel/destinations/list.
- For vaccination of persons with primary and secondary immunodeficiencies, see Table 13, *"Vaccination of persons with primary and secondary immunodeficiencies," in General Recommendations on Immunization (ACIP)*, available at http://www.cdc.gov/mmwr/pdf/rr/rr6002.pdf.; and American Academy of Pediatrics, "Immunization in Special Clinical Circumstances," in Kimberlin DW, Brady MT, Jackson MA, Long SS eds. *Red Book: 2015 report of the Committee on Infectious Diseases*. 30th ed. Elk Grove Village, IL: American Academy of Pediatrics.

1. **Hepatitis B (HepB) vaccine. (Minimum age: birth)**
   Routine vaccination:
   At birth:
   - Administer monovalent HepB vaccine to all newborns before hospital discharge.
   - For infants born to hepatitis B surface antigen (HBsAg)-positive mothers, administer HepB vaccine and 0.5 mL of hepatitis B immune globulin (HBIG) within 12 hours of birth. These infants should be tested for HBsAg and antibody to HBsAg (anti-HBs) at age 9 through 18 months (preferably at the next well-child visit) or 1 to 2 months after completion of the HepB series if the series was delayed; CDC recently recommended testing occur at age 9 through 12 months; see http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6439a6.htm.
   - If mother's HBsAg status is unknown, within 12 hours of birth administer HepB vaccine regardless of birth weight. For infants weighing less than 2,000 grams, administer HBIG in addition to HepB vaccine within 12 hours of birth. Determine mother's HBsAg status as soon as possible and, if mother is HBsAg-positive, also administer HBIG for infants weighing 2,000 grams or more as soon as possible, but no later than age 7 days.

   Doses following the birth dose:
   - The second dose should be administered at age 1 or 2 months. Monovalent HepB vaccine should be used for doses administered before age 6 weeks.
   - Infants who did not receive a birth dose should receive 3 doses of a HepB-containing vaccine on a schedule of 0, 1 to 2 months, and 6 months starting as soon as feasible. See Figure 2.
   - Administer the second dose 1 to 2 months after the first dose (minimum interval of 4 weeks), administer the third dose at least 8 weeks after the second dose AND at least 16 weeks after the **first** dose. The final (third or fourth) dose in the HepB vaccine series should be administered **no earlier than age 24 weeks**.
   - Administration of a total of 4 doses of HepB vaccine is permitted when a combination vaccine containing HepB is administered after the birth dose.

   Catch-up vaccination:
   - Unvaccinated persons should complete a 3-dose series.
   - A 2-dose series (doses separated by at least 4 months) of adult formulation Recombivax HB is licensed for use in children aged 11 through 15 years.
   - For other catch-up guidance, see Figure 2.
2. **Rotavirus (RV) vaccines. (Minimum age: 6 weeks for both RV1 [Rotarix] and RV5 [RotaTeq])**
   Routine vaccination:
   Administer a series of RV vaccine to all infants as follows:
   1. If Rotarix is used, administer a 2-dose series at 2 and 4 months of age.
   2. If RotaTeq is used, administer a 3-dose series at ages 2, 4, and 6 months.
   3. If any dose in the series was RotaTeq or vaccine product is unknown for any dose in the series, a total of 3 doses of RV vaccine should be administered.

   Catch-up vaccination:
   - The maximum age for the first dose in the series is 14 weeks, 6 days; vaccination should not be initiated for infants aged 15 weeks, 0 days or older.
   - The maximum age for the final dose in the series is 8 months, 0 days.
   - For other catch-up guidance, see Figure 2.
3. **Diphtheria and tetanus toxoids and acellular pertussis (DTaP) vaccine. (Minimum age: 6 weeks. Exception: DTaP-IPV (Kinrix, Quadracel): 4 years)**
   Routine vaccination:
   - Administer a 5-dose series of DTaP vaccine at ages 2, 4, 6, 15 through 18 months, and 4 through 6 years. The fourth dose may be administered as early as age 12 months, provided at least 6 months have elapsed since the third dose.
   - Inadvertent administration of 4th DTaP dose early: If the fourth dose of DTaP was administered at least 4 months, but less than 6 months, after the third dose of DTaP, it need not be repeated.
3. **Diphtheria and tetanus toxoids and acellular pertussis (DTaP) vaccine (cont'd)**
   Catch-up vaccination:
   - The fifth dose of DTaP vaccine is not necessary if the fourth dose was administered at age 4 years or older.
   - For other catch-up guidance, see Figure 2.
4. ***Haemophilus influenzae* type b (Hib) conjugate vaccine. (Minimum age: 6 weeks for PRP-T [ActHIB, DTaP-IPV/Hib (Pentacel) and Hib-MenCY (MenHibrix)], PRP-OMP (PedvaxHIB or COMVAX), 12 months for PRP-T (Hiberix))**
   Routine vaccination:
   - Administer a 2- or 3-dose Hib vaccine primary series and a booster dose (dose 3 or 4 depending on vaccine used in primary series) at age 12 through 15 months to complete a full Hib vaccine series.
   - The primary series with ActHIB, MenHibrix, or Pentacel consists of 3 doses and should be administered at 2, 4, and 6 months of age. The primary series with PedvaxHib or COMVAX consists of 2 doses and should be administered at 2 and 4 months of age, a dose at age 6 months is not indicated.
   - One booster dose (dose 3 or 4 depending on vaccine used in primary series) of any Hib vaccine should be administered at age 12 through 15 months. An exception is Hiberix vaccine. Hiberix should only be used for the booster (final) dose in children aged 12 months through 4 years who have received at least 1 prior dose of Hib-containing vaccine.
   - For recommendations on the use of MenHibrix in patients at increased risk for meningococcal disease, please refer to the meningococcal vaccine footnotes and also to MMWR February 28, 2014 / 63(RR01);1-13, available at http://www.cdc.gov/mmwr/PDF/rr/rr6301.pdf.

   Catch-up vaccination:
   - If dose 1 was administered at ages 12 through 14 months, administer a second (final) dose at least 8 weeks after dose 1, regardless of Hib vaccine used in the primary series.
   - If both doses were PRP-OMP (PedvaxHIB or COMVAX), and were administered before the first birthday, the third (and final) dose should be administered at age 12 through 59 months and at least 8 weeks after the second dose.
   - If the first dose was administered at age 7 through 11 months, administer the second dose at least 4 weeks later and a third (and final) dose at age 12 through 15 months or 8 weeks after second dose, whichever is later.
   - If first dose is administered before the first birthday and second dose administered at younger than 15 months, a third (and final) dose should be administered 8 weeks later.
   - For unvaccinated children aged 15 months or older, administer only 1 dose.
   - For other catch-up guidance, see Figure 2. For catch-up guidance related to MenHibrix, please see the meningococcal vaccine footnotes and also *MMWR* February 28, 2014 / 63(RR01);1-13, available at http://www.cdc.gov/mmwr/PDF/rr/rr6301.pdf.

   Vaccination of persons with high-risk conditions:
   - Children aged 12 through 59 months who are at increased risk for Hib disease, including chemotherapy recipients and those with anatomic or functional asplenia (including sickle cell disease), human immunodeficiency virus (HIV) infection, immunoglobulin deficiency, or early component complement deficiency, who have received either no doses or only 1 dose of Hib vaccine before 12 months of age, should receive 2 additional doses of Hib vaccine 8 weeks apart; children who received 2 or more doses of Hib vaccine before 12 months of age should receive 1 additional dose.
   - For patients younger than 5 years of age undergoing chemotherapy or radiation treatment who received a Hib vaccine dose(s) within 14 days of starting therapy or during therapy, repeat the dose(s) at least 3 months following therapy completion.
   - Recipients of hematopoietic stem cell transplant (HSCT) should be revaccinated with a 3-dose regimen of Hib vaccine starting 6 to 12 months after successful transplant, regardless of vaccination history; doses should be administered at least 4 weeks apart.
   - A single dose of any Hib-containing vaccine should be administered to unimmunized* children and adolescents 15 months of age and older undergoing an elective splenectomy; if possible, vaccine should be administered at least 14 days before procedure.

For further guidance on the use of the vaccines mentioned below, see: http://www.cdc.gov/vaccines/hcp/acip-recs/index.html.

4. ***Haemophilus influenzae*** **type b (Hib) conjugate vaccine (cont'd)**
   - Hib vaccine is not routinely recommended for patients 5 years or older. However, 1 dose of Hib vaccine should be administered to unimmunized* persons aged 5 years or older who have anatomic or functional asplenia (including sickle cell disease) and unvaccinated persons 5 through 18 years of age with HIV infection.

   ** Patients who have not received a primary series and booster dose or at least 1 dose of Hib vaccine after 14 months of age are considered unimmunized.*

5. **Pneumococcal vaccines. (Minimum age: 6 weeks for PCV13, 2 years for PPSV23)**

   Routine vaccination with PCV13:
   - Administer a 4-dose series of PCV13 vaccine at ages 2, 4, and 6 months and at age 12 through 15 months.
   - For children aged 14 through 59 months who have received an age-appropriate series of 7-valent PCV (PCV7), administer a single supplemental dose of 13-valent PCV (PCV13).

   Catch-up vaccination with PCV13:
   - Administer 1 dose of PCV13 to all healthy children aged 24 through 59 months who are not completely vaccinated for their age.
   - For other catch-up guidance, see Figure 2.

   Vaccination of persons with high-risk conditions with PCV13 and PPSV23:
   - All recommended PCV13 doses should be administered prior to PPSV23 vaccination if possible.
   - For children 2 through 5 years of age with any of the following conditions: chronic heart disease (particularly cyanotic congenital heart disease and cardiac failure); chronic lung disease (including asthma if treated with high-dose oral corticosteroid therapy); diabetes mellitus; cerebrospinal fluid leak; cochlear implant; sickle cell disease and other hemoglobinopathies; anatomic or functional asplenia; HIV infection; chronic renal failure; nephrotic syndrome; diseases associated with treatment with immunosuppressive drugs or radiation therapy, including malignant neoplasms, leukemias, lymphomas, and Hodgkin disease; solid organ transplantation; or congenital immunodeficiency:
     1. Administer 1 dose of PCV13 if any incomplete schedule of 3 doses of PCV (PCV7 and/or PCV13) were received previously.
     2. Administer 2 doses of PCV13 at least 8 weeks apart if unvaccinated or any incomplete schedule of fewer than 3 doses of PCV (PCV7 and/or PCV13) were received previously.
     3. Administer 1 supplemental dose of PCV13 if 4 doses of PCV7 or other age-appropriate complete PCV7 series was received previously.
     4. The minimum interval between doses of PCV (PCV7 or PCV13) is 8 weeks.
     5. For children with no history of PPSV23 vaccination, administer PPSV23 at least 8 weeks after the most recent dose of PCV13.
   - For children aged 6 through 18 years who have cerebrospinal fluid leak; cochlear implant; sickle cell disease and other hemoglobinopathies; anatomic or functional asplenia; congenital or acquired immunodeficiencies; HIV infection; chronic renal failure; nephrotic syndrome; diseases associated with treatment with immunosuppressive drugs or radiation therapy, including malignant neoplasms, leukemias, lymphomas, and Hodgkin disease; generalized malignancy; solid organ transplantation; or multiple myeloma:
     1. If neither PCV13 nor PPSV23 has been received previously, administer 1 dose of PCV13 now and 1 dose of PPSV23 at least 8 weeks later.
     2. If PCV13 has been received previously but PPSV23 has not, administer 1 dose of PPSV23 at least 8 weeks after the most recent dose of PCV13.
     3. If PPSV23 has been received but PCV13 has not, administer 1 dose of PCV13 at least 8 weeks after the most recent dose of PPSV23.
   - For children aged 6 through 18 years with chronic heart disease (particularly cyanotic congenital heart disease and cardiac failure), chronic lung disease (including asthma if treated with high-dose oral corticosteroid therapy), diabetes mellitus, alcoholism, or chronic liver disease, who have not received PPSV23, administer 1 dose of PPSV23. If PCV13 has been received previously, then PPSV23 should be administered at least 8 weeks after any prior PCV13 dose.
   - A single revaccination with PPSV23 should be administered 5 years after the first dose to children with sickle cell disease or other hemoglobinopathies; anatomic or functional asplenia; congenital or acquired immunodeficiencies; HIV infection; chronic renal failure; nephrotic syndrome; diseases associated with treatment with immunosuppressive drugs or radiation therapy, including malignant neoplasms, leukemias, lymphomas, and Hodgkin disease; generalized malignancy; solid organ transplantation; or multiple myeloma.

6. **Inactivated poliovirus vaccine (IPV). (Minimum age: 6 weeks)**

   Routine vaccination:
   - Administer a 4-dose series of IPV at ages 2, 4, 6 through 18 months, and 4 through 6 years. The final dose in the series should be administered on or after the fourth birthday and at least 6 months after the previous dose.

   Catch-up vaccination:
   - In the first 6 months of life, minimum age and minimum intervals are only recommended if the person is at risk of imminent exposure to circulating poliovirus (i.e., travel to a polio-endemic region or during an outbreak).
   - If 4 or more doses are administered before age 4 years, an additional dose should be administered at age 4 through 6 years and at least 6 months after the previous dose.
   - A fourth dose is not necessary if the third dose was administered at age 4 years or older and at least 6 months after the previous dose.

6. **Inactivated poliovirus vaccine (IPV). (Minimum age: 6 weeks) (cont'd)**
   - If both OPV and IPV were administered as part of a series, a total of 4 doses should be administered, regardless of the child's current age. If only OPV were administered, and all doses were given prior to 4 years of age, one dose of IPV should be given at 4 years or older, at least 4 weeks after the last OPV dose.
   - IPV is not routinely recommended for U.S. residents aged 18 years or older.
   - For other catch-up guidance, see Figure 2.

7. **Influenza vaccines. (Minimum age: 6 months for inactivated influenza vaccine (IIV), 2 years for live, attenuated influenza vaccine [LAIV])**

   Routine vaccination:
   - Administer influenza vaccine annually to all children beginning at age 6 months. For most healthy, nonpregnant persons aged 2 through 49 years, either LAIV or IIV may be used. However, LAIV should NOT be administered to some persons, including 1) persons who have experienced severe allergic reactions to LAIV, any of its components, or to a previous dose of any other influenza vaccine; 2) children 2 through 17 years receiving aspirin or aspirin-containing products; 3) persons who are allergic to eggs; 4) pregnant women; 5) immunosuppressed persons; 6) children 2 through 4 years of age with asthma or who had wheezing in the past 12 months; or 7) persons who have taken influenza antiviral medications in the previous 48 hours. For all other contraindications and precautions to use of LAIV, see *MMWR* August 7, 2015 / 64(30);818-25 available at http://www.cdc.gov/mmwr/pdf/wk/mm6430.pdf.

   For children aged 6 months through 8 years:
   - For the 2015-16 season, administer 2 doses (separated by at least 4 weeks) to children who are receiving influenza vaccine for the first time. Some children in this age group who have been vaccinated previously will also need 2 doses. For additional guidance, follow dosing guidelines in the 2015-16 ACIP influenza vaccine recommendations, *MMWR* August 7, 2015 / 64(30);818-25, available at http://www.cdc.gov/mmwr/pdf/wk/mm6430.pdf.
   - For the 2016-17 season, follow dosing guidelines in the 2016 ACIP influenza vaccine recommendations.

   For persons aged 9 years and older:
   - Administer 1 dose.

8. **Measles, mumps, and rubella (MMR) vaccine. (Minimum age: 12 months for routine vaccination)**

   Routine vaccination:
   - Administer a 2-dose series of MMR vaccine at ages 12 through 15 months and 4 through 6 years. The second dose may be administered before age 4 years, provided at least 4 weeks have elapsed since the first dose.
   - Administer 1 dose of MMR vaccine to infants aged 6 through 11 months before departure from the United States for international travel. These children should be revaccinated with 2 doses of MMR vaccine, the first at age 12 through 15 months (12 months if the child remains in an area where disease risk is high), and the second dose at least 4 weeks later.
   - Administer 2 doses of MMR vaccine to children aged 12 months and older before departure from the United States for international travel. The first dose should be administered on or after age 12 months and the second dose at least 4 weeks later.

   Catch-up vaccination:
   - Ensure that all school-aged children and adolescents have had 2 doses of MMR vaccine; the minimum interval between the 2 doses is 4 weeks.

9. **Varicella (VAR) vaccine. (Minimum age: 12 months)**

   Routine vaccination:
   - Administer a 2-dose series of VAR vaccine at ages 12 through 15 months and 4 through 6 years. The second dose may be administered before age 4 years, provided at least 3 months have elapsed since the first dose. If the second dose was administered at least 4 weeks after the first dose, it can be accepted as valid.

   Catch-up vaccination:
   - Ensure that all persons aged 7 through 18 years without evidence of immunity (see *MMWR* 2007 / 56 [No. RR-4], available at http://www.cdc.gov/mmwr/pdf/rr/rr5604.pdf) have 2 doses of varicella vaccine. For children aged 7 through 12 years, the recommended minimum interval between doses is 3 months (if the second dose was administered at least 4 weeks after the first dose, it can be accepted as valid); for persons aged 13 years and older, the minimum interval between doses is 4 weeks.

10. **Hepatitis A (HepA) vaccine. (Minimum age: 12 months)**

    Routine vaccination:
    - Initiate the 2-dose HepA vaccine series at 12 through 23 months; separate the 2 doses by 6 to 18 months.
    - Children who have received 1 dose of HepA vaccine before age 24 months should receive a second dose 6 to 18 months after the first dose.
    - For any person aged 2 years and older who has not already received the HepA vaccine series, 2 doses of HepA vaccine separated by 6 to 18 months may be administered if immunity against hepatitis A virus infection is desired.

    Catch-up vaccination:
    - The minimum interval between the 2 doses is 6 months.

For further guidance on the use of the vaccines mentioned below, see: http://www.cdc.gov/vaccines/hcp/acip-recs/index.html.

10. Hepatitis A (HepA) vaccine (cont'd)

Special populations:

- Administer 2 doses of HepA vaccine at least 6 months apart to previously unvaccinated persons who live in areas where vaccination programs target older children, or who are at increased risk for infection. This includes persons traveling to or working in countries that have high or intermediate endemicity of infection; men having sex with men; users of injection and non-injection illicit drugs; persons who work with HAV-infected primates or with HAV in a research laboratory; persons with clotting-factor disorders; persons with chronic liver disease; and persons who anticipate close personal contact (e.g., household or regular babysitting) with an international adoptee during the first 60 days after arrival in the United States from a country with high or intermediate endemicity. The first dose should be administered as soon as the adoption is planned, ideally 2 or more weeks before the arrival of the adoptee.

11. Meningococcal vaccines. (Minimum age: 6 weeks for Hib-MenCY [MenHibrix], 9 months for MenACWY-D [Menactra], 2 months for MenACWY-CRM [Menveo], 10 years for serogroup B meningococcal [MenB] vaccines: MenB-4C [Bexsero] and MenB-FHbp [Trumenba])

Routine vaccination:

- Administer a single dose of Menactra or Menveo vaccine at age 11 through 12 years, with a booster dose at age 16 years.
- Adolescents aged 11 through 18 years with human immunodeficiency virus (HIV) infection should receive a 2-dose primary series of Menactra or Menveo with at least 8 weeks between doses.
- For children aged 2 months through 18 years with high-risk conditions, see below.

Catch-up vaccination:

- Administer Menactra or Menveo vaccine at age 13 through 18 years if not previously vaccinated.
- If the first dose is administered at age 13 through 15 years, a booster dose should be administered at age 16 through 18 years with a minimum interval of at least 8 weeks between doses.
- If the first dose is administered at age 16 years or older, a booster dose is not needed.
- For other catch-up guidance, see Figure 2.

Clinical discretion:

- Young adults aged 16 through 23 years (preferred age range is 16 through 18 years) may be vaccinated with either a 2-dose series of Bexsero or a 3-dose series of Trumenba vaccine to provide short-term protection against most strains of serogroup B meningococcal disease. The two MenB vaccines are not interchangeable; the same vaccine product must be used for all doses.

Vaccination of persons with high-risk conditions and other persons at increased risk of disease:

Children with anatomic or functional asplenia (including sickle cell disease):

Meningococcal conjugate ACWY vaccines:

1. Menveo
   - *Children who initiate vaccination at 8 weeks:* Administer doses at 2, 4, 6, and 12 months of age.
   - *Unvaccinated children who initiate vaccination at 7 through 23 months:* Administer 2 doses, with the second dose at least 12 weeks after the first dose AND after the first birthday.
   - *Children 24 months and older who have not received a complete series:* Administer 2 primary doses at least 8 weeks apart.
2. MenHibrix
   - *Children who initiate vaccination at 6 weeks:* Administer doses at 2, 4, 6, and 12 through 15 months of age.
   - If the first dose of MenHibrix is given at or after 12 months of age, a total of 2 doses should be given at least 8 weeks apart to ensure protection against serogroups C and Y meningococcal disease.
3. Menactra
   - *Children 24 months and older who have not received a complete series:* Administer 2 primary doses at least 8 weeks apart. If Menactra is administered to a child with asplenia (including sickle cell disease), do not administer Menactra until 2 years of age and at least 4 weeks after the completion of all PCV13 doses.

Meningococcal B vaccines:

1. Bexsero or Trumenba
   - *Persons 10 years or older who have not received a complete series.* Administer a 2-dose series of Bexsero, at least 1 month apart. Or a 3-dose series of Trumenba, with the second dose at least 2 months after the first and the third dose at least 6 months after the first. The two MenB vaccines are not interchangeable; the same vaccine product must be used for all doses.

Children with persistent complement component deficiency (includes persons with inherited or chronic deficiencies in C3, C5–9, properidin, factor D, factor H, or taking eculizumab (Soliris®)):

Meningococcal conjugate ACWY vaccines:

1. Menveo
   - *Children who initiate vaccination at 8 weeks:* Administer doses at 2, 4, 6, and 12 months of age.
   - *Unvaccinated children who initiate vaccination at 7 through 23 months:* Administer 2 doses, with the second dose at least 12 weeks after the first dose AND after the first birthday.
   - *Children 24 months and older who have not received a complete series:* Administer 2 primary doses at least 8 weeks apart.
2. MenHibrix
   - *Children who initiate vaccination 6 weeks:* Administer doses at 2, 4, 6, and 12 through 15 months of age.
   - If the first dose of MenHibrix is given at or after 12 months of age, a total of 2 doses should be given at least 8 weeks apart to ensure protection against serogroups C and Y meningococcal disease.

11. Meningococcal vaccines (cont'd)

3. Menactra
   - *Children 9 through 23 months:* Administer 2 primary doses at least 12 weeks apart.
   - *Children 24 months and older who have not received a complete series:* Administer 2 primary doses at least 8 weeks apart.

Meningococcal B vaccines:

1. Bexsero or Trumenba
   - *Persons 10 years or older who have not received a complete series.* Administer a 2-dose series of Bexsero, at least 1 month apart. Or a 3-dose series of Trumenba, with the second dose at least 2 months after the first and the third dose at least 6 months after the first. The two MenB vaccines are not interchangeable; the same vaccine product must be used for all doses.

For children who travel to or reside in countries in which meningococcal disease is hyperendemic or epidemic, including countries in the African meningitis belt or the Hajj

- administer an age-appropriate formulation and series of Menactra or Menveo for protection against serogroups A and W meningococcal disease. Prior receipt of MenHibrix is not sufficient for children traveling to the meningitis belt or the Hajj because it does not contain serogroups A or W.

For children at risk during a community outbreak attributable to a vaccine serogroup

- administer or complete an age- and formulation-appropriate series of MenHibrix, Menactra, or Menveo, Bexsero or Trumenba.

For booster doses among persons with high-risk conditions, refer to *MMWR* 2013 / 62(RR02);1-22, available at http://www.cdc.gov/mmwr/preview/mmwrhtml/rr6202a1.htm.

For other catch-up recommendations for these persons, and complete information on use of meningococcal vaccines, including guidance related to vaccination of persons at increased risk of infection, see *MMWR* March 22, 2013 / 62(RR02):1-22, and *MMWR* October 23, 2015 / 64(41); 1171-1176 available at http://www.cdc.gov/mmwr/pdf/rr/rr6202.pdf, and http://www.cdc.gov/mmwr/pdf/wk/mm6441.pdf.

12. Tetanus and diphtheria toxoids and acellular pertussis (Tdap) vaccine. (Minimum age: 10 years for both Boostrix and Adacel)

Routine vaccination:

- Administer 1 dose of Tdap vaccine to all adolescents aged 11 through 12 years.
- Tdap may be administered regardless of the interval since the last tetanus and diphtheria toxoid-containing vaccine.
- Administer 1 dose of Tdap vaccine to pregnant adolescents during each pregnancy (preferred during 27 through 36 weeks gestation) regardless of time since prior Td or Tdap vaccination.

Catch-up vaccination:

- Persons aged 7 years and older who are not fully immunized with DTaP vaccine should receive Tdap vaccine as 1 (preferably the first) dose in the catch-up series; if additional doses are needed, use Td vaccine. For children 7 through 10 years who receive a dose of Tdap as part of the catch-up series, an adolescent Tdap vaccine dose at age 11 through 12 years should NOT be administered. Td should be administered instead 10 years after the Tdap dose.
- Persons aged 11 through 18 years who have not received Tdap vaccine should receive a dose followed by tetanus and diphtheria toxoids (Td) booster doses every 10 years thereafter.
- Inadvertent doses of DTaP vaccine:
  - If administered inadvertently to a child aged 7 through 10 years may count as part of the catch-up series. This dose may count as the adolescent Tdap dose, or the child can later receive a Tdap booster dose at age 11 through 12 years.
  - If administered inadvertently to an adolescent aged 11 through 18 years, the dose should be counted as the adolescent Tdap booster.
- For other catch-up guidance, see Figure 2.

13. Human papillomavirus (HPV) vaccines. (Minimum age: 9 years for 2vHPV [Cervarix], 4vHPV [Gardasil] and 9vHPV [Gardasil 9])

Routine vaccination:

- Administer a 3-dose series of HPV vaccine on a schedule of 0, 1-2, and 6 months to all adolescents aged 11 through 12 years. 9vHPV, 4vHPV or 2vHPV may be used for females, and only 9vHPV or 4vHPV may be used for males.
- The vaccine series may be started at age 9 years.
- Administer the second dose 1 to 2 months after the first dose (minimum interval of 4 weeks); administer the third dose 16 weeks after the second dose (minimum interval of 12 weeks) and 24 weeks after the first dose.
- Administer HPV vaccine beginning at age 9 years to children and youth with any history of sexual abuse or assault who have not initiated or completed the 3-dose series.

Catch-up vaccination:

- Administer the vaccine series to females (2vHPV or 4vHPV or 9vHPV) and males (4vHPV or 9vHPV) at age 13 through 18 years if not previously vaccinated.
- Use recommended routine dosing intervals (see Routine vaccination above) for vaccine series catch-up.

CS260933-A

Index

M.A. Goldstein (ed.), *The MassGeneral Hospital for Children Adolescent Medicine Handbook*, DOI 10.1007/978-3-319-45778-9