FIRST AID FOR THE®

USMLE® STEP 3

Fifth Edition

A RESIDENT-TO-RESIDENT GUIDE

Prepare for the USMLE® Step 3 with this updated, comprehensive review

Improve your ability to choose the "next step" in patient management

Test your clinical knowledge with vignette-style Q&As

Refine your diagnostic skills with 100 high-yield CCS cases

Gain confidence in answering foundational science questions

Mc Graw Hill Education

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FIRST AID FOR THE® USMLE Step 3

Fifth Edition

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DEDICATION

To Tai Le, who brought us immeasurable love and joy.

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Contents

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Preface

With *First Aid for the USMLE Step 3*, we continue our commitment to providing residents and international medical graduates with the most useful and up-to-date preparation guides for the USMLE exams. This fifth edition represents a thorough review in many ways and includes the following:

- An updated review of hundreds of high-yield Step 3 topics, presented in a format designed to highlight board-relevant information.
- A renewed emphasis on integrated pathophysiology and on the "next step" in diagnosis and management.
- More high-yield vignette-style "flash cards" and full-color images designed to enhance study.
- A thoroughly revised exam preparation guide for the USMLE Step 3 with proven test-taking strategies based on the 2-day exam.
- A high-yield guide to the Computer-based Case Simulations (CCS) that includes invaluable tips and shortcuts.
- 100 updated cases with management strategies similar to those of the actual CCS.

We invite you to share your thoughts and ideas to help us improve *First Aid for the USMLE Step 3*. See How to Contribute, p. xiii.

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How to Contribute

To help us continue to produce a high-yield review source for the USMLE Step 3 exam, you are invited to submit any suggestions or corrections. We also offer paid internships in medical education and publishing ranging from three months to one year (see below for details).

Please send us your suggestions for:

- Study and test-taking strategies for the computerized USMLE Step 3.
- New facts, mnemonics, diagrams, and illustrations.
- CCS-style cases.
- Low-yield topics to remove.

For each entry incorporated into the next edition, you will receive up to a $20 Amazon gift card as well as personal acknowledgment in the next edition. Diagrams, tables, partial entries, updates, corrections, and study hints are also appreciated, and significant contributions will be compensated at the discretion of the authors. Also let us know about material in this edition that you feel is low yield and should be deleted.

The preferred way to submit entries, suggestions, or corrections is via the First Aid Team's blog at:

www.firstaidteam.com

Please include name, address, school affiliation, phone number, and e-mail address (if different from the address of origin). We can also be contacted at **firstaid@scholarrx.com**.

NOTE TO CONTRIBUTORS

All entries become property of the authors and are subject to editing and reviewing. Please verify all data and spellings carefully. If similar or duplicate entries are received, only the first entry received will be used. Include a reference to a standard textbook to facilitate verification of the fact. Please follow the style, punctuation, and format of this edition if possible.

INTERNSHIP OPPORTUNITIES

The author team is pleased to offer part-time and full-time paid internships in medical education and publishing to motivated physicians. Internships may range from three months (eg, a summer) up to a full year. Participants will have an opportunity to author, edit, and earn academic credit on a wide variety of projects, including the popular First Aid series. Writing/editing experience, familiarity with Microsoft Word, and Internet access are desired. For more information, e-mail a résumé or a short description of your experience along with a cover letter to the authors at **firstaid@scholarrx.com.**

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CHAPTER 1

GUIDE TO THE USMLE STEP 3

KEY FACT

For Step 3 eligibility, USMLE recommends that you should have 1 year (or almost 1 year) of postgraduate training in a graduate medical education program that is US-accredited and meets state board licensing requirements.

USMLE Step 3

The USMLE® Step 3 is one of the last steps one must take toward becoming a licensed physician. The exam assesses the extent to which one can apply medical knowledge to the unsupervised practice of medicine. For international medical graduates (IMGs) who are applying for residency training in the United States, it also represents an opportunity to strengthen the residency application. The Step 3 exam focuses on the initial and long-term management of common clinical problems in different settings.

In this section, we will provide an overview of the Step 3 exam and will offer you proven approaches toward conquering it. For a detailed description of Step 3, visit www.usmle.org or refer to the two booklets provided on the USMLE Web site: *USMLE Step 3 Content Description and General Information* and *USMLE Step 3 Sample Test Questions*.

HOW IS STEP 3 STRUCTURED?

The Step 3 exam is administered on two separate days that need not be consecutively scheduled. The first day of the exam covers the Foundations of Independent Practice. The second day emphasizes Advanced Clinical Medicine and is discussed in detail in the Primum® Computer-based Case Simulations (CCS) section.

Foundations of Independent Practice (FIP): Day 1 of testing lasts 7 hours and consists of six blocks of 38–40 multiple-choice questions for a total of 235 questions. Test takers are given a maximum of 60 minutes to complete each block. There is a 45-minute break as well as an optional 5-minute tutorial. Break time can be extended if a test taker skips the optional tutorial or finishes a test block early. Once you finish a test block, you cannot go back to it.

The content material on day 1 focuses on the basic principles required for the provision of effective health care. This includes basic foundational science (ie, knowledge of the underlying mechanisms of both normal and abnormal physiologic processes); knowledge of the history and PE, the diagnostic process, and use of studies in diagnosing diseases; the principles and interpretation of biostatistics, epidemiology, and population health; and the application of social sciences, including interpersonal skills, medical ethics, systems-based practice, and patient safety, to the provision of health care. Also included on day 1 are items that test one's ability to interpret the medical literature and pharmaceutical advertisements.

Advanced Clinical Medicine (ACM): Day 2 lasts approximately 9 hours and consists of six blocks of 30 multiple-choice questions for a total of 180 questions. Test takers are given 45 minutes to complete each block. There is an optional 5-minute tutorial. Day 2 also includes a CCS component with 13 case simulations. Each case is allotted 10 or 20 minutes. There is also an optional 7-minute CCS tutorial and a 45-minute break. As on day 1, test takers can add time to the break by completing a test block early or by skipping the optional tutorial. At the end of the day, there is an optional survey.

Day 2 of the exam focuses on the test taker's ability to apply medical knowledge in the context of patient management and the evolving manifestations of disease over time. The test focuses on knowledge of medical decision making, diagnosis and management, and disease prognosis and outcome. Additional

emphasis is placed on screening and health maintenance management. Tables 1-1 and 1-2 graphically depict the areas of concentration of the revised Step 3 exam.

WHAT TYPES OF QUESTIONS ARE ASKED?

Virtually all questions on Step 3 are case based. A substantial amount of extraneous information may be given, or a clinical scenario may be followed by a question that one could answer without actually reading the case. It is your job to determine which information is superfluous and which is pertinent to the case at hand. There are three question formats:

- **Single items:** This is the most frequent question type. It consists of the traditional single-best-answer question with 4–5 choices.
- **Multiple-item sets:** This consists of a clinical vignette followed by 2 or 3 questions regarding that case. These questions can be answered independently. Again, there is only one best answer.
- **Cases:** This is a clinical vignette followed by 2–5 questions. You actually receive additional information as you answer questions, so it is important that you answer questions sequentially without skipping. As a result, once you proceed to the next question in the case, you cannot change the answer to the previous question.

KEY FACT

For long vignettes, read the question stem first, and then read the case.

TABLE 1-1. Step 3 Content Areas Tested

Category	Percent of Overall Content
General Principles of Foundational Science[a]	1–3%
Biostatistics and Epidemiology/Population Health and Interpretation of the Medical Literature Social Science	14–18%
Immune System Blood and Lymphoreticular System Behavioral Health Nervous System and Special Senses Skin and Subcutaneous Tissue Musculoskeletal System Cardiovascular System Respiratory System Gastrointestinal System Renal and Urinary System Pregnancy, Childbirth, and the Puerperium Female Reproductive System and Breast Male Reproductive System Endocrine System Multisystem Processes and Disorders	80–85%

[a]This category includes test items covering underlying physiologic mechanisms that are normal and not limited to specific organ systems.

TABLE 1-2. Step 3 Competencies Tested[a]

Competency	Day 1: FIP	Day 2: ACM
Medical Knowledge/Scientific Concepts	18–22%	
Patient Care: Diagnosis History/PE Laboratory/Diagnostic Studies Diagnosis	40–45%	
Prognosis/Outcome		20–25%
Patient Care: Management Health Maintenance/Disease Prevention Pharmacotherapy Clinical Interventions Mixed Management Surveillance for Disease Recurrence		75–80%
Communication and Professionalism	8–12%	
Systems-based Practice/Patient Safety and Practice-based Learning	22–27%	

[a]The competencies listed in rows 2–4 (Patient Care: Diagnosis and Management) are also tested on the CCS.

Questions are organized by clinical setting and include an outpatient office/community health center, an inpatient hospital, and an ED. The clinical care situations you will encounter in these settings include:

- **Initial workup:** This is characterized by the initial assessment and management of clinical issues among patients typically seen in an outpatient setting.
- **Continuing care:** This physician-patient encounter typically occurs in an ambulatory context but may also take place in an inpatient setting. The encounter focuses on the management of previously diagnosed conditions and issues surrounding health maintenance. Encounters are characterized by the evaluation and management of acute exacerbations or complications of chronic and progressive medical illnesses.
- **Urgent intervention:** This encounter tests the prompt recognition and management of life-threatening emergencies, typically in EDs or in the context of hospitalized patients.

KEY FACT

Remember that Step 3 tends to focus on outpatient continuing-management scenarios.

When approaching vignette questions, you should keep a few things in mind:

- Be sure to note the age and race of the patient in each clinical scenario. When ethnicity is given, it is often relevant. Know these associations well (see high-yield facts), especially for more common diagnoses.
- Be able to recognize key facts that distinguish major diagnoses.
- Questions often describe clinical findings rather than naming eponyms (eg, they cite "audible hip click" instead of "positive Ortolani sign").

HOW ARE THE SCORES REPORTED?

Like the Step 1 and 2 score reports, your Step 3 report includes your pass/fail status, a score with a three-digit scale, and a graphical performance profile organized by discipline and disease process. A minimum score of 196 is required for passing. According to the USMLE, the mean score for first-time test takers from accredited US medical schools ranges from 222 to 225 with a standard deviation of approximately 16.

According to recent data from the USMLE Web site, approximately 98–100% of graduates from US and Canadian medical schools passed Step 3 on their first try, whereas 88% of IMGs passed on their first attempt. For detailed, year-to-year performance, visit www.usmle.org/performance-data/.

KEY FACT

As part of its multiple-choice questions, the exam tests your ability to understand and interpret medical journal abstracts and pharmaceutical advertisements.

KEY FACT

Check the "FAQ" and "Scores" tabs of the USMLE Web site for the latest score information.

HOW DO I REGISTER TO TAKE THE EXAM?

The process of registering for the Step 3 exam varies depending on whether you are a US or a Canadian-based medical student, an allopathic or osteopathic student, or a student living outside the United States or Canada. For US and Canadian medical students, application is made through the Web site of the Federation of State Medical Boards (FSMB), www.fsmb.org. The registration was $850 for eligibility periods ending in 2018. Note again that the 2 days of the exam do not need to be scheduled consecutively.

Your scheduling permit is sent via e-mail to the e-mail address provided on the application materials. Once you have received your scheduling permit, it is your responsibility to print it and decide when and where you would like to take the exam. To see a list of Prometric locations near you and to arrange a time to take the exam, call Prometric's toll-free number or visit www.prometric.com.

KEY FACT

The exam is scheduled on a "first-come, first-served" basis, so contact Prometric as soon as you receive your scheduling permit!

The electronic scheduling permit you receive will contain the following important information:

- Your USMLE identification number
- The 90-day eligibility period in which you may take the exam
- Your "scheduling number," which you will need to make your exam appointment with Prometric
- Your Candidate Identification Number, or CIN, which you must enter at your Prometric workstation to access the exam

Prometric has no access to these codes or your scheduling permit and will not be able to supply them for you. You will not be allowed to take Step 3 unless you present your permit, printed ahead of time, along with an unexpired, government-issued photo identification that contains your signature (eg, a driver's license or passport). Make sure the name on your photo ID exactly matches the name that appears on your scheduling permit.

WHAT IF I NEED TO RESCHEDULE THE EXAM?

You can change your date and/or center within your 3-month eligibility period at no charge by contacting Prometric, as long as you do so 31 or more days before your scheduled test date. A fee will apply if you reschedule between 5 and 30 days before your test date, and a larger fee will apply if you reschedule less than 5 days before your test date. You may not reschedule your test the day before. If you need to re-schedule outside your initial eligibility period, you can apply for a single 3-month extension (eg, April/May/June can be extended

through July/August/September) after your eligibility period has begun (go to www.nbme.org for more information). For other rescheduling needs, you must submit a new application along with another application fee.

WHAT ABOUT TIME?

Time is of special interest on the exam. As you take the exam, the computer will keep track of how much time has elapsed. However, the computer will show you only how much time remains in a given test block, not how much time is left in the entire test (unless you look at the full clock by using the Alt-T command). Therefore, it is up to you to determine whether you are pacing yourself properly. Note that on both days of the exam, you have approximately 75 seconds per multiple-choice question. If you feel that you can't answer a question within a reasonable time, take an educated guess and move on, as there are no penalties for wrong answers.

KEY FACT

Never, ever leave a question blank! You can always mark it and come back later.

It should be noted that a total of 45 minutes is allowed for break time. You choose how to allot those 45 minutes and you may take all 45 minutes at once or split the period into multiple breaks. However, you can elect not to use all of your break time, or you can gain extra break time either by skipping the tutorial or by finishing a block ahead of the allotted time. The computer will not warn you if you have used more than your allotted break time.

IF I LEAVE DURING THE EXAM, WHAT HAPPENS TO MY SCORE?

You are considered to have started the exam once you have entered your CIN onto the computer screen. For an official score to be recorded, however, you must finish the entire exam. This means that you must start an exam block and either finish it or run out of time. If you do not complete all the blocks, your USMLE score transcript will document your exam as an incomplete attempt, and no actual score will be reported.

The exam ends when all blocks have been completed or time has elapsed. As you leave the testing center, you will receive a written test-completion notice to document your completion of the exam.

HOW LONG WILL I HAVE TO WAIT BEFORE I GET MY SCORES?

The USMLE typically reports scores 3–4 weeks after the examinee's test date. During peak periods, however, it may take up to 8 weeks for scores to be made available. Official information concerning the time required for score reporting is posted on the USMLE Web site.

USMLE/NBME RESOURCES

We strongly encourage you to use and study the free materials provided by the testing agencies (Table 1-3) as well as those found on the USMLE Web site at www.usmle.org/practice-materials/index.html. These include:

- *USMLE Step 3 Content Description and General Information*
- *USMLE Step 3 Sample Test Questions*
- *Tutorial and Practice Test Items for Multiple-Choice Questions*
- *Primum Computer-based Case Simulations (CCS)*

In addition, computer-based practice tests are available for a fee through the NBME for those who seek to become familiar with the Prometric test center environment.

TABLE 1-3. Testing Agencies

National Board of Medical Examiners (NBME) Department of Licensing Examination Services 3750 Market Street Philadelphia, PA 19104-3102 215-590-9500 Fax: 215-590-9460 www.nbme.org	**Federation of State Medical Boards (FSMB)** 400 Fuller Wiser Road Euless, TX 76039 817-868-4000 Fax: 817-868-4099 www.fsmb.org
Educational Commission for Foreign Medical Graduates (ECFMG) 3624 Market Street Philadelphia, PA 19104-2685 215-386-5900 Fax: 215-386-9196 www.ecfmg.org	**USMLE Secretariat** 3750 Market Street Philadelphia, PA 19104-3102 215-590-9700 Fax: 215-590-9460 www.usmle.org

Primum Computer-Based Case Simulations

This computerized patient simulation is administered on the second day of the Step 3 exam. You will be given 13 cases over 4 hours and will have up to 10 or 20 minutes to complete each case. As with the rest of the Step 3 exam, the CCS aims to test your ability to properly diagnose and manage common conditions in a variety of patient settings. Many of the conditions tested are obvious or easily diagnosed.

Clinical problems presented on the CCS may be acute or chronic and may range from mild to life-threatening. Cases may last anywhere from a few minutes to a few months in simulated time, but you will be allotted only 10 or 20 minutes of real time to complete each. Regardless of the setting (eg, office, ED, ICU), you will serve as the patient's primary physician and will assume complete responsibility for his or her care.

REVIEWING A CASE

If you wish to excel on the CCS, there is no substitute for downloading and trying out the sample cases from the USMLE Web site (www.usmle.org/practice-materials/index.html). Devoting at least a few hours to these cases and familiarizing yourself with the CCS interface will improve your performance on the exam regardless of your level of computer expertise.

For each case, you will be presented with a chief complaint, vital signs, and a history of present illness (HPI). You will then initiate patient management, continue care, and advance the case by taking one of the following four actions represented on the computer screen:

1. **Get interval history or PE.** You can obtain either a focused or a full PE. You can also obtain an interval history to see how a patient is doing. Getting an interval history or performing a PE will automatically advance the clock in simulated time.

Quick tips and shortcuts:

- If the patient's vital signs are unstable, remember that you may have to write some orders (eg, IV fluids, oxygen, type and cross-match) before performing the PE.
- Remember to keep the PE focused. Conducting a full PE may be wasteful and may cost you valuable simulated time. You can always perform additional exam components as they become necessary.

2. **Write order or review chart.** You can manage the patient by typing orders. For example, you can order tests, monitoring, treatments, procedures, consultations, and counseling. The order sheet on the CCS is formatted as free-text entry, so you can type whatever you choose; the computer has a 12,000-term vocabulary that can accommodate approximately 2500 orders or actions.

KEY FACT

Cases can, and frequently do, end in < 20 minutes.

KEY FACT

You will see few diagnostic "zebras" on the CCS. The focus here is on management, management, management!

KEY FACT

Orders on the CCS require free-text entry. There are no multiple-choice options here!

When you order a medication, you will also need to specify the route and frequency of administration. If a patient comes into a case with preexisting medications, these meds will appear on the order sheet with an order time of "Day 1 @00:00." The medications will continue to be administered unless you decide to cancel them. Unlike the interval history or PE, you must manually advance simulated time to see the results of your orders.

Quick tips and shortcuts:

- As long as the computer can recognize the first three characters of your order, it can provide a list of orders from which to choose.
- When inputting an order, simply type the name of the test, therapy, or procedure you wish to obtain. Don't type verbs such as "get," "administer," or "do."
- Complete the sample cases to get a sense of the types of abbreviations that the computer will recognize (eg, CBC, CXR, ECG).
- Familiarize yourself with the routes of administration and dosing frequencies of common medications. You do not need to know dosages or drip rates.
- Never assume that other health care staff or consultants will write orders for you. On the contrary, you are responsible for writing all orders, including routine actions such as IV fluids, oxygen, monitoring, and diabetic diet. If a patient is preoperative, don't forget NPO, type and cross-match, and antibiotics if necessary.
- You can always change your mind about an order and cancel it as long as the clock has not advanced.
- Review any preexisting medications on the order sheet. Sometimes the patient's problem may be due to a preexisting medication adverse effect or a drug interaction!

3. **Obtain results or see patient later.** To determine how a given case evolves after you have entered your orders, you must advance the clock. You can specify a time to see the patient either in the future or when the next results become available. Upon advancing the clock, you may receive messages from the patient, family, or health care staff updating you on the patient's status before the specified time or results are made available. If you stop a clock advance to a future time (eg, a follow-up appointment) to review results from previous orders, that future event will be canceled.

Quick tips and shortcuts:

- Before advancing the clock, ask yourself whether the patient will be stable during that time period. Also ask yourself whether the patient is in the appropriate location or whether he or she should be transferred to another setting.
- If you receive an update while the clock is advancing, be sure to review your current management, especially if the patient's condition is worsening.

4. **Change location.** In the simulated exam, you will have an outpatient office with admitting privileges to a 400-bed tertiary-care facility. As in real life, the patient will typically present to you in either an office or an ED. Once you've done all you can for the patient, you can elect to transfer him or her to another setting, such as the ward or the ICU, for appropriate care. Note that in the context of the CCS, "ICU" is a blanket term that encompasses all types of intensive care, including medical, surgical, pediatric, obstetrics, and neonatal. Where appropriate, the patient may be discharged home with follow-up.

Quick tips and shortcuts:

- Always ask yourself if the patient is in the right setting to receive optimal management.
- Remember that you will remain the patient's primary physician regardless of where he or she goes.
- When changing locations (and especially when discharging the patient), remember to discontinue orders that are no longer needed.
- Remember that patients who are discharged home will require a follow-up appointment.
- Before discharging a patient, think about whether he or she needs any health maintenance or counseling.

KEY FACT

Wherever the patient goes, you go!

KEY FACT

The final diagnosis and reasons for consultation do not count toward your score!

FINISHING THE CASE

On the CCS, each case ends when you have used up your allotted 10 or 20 minutes. If the measurement objectives for the case have already been met before this period has elapsed, the computer may ask you to exit early. Toward the end, you will be given a warning that the case is about to conclude. You will then be given an opportunity to cancel existing orders as well as to write new short-term orders. You will be asked for a final diagnosis before exiting.

HOW IS THE CCS GRADED?

Your grade will be determined by a scoring algorithm that is based on generally accepted practices of care. This algorithm allows for wide variation and recognizes that there may be more than one appropriate way to approach a case. In general, you will gain points for appropriate management actions and will lose points for actions that are not indicated or are potentially harmful to your patient. These actions are weighted such that key actions (eg, ordering an emergent needle thoracostomy for a patient with tension pneumothorax) will earn you a comparatively greater number of points, whereas highly inappropriate actions (eg, ordering a liver biopsy for a patient with an ear infection) will cost you relatively more points.

Note, however, that even if your management actions are correct, you may not be given full credit for them if you perform them out of sequence or following an inappropriate delay in simulated time. Unnecessary or excessive orders—even if they pose no risk to the patient—will cost you points as well. The bottom line is that the CCS tends to reward thorough but efficient medicine.

HIGH-YIELD STRATEGIES FOR THE CCS

As mentioned earlier, it is essential that you practice the sample CCS cases before taking the actual exam. Make sure you do both outpatient and inpatient cases. Try different abbreviations to get a feel for the vocabulary you should use when you write orders. You can also apply different approaches toward the same case to see how the computer reacts.

Read through the 100 cases in Chapter 19, High-Yield CCS Cases. They will show you how clinical conditions can present and play out in the CCS. Remember that the computer wants you to do the right things at the right times while incurring minimal waste and risk to the patient. When taking the exam, also bear the following in mind:

- **Read the HPI carefully.** Use the HPI to develop a short differential that will direct your PE and initial management. Often the diagnosis will become apparent to you before you begin the PE. Jot down pertinent positives and negatives so that you don't have to come back and review the chart. Keep in mind any drug allergies that the patient might have.
- **Remember that unstable patients need immediate management.** If a patient's vital signs are unstable, you may want to take some basic management measures, such as administering IV fluids and oxygen, before starting the PE. With unstable patients, your goal should be to order tests that will help identify and manage the patient's underlying condition while incurring minimal delay.
- **Consultants are rarely helpful.** Although you will earn some points for calling a consultant for an indicated procedure (eg, a surgeon for an appendectomy), consultants will generally offer little in the way of diagnostic or management assistance.
- **Don't forget health maintenance, education, and counseling.** After treating tension pneumothorax, counsel the patient about smoking cessation if the HPI mentions that he or she is an active smoker.
- **Don't treat the patient alone.** The computer will not permit you to treat a patient's family or sexual partner, but it will allow you to provide education or counseling. If a female patient is of childbearing age, check a pregnancy test before starting a potentially teratogenic treatment.
- **Some patients will worsen despite good care, while others will improve despite poor management.** If a case is not going your way, reassess your approach to make sure you're not missing anything. If you're confident about your diagnosis and management strategy, stop second-guessing it. Sometimes the CCS tests your ability to handle difficult clinical situations.

KEY FACT

A patient whose condition is worsening may reflect the testing goals of the case rather than an error on your part.

CHAPTER 2

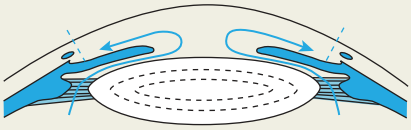
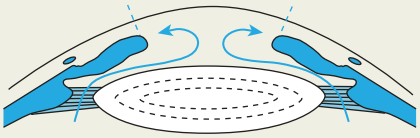
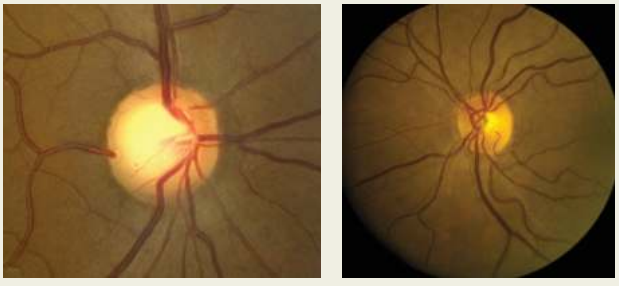
AMBULATORY MEDICINE

Ophthalmology

GLAUCOMA

An optic neuropathy associated with ↑ intraocular pressure (IOP) > 21 mm Hg and vision loss if untreated. Table 2-1 contrasts open-angle with closed-angle glaucoma.

TABLE 2-1. Open-Angle vs Closed-Angle Glaucoma

	Open-Angle Glaucoma	Closed-Angle Glaucoma
Etiology	The angle between the iris and cornea is open, but the drainage canals are blocked; most common 	The angle between the iris and cornea (anterior chamber angle) is closed, impairing drainage 
Risk factors	Africans, Hispanics, age > 60 years of age, steroid users, eye trauma, high myopia (nearsightedness), hypertension, and ⊕ family history	Asians, increasing age, women, high hyperopia (farsightedness), and ⊕ family history
Symptoms	Chronic; gradual loss of peripheral vision	Acute; presents with eye pain, headache, nausea, conjunctival injection, halos around lights, and fixed, dilated pupils
Diagnosis	High IOP and an ↑ cup-to-disk ratio (> 50%) (A, glaucomatous nerve; B, normal optic nerve)  **A** **B**	High IOP (≥ 30 mm Hg; normal 12–22 mm Hg)
Treatment	First line: Prostaglandin agonist (eg, latanoprost) Second line: α2-adrenergic agonist (eg, brimonidine) Nonselective topical β-blockers (eg, timolol, levobunolol) Topical carbonic anhydrase inhibitors (eg, dorzolamide, brinzolamide)	First line: Topical, oral, or IV carbonic anhydrase inhibitors (eg, acetazolamide) Topical β-adrenergic antagonists (eg, timolol) Topical α2-adrenergic agonists (eg, brimonidine) Topical miotics (eg, pilocarpine) Second line: If IOP > 50, start hyperosmotic agents (eg, glycerine, mannitol) Definitive treatment: Laser peripheral iridotomy after resolution or prophylaxis in high-risk individuals

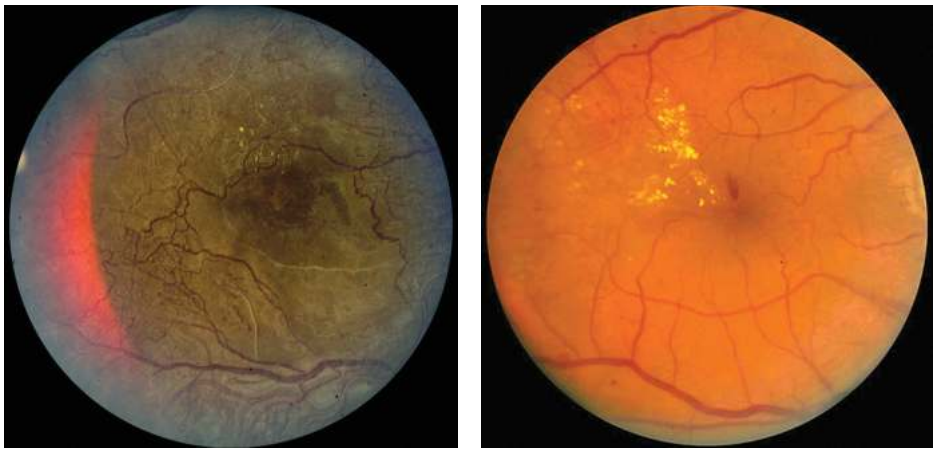
Images A and B reproduced with permission from USMLE-Rx.com; courtesy of Dr. Nicholas Mahoney.

DIABETIC RETINOPATHY

- **Painless:** Gradual vision loss in diabetic patients. The leading cause of blindness in the United States. Divided into nonproliferative and proliferative forms (see Figure 2-1).
- **Hx/PE:** Funduscopic findings include neovascularization, microaneurysms, flame hemorrhages, exudate, and macular edema.
- **Tx:** For proliferative retinopathy, first line: Laser photocoagulation, intravitreal anti-vascular endothelial growth factor (anti-VEGF). Severe: Vitrectomy if large vitreous hemorrhage or significant macular traction.
- **Prevention:** Diabetics should have a comprehensive ophthalmologic screening annually. Progression can be slowed with tight glucose and BP control.

HERPES ZOSTER OPHTHALMICUS

- Infection of the V1 branch of CN V (the ophthalmic division of the trigeminal nerve; see Figure 2-2). Most common in immunocompromised individuals or the aging population > 65.
- **Hx/PE:** Presents with fever, headache, malaise, periorbital burning/itching, conjunctivitis, keratitis, ↑ IOP, optic neuropathy, and cranial nerve palsies. Vesicles are purulent and progress to crusting following a dermatomal pattern and do NOT cross the midline.
- **Tx:** IV acyclovir/valacyclovir/famciclovir within 72 hours after the appearance of the rash ↓ the incidence of late ocular complications (eg, corneal scarring, glaucoma, cataract). Refer immediately to an ophthalmologist. Steroids are contraindicated.



A B

FIGURE 2-1. Diabetic Retinopathy. (**A**) Proliferative form with clinically significant macular edema, neovascularization. (**B**) Nonproliferative form with exudates, dot-blot hemorrhages and microaneurysms. (Reproduced with permission from USMLE-Rx.com.)

Q

A 42-year-old woman presents with headache, nausea, vomiting, and a red eye that has progressively worsened since this morning. She also notes vision changes. Exam reveals conjunctival injection; a mid-range fixed, dilated pupil; and no focal weaknesses in the extremities. What should you do next?

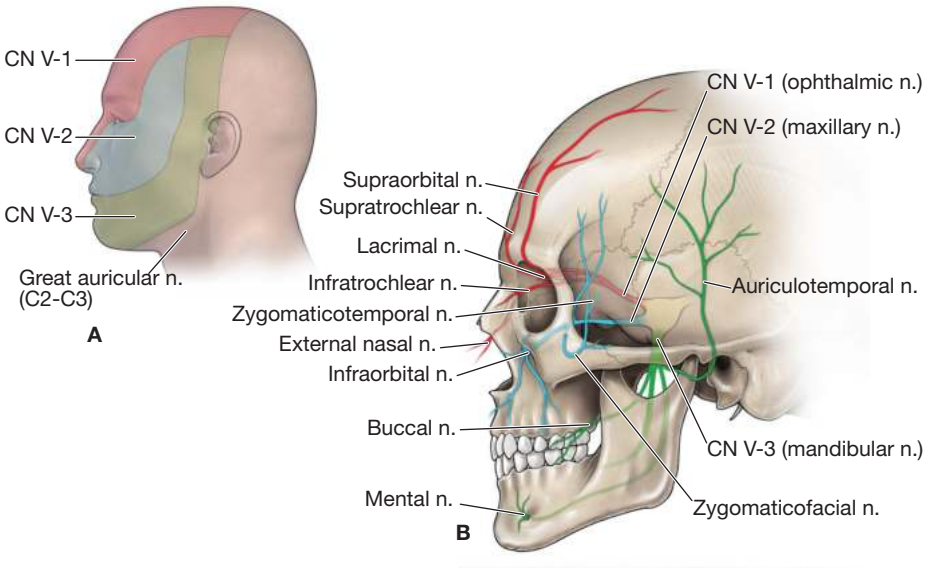


FIGURE 2-2. Trigeminal nerve. (**A**) CN V and its cutaneous fields of the face. (**B**) Branches of CN V in the face. (Modified with permission from Morton DA et al. *The Big Picture: Gross Anatomy.* New York: McGraw-Hill, 2011, Fig. 20-1A and B.)

Ear, Nose, and Throat

INFLUENZA

An acute respiratory illness caused by influenza A or B. Occurs primarily during the fall and winter.

History/PE

Presents following an incubation period of 1–2 days with acute-onset upper and lower respiratory tract symptoms, myalgias, fevers, and weakness.

Diagnosis

- **Initial test:** Rapid antigen tests have a sensitivity of only 40–60%.
- **Definitive:** Polymerase chain reaction (PCR) testing (24 hours) or viral culture (3–7 days).
- Include CXR for older adults (> 50 years of age or in nursing home) or high-risk patients with comorbidities (eg, DM, cardiopulmonary disease) to exclude pneumonia.

KEY FACT

Prophylaxis/treatment with zanamivir and oseltamivir is most effective within 48 hours of exposure or symptom onset.

Treatment

- Antiviral drugs zanamivir and oseltamivir can be used prophylactically or to treat existing infection in at-risk individuals; most effective when given within 48 hours of exposure or at symptom onset.
- Most influenza strains have become resistant to amantadine and rimantadine.

A

Use tonometry to check IOP. A pressure of ≥ 30 mm Hg confirms the diagnosis of acute closed-angle glaucoma. Emergent referral to ophthalmology and possible hospitalization to reduce IOP. Treatment includes topical β-blocker (timolol), IV acetazolamide, and topical steroids.

Complications

2° bacterial pneumonia, often from *Streptococcus pneumoniae*, is responsible for one-quarter of influenza-related deaths.

HEARING LOSS

Common in elderly persons. Table 2-2 contrasts conductive with sensorineural hearing loss.

KEY FACT

Otosclerosis is the most common cause of conductive hearing loss in young adults.

ALLERGIC RHINITIS

Affects up to 20% of the adult population. Patients may also have asthma and atopic dermatitis.

History/PE

- Presents with congestion, rhinorrhea, sneezing, eye irritation (eg, redness, swelling), and postnasal drip.
- Induced by environmental allergens such as pollens, animal dander, dust mites, and mold spores. May be seasonal.
- Exam reveals edematous, pale mucosa; cobblestoning in the pharynx; scleral injection; and blue, boggy turbinates.

Diagnosis

- By clinical exam.
- Skin-prick testing to a standard panel of antigens can be performed.
- Blood testing for specific IgE antibodies via radioallergosorbent testing.

Treatment

- **Allergen avoidance:** Use dust mite–proof covers on bedding and remove carpeting. Keep the home dry and avoid pets.
- **Medications:**
  - **Intermittent symptoms:** Oral or intranasal antihistamines (diphenhydramine, fexofenadine, olopatadine) block the effects of histamine released by mast cells. Selective antihistamines such as fexofenadine may cause less drowsiness than nonselective agents such as diphenhydramine. Decongestants (pseudoephedrine) have α-adrenergic agonist effects and result in vasoconstriction.
  - **Chronic symptoms:** Intranasal corticosteroids, nasal saline rinses.
  - **Severe acute symptoms:** Intranasal antihistamine sprays, intranasal cromolyn, intranasal anticholinergic sprays (ipratropium), and short courses of oral corticosteroids.
  - **Severe chronic symptoms:** Immunotherapy ("allergy shots")—slow to take effect, but useful for difficult-to-control symptoms. Sublingual immunotherapy for house dust mite or grass pollen. First dose must be given in the presence of a physician to monitor signs of severe systemic or local allergic reaction.

EPISTAXIS

Bleeding from the nose or nasopharynx. Roughly 90% of cases are anterior nasal septum bleeds at the Kiesselbach plexus (see Figure 2-3). The most common etiology is local trauma 2° to digital manipulation. Other causes include dryness of the nasal mucosa, nasal septal deviation, use of antiplatelet medications, bone abnormalities in the nares, rhinitis, intranasal steroid side effect, and bleeding diatheses.

Q 1

A 71-year-old man with a history of well-controlled asthma presents in November for his annual checkup. He has no complaints, and his PE findings are unremarkable. He received the pneumococcal vaccine 3 years ago. What should he be given before the completion of his visit?

Q 2

A 68-year-old woman is brought to your office because her son is concerned that she is losing her memory. He describes several instances in which she forgot what he had just told her, adding that she was recently unaware that he was calling to her at a crowded park. She spends most of her time at home watching television. What is the diagnosis?

TABLE 2-2. Conductive vs Sensorineural Hearing Loss

	Conductive	Sensorineural
Location of damage	Outer and middle ear	Inner ear
Diagnosis	Weber test: A vibrating tuning fork in the middle of the patient's forehead will sound louder in the affected ear Rinne test: Place a vibrating tuning fork against the patient's mastoid bone and replace immediately near the external meatus once it is no longer audible; bone conduction will be audible longer than air conduction	Weber test: A vibrating tuning fork in the middle of the patient's forehead will sound louder in the normal ear Rinne test: Same maneuver; air conduction will be audible longer than bone conduction
Examples	Cerumen impaction Otitis media Otitis externa Tumor/mass Otosclerosis (progressive fixation of stapes) Foreign bodies Barotrauma Perforation of tympanic membrane	Presbycusis (age-related) Drug-induced (eg, aspirin, aminoglycosides)

History/PE

- **Posterior bleeds:** Most commonly from the sphenopalatine artery. More brisk and less common than anterior bleeds; blood is swallowed and may not be seen.
- **Anterior bleeds:** Usually less severe; bleeding is visible as it exits the nares.

Treatment

- **First line:** Prolonged and sustained direct pressure and topical nasal vasoconstrictors (phenylephrine or oxymetazoline).
- **Refractory bleeding:** Cauterize with silver nitrate or insert nasal packing (with antibiotics covering *S aureus* to prevent toxic shock syndrome).
- **Severe bleeding:** Type and screen, obtain IV access, and consult an ENT surgeon.

1 **A**

Annual influenza vaccination is recommended for all patients > 6 months of age who lack contraindications (eg, severe allergy/anaphylaxis to egg protein). The live attenuated vaccine should not be used in populations who are pregnant, immunosuppressed, or have taken influenza antiviral medications within 48 hours.

2 **A**

Presbycusis, or age-related hearing loss. Hearing loss in elderly persons must be evaluated. Patients may have difficulty distinguishing voices in a crowd, which is often misinterpreted as memory loss. Patients may become socially isolated.

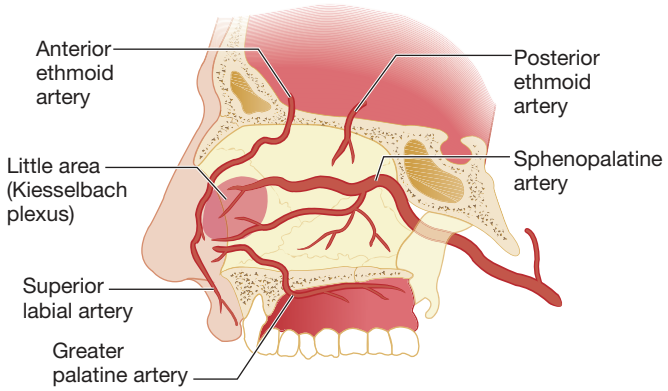


FIGURE 2-3. Blood supply to the nasal cavity. The most common site of hemorrhage is from the Kiesselbach plexus. The most common site of posterior hemorrhage is from the sphenopalatine artery. (Reproduced with permission from Tintinalli JE et al. *Tintinalli's Emergency Medicine: A Comprehensive Study Guide,* 7th ed. New York: McGraw-Hill, 2011, Fig. 239-1.)

Dermatology

"DERM TERMS"

Table 2-3 gives examples of common dermatologic lesions.

ATOPIC DERMATITIS (ECZEMA)

Chronic, inflammatory condition associated with frequent flares.

- Characterized by an early age of onset.
- Associated with ⊕ family history and personal history of atopic triad—asthma, allergic rhinitis, atopic dermatitis.
- Associated with ↑ serum IgE and recurrent skin infections.

History/PE

Intensely pruritic, lichenified plaques often found on flexor surfaces. May also appear anywhere on the body (see Figure 2-4).

Differential

Seborrheic dermatitis, contact/irritant dermatitis, impetigo.

Diagnosis

Clinical.

Treatment

- **First line** is preventative therapy: Keep skin moisturized with topical emollients. Avoid hot water, dry environments, harsh soaps, fragranced products. Topical steroids only for flares.
- **First-line steroid-sparing agents:** Topical tacrolimus/pimecrolimus (useful in areas where steroids are contraindicated, such as eyelids/groin).
- Oral antihistamines to treat itch and antibiotics to treat superimposed impetigo.

CONTACT DERMATITIS

Caused by exposure to allergens in the environment; may lead to acute, subacute, or chronic eczematous inflammation.

- **Irritant contact dermatitis:** Non–immune-mediated irritation caused by a substance; no clear borders.
- **Allergic contact dermatitis:** Immune-mediated Type IV hypersensitivity; usually occurs as a demarcated rash.

History/PE

- Patients complain of itching, burning, and pruritus.
- **Acute:** Presents with papular erythematous lesions and sometimes with vesicles, weeping erosions where vesicles have ruptured, crusting, and excoriations. The pattern of lesions often reflects the mechanism of exposure (see Figure 2-5).
- **Chronic:** Characterized by hyperkeratosis and lichenification.

KEY FACT

Leukoplakia consists of white patches/plaques on the oral mucosa that cannot be removed by rubbing (unlike pseudomembraneous candidiasis, which can be scraped off). Chewing tobacco is a risk factor.

KEY FACT

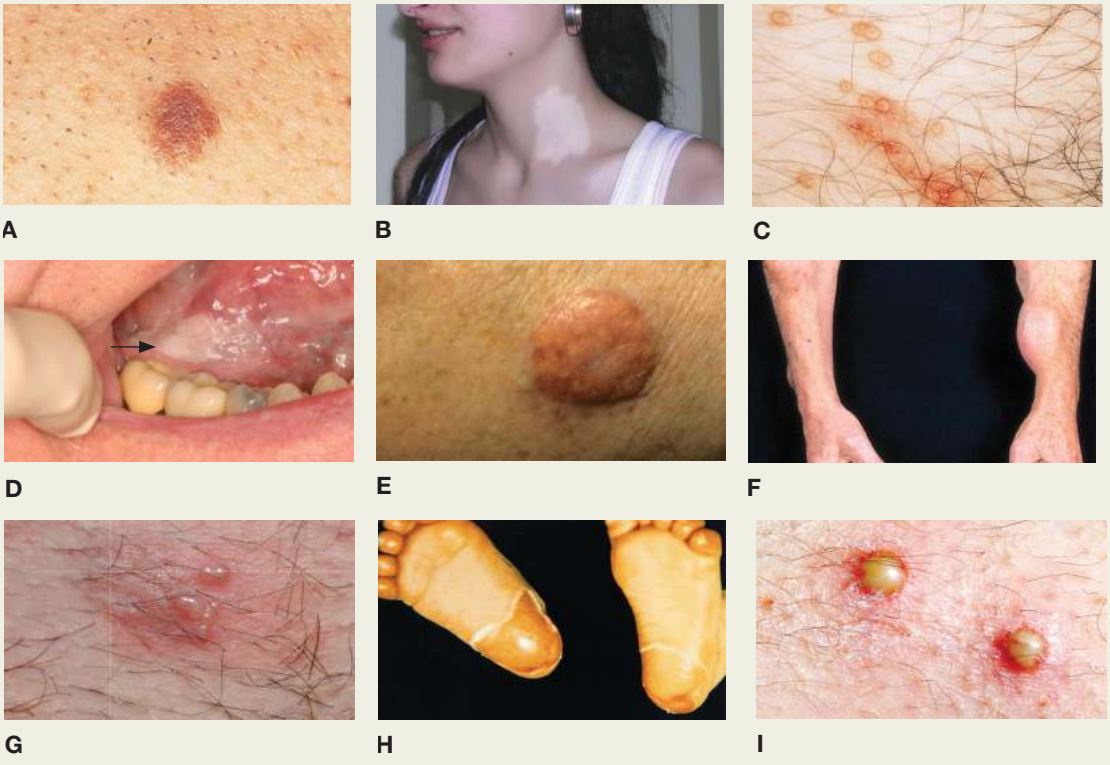
For atopic dermatitis, steroids are only indicated for acute exacerbations.

KEY FACT

Common causes of contact dermatitis include nickel (earrings, watches, necklaces) and poison ivy.

TABLE 2-3. Types of Dermatologic Lesions

Type	Description	Example
Macule	Flat, circumscribed, < 0.5 cm in diameter	Lentigo, café-au-lait spot, nevi (Image A)
Patch	Flat, > 0.5 cm in diameter	Café-au-lait spot, vitiligo (Image B)
Papule	Elevated, palpable, < 0.5 cm in diameter	Nevi, molluscum contagiosum (Image C)
Plaque	Elevated, palpable, > 0.5 cm in diameter	Psoriasis, lichen simplex chronicus, oral leukoplakia (Image D)
Nodule	Circumscribed, elevated, solid, 0.5–2.0 cm in diameter; located in the epidermis or deeper	Rheumatoid nodules, xanthomas (Image E)
Tumor	Large, circumscribed, solid; located deep in tissue	Neoplasms (Image F)
Vesicle	Circumscribed, elevated, fluid-filled, < 0.5 cm in diameter	Herpes lesions (Image G), varicella-zoster lesions
Bullae	Circumscribed, elevated, fluid-filled, > 0.5 cm in diameter	Coma blisters, pemphigus (Image H), epidermolysis bullosa
Pustule	Circumscribed, elevated, purulent	Folliculitis, acne, pyoderma (Image I)



Images A and C reproduced with permission from Longo DL et al. *Harrison's Principles of Internal Medicine,* 18th ed. New York: McGraw-Hill, 2012, Figs. 51-2 and 183-1. Images B, D, F, H, and I reproduced with permission from Goldsmith LA et al. *Fitzpatrick's Dermatology in General Medicine,* 8th ed. New York: McGraw-Hill, 2012, Figs. 74-4, 76-9, 129-1, 200-32, and 5-15. Images E and G reproduced with permission from Wolff K et al. *Fitzpatrick's Color Atlas and Synopsis of Clinical Dermatology,* 7th ed. New York: McGraw-Hill, 2013, Figs. 15-14 and 27-31.

Diagnosis

- Clinically diagnosed in the setting of a possible exposure.
- Patch testing can be used to elicit the reaction with the agent that caused the dermatitis.
- Consider the occupation and hobbies of the individual in relation to exposure site to determine whether they suggest a diagnosis.

Treatment

- **Prevention:** Avoid causative agents.
- **Mild:** Cold compresses and oatmeal baths help soothe the area +/− topical steroids.
- **Severe:** A short course of oral steroids if a large region of the body is involved.

PSORIASIS

An immune-mediated skin disease. Often chronic with a probable genetic predisposition.

History/PE

Presents with well-demarcated pink plaques with silvery scale on the knees, elbows, gluteal cleft, and scalp (see Figure 2-6). Nails may show pitting and onycholysis.

Treatment

- **Limited disease:** Topical steroids, topical vitamin D analogs, topical retinoids.
- **Generalized disease (involving > 30% of the body):** UVB light exposure; PUVA (psoralen and UVA) if UVB is not effective.
- **Severe:** Methotrexate, acitretin, and anti–tumor necrosis factor agents.

ERYTHEMA NODOSUM

An inflammatory condition that is characterized by tender red or violet nodules. More common in women. Although often idiopathic, it may also be 2° to sarcoidosis, inflammatory bowel disease, and infections (streptococcal infection, coccidioidomycosis, tuberculosis).

History/PE

- Tender red or violet nodules may be preceded by fever, malaise, and arthralgias in the context of a recent URI or diarrheal illness.
- Exam reveals deep-seated, poorly demarcated, painful red nodules without ulceration on the shins (see Figure 2-7).

Differential

Cellulitis, trauma, thrombophlebitis.

Treatment

- **Mild:** Treat the underlying disease, which is usually self-limited. NSAIDs are helpful for pain.
- **Severe or unresolved cases:** Potassium iodide drops and systemic corticosteroids may be of benefit.

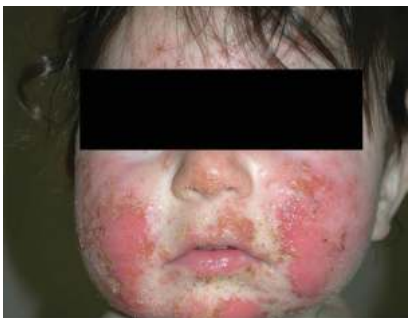


FIGURE 2-4. Severe atopic dermatitis. Pruritic scaly erythematous plaques of the face, with superimposed impetigo. (Reproduced with permission from USMLE-Rx.com.)

KEY FACT

Psoriatic arthritis characteristically involves the distal interphalangeal (DIP) joints.

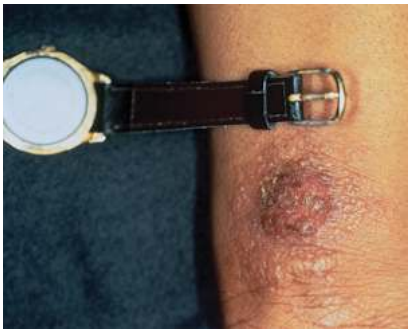


FIGURE 2-5. Contact dermatitis. The erythematous, edematous base of the rash corresponds to the posterior surface of the watch. (Used with permission of the Department of Dermatology, Wilford Hall USAF Medical Center and Brooke Army Medical Center, San Antonio, TX, as published in Knoop KJ et al. *The Atlas of Emergency Medicine,* 2nd ed. New York: McGraw-Hill, 2010, Fig. 13-50.)

Q

A 24-year-old medical student develops a rash when he puts on a pair of latex examination gloves. What is the mechanism leading to this rash?

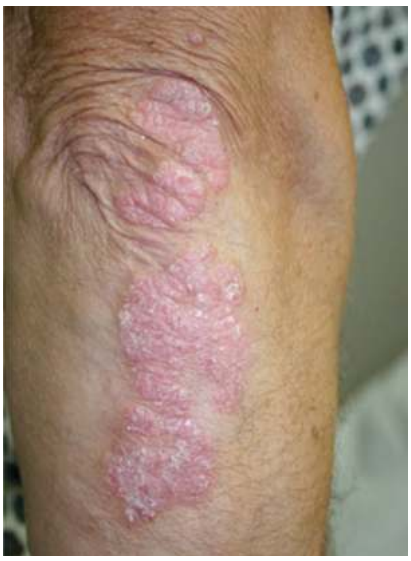


FIGURE 2-6. Psoriasis. Note the well-demarcated, erythematous plaque with micaceous silvery scale of the elbow. (Reproduced with permission from USMLE-Rx.com.)

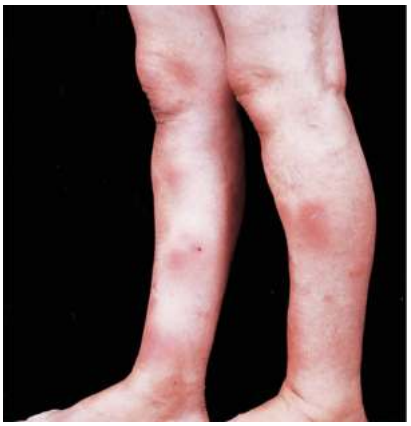


FIGURE 2-7. Erythema nodosum. Note the bilateral erythematous nodules localized over the shins. (Reproduced with permission from Goldsmith LA et al. *Fitzpatrick's Dermatology in General Medicine,* 8th ed. New York: McGraw-Hill, 2012, Fig. 70-2.)

A

Allergic contact dermatitis is a result of delayed contact (type IV) hypersensitivity caused by allergen-primed memory T lymphocytes (vs irritant contact dermatitis, which results from cytokines released following irritant contact).

ROSACEA

Most common among people with fair skin, light hair or eyes, and those who have frequent flushing.

History/PE

- Presents with erythema and with inflammatory papules that mimic acne and appear on the cheeks, forehead, nose, and chin.
- Open and closed comedones (whiteheads and blackheads) are not present.
- Recurrent flushing may be elicited by spicy foods, alcohol, or emotional reactions.
- Rhinophyma (an enlarged nose with an irregular texture) occurs late in the disease course and results from sebaceous gland hyperplasia (see Figure 2-8).
- Patients may have ocular symptoms such as blepharitis, dry eyes, conjunctival injection, and lid margin telangiectasias.

Differential

The absence of comedones and the patient's age (older in rosacea versus younger in acne) help distinguish rosacea from acne vulgaris.

Treatment

- **Initial therapy:** The goal is to control rather than cure the chronic disease. Use mild cleansers, azelaic acid, and/or metronidazole topical gel +/− oral antibiotics as initial therapy.
- **Persistent symptoms:** Treat with oral antibiotics (doxycycline, minocycline) and tretinoin cream.
- **Maintenance therapy:**
  - **First line:** Topical metronidazole.
  - Clonidine or α-blockers may be effective in the management of flushing, and patients should avoid triggers.
  - Consider referral for surgical evaluation if rhinophyma is present and is not responding to treatment.
  - Any patient with ocular symptoms (eg, grittiness, dryness) should be started on oral or topical local antibiotics and ocular lubricants.

ERYTHEMA MULTIFORME

An acute inflammatory disease (type IV hypersensitivity). Etiologic factors: herpes simplex virus (HSV), *Mycoplasma pneumoniae*, and sulfa drugs. Many cases are idiopathic and recurrent.

History/PE

- May be preceded by malaise, fever, itching or burning at the location where eruptions occur.
- Presents with sudden onset of rapidly progressive, symmetric lesions.
- Targetoid papules are typically located on the back of the hands and on the palms (see Figure 2-9), soles, and limbs but may be found anywhere. Lesions recur in crops for 2–3 weeks.

Diagnosis

Typically a clinical diagnosis.

Treatment

- **Mild cases:** Histamine blockers for pruritus.
- **Moderate (many targetoid lesions):** Prednisone for 1–3 weeks.
- Azathioprine has been helpful in refractory cases.
- When HSV causes recurrent erythema multiforme (EM), maintenance acyclovir or valacyclovir can ↓ recurrences of both.

PEMPHIGUS VULGARIS

- An autoimmune disease which results from autoantibodies targeting desmoglein in the desmosomal complex in skin cells. Pemphigus vulgaris is the most common subtype of pemphigus.
- **Hx/PE:** Presents with flaccid bullae and erosions where bullae have been unroofed (see Figure 2-10). Oral lesions usually precede skin lesions. Nikolsky sign is elicited when gentle lateral traction on the skin separates the epidermis from underlying tissue.
- **Dx:** Skin biopsy.
- **Tx:** Corticosteroids and immunosuppressive agents.
- **Cx:** If it is not treated early, the disease usually generalizes and can affect the esophagus.

BULLOUS PEMPHIGOID

- An autoimmune disease characterized by antibodies against the basement membrane that leads to subepidermal bullae. More common than pemphigus vulgaris. Occurs in those > 60 years of age (the median age at onset is 80 years).
- **Hx/PE:** Presents as large, tense bullae and erythematous patches with few other symptoms (see Figure 2-11). In contrast to pemphigus vulgaris, Nikolsky sign is not present.
- **Differential:** Pemphigus vulgaris, dermatitis herpetiformis.
- **Dx:** Skin biopsy, with confirmation via immuno- and histopathology.
- **Tx:** Topical steroids.

ACNE VULGARIS (COMMON ACNE)

- Results from ↑ pilosebaceous gland activity, *Propionibacterium acnes*, and occlusion of follicles.
- **Hx/PE:** Characterized by closed comedones (whiteheads), open comedones (blackheads), inflammatory papules, nodules, and scars. Typically seen over the face, back, and chest.
- **Differential:** Rosacea, folliculitis.
- **Dx:** Clinical.
- **Tx: First line** is topical benzoyl peroxide, topical retinoids, or topical antibiotics such as erythromycin. **Second line:** Addition of oral antibiotics such as minocycline or doxycycline. **Refractory acne:** Isotretinoin but is teratogenic and should thus be prescribed with caution in women of childbearing age.

HERPES ZOSTER (SHINGLES)

Caused by reactivated varicella-zoster virus, which is dormant in the dorsal roots of nerves. Risk factors: ↑ age and immunosuppression. Sequelae: postherpetic neuralgia.

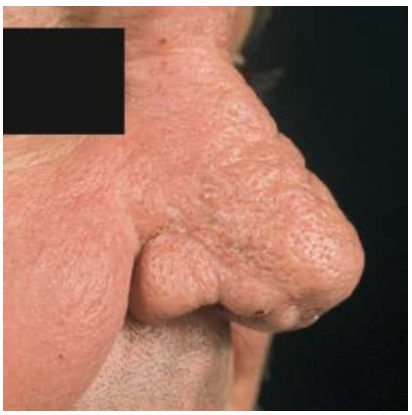


FIGURE 2-8. Rhinophyma. (Reproduced with permission from Wolff K et al. *Fitzpatrick's Color Atlas & Synopsis of Clinical Dermatology,* 5th ed. New York: McGraw-Hill, 2005, 11.)

KEY FACT

Pemphigus vulgaris presents with flaccid bullae, whereas bullous pemphigoid is characterized by tense bullae.

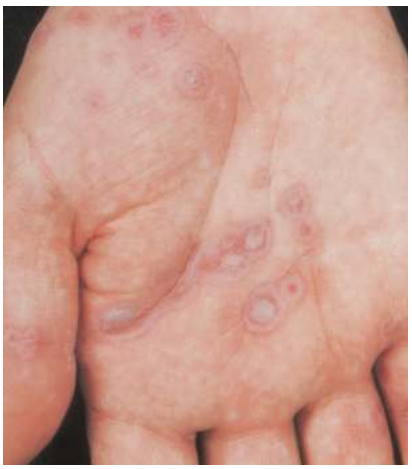


FIGURE 2-9. Erythema multiforme. Note the typical targetoid lesions on the palm. (Reproduced with permission from Goldsmith LA et al. *Fitzpatrick's Dermatology in General Medicine,* 8th ed. New York: McGraw-Hill, 2012, Fig. 39-3.)

Q

A 26-year-old man presents with targetoid papules that appeared on his palms 2 days ago. He states that he was recently prescribed a new antiseizure medication for his epilepsy. He denies any other symptoms, and exam reveals no other lesions. What is the diagnosis?

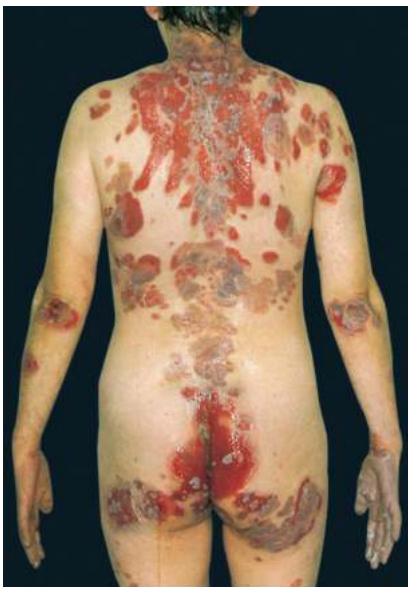


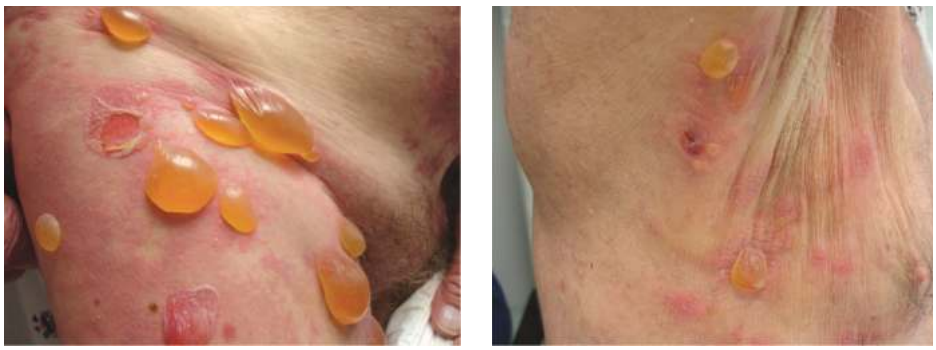
FIGURE 2-10. Pemphigus vulgaris. Note the extensive erosions due to blistering and the intact, flaccid blisters at the lower border of the eroded lesions. (Reproduced with permission from Goldsmith LA et al. *Fitzpatrick's Dermatology in General Medicine,* 8th ed. New York: McGraw-Hill, 2012, Fig. 54-3.)

KEY FACT

When prescribing isotretinoin for refractory acne, concomitant contraception and pregnancy tests are necessary. Adverse effects include hypertriglyceridemia and elevated liver function tests (LFTs) (need baseline and subsequent lipid panel and LFTs).

A

Erythema multiforme 2° to the new antiseizure medication. EM differs from Stevens-Johnson syndrome/toxic epidermal necrolysis in that lesions are generally localized to the extremities (vs spreading from the face and trunk), and the disease course is usually less severe.



A B

FIGURE 2-11. Bullous pemphigoid. (A) Large, tense bullae and erythematous patches are seen on the thighs and lower legs. (B) Urticarial plaques with overlying tense vesicles and bullae are seen in the axilla. (Reproduced with permission from Goldsmith LA et al. *Fitzpatrick's Dermatology in General Medicine,* 8th ed. New York: McGraw-Hill, 2012, Fig. 56-3.)

History/PE

Presents with the painful vesicles evolving into crusted lesions in a dermatomal distribution that do not cross the midline. Lesions are typically preceded by paresthesias in the area of distribution.

Differential

Contact dermatitis.

Diagnosis

Largely clinical. PCR or culture can be confirmatory.

Treatment

- **Pain management:** NSAID first line for mild to moderate pain. Topical analgesics containing capsaicin (effective for temporary relief of neuropathic pain or postherpetic neuralgia).
- **Antiviral treatment** with acyclovir, valacyclovir, or famciclovir: If initiated within 72 hours of rash onset can ↓ the duration of illness and may also ↓ the occurrence of postherpetic neuralgia. Use of glucocorticoids is controversial and is generally not recommended.
- Patients are contagious until crusts have formed over the vesicles. Keep the area covered to prevent the spread of virus to immunocompromised patients.
- **Vaccination** is recommended for people ≥ 60 years of age and helps ↓ the risk of both shingles and postherpetic neuralgia.

DERMATOPHYTOSES

Dermatophytes attach to and proliferate on the superficial layers of the epidermis, nails, and hair. Examples are given in Table 2-4.

BASAL CELL CARCINOMA

- The most common skin cancer. Slow growing and rarely metastasizes. Caused by excessive sun exposure.
- **Hx/PE:** Pearly papules with central depression that may be ulcerated (see Figure 2-12). Most commonly found on sun-exposed areas.

TABLE 2-4. Common Dermatophytoses

Condition	Description	Treatment
Tinea corporis	Annular plaques with a thin scale and central clearing (Image A)	Griseofulvin, itraconazole, clotrimazole cream
Tinea pedis	Red, scaly soles with maceration and fissuring between the toes +/− blisters (Image B)	Griseofulvin, terbinafine, itraconazole, antifungal powders
Tinea versicolor	Hypopigmented macules in areas of sun-induced pigmentation; reddish-brown appearance in winter (Image C)	Itraconazole, topical selenium sulfide/ketoconazole
Onychomycosis	Hyperkeratosis and yellowing of the nail plate; scaling (Image D)	Oral: Terbinafine
Tinea capitis	Erythema and scaling of the scalp with thickened, broken-off hairs and scalp kerion (Image E)	Oral: Griseofulvin, itraconazole

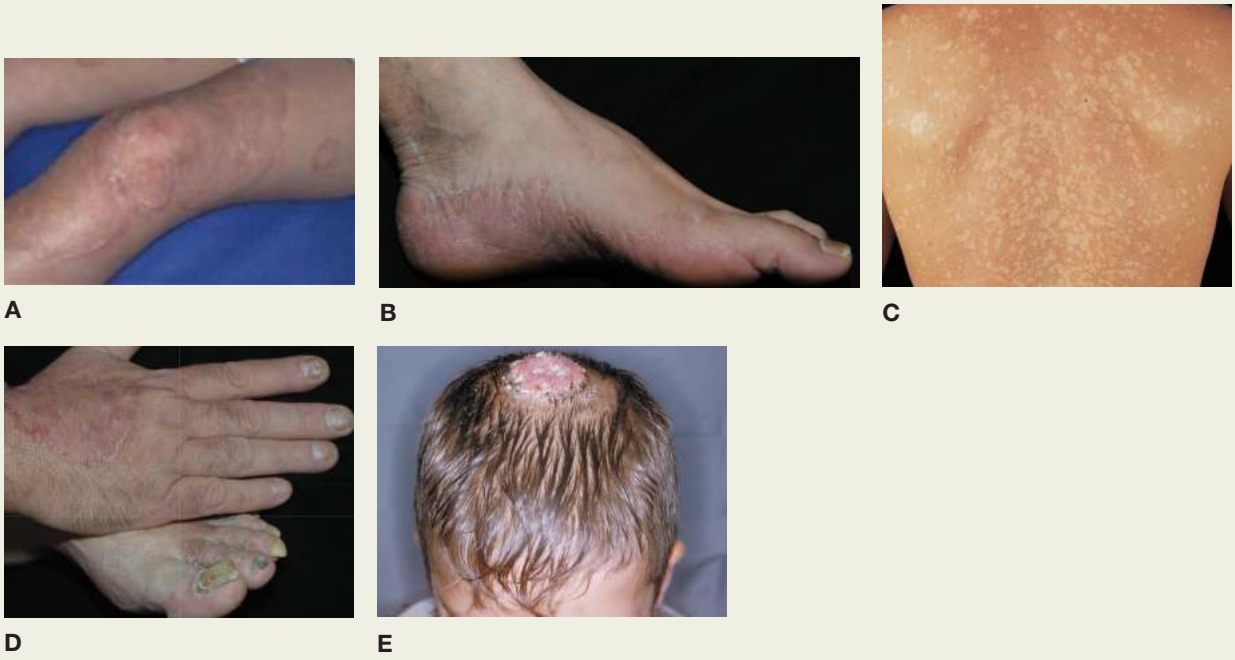


Image A reproduced with permission from Stern SD et al. *Symptom to Diagnosis: An Evidence-Based Guide,* 2nd ed. New York: McGraw-Hill, 2010, Fig. 24-11. Images B–D reproduced with permission from Wolff K et al. *Fitzpatrick's Color Atlas and Synopsis of Clinical Dermatology,* 7th ed. New York: McGraw-Hill, 2013, Figs. 26-29, 26-19, and 26-32. Image E reproduced from the Centers for Disease Control and Prevention, Atlanta, GA.

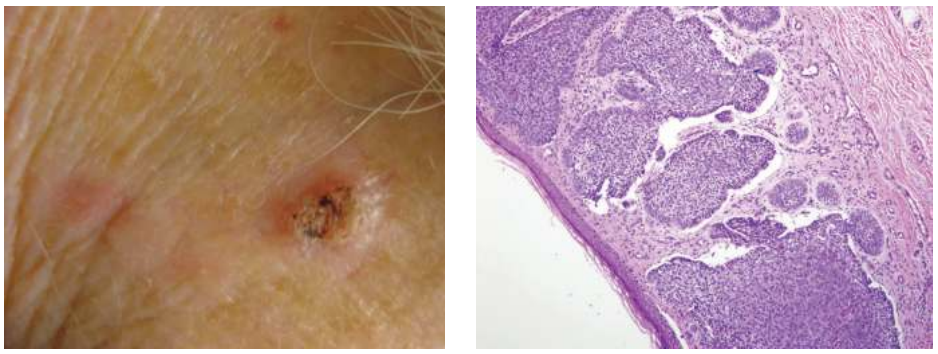
- **Dx:** Skin biopsy shows palisading cells with retraction.
- **Tx:** Curettage, cryosurgery, radiation, or excision by surgery depending on the size, location, and histology of the tumor as well as on prior treatment and cosmetic considerations. Mohs micrographic surgery for lesions on areas of the face that are difficult to reconstruct.

SQUAMOUS CELL CARCINOMA

- The second most common skin cancer. Risk factors: history of actinic keratosis (see Figure 2-13), immunosuppression, smoking, arsenic exposure, and exposure to industrial carcinogens.
- **Hx/PE:** Pink plaques with scale or erosion; may spread to regional lymph nodes.

Q

A 71-year-old man complains of a lesion on his right flank that was preceded by tingling in the same area 1 day ago. Exam reveals a 4-inch band of painful vesicles with 2° crusting and a clear midline border. What test do you send to confirm your clinical diagnosis?



A B

FIGURE 2-12. Basal cell carcinoma. (**A**) 59-year-old Caucasian man with a 6-month history of a bleeding 7-mm pearly plaque with a rolled border, peripheral arborizing telangiectasias, and central ulceration involving the left lateral neck. (**B**) Nests or lobules of uniform basaloid cells extending downward from the epidermis. The nests are surrounded by a loose stroma and cleft-like retraction spaces. (Reproduced with permission from USMLE-Rx.com.)

- **Dx:** Skin biopsy.
- **Tx:** Surgical excision for larger lesions; actinic keratoses may be treated with topical chemotherapeutics or liquid nitrogen. Mohs micrographic surgery for lesions on areas of the face that are difficult to reconstruct.

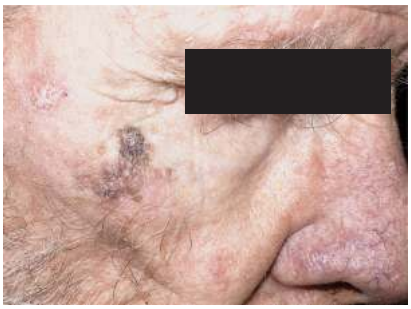


FIGURE 2-13. Actinic keratosis. Premalignant precursor to squamous cell carcinoma. Presents as gritty or scaly plaques on areas of sun exposure. (Reproduced with permission from Wolff K et al. *Fitzpatrick's Color Atlas and Synopsis of Clinical Dermatology,* 7th ed. New York: McGraw-Hill, 2013, Fig. 10-28.)

MELANOMA

- Malignant proliferation of melanocytes. Risk factors: sun exposure, fair skin, a ⊕ family history, a large number of nevi, and dysplastic nevi.
- **Hx/PE:** Look for nevi with an irregular appearance (**ABCDE** = **A**symmetry, **B**order irregularity, **C**olor irregularity, **D**iameter > 6 mm, **E**volution).
- **Dx:** Skin biopsy (melanocytes with cellular atypia); imaging may be warranted for metastatic evaluation.
- **Tx:** Surgical excision; adjuvant therapy for patients with advanced disease.

Genitourinary Disorders

ERECTILE DYSFUNCTION

Inability to achieve or maintain an erection sufficient for penetration and ejaculation. Associated with increasing age. Etiologies are as follows:

- **Psychological:**
  - Symptoms often have a sudden onset.
  - Patients are unable to sustain or sometimes even obtain an erection.
  - Patients have normal nocturnal penile tumescence (those with organic causes do not).
- **Organic:**
  - **Endocrine:** DM, hypothyroidism or thyrotoxicosis, pituitary or gonadal disorders, ↑ prolactin.
  - **Vascular:** Atherosclerosis, vascular steal.
  - **Neurologic:** Stroke, DM, multiple sclerosis, spinal surgery, neuropathy.
  - **Exogenous:** β-blockers, selective serotonin reuptake inhibitors, α-blockers, clonidine, CNS depressants, anticholinergics, chronic opioids, tricyclic antidepressants.

A

Although a clinical exam is typically sufficient for the diagnosis of herpes zoster, a PCR of fluid from the lesion can be confirmatory. NSAIDs may be useful for pain control, and antiviral therapy may speed resolution and ↓ the likelihood of postherpetic neuralgia.

History/PE

- Findings that suggest an organic cause: Small testes, evidence of Peyronie disease, ↓ perineal sensation/cremaster reflex, or evidence of peripheral neuropathy/vasculopathy.
- Assess peripheral pulses: Look for skin atrophy, hair loss, and low skin temperature.

Diagnosis

- Obtain testosterone level if there is concern about 2° causes.
- Check thyroid-stimulating hormone, prolactin, and glucose if there is a concern regarding diabetes.

Treatment

- **First line:**
  - Treat underlying disease (eg, testosterone for hypogonadism).
  - Oral phosphodiesterase type 5 (PDE-5) inhibitors (sildenafil, tadalafil, vardenafil): Relaxation of smooth muscle in the corpora cavernosa results in improved blood flow causing tumescence. Adverse effects include flushing, headache, ↓ BP.
- **Contraindicated:** Concurrent nitrates or α-blockers as they may cause refractory hypotension.
- **Failure of medical therapy:** An external penile pump, inflatable penile prosthesis, vascular surgery.
- **Psychological treatment:** Behavioral treatment for depression and anxiety. A PDE-5 inhibitor may be effective for psychogenic causes.

BENIGN PROSTATIC HYPERPLASIA

Hyperplasia of the prostate, leading to bladder outlet obstruction. Risk ↑ with age; common in patients > 45 years of age. In patients < 45 years of age with urinary retention, consider urethral stricture or a neuropathic etiology.

History/PE

- Patients complain of frequency, urgency, nocturia, ↓ force and size of the urinary stream, and incomplete emptying leading to overflow incontinence.
- Exam reveals a firm, rubbery, smooth prostatic surface (vs rock-hard areas that suggest prostate cancer).

Diagnosis

- Diagnosed by history and exam. Check a UA for infection or hematuria, both of which should prompt further evaluation.
- Prostate-specific antigen (PSA) is ↑ in up to 50% of patients but is not diagnostically useful.

Treatment

- **First line:** α-blockers (terazosin), 5α-reductase inhibitors (finasteride).
- Avoid anticholinergics, antihistamines, or narcotics.
- Refractory to medical treatment: Transurethral resection of the prostate; indications include recurrent urinary tract infections, bladder stones, hematuria, episodes of acute urinary retention, and renal failure 2° to obstruction.

Q 1

A patient presents for evaluation of a pigmented skin lesion. Biopsy reveals melanocytes with marked atypia characteristic of melanoma. What feature is the most important prognostic factor?

Q 2

A 74-year-old man presents with inability to maintain an erection. Although the problem started several years ago, he states that he ignored it because he thought it was a normal part of aging. How should the patient be counseled?

Q 3

A 70-year-old man is prescribed terazosin for his benign prostatic hyperplasia. How does the drug treat this condition, and what other medical condition does its mechanism of action address?

TESTICULAR MASSES/GROIN PAIN IN MEN

Epididymitis/Orchitis

- **Epididymitis** is defined as an acute infection that results in posterior and superior testicular tenderness. It is the most common cause of scrotal pain in adults.
- **Orchitis** is associated with diffuse testicular pain.
  - In men > 35 years of age, *Escherichia coli* is the most common cause.
  - In men < 35 years of age, *Chlamydia* is most common.
- **Dx:** CBC, UA and urine culture, Gram stain for gonococcal infection and trichomoniasis, nucleic acid amplification tests for *Neisseria gonorrhoeae* and *Chlamydia trachomatis*, Doppler ultrasound (shows ↑ blood flow).
- **Tx:** Antibiotics and supportive therapy (analgesics, ice packs, scrotal support and elevation).

Testicular Torsion

- A urologic emergency that requires immediate intervention owing to the potential for resulting infertility.
- **Hx/PE:** The affected testicle sits higher and is painful. Cremasteric reflex may be absent on the affected side.
- **Dx:** Doppler ultrasound (shows ↓ blood flow).
- **Tx:** Manual detorsion or surgical intervention. Surgical orchiopexy of bilateral testicles should follow.

Health Care Maintenance

CANCER SCREENING

Table 2-5 outlines recommended guidelines for the screening of common forms of cancer.

OTHER ROUTINE SCREENING

- **HIV infection:** Screening for HIV infection is recommended for individuals 15 to 65 years of age at least once, with annual screening for individuals with high-risk factors. Women should be screened with each pregnancy.
- **Hypertension:** BP screening should be done every 2 years in normotensive adults and every year for those with a systolic BP of 120–139 or a diastolic BP of 80–90. For young patients (age < 50 years of age) with an ↑ BP, look for 2° causes of hypertension, such as chronic kidney disease, pheochromocytoma, thyroid/parathyroid disease, sleep apnea, renovascular disease, Cushing syndrome, coarctation of the aorta, and 1° hyperaldosteronism.
- **Hyperlipidemia:** The US Preventive Services Task Force (USPSTF) strongly recommends screening men ≥ 35 years of age and women ≥ 45 years of age for lipid disorders. In the setting of coronary artery disease (CAD) risk factors, screening should begin earlier (20–45 years of age). Treatment measures are outlined in Chapter 3. Risk factors that modify LDL goals include:
  - Cigarette smoking.
  - Hypertension (BP ≥ 140/90 or on antihypertensive medication).

1 **A**

Depth of invasion of the melanoma.

2 **A**

Although erectile dysfunction is associated with age, it is still considered abnormal, and patients with erection difficulties should be adequately evaluated for all potential causes.

3 **A**

α_1-blockers such as terazosin act on smooth muscle in the prostate, bladder neck, and urethra. They also act on vascular smooth muscle, causing vasodilation; therefore, they can work to lower hypertension as well.

TABLE 2-5. Recommended Cancer Screening Guidelines

Type	Recommendations
Cervical cancer	A Pap smear is recommended starting at age 21 until age 75 regardless of sexual activity; (stop at age 65 if patient has three consecutive ⊖ screenings) Screen every 3 years if patient has had a normal Pap Those > 30 years of age may ↑ the screening interval to 5 years if the Pap is performed with HPV PCR testing
Breast cancer	Mammography should be conducted every 2 years after age 50 (earlier if there is a ⊕ family history at a young age) When mammographic screening should begin is controversial. The USPSTF recommends: Biennial screening mammography for women 50–74 years of age For patients in their 40s, the decision to begin screening should be thoroughly discussed with their doctors
Colorectal cancer	In patients without a family history of colorectal cancer, screening should start at 50 years of age. A colonoscopy every 10 years is recommended, but other accepted screening tools include flexible sigmoidoscopy every 3-5 years or an annual hemoccult If a first-degree relative has colon cancer, begin screening at age 40 or when the patient is 10 years younger than the age at which that relative was diagnosed, whichever comes first American College of Gastroenterology recommends that African-Americans be screened at age 40–45 for colon cancer
Prostate cancer	Controversial. USPSTF 2017 Guidelines recommend: Men 55–69 years of age: Decision to initiate screening should be individualized based on risk factors (eg, family history, African-American, or urinary changes) Men > 69 years: Recommend against PSA-based screening for prostate cancer
Lung cancer	Controversial. The USPSTF recommends annual screening for lung cancer with a low-dose CT scan at 55–80 years of age if the patient has a 30-pack-year smoking history and is currently smoking or quit within the past 15 years

- Patient has history of CAD or non-CAD atherosclerosis (eg, peripheral artery disease, carotid artery stenosis).
- Diabetes.
- A family history of cardiovascular disease before age 50 in male relatives or age 60 in female relatives.
- Obesity.

- **Diabetes:** The ADA recommends testing for diabetes or prediabetes in all adults with a BMI ≥ 25 kg/m^2 and one or more additional risk factors for diabetes (see below). For those without risk factors, testing should begin at age 45. A fasting plasma glucose, a 2-hour oral glucose tolerance test, or an HbA_{1c} (≥ 6.5%) is appropriate. Additional risk factors for diabetes are as follows:
  - A family history of DM in a first-degree relative.
  - Habitual physical inactivity.
  - High-risk ethnic or racial group (eg, African-American, Hispanic, Native American, Asian-American, Pacific Islander).
  - A history of delivering a baby weighing > 4.1 kg (9 lb) or gestational diabetes.
  - Hypertension (BP ≥ 140/90).
  - Dyslipidemia.
  - Polycystic ovarian syndrome.
  - A history of vascular disease.
- **Osteoporosis:** The USPSTF recommends that women ≥ 65 years of age be screened no more than every 2 years by DEXA scan. Screening should

Q

A 41-year-old woman with no significant medical history comes to your clinic for her first checkup. Her mother had type 2 DM. Her PE findings, including BMI, are normal. Which screening tests might you recommend?

begin earlier for postmenopausal women who are at ↑ risk for osteoporotic fractures (eg, low weight, low estrogen state, long-term use of oral or injected steroids). DEXA is the screening test of choice.

- **Abdominal aortic aneurysm (AAA):** The USPSTF recommends one-time screening for AAA in men 65–75 years of age who have smoked at any time. Abdominal ultrasound is the screening test of choice.

IMMUNIZATIONS

Table 2-6 lists indications for adult immunizations.

TABLE 2-6. Indications for Immunization in Adults

Immunization	Indication/Recommendation
Tetanus	Give 1° series in childhood followed by boosters every 10 years (see Chapter 4)
Hepatitis B	Administer to all infants and to patients at ↑ risk (eg, IV drug users, health care providers, those with chronic liver disease)
Pneumococcal	Give to those ≥ 65 years of age or to any patient at ↑ risk (eg, patients with splenectomy, chronic obstructive pulmonary disease, or diabetes; alcoholics; or immunocompromised patients such as those on chemotherapy, posttransplant, or HIV ⊕)
Influenza	Give annually to all patients > 6 months of age
Hepatitis A	Give to those traveling to endemic areas, those with chronic liver disease (HBV or HCV), and IV drug abusers
Zoster	Recommended for all patients ≥ 60 years of age who have no contraindications, including those who report a previous episode of zoster or who have chronic medical conditions
Smallpox	Currently recommended only for those working in laboratories in which they are exposed to the virus
Meningococcal	The CDC recommends that all children 11–12 years of age be vaccinated and that a booster dose be given at age 16

A

A Pap smear and hypertension screening. A diabetes workup (eg, a fasting glucose test, a 2-hour glucose tolerance test, or an HbA_{1c}) is not needed as the patient is < 45 years of age with a normal BMI. Given the patient's age, a screening mammogram is controversial. It is important to discuss the risks, benefits, and alternatives of screening before proceeding.

CHAPTER 3

CARDIOLOGY

KEY FACT

Major risk factors for ischemic heart disease:

- Age > 65 years
- Diabetes mellitus
- Family history
- Hyperlipidemia
- Hypertension
- Male gender
- Smoking

KEY FACT

Unstable angina is any new angina in previously asymptomatic patients or accelerating or new angina at rest in patients with prior stable angina. In patients with known stable angina, unstable angina may present with acceleration or worsening of prior anginal symptoms.

KEY FACT

Certain patients—including people with diabetes, women, and elderly persons—can present with ischemic disease with highly atypical symptoms. Diabetes is considered a CAD risk equivalent.

Ischemic Heart Disease

The 1° cause of ischemic heart disease is atherosclerotic occlusion of the coronary arteries. In addition to individual patient risk factors, a major risk factor for ischemic heart disease is family history, particularly of early coronary artery disease (CAD) in a first-degree relative, as defined by significant disease in male relatives before age 55 or in female relatives before age 65.

History/PE

- May be asymptomatic or present as follows:
  - Stable angina: Typical substernal chest pressure or shortness of breath that is exacerbated by exertion and relieved by rest or nitroglycerin. Reflects a stable, flow-limiting plaque.
  - Unstable angina or MI (acute coronary syndrome): Chest pressure and/or shortness of breath that occur at rest or with minimal exertion, often with a duration of > 20 minutes. Pain tends not to improve markedly with nitroglycerin or recurs soon after its use. Reflects plaque rupture with formation of a clot in the lumen of the blood vessel.
  - Not all patients present with typical anginal symptoms. Ask about other symptoms that are considered "anginal equivalents," such as dyspnea, nausea, and diaphoresis. Some patients may complain of indigestion.
- Exam may be normal when patients are asymptomatic. During episodes of angina, a left ventricular S4 or a mitral regurgitation murmur may occasionally be heard on cardiac auscultation.
- Look for signs of heart failure (eg, ↑ jugular venous pulse [JVP], inspiratory crackles, hepatomegaly, lower extremity edema) that could be due to prior MI and may be causing left ventricular dysfunction.
- Look for vascular disease elsewhere (eg, carotid, abdominal, and femoral bruits; asymmetric or diminished pulses; and lower extremity ischemic ulcers).
- Other potential signs include diaphoresis and the Levine sign (clenched right fist held over the chest when describing pain).

Differential

Consider pericarditis, pulmonary embolism, pneumothorax, aortic dissection, peptic ulcer, esophageal disease (including diffuse esophageal spasm), gastroesophageal reflux disease (GERD), and musculoskeletal causes. Chest pain from anxiety should be a diagnosis of exclusion.

Diagnosis

- **Initial workup:** +/− ECG changes (ST-segment elevation/depression/Q waves) in the distribution of the coronary arteries (see Table 3-1, Table 3-2, and Figure 3-1); elevated cardiac biomarkers (troponin, creatine kinase [CK], CK–MB fraction). Consider tests (eg, CXR, D-dimer) to evaluate for other causes of chest pain. Non-ST-segment-elevation MI (NSTEMI) can be distinguished from unstable angina by the presence of elevated cardiac biomarkers.
- **Stress testing:** Exercise, dobutamine, or vasodilator stress; ECG, echocardiography, or radionuclide imaging to assess perfusion (see the discussion of advanced cardiac evaluation below).
- **Cardiac catheterization:** Defines anatomy and the location and severity of lesions; can also be used for reperfusion. ST-segment-elevation MI (STEMI) is a high-risk MI that requires emergency catheterization for reperfusion.

TABLE 3-1. Arterial Supply of the Heart in Right-Dominant Coronary Circulation

Left Anterior Descending (LAD) Artery	Left Circumflex Artery	Right Coronary Artery/ Posterior Descending Artery (RCA/PDA)
Apex	Lateral wall of LV	Lateral wall of right ventricle (RV)
Anterior wall of left ventricle (LV)	Posterior wall of LV (20%)	Posterior wall of LV (80%)
Anterior two-thirds of interventricular septum (IVS)	Posterior one-third of IVS (20%)	Posterior one-third of IVS (80%)
		SA node
		AV node

Treatment

- **Acute coronary syndrome:**
  - **Initial treatment:** Anticoagulation (low molecular weight heparin [LMWH], unfractionated heparin), aspirin, nitroglycerin, supplemental O_2, and a β-blocker in hemodynamically stable patients. Antiplatelet agents (clopidogrel, prasugrel, ticagrelor) are often used as well if a percutaneous stent is placed. Glycoprotein IIb/IIIa antagonists (abciximab, eptifibatide, tirofiban) or bivalirudin may be used in the catheterization laboratory when angioplasty is pursued.
  - STEMIs or NSTEMIs with high-risk features should be managed by percutaneous coronary intervention (PCI) if available at that hospital. If PCI is unavailable or cannot be initiated within 90 minutes, tPA should be given. If possible, an angiotensin converting enzyme inhibitor (ACEI) should be started before discharge.
- **Angina:** β-blockers ↓ HR, ↑ myocardial perfusion time, and ↓ cardiac workload, which ↓ exertional angina. If symptoms arise on a β-blocker, a long-acting nitrate or calcium channel blocker (CCB) can be added. Ranolazine can be added for refractory angina.

2° Prevention

- Risk-factor modification (to slow progression): Control diabetes, ↓ BP, ↓ cholesterol (specifically LDL), and encourage smoking cessation.
- **Prevention of MI:** Aspirin; clopidogrel can be given to aspirin-sensitive patients.
- **Drugs that improve mortality after MI:** Aspirin, β-blockers, ACEIs (or angiotensin receptor blockers [ARBs] in ACEI-intolerant patients), hydroxymethylglutaryl-coenzyme A [HMG-CoA] reductase inhibitors (statins), and spironolactone in high-risk subgroups. Antiplatelet agents are used following coronary stent placement, usually for a minimum of 12 months.

TABLE 3-2. ECG Findings with MI in Right-Dominant Coronary Circulation

Area of Infarct	Coronary Artery Involved	Leads with ST Changes
Inferior wall (RV)	RCA/PDA	II, III, aVF
Septum	LAD	V2, V3
Lateral wall (LV)	Left circumflex	I, aVL, V5, V6

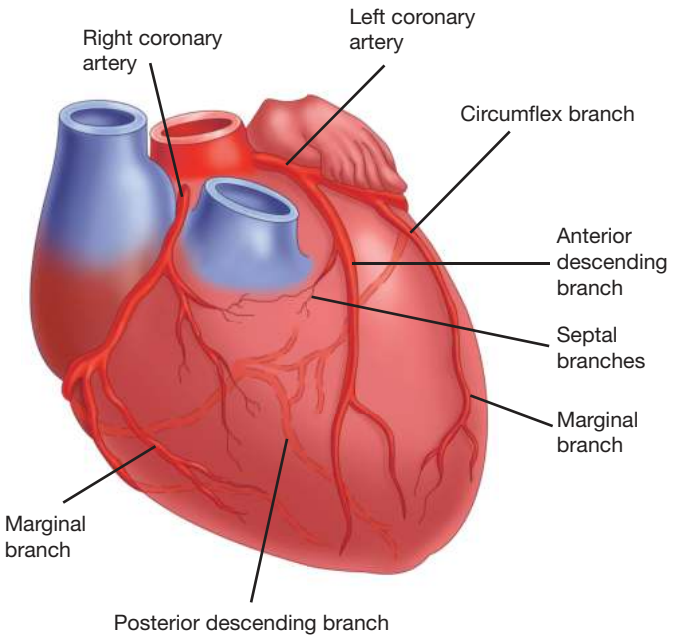


FIGURE 3-1. Coronary artery anatomy. (Reproduced with permission from Le T, Krause K. *First Aid for the Basic Sciences: Organ Systems,* 2nd ed. New York: McGraw-Hill, 2011, Fig. 1-9.)

KEY FACT

Any condition that causes delayed left ventricular emptying (eg, aortic stenosis, left bundle branch block [LBBB]) can be associated with paradoxical splitting. Delayed emptying leads to delayed A2, with P2 heard before A2. On inspiration, A2 and P2 move closer together, eliminating a split S2.

KEY FACT

Half of patients with moderate to severe acute mitral regurgitation have no audible murmur.

KEY FACT

Ventricular septal defects (VSDs) produce holosystolic murmurs that radiate throughout the precordium, often with a thrill. They are the most common cardiac malformation at birth.

Valvular Disease

Table 3-3 describes the clinical characteristics and treatment of common valvular lesions.

Heart Failure

Defined as inability of the heart to pump adequate blood to meet the demands of the body. One categorization scheme includes:

- Systolic heart failure.
- Diastolic heart failure.
- Heart failure related to valvular disease.
- Heart failure related to arrhythmias.

SYSTOLIC HEART FAILURE

Weakened pump function of the heart. Sometimes referred to as "heart failure with reduced ejection fraction" (HFrEF). Common causes include ischemic heart disease, long-standing hypertension, toxins (eg, alcohol), and viral or idiopathic cardiomyopathy in younger patients.

History/PE

- Poor exercise tolerance, exertional dyspnea, and easy fatigability.
- Orthopnea or paroxysmal nocturnal dyspnea, poor appetite, RUQ pain, and ankle swelling (due to volume overload).
- Exam often reveals inspiratory crackles (may be absent in chronic heart failure); a diffuse left-displaced point of maximal impulse (PMI), reflecting cardiomegaly; an S3 gallop, ↑ JVP; and lower extremity edema. Cool extremities and/or confusion may suggest low cardiac output.

TABLE 3-3. Presentation and Treatment of Select Valvular Lesions

Lesion	Symptoms	Exam	Treatment	Comments
Mitral stenosis	Symptoms of heart failure; hemoptysis; atrial fibrillation (AF)	Diastolic murmur best heard at the apex; opening snap; usually does not radiate	HR control, balloon valvuloplasty, valve replacement	Usually caused by rheumatic fever
Mitral regurgitation	Has a long asymptomatic period; when severe or acute, presents with symptoms of heart failure	Blowing systolic murmur at the apex, radiating to the axilla. The posterior leaflet may lead to a murmur along the sternal border	If acute, surgery is always required. For chronic mitral regurgitation, repair or replace the valve when symptomatic or if the ejection fraction (EF) is $<$ 60%. Surgery is indicated in some patients with an EF $>$ 60% (new AF, pulmonary hypertension)	Long-standing regurgitation dilates the atrium, increasing the chance of AF
Mitral valve prolapse	Generally asymptomatic, although patients can complain of nonspecific symptoms such as palpitations or dyspnea; symptoms are unreliable indicators	Midsystolic click; also murmur if mitral regurgitation is present (murmur increased by Valsalva maneuvers)	Endocarditis prophylaxis is not required	Questionable association with palpitations and panic attacks. The most common cause of mitral regurgitation
Aortic stenosis	Chest pain, syncope, heart failure, shortness of breath	Harsh systolic crescendo-decrescendo murmur radiating to the carotids along the right sternal border. Signs of severe stenosis: a small and slow carotid upstroke (parvus et tardus), a late-peaking murmur, and a loss of clear S2	Avoid overdiuresis; avoid vasodilators such as nitrates and ACEIs given fixed obstruction. Surgery, transcatheter valve replacement, or balloon valvuloplasty for all symptomatic patients	Once symptoms appear, mortality is 50% at 3 years
Aortic regurgitation	Usually asymptomatic until advanced; then presents with symptoms of heart failure	**Chronic:** Soft, high-pitched diastolic murmur along the left sternal border. Radiates toward the apex. Wide pulse pressure and associated signs (eg, the Traube sign, Duroziez murmur) **Acute:** Low-pitched early diastolic murmur. May not have wide pulse pressure and associated signs (because LV stroke volume not increased)	Afterload reduction with ACEIs, hydralazine; valve replacement if symptomatic or in the setting of a ↓ EF	Many cases are associated with aortic root disease, dissection, syphilis, ankylosing spondylitis, and Marfan syndrome

Differential

Deconditioning, lung disease (eg, chronic obstructive pulmonary disease [COPD], chronic thromboembolic pulmonary hypertension, 1° pulmonary hypertension), other categories of heart failure (eg, diastolic dysfunction), other causes of edema (eg, cirrhosis, vascular incompetence, low albumin, nephrotic syndrome).

Diagnosis

- The history and exam are suggestive, but determination of the EF via an imaging study (eg, echocardiography, radionuclide imaging, cardiac MRI) confirms the diagnosis.
- Look for the cause of the low EF:
  - Perform a stress test or cardiac catheterization to look for CAD; evaluate for thyroid and renal disease.
  - Look for a history of alcohol use or exposure to offending cardiotoxic medications such as doxorubicin.
  - Consider dilated cardiomyopathy in postpartum women.
  - Consider myocardial biopsy in selected cases to evaluate for infiltrative disease or other rare causes when other evaluations are inconclusive.

Treatment

- Based on optimizing cardiac output via the following mechanisms:
  - ↓ Preload (reducing cardiac filling pressures).
  - ↓ Wall stress and optimization of cardiac contractility.
  - ↓ Afterload (making it easier for the heart to pump systemically).
- **Maintenance medications** include:
  - **Preload reduction:** Diuretics (furosemide, bumetanide, torsemide).
  - **↓ Wall stress:** β-blockers (metoprolol, bisoprolol, carvedilol).
  - **Optimization of contractility:** Digoxin (may lower the frequency of hospitalizations and improve symptoms but does not ↓ mortality).
  - **Afterload reduction:** Renin-angiotensin-aldosterone antagonists (ACEIs/ARBs; spironolactone if potassium and creatinine are not ↑ and the patient is on optimal dosages of β-blockers and ACEIs/ARBs). Hydralazine and nitrates may be useful additions to ACEIs/ARBs in African-American patients or an alternative to ACEIs/ARBs in patients with kidney disease/hyperkalemia. Spironolactone improves mortality in symptomatic systolic heart failure. ACEI or ARB can be replaced by an angiotensin receptor-neprilysin inhibitor in appropriate patients with mild to moderate disease.
- **Exacerbations:** Give loop diuretics such as furosemide when the patient is volume overloaded. These are given first in IV form and then transitioned to oral form once the patient is closer to euvolemia. β-blockers and afterload reduction agents can be initiated once the patient is euvolemic.
- **Implantable cardiac defibrillators (ICDs)** are associated with ↓ mortality from ventricular tachycardia and ventricular fibrillation (VT/VF) in heart failure patients who are symptomatic and have a ↓ EF (< 35%). Cardiac resynchronization therapy (CRT) is sometimes indicated in heart failure patients with both a ↓ EF and intraventricular conduction delay (QRS > 120 msec).
- Treat the underlying cause of the systolic heart failure (eg, CAD).

KEY FACT

Systolic heart failure is associated with a low EF, whereas diastolic heart failure often has a normal to elevated EF.

KEY FACT

ACEIs, ARBs, and spironolactone all cause hyperkalemia and should be avoided or used cautiously in patients with hyperkalemia and/or renal impairment.

KEY FACT

VT leading to VF is a common cause of death in patients with a ↓ EF. Thus, ICD placement is indicated for patients with an EF < 35%, and CRT is indicated for those with a ↓ EF and intraventricular delay.

DIASTOLIC HEART FAILURE

During diastole, the heart is stiff and does not relax well, resulting in ↑ diastolic filling pressure. However, the EF is often normal, so diastolic heart failure is sometimes referred to as "heart failure with preserved ejection fraction"

(HFpEF). Hypertension with left ventricular hypertrophy (LVH) is the most common cause; other causes include hypertrophic cardiomyopathy and infiltrative diseases.

History/PE

- Signs and symptoms are the same as those of systolic heart failure.
- Exam findings are like those of systolic heart failure. Listen for an S4 rather than an S3 (if rhythm is regular) or an irregular rhythm (atrial fibrillation [AF] is commonly associated with diastolic dysfunction).

Diagnosis

Echocardiography shows preserved EF, often accompanied with ventricular hypertrophy. Biopsy may be needed to establish the underlying diagnosis if infiltrative disease is suspected. Cardiac MRI is becoming an increasingly popular modality for this purpose.

Treatment

- Initially control hypertension. Give diuretics to control volume overload and symptoms, but avoid overdiuresis, which can ↓ preload and cardiac output.
- Manage arrhythmias (eg, AF) that are frequently associated with diastolic dysfunction.
- Control renal and vascular disease, both of which are thought to be associated with diastolic heart disease.

KEY FACT

Important 2° causes of diastolic heart failure:

- Sarcoidosis
- Amyloidosis
- Hemochromatosis
- Scleroderma
- Fibrosis (radiation, surgery)

KEY FACT

Active ischemia can acutely worsen diastolic dysfunction and cause systolic dysfunction, so treat any coexisting CAD in patients with diastolic heart failure.

HEART FAILURE RELATED TO VALVULAR DISEASE

- Right-sided valvular lesions can cause profound edema that is refractory to diuresis.
- Left-sided valvular lesions can produce heart failure.

HEART FAILURE RELATED TO ARRHYTHMIAS

- Often apparent from either patient-reported palpitations or ECG findings.
- Rhythms that can cause symptoms of heart failure include both tachyarrhythmias (eg, rapid AF) and bradyarrhythmias. Others present abruptly with palpitations, shortness of breath, or even syncope.

Cardiomyopathy

Table 3-4 outlines the types and clinical presentations of cardiomyopathies as well as their treatment. Echocardiography is useful for the diagnosis of all types of cardiomyopathy.

Q 1

A 58-year-old woman with long-standing hypertension is admitted to the hospital with dyspnea on exertion and bibasilar crackles, and you suspect heart failure. Which imaging modality would confirm your diagnosis?

Q 2

A 54-year-old business executive develops chest pain while at work. His vital signs remain stable. The chest pain is partially relieved by nitroglycerin but worsens with cough and deep inspiration. He is brought to the ED, where his ECG reveals diffuse ST-T elevations. His cardiac biomarkers are normal. What is the appropriate treatment?

Pericardial Disease

PERICARDITIS

Inflammation of the pericardial sac. Acute (< 6 weeks; most common), subacute (6 weeks to 6 months), or chronic (> 6 months). Causes include bacterial or viral infection (especially enterovirus), mediastinal radiation, post-MI

TABLE 3-4. Types and Features of Cardiomyopathies

Type	Associated Symptoms and Conditions	Distinguishing Features	Treatment
Dilated	Ischemia, tachycardia, hypertension, alcohol, and Chagas disease (in South America)	If the offending source or stimulus is removed, alcoholic and tachycardia-induced cardiomyopathies can be almost completely reversible	ACEIs, ARBs, β-blockers, and spironolactone; Digoxin can improve symptoms but does not improve mortality
Restrictive	Sarcoid, amyloid, hemochromatosis, cancer, and glycogen storage disease	Echocardiography shows left ventricular hypertrophy (LVH), whereas ECG frequently shows low voltage. Biopsy is occasionally required to determine the cause	Directed at the underlying cause and symptom management with diuretics
Hypertrophic	Genetically inherited in an autosomal dominant pattern; associated with sudden cardiac death	Echocardiography may reveal a normal EF and an asymmetrically thickened ventricle	Avoid inotropes, vasodilators, and excessive diuresis

KEY FACT

Chronic constrictive pericarditis often presents with ascites, hepatomegaly, and distended neck veins. A common cause in North America is prior pericardiotomy (from cardiac surgery). TB is a cause that is uncommon in North America.

(Dressler syndrome), cancer, rheumatologic diseases (systemic lupus erythematosus [SLE], rheumatoid arthritis [RA]), uremia, tuberculosis (TB), and prior cardiac surgery. May also be idiopathic (the most common cause of acute cases).

History/PE

- Presents with chest pain that is often improved with sitting up or leaning forward. The pain may radiate to the back and to the left trapezial ridge.
- If a large effusion is present, the patient may be short of breath.
- Exam may reveal a pericardial friction rub (a leathery sound that can be present in multiple stages of the cardiac cycle).

Differential

Myocardial ischemia, aortic dissection, pneumonia, pulmonary embolism, pneumothorax.

Diagnosis

- A number of clinical and ECG features can distinguish pericarditis from acute MI (see Table 3-5).
- First diagnostic test: ECG (see Figure 3-2).

1 A

Transthoracic echocardiography (TTE). TTE provides specific information, such as left ventricular ejection factor (LVEF) and diastolic compliance and relaxation, which can confirm the diagnosis of systolic and diastolic heart failure. It also yields information about specific etiologies or precipitants such as valvular or wall motion abnormalities.

2 A

NSAIDs. The patient most likely has pericarditis, which is a clinical diagnosis.

TABLE 3-5. Pericarditis vs Acute MI

	Pericarditis	MI
Clinical	Pain improves with sitting up or leaning forward; sometimes pleuritic	Pain is not alleviated or exacerbated by position
ECG	Diffuse ST-segment elevation, often with upward concavity (see Figure 3-2); PR-segment depression, particularly in the limb leads; ST-T changes tend to normalize more rapidly than those in MI	ST-segment elevation is localized to the distribution of coronary arteries, often with downward concavity; reciprocal ST depressions can be present

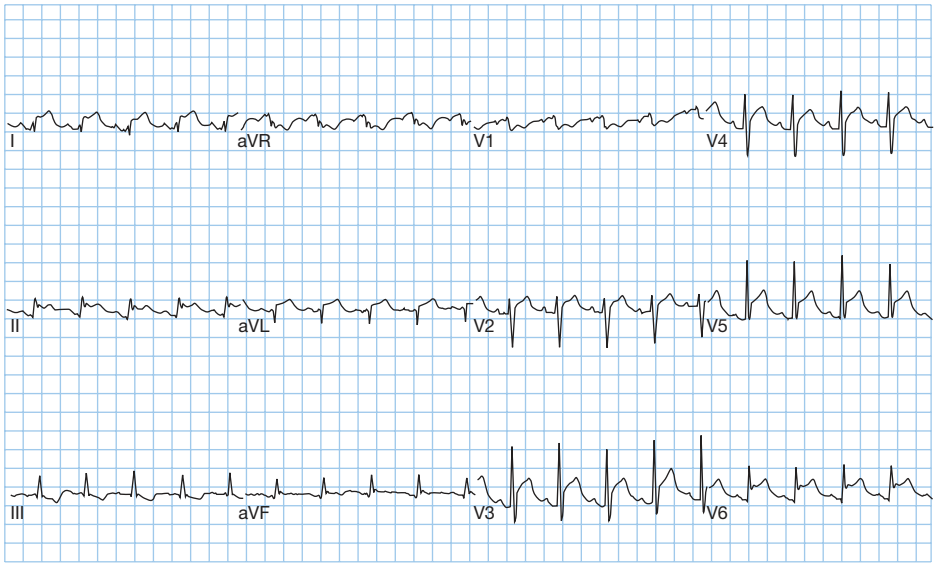


FIGURE 3-2. Pericarditis. Note diffuse ST-segment elevation and PR depression.

- Echocardiography may reveal an associated pericardial effusion.
- Search for an underlying cause (ie, take a history for viral illness, radiation exposure, and malignancy). Check antinuclear antibody (ANA), PPD, blood cultures if febrile, and renal function.

Treatment

- Where possible, treat the underlying disorder (eg, SLE, advanced renal failure).
- For viral or idiopathic pericarditis, give NSAIDs, colchicine, or aspirin. Avoid NSAIDs or steroids in early post-MI pericarditis, as they may interfere with scar formation.

Complications

Patients may develop a clinically significant pericardial effusion and tamponade (see below).

PERICARDIAL EFFUSION AND CARDIAC TAMPONADE

Accumulation of fluid (usually chronic) or blood (usually acute and posttraumatic/postsurgical) in the pericardial cavity surrounding the heart.

History/PE

- Symptomatology often depends on the rate of fluid accumulation. If acute, patients may present with shock. If chronic, patients may present with shortness of breath and heart failure (if gradual, several liters of fluid may accumulate).
- In patients with pericardial effusions and tamponade physiology, exam classically reveals distant or muffled heart sounds, ↑ JVP, and pulsus paradoxus (a drop of > 10 mm Hg in systolic BP [blood pressure] during inspiration). Pulsus paradoxus may be absent in a patient with tamponade physiology if there is concurrent aortic regurgitation or atrial septal defect.

Differential

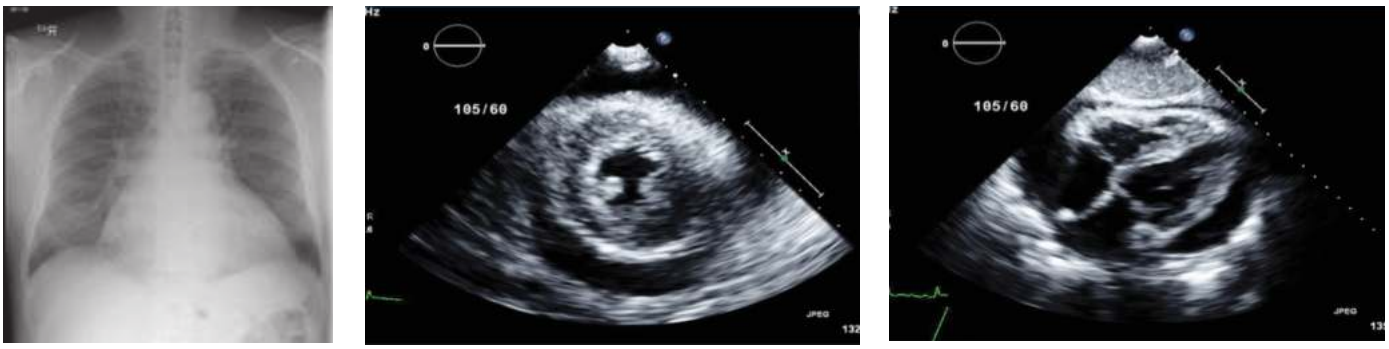
Pneumothorax, acute MI, heart failure.

KEY FACT

Pulsus paradoxus occurs in tamponade: inspiration → ↑ venous return to the right side of the heart → ↓ LV filling and output (pericardial fluid creates a fixed volume, so increases in right-sided volume → ↓ left-sided volume).

Q

A 64-year-old woman suddenly develops hypotension and shortness of breath 1 day after CABG surgery. Exam reveals JVD and muffled heart sounds, and bedside pulsus paradoxus is present. Besides ordering an urgent echocardiogram, what are your next therapeutic steps?



A B C

FIGURE 3-3. Pericardial effusion and tamponade. (**A**) CXR with enlargement of the cardiac silhouette ("water-bottle heart") in a patient with a pericardial effusion. (**B** and **C**) Transthoracic echocardiogram images show a large pericardial effusion with collapse of the right atrium and right ventricle in early diastole in a patient with cardiac tamponade. (Reproduced with permission from USMLE-Rx.com.)

KEY FACT

Always check a bedside pulsus paradoxus when tamponade is suspected. Echocardiography is the diagnostic procedure of choice.

Diagnosis

- **Initial test:** Echocardiography is needed to confirm the diagnosis.
- CXR may reveal an enlarged cardiac silhouette (see Figure 3-3), and ECG may show low voltages and electrical alternans (beat-to-beat variation in R-wave amplitude).

Treatment

- Consider emergent pericardiocentesis for patients with post–chest trauma shock as well as for those whose echocardiogram shows evidence of tamponade physiology.
- Also consider a pericardial window for those with recurrent or malignant effusions. While evaluation with echocardiography is being pursued, give IV fluids to maintain preload and systemic BP.

Advanced Cardiac Evaluation

- Indications for stress testing include diagnosis of CAD/evaluation of symptoms, preoperative evaluation, risk stratification in patients with known disease, and decision making about the need for revascularization.
- Contraindications include severe aortic stenosis, acute coronary syndrome, acute pulmonary embolus, unstable arrhythmias, and decompensated heart failure.
- Testing consists of a stressing modality and an evaluating modality (see Tables 3-6 and 3-7).
- Within pharmacologic stressing modalities, dobutamine ↑ cardiac contractility, whereas adenosine and dipyridamole dilate the coronary arteries (the latter ↑ blood flow in healthy arteries but not in already maximally dilated diseased arteries, creating a differential flow that can be detected on nuclear imaging).

Hypertension

A major contributor to cardiovascular disease; more common with increasing age and among African-Americans.

A

Administer IV fluids and pursue emergent therapeutic pericardiocentesis or pericardial window.

TABLE 3-6. Stressing Modalities in Cardiac Testing

Modality	Pros	Cons
Treadmill	Good for patients who can exercise lightly	Lower sensitivity in women
Dobutamine	Good for patients who cannot exercise	Patients can feel poorly because of β-agonism
Adenosine or dipyridamole (with nuclear imaging)	Good for patients who cannot exercise	Can cause bronchospasm; use caution in patients with asthma/COPD

History/PE

- Asymptomatic unless severe. If severe without symptoms, it is termed "hypertensive urgency." If severe with symptoms or evidence of organ damage (dizziness, lightheadedness), it is termed "hypertensive emergency."
- BP > 130/80.
- A displaced PMI or an S4 suggests LVH.
- Listen for bruits, which indicate peripheral vascular disease.
- Examine fundi, which can show AV nicking and "copper-wire" changes to the arterioles. In severe hypertension, look for papilledema and retinal hemorrhages.
- Look for signs suggestive of 2° hypertension.

Differential

The vast majority of cases are due to essential (1°) hypertension, but in the right clinical settings or in cases of refractory hypertension, consider 2° causes (see Table 3-8).

Diagnosis

- Diagnosed in the setting of a BP > 130/80 on two or more readings obtained on two or more separate occasions (elevation of either systolic or diastolic BP). Note: the previous definition of BP > 140/90 has been

TABLE 3-7. Evaluating Modalities in Cardiac Testing

Modality	Pros	Cons
ECG	Inexpensive, fast	Cannot localize the lesion; cannot use with baseline ST-segment abnormalities or LBBB; cannot use if the patient is on digoxin
Echocardiography	Better than ECG in patients with LBBB; cheaper than nuclear imaging	Quality is provider dependent, which may limit the usefulness of images
Radionuclide tracer (thallium or technetium)	Localizes ischemia; localizes infarcted tissue	Expensive; usefulness can be limited in extensive, multivessel CAD with balanced ischemia in different regions

Q

A 65-year-old Caucasian man who has a history of diabetes and is currently on metformin has BP readings of 150/90 and 140/95 on multiple office visits. You start him on an ACEI, but he returns for follow-up complaining of a dry cough with a measured BP of 145/92. What is your BP goal for this patient, and what are additional options for treating his hypertension?

TABLE 3-8. Causes of 2° Hypertension

Causes	Examples
Endocrine	Cushing syndrome, Conn syndrome (aldosterone-producing tumor), hyperthyroidism, pheochromocytoma
Renal	Chronic kidney disease (CKD); renal artery stenosis (listen for an abdominal bruit)
Medications	OCPs, NSAIDs
Other	Fibromuscular dysplasia of the renal arteries and aortic coarctation (in younger patients), obstructive sleep apnea, alcohol

updated to reflect the 2017 American College of Cardiology/American Heart Association (ACC/AHA) hypertension guidelines.

- Based on the 2017 ACC/AHA guidelines, a systolic BP of 120–139 and a diastolic BP of < 80 is considered "elevated." There is no longer the designation of "prehypertension."
- Stage 1 hypertension: Systolic BP between 130–139 or diastolic BP between 80–89.
- Stage 2 hypertension: Systolic BP of at least 140 or diastolic BP of at least 90.

Treatment

- Based on the most recent guidelines, the goal BP for almost all patients, including those with diabetes or CKD, is < 130/80. This represents a change from earlier guidelines, which recommended a goal of < 140/90 in those with diabetes and those with renal insufficiency. (Note: The goal BP recommended in the last several guidelines has been the subject of controversy.)
- New guidelines also suggest initiating treatment with two medications for Stage 2 hypertension, with the goal BP of < 130/80.
- Interventions include the following:
  - **Step 1—lifestyle modification:** Weight loss, exercise, ↓ sodium intake, smoking cessation.
  - **Step 2—medications:** First-line agents include thiazide diuretics, CCBs, ACEIs, or ARBs unless there is a more specific indication for another class of drugs (see Table 3-9). Thiazide diuretics and CCBs considered first line for African-Americans.
  - Control other cardiovascular risk factors, such as diabetes, smoking, and hypercholesterolemia.

KEY FACT

The goal BP in almost all patients including those with diabetes or CKD is < 130/80.

KEY FACT

The treatment of hypertension in African-American patients should begin with thiazide diuretics or CCBs.

Complications

Long-standing hypertension contributes to CAD, heart failure (both systolic and diastolic), peripheral vascular disease, renal failure, and stroke.

A

Thiazide diuretics, CCBs, ACEIs, and ARBs are all therapeutic options. The BP goal for this patient would be < 130/80. In light of his cough (a potential adverse effect of ACEIs), you could switch the patient to an ARB and add a second medication to achieve goal BP.

Aortic Dissection

Increased risk among patients with a history of long-standing hypertension, cocaine use, aortic aneurysm, or aortic root disease such as Marfan syndrome or Takayasu arteritis.

TABLE 3-9. Antihypertensive Medications

Commonly Used Classes	Optimal Use	Main Adverse Effects
Thiazide diuretics	First line	↓ Excretion of calcium and uric acid, hyperglycemia, hyperlipidemia, hyponatremia
β-blockers	Not recommended as a first line; useful in ↓ EF, angina, and CAD	Bradycardia, erectile dysfunction, bronchospasm in asthmatics
ACEIs	First line, preferred over thiazides or CCBs in patients with CKD with or without diabetes, also useful in patients with ↓ EF and in patients with diabetes with microalbuminuria	Dry cough, angioedema, hyperkalemia, acute kidney injury
ARBs	Same as ACEIs	Hyperkalemia; do not cause cough associated with ACEIs
CCBs	First line	Lower extremity edema

History/PE

- Presents with sudden onset of severe chest pain that sometimes radiates to the back, often described as a burning, searing, or tearing pain. May also present with neurologic symptoms resulting from involvement of vessels supplying the brain or spinal cord.
- On exam, evaluate for a murmur consistent with aortic regurgitation, asymmetric pulses and BP, and neurologic findings.

Differential

MI (aortic dissection can also cause an MI if it extends into a coronary artery), pulmonary embolism, pneumothorax.

Diagnosis

- Requires a high index of suspicion.
- **Initial test:** CT with IV contrast is diagnostic and shows the extent of dissection (see Figure 3-4).
- CXR has low sensitivity but may show a widened mediastinum or a hazy aortic knob. Transesophageal echocardiography (TEE) is highly sensitive and specific.
- MRI may also be used but can be time-consuming and not optimal for unstable patients.

Treatment

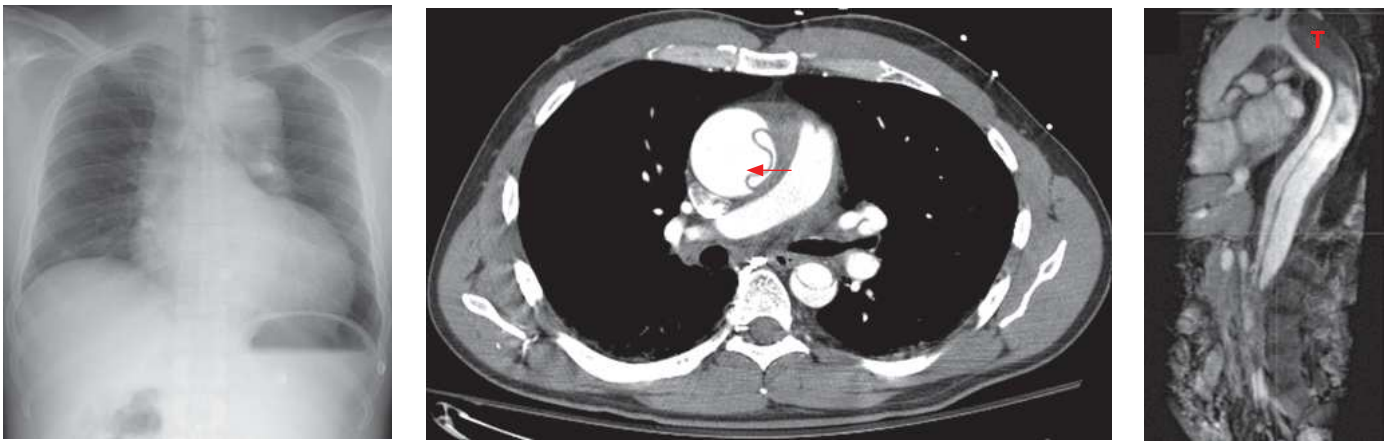
- **Initial medical stabilization:** Aggressive HR and BP control, first with β-blockers (typically IV esmolol) and then with IV nitroprusside if needed.
- **Ascending dissection—Stanford type A (involves the ascending aorta):** Emergent surgical repair.

KEY FACT

Risk factors for aortic aneurysm include age > 60 years, smoking, hypertension, a family history of aortic aneurysm, and hypercholesterolemia. The risk of rupture is low for aneurysms < 4 cm but ↑ with those ≥ 5 cm.

Q

A 69-year-old hospital administrator presents to the ED with severe, tearing chest pain that radiates to his back. CXR is unrevealing. Given your concern for potential aortic dissection, what is the next diagnostic step?



A B C

FIGURE 3-4. Aortic dissection. (**A**) Frontal CXR showing a widened mediastinum in a patient with an aortic dissection. (**B**) Transaxial contrast-enhanced CT showing a dissection involving the ascending and descending aorta (*arrow*, false lumen). (**C**) Sagittal MRA image showing a dissection involving the descending aorta, with a thrombus (T) in the false lumen. (Images A and C reproduced with permission from USMLE-Rx.com. Image B reproduced with permission from Doherty GM. *Current Diagnosis & Treatment: Surgery,* 13th ed. New York: McGraw-Hill, 2010, Fig. 19-17.)

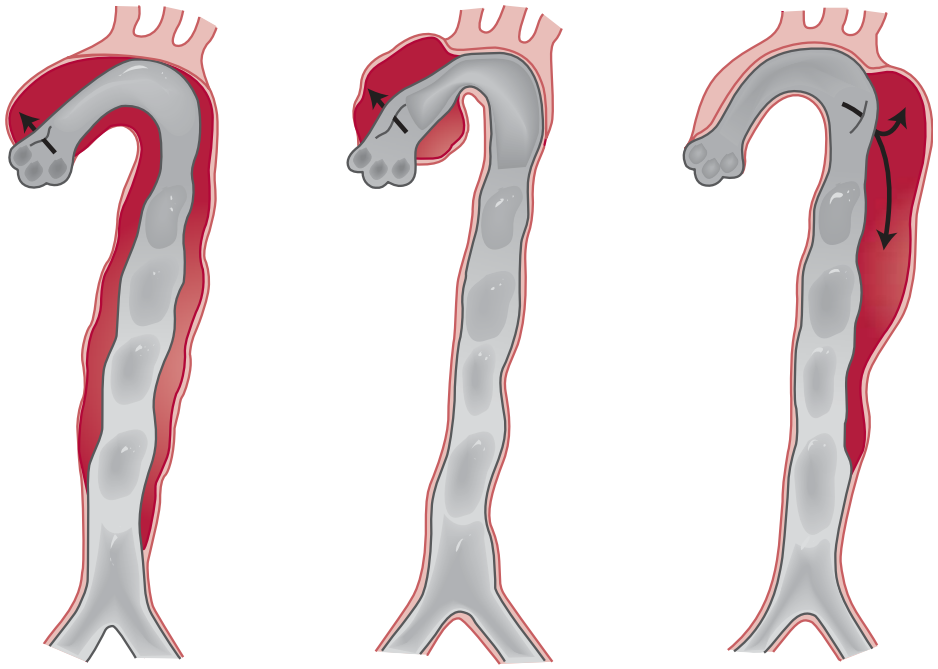
KEY FACT

Surgery is indicated for rapidly expanding aneurysms (> 0.5 cm/year) as well as for large aneurysms to avert the catastrophe of dissection.

- **Descending dissection—Stanford type B (distal to the left subclavian artery):** Medical management with β-blockers is indicated unless there is intractable pain, progressive dissection in patients with chest pain, or vascular occlusion of the aortic branches (see Figure 3-5).

Complications

Aortic rupture, acute aortic regurgitation, tamponade, MI, neurologic impairment, limb or mesenteric ischemia, renal ischemia.



A B

FIGURE 3-5. Ascending vs descending aortic dissection. (**A**) Proximal or ascending (type A). (**B**) Distal or descending (type B). (Reproduced with permission from Doherty GM. *Current Diagnosis & Treatment: Surgery,* 13th ed. New York: McGraw-Hill, 2010, Fig. 19-16.)

A

Chest CT with IV contrast. TEE is appropriate for patients with a history of allergic reaction to IV contrast.

Peripheral Vascular Disease

Atherosclerotic disease of vessels other than the coronary arteries. Risk factors are similar to those for CAD and include smoking, diabetes, hypercholesterolemia, hypertension, and increasing age.

History/PE

Depends on the affected organ(s).

- **Abdominal aortic aneurysm:** Palpate for a pulsatile mass in the abdominal midline.
- **Mesenteric ischemia:** Postprandial abdominal pain and food avoidance ("food fear"), bloody diarrhea. On exam, no specific findings. May observe thin habitus because of weight loss from avoidance of food.
- **Lower extremity disease:** Claudication, leg ulceration or nonhealing wounds, rest pain. Look for ulcers and nonhealing wounds, diminished pulses, ↓ ankle-brachial indices, skin atrophy, and loss of hair. Listen for bruits over affected vessels (abdominal, femoral, popliteal).
- **Kidneys:** Usually asymptomatic but may present with difficult-to-control hypertension. Listen for a bruit during systole and diastole (highly specific for renal artery stenosis).
- **CNS:** Stroke and transient ischemic attack (see Chapter 13).

Differential

- **Abdominal pain:** Stable symptoms can mimic peptic ulcer disease or biliary colic. If the colon is predominantly involved, episodes of pain and bloody stool can look like infectious colitis.
- **Lower extremities:** Spinal stenosis can produce lower extremity discomfort similar to claudication. Claudication improves with rest (except for severe peripheral arterial disease with rest claudication), but spinal stenosis classically improves with sitting forward (lumbar flexion improves spinal stenosis symptoms).

Diagnosis

- **Mesenteric disease:** Angiography reveals lesions. A diagnosis of exclusion.
- **Lower extremity disease:** Ankle-brachial index (compares BP in the lower and upper extremities) and Doppler ultrasound. Angiography or magnetic resonance angiogram (MRA) is used in preparation for revascularization but is generally not used for diagnosis.
- **Renal artery stenosis:** CT angiography, MRA, conventional angiography, or ultrasound with Doppler flow (technically difficult).

Treatment

- Control modifiable risk factors, especially smoking.
- **Mesenteric disease:** Treat with surgical revascularization or angioplasty.
- **Lower extremity disease:** Treat with exercise (to improve functional capacity), surgical revascularization, and sometimes angioplasty. Cilostazol is moderately useful (improves pain-free walking distance by 50%), whereas pentoxifylline is of marginal benefit. Antiplatelet therapy (aspirin, clopidogrel) is indicated to prevent cardiovascular events.
- **Renal artery stenosis:** Surgery or angioplasty may be of benefit.

KEY FACT

Peripheral vascular disease is a predictor of CAD.

KEY FACT

Patients with acute vessel occlusion from an embolus or an in-situ thrombus present with sudden pain (abdominal or extremity). This represents an emergency.

Q

A 73-year-old man with a history of diabetes mellitus, but with no history of clinical CAD, comes to your office for the results of his recent bloodwork. His fasting lipid panel is significant for an LDL of 130 mg/dL, and his 10-year risk of atherosclerotic cardiovascular disease is 7%. In addition to educating him on diet and lifestyle changes, what action should you take?

Hypercholesterolemia

One of the principal factors contributing to atherosclerotic vascular disease. ↑ LDL and ↓ HDL are the 1° contributors. Can be idiopathic, genetic, or 2° to other diseases, such as diabetes, nephrotic syndrome, and hypothyroidism.

History/PE

- Generally asymptomatic unless the patient develops ischemia (eg, angina, stroke, claudication) or unless severe hypertriglyceridemia leads to pancreatitis.
- Look for evidence of atherosclerosis (eg, carotid, subclavian, abdominal and other bruits; diminished or asymmetric pulses; or ischemic foot ulcers or other skin or hair changes).
- Look for xanthomas over the tendons, above the upper eyelid, and on the palms.

Diagnosis

- **Initial test:** Order a lipid panel. A full panel consists of total cholesterol, HDL, LDL, and triglycerides.
- In many cases, a nonfasting lipid profile can be obtained for ease of testing. Fasting and nonfasting total cholesterol and HDL values vary very little. However, triglyceride values ↑ following a meal. If triglyceride values are of concern, fasting levels should be obtained.
- A fasting profile may also be helpful for quantifying LDL. Traditionally, LDL has not been measured directly but calculated on the basis of total cholesterol, HDL, and triglycerides (via the Friedewald equation). High triglycerides (> 400 mg/dL) make LDL calculation unreliable. However, newer assays can measure LDL directly.
- Look for other contributing conditions. Check glucose and TSH, check body weight, and consider nephrotic syndrome.
- In patients with a family history of early heart disease, consider novel risk factors such as homocysteine, Lp(a), and C-reactive protein (CRP). These can be treated with folic acid supplementation, niacin, and statins, respectively.

KEY FACT

The Friedewald equation can be used to calculate LDL cholesterol (in mg/dL): LDL = Total cholesterol – HDL – (TG/5)

Treatment

Aimed at preventing pancreatitis when triglycerides are very high (generally > 1000 mg/dL) and at preventing atherosclerotic disease (see Table 3-10).

KEY FACT

LDL control is the 1° cholesterol-related goal in patients with CAD or diabetes. Recommendations for LDL goals have recently changed from absolute target values to percent reduction based on risk profile.

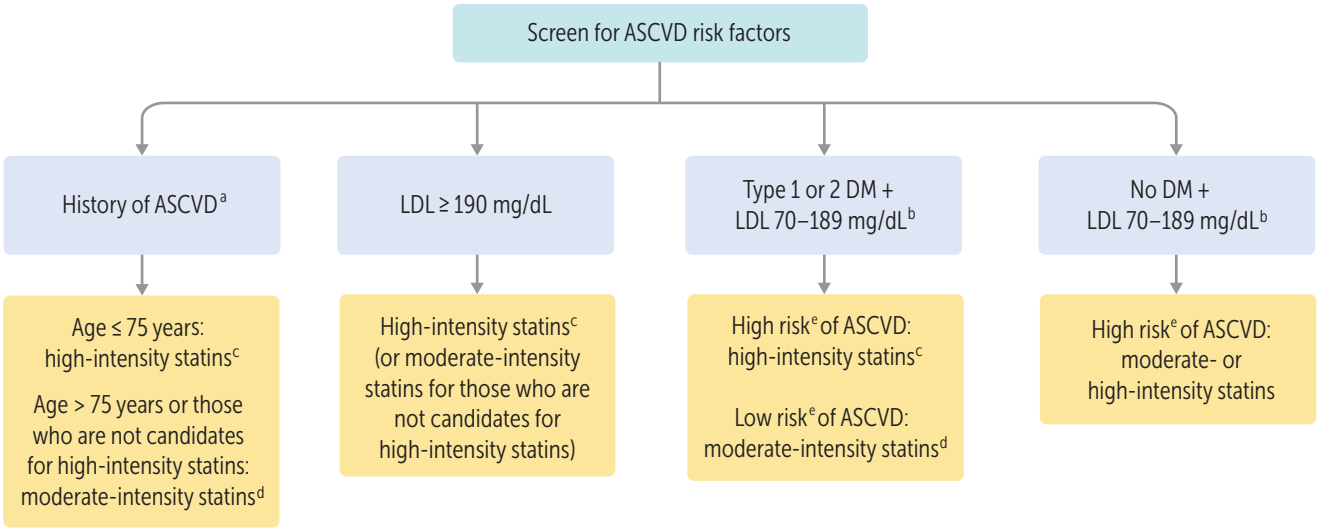
- **LDL:**
  - Traditional treatment has been based on goal LDL (eg, in patients with diabetes or CAD, the goal LDL was < 70 mg/dL; lower-risk patients had higher LDL goals). However, recent guidelines recommend percent reductions in LDL rather than absolute goals (eg, a 50% reduction in LDL in high-intensity treatment and a 30–50% reduction in moderate-intensity treatment) based on patient risk profiles (see Figure 3-6).
  - The mainstay of treatment is diet, exercise, and a statin. LDL control is the 1° cholesterol-related goal in patients with CAD or diabetes.
- **HDL:** Can be modestly ↑ with fibrate or nicotinic acid. Although ↓ HDL has been associated with an ↑ risk of cardiovascular events, there is no definitive clinical benefit to using medications to ↑ HDL.
- **Triglycerides:** If > 500 mg/dL, recommend dietary modification (↓ total fat, ↓ saturated fat, ↓ alcohol) and aerobic exercise, and begin medication

A

Start moderate-intensity statin therapy with a goal LDL reduction of 30–50%.

TABLE 3-10. Mechanisms and Features of Cholesterol-Lowering Medications

Medication	Primary Effect	Adverse Effects	Comments
HMG-CoA reductase inhibitors ("statins")	↓ LDL	Hepatitis, myositis	Potent LDL-lowering medication; the only medication to show a mortality benefit
Cholesterol absorption inhibitors (ezetimibe)	↓ LDL	Generally well tolerated but can cause diarrhea and arthralgias	Introduced in 2003; no independent mortality benefit but improves cardiovascular outcomes when added to statins in patients hospitalized for acute coronary syndrome
Fibrates (gemfibrozil)	↓ Triglycerides, slightly ↑ HDL	Potentiates myositis with statins	
Bile acid–binding resins	↓ LDL	Bloating and cramping	Many patients cannot tolerate GI adverse effects
Nicotinic acid (niacin)	↓ LDL, ↑ HDL	Hepatitis, flushing	Causes flushing, which can be ↓ by taking aspirin beforehand



[a] Atherosclerotic cardiovascular disease (ASCVD) = acute coronary syndrome, MI stable/unstable angina, revascularization procedures, stroke/TIA, peripheral arterial disease.

[b] In patients 40–75 years of age.

[c] High-intensity statins = atorvastatin, 40–80 mg; rosuvastatin, 20–40 mg (reduce LDL by ≥50%).

[d] Moderate-intensity statins = atorvastatin, 10–20 mg; rosuvastatin, 5–10 mg; simavastatin, 20–40 mg; pravastatin, 40–80 mg; lovastatin, 40 mg; extended-release fluvastatin, 80 mg; fluvastatin, 40 mg BID; pitavastatin 2–4 mg (reduce LDL by 30–50%).

[e] Estimated 10-year ASCVD risk: low risk is < 7.5%; high risk is ≥ 7.5%.

FIGURE 3-6. Guidelines for the treatment of hyperlipidemia with statin therapy. (Data from Stone NJ, et al. *Circulation*. 2014 Jun 24;129(25 Suppl 2): S1-45; Reproduced with permission from USMLE-Rx.com.)

(fibrate or nicotinic acid). At lower levels, treatment can begin with diet and exercise, and medication can be added as needed. Treat diabetes and other concurrent metabolic syndrome risk factors if present.

Endocarditis

Inflammation of the heart valves. Can be infective or noninfective. Infective endocarditis (IE) is commonly seen in IV drug abusers, hemodialysis patients, and those with valvular lesions or prosthetic heart valves. Valvular thrombi are composed of bacteria and platelets and are devoid of WBCs. IE is further distinguished as follows:

- **Acute IE (days):** Usually affects normal heart valves and is most often caused by *S aureus* and β-hemolytic streptococci. IV drug users typically have *S aureus* organisms and right heart involvement.
- **Subacute IE (weeks to months):** Usually colonizes a previously damaged valve in the setting of bacteremia from oral surgery or poor dentition. It is most often caused by the viridans group of streptococci. The aortic and mitral valves are most commonly affected.

History/PE

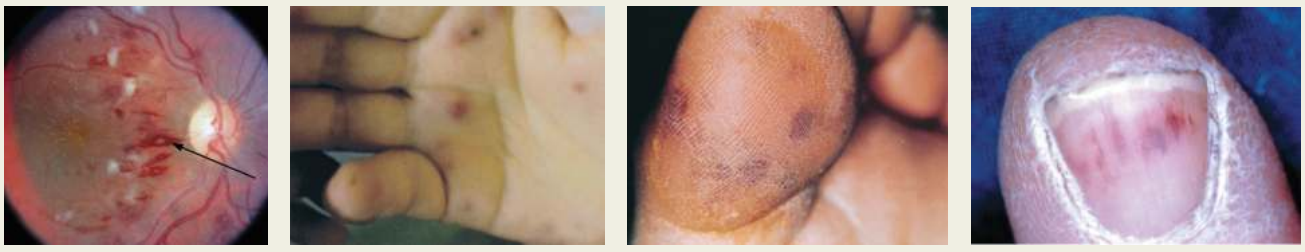
- **Acute IE:** Presents with fever, rigors, heart failure from valve destruction, and symptoms related to systemic emboli (neurologic impairment, back pain, pulmonary symptoms).
- **Subacute IE:** Characterized by weeks to months of fever, malaise, and weight loss. Also presents with symptoms of systemic emboli.
- **Noninfective endocarditis:** Generally asymptomatic. Can cause heart failure by destroying valves.
- Listen for a new murmur.
- Look for involvement of multiple organs (see Table 3-11).

KEY FACT

Streptococcus bovis bacterial endocarditis should raise suspicion for occult GI malignancy. These patients need a colonoscopy.

TABLE 3-11. Exam Findings and Organ Systems Affected in Infective Endocarditis

Organ System	Findings
Neurologic	Focal neurologic deficits; tenderness to percussion or palpation of the spine
Ophthalmologic	Roth spots, white-centered hemorrhages (Image A, *arrow*)
Integumentary (extremities)	Osler nodes (Image B), deep-seated hand/foot nodules, painful and reflect microthrombi and immune-mediated vasculitis, or Janeway lesions (Image C), small skin infarctions, painless and reflect microabscesses; splinter hemorrhages (Image D) and petechiae



A B C D

Image A reproduced with permission from USMLE-Rx; courtesy of Nicholas Mahoney, MD. Images B and C reproduced with permission from Hall JB et al. *Principles of Critical Care,* 3rd ed. New York: McGraw-Hill, 2005, Figs. 49-1 and 49-2. Image D reproduced with permission from USMLE-Rx.

TABLE 3-12. Causes of Endocarditis

Acute	Subacute	Culture Negative	NBTE (Marantic Endocarditis)	Verrucous (Libman-Sacks)
Most commonly *S aureus*	Viridans streptococci *Enterococcus* *Staphylococcus epidermidis* Gram ⊖ rods *Candida*	HACEK organisms[a] *Coxiella burnetii* Noncandidal fungi	Thrombus formation on the valve seen in many cancers	Seen in lupus; vegetation is composed of fibrin, platelets, immune complexes, and inflammatory cells

[a]**HACEK** organisms: ***H****aemophilus aphrophilus* and ***H*** *parainfluenzae,* ***A****ctinobacillus actinomycetemcomitans,* ***C****ardiobacterium hominis,* ***E****ikenella corrodens,* ***K****ingella kingae.*

Differential

The differential diagnosis of endocarditis is outlined below and in Table 3-12.

- **For vegetation found on echocardiography:** IE, nonbacterial thrombotic endocarditis (NBTE, also known as marantic endocarditis), verrucous endocarditis (Libman-Sacks endocarditis), valve degeneration.
- **For bacteremia:** IE, infected hardware (eg, from a central line), abscess, osteomyelitis.

Diagnosis

- Noninfective endocarditis is usually an incidental finding on echocardiography. It may be found during the workup of systemic emboli.
- IE is diagnosed by a combination of lab and clinical data. If suspicious, obtain at least three sets of blood cultures and an echocardiogram. If transthoracic echocardiography (TTE) is ⊖, proceed to TEE (more sensitive). ⊕ Blood cultures and echocardiogram findings together are strongly suggestive of IE. The modified Duke criteria are often used for diagnosis (see Table 3-13).

Treatment

- Treat with prolonged antibiotic therapy, generally for 4–6 weeks (can be as short as 2 weeks for small subgroups of patients; > 6 weeks for patients with highly virulent organisms). Begin empiric therapy with gentamicin and antistaphylococcal penicillin (oxacillin or nafcillin). If there is a risk of methicillin-resistant *S aureus* (MRSA), treat empirically with vancomycin instead of oxacillin/nafcillin.
- Valve replacement is appropriate for fungal endocarditis, HF from valve destruction, valve ring abscess, cardiac conduction abnormalities, persistently ⊕ blood cultures despite antibiotic treatment, large or mobile vegetations, or systemic emboli despite adequate antibiotic therapy.
- Following treatment for IE, patients should receive endocarditis prophylaxis.
- For NBTE, treat the underlying disorder (often malignancy). Systemic anticoagulation (LMWH or unfractionated heparin) is useful for preventing recurrent emboli. Surgery is rarely indicated.
- For verrucous endocarditis, no treatment is required. Patients should receive endocarditis prophylaxis (see below).

KEY FACT

Any patient with *S aureus* bacteremia should be evaluated for endocarditis with echocardiography.

KEY FACT

Surgery is indicated in the setting of hemodynamic instability, heart-failure symptoms, valvular destruction, conduction abnormalities, perivalvular extension, fungal endocarditis, or persistently ⊕ blood cultures. Surgery should not be delayed while the acute infection is cleared with antibiotics.

Q

A 26-year-old IV drug user is admitted to the hospital with fevers and chills. Despite broad antibiotic therapy, blood cultures remain persistently ⊕, but TTE is normal. Given your suspicion of infective endocarditis, what is your next step?

TABLE 3-13. Modified Duke Criteria for the Diagnosis of Infective Endocarditis[a,b]

Duke Criterion	Definition
	Major Criteria
1. Microbiologic evidence of IE	Typical organisms isolated from two separate blood cultures: ■ Viridans streptococci, *S aureus,* HACEK organisms, or *S bovis* OR ■ Community-acquired enterococci in the absence of an alternative 1° site of infection Persistently ⊕ blood cultures with other organisms: ■ At least two ⊕ cultures drawn >12 hours apart OR ■ All of three or a majority of four ⊕ cultures, with the first and last drawn > 1 hour apart ■ One ⊕ culture (or phase I IgG > 1:800) for *Coxiella burnetii*
2. Evidence of endocardial involvement	Echocardiogram showing one of the following: ■ An oscillating intracardiac mass with no alternative explanation ■ An abscess ■ New partial dehiscence of a prosthetic valve ■ New valvular regurgitation
	Minor Criteria
1. Predisposition to IE	Previous IE, IV drug use, a prosthetic heart valve, or a cardiac lesion causing turbulent blood flow
2. Fever > 38°C (100.4°F)	
3. Vascular phenomena	Arterial emboli, pulmonary infarcts, mycotic aneurysms, intracranial or conjunctival hemorrhage, Janeway lesions
4. Immunologic phenomena	Glomerulonephritis, Osler nodes, Roth spots, ⊕ RF
5. Microbiologic findings not meeting major criteria	

[a]The definitive diagnosis of IE requires two major criteria, one major and three minor criteria, or five minor criteria.

[b]The diagnosis of possible IE requires one major and one minor criterion or three minor criteria.

Prevention

A

Order a TEE, which is more sensitive than TTE for visualizing vegetations and diagnosing endocarditis. When endocarditis is suspected clinically but TTE is normal, a TEE is indicated to better confirm or rule out infection.

Endocarditis prophylaxis is indicated only in patients whose cardiac conditions are associated with the highest risk of an adverse outcome from endocarditis. These include:

- **Congenital cardiac disease:**
  - Unrepaired cyanotic disease, including those with palliative shunts and devices.
  - Congenital cardiac defects that have been completely repaired during the first 6 months after the repair (endothelialization occurs after 6 months).

  - Repaired congenital cardiac disease with residual defects that may inhibit endothelialization.
- **Other:**
  - Prosthetic heart valves (both homograft and bioprosthetic).
  - A patient history of prior IE.
  - Cardiac transplant patients with cardiac valvulopathy.
- **Guidelines for antibiotic prophylaxis:**
  - **Dental procedures:** All dental procedures that involve the manipulation of gingival tissue or the periapical region of teeth, as well as procedures involving perforation of the oral mucosa (not for routine anesthetic injections through noninfected tissue, dental radiographs, bleeding from trauma, adjustment of orthodontic devices, or shedding of deciduous teeth).
  - **Respiratory tract procedures:** Any of the above-mentioned cardiac patients who are undergoing an invasive procedure of the respiratory tract that involves incision (eg, tonsillectomy) or biopsy of the respiratory mucosa (includes bronchoscopy with biopsy).
  - **Skin procedures:** Any of the above-mentioned cardiac patients who are undergoing procedures involving infected skin or musculoskeletal tissue.
  - **GI and GU procedures:** Prophylaxis is not recommended even for high-risk patients but may be considered in special scenarios involving the above-mentioned cardiac patients.
  - **Prophylactic regimens:** Amoxicillin (or clindamycin, azithromycin, or cephalexin for those with penicillin allergy) 30–60 minutes before the procedure.

KEY FACT

Don't forget—IE generally requires prolonged antibiotic therapy for 4–6 weeks.

Complications

Spinal osteomyelitis, valve destruction and heart failure, stroke and pulmonary or renal damage (from septic emboli), metastatic abscesses, mycotic aneurysms.

NOTES

CHAPTER 4

EMERGENCY MEDICINE

Trauma

The acute management of trauma patients follows a linear algorithm that should be performed in the same order every time: the **ABCDE** approach (1° survey) followed by **FAST** (**F**ocused **A**ssessment with **S**onography in **T**rauma) and the 2° survey. This ensures that no important steps in the initial assessment and resuscitation will be skipped.

In actual practice, multiple steps occur simultaneously (eg, IV fluids are administered as an airway is being secured). However, the USMLE often asks about the "next step," thereby testing your understanding of the algorithm rather than your ability to manage multiple therapeutic approaches at the same time. It is the team leader's responsibility to ensure that the 1° survey is completed before the 2° survey is begun.

MNEMONIC

Glasgow Coma Scale—

Less than 8…Intubate!

KEY FACT

Hemodilution does not occur in acute hemorrhage, so hematocrit will be normal initially; don't be falsely reassured. Patients don't bleed normal saline, so limit crystalloid resuscitation and administer blood products.

KEY FACT

When initially assessing disability in trauma, put your tuning fork away. Is the patient talking, moving, following commands, and can he feel his arms and legs? Good!

THE 1° SURVEY

- **A**—**A**irway maintenance with cervical spine control. Indications for a definitive airway (eg, intubation, cricothyroidotomy):
  - Patient cannot protect his airway.
  - Patient cannot be ventilated by bag-valve mask (eg, facial trauma).
  - Impending or complete airway failure (eg, inhalation burn, severe head/neck trauma). Includes failure to oxygenate or ventilate as expected.
  - Any of the above conditions expected in the immediate future.
- **B**—**B**reathing with ventilation. Quickly evaluate for and treat causes of impending cardiopulmonary failure/death (eg, tension or open pneumothorax, massive hemothorax, or airway obstruction).
- **C**—**C**irculation with hemorrhage control.
  - Resuscitation: Think short and fat IV lines—2 large-bore (14- or 16-gauge) IVs. Central lines have high flow resistance and take too long to insert. May also use intraosseous cannulation.
  - 16-gauge IV 150 cc/min flow rate > 16-gauge triple-lumen port 70 cc/min flow rate. Flow resistance ↑ with catheter length.
  - Resuscitate with 2 L of crystalloid. If further resuscitation is needed based on unstable vital signs or ongoing bleeding, switch to O negative blood.
- **D**—**D**isability determined by a brief neurologic exam—assessing mental status and size of pupils—and Glasgow Coma Scale (GCS) score. A depressed GCS = patient cannot protect airway (see Figure 4-1).
- **E**—**E**xposure/Environmental control: Completely undress the patient to assess for injury, but avoid hypothermia.

Eye Opening (E)	Verbal Response (V)	Motor Response (M)
4 Spontaneous	**5** Oriented	**6** Obeys commands
3 Responds to voice	**4** Confused speech	**5** Localizes pain
2 Responds to pain	**3** Inappropriate speech	**4** Withdraws to pain
1 No response	**2** Incomprehensible	**3** Abnormal flexion
	1 No response	**2** Abnormal extension
		1 No response

FIGURE 4-1. Glasgow Coma Scale. Best response of E + V + M = 15, ≤ 8 = comatose.

THE 2° SURVEY

Consists of total patient evaluation and is the time to order appropriate lab tests and radiographs based on the mechanism of injury, past medical history, and physical exam findings.

- **Conduct a focused PE:**
  - **Head and skull:** Inspect for trauma, pupils, and loss of consciousness. Look for ecchymosis around the eyes (see Figure 4-2) and hemotympanum, which point to a basilar skull fracture. Inspect the ears and nose for cerebral spinal fluid (CSF) leakage. If a septal hematoma is present, it will need to be drained once the patient is stabilized. Assess for midface instability, ocular/orbital trauma, or intraoral injuries. Ecchymosis of the mastoid process (Battle sign) is a late sign of basilar skull fracture and is rarely found on initial presentation.
  - **Neck:** Look for trauma or a pulsatile/expanding hematoma; palpate for midline cervical spine tenderness, crepitus, and tracheal deformity.
  - **Chest:** Listen for equal bilateral breath sounds. (If absent/asymmetric or if there is crepitus on palpation of the chest, suspect pneumothorax. Listen for clear heart sounds (if muffled and accompanied by jugular venous distention [JVD], suspect cardiac tamponade). Inspect for irregular or paradoxical breathing patterns resulting from multiple rib fractures (ie, flail chest). A new diastolic murmur after trauma suggests aortic dissection.
  - **Abdomen:** Inspect the abdomen and flanks for signs of trauma, usually indicated by bruising. Palpate the pelvis for tenderness or instability. Do not compress the pelvis anteriorly/posteriorly; if the patient has an "open-book" fracture, doing so will make it significantly worse.
  - **Perineum/rectum/vagina:** Assess for trauma, including urethral bleeding (suggests urethral tear). Check for prostate position, rectal tone, and rectal blood. Check women for vaginal trauma and blood in the vaginal vault.
  - **Musculoskeletal system:** Look for evidence of trauma, including contusions, lacerations, and deformities. Inspect the extremities for tenderness, crepitus, abnormal range of motion, and sensation. An externally rotated, shortened leg suggests hip fracture.
  - **Back, axilla, perineum:** Look for hidden injuries. Roll the patient! Don't miss the gunshot wound to the back because you were worried about the one on the front.
- **Assess and reassess:** Traumatic injuries can dynamically change.
- Obtain an **AMPLE** history: Inquire about **A**llergies, **M**edications, **P**ast medical history, **L**ast oral intake, **E**vents/**E**nvironmental factors related to the injury. If the patient can speak, ask about other symptoms that may not be obvious on exam. Obtain as much information as possible from EMTs/paramedics about the circumstances of the trauma.
- **Imaging:**
  - **Head and skull:** Obtain a CT of the head and face if there is evidence of trauma. Maintain a low threshold for scanning intoxicated patients, elderly patients, and those on blood thinners.
  - **Neck:** Maintain in-line immobilization and protection with a hard cervical collar. Obtain a cervical spine CT if a fracture cannot be cleared clinically by National Emergency X-Radiography Utilization Study (NEXUS) criteria.

FIGURE 4-2. Raccoon eyes. Bilateral periorbital ecchymosis, which is suggestive of basilar skull fracture. (Reproduced from Bouchaouch A et al. *Pan Afr Med J.* 2015;21:155.)

KEY FACT

Cushing triad indicates ↑ intracranial pressure, as from a closed-head injury. Occurs in a stepwise fashion: Systolic hypertension ↑ cerebral perfusion pressure resulting in reflex bradycardia followed by irregular respirations (Cheyne-Stokes)—a late sign indicative of herniation.

KEY FACT

Beck triad (JVD, muffled heart tones, and hypotension) indicates cardiac tamponade. Pulsus paradoxus is rarely assessed in the trauma setting (low sensitivity, time-consuming). Bedside echocardiography can help to diagnose quickly whether there is right ventricular collapse.

KEY FACT

The spleen is the most commonly injured solid organ in blunt abdominal trauma…and spleens bleed!

KEY FACT

Must meet all NEXUS criteria to not need imaging: No midline cervical spine tenderness, No focal neurologic deficit, Normal alertness, No intoxication, No painful distracting injury.

KEY FACT

A ⊖ FAST does not rule out intra-abdominal injury. It is a point-of-care screening tool for blood in the abdomen or pericardial fluid.

- **Chest:** Rapidly assess for pneumothorax with ultrasound. Obtain a CXR in all patients with significant trauma. Penetrating thoracic wounds or clinical concern for major intrathoracic trauma often requires a chest CT angiography.
- **Abdomen:** Obtain a pelvic x-ray; do a FAST scan, and/or an abdominal CT if indicated. Diagnostic peritoneal lavage is never done.
- **Urinary system:** If there is blood at the urethral meatus or a "high-riding" prostate, consult urology for a urethrogram. Do not insert a Foley.
- **Musculoskeletal system:** Obtain an arteriogram if vascular injury is suspected (eg, pulsating or expanding hematoma, distal perfusion deficit). Obtain radiographs as needed for extremity injuries. Knee dislocations (not patellar dislocations) require a CT angiogram to rule out popliteal artery injury.

Management of Emergent Procedures

You should be familiar with the indications for a variety of emergent procedures.

- **Intubation:** Airway failure, respiratory failure, depressed GCS, or flail chest (serial rib fractures in at least two places create a paradoxically moving chest wall) will likely require intubation to assist with breathing.
- **Cricothyroidotomy:** Can't ventilate and can't intubate? It's time to get out the scalpel.
- **Needle thoracostomy:** Only for tension pneumothorax and only a temporizing step prior to chest tube insertion. Inserting a chest tube takes several minutes. A 14-gauge needle to the second intercostal space midclavicular line takes seconds.
- **Tube thoracostomy** (aka chest tube): The treatment for pneumothorax and hemothorax.
- **Pericardiocentesis:** Perform if ultrasound shows a pericardial effusion with tamponade physiology.
- **Emergent thoracotomy:** For patients in extremis with suspected penetrating injury to the heart or disruption of major vessels (aorta, pulmonary artery).

Shock

A major complication of both medical and surgical emergencies. Rapid clinical assessment of circulatory status includes pulse, skin color, and level of consciousness. The evolution of the symptoms of shock is shown in Figure 4-3.

- Low BP does not in itself represent shock. Shock is a physiologic O_2 supply/demand mismatch. ↓ Tissue perfusion leads to cell hypoxia with subsequent dysfunction and eventual tissue death. Consequently, liver function tests (LFTs), creatinine, and troponin may be ↑ in severe shock. Lactic acid is a useful marker for tissue hypoperfusion or tissue death.
- Classically, shock has been divided into four types by physiologic response: hypovolemic, cardiogenic, distributive, and obstructive. Distributive shock is further subdivided into septic, anaphylactic, and neurogenic shock. These types are reviewed in Table 4-1.

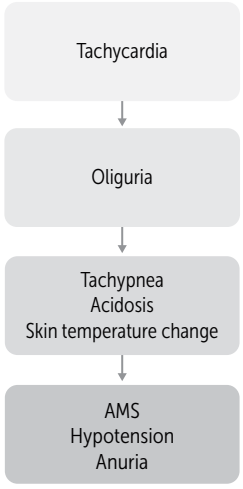


FIGURE 4-3. Evolution of shock.
(Reproduced from USMLE-Rx.com.)

TABLE 4-1. Hemodynamic Characteristics of Shock

Type	Major Causes	Preload	Cardiac Output	Afterload	Treatment
Hypovolemic	Trauma, blood loss, burns, dehydration	↓	↓	↑	IV fluids: Crystalloid/blood
Cardiogenic	MI, heart failure, arrhythmia, structural heart disease (eg, severe mitral regurgitation, ventricular septal defect)	↑	↓	↑	Treat the cause and give vasopressors (dopamine; norepinephrine or dobutamine if necessary)
Distributive	Septic: Bacteremia Anaphylactic: Allergic reaction Neurogenic: Spinal cord trauma (autonomic dysfunction)	↓	↑	↓	Septic shock: fluids, antibiotics, +/− vasopressors Anaphylactic shock, diphenhydramine and steroids; epinephrine if severe
Obstructive	Tamponade, tension pneumothorax, pulmonary embolism (PE)	↓ or ↑	↓	↑	Tamponade: Pericardiocentesis PE: Fluids and thrombolytics

Treatment

- Correct the underlying cause. A good first step is to administer O_2 and IV fluids (use caution in cardiogenic shock). Urine output and lactate are surrogate markers to guide the clinician's treatment approach.
- Keep in mind that shock is a symptom of a disease process, not the disease itself.

KEY FACT

With increasing blood loss, a patient's mental status progresses from anxiety to agitation to confusion and then to lethargy/unconsciousness.

Orthopedic Injuries

Patients present to the ED with a variety of orthopedic complaints, a detailed discussion of which is beyond the scope of this book. This section provides a high-yield summary of common and dangerous conditions, their diagnostic workup, and their initial management. In general, any compromise of blood flow or nerve function due to fracture/dislocation is an indication for an emergent reduction.

ANKLE INJURIES

- Traumatic ankle injuries are among the most common orthopedic complaints encountered in the ED. The spectrum of injury ranges from sprains (damage to a ligament) to significant fracture requiring operative intervention.
- In general, the Ottawa ankle rules (see Figure 4-4) guide the clinician in determining which patients need radiographic imaging.
- If there is concern for syndesmotic disruption between the tibia and fibula, rupture of the deltoid ligament, or ankle instability due to fractures, stress views of the ankle should also be added (x-ray in supination/external rotation).

KNEE INJURIES

- Knee pain is another common reason patients present to the ED. Several exam maneuvers should be performed to assess for certain injuries.

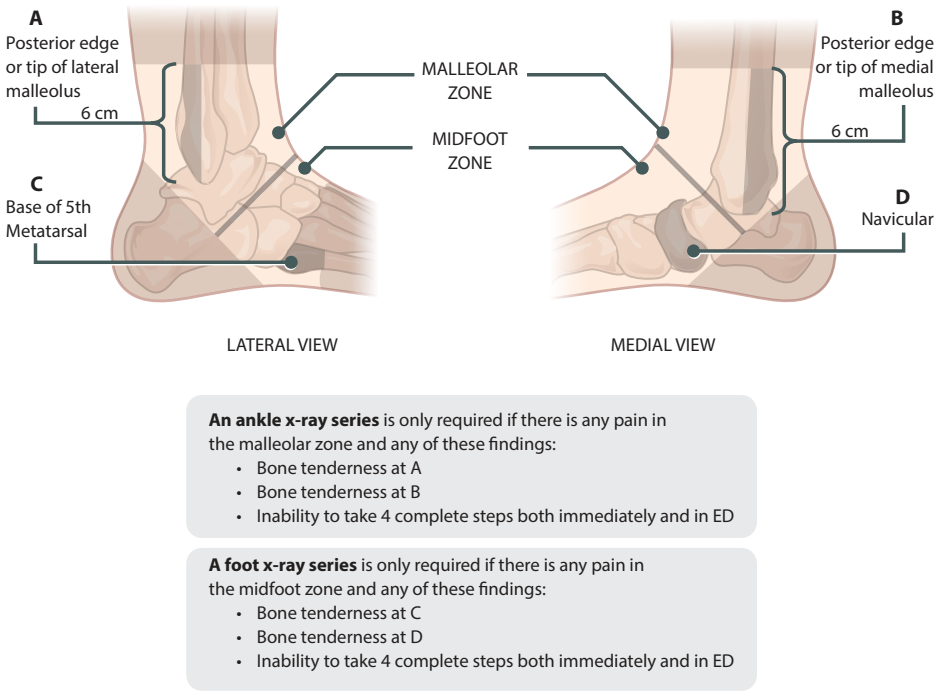


FIGURE 4-4. Ottawa ankle rules. (Reproduced with permission from USMLE-Rx.com.)

- A locking sensation on passive range of motion or pain with axial loading may be a sign of meniscal injury.
- Active range of motion not resulting in full extension or inability to lift against resistance can indicate quadriceps or patellar tendon rupture.
- The Lachman test and posterior drawer test assess anterior cruciate ligament and posterior cruciate ligament integrity respectively.
- Varus/valgus stress assesses the integrity of the medial/lateral collateral ligaments.

- Knee dislocation in obese patients may occur after only minor trauma and may self-reduce before presentation to the ED.

HIP INJURIES

- The differential for hip pain is highly dependent on the age of the patient.
  - Children and adolescents (particularly if they are obese) are at risk for a slipped capital femoral epiphysis (see Figure 4-5) or Legg-Calvé-Perthes disease (avascular necrosis of the femoral head; typically affects children 4–8 years of age). If the hip pain was preceded by a recent URI, the patient may be suffering from toxic synovitis. Keep in mind that the presenting complaint for hip issues in children may be knee pain.
  - Older patients are at high risk for "hip fractures" (technically a proximal femur fracture) 2° to osteopenia. Classically, the affected limb is shortened and externally rotated.
- Other causes of hip pain include osteoarthritis and trochanteric bursitis. In addition, patients of all ages are at risk for hip dislocation.
  - A dislocation typically occurs when a tremendous amount of force is thrust upon the hip joint (eg, when a flexed knee hits a dashboard in a motor vehicle accident).

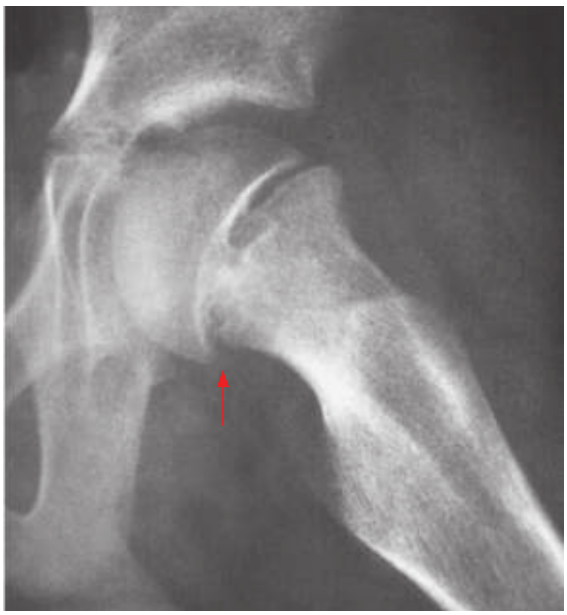


FIGURE 4-5. Slipped capital femoral epiphysis. Note the appearance of "ice cream about to fall off the cone" (*arrow*). (Reproduced with permission from Chen MY et al. *Basic Radiology,* 2nd ed. New York: McGraw-Hill, 2011, Fig. 6-1B.)

- The vascular supply to the femoral head may be strained or severed in a hip dislocation placing the patient at risk of developing avascular necrosis of the femoral head as a delayed complication. Expeditious reduction is indicated to minimize the risk to the artery.

- All joints in the body are at risk for septic arthritis, which involves direct inoculation of the joint or hematogenous spread of pathogens.
  - Patients may be febrile with exquisite tenderness on ranging the joint.
  - Labs show an ↑ WBC count, C-reactive protein, and erythrocyte sedimentation rate.
  - Joint aspirate with a WBC count > 100,000/mm^3 is compatible with septic arthritis. A synovial fluid aspirate lactate > 10 mmol/L is very sensitive for septic arthritis.
  - Treatment consists of IV antibiotics and joint washout by an orthopedic surgeon.

ARM INJURIES

Shoulder Dislocation

Most commonly anterior, but posterior dislocations occur with seizures and electrical injuries causing violent muscle contractions. Presents with pain and obvious asymmetry to the affected shoulder with inability to lift the arm.

- **Dx:** Clinical but confirmed with unilateral shoulder x-ray—to rule out fracture, subluxation, acromioclavicular joint separation.
- **Tx:** Shoulder reduction under conscious sedation after which pain is usually resolved.

Forearm Fractures

- Classified by the distribution of the fracture lines in the radius and ulna and are a favorite USMLE test question.
  - **Monteggia fracture:** An ulnar shaft fracture with a radial head dislocation.

- **Galeazzi fracture:** A distal 1/3 radius fracture with a distal radioulnar dislocation.
- **Colles fracture:** A distal radius fracture with dorsal displacement after a **F**all **O**nto **O**ut**S**tretched **H**and (**FOOSH**) injury. Most common in elderly osteopenic women.

- **Tx:** Includes pain control, reduction of the fracture, splinting, and orthopedic follow-up.

ORTHOPEDIC PEARLS

- Tenderness over the scaphoid bone requires splinting even if initial x-rays are ⊖ to help prevent future complication of avascular necrosis. A scaphoid fracture may take several days to become visible on x-rays.
- Compartment syndrome typically features good pulses and sensation until it reaches an advanced state. Excruciating pain with passive movement is the earliest clinical sign.
- Ankle injuries may lead to proximal fibula injury (Maisonneuve fracture) and are at higher risk for compartment syndrome.
- Shoulder dislocations may lead to axillary nerve injury.
- Supracondylar fractures in children may lead to radial nerve injury.
- Clavicle fractures are typically treated conservatively with a sling.
- The first rib, proximal clavicle, sternum, scapula, and femur require significant force to fracture. Look for other injuries.

MNEMONIC

6 P's of compartment syndrome—

Pain
Paresthesia
Pulselessness
Pallor
Paralysis
Poikilothermia

KEY FACT

After a premature ventricular contraction (PVC), the sinus rhythm resumes after repolarization and a compensatory pause. After a premature atrial contraction (PAC), however, the sinus rhythm resets as if the PAC were a normal beat.

KEY FACT

"Geminy" refers to the sequence of normal beats with PVCs. Bigeminy is a pattern of one normal beat followed by a PVC; trigeminy is a pattern with two normal beats followed by a PVC.

Common Dysrhythmias

Tables 4-2 and 4-3 illustrate a variety of important dysrhythmias. In general, these can be subdivided into narrow-complex arrhythmias originating in the atria and wide-complex arrhythmias originating in the ventricles or secondary to conduction pathway abnormalities. These can further be subdivided into "tachy" and "brady" arrhythmias.

Advanced Cardiac Life Support

Provides a framework for resuscitating a critically ill medical patient. Circulation is addressed before airway and breathing, with cardiopulmonary resuscitation (CPR) being performed before attempting intubation. Epinephrine remains an advanced cardiac life support (ACLS) drug, as it ↑ the rate of return of spontaneous circulation but has been found to have no effect on survival to discharge.

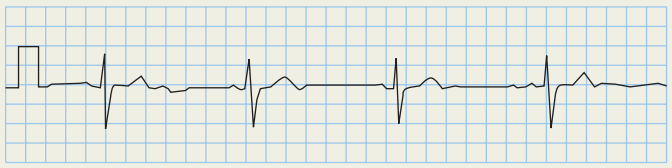
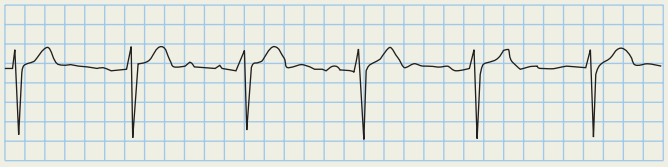
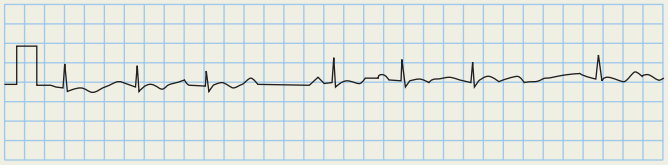
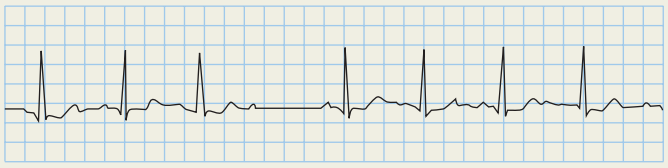
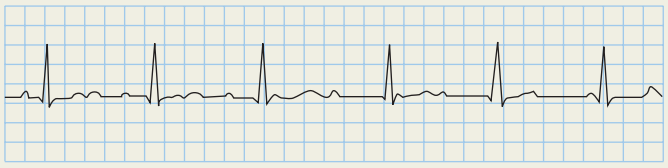
UNSTABLE BRADYCARDIA

History/PE

Symptomatic bradycardia, including hypotension, chest pain, altered mental status, or other signs of shock, is usually due to one of the following:

- High vagal tone (cholinergic toxicity, inferior MI, digoxin toxicity).
- Conduction abnormalities (sick sinus syndrome, AV-nodal blocks, diseases such as Lyme carditis or multiple myeloma).
- Medication effects (β-blockers, calcium channel blockers).

TABLE 4-2. Common Bradyarrhythmias

Bradyarrhythmia	Example
Sinus bradycardia HR < 60	
1° AV block PR interval > 120 ms	
2° "Mobitz I" (Wenckebach) Progressive PR interval until dropped QRS	
2° "Mobitz II" Constant PR interval until randomly dropped QRS	
3° AV block Complete P-QRS dissociation	

Treatment

The underlying cause influences the efficacy of the treatment approach:

- High vagal tone responds to atropine.
- Conduction abnormalities often require a manual or chemical override of the conduction system, including cardioactive drugs and pacing.
  - **Transcutaneous pacing:** Place pads on the chest/back, set to the desired rate, and ↑ amperage until you have mechanical capture. If possible, sedate.
  - **Transvenous pacing:** Place a cordis central line and float a pacing wire to the heart. This takes about 15 minutes but provides the most definitive management until a permanent pacemaker can be placed.
  - **Chemically:** Dopamine or epinephrine.
- Unfortunately, conditions such as β-blocker overdose lead to ⊖ chronotropy and ⊖ inotropy. In many cases, even pacing remains ineffective.

MNEMONIC

ACLS Guidelines—

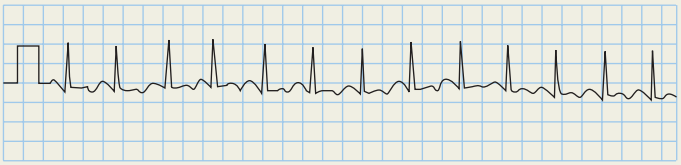
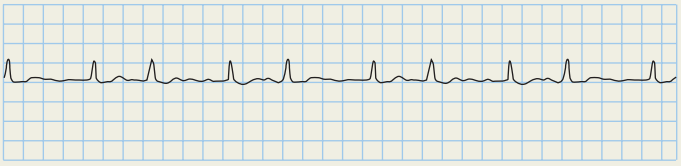
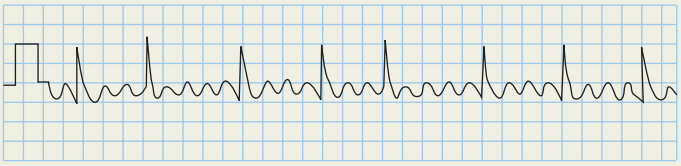
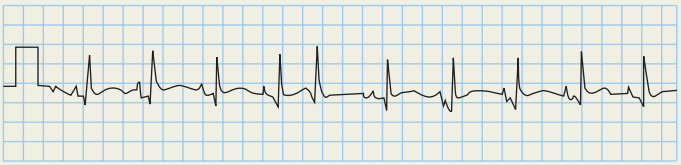
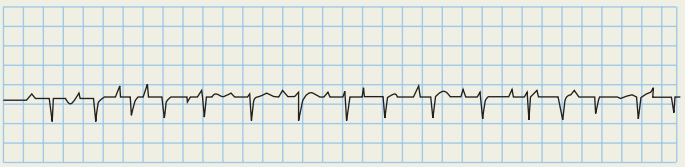
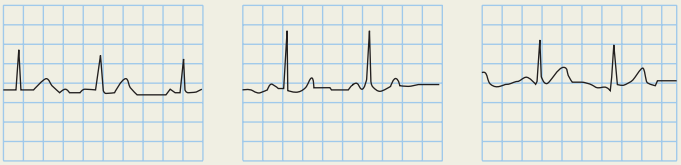
CAB

Circulation, **A**irway, **B**reathing
Additional **DEF**
Drugs, **E**lectricity (shock), **F**luids

KEY FACT

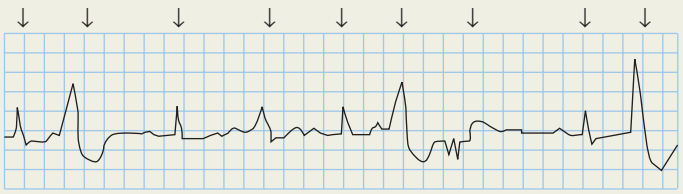
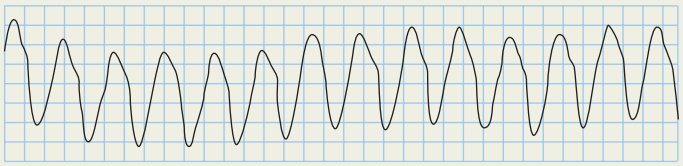
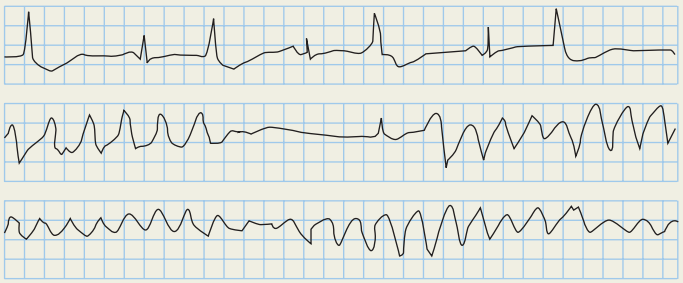
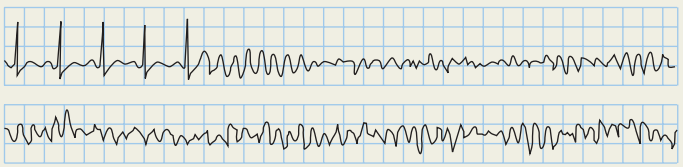
Transcutaneous pacing will lead to contraction of the chest wall and sternocleidomastoid muscles. This pulsation is easily mistaken for a carotid pulse. Check femoral pulses instead.

TABLE 4-3. Common Tachyarrhythmias

Tachyarrhythmia	Example
Supraventricular Tachyarrhythmias	
Sinus tachycardia Regular intervals; HR > 100	
Atrial fibrillation (AF) Irregularly irregular intervals; HR > 100	
Atrial flutter Circulating atrial reentrant activity with occasional conducted beats	
Premature atrial contraction Abnormally conducted atrial beat	
Multifocal atrial tachycardia Instead of just the SA node conducting beats, there are multiple ectopic atrial focuses conducting beats	
Wolff-Parkinson-White syndrome Slurred upstroke = delta wave Shortened PR interval	

(continues)

TABLE 4-3. Common Tachyarrhythmias *(continued)*

Tachyarrhythmia	Example
Ventricular Tachyarrhythmias	
Premature ventricular contraction (unifocal vs multifocal) Ectopic ventricular electrical depolarization; no conducted beat	
Ventricular tachycardia (VT) (monomorphic vs polymorphic) Pathologic recurrent ventricular depolarization	
Torsades de pointes (a type of VT that can lead to ventricular fibrillation [VF] as well)	
Ventricular fibrillation Pathologic electrical dysfunction from a ventricular focus	

CARDIAC ARREST

In the event of cardiac arrest, start CPR immediately using end-tidal CO_2 to monitor quality. As chest compressions are being performed, begin bag-valve-mask ventilation, rapidly obtain vascular access (or interosseous access), and attach defibrillator pads to the patient. At the first rhythm check, you will find one of four electrical patterns: VF, pulseless VT, asystole, or pulseless electrical activity (PEA).

- **Asystole or PEA:** CPR and epinephrine. No defibrillation, atropine, or pacing.
- **VF or pulseless VT:**
  - CPR with epinephrine q 3–5 minutes + defibrillation with 200 J (biphasic) or 360 J (monophasic) + antiarrhythmic agent (amiodarone 300 mg IV once followed by a 150-mg dose in 3–5 minutes if still in a shockable rhythm).
  - If torsades de pointes develops, give magnesium 1–2 g IV.
- Identify and treat the **H**s and **T**s:
  - Hypothermia → warm them up.

KEY FACT

Check a finger stick blood sugar as part of your vitals for any unstable patient—you might be missing easy-to-fix hypoglycemia.

- H+ (acidosis) → reverse acidosis.
- Hypo-/Hyperkalemia → either give or remove K^+.
- Hypoxia → 100% O_2; secure/establish airway.
- Hypovolemia → fluid replacement.
- Thrombosis (PE, MI) → thrombolytics.
- Tamponade → pericardiocentesis.
- Tension pneumothorax → needle decompression.
- Toxins → antidote (eg, hydroxocobalamin in cyanide toxicity).

TACHYCARDIA

Tachycardia is defined as a heart rate > 100 bpm. Sinus tachycardia has an underlying cause that must be addressed (eg, dehydration, fever, pain) and will not be reviewed here in detail. The treatment of sinus tachycardia with rate-limiting agents is likely harmful, as the heart rate is compensatory to an underlying process and the compensatory mechanism is removed. Tachydysrhythmias can result from:

- Self-sustained conduction pathways (eg, SVT).
- Multiple foci of automaticity (atrial flutter, AF).
- Ventricular focus (VT).

Treatment

- **Unstable tachycardia** (eg, shortness of breath, chest pain, hypotension, ischemic ECG changes): Requires immediate synchronized cardioversion.
- **Stable tachycardia:** Attempt vagal maneuvers first and then escalate therapy as follows:
  - **Narrow, regular complex** (eg, SVT): Adenosine.
  - **Narrow, irregular complex** (eg, AF): Rate control (metoprolol, diltiazem).
  - **Wide complex** (eg, VT): Amiodarone.
  - All of the above rhythms can be electrically cardioverted if medical therapy fails.
- **Special cases:**
  - Do not cardiovert stable AF that has been present for > 48 hours. Obtain a transesophageal echocardiogram first to assess for an atrial thrombus.
  - In torsades de pointes, give magnesium 1–2 g IV and provide either chemical or electrical overdrive pacing (may resolve with ↑ heart rate).

KEY FACT

Patients with stable tachycardia can be treated medically. Consider sedation and pain medications for any cardioversion.

MYOCARDIAL INFARCTION

Also known as heart attack, MI usually presents with a primary complaint of chest pain that may radiate to the arm, neck, or back and that is often accompanied by other symptoms, including shortness of breath, sweating, nausea and vomiting, palpitations, lightheadedness, and fatigue.

Diagnosis

- Patients often appear anxious and/or have an impending feeling of doom.
- ECG within 10 minutes of patient arrival to ED. The coronary artery involved produces a predictable pattern of electrical changes on an ECG (see the Cardiology chapter, Table 3-2, for a review of ECG changes with MI).
- Further confirmatory blood work includes troponin and less often creatine kinase–MB fraction.

Treatment

In the ED, treatment includes aspirin, oxygen, nitroglycerin, and analgesia. (Morphine was standard analgesic therapy but has recently become controversial in the literature.) Mainstay of therapy, however, is emergent revascularization of the offending occluded artery.

Toxicology

In general, there are several things you need to inquire about or obtain when treating a poisoned patient:

- Time and type of ingestion.
- Quantity and route of ingestion.
- Comorbidities.
- Vitals.
- ECG.
- Pupils, bowel sounds, skin exam, reflexes, and clonus.
- Respiratory/heart rate, mental status.

Also bear in mind that while patients on the USMLE are always truthful, "real" patients may intentionally provide you with false information out of concern for the legal implications of substance abuse or if they overdosed for intentional self-harm.

TOXIDROMES

Table 4-4 lists symptoms and signs associated with common toxin-induced syndromes ("toxidromes"). Table 4-5 outlines several hypothetical scenarios involving toxidromes. Some additional toxicology pearls are as follows:

- If a patient appears altered or intoxicated, don't forget to check a blood sugar first!
- Do not intubate patients with aspirin toxicity unless you absolutely must. Because the mechanical ventilator will never match these patients' high minute volume, they will become more acidotic and die.
- In all overdoses, send an acetaminophen and aspirin level.
- In smoke inhalation, consider carbon monoxide and cyanide toxicity.
- Serotonin syndrome kills (see Chapter 17).
- Neuroleptic malignant syndrome can look like serotonin syndrome but develops more slowly (> 24 hours) and features rigidity rather than clonus (see Chapter 17).
- Lithium toxicity may require dialysis.
- Digoxin toxicity may require antibody fragment administration (digoxin immune fab).
- Charcoal is useful only in ingestions that occurred < 60 minutes ago. Multidose activated charcoal can be given for "gut dialysis" (removal of toxins from the enterohepatic circulation).
- Whole bowel irrigation (similar to a colonoscopy prep) is indicated for "body packers" and for children with visible lead paint chips on x-ray, as well as for certain other ingestions.

KEY FACT

With a paucity of data to support their theoretical benefits, induced emesis and gastric lavage have fallen out of favor. Gastric lavage is rarely performed in practice today and induced emesis not at all.

KEY FACT

Body packers are professional drug smugglers with drug packages prepared to withstand the GI tract. Body stuffers swallow/stuff drug bags in a panic when they are confronted by police. Stuffers are at much greater risk of experiencing toxicity from bag rupture.

MNEMONIC

Indications for emergent hemodialysis—

AEIOU

Metabolic **A**cidosis that cannot be corrected with $NaHCO_3$
Severe **E**lectrolyte imbalances (eg, hyperkalemia)
Toxic **I**ngestions (eg, lithium or aspirin)
Fluid **O**verload that is resistant to treatment with diuretics
Uremia (eg, uremic encephalopathy, uremic serositis, uremic pericarditis)

Q

A 73-year-old woman who has had palpitations for 4 days presents with AF with rapid ventricular response. Other than mild shortness of breath, she is hemodynamically stable. What is the best management approach?

TABLE 4-4. Classic Toxidromes

Toxidrome	Symptoms/Signs	Examples
Cholinergic	DUMBELS: **D**iarrhea, **U**rination, **M**iosis, (**B**ronchorrhea **B**ronchospasm **B**radycardia) **E**mesis, **L**acrimation, **S**alivation	Muscarine-containing mushrooms, organophosphates, pilocarpine, pyridostigmine
Anticholinergic	"Hot as a hare, red as a beet, dry as a bone, mad as a hatter, blind as a bat": fever, skin flushing, dry mucous membranes, psychosis, mydriasis; also tachycardia and urinary retention	Antihistamines, antipsychotics, atropine, Jimson weed, scopolamine, tricyclic antidepressants
Opioid	Triad of coma, respiratory depression, and miosis; also bradycardia, hypothermia, and diminished bowel sounds	Heroin, morphine, oxycodone
Sedative-hypnotic	CNS depression, respiratory depression, and coma	Alcohol, barbiturates, benzodiazepines
Sympathomimetic	Disorientation, panic, seizures, hypertension, tachycardia, and tachypnea	Amphetamines, cocaine, PCP
Extrapyramidal	Parkinsonian symptoms: tremor, torticollis, trismus, rigidity, oculogyric crisis, opisthotonos, dysphonia, and dysphagia	Haloperidol, metoclopramide, phenothiazines

Abdominal Pain

Pain is poorly localized by patients, and many conditions have symptoms that substantially overlap. Approximately 50% of patients presenting to the ED will not receive a diagnosis for their discomfort. Common abdominal conditions are discussed in Chapter 7 of this book. What follows is a discussion of conditions that require emergent treatment.

EPIGASTRIC PAIN

Discomfort in this region may be due to intra-abdominal or intrathoracic processes. Broaden the differential appropriately in elderly persons, in women, and in patients with diabetes.

Differential

- **Intra-abdominal processes:** Pancreatitis (alcohol, gallstones), gastritis/peptic ulcer disease (PUD) (heavy use of ethanol/NSAIDs).
- **Intrathoracic processes:** Lower lobe pneumonia or an inferior MI.

A

Rate control. Paroxysmal AF may also lead to atrial clot formation. Cardioversion should be attempted only if a mural thrombus has been ruled out.

TABLE 4-5. Scenarios Involving Toxidromes

Vignette	Toxidrome	Treatment
A 25-year-old man is pushed out of the back seat of a car in front of the ED before the car takes off speeding. The triage nurse finds the patient apneic and cyanotic with a thready pulse. He is tachycardic and hypoxic, and his pupils are constricted and minimally reactive. The patient has multiple scars on his arms and neck. Bag-valve-mask ventilations are provided.	This patient has likely overdosed on an opiate such as oxycodone or heroin and is suffering from opioid toxidrome. Given the scars on his arms (track marks) and neck (from "jugging"), he likely injected the opiate.	Administer naloxone Long-acting opiates (eg, methadone) need repeat doses and hence will likely require admission Pulmonary edema may occur in some cases
A 17-year-old girl is brought to the ED by her parents for acting erratically. She is unable to give a history and is speaking nonsensically while picking at her clothing. Her pupils are 6 mm and reactive, and no nystagmus is present. She has no axillary moisture. Palpation of her abdomen reveals a suprapubic mass. Her reflexes are normal. She is tachycardic and has a temperature of 38.1°C (100.4°F).	This patient appears to have ingested an anticholinergic, as evidenced by her dry skin, mydriasis, ↑ temperature, mental status changes, and urinary retention (distended bladder). The repetitive picking behavior is typical. ECG shows a QRS of 108 msec with a sloped R′ in aVR.	Most patients require only observation and benzodiazepines for symptom control; improvement with physostigmine confirms the diagnosis Watch for QRS widening and subsequent seizures or arrhythmia; administer sodium bicarbonate to narrow the QRS as antihistamines have sodium channel-blocking properties similar to tricyclic antidepressants
A 42-year-old man is brought in for erratic behavior after partying all night. He is diaphoretic and must be restrained by security. A limited PE reveals mydriasis but no other significant abnormalities. After administration of lorazepam 2 mg IM, the patient becomes more cooperative and states that he has chest pain. An ECG shows sinus tachycardia with concerning ST-segment changes in the lateral leads.	The sympathomimetic toxidrome can be triggered by drugs like PCP, methamphetamine, or, as in this case, cocaine. Chemical restraints are always preferred over physical ones, as physically restrained patients will remain agitated, fight the restraints, and develop hyperthermia and rhabdomyolysis.	Treat cocaine-associated chest pain as you would regular chest pain; 6% of cocaine chest pain cases will result in MI The use of β-blockers to treat cocaine overdose remains controversial Benzodiazepines are the mainstay of treatment in light of concern over unopposed α-adrenergic stimulation
A 40-year-old man finds his father pulseless in the garden shed with a letter by his side 2 days after his mother's death. The son's attempts at mouth-to-mouth resuscitation and chest compressions prove futile. Shortly thereafter, the son loses control of his bowel and bladder, develops rhinorrhea, and coughs up copious amounts of sputum. His HR is found to be 38 bpm.	Exposure to cholinergic toxins results in **SLUDGE** (**S**alivation, **L**acrimation, **U**rination, **D**iarrhea, **G**I distress, and **E**mesis). Exposure can be intentional but may also be accidental (as in carbamate [insecticide] exposure).	The antidote is atropine In organophosphate poisoning, early administration of pralidoxime prevents aging of the chemical bond that inhibits cholinesterase
Three young men are stopped near the Canadian border for driving 63 mph in a 65-mph zone. Before a search of the car can be conducted, one of the occupants eats an entire bag of their contraband. Shortly thereafter, he tells his friends that he is "freaking out." While under arrest, the patient finds that parts of the police cruiser taste like his favorite fruit.	The patient is experiencing a hallucinogenic toxidrome. A variety of substances can induce this state, most commonly LSD and marijuana.	Although hemodynamic instability can occur with high drug doses, most patients just need control of agitation if present; give benzodiazepines as needed
A 5-year-old boy is brought to the ED obtunded and tachypneic. His younger brother reports that the boy had been drinking "candy juice" that he found in the garage. A blood glucose level is normal.	The sedative-hypnotic toxidrome is frequently seen in the ED, often in the form of benzodiazepine abuse or alcohol intoxication—or, in this case, ethylene glycol from antifreeze.	Patients with sedative-hypnotic toxidrome often require only supportive care; however, in the setting of ethylene glycol ingestion, the patient may need fomepizole or ethanol and potentially dialysis

Treatment

- **First step in managing both gastritis and peptic ulcers:** Withdrawal/removal of the offending agent (alcohol, NSAIDs). Both conditions are then treated conservatively with pain control and acid-lowering medications such as H_2 blockers and proton pump inhibitors.
- Pancreatitis requires analgesia and IV fluids. Patients can become severely dehydrated by pancreatic sequestration of fluids caused by its massive inflammation. As in gastritis and PUD, removal of the offending agent is necessary. The Ranson criteria allow the clinician to estimate the mortality of pancreatitis and help determine disposition.

Complications

In PUD, there is a risk of erosion into a gastric vessel, which can be life-threatening, or through the gastric wall, causing perforation.

- Gastric hemorrhage is managed with upper endoscopy and clipping of the offending vessel.
- Gastric perforation requires operative management.

RLQ PAIN

Can indicate a variety of conditions, especially in young women. The history often does not suffice to establish a diagnosis. The differential includes appendicitis, ovarian torsion, ruptured ovarian cyst, ectopic pregnancy, tubo-ovarian abscess, pelvic inflammatory disease (PID), renal calculus at the ureterovesical junction.

Appendicitis

- Has a bimodal distribution, affecting teenagers/young adults and those ~60 years of age. Caused by a fecalith or occlusion of the appendix by swollen lymphoid tissue, leading to bacterial overgrowth. Left untreated, the infection may lead to rupture of the appendix.
- **Hx/PE:** Classic signs and symptoms include pain in the periumbilical area that migrates to the RLQ, anorexia, and pain with jumping.
- **Dx:** CT of the abdomen with IV contrast may quickly rule the diagnosis in or out. In children, ultrasound is preferred. MRI is a reasonable diagnostic modality in pregnancy. The Rovsing sign and the obturator sign are not sensitive or specific enough to confirm or rule out the diagnosis.
- **Tx:** Antibiotics for GI flora and immediate surgical consultation.

LLQ PAIN

Diverticulitis

- Inflammation and microperforation of the diverticula. One of the most common causes of left lower quadrant (LLQ) pain.
- **Hx/PE:** Presents with fever, chills, nausea, vomiting, and abdominal pain of gradual onset. Patients may have a history of long-standing constipation prior to the pain but often complain of diarrhea while in pain. Exam ⊕ for LLQ tenderness with local peritoneal signs and often rebound.
- **DDx:** Ulcerative colitis, Crohn disease, perforating colon cancer, ectopic pregnancy, PID, ovarian torsion, ovarian cyst rupture.
- **Dx:** Clinical diagnosis. CT scan is also used for diagnosis and aids in the identification of complications such as abscess and perforation (see Figure 4-6). Do not perform colonoscopy on these patients while infection is

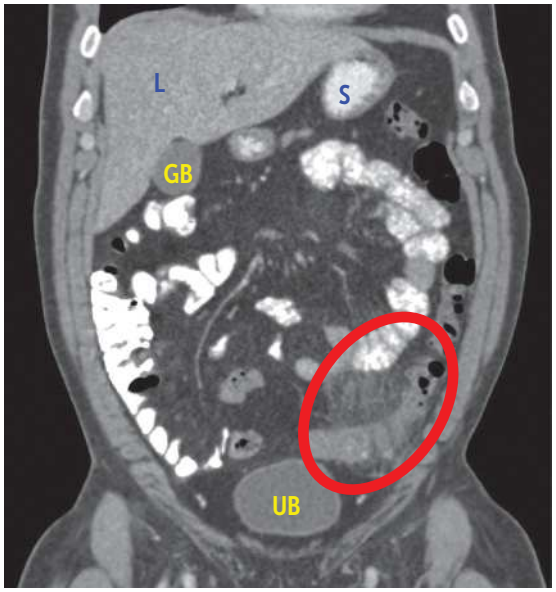


FIGURE 4-6. Acute diverticulitis. Coronal reconstruction from a contrast-enhanced CT demonstrates sigmoid diverticula with perisigmoid inflammatory "fat stranding." The area of abnormality is circled in red. (*L*, liver; *S*, stomach; *GB*, gallbladder; *UB*, urinary bladder.)
(Reproduced with permission from USMLE-Rx.com.)

present, as they are at high risk for perforation. Obtain a CBC and blood cultures.
- **Tx:** Bowel rest, antimicrobial coverage of gram ⊖ and anaerobic organisms (eg, ciprofloxacin and metronidazole), and pain control. If perforation or abscess, surgical consult and admission.
- **Complications:** Abscess, obstruction, sepsis, death.

KEY FACT

If diverticulitis is suspected, do not perform lower endoscopy until the acute process resolves, as patients are at high risk for perforation. Following resolution of the infection, colonoscopy is necessary to rule out malignancy.

Abdominal Aortic Aneurysm

Risk factors include age > 60, atherosclerosis, and smoking. Underlying mechanisms are as follows:

- Weakness in the connective tissue of the tunica muscularis leads to bulging out of the vessel, typically inferior to the origin for the renal arteries.
- Wall stress is directly correlated to diameter (Laplace's law); once a critical threshold is passed, the aneurysm will rupture. Rupture occurs into the retroperitoneal space, which can hold enough blood volume to cause the patient to exsanguinate within minutes.

History/PE

- Presents with back pain/abdominal pain and syncope.
- Leg pain/paresthesias 2° to occlusion of the artery of Adamkiewicz leads to spinal cord infarcts.

Diagnosis

- Pulsatile abdominal mass may be palpated or abdominal bruit may be heard.
- Ultrasound can assess for the presence of abdominal aortic aneurysm (AAA) but not rupture.
- CT angiography of the abdomen/pelvis can detect rupture.

Treatment

- A ruptured AAA requires immediate resuscitation and emergent operative repair.
- Several large-bore (14- to 16-gauge) IVs should be inserted for resuscitation with blood products.
- Reverse coagulopathy.
- Do not manipulate BP with pressors (more pressure = more bleeding).

Sexual Assault

Begin by diagnosing and treating the patient's physical and emotional injuries. Then collect legal evidence and document that evidence carefully. Your main concern should always be the well-being of the patient. Information should include the following:

- Ascertain any injuries sustained during the assault.
- Determine the risk of pregnancy. When was the last menstrual period? Any birth control?
- Find out where, when, and how the assault occurred. What happened during the assault? Determine the number of assailants; the use of force, weapons, objects, or restraints; which orifices were penetrated; and whether alcohol and/or drugs were involved.
- Determine what happened after the assault. Are there any specific symptoms or pains? Did the patient bathe, defecate, urinate, brush teeth, or change clothes? Has the patient had sexual intercourse in the last 72 hours?

Diagnosis

- Assess for pelvic trauma that may require immediate intervention.
- The collection of physical evidence (eg, debris, fingernail scrapings, dried secretions from the skin, pubic hairs) is often restricted to certified personnel.
- Medically indicated testing includes a pregnancy test.
- Nucleic acid amplification testing for gonorrhea and chlamydia; a wet mount and culture for trichomoniasis, bacterial vaginosis, and candidiasis; serology for syphilis; and hepatitis B virus (HBV)/HIV testing should be done later as they will not be positive early after exposure.

Treatment

- Treat traumatic injuries.
- Infection prevention: Gonorrhea and chlamydia prophylaxis. HIV prophylaxis in high-risk populations.
- Pregnancy prevention: Administer ethinyl estradiol/norgestrel or levonorgestrel. Offer counseling.

Animal and Insect Bites

KEY FACT

Tearing dog bites cause considerably more physical trauma, but puncture-like cat bites are more likely to become infected.

Animal bites are a common reason patients present to the ED. The management of bite wounds requires a fine balance between reducing the risk of infection and achieving cosmesis.

- Animal bites result in tissue destruction and inoculation of the wound with oral flora. Depending on the animal, the patient may be at risk for a variety of complications.
- Dog bites produce large, torn wounds (bite and then shake/pull).

- Dogs have relatively clean mouths, so wounds may be sutured unless they are on the hand.
- Cat bites cause deep penetrative wounds (high risk of anaerobic infection).
- The kicking action of a cat's hind legs may lead to inoculation with *Bartonella henselae*.

Treatment

- Antibiotic prophylaxis should be provided even if the wound is not repaired. Amoxicillin/clavulanate or a similar agent that covers oral flora is preferred.
- Wounds should be irrigated at high pressure with copious amounts of fluid. A wound may be loosely approximated rather than sutured tightly to prevent further wound contamination without creating an anaerobic environment.
- Centers for Disease Control and Prevention recommendations on the treatment of rabies are as follows:
  - If the animal can be observed and does not display symptoms of rabies after 10 days, no vaccine is necessary.
  - If the patient slept in the same room as a bat, vaccinate.
  - There have been no documented cases of rabies transmitted by a rodent (including squirrels).
  - Don't forget to address wound care and tetanus status.
  - Give human rabies immunoglobin to all patients who were not previously immunized. If possible, inject half around the bite and half IM elsewhere.
  - Vaccine should be administered in four doses on days 0, 3, 7, and 14.
  - Those previously vaccinated need only two vaccine doses.
  - Immunocompromised patients still get the fifth dose of the vaccine (as in the previous recommendations) at day 28.
- Table 4-6 summarizes bite types (including human), associated infecting organisms, and appropriate treatment.

KEY FACT

Scorpion stings are treated with antivenom and benzodiazepines to control agitation and involuntary muscle movements. Monitor for hypertension, arrhythmias, and pancreatitis.

KEY FACT

For monkey bites, add postexposure prophylactic valacyclovir or acyclovir x 14 days. Herpes B virus from monkeys has an 80% fatality rate.

Tetanus

Trismus (ie, lockjaw), glottic spasm, and convulsive spasms caused by *Clostridium tetani*. High-risk patients include older adults (due to inadequate immunization), IV drug users, and skin ulcer patients.

- The tetanus toxin affects modulatory motor neurons that normally secrete gamma-aminobutyric acid (GABA) to suppress motor impulses. As GABA levels in the synaptic cleft decline, even small, accidental impulses will produce muscle contractions. This results in a generalized tonic state in which all striated muscles begin to contract.
- Because the posterior muscle groups of the torso are stronger than the anterior groups, patients in the most advanced disease states are often arched with contracted arms (biceps stronger than triceps). This is called opisthotonos.
- Although the heart muscle is not affected, tetanus may lead to respiratory arrest, hyperthermia and rhabdomyolysis, and subsequent death.

KEY FACT

Although "rusty nails" are associated with tetanus, any anaerobic wound with soil contamination can lead to the disease.

Treatment

- Benzodiazepines to control muscle spasms; neuromuscular blockade if needed to control the airway.
- Metronidazole is the antibiotic of choice.
- Administer tetanus immune globulin (TIG) and/or adsorbed tetanus and diphtheria toxoid vaccine as indicated in Table 4-7.

Q 1

A 25-year-old man becomes involved in a bar fight and sustains a "fight bite" (closed-fist injury) to his hand. The wound culture grows gram ⊖ rods. What is the most likely pathogen, and how should it be treated?

Q 2

A 37-year-old known IV drug user is brought to the ED with trismus and facial grimacing 30 minutes after using heroin. What is the most likely diagnosis?

TABLE 4-6. Bite Types, Infecting Organisms, and Treatment

Bite Type	Likely Organisms/Toxins	Treatment
Dog	α-hemolytic streptococci, *S aureus, Pasteurella multocida,* and *anaerobes*	Amoxicillin/clavulanate or a first-generation cephalosporin +/− tetanus and rabies prophylaxis
Cat	*P multocida* (high rate of infection), anaerobes	Amoxicillin/clavulanate +/− tetanus prophylaxis
Human	Polymicrobial. Viridans streptococci, *Eikenella corrodens*	Second- or third-generation cephalosporins, dicloxacillin + penicillin, amoxicillin/clavulanate or clarithromycin +/− tetanus prophylaxis, HBV vaccine, hepatitis B immune globulin, and postexposure human HIV prophylaxis
Rodent	*Streptobacillus moniliformis, P multocida, Leptospira* spp	Penicillin VK or doxycycline
Bat	Rabies and other viruses	Vaccination against rabies
Snake	*Pseudomonas aeruginosa, Proteus* spp, *Bacteroides fragilis, Clostridium* spp, venom	Antivenom as appropriate. Venomous snakes (eg, coral snake, pit viper, rattlesnake) do not require prophylactic antibiotics; ampicillin/sulbactam (or, alternatively, a fluoroquinolone or clindamycin + TMP-SMX) is given to combat the snake's oral flora if infection develops Monitor for rhabdomyolysis, neurologic impairment, coagulopathy, and serum sickness
Spider	Venom (can cause tissue necrosis and/or rigid paralysis, depending on species)	Antivenom as appropriate; otherwise supportive care (analgesics, antihistamines, wound irrigation/debridement) Tetanus prophylaxis

Anaphylaxis

Patients who are presensitized to certain antigens may develop a significant type I hypersensitivity (allergic) reaction on exposure. True anaphylaxis is associated with significant mortality, usually from airway occlusion rather than from hypotension (which is easily treated with IV fluids and pressors).

1 A

Eikenella corrodens, the most likely pathogen, is common in human bite infections that are sustained in closed-fist injuries. Treat with amoxicillin/clavulanate.

2 A

Strychnine poisoning, which can look just like tetanus. When heroin is "cut," drug dealers often use white, bitter chemicals so that the drug still tastes pure. Strychnine antagonizes glycine (an inhibitory neurotransmitter) in the spinal cord. Give benzodiazepines.

TABLE 4-7. Tetanus Prophylaxis Schedule

History of Adsorbed Tetanus Toxoid (Doses)	Non-Tetanus-Prone Wounds	Tetanus-Prone Wounds[a]	
	Td	Td	TIG
Unknown or < 3 doses	√	√	√
Three doses:			
Last dose ≥ 5 years		√	
Last dose ≥ 10 years	√	√	

[a]Tetanus-prone wounds are those that are present for > 6 hours; are nonlinear; are > 1 cm deep; and show signs of infection, devitalized tissue, and contamination

- IgE-mediated cytokine release in response to an antigen triggers a variety of reactions. The predominant cytokine is IL-4 causing a release of histamine. Histamine can also be released independent of IgE by direct mast cell stimulation (eg, morphine, IV contrast dye).
- In addition to vasodilation, the capillary bed becomes leaky and significant edema ensues. Edema may occur superficially (facial swelling), in the gut (leading to nausea/vomiting/abdominal pain), and in the airway (placing the patient at risk for airway occlusion). The latter is exacerbated by induced bronchospasm as well as bronchorrhea.
- Anaphylaxis also leads to systemic vasodilation, resulting in hypotension despite high cardiac output (distributive shock).

KEY FACT

Type I: Anaphylactic/immediate (IgE)
Type II: Cytotoxic (antibody mediated)
Type III: Immune complex
Type IV: Delayed (CD4 mediated)

Diagnosis

A clinical diagnosis. Patients often present with significant hives and obvious swelling along with a history of allergic reactions. To meet the diagnostic criteria for anaphylaxis, two organ systems must be involved (eg, hives and abdominal pain or vomiting). No lab tests or imaging studies aid in diagnosis.

Treatment

Several treatment modalities are available for patients with an allergic reaction or anaphylaxis:

- Epinephrine: Can be given any route. IM is the fastest to administer.
- Histamine blockade (diphenhydramine for H_1 blockade; famotidine for H_2 blockade).
- Steroids.
- Nebulized albuterol (for wheezing).
- Early intubation if necessary.

Angioedema

There are two types of angioedema: hereditary and acquired (eg, related to angiotensin-converting enzyme inhibitors [ACEIs]). The condition becomes an emergency if it involves the tongue or upper airway (see Figure 4-7). Underlying mechanisms include the following:

- The complement system is a cascade that ends in the formation of the "membrane attack complex," which disrupts the cell walls of pathogens. C1 is the first step in this cascade. In hereditary angioedema, C1 is not inhibited, so it may inappropriately trigger the cascade.
- An autosomal dominant mutation leads to a deficiency of C1 esterase (aka C1 inhibitor). C1 then becomes overactive, leading to the production of kallikrein. Subsequently, kininogen and therefore bradykinin levels can be ↑.
- Bradykinin enhances vascular permeability, which in turn produces significant tissue edema. ACEIs also ↑ bradykinin.

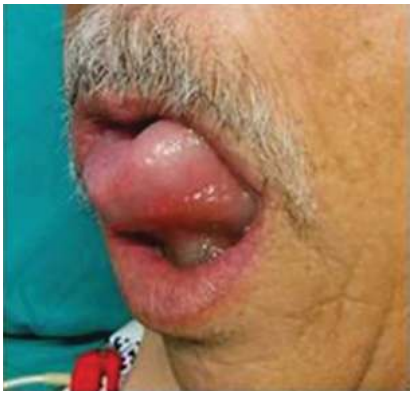


FIGURE 4-7. Angioedema. (Reproduced from Marquez A et al. *Case Rep Anesthesiol.* 2014;2014:693191.)

Diagnosis

- Clinical.
- C1 esterase inhibitor levels confirm the diagnosis but are not available for immediate decision making in the ED.

Treatment

- Most treatment modalities available for anaphylaxis have no effect on the course of angioedema.
- Provide airway protection.

- Fresh frozen plasma contains C1 esterase inhibitor and may ↓ the severity of hereditary angioedema.
- Concentrated C1 esterase inhibitor is available but is costly.

Environmental Emergencies

COLD EMERGENCIES

Frostbite

KEY FACT

Do not rewarm frostbite until refreezing can be prevented.

- Cold injury with pallor and loss of cold sensation resulting from exposure to cold air or direct contact with cold materials. Nonviable structures demarcate and slough off. May be superficial or deep:
  - **Superficial:** Injury to cutaneous and subcutaneous tissue. Skin is soft under a frozen surface. Large, clear, fluid-filled vesicles develop within 2 days (indicating a good prognosis); sloughing leaves new skin that is pink and hypersensitive.
  - **Deep:** Injury to the above tissues plus deep structures (muscle, bone). Skin is hard under a frozen surface.
- **Tx:** Rapidly rewarming once refreezing can be prevented. Circulating water at 40°C (104°F); wound care; tetanus prophylaxis.

Hypothermia

Defined as a core body temperature of < 35°C (< 95°F). Caused by environmental exposure, alcohol ingestion, drugs (barbiturates, benzodiazepines, narcotics), hypoglycemia, CNS or hypothalamic dysfunction (via loss of stimulus of shivering response and adrenal activity), hypothyroidism, skin disorders, and sepsis.

Diagnosis

KEY FACT

No one is dead until they're warm and dead.

Look for arrhythmias and/or Osborn/J waves (positive deflection in the QRS complex) on ECG (see Figure 4-8).

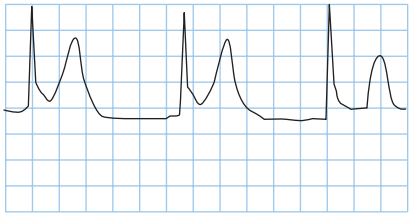


FIGURE 4-8. Sinus bradycardia, Osborn wave. J-point elevation with ST-segment elevation and a prolonged QT interval (0.56 sec) is seen in a patient with hypothermia.

Treatment

- Airway, Breathing, Circulation (ABCs), CPR (in the event of cardiac arrest), and stabilization. Rewarming:
  - **Passive external:** Blankets should be used only in patients who shiver. Once shivering stops, the patient no longer generates heat, and additional methods of rewarming must be used.
  - **Active external:** Warmed blankets, warm-air circulatory blankets, hot-water bottles.
  - **Active internal:** Warm humidified O_2; heated IV fluids; gastric, colonic, bladder, or peritoneal lavage; thoracic lavage; extracorporeal rewarming.
- **Monitoring:** Do not pronounce patients dead until they have been rewarmed to 35°C (95°F); full recovery is not uncommon.

Complications

Associated with a risk of dysrhythmias, especially VF at core temperatures of < 30°C (86°F).

HEAT EMERGENCIES

Heat Exhaustion

- Extreme fatigue with profuse sweating. Also presents with nausea/vomiting and a dull headache.
- **Hx/PE:** Body temperature is normal or slightly ↑. Patients are tachypneic, tachycardic, and hypotensive.
- **Tx:** Treat with IV normal saline and a cool environment.

Heat Stroke

- Elevation of body temperature above normal as a result of temperature dysregulation (> 40°C [104°F]). A true emergency. Monitor for convulsions and cardiovascular collapse.
- **Hx/PE:** Presents with ↑ body temperature, altered mental status, and possibly paradoxical shivering. Patients have hot, dry skin, often with no sweating. Ataxia may be seen.
- **Tx:** Treat with aggressive cooling. Remove from the heat source and undress. Use an atomized tepid water spray in combination with fans and apply ice packs to the groin/axillae (some facilities use cooled IV fluids run through a central line). Treat seizures with benzodiazepines.

KEY FACT

Heat stroke presents with altered mental status and ↑ temperature, often with no sweating.

Burns

Burn victims pose highly complex challenges. Not only are they prone to dehydration, hypothermia, and infection from their compromised skin barrier, but they are also at risk for airway compromise (inhalational burn), trauma (when attempting to escape fire), and toxicity from inhaled gases (primarily carbon monoxide and cyanide).

History/PE

- Airway is of utmost importance. Whether the patient has perioral or intraoral burns, carbonaceous sputum, or a hoarse voice, intubate early.
- Gauge the body surface area (BSA) involved. Observe the rule of 9's:
  - **Adults:** 9% BSA for the head and each arm; 18% BSA for the back torso, the front torso, and each leg.
  - **Children:** 9% BSA for each arm; 18% BSA for the head, back torso, and front torso; and 14% BSA for each leg.
- Determine the depth of the burn (see Table 4-8 and Figure 4-9).

Treatment

- **Prehospital treatment:**
  - Administer IV fluids and high-flow O_2.
  - Remove the patient's clothes and cover with clean sheets or dressings.
  - Give pain medications.
- **In-hospital treatment:**
  - Early airway control is critical.
  - Fluid resuscitation: Appropriate for patients with > 20% BSA second-degree burns. Give 4 cc/kg per % total BSA (Parkland formula) over 24 hours—the first half over the first 8 hours and the second half over the next 16 hours. Keep in mind that the clock starts at the time of the burn. Don't fall behind with fluid resuscitation; you will never catch up in these patients.

Q 1

A 20-year-old woman is pulled unconscious from a cold lake 5 minutes after her sailboat capsized. Despite the problems associated with hypothermia, her near-drowning is likely to have a better outcome than other causes of hypoxia. Why is this the case?

Q 2

A 35-year-old migrant worker with no past medical history has a syncopal episode while harvesting tobacco. Exam reveals diminished mentation, tachypnea, and rales. His bloodwork reveals hypovolemic hyponatremia, hypoglycemia, leukocytosis, and ↑ LFTs. What diagnosis can account for all these abnormalities?

Q 3

A 20-year-old, 154-lb (70-kg) college student was attempting to light a campfire when his shirt caught on fire. Because of the remote location, it took EMS 2 hours to bring the patient to the ED. On exam, you estimate a 30% body surface full-thickness burn. What is the initial fluid administration rate?

TABLE 4-8. Burn Classification

Severity of Burn	Tissue Involvement	Findings
First degree	Epidermis only	Red and painful
Second degree (superficial)	Epidermis and superficial dermis	Red, wet, and painful with blisters
Second degree (deep)	Epidermis and deep dermis	White, dry, and painful
Third degree	Epidermis and entire dermis	Charred/leathery, pearly white, and nontender
Fourth degree	Below the dermis to bone, muscle, and fascia	

KEY FACT

Loss of sensation—meaning the patient says the burn does not hurt—is indicative of third-degree burn.

- Maintain a urine output of 1 cc/kg/hr.
- Tetanus prophylaxis; pain control. Prophylactic antibiotics are of no benefit.

- **Disposition:**
  - **Minor burns:** Discharge with pain medications.
  - **Moderate burns** (partial-thickness 15–25% BSA or full-thickness < 10% BSA): Admit to the hospital.
  - **Major burns** (partial-thickness > 25% BSA or full-thickness > 10% BSA; burns to the face, hands, joints, feet, or perineum; electrical or circumferential burns): Refer to a burn center.

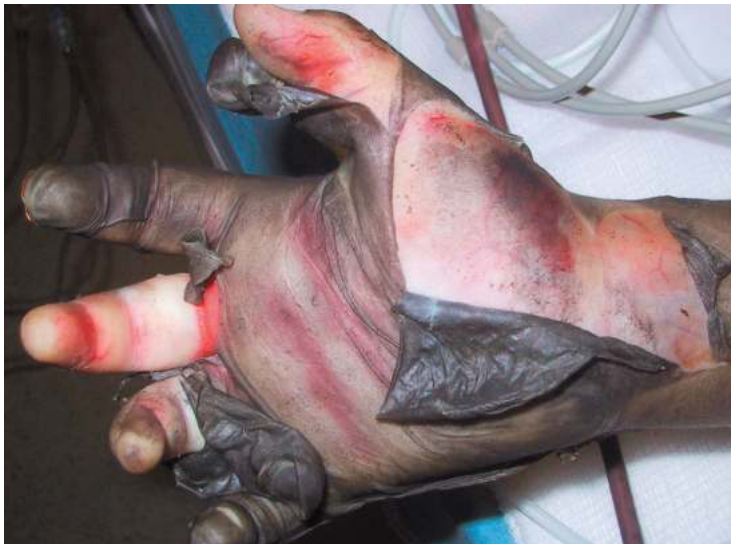


FIGURE 4-9. Third-degree burns. (Reproduced with permission from Goldsmith LA et al. *Fitzpatrick's Dermatology in General Medicine,* 8th ed. New York: McGraw-Hill, 2012, Fig. 95-1D.)

1 A

Activation of the diving reflex (reflex bradycardia and breath holding), which reduces metabolic demands and the effects of hypoxemia, shunts blood to the vital organs and limits aspiration of water.

2 A

Exertional heat stroke.

3 A

The rate should be 0.5 x 70 kg × 4 cc/kg × 30% ÷ 6 hours = 700 cc/hr. The Parkland formula requires that half the volume be given in the first 8 hours (0.5), is weight based (70 kg × 4 cc/kg), and depends on the surface area burned (30%). Why divide by 6 hours and not 8? Because we're already 2 hours in from the initial burn.

Electrical Injuries

Electrical current flows most easily through tissues of low resistance, such as nerves, blood vessels, mucous membranes, and muscles. The current pathway determines which organs are affected. External injuries do not predict internal injuries.

History/PE

Symptoms vary with the nature of the current.

- **Alternating current (household and commercial):**
  - Associated with explosive exit wounds (see Figure 4-10).
  - Effects are worse with alternating current than with direct current at the same voltage.
  - VF is common.
- **Direct current (industrial, batteries, lightning):**
  - Causes discrete exit wounds.
  - Asystole is common.

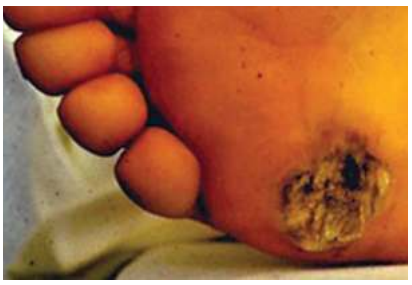


FIGURE 4-10. Electrical burn exit wound. Current flows through the body from the entrance point, until finally exiting where the body is closest to the ground. This foot suffered massive internal injuries, which weren't readily visible, and had to be amputated a few days later. (Reproduced from the United States Department of Labor).

Treatment

- CABs as above; IV fluids for severe burns.
- Administer pain medications and treat burns.
- In mass casualty events (eg, a lightning strike into a crowd), perform reverse triage and prioritize pulseless patients, as return of spontaneous circulation is very likely.
- Treat myoglobinuria with IV fluids to maintain a urine output of 1.5–2.0 cc/kg/hr.
- Tetanus prophylaxis.
- Asymptomatic patients with low-voltage (< 1000-V) burns can be discharged.

Ophthalmology

OCULAR TRAUMA

Corneal Abrasion

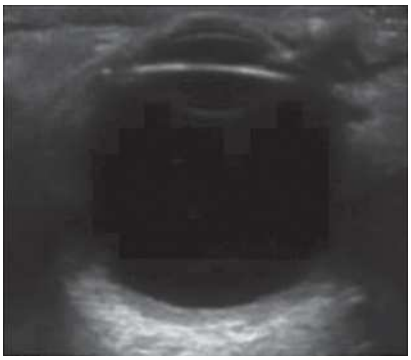
- **Hx/PE:** Presents with pain out of proportion to the exam as well as with a foreign-body sensation and photophobia.
- **Dx:** Fluorescein staining (cobalt-blue light source via slit-lamp or Wood lamp examination) reveals an abraded area.
- **Tx:** Treat with topical broad-spectrum antibiotics (eg, gentamicin, sulfacetamide, bacitracin), tetanus prophylaxis, and oral analgesics.

Ruptured Globe

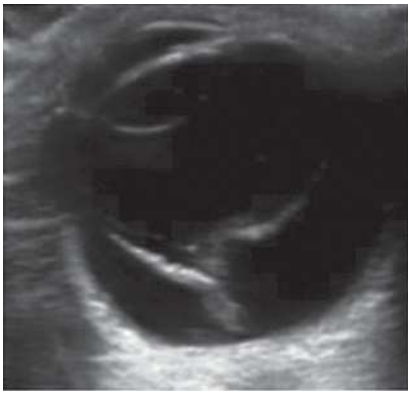
- **Hx/PE:** Presents with trauma and loss of vision. Exam may reveal a vitreous humor leak leading to a teardrop-shaped pupil and a marked ↓ in visual acuity. Seidel test: Apply fluorescein to the cornea; if there is cascading of fluid like a waterfall, then globe perforation has occurred.
- **Dx:** Diagnosis can often be made only by clinical means. Ocular ultrasound or tonometry will worsen the injury.
- **Tx:** Manage with a rigid eye shield to prevent pressure on the globe. An immediate ophthalmologic consultation is necessary.

KEY FACT

A CT scan of the orbit, though sometimes helpful, usually reveals more about damage to the temporal bone than about injury to the eyeball itself.



A



B

FIGURE 4-11. Ocular ultrasound showing normal retina (A) and retinal detachment (B). (Reproduced from Jacobsen B et al. *West J Emerg Med.* 2016;17(2):196–200.)

KEY FACT

Timeline of neonatal conjunctivitis (ophthalmia neonatorum):

- Within 24 hours = chemical.
- 2–5 days = gonorrheal.
- 5–14 days = chlamydial.

Ocular Foreign Body

- **Hx/PE:** Presents with a foreign-body sensation.
- **Dx:** Superficial foreign bodies can often be seen on slit lamp exam; deep foreign bodies may be seen on ultrasound.
- **Tx:** Remove superficial foreign bodies with a wet cotton tip or needle (embedded). Call ophthalmology for deep foreign bodies or perforated globes.

Retinal Detachment

- **Hx/PE:** Patients present with "flashing lights" in vision. Painless, and may occur spontaneously or after trauma.
- **Dx:** Ocular ultrasound shows a detached retina (see Figure 4-11).
- **Tx:** Urgent ophthalmology consult.

CONJUNCTIVITIS

Allergic Conjunctivitis

- Intensely pruritic, watery eyes. Most commonly affects males with a family history of atopy.
- **Hx/PE/Dx:** Look for diffuse conjunctival injection with normal visual acuity. Lid edema and cobblestone papillae may be seen under the upper lid.
- **Tx:** Treat with topical antihistamine/vasoconstrictor preparations such as naphazoline/pheniramine. Cool compresses are also of benefit.

Bacterial Conjunctivitis

- Painful, red eye that is usually unilateral. Causative organisms include *Staphylococcus*, *Streptococcus*, *Neisseria gonorrhoeae*, and *Chlamydia trachomatis* (in newborns and sexually active adults).
- **Hx/PE:** Presents with photophobia, a gritty foreign-body sensation, and a purulent exudate.
- **Dx:** Diffuse conjunctival injection with normal visual acuity. Bacteria can be seen on Gram stain.
- **Tx:** Treat staphylococcal and streptococcal infection with topical 10% sulfacetamide or aminoglycoside. For suspected *N gonorrhoeae*, IV ceftriaxone and topical erythromycin or tetracycline (if left untreated, can lead to blindness and sepsis). PO doxycycline or PO/topical erythromycin is appropriate for chlamydial infection (if left untreated, can lead to corneal scarring and/or *C trachomatis* pneumonia). Warm compresses and frequent flushes are also of benefit.

Viral Conjunctivitis ("Pink Eye")

- **Hx/PE:** Presents as an irritated, red eye with watery discharge and crusting. Frequently bilateral, and often occurs in conjunction with cold symptoms (eg, rhinorrhea, sore throat, cough).
- **Dx:** Diffuse conjunctival injection with normal vision and preauricular lymphadenopathy. Multiple superficial punctate corneal lesions are seen on fluorescein staining.
- **Tx:** Generally no treatment is necessary.

Chemical Conjunctivitis

- Caused by acid or alkali exposure.
- **Dx:** Determine pH from litmus paper. Coagulation necrosis is associated with acid burns, liquefaction necrosis with alkali burns.

- **Tx:** IRRIGATION! Do not delay irrigation for pH checking! Normal saline with a Morgan lens and regular tap water with an eye wash station are common methods. Irrigate until pH is approaching normal. Keep in mind that the pH of normal saline is about 5.5, so you will never get the pH to be 7, no matter how much you irrigate.

OTHER CONDITIONS OF THE EYE

- **Dacryostenosis:** Congenital nasolacrimal duct obstruction (can lead to conjunctivitis).
- **Hordeolum:** Infection of the meibomian glands; most frequently caused by *S aureus*.
- **Periorbital/preseptal cellulitis:** Infection of the tissue around the eye/eyelid, usually caused by *S aureus*. If there is pain on eye movement or proptosis, treat as orbital cellulitis, a vision-threatening emergency. IV antibiotics (vancomycin, piperacillin/tazobactam) and an emergent ophthalmology consult are needed.
- **Blepharoconjunctivitis:** Concurrent inflammation of the conjunctiva and eyelid.
- **Keratitis:** Inflammation of the cornea; may be caused by syphilis, HSV, or UV light exposure.
- **Uveitis:** Inflammation of the inner eye (iris or retina); usually 2° to inflammatory diseases (eg, SLE).
- **Hyphema:** Blood in the anterior chamber of the eye; usually 2° to trauma.
- **Xerophthalmia:** Dry eyes.
- **Strabismus** ("lazy eye"): Can lead to blindness (amblyopia) if not treated during childhood.
- **Presbyopia:** Normal age-related reduction in accommodation.
- **Cataracts:** Painless, progressive loss of vision; absent red reflex.
- **Glaucoma:** Refer to Chapter 2 for a detailed discussion of open- and closed-angle glaucoma.

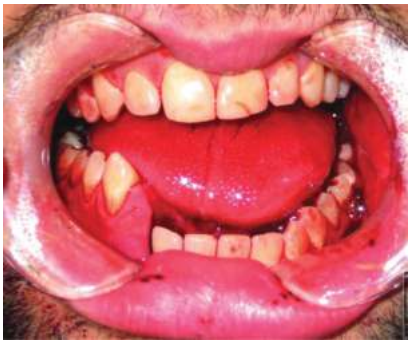
Dental Emergencies

DENTAL AVULSION

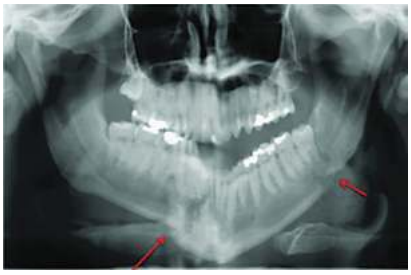
Fractures of the teeth are classified by the deepest layer violated (enamel, dentin, or pulp). They should be evaluated by a dentist within 24 hours. Complete removal of the tooth from its socket, or an avulsion, requires reimplantation within 2–3 hours of injury.

Treatment

- Wash the tooth in clean water to remove debris. Do not scrub; doing so will also remove the periodontal ligaments. Then attempt to reimplant the tooth in its socket.
- If this is not possible (eg, if the tooth doesn't fit or the patient is unconscious and likely to swallow it), place the tooth in an isotonic solution such as sterile saline or milk. There are also commercially available solutions for this purpose.
- Further treatment depends on the amount of time the tooth has been "dry." The patient should be referred to a dentist or an oral surgeon.



A



B

FIGURE 4-12. Mandibular fracture. (**A**) Step off between the right mandibular canine and lateral incisor and general malocclusion. (**B**) Panoramic radiograph demonstrating displaced right mandibular parasymphysis/body fracture and left mandibular angle fracture (*arrows*). (Reproduced from Susarla S et al. *Eplasty.* 2014;14:ic38.)

KEY FACT

Water-soluble contrast leads to chemical pneumonitis if aspirated. Barium contrast leads to peritonitis if a perforation is present. Choose your contrast agent carefully!

MANDIBULAR FRACTURE

Consider fracture of the mandible in any patient with blunt-force trauma to the face with subsequent jaw pain, asymmetry, and/or difficulty speaking/eating. Because of the semiannular shape of the mandible, contrecoup fractures (fractures at a site other than the point of impact) are likely. Be sure to stabilize the patient's airway before focusing on facial injuries.

History/PE

Malalignment of the teeth (malocclusion), ecchymosis of the floor of the mouth, intraoral lacerations (including open fractures into the mouth), dental fractures, inferior alveolar or mental nerve paresthesia, trismus (see Figure 4-12A).

Diagnosis

Confirmed with a panoramic dental x-ray, AP/oblique plain films, or a CT of the face (see Figure 4-12B).

Treatment

- Clindamycin or amoxicillin/clavulanate against anaerobic oral flora. Tetanus prophylaxis if needed.
- Analgesia; immobilization of the jaw.
- Refer to an oral surgeon.

Radiology and Other Diagnostic Testing

Appropriate radiology screening modalities and confirmation for various diagnoses are listed by test below:

- **CT with contrast:** Abdominal abscess, abdominal trauma, aortic aneurysm/dissection, appendicitis, bowel perforation, chest mass/trauma, colitis, diverticulitis, hemoptysis, hydronephrosis, intestinal obstruction, persistent hematuria, PE, tumor diagnosis/staging. Contrast timing allows radiologist to see certain things better (angiogram vs venogram).
- **CT without contrast:** Head trauma (including skull fracture), intracranial bleed, nephrolithiasis, suspected spinal trauma/fracture.
- **MRI with and without contrast:** Brain/spinal tumor/infection, joint imaging, multiple sclerosis, osteomyelitis, vascular imaging, spinal cord compression.
- **Plain film:** Chest mass/trauma, hemoptysis, intestinal obstruction/perforation, fractures, pneumonia.
- **Duplex ultrasound:** Carotid stenosis, deep venous thrombosis.
- **Ultrasound:** AAA screening, appendicitis (in pediatric/pregnant patients), gallstones/cholecystitis, hydronephrosis, intussusception, liver screening, pregnancy/most gynecologic pathology, pyloric stenosis, scrotal pathology (torsion, hydrocele, epididymitis/orchitis, scrotal mass).
- **Barium swallow:** Esophageal obstruction.
- **Barium enema:** Colonic masses (single contrast), inflammatory bowel disease/diverticulosis (double contrast).
- **Upper (or lower) endoscopy:** Esophageal obstruction, hematemesis, PUD, upper (or lower) GI bleeding.
- **Cystoscopy:** Persistent hematuria.
- **HIDA scan:** Cholecystitis.
- **V/Q scan:** PE.

CHAPTER 5

ENDOCRINOLOGY

Diabetes Mellitus

Diabetes mellitus (DM) results from ↓ insulin secretion (type 1) or from tissue resistance to insulin (type 2), leading to hyperglycemia (see Table 5-1). Complications include microvascular disease (retinopathy, nephropathy, neuropathy) and macrovascular disease (atherosclerosis).

TYPE 1 DIABETES MELLITUS

MNEMONIC

The 3 P's of diabetes:

Polyuria
Polydipsia
Polyphagia

Type 1 DM is caused by immune-mediated destruction of insulin-producing pancreatic β-cells, leading to insulin deficiency. It accounts for < 10% of all cases of DM.

History/PE

- Polyuria, polydipsia, polyphagia—the 3 P's of diabetes—can be severe. Patients may also have rapid or unexplained weight loss, blurry vision, or recurrent infections (eg, candidiasis).
- Patients are often young (< 30 years).

Differential

Pancreatic disease (eg, chronic pancreatitis), glucagonoma, Cushing disease, iatrogenic factors (eg, high-dose glucocorticoids), gestational diabetes, diabetes insipidus.

TABLE 5-1. Type 1 vs Type 2 DM

	Type 1 (Insulin-Dependent DM)	Type 2 (Non-Insulin-Dependent DM)
Pathophysiology	Failure of the pancreas to secrete insulin as a result of autoimmune destruction of β cells	Insulin resistance and inadequate insulin secretion by the pancreas to compensate
Incidence	10%	90%
Age (exceptions are common)	< 30 years	> 40 years
Association with obesity	No	Yes
Common symptoms	Polydipsia, polyuria, weight loss	Usually asymptomatic, can cause fatigue, weight changes
Diabetic ketoacidosis	Common	Rare
Genetic predisposition	Weak, polygenic	Strong, polygenic
Association with human leukocyte antigen (HLA) system	Yes (HLA-DR3 and HLA-DR4)	No
Serum C-peptide	↓; Can be normal during the "honeymoon period"	↓ Late in the disease

Diagnosis

Requires at least one of the following:

- A random plasma glucose concentration of ≥ 200 mg/dL with classic symptoms of diabetes.
- Two fasting plasma glucose levels of ≥ 126 mg/dL on more than one occasion.
- A 2-hour postprandial glucose level of ≥ 200 mg/dL after a 75-g oral glucose tolerance test on two separate occasions.
- A hemoglobin A_{1c} (HbA_{1c}) > 6.5%.

Treatment

- **First line:** Start insulin (see Table 5-2). Both basal and bolus insulin are required.
- Most patients with type 1 DM are on a multiple-daily-injection (MDI) regimen consisting of a premeal short-acting insulin (eg, lispro or aspart) and a bedtime long-acting insulin (glargine) or twice-daily neutral protamine Hagedorn (NPH) or detemir.
- Consider screening newly diagnosed type 1 diabetics for other autoimmune diseases such as thyroid disease or celiac disease.

KEY FACT

Latent autoimmune diabetes in adults can present as type 2 DM. While patients may initially respond to oral medications, they will eventually require insulin.

KEY FACT

All type 1 diabetics require insulin! Oral hypoglycemic agents DO NOT work in type 1 DM, as there are no functional pancreatic islet cells to stimulate.

TYPE 2 DIABETES MELLITUS

Common disorder with two etiologies: insufficient insulin secretion and ↑ insulin resistance (see Table 5-1). Prevalence is rising with increasing rates of obesity.

- Characterized by impaired insulin secretion, insulin resistance, and excessive hepatic glucose production.
- In its early stages, glucose tolerance remains near normal despite insulin resistance. After an initial period of insulin resistance and ↑ insulin secretion, pancreatic β-cell function falters and fails to meet peripheral demand.

KEY FACT

Metabolic syndrome refers to clinical combinations of ↑ serum glucose, abdominal obesity, hypertension, ↑ LDL, and ↓ HDL. It can progress to type 2 DM and increases the risk of coronary artery disease (CAD).

TABLE 5-2. Types of Insulin

Insulin	Onset of Action	Duration of Action	Dosing Schedule
Short acting:			
Aspart	10–20 minutes	1–3 hours	3–4x daily, usually with meals
Lispro	5–10 minutes	30–90 minutes	
Regular	30–60 minutes	5–8 hours	3–4x daily, usually with meals
			Varies, usually twice daily with NPH
Intermediate acting:			
NPH	2–4 hours	6–10 hours	Usually twice daily with regular insulin
Long acting:			
Detemir	2 hours	20 hours	Once or twice daily
Glargine	1–4 hours	24 hours	Once daily

History/PE

- Symptoms are similar to those of type 1 DM. Because of the insidious onset of hyperglycemia, patients may be asymptomatic at the time of diagnosis.
- ↑ BMI or strong family history of DM.

Differential

- **Pancreatic insufficiency:** Chronic pancreatitis, hemosiderosis, subtotal pancreatectomy, hemochromatosis.
- **Endocrinopathies:** Cushing syndrome, acromegaly, glucagonoma, gestational diabetes, diabetes insipidus.
- **Drugs:** Glucocorticoids, thiazides, niacin, HIV protease inhibitors, tacrolimus.

Diagnosis

Similar to that of type 1 DM. Consider screening asymptomatic adults with a BMI > 25 or strong family history of DM.

Treatment

- **First line:** Lifestyle changes are first-line treatment. Diet, weight loss, and exercise are critical in that they ↑ insulin sensitivity and ↓ blood glucose levels. Goal HbA_{1c} for most patients is < 7%.
- Start oral therapy in patients whose diabetes is not controlled by weight loss, diet, or exercise. Best initial medical therapy is metformin.
- If HbA_{1c} is still elevated, add a second medication (see Table 5-3).
- If the patient continues to have inadequate control on oral antidiabetic drugs, insulin is either added to the oral regimen or used to replace it. Dosing depends on the type of insulin (see Table 5-2). Consider long-acting insulin (detemir or glargine) if insulin is added to oral hypoglycemic therapy (given in the morning or at bedtime).
- For those who require more intense therapy, a split/mixed regimen of regular or short-acting and NPH or glargine insulin may be used (usually a basal-bolus regimen of glargine with premeal aspart or lispro).
- Long-term management (see next section) includes monitoring blood glucose and checking a fasting glucose level once a day; otherwise, it is similar to that of type 1 DM.

KEY FACT

Step 3 loves to ask about lifestyle changes in diseases like diabetes!

KEY FACT

Metformin should not be administered to patients with renal failure, conditions predisposing to lactic acidosis, or concurrent use of a contrast agent.

LONG-TERM MANAGEMENT OF DIABETES MELLITUS

DM is closely linked to multiple vascular complications, many of which can be prevented with improved glycemic control (see Table 5-4).

- Check HbA_{1c} every 3 months (goal HbA_{1c} < 7%).
- Order yearly urine microalbumin to look for nephropathy.
- Instruct patients to inspect feet daily; obtain yearly foot exam with microfilament sensation testing.
- Conduct yearly dilated eye exam to look for retinopathy.
- Manage CAD risk factors.
  - Encourage smoking cessation.
  - Keep BP below 130/80 mm Hg. First-line treatment of hypertension is angiotensin-converting enzyme inhibitors (ACEIs) such as lisinopril or angiotensin receptor blocker (ARB), which help protect against nephropathy.
  - Treat hyperlipidemia with statins.
- Counsel on consistent carbohydrate intake; refer to dietician if necessary.

TABLE 5-3. Oral Diabetes Medications

Medication	Examples	Mechanism of Action	Adverse Effects	Contraindications
Biguanides	Metformin	Inhibit hepatic gluconeogenesis, ↑ glucose utilization, ↓ insulin resistance, ↓ postprandial glucose levels	Lactic acidosis, diarrhea, GI discomfort, metallic taste, weight loss	Renal insufficiency, any form of acidosis, liver disease, severe hypoxia
Sulfonylureas	First generation: Chlorpropamide Second generation: Glipizide, glyburide	↑ Insulin secretion and ↑ peripheral insulin sensitivity	Hypoglycemia, weight gain, type IV hypersensitivity reactions	Renal/liver disease
Meglitinides	Repaglinide	↑ Insulin secretion. (work like sulfonylureas by stimulating the release of insulin from the pancreas)	Hypoglycemia	Renal/liver disease
α-Glucosidase inhibitors	Acarbose	↓ Glucose absorption (↓ carbohydrate absorption from the GI tract, ↓ insulin demand)	↑ Flatulence, GI discomfort, ↑ liver function tests (LFTs)	Renal/liver disease
Thiazolidinediones ("glitazones")	Rosiglitazone, pioglitazone	↓ Insulin resistance, ↑ glucose utilization (↑ insulin sensitization, ↓ hepatic gluconeogenesis and insulin receptor upregulation)	Hepatocellular injury, anemia, pedal edema, heart failure (HF)	Liver disease, HF (class III/IV), LFTs > two times normal
Glucagon-like peptide-1 (GLP-1) agonists	Exenatide Liraglutide	↑ Postprandial glucose utilization	Nausea, vomiting, weight loss, hypoglycemia	Renal disease
Dipeptidyl peptidase inhibitors	Sitagliptin, vildagliptin	Same as that of GLP-1 agonists	Same as those of GLP-1 agonists	Same as that of GLP-1 agonists
SGLT2 inhibitors	Canaglifozin	↓ Renal glucose reabsorption	Urinary tract infections, hypoglycemia	Renal disease

- Ensure patients are up-to-date on pneumococcal and yearly flu vaccinations.
- Treat complications of diabetes.
  - Gastroparesis is slowed gastric emptying causing nausea, bloating, constipation. Treat with a promotility agent such as metoclopramide.
  - Erectile dysfunction (often related to microvascular disease and neuropathy) can be treated with phosphodiesterase inhibitors such as sildenafil.

KEY FACT

The risk of microvascular complications in DM is ↓ by tight glycemic control.

DIABETIC KETOACIDOSIS

Occurs when a lack of insulin leads to ↑ catabolism causing hyperglycemia, acidosis, and hyperkalemia. It can be precipitated by stressors such as infection or surgery. It is typically seen in type 1 DM and may be the initial presentation.

Q

A 45-year-old obese man presents with polyuria and weight loss. What level of serum glucose is diagnostic of DM?

TABLE 5-4. Vascular Complications of Diabetes Mellitus

	Presentation	Diagnosis	Management
Neuropathy	Primarily a symmetrical sensory polyneuropathy affecting the distal lower extremities; ↑ the risk of diabetic foot ulcers (see Figure 5-1)	Clinical	Prevention is key, including daily self-inspection of feet and yearly foot exams. First-line treatment includes gabapentin or pregabalin and focuses on symptom relief
Nephropathy	Usually asymptomatic but may present with bilateral lower extremity edema from nephrotic syndrome	Best initial test is yearly urine microalbumin. Definitive diagnosis is made by renal biopsy showing Kimmelstiel-Wilson lesions (not necessary in most cases)	ACEIs and aggressive BP management (goal is <130/80) can help prevent progression to end-stage renal disease
Retinopathy	Often asymptomatic; can also present with blurry vision	Yearly dilated eye exam to look for proliferative retinopathy with abnormal new blood vessels	First line treatment: Laser therapy; 2nd line: Intravitreous injection of vascular endothelial growth factor inhibitor such as bevacizumab
Atherosclerosis	Manifestations vary but may present as MI or stroke	May be diagnosed as CAD	Treat hyperlipidemia with statins; implement aggressive management of risk factors (eg, hypertension obesity, smoking)

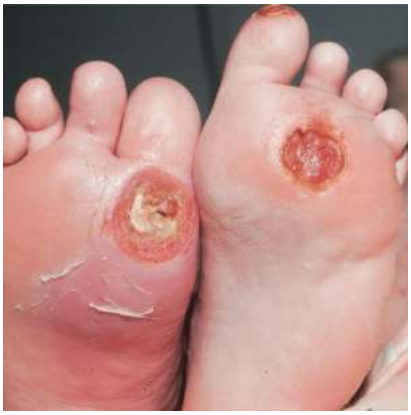


FIGURE 5-1. Neuropathic ulcers in a diabetic. (Reproduced with permission from Tintinalli JE et al. *Tintinalli's Emergency Medicine,* 7th ed. New York: McGraw-Hill, 2011, Fig. 247-3.)

A

A serum glucose level of ≥ 200 mg/dL is diagnostic of DM in a symptomatic patient.

History/PE

- Abdominal pain.
- "Fruity" breath odor.
- Kussmaul hyperpnea (↑ in depth and rate of breathing).
- Dehydration.

Diagnosis

- Initial labs: Electrolytes (including calculated anion gap) and arterial blood gas (ABG).
  - Serum electrolytes (↑ anion gap, ↑ glucose, ↑ K, ↓ bicarbonate).
  - ABG (pH < 7.3).
- Diagnosis can be confirmed with serum and urine ketones (β-hydroxybutyrate and acetoacetate).
- Other tests to consider: CBC, UA, urine culture, CXR, blood cultures.

Treatment

- Begin initial therapy of IV fluids and IV insulin.
- Monitor electrolytes every 2 hours. Add glucose to IV fluids when serum glucose drops below 250 mg/L.
- Add potassium to fluids when serum K drops below 4.5.
- Continue IV insulin until anion gap normalizes, then switch to subcutaneous basal-bolus insulin with an overlap of IV Insulin for at least 2 hours.

HYPERGLYCEMIC HYPEROSMOLAR STATE

Markedly ↑ plasma glucose leads to ↑ plasma osmolality and serum volume depletion. The presence of small amounts of insulin inhibits ketosis and

acidosis. Hyperglycemic hyperosmolar state (HHS) can be precipitated by infection, medications (eg, β-blockers, steroids, thiazides), or dehydration. It is typically seen in type 2 DM.

History/PE

Patients are acutely ill and dehydrated with altered mental status.

Diagnosis

- Electrolytes (serum glucose > 600 mg/dL, normal anion gap, normal bicarbonate).
- ABG (pH > 7.3).
- Serum osmolality (> 310 mOsm/kg).

Treatment

- **First line:** IV fluids.
- Monitor and replace sodium, potassium, phosphate, and glucose every 2 hours. Give IV insulin only if glucose levels remain elevated after sufficient fluid resuscitation.

KEY FACT

Don't forget to look for underlying causes of diabetic ketoacidosis (DKA) such as infection, MI, surgery, stress. It can also be the presenting symptom for type 1 DM.

KEY FACT

In DKA, serum K is often elevated at presentation due to insulin deficiency and acidemia causing ↑ extracellular K. Monitor closely, as this can drop rapidly when insulin is started.

KEY FACT

In patients with HHS, neurologic symptoms such as lethargy, focal signs, and obtundation are common. In patients with DKA, hyperventilation and abdominal pain are most frequently seen.

Thyroid Disorders

The thyroid gland helps regulate multiple metabolic functions. Thus, a hyper- or hypo-functioning gland affects multiple organ systems with a wide variety of presenting symptoms. Table 5-5 lists distinguishing features of hypo- and hyperthyroidism.

1° HYPOTHYROIDISM

Characterized by a ↓ free T_4. It is most commonly caused by Hashimoto thyroiditis, which also causes ↑ thyroid-stimulating hormone (TSH).

History/PE

Fatigue, weight gain, constipation, dry skin (see Table 5-5).

Differential

Hashimoto thyroiditis, medication effect (lithium, amiodarone), subacute thyroiditis, amyloidosis, iatrogenic post-ablative therapy or thyroidectomy.

Diagnosis

- **Best initial tests:** TSH (↑) and free T_4 (↓).
- Check antithyroid peroxidase antibodies (elevated in Hashimoto thyroiditis).

Treatment

Patients require oral replacement therapy with levothyroxine.

Complications

Myxedema coma is a form of severe hypothyroidism characterized by altered mental status, hypothermia, and hemodynamic instability. Treat with IV levothyroxine.

Q 1

A 20-year-old woman with type 1 DM presents with abdominal pain. Labs reveal a glucose level of 270 mg/dL, HCO3 14, and an anion gap of 20. She is started on IV fluids and insulin. Repeat labs show glucose of 190 mg/dL, HCO3 16, anion gap 17. What is the next step in management?

Q 2

An 8-year-old boy presents with a 2-day history of a productive cough and a fever of 38.4°C (101.1°F). Labs reveal leukocytosis, a blood glucose level of 341 mg/dL, a serum bicarbonate level of 13 mEq/L, and a UA positive for 2+ ketones. CXR reveals lobar pneumonia. Which serum ketone is likely elevated?

TABLE 5-5. Clinical Presentation of Functional Thyroid Disease

	Hypothyroidism	Hyperthyroidism
General	Fatigue, lethargy	Hyperactivity, nervousness, fatigue
Temperature	Cold intolerance	Heat intolerance
GI	Constipation leading to ileus; weight gain despite a poor appetite	Diarrhea; weight loss despite a good appetite
Cardiac	Bradycardia, pericardial effusion, hyperlipidemia	Tachycardia, atrial fibrillation, HF; systolic hypertension, ↑ pulse pressure
Neurologic	Delayed deep tendon reflexes	Fine resting tremor; apathetic hyperthyroidism (elderly)
Menstruation	Heavy	Irregular, amenorrhea
Dermatologic	Dry, coarse skin; thinning hair; thin, brittle nails; myxedema	Warm, sweaty skin; fine, oily hair; nail separation from matrix
Other	Arthralgias/myalgias	Osteoporosis

1° HYPERTHYROIDISM

Characterized by ↑ free T_4 level. Most common cause is Graves disease, although subacute thyroiditis can also cause transient symptoms of hyperthyroidism.

KEY FACT

Pregnancy is an absolute contraindication to radioactive iodine uptake (RAIU) tests. Instead, measure thyroid-stimulating immunoglobulin.

History/PE

Weight loss, tachycardia, anxiety (see Table 5-5).

Differential

Graves disease, subacute thyroiditis (patient presents initially with hyperthyroidism followed by hypothyroidism, may also have tender nodule), toxic adenoma, multinodular goiter.

Diagnosis

- **Initial tests:** TSH (usually ↓) and free T_4 (↑). Normal free T_4 levels can be seen in initial stages of Hashimoto and subacute thyroiditis.
- RAIU test results can differentiate between Graves disease and subacute thyroiditis (see Table 5-6).

Treatment

- **First line:** Propylthiouracil or methimazole, which block thyroid hormone synthesis.
  - Give β blockers for symptomatic treatment of tachycardia or tremors.
- Radioactive iodine (RAI) therapy ablates the gland, or thyroidectomy can be considered for pregnant patients or those with large goiters.
- All patients who have undergone RAI therapy or thyroidectomy will develop hypothyroidism and require levothyroxine.

1 **A**

Continue the insulin drip and add glucose. Insulin drip should be continued until the anion gap closes, not until the glucose normalizes.

2 **A**

β-Hydroxybutyrate.

TABLE 5-6. Differential and Treatment of Functional Thyroid Disease

	Graves Disease	Subacute Thyroiditis	Hashimoto Thyroiditis
Etiology/ pathophysiology	Antibody directed at TSH receptor; more prevalent in female patients	Viral (possibly mumps or coxsackievirus)	Autoimmune disorder
Symptoms/exam	Hyperthyroidism; diffuse, painless goiter Proptosis (also called exophthalmos; see Figure 5-2A), lid lag, diplopia, conjunctival injection Pretibial myxedema (see Figure 5-2B)	Hyperthyroidism followed by hypothyroidism Tender thyroid Malaise, upper respiratory tract symptoms, fever early on	Occasionally presents with hyperthyroidism (hashitoxicosis) followed by hypothyroidism; painless thyroid enlargement
Diagnosis	↑ RAIU scan, ⊕ thyroid-stimulating immunoglobulin	↓ RAIU scan, ↑ erythrocyte sedimentation rate	⊕ Anti-TPO antibody
Disease-specific treatment	Propylthiouracil, methimazole, thyroid ablation with ^{131}I, thyroidectomy Ophthalmopathy may require surgical decompression, steroids, or orbital radiation	NSAIDs for pain control, steroids for severe pain Self-limited	Levothyroxine

Complications

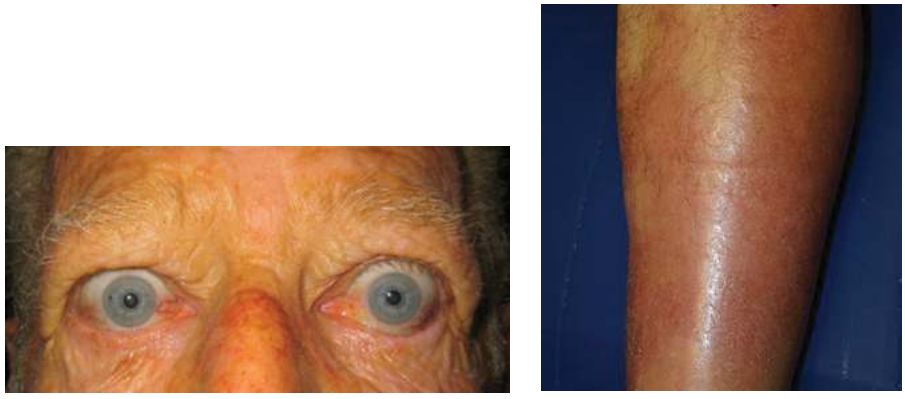
Thyroid storm is a severe form of hyperthyroidism characterized by high fever, tachycardia, cardiac failure, dehydration and altered mental status. Treat supportively with propranolol for tachycardia, glucocorticoids (block conversion of T_4 to T_3), and methimazole or propylthiouracil.

KEY FACT

Methimazole should not be given during pregnancy because it can cause congenital anomalies. Instead, consider using propylthiouracil or thyroidectomy.

2° HYPERTHYROIDISM

- Extremely rare condition in which there is ↑ TSH with ↑ T_4. It is almost always caused by pituitary adenoma.
- **Hx/PE:** Same as primary hypothyroidism. May also present with visual changes and other hormonal abnormalities.
- **Dx:** Best initial tests are TSH (↑) and T_4 (↑). Check brain MRI for adenoma.
- **Tx:** Remove tumor if present. Treat symptomatically with β-blockers, if needed.



A B

FIGURE 5-2. Physical signs of Graves disease. (A) Graves ophthalmopathy. (B) Pretibial myxedema. (Reproduced with permission from USMLE-Rx.com.)

Q 1

A 30-year-old woman presenting with weight loss and heat intolerance is found to be tachycardic. Labs reveal a suppressed TSH and an ↑ T_4 level. What is the most common cause of these findings?

Q 2

A 55-year-old man complains of hoarseness and difficulty swallowing. As a teenager, he received external radiation to treat his severe acne. Exam reveals a palpable thyroid nodule. His TSH level is 1.5 mIU/L. What is the next step in diagnosis?

THYROID NODULES

More common in older women; they can be benign or malignant. Hyperfunctioning ("hot") nodules are rarely malignancy; therefore, checking TSH levels is the first step in evaluation. Risk factors for malignancy include a history of head or neck irradiation, family or personal history of thyroid disease or multiple endocrine neoplasia (MEN), and a rapidly growing nodule.

History/PE

- May be asymptomatic or present as a single firm, palpable nodule.
- Often found incidentally on radiologic studies that are ordered for other purposes.
- Cervical lymphadenopathy, dysphagia, dyspnea and hoarseness should raise concern.

Differential

- The differential for thyroid nodules includes:
  - **Benign:** Adenomatous thyroid nodule; thyroglossal duct cyst.
  - **Malignant:** 1° thyroid cancer, thyroid lymphoma, metastatic cancer.
- Subtypes of malignant lesions include:
  - **Papillary:** Most common; spreads lymphatically; has an excellent prognosis, with a 10-year survival rate of > 95%.
  - **Follicular:** The second most common subtype; spreads locally and hematogenously. Can metastasize to the bone and lungs. Has a 10-year survival rate of ~ 90%.
  - **Medullary:** A tumor of parafollicular C cells. May secrete calcitonin. 15% familial or associated with MEN 2A or 2B.
  - **Anaplastic:** Undifferentiated. Has a poor prognosis; usually occurs in older patients.

Diagnosis

- **Best initial test:** TSH.
  - Normal or high: Obtain an ultrasound to select a nodule for biopsy with FNA—the most accurate method for evaluating thyroid nodules.
  - Low: Conduct an RAI uptake and scan to identify whether the nodule is functioning ("hot") or nonfunctioning ("cold"). Functioning nodules are almost always benign, whereas those that are nonfunctioning are associated with a 15% chance of malignancy. Cold nodules should undergo biopsy with FNA.
- Figure 5-3 outlines subsequent steps in the evaluation and treatment of thyroid nodules.

Treatment

Contingent on FNA or RAI uptake results (see Figure 5-3):

- **Follicular cells or malignancy:** Surgery.
- **Benign:** Serial follow-up.
- **Indeterminate:** Repeat FNA under ultrasound guidance.
- **Hot nodules:** Ablation/resection or medical management.

MNEMONIC

Characteristics of thyroid nodules:

90% of nodules are benign.
90% of nodules are cold (nonfunctioning) on RAI uptake scan; 15%–20% of these are malignant (vs 1% of hot, or functioning, nodules).
90% of thyroid malignancies present as a thyroid nodule.
> **90%** of thyroid cancers are either papillary or follicular.

KEY FACT

Papillary and follicular thyroid cancer are the most common 1° thyroid cancers and carry the best prognosis.

KEY FACT

Ultrasound features suggestive of malignancy include hypoechogenicity, microcalcification, irregular margins, ↑ vascular flow, and size > 3 cm.

KEY FACT

Thyroglobulin is a good marker for the presence of thyroid tissue and can be used to determine if malignancy has recurred or if residual cancer remains after treatment.

1 A

Graves disease.

2 A

The patient's clinical presentation, history of irradiation, and normal TSH level raise suspicion for malignancy. Order an ultrasound of the thyroid to isolate the nodule or nodules to be screened for thyroid cancer by fine-needle aspiration (FNA).

Hypercalcemia

Most commonly caused by 1° hyperparathyroidism, often detected on routine labs.

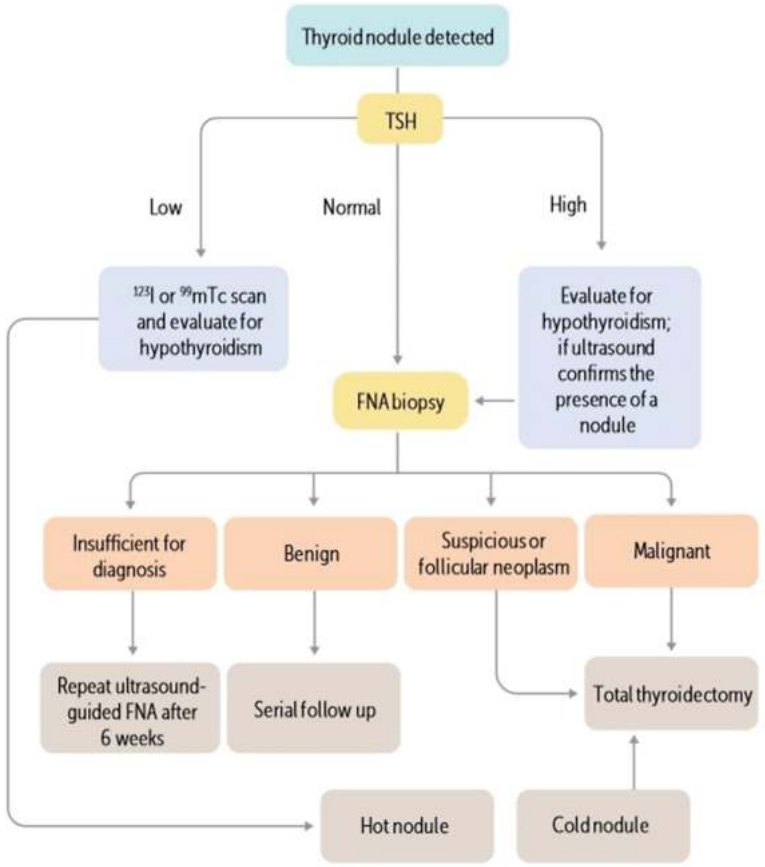


FIGURE 5-3. Workup and treatment of a thyroid nodule. (Reproduced with permission from USMLE-Rx.com.)

History/PE

Many patients are asymptomatic. Symptoms range from mild nausea to obtundation, and may include fatigue, constipation, polyuria, polydipsia, abdominal pain.

Differential

- 1° hyperparathyroidism (parathyroid adenoma or multiglandular disease).
- Vitamin D excess, thiazides, sarcoidosis.
- Malignancy: Parathyroid hormone (PTH)-related protein (lung and breast cancers are most common), bony metastases.

Diagnosis

- **Best initial test:** PTH level.
  - ↑ PTH with ↑ Ca indicates 1° hyperparathyroidism.
  - Normal or ↓ PTH with ↑ Ca indicates 2° cause such as malignancy.
- Other tests to consider: Serum protein electrophoresis, vitamin D levels, CXR.

Treatment

- **First line:** For acute hypercalcemia, IV hydration with normal saline.
- **Second line:** Bisphosphonates (IV zoledronic acid or pamidronate) and calcitonin.
- If persistently elevated despite fluids, furosemide can promote renal calcium excretion.

MNEMONIC

Hypercalcemia causes—

Stones, bones, moans, and groans

Stones—nephrolithiasis
Bones—osteoporosis, fractures
Moans—abdominal pain, nausea
Psychic **g**roans—confusion, altered mental status

KEY FACT

Not all diuretics act alike! Thiazide diuretics can cause hypercalcemia by increasing calcium resorption. Loop diuretics promote calcium excretion ("Loops Lose Calcium") and can be used to treat hypercalcemia.

KEY FACT

Hypercalcemic crisis (Ca > 13) presents with altered mental status, polyuria, short QT syndrome, and severe dehydration. Consider emergent dialysis.

- Definitive therapy focuses on correcting the underlying cause (see Figure 5-4).
  - Parathyroidectomy for parathyroid adenoma.
  - Chemotherapy for malignancy.

Osteoporosis

A common metabolic bone disease characterized by ↓ bone strength, low bone mass, and skeletal fragility, resulting in an ↑ risk of fracture. More common among inactive, postmenopausal Caucasian women; other risk factors include a ⊕ family history, steroid use, smoking, and alcohol.

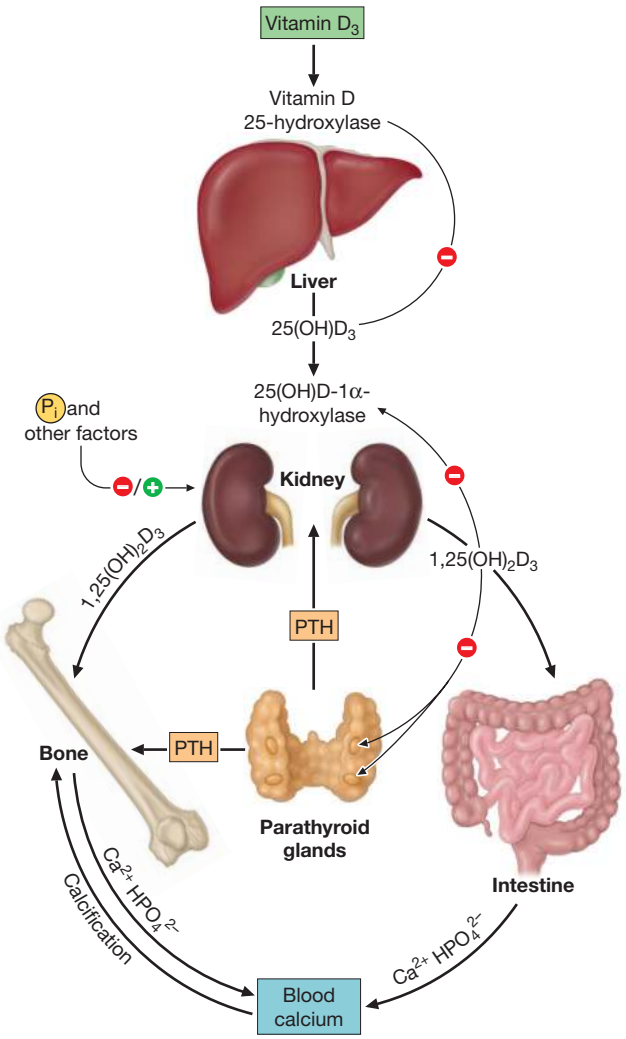


FIGURE 5-4. Relationship between calcium, vitamin D, and PTH. A reduction in serum calcium prompts a proportional increase in the secretion of PTH and mobilizes additional calcium from the bone. PTH promotes the synthesis of 1,25(OH)2D in the kidney, which stimulates the mobilization of calcium from bone and intestine and regulates the synthesis of PTH by negative feedback. (Reproduced with permission from Longo DL et al. *Harrison's Principles of Internal Medicine,* 18th ed. New York: McGraw-Hill, 2012, Fig. 352-5.)

History/PE

Commonly asymptomatic. Patients may present with vertebral compression fractures (resulting in loss of height and progressive thoracic kyphosis), or wrist or hip fracture following minimal trauma.

Differential

Osteomalacia (inadequate bone mineralization), hyperparathyroidism, multiple myeloma, metastatic carcinoma (pathologic fracture).

Diagnosis

- All women > 65 years of age, as well as those 40–60 years of age with at least one risk factor for osteoporotic fractures after menopause, should be screened with a DEXA scan of the spine and hip. DEXA results are categorized as follows:
  - **T-score > −1.0:** Normal.
  - **T-score −1.0 to −2.5:** Osteopenia ("low bone density").
  - **T-score < −2.5:** Osteoporosis.
  - **T-score < −2.5 with a fracture:** Severe osteoporosis.
- Rule out 2° causes, including smoking, alcoholism, renal failure, hyperthyroidism, multiple myeloma, 1° hyperparathyroidism, vitamin D deficiency, hypercortisolism, heparin use, and long-term steroid use.

Treatment

- All postmenopausal women should be counseled on lifestyle changes including calcium/vitamin D supplementation, weight-bearing exercise, and smoking cessation.
- Treat when the T-score is < −2.5 or when the T-score is < −1.0 in a patient with high risk factors for osteoporotic fractures.
- **First line:** Bisphosphonates (alendronate, risedronate), which inhibit osteoclastic activity.
- **Second line**: Selective estrogen receptor modulators (SERMs) such as raloxifene, which ↑ bone mineral density and ↓ bone resorption; denosumab, a RANK ligand inhibitor; and teriparatide (PTH analog) or calcitonin.
- A DEXA scan should be repeated 1–2 years after the initiation of drug therapy. If the T-score is found to have worsened, combination therapy (eg, a SERM and a bisphosphonate) or a change in therapy should be initiated, with consideration given to ruling out 2° causes.

Cushing Syndrome (Hypercortisolism)

Results from excess levels of exogenously administered glucocorticoids or endogenous overproduction of cortisol. The most common cause is iatrogenic Cushing syndrome due to exogenous glucocorticoids. The second most common form is Cushing disease, which results from pituitary hypersecretion of adrenocorticotropic hormone (ACTH).

KEY FACT

Excess ACTH may be produced by pituitary adenomas (Cushing disease) or by extrapituitary ACTH-producing tumors (eg, small-cell lung cancer).

History/PE

- Presents with skin atrophy and proximal muscle weakness. Areas of fat distribution (moon face, buffalo hump) are characteristic (see Figure 5-5).
- Psychiatric disturbances, hypertension, hyperglycemia, oligomenorrhea, growth retardation, and hirsutism.
- Muscle wasting, easy bruising, and striae.

Q

A 68-year-old woman presents to her primary care physician for a routine checkup. The physician orders a DEXA scan of the spine and hip. What T-score value denotes osteoporosis?

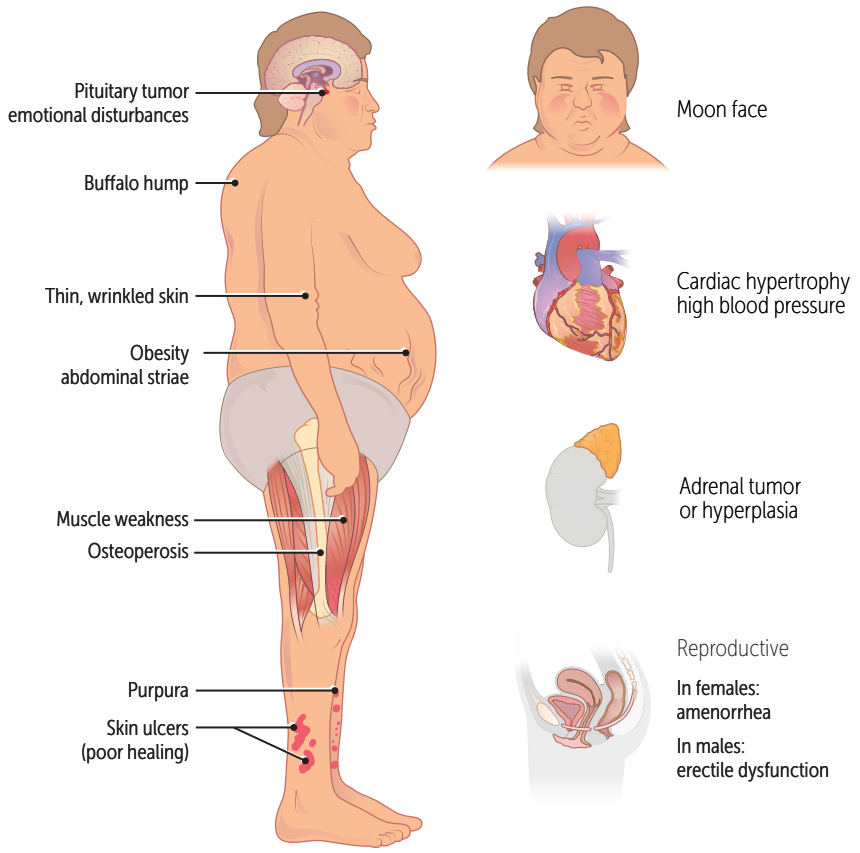


FIGURE 5-5. Clinical features of Cushing syndrome. (Reproduced with permission from USMLE-Rx.com.)

Differential

DM, chronic alcoholism, depression, obesity due to other causes, long-term steroid use, adrenogenital syndrome, acute stress.

Diagnosis

KEY FACT

Adrenal overproduction of cortisol can be due to adrenal adenomas or carcinomas (usually unilateral) or adrenal hyperplasia (bilateral). Check CT of the abdomen to determine cause.

- **Best initial test:** Overnight dexamethasone test or measurement of urinary or salivary cortisol to confirm the diagnosis of cortisol excess. See Figure 5-6.
  - The overnight test consists of administration of 1 mg of dexamethasone at 11 PM and measurement of serum cortisol at 8 AM the next morning. An 8 AM serum cortisol value of < 2 μg/dL is normal in most patients.
- If hypercortisolism, measure ACTH level to determine whether ACTH is independent or dependent. See Table 5-7.
- For ACTH-independent hypercortisolism (↓ ACTH), order abdominal CT to look for adrenal pathology.
- For ACTH-dependent hypercortisolism (↑ ACTH), determine location by performing a high-dose dexamethasone suppression test.
  - If the high-dose dexamethasone suppresses ACTH, the origin is pituitary.
  - If ACTH is not suppressed, the origin is ectopic production of ACTH.

Treatment

- Patients with Cushing disease are usually treated by transsphenoidal microsurgical excision of the pituitary adenomas.

A

T-score < -2.5.

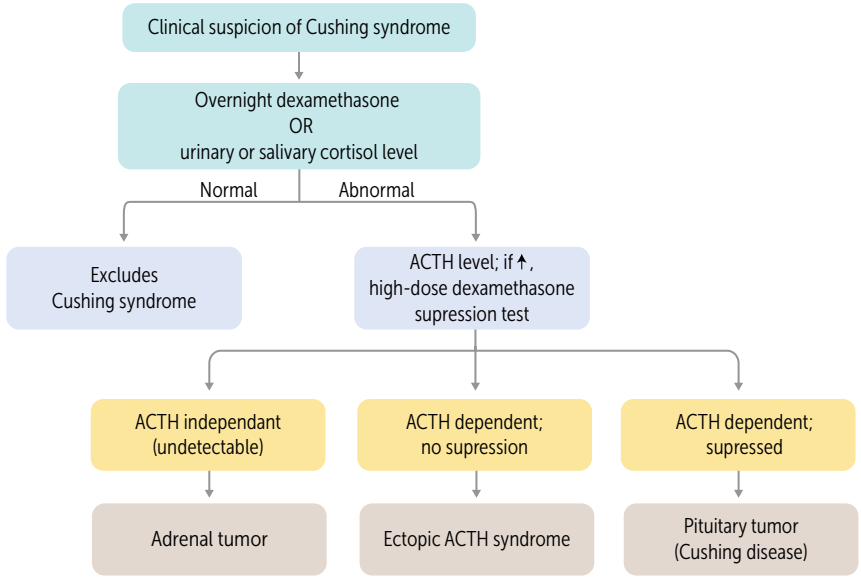


FIGURE 5-6. Diagnostic evaluation of Cushing syndrome. (Reproduced with permission from USMLE-Rx.com.)

- Adrenal adenomas are treated with unilateral adrenalectomy.
- Bilateral adrenal hyperplasia is cured with bilateral total adrenalectomy. Patients will require lifelong daily glucocorticoid and mineralocorticoid replacement.
- Ectopic ACTH-secreting tumor: Surgical resection of the tumor.
- Exogenous steroids: Minimize use.

Adrenal Insufficiency

1° adrenal insufficiency, or Addison disease, is most commonly caused by autoimmune adrenalitis. Adrenal crisis may occur in previously undiagnosed patients in the setting of serious infection or other acute stressors and in patients with known 1° adrenal insufficiency who do not take a "stress dose" of glucocorticoid during an infection or other major illness.

TABLE 5-7. Laboratory Characteristics of Endogenous Cushing Syndrome

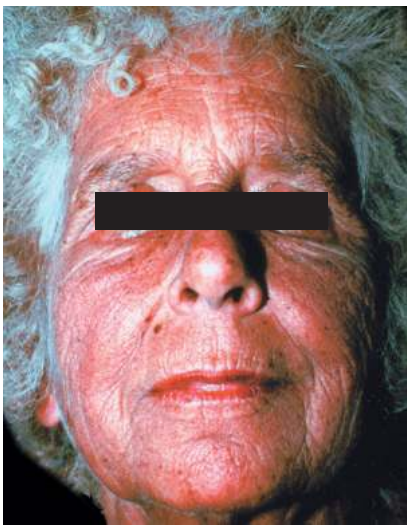
	ACTH Dependent	ACTH Independent
Plasma cortisol	↑	↑
Urinary cortisol	↑	↑
ACTH	↑	↓ or undetectable
Source	Pituitary (suppressible) Ectopic (nonsuppressible)	Adenoma (↓ DHEA) Carcinoma (↑ DHEA)

Q 1

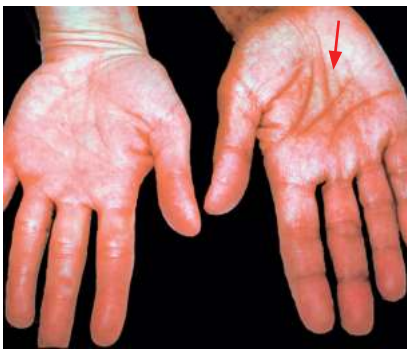
A 30-year-old woman with a history of systemic lupus erythematosus (SLE) presents with ↑ truncal obesity, a fatty hump between her shoulders. She is on long-term steroids. What is the next best step in management?

Q 2

A 65-year-old man with a known recent diagnosis of melanoma presents with vague complaints of dizziness, weakness, fatigue, and weight loss. Basic lab testing reveals hyponatremia. What testing will help determine the diagnosis?



A



B

FIGURE 5-7. Addison disease. (**A**) Note the characteristic hyperpigmentation. (**B**) Hyperpigmented palmar creases (right, arrow) compared with the palm of an unaffected person (left). (Reproduced with permission from Goldsmith LA et al. *Fitzpatrick's Dermatology in General Medicine*, 8th ed. New York: McGraw-Hill, 2012, Fig. 151-12.)

History/PE

- **Common features:** Chronic malaise; fatigue that is worsened by exertion and improved with bed rest; generalized weakness, weight loss.
- **Additional features** (more common in 1° adrenal insufficiency):
  - Hypotension; postural dizziness or syncope due to volume depletion resulting from aldosterone deficiency.
  - Electrolyte abnormalities: Hyponatremia and hyperkalemia (mild hyperchloremic acidosis) due to mineralocorticoid deficiency (60–65% of patients); salt craving in some patients.
  - Hyperpigmentation due to production of proopiomelanocortin (brownish discoloration); occurs primarily with 1° adrenal insufficiency (see Figure 5-7).

Differential

- **1° adrenal insufficiency:** Adrenal failure due to autoimmune disease (idiopathic), metastatic tumors, hemorrhagic infarction (from coagulopathy or septicemia), adrenalectomy, or granulomatous disease (TB, sarcoid).
- **2° adrenal insufficiency:** Results from ↓ ACTH production from the pituitary. May be due to withdrawal of exogenous steroids or hypothalamic/pituitary pathology (tumor, infarct, trauma, infection, iatrogenic).

Diagnosis

- Measure 8 AM serum cortisol and plasma ACTH to confirm low serum cortisol levels. Then check a cosyntropin stimulation test, which measures cortisol before and after administration of synthetic ACTH.
  - An AM serum cortisol < 5 μg/dL or a serum cortisol < 20 μg/dL after an ACTH stimulation test makes the diagnosis more likely.
- If the cause is unclear, the plasma ACTH level distinguishes 1° from 2° adrenal failure (see Table 5-8).

Treatment

- **First line:** For stable patients with chronic adrenal insufficiency, steroids (hydrocortisone or prednisone).
- Add fludrocortisone for patients with persistent orthostatic hypotension, hyponatremia, or hyperkalemia.
- Patients should be instructed to take ↑ doses (stress doses) of glucocorticoid during times of stress or illness.

TABLE 5-8. 1° vs 2° Adrenal Insufficiency

	Addison Disease	2° Adrenal Insufficiency
ACTH	↑	↓
Cortisol after ACTH challenge	↓	↑
Aldosterone	↓	Normal
Na	↓	Normal or ↓
K	↑	Normal

1 **A**

Exogenous steroids can cause iatrogenic Cushing syndrome. If possible, discontinue or taper steroids prior to evaluation for endogenous Cushing syndrome.

2 **A**

AM serum cortisol and AM serum ACTH.

Complications

Adrenal crisis is a life-threatening emergency that requires immediate treatment. Start immediate fluid resuscitation. If the diagnosis of adrenal failure has not been established, start with dexamethasone (does not interfere with the measurement of plasma cortisol). If the diagnosis of adrenal failure is known, treat with hydrocortisone.

KEY FACT

Infection, surgery, or other stressors can trigger an Addisonian crisis with symptomatic adrenal insufficiency, confusion, and vasodilatory shock. These patients require immediate fluid resuscitation and IV hydrocortisone.

Hyperaldosteronism

A state of excess mineralocorticoids, most often caused by aldosterone producing adenoma.

Differential

- **1° hyperaldosteronism:** Due to excess secretion of aldosterone, resulting in ↑ sodium reabsorption and potassium secretion. Most commonly caused by an aldosterone-producing adenoma.
- **2° hyperaldosteronism:** Caused by renin-secreting tumors, renovascular disease such as renal artery stenosis and malignant hypertension, and edematous states with ↓ arterial volume (HF, cirrhosis, nephrotic syndrome).

History/PE

Presents with hypertension, hypokalemia (causes symptoms of muscle weakness and can cause arrhythmia), metabolic alkalosis, and mild hypernatremia.

Diagnosis

- **Best initial tests:** Plasma renin activity (PRA) and plasma aldosterone concentration (PAC).
  - Look for low PRA, resistant hypertension, and a PAC that is inappropriately high for the PRA (PAC/PRA ratio > 20).
  - Saline infusion confirms diagnosis (↑ PAC despite ↑ Na levels).
- CT scan can help differentiate between unilateral adenoma vs bilateral adrenal hyperplasia.
- Confirm diagnosis with adrenal venous sampling to measure aldosterone level.

Treatment

- Surgical adrenalectomy for unilateral adrenal adenoma.
- Treat bilateral adrenal hyperplasia medically with spironolactone.

Prolactinoma

The most common functioning pituitary tumor; characterized by hypersecretion of prolactin.

History/PE

- ↓ GnRH leads to ↓ follicle-stimulating hormone and luteinizing hormone, which ↓ progesterone and estrogen levels (testosterone in males).
- Presents differently in men and women; usually appears later in men.
  - Women typically present with galactorrhea and amenorrhea in the absence of pregnancy and with osteopenia due to ↓ estrogen.

Q 1

A 60-year-old man with a history of erectile dysfunction presents with headaches and associated temporal field visual loss. Lab testing reveals ↑ prolactin levels. What is the imaging test of choice?

Q 2

A 40-year-old woman with a history of difficult-to-control hypertension presents with a headache. A review of systems reveals associated palpitations and diaphoresis. On exam, she is found to have a BP of 200/100. What lab test will yield the suspected diagnosis?

KEY FACT

MRI is the best imaging method to identify mass lesions.

KEY FACT

Always check a pregnancy test in women with amenorrhea and galactorrhea!

- Men develop impotence, ↓ libido, and often, with larger adenomas, symptoms related to mass effect (eg, CN III palsy, diplopia, temporal field visual loss, headache).

Differential

Pregnancy, hypothyroidism, stress, nipple stimulation. Drugs including antipsychotics (haloperidol, phenothiazines), antiemetics (metoclopramide).

Diagnosis

MRI to identify mass lesions (see Figure 5-8).

Treatment

- **First line:** Dopamine agonists (cabergoline, bromocriptine), which ↓ the size and secretion of > 90% of lactotroph adenomas.
- **Second line:** Transsphenoidal surgery if medical therapy is not tolerated or if the tumor is large.
- Asymptomatic patients without hypogonadism can be followed with serial prolactin levels.

Acromegaly

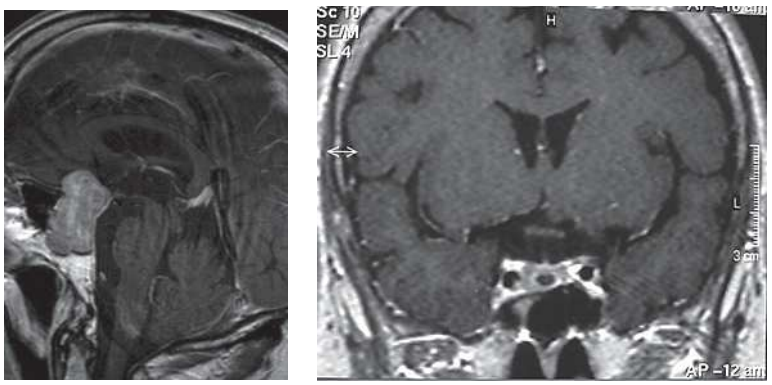
Abnormal growth of bones and soft tissue resulting from ↑ growth hormone levels, most commonly caused by a functional pituitary tumor. Excess growth hormone may also cause DM and hypertension.

History/PE

Patients may notice ↑ ring size, ↑ hat size, ↑ shoe size.

Diagnosis

- **Best initial test:** Serum insulin-like growth factor (IGF)-1 level. Growth hormone (GH) stimulates production of IGF. Unlike GH, IGF-1 levels have little variability based on sleep or food intake.



A B

FIGURE 5-8. Pituitary adenomas. (**A**) Macroadenoma. Sagittal post-contrast MRI shows a large, heterogeneously enhancing mass in the midline expanding the sella and extending into the anterior cranial fossa of a 42-year-old woman with loss of peripheral vision. (**B**) Microadenoma. Brain MRI shows mass measuring 8 × 6 mm. (Image A reproduced with permission from USMLE-Rx.com; image B reproduced from Talaei A et al. *J Med Case Rep.* 2014;8:38.)

1 **A**

MRI to assess the pituitary for possible prolactinoma.

2 **A**

Urine- or plasma-free metanephrines and normetanephrines.

- **Next best test:** Oral glucose tolerance test. Take measurement of GH before and 2 hours after ingestion of 75 g of glucose. Failure to suppress growth confirms diagnosis.
- Conduct MRI to look for pituitary mass.

Treatment

- Transsphenoidal resection of adenoma is curative.
- Masses that are not amenable to resection should be treated with somatostatin analogues such as octreotide or lanreotide.

Multiple Endocrine Neoplasia

A group of familial autosomal dominant syndromes (see Table 5-9).

PHEOCHROMOCYTOMA

A catecholamine-secreting tumor (also called adrenal medullary tumor) that secretes epinephrine, norepinephrine, and dopamine. Most are benign; however, 10–15% are malignant and can present with metastatic disease.

History/PE

Clinical syndrome that typically presents with hypertension, headaches, palpitations, and sweating.

Diagnosis

- **Best initial test:** Urinary or plasma free metanephrines and normetanephrines.
- Confirm diagnosis with CT or MRI (see Figure 5-9).

Treatment

- **First line:** Phenoxybenzamine is an irreversible α-blocker. This must be followed by a β-blocker (propranolol) to prevent hypertensive crisis.
- Surgical resection is curative if tumor is not metastatic.

MNEMONIC

The 3 P's of 1° MEN:

Parathyroid hyperplasia
Pancreatic islet cell tumor
Pituitary adenoma

KEY FACT

Screen for pheochromocytoma with 24-hour urinary fractionated metanephrines.

TABLE 5-9. Characteristics of MEN Syndromes

Syndrome	Type	Characteristics
Wermer syndrome	MEN 1	Parathyroid hyperplasia Pancreatic islet cell tumor Pituitary adenoma
Sipple syndrome	MEN 2A	Parathyroid hyperplasia Thyroid medullary cancer Pheochromocytoma
	MEN 2B	Thyroid medullary cancer Pheochromocytoma Mucocutaneous neuromas Ganglioneuromatosis of the colon Marfan-like habitus

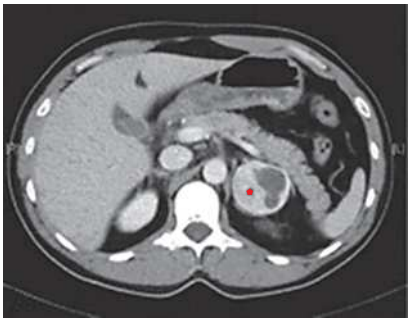


FIGURE 5-9. Pheochromocytoma. Abdominal CT shows a left adrenal mass of 50 mm in diameter with rounded, well-defined edges, and hyperdense areas of cystic necrosis inside (*asterisk*). (Reproduced from Martinez-Quintana E et al. *Int J Endocrinol Metab.* 2013;11(1):48-51.)

NOTES

CHAPTER 6

ETHICS AND STATISTICS

Basic Principles

Be familiar with the following principles:

- **Autonomy:** The right to make decisions for oneself in accordance with one's own system of morals and beliefs.
- **Paternalism:** Providing for your perception of patients' needs without their input.
- **Beneficence:** Action intended to bring about a good outcome.
- **Nonmaleficence:** Action not intended to bring about harm.
- **Truth telling:** Revealing all pertinent information to patients.
- **Proportionality:** Ensuring that a medical treatment or plan is commensurate with the illness and with the goals of treatment.
- **Distributive justice:** Allocation of resources in a manner that is fair and just, though not necessarily equal.

KEY FACT

Patients have the right to refuse care as long as they can understand and articulate the risks and benefits.

Autonomy

INFORMED CONSENT

Involves discussing diagnoses and prognoses with patients as well as any proposed treatment, its risks and benefits, and its alternatives. Only with such information can a patient reach an informed decision. Do not conceal a diagnosis from a patient, as doing so would violate the principle of truth telling. However, respect your patients' wishes if they ask you to share only certain things with them. Under emergent circumstances, if a patient's wishes are unknown, consent is implied.

RIGHTS OF MINORS

The treatment of patients < 18 years of age requires parental consent unless:

- They are emancipated (ie, financially independent, married, pregnant, raising children, living on their own, or serving in the armed forces).
- They are requesting contraception or treatment of pregnancy, sexually transmitted diseases, or psychiatric illness. Note that many states require parental consent or notice for termination of pregnancy in a minor.

Most Step 3 exam questions on parental consent will deal with situations such as those cited above. In general, this means that for the Step 3 exam, the governing principle should be to let minors make their own decisions.

Competency

COMPETENCY VS CAPACITY

The terms "competency" and "capacity" should not be used interchangeably. Competency is a legal determination made only by a court, whereas capacity is a clinical assessment. Both capacity and competency involve the doctor's assessment of a patient's ability to think, reason, and act rationally (though not necessarily wisely). Incapacity may be temporary and situational; it is applied to a specific clinical question/scenario (eg, "can the patient refuse a platelet infusion despite his untreated schizoaffective disorder") and is not broadly

assigned (eg, "this patient does not have capacity"). Incompetence is more permanent (eg, severe dementia), and incompetent patients are generally assigned a surrogate or guardian by the court.

DETENTION AND USE OF RESTRAINTS

Psychiatric patients may be involuntarily hospitalized only if they are a danger to themselves or to others (in accordance with the principle of beneficence). The use of restraints can be considered if a patient is at risk of doing harm to self or others, but such use must be evaluated on at least a daily basis.

DURABLE POWER OF ATTORNEY FOR HEALTH CARE

Durable power of attorney (DPoA) has two related meanings. First, it can refer to a document signed by the patient assigning a surrogate decision maker if he or she becomes incapacitated. Second, it can refer to the person to whom that authority has been granted.

SURROGATE/PROXY

A surrogate or proxy is defined as an alternate decision maker who is designated by the patient (or DPoA) and charged with making decisions in accordance with the patient's preferences.

Confidentiality

IMPORTANCE OF CONFIDENTIALITY (AND HIPAA)

Maintaining the confidentiality of patient information is critical. Violations are unethical, may have legal implications, and may irreparably harm the patient-physician relationship. The Health Insurance Portability and Accountability Act of 1996 (HIPAA) outlines rules and guidelines for preserving patient privacy.

WHEN TO VIOLATE CONFIDENTIALITY

If a physician learns about a threat to an individual's life or well-being (ie, a danger to self or to others), violating confidentiality is mandatory. In a similar manner, information about child abuse or elder abuse must be reported. Intimate partner violence is not a mandated reportable condition.

REPORTABLE CONDITIONS

The list of reportable conditions varies by state but often includes HIV/AIDS, syphilis, gonorrhea, chlamydia, TB, mumps, measles, rubella, smallpox, and suspected bioterrorist events. Such reporting is mandatory, is anonymous, and does not constitute a violation of patient confidentiality.

ASKING FOLLOW-UP QUESTIONS

Follow-up questions should be used to clarify unclear issues, such as which family members can be included in discussions of care, who is the primary surrogate, and what patients want to know about their own conditions.

KEY FACT

Capacity can be assessed by any doctor, but it often becomes a psychiatric consult if unclear.

Q

A 22-year-old Jehovah's Witness presents with GI bleeding but states that he does not want a blood transfusion. His hematocrit falls from 40 to 22%, and his BP falls as well. The patient is urged to accept lifesaving treatments but refuses. When his BP reaches a critical level, one of his physicians initiates plans to transfuse. The rest of the team vetoes the plan. What ethical principles are involved, and which principle trumps the other?

End-of-Life Care

Patients in the end stages of a terminal illness have the right to obtain medical treatment that is intended to preserve human dignity in dying. The best means of reaching an agreement with the patient and family regarding end-of-life care is to continue to talk about the patient's condition and to resolve decision-making conflicts. Ultimately, this is the same task that an ethics consultant would attempt to perform for the physician and the patient.

There is a growing body of literature addressing the importance of cultural issues in end-of-life care. In the United States, emphasis is placed on patient autonomy, full disclosure of medical information, and shared decision making. However, members of other cultures may lend more credibility to family-based decisions, particular methods of diagnosis communication, and the importance of subjective aspects of illness. It is important to elicit and respect these cultural frameworks and dynamics in end-of-life care.

KEY FACT

The Elisabeth Kübler-Ross psychological stages at the end of life are denial, anger, bargaining, depression, and acceptance.

ADVANCE DIRECTIVES

Advance directives are oral or written instructions regarding what a patient would want in the event that the patient loses capacity to make health-care decisions. These instructions can be detailed or broad. Oral statements are ethically binding but are not legally binding in all states. Remember that an informed, competent adult can refuse treatment even if it means that doing so would lead to death. Such instructions must be honored.

DO NOT RESUSCITATE ORDERS/CODE STATUS

KEY FACT

Do not resuscitate ≠ do not treat!

The express wishes of a patient (eg, "I do not want to be intubated") supersede the wishes of family members or surrogates. Physicians should inquire about and follow DNR orders during each hospitalization. If code status has not been addressed and the matter becomes relevant, defer to the surrogate.

PAIN IN TERMINALLY ILL PATIENTS

Terminally ill patients are often inadequately treated for pain. Prescribe as much narcotic and non-narcotic medication as needed to relieve patients' pain and suffering. Do not worry about addiction in this setting. Two thirds of terminally ill patients reported moderate to severe pain in the last 3 days of life.

THE PRINCIPLE OF "DOUBLE EFFECT"

Actions can have more than one consequence, some intended, others not. Unintended medical consequences are acceptable if the intended consequences are legitimate and the harm proportionately smaller than the benefit. For example, a dying patient can be given high doses of analgesics even if it may unintentionally shorten life.

PERSISTENT VEGETATIVE STATE

Defined as a state in which the brainstem is intact, and the patient has sleep-wake cycles, but there is no awareness, voluntary activity, or ability to interact with the environment. Reflexes may be normal or abnormal. Some patients survive this way for 5 years or more, with the aggregate annual cost reaching into the billions of dollars.

A

This is a conflict between beneficence and autonomy. The physician aims to bring a good outcome for the patient (beneficence), but the patient is deciding in accordance with his belief system (autonomy). The principle of autonomy trumps beneficence in this situation.

QUALITY OF LIFE

Quality of life refers to a subjective evaluation of a patient's current physical, emotional, and social well-being. This must be evaluated from the perspective of the patient.

PHYSICIAN-ASSISTED SUICIDE AND EUTHANASIA

Physician-assisted suicide is currently legal only in six states (WA, OR, MT, VT, CA, CO) and refers to physicians prescribing medication to hasten death. Each state has slightly different criteria; generally, patients must be informed and competent, have a prognosis of 6 months or less, and must be able to self-administer the drug. Euthanasia refers to the physician directly participating in the administration of medication to end life.

KEY FACT

Euthanasia is illegal in all states.

PALLIATION AND HOSPICE

Palliative care focuses on reducing symptom burden and improving quality of life for patients with serious medical conditions, such as cancer, heart failure, chronic obstructive pulmonary disease, and amyotrophic lateral sclerosis (ALS). A patient may still undergo treatment with curative intent and receive palliative care. Hospice is a related specialty that focuses on providing this care in patients who are no longer receiving curative treatment. Both involve interdisciplinary collaboration (MD, RN, chaplain, social worker) to manage the patient's psychosocial and physical well-being in a manner that preserves dignity and maximizes comfort.

KEY FACT

Palliative care is appropriate for any patient with a high symptom burden, even those with a good prognosis. Hospice is appropriate for patients with a prognosis of 6 months or less.

WITHDRAWAL OF TREATMENT

Withdrawal of treatment is the removal of life-sustaining treatment and is legally and ethically no different from never starting treatment. The decision to withdraw treatment may come from the patient, an advance directive, a DPoA, or—absent any of these—the patient's closest relative and/or a physician. It is easiest when all parties are in agreement, although this is not required. When there is conflict, the patient's wishes take precedence. In futile cases or those involving extreme suffering, a physician may withdraw or withhold treatment; if the family disagrees, the physician should seek input from an ethics committee or obtain a court's approval.

Biostatistics

Not everyone with a given disease will test positive for that disease, and not everyone with a positive test result has the disease.

SENSITIVITY AND SPECIFICITY

Sensitivity is the probability that a person with a disease will have a positive result on a test (true positive rate). Specificity is the probability that a person without the disease will have a negative result on a test (true negative rate). High specificity is desirable for a confirmatory test.

Ideally, a test will be highly sensitive and specific, but this is rare. A test that is highly sensitive but not specific will yield many false positives, whereas one that is highly specific but not sensitive will yield many false negatives.

KEY FACT

Remember: sense (sensitivity) who does have a disease; specify (specificity) who does not.
SPIN: SPecificity rules IN
SNOUT: SeNsitivity rules OUT

Q

You have a test that has a sensitivity of 0.95 and a specificity of 0.95. How helpful is this test in your diagnostic reasoning for a disease prevalence of 50%?

PREDICTIVE VALUES

Positive predictive value (PPV) is the probability that a person with a positive test result has the disease (true positives/all positives; see Table 6-1). If a disease has a greater prevalence, then the PPV is higher. Negative predictive value (NPV) is the probability that a person with a negative test result is disease free (see Table 6-1). A test has a higher NPV value when a disease has a lower prevalence. It is important to note that PPV and NPV can be determined only if the incidence in the sample is representative of the population. For example, if the data for Table 6-1 are derived from a case-control study, then the PPV and NPV cannot be calculated. Generally, one needs a cohort study design to get PPV or NPV.

INCIDENCE

Defined as the number of new cases of a given disease per year; for example, four cases of X per year.

PREVALENCE

Defined as the total number of existing cases of a given disease in the entire population; for example, 20 people have X (right now).

ABSOLUTE RISK

Defined as the probability of an event in a given time period; for example, 0.1% chance of developing X in 10 years.

RELATIVE RISK

Used to evaluate the results of cohort (prospective) studies. The relative risk (RR) compares the incidence of a disease in a group exposed to a particular risk factor with the incidence in those not exposed to the risk factor (see Table 6-2). An RR < 1 means that the event is less likely in the exposed group; conversely, an RR > 1 signifies that the event is more likely in that group.

ODDS RATIO

Used in case-control (retrospective) studies. The odds ratio (OR) compares the rate of exposure among those with and without a disease (see Table 6-2). It is considered less accurate than RR, but in rare diseases the OR approximates the RR.

KEY FACT

RR is used in prospective studies to calculate risk of developing a disease with a particular exposure. OR is used in retrospective studies to look at who has the exposure from among those who are known to have the disease.

A

Very helpful. Both positive and negative results make significant changes in disease probability and can confirm or disprove a diagnosis. This is the situation in which a laboratory test is most helpful. The test would not be helpful for a disease prevalence of 1%; most of the positives will be false positives, so further evaluation will be necessary. It would not be helpful for a disease prevalence of 90%; the positive result adds nothing to your clinical suspicion, and a negative test is likely to be a false negative.

TABLE 6-1. Determination of PPV and NPV

	Disease Present	No Disease	
Positive test	a	b	PPV = a/(a + b)
Negative test	c	d	NPV = d/(c + d)
	Sensitivity = a/(a + c)	Specificity = d/(b + d)	

TABLE 6-2. Determination of RR and OR

	Disease Develops	No Disease	
Exposure	a	b	RR = [a/(a + b)]/[c/(c + d)]
No exposure	c	d	OR = ad/bc

ABSOLUTE RISK REDUCTION OR ATTRIBUTABLE RISK

Measures the risk accounted for by exposure to a given factor, taking into account the background of the disease. It is useful in randomized controlled trials. Numerically, absolute risk reduction (ARR) = the absolute risk (rate of adverse events) in the placebo group minus the absolute risk in treated patients.

RELATIVE RISK REDUCTION

Also used in randomized controlled trials; this is the ratio between two risks. Numerically, relative risk reduction (RRR) = [the event rate in control patients minus the event rate in experimental patients] plus the event rate in control patients.

RRR can be deceptive and is clinically far less important than ARR. Consider a costly intervention that reduces the risk of an adverse event from 0.01% to 0.004%. ARR is 0.01 − 0.004 = 0.006%, but RRR is (0.01 − 0.004)/0.01 = 0.6, or 60%! Would you order this intervention?

KEY FACT

ARR and RRR give different values and should not be confused. ARR is a much better measure of benefit; because it is a ratio, RRR can look deceptively large. Watch out for drug advertising that touts RRR.

NUMBER NEEDED TO TREAT

The number of patients needed to treat (NNT) = who would need to be treated to prevent one event. NNT = 1/ARR. In the example above, the NNT is 167.

STATISTICAL SIGNIFICANCE/*P* VALUE

The *P* value expresses the likelihood that an observed outcome was due to random chance. A *P* value < .05 is generally accepted as indicating that an outcome is statistically significant.

CONFIDENCE INTERVAL

Like the *P* value, the confidence interval (CI) expresses the certainty that the observation is real or is a product of random chance. Used with ORs and RR, the 95% CI indicates that the observed risk or odds have a 95% chance of being within the interval. Thus, in Figure 6-1, the RR of cancer with smoking is 2.0 with a 95% CI of 1.3–3.5—meaning that the observed RR of cancer was 2.0, and there is a 95% certainty that the actual RR of cancer from smoking falls somewhere between 1.3 and 3.5.

KEY FACT

If a 95% CI includes 1.0, the results are not significant. Therefore, if an RR is 1.9, but the 95% CI is 0.8–3.0, the RR is not significant.

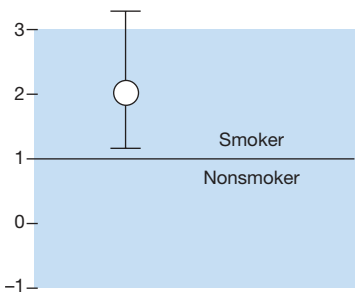


FIGURE 6-1. Relative risk of cancer.

Study Design

Statistical analyses are used as a means of assessing relationships between events and outcomes. They do not prove irrefutably that a relationship exists but point to the likelihood of this being the case. The validity of the results depends on the strength of the design.

KEY FACT

Beware! Many of these types of surveys are subject to recall bias, where patients with a disease may be more likely to report a previous exposure.

SURVEYS

Self-reports of symptoms, exposures, feelings, and other subjective data. Such data may be analyzed with descriptive statistics or qualitative methodologies.

PROSPECTIVE AND RETROSPECTIVE STUDIES

- **Prospective studies** assess future outcomes relating to present or future events; this enables the study designer to control for bias and to modify inputs/exposures.
- **Retrospective studies** relate to outcomes from past events. They may be less reliable than prospective studies.

COHORT STUDIES

In a cohort study (see Figure 6-2), a population is observed over time, grouped by exposure to a particular factor, and watched for a specific outcome. Such studies are not good for rare conditions. Studies can be prospective or retrospective. Use RR to interpret results. Examples include the Nurses' Health Study and the Framingham Heart Study.

CASE-CONTROL STUDIES

A case-control study (see Figure 6-3) is a retrospective study involving a group of people with a given disease and an otherwise similar group of people without the disease who are compared for exposure to risk factors. Case-control studies are good for rare diseases. Use OR to interpret results.

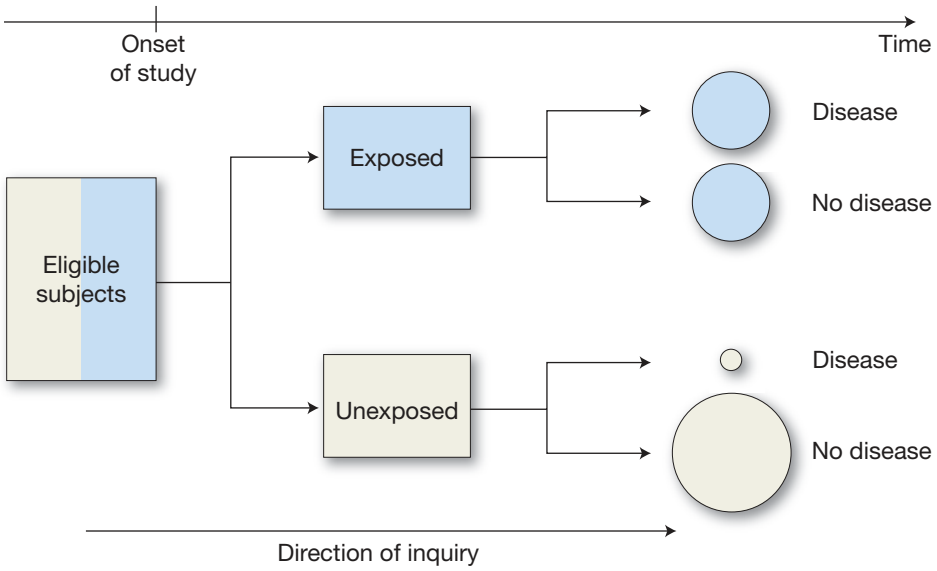


FIGURE 6-2. Schematic diagram of a cohort study. Shaded areas in the diagram represent exposed persons; unshaded areas represent unexposed persons. (Reproduced with permission from Greenberg RS et al. *Medical Epidemiology,* 4th ed. New York: McGraw-Hill, 2005, Fig. 8-2.)

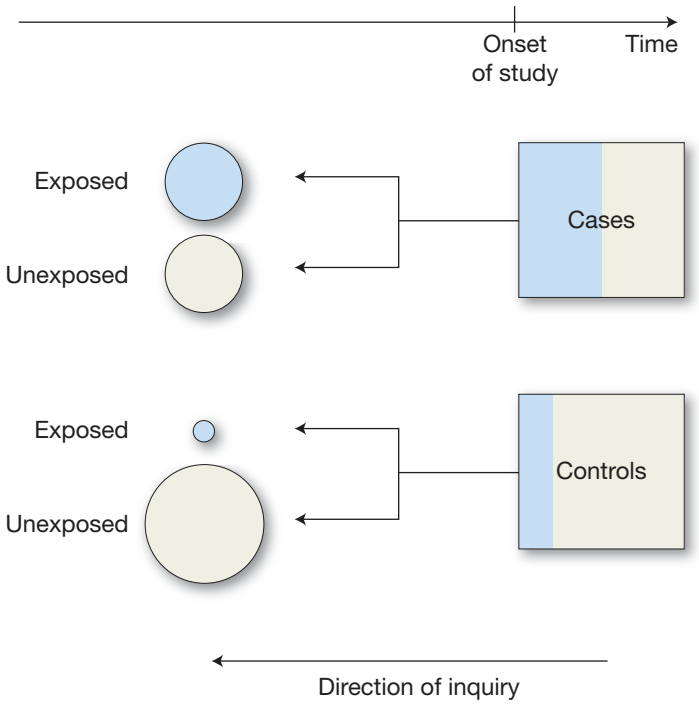


FIGURE 6-3. Schematic diagram of a case-control study. (Reproduced with permission from Greenberg RS et al. *Medical Epidemiology,* 4th ed. New York: McGraw-Hill, 2005, Fig. 9-1.)

RANDOMIZED CONTROLLED TRIALS

A prospective study that randomly assigns participants to a treatment group or to a placebo group (see Figure 6-4). The placebo group and the treatment group are then compared to determine if the treatment made a difference. The double-blind randomized controlled trial is the gold standard of experimental design.

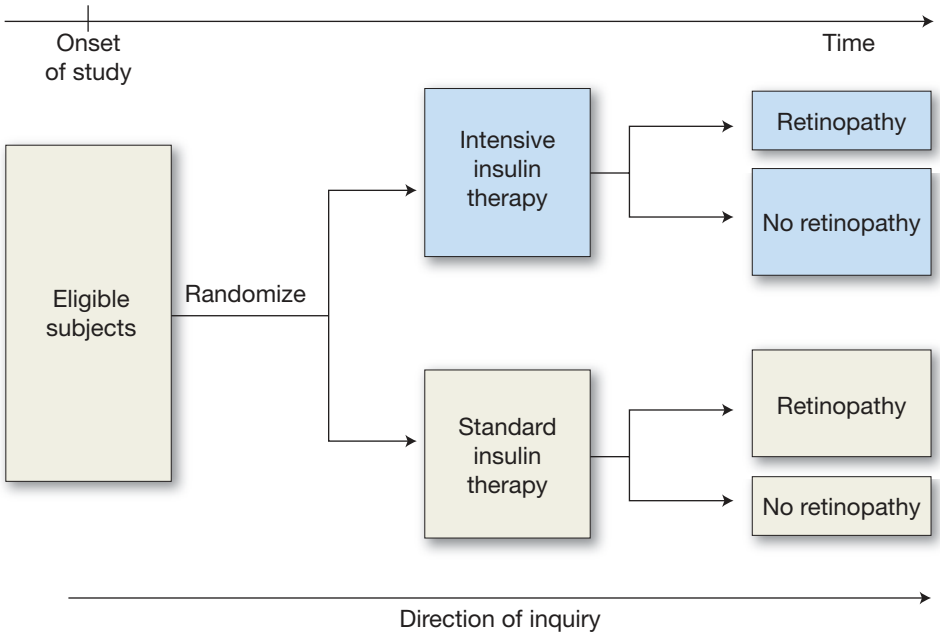


FIGURE 6-4. Schematic diagram. (Reproduced with permission from Greenberg RS et al. *Medical Epidemiology,* 4th ed. New York: McGraw-Hill, 2005, Fig. 7-2.)

NOTES

CHAPTER 7

GASTROENTEROLOGY

Esophageal Pathology

Broadly defined as dysphagia, or difficulty swallowing food.

History/PE

Patients may complain of food that "sticks" or "hangs up." May have associated odynophagia (pain with swallowing).

Differential

If difficulty is with solids alone, consider the following:

- **Lower esophageal ring (Schatzki ring):** Characterized by intermittent symptoms or sudden obstruction with a food bolus due to an esophageal stricture, often associated with a hiatal hernia.
- **Zenker diverticulum:** Outpouching above the upper esophageal sphincter. Presents with foul-smelling breath and food regurgitation.
- **Plummer-Vinson syndrome:** Triad of dysphagia, cervical esophageal webs, and iron-deficiency anemia. Associated with esophageal cancer.
- **Peptic stricture:** Progressive symptoms with long-standing heartburn (see Figure 7-1A).
- **Carcinoma**: Progressive symptoms in an older patient, often with weight loss.
  - Squamous cell carcinoma (SCC): ↑ Risk with tobacco, ethanol, poor diet.
  - Adenocarcinoma: ↑ Risk with tobacco, obesity, gastroesophageal reflux disease (GERD), poor diet.
- **Esophagitis:** Inflammation can be 2° to a number of causes:
  - **Gastroesophageal reflux:** Reflux of acid and stomach contents through the lower esophageal sphincter (LES).
  - **Pill esophagitis:** Usually caused by taking a pill with little or no fluid before lying down. Associated medications: doxycycline, NSAIDs, and bisphosphonates.
  - **Opportunistic infections:** *Candida*, herpes simplex virus (HSV), and cytomegalovirus (CMV). Usually occur in immunocompromised patients (eg, HIV, chemotherapy, diabetes).
  - **Eosinophilic esophagitis:** Chronic inflammatory disease mediated by IL-5. Usually found in young men with a history of respiratory allergies.

KEY FACT

Think cancer in older patients with worsening dysphagia, weight loss, and heme ⊕ stools.

If difficulty is with both solids and liquids, consider:

- **Achalasia:** Progressive symptoms that worsen at night with no heartburn. Look for a "bird's beak" on barium swallow (see Figure 7-1B).
- **Esophageal spasm:** Intermittent symptoms with chest pain. Triggered by acid, stress, and hot and cold liquids. Diagnosed by esophageal manometry. Look for "corkscrew esophagus" on barium swallow (see Figure 7-1C).
- **Scleroderma:** Progressive symptoms with heartburn and Raynaud phenomenon. Lower esophageal pressure and aperistalsis of the distal esophagus leads to reflux (**CREST** syndrome: **C**alcinosis cutis, **R**aynaud phenomenon, **E**sophageal dysmotility, **S**clerodactyly, and **T**elangiectasia).

KEY FACT

Think food impaction when a patient has sudden difficulty swallowing—even swallowing saliva.

Diagnosis

Workup includes esophagogastroduodenoscopy (EGD) and/or barium swallow.

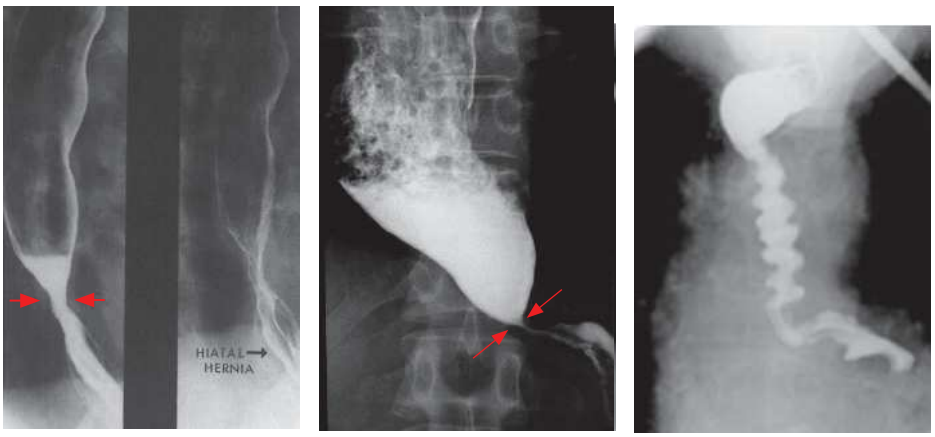


FIGURE 7-1. Esophageal disease on barium esophagram. **(A)** Peptic stricture (*arrow*) secondary to GERD above a hiatal hernia (*right*). **(B)** Achalasia. Note the dilated esophagus tapering to a "bird's beak" narrowing at the LES. **(C)** Esophageal spasm. (Image A reproduced with permission from Chen MY et al. *Basic Radiology,* 2nd ed. New York: McGraw-Hill, 2011, Fig. 10-14. Image B reproduced with permission from Doherty GM. *Current Diagnosis & Treatment: Surgery,* 13th ed. New York: McGraw-Hill, 2010, Fig. 20-5. Image C reproduced with permission from USMLE-Rx.com.)

Gastroesophageal Reflux Disease

Results when the LES is weakened by ↑ pressure or ↓ tone. Risk factors include:

- ↑ **Pressure:** Hiatal hernia, obesity, collagen vascular disease, pregnancy.
- ↓ **Tone:** Alcohol, caffeine, nicotine, chocolate, fatty foods.

History/PE

- Presents with a burning sensation beneath the sternum.
- Symptoms usually worsen after meals, on reclining, and with tight clothes.

Differential

Cardiovascular causes of chest pain, esophageal motility disorders, peptic ulcer.

Diagnosis

For classic symptoms, diagnosis is usually based on response to treatment. EGD and ambulatory pH monitoring are warranted only if therapy fails.

Treatment

- **Lifestyle modification:** Elevate the head of the bed; avoid cigarettes and NSAIDs; promote weight loss.
- **Drugs:** Prescribe antacids, H_2 blockers, or proton pump inhibitors (PPIs). If symptomatic relief is achieved with an H_2 blocker or a PPI, discontinuation of treatment after 8–12 weeks may be successful.
- **Other:**
  - If refractory to medical therapy, consider evaluation for Nissen fundoplication or hiatal hernia repair.
  - Further workup (usually EGD) is warranted for signs or symptoms of more serious disease (eg, weight loss, anemia, heme ⊕ stools, signs of obstruction, advanced age [especially white men > 45 years]).

KEY FACT

H_2 blockers (eg, ranitidine, famotidine) are competitive antagonists of histamine on the H_2 receptor of parietal cells, preventing parietal cells from secreting acid.

KEY FACT

PPIs irreversibly block proton pumps of gastric parietal cells, which form the last stage of gastric acid secretion.

Q 1

A 56-year-old man presents for a routine PE and mentions that he has had increasing difficulty swallowing over the past 6 months, more with solids than with liquids. He adds that he does not drink alcohol. What is the likely diagnosis?

Q 2

A 56-year-old woman presents with abdominal pain that worsens with eating. Two months earlier, she was given a diagnosis of osteoarthritis. What is the likely cause?

Peptic Ulcer Disease

The most common sites of peptic ulcer disease (PUD) are the stomach and duodenum. *Helicobacter pylori* infection and NSAID use are the most common causes. Zollinger-Ellison syndrome, HSV and CMV infections, and cocaine use are less common etiologies.

History/PE

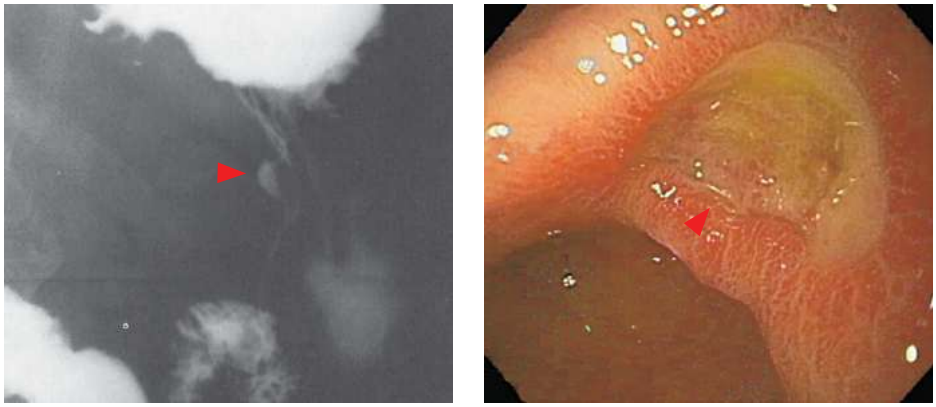
- PUD presents with "gnawing" or "aching" epigastric pain.
- Advanced disease may present with upper GI bleeding, perforation, or penetration into adjacent structures (eg, the pancreas, vascular structures such as the superior mesenteric artery, and the bile ducts), leading to hemodynamic instability and associated symptoms such as pancreatitis.
- Symptoms are often distinguished by disease site:
  - **Duodenal ulcers:** Pain is relieved by eating.
  - **Gastric ulcers:** Pain worsens with food.
- **Red flags:** Advanced age (> 55 years), dysphagia, persistent vomiting, anemia, GI bleeding (heme + stool), abdominal masses, lymphadenopathy, unintended weight loss, and family history of GI cancer.

KEY FACT

Zollinger-Ellison syndrome, associated with MEN 1, presents with abdominal pain, chronic diarrhea, and ulcer disease. Diagnose with elevated fasting serum gastrin or secretin stimulation test.

Diagnosis

- For healthy patients < 55 years of age without alarm symptoms, assess response to treatment.
- Look for *H pylori* infection in patients < 55 years of age with active PUD, history of PUD, or history of mucosa-associated lymphoid tissue lymphoma or gastric cancer.
  - Urea breath test: Detects active infection and resolution 4-6 weeks after treatment; patients must be off PPIs for 2 weeks and off antibiotics and bismuth for 4 weeks.
  - Fecal antigen test: Useful for initial diagnosis and detecting resolution of infection, but as above, patients must be off antibiotics, PPIs, and bismuth; false positives and false negatives possible after treatment and with hematochezia.



A B

FIGURE 7-2. Gastric ulcer. (**A**) Gastric ulcer on barium upper GI. A benign gastric ulcer can be seen as pooling of contrast (*arrowhead*) extending beyond the adjacent gastric wall. (**B**) Benign gastric ulcer on endoscopy. (Image A reproduced with permission from Longo DL et al. *Harrison's Principles of Internal Medicine,* 18th ed. New York: McGraw-Hill, 2012, Fig. 291-2A. Image B reproduced with permission from Chen MY et al. *Basic Radiology.* New York: McGraw-Hill, 2004, Fig. 10-21.)

1 A

Esophageal adenocarcinoma; unlike SCC of the esophagus, is not associated with alcohol; usually presents as an obstructive lesion causing progressive dysphagia to solids and then liquids

2 A

Gastric ulcer 2° to the use of NSAIDs for joint pain.

- Serum antibody: Detects IgG to *H pylori* but cannot distinguish active from treated infection.
- In older patients, those unresponsive to treatment, or with any alarm symptoms, consider EGD.
- Benign appearing ulcers—smooth and round edge, flat base, exudate—do not need to be biopsied.

Treatment

- Discontinue aspirin and NSAIDs; promote smoking cessation and encourage weight loss.
- Give PPIs to control symptoms, ↓ acid secretion, and heal the ulcer.
- For *H pylori* infection, initiate multidrug therapy. Two of the following drugs may be used—amoxicillin, clarithromycin, or metronidazole—along with a PPI (omeprazole, lansoprazole) for 10–14 days.
- Indications for surgery include recurrent/refractory upper GI bleed, gastric outlet obstruction, recurrent/refractory ulcers, perforation, and Zollinger-Ellison syndrome.

Inflammatory Bowel Disease

Describes two distinct chronic idiopathic inflammatory diseases: Crohn disease and ulcerative colitis (see Table 7-1 and Figures 7-3 and 7-4).

Irritable Bowel Syndrome

A GI disorder characterized by abdominal pain and altered bowel function (diarrhea or constipation), with or without bloating. Possible etiologies include altered gut motor function, autonomic nervous system abnormalities, and psychological factors.

History/PE

- Presents with abdominal pain with complete or incomplete relief with defecation. Pain poorly localized, migratory, and variable in nature.
- Intermittent diarrhea or constipation.
- May also present with a feeling of incomplete rectal evacuation, urgency, passage of mucus, and bloating.

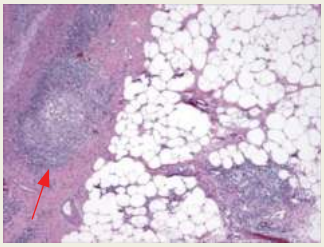
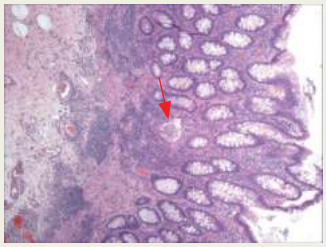
KEY FACT

Pain that is unrelated to defecation or is induced by activity, menstruation, or urination is unlikely to be IBS.

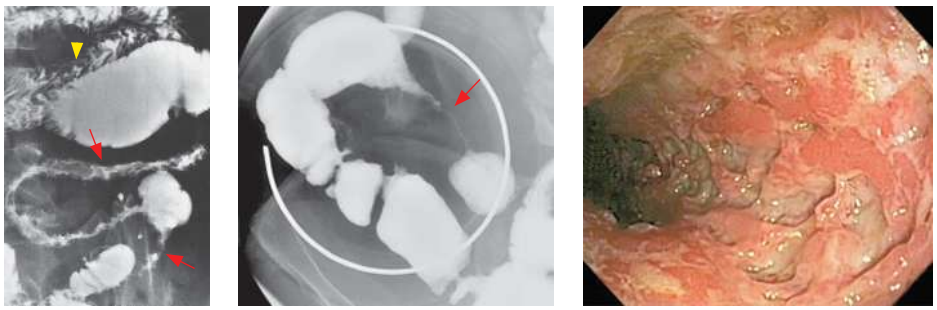
Diagnosis

- A diagnosis of exclusion is based primarily on the history and physical exam. Basic labs to exclude other causes should include CBC, basic metabolic panel, calcium, thyroid-stimulating hormone (TSH), and stool ova and parasites (O&P).
- The Rome IV criteria, used for symptomatic diagnosis, define IBS as recurrent abdominal pain on average at least 1 day/week in the last 3 months, associated with two or more of the following:
  - Related to defecation.
  - Associated with a change in frequency of stool.
  - Associated with a change in the form/appearance of stool.

TABLE 7-1. Crohn Disease vs Ulcerative Colitis

	Crohn Disease	Ulcerative Colitis
Pathology	Skip lesions Transmural inflammation; noncaseating granulomas (**A**), found in 30% of cases, diagnostic if infectious causes are excluded  **A**	Continuous, uniform involvement with a "lead pipe" appearance Limited to mucosa; crypt abscesses (**B**) and microulcerations, but no granulomas  **B**
Anatomic location	Anywhere from the mouth to the anus Most commonly affecting the terminal ileum, small bowel, and colon	Usually involves the rectum but can involve all or part of the colon Does not involve the GI tract outside the colon and rectum
Epidemiology	Bimodal distribution (20s and 50–70) More common among those of Jewish ancestry	Bimodal distribution (15–30 and 60–80) More common among those of Jewish ancestry
Symptoms	GI: Colicky right lower quadrant pain; diarrhea (often with mucus, usually nonbloody); perirectal abscess/fistula; oral ulcers Other: Fever, weight loss, erythema nodosum, pyoderma gangrenosum (see Figure 7-5), iritis and episcleritis, arthritis, gallstones, kidney stones	GI: Cramping abdominal pain, urgency, and bloody diarrhea Other: Weight loss, fatigue, arthritis, uveitis and episcleritis, erythema nodosum, pyoderma gangrenosum (see Figure 7-5)
Diagnosis	Labs: Anemia: Chronic disease or iron, vitamin B_{12}, or folate deficiency Erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP) may be ↑ Anti-*Saccharamycyes cerevisiae* antibody (ASCA) ⊕ Imaging: Cobblestoning and fistulas on barium enema CT may show abscesses, fistulas, and strictures Confirmed with pathologic diagnosis via colonoscopy	Labs: Anemia: Normocytic or iron deficiency ↑ ESR or CRP Perinuclear antineutrophil cytoplasmic antibody (p-ANCA) ⊕ Imaging: Lead-pipe colon and loss of haustra on barium enema Confirmed with pathologic diagnosis via colonoscopy
Treatment	Mild to moderate: Oral corticosteroids +/− azathioprine, 6-mercaptopurine, or methotrexate; limited role of 5-ASA with poor efficacy Refractory disease: IV steroids +/− anti-TNF therapy Rule out perforations, fistulas, megacolon, or abscesses; resection may be needed	Mild: 5-ASA compounds Moderate: Oral corticosteroids +/− azathioprine, 6-mercaptopurine, or methotrexate Refractory disease: IV steroids +/− cyclosporine +/− anti-TNF therapy Rule out toxic megacolon; resection may be needed
Other	Surveillance colonoscopy 8 years after diagnosis to evaluate for colorectal cancer, and at least annually thereafter	Associated with 1° sclerosing cholangitis and autoimmune liver disease Surveillance colonoscopy 8–10 years after diagnosis (unless limited to the rectum) to evaluate for colorectal cancer, at and least annually thereafter

Images A and B reproduced with permission from USMLE-Rx.com.



A B C

FIGURE 7-3. Crohn disease. (**A**) Small bowel follow-through (SBFT) barium study shows skip areas of narrowed small bowel with nodular mucosa (*arrows*) and ulceration. Compare with normal bowel (*arrowhead*). (**B**) Spot compression image from SBFT shows "string sign" narrowing (*arrow*) due to stricture. (**C**) Deep ulcers in the colon of a patient with Crohn disease, seen at colonoscopy. (Image A reproduced with permission from Chen MY et al. *Basic Radiology.* New York: McGraw-Hill, 2004, Fig. 10-30. Image B reproduced with permission from USMLE-Rx.com. Image C reproduced with permission from Longo DL et al. *Harrison's Principles of Internal Medicine,* 18th ed. New York: McGraw-Hill, 2012, Fig. 291-4B.)

Treatment

- High-fiber diet, exercise, and adequate fluid intake.
- Tricyclic antidepressants often used even in the absence of depression, especially in the setting of chronic pain and diarrhea.

Diarrhea

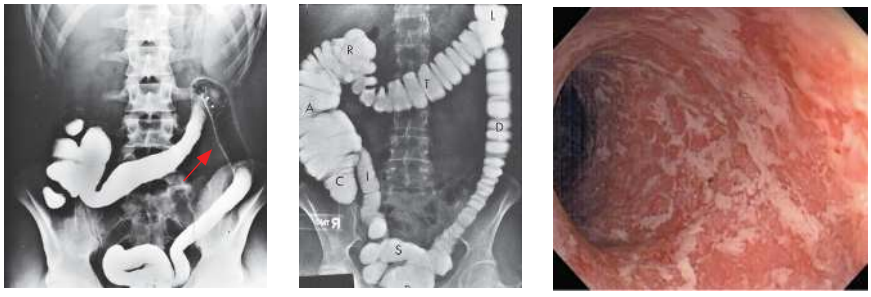
Described as watery consistency and/or ↑ frequency of bowel movements. Typically characterized as acute or chronic.

- **Acute diarrhea:** Duration of < 2 weeks; usually infectious.
- **Chronic diarrhea:** Lasting > 4–6 weeks.

Tables 7-2 and 7-3 outline the etiology, presentation, and treatment of acute and chronic diarrhea.

KEY FACT

If a patient with diarrhea has recently been on antibiotics, think *Clostridium difficile.*



A B C

FIGURE 7-4. Ulcerative colitis. (**A**) Radiograph from a barium enema showing a featureless ("lead pipe") colon with small mucosal ulcerations (*arrow*). Compare with normal haustral markings in (**B**). (**C**) Diffuse mucosal ulcerations and exudates at colonoscopy in chronic ulcerative colitis. (Image A reproduced with permission from Doherty GM. *Current Diagnosis & Treatment: Surgery,* 13th ed. New York: McGraw-Hill, 2010, Fig. 30-17. Image B reproduced with permission from Chen MY et al. *Basic Radiology.* New York: McGraw-Hill, 2004, Fig. 10-10A. Image C reproduced with permission from Longo DL et al. *Harrison's Principles of Internal Medicine,* 18th ed. New York: McGraw-Hill, 2012, Fig. 291-4A.)

Q 1

A 27-year-old man comes to your office complaining of diarrhea and weight loss. He states that his diarrhea often contains mucus but denies any blood in his stool. He also describes having difficulty eating food because of ulcers in his mouth. What is the next step in management?

Q 2

A 30-year-old woman complains of vague, cramping abdominal pain that is improved with defecation. She is recently divorced and expresses concern over custody of her children. What is the likely diagnosis?

TABLE 7-2. Characteristics of Acute Diarrhea

Cause	History	Symptoms/Signs	Labs	Treatment
Bacterial	History may be unremarkable Look for a history of foreign travel or consumption of raw, undercooked, or unpasteurized products A history of recent antibiotic use suggests *C difficile*	Symptoms are often severe Bloody diarrhea suggests enterohemorrhagic *E coli* (EHEC) Patients may complain of fever	Obtain ↑ Fecal WBCs Obtain guaiac ⊕ stool in the case of hemorrhagic disease Culture and sensitivity may reveal the pathogen (be sure to ask specifically to test for EHEC when appropriate) Request a *C difficile* toxin assay when appropriate	Most cases of bacterial diarrhea will resolve with symptomatic treatment (fluids, electrolytes) Avoid antibiotics if possible in light of potentially ↑ release of endotoxin TMP-SMX or macrolides can be used to treat most cases of invasive diarrhea Antibiotics are contraindicated in EHEC Metronidazole or oral vancomycin is used to treat *C difficile* Avoid loperamide
Viral	Family or friends may have similar symptoms	Symptoms are usually milder and of shorter duration than bacterial illness Fever is unusual	Labs are generally nonspecific	Supportive care with loperamide, bismuth, and probiotics may be helpful
Parasitic	*Giardia* is associated with day-care outbreaks and foreign travel *Entamoeba* is associated with foreign travel	Parasitic illnesses can cause prolonged symptoms if left untreated	Obtain ↑ fecal WBCs Check stool O&P smear Consider checking HIV status	Metronidazole is the treatment of choice for most parasitic illnesses

Celiac Sprue

An autoimmune disorder in which an inflammatory response to dietary gluten causes small bowel villous atrophy and crypt hypertrophy, resulting in malabsorption. More common in those of northern European ancestry.

History/PE

- Presents with abdominal discomfort, flatulence.
- Commonly associated with iron-deficiency anemia, with severe cases demonstrating chronic diarrhea, steatorrhea, fractures, coagulopathy.
- Associated with dermatitis herpetiformis and ↑ risk of GI malignancies.

Diagnosis

- Biopsy reveals flattening or loss of villi.
- Antibody assays are ⊕ for tissue transglutaminase IgA (tTG-IgA) and may be falsely ⊖ with IgA deficiency.

Treatment

Institute a gluten-free diet. Gluten is found in most grains in the Western world (eg, wheat, barley, rye, some oats, additives, many prepared foods).

1 **A**

In light of his age and presenting symptoms, this patient needs a colonoscopy and an evaluation for possible Crohn disease.

2 **A**

Irritable bowel syndrome. The patient has pain associated with defecation, and her background points to recent stressors.

TABLE 7-3. Characteristics of Chronic Diarrhea

Type	Characteristics	Causes	Diagnosis	Treatment
Osmotic	↑ Stool osmotic gap Malabsorption associated with bloating and gas	Lactose intolerance Magnesium supplements Sorbitol, lactulose, or mannitol ingestion	Usually made by the history	Stop the offending agent Lactose enzyme tablets can be helpful in those with lactose intolerance
Secretory	Caused by mucosal oversecretion Normal stool osmotic gap	Hormonal stimulation (gastrin, vasoactive intestinal peptide) Viruses Bacterial toxins	Serum gastrin level and secretin stimulation test if a hormonal cause is suspected	Varies with the cause
Exudative	Associated with mucosal inflammation	IBD or celiac disease TB Colon cancer	↑ ESR or CRP Colonoscopy	Treat the underlying cause
Rapid transit	↑ Gut motility	Hyperthyroidism IBS Laxative abuse Carcinoid Antibiotics (erythromycin)	Check TSH Take a thorough history	Treat the underlying cause
Slow transit	↓ Gut motility	Microscopic colitis Diabetes Radiation damage Scleroderma Small bowel bacterial overgrowth	Colonoscopy in addition to history	Treat the underlying cause A short course of antibiotics can be given to patients with bacterial overgrowth

Upper GI Bleed

Bleeding in the section of the GI tract extending from the upper esophagus to the duodenum to the ligament of Treitz. The most common causes include PUD, gastritis, varices (caused by cirrhosis with portal hypertension), and Mallory-Weiss syndrome (caused by excessive vomiting) (see Figure 7-6).

History/PE

- May present with dizziness, lightheadedness, weakness, and nausea.
- Patients may report vomiting blood or dark brown contents (hematemesis—vomiting of fresh blood, clots, or coffee-ground-like material) or passing of black stool (melena—dark, tarry stools composed of degraded blood from the upper GI tract). Severe upper GI bleeds can present as bright red blood in stool (hematochezia).
- Associated with pallor +/− abdominal pain, tachycardia, and hypotension; rectal exam with gross blood or occult guaiac ⊕ stool.
- If patients show signs of cirrhosis (telangiectasias, spider angiomata, gynecomastia, testicular atrophy, palmar erythema, caput medusae), think varices.
- Vital signs reveal tachycardia at 10% volume loss, orthostatic hypotension at 20% blood loss, and shock at 30% loss.

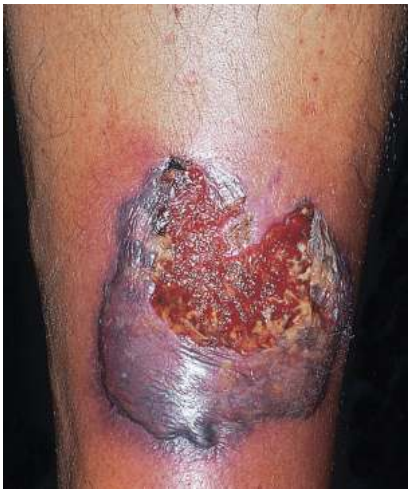
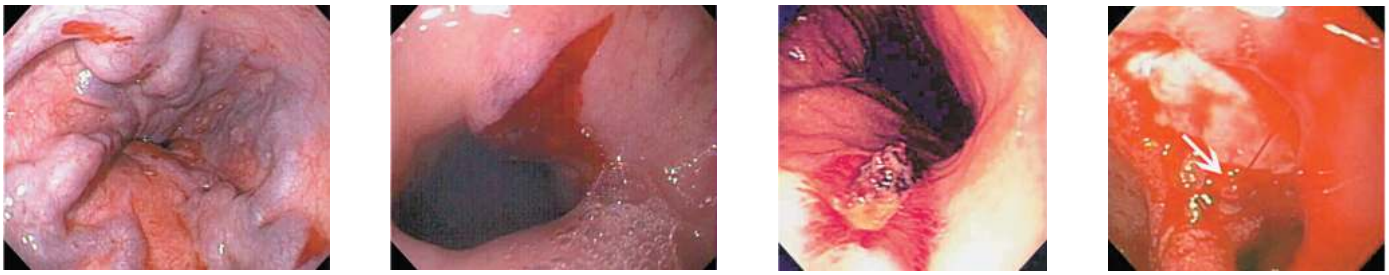


FIGURE 7-5. Pyoderma gangrenosum. (Reproduced with permission from Wolff K et al. *Fitzpatrick's Color Atlas & Synopsis of Clinical Dermatology,* 5th ed. New York: McGraw-Hill, 2005: 153.)



A B C D

FIGURE 7-6. Causes of upper GI bleed at endoscopy. (**A**) Esophageal varices. (**B**) Mallory-Weiss tear. (**C**) Gastric ulcer with protuberant vessel. (**D**) Duodenal ulcer with active bleeding (*arrow*). (Reproduced with permission from Longo DL et al. *Harrison's Principles of Internal Medicine,* 18th ed. New York: McGraw-Hill, 2012, Figs. 291-17, 291-20, and 291-16D and E.)

KEY FACT

Melena is suggestive of, though not exclusive to, an upper GI bleed. Hematochezia is suggestive of, though not exclusive to, a lower GI bleed. Consider GI transit time.

Diagnosis

- Assess the severity of the bleed beginning with patient stabilization.
- Check hematocrit (may be normal in acute blood loss), platelet count, prothrombin time/partial thromboplastin time (PT/PTT), and liver function tests (LFTs). ↑ blood urea nitrogen indicates digestion of blood. Type and screen early.
- If perforation is suspected, obtain upright and abdominal x-rays or a CT scan.
- Endoscopy can be both diagnostic and therapeutic.

Treatment

- Start by stabilizing the patient. Use at least two large-bore peripheral IV catheters. Transfusion and intravascular volume replacement can be initiated if indicated. Treat empirically with a PPI (can be stopped later if not appropriate).
- Consult GI and surgery if bleeding does not stop or if difficulty is encountered with resuscitation 2° to a brisk bleed.
- Treat variceal bleeds with octreotide, PPIs, endoscopy band ligation, or sclerotherapy. If the bleed is severe, balloon tamponade is appropriate, followed by embolization, transjugular intrahepatic portosystemic shunt (TIPS), or a surgical shunt if endoscopic therapy fails.
- To prevent variceal bleeds, treat patients with known varices with nonselective β-blockers (eg, propranolol), obliterative endoscopic therapy, shunting. Consider evaluation for liver transplant in cases of underlying cirrhosis as definitive treatment.
- For PUD, use PPIs, endoscopic epinephrine injection, thermal contact, and ligation with clip placement. Evaluate and treat for *H pylori*.
- Mallory-Weiss tears usually stop bleeding spontaneously.
- Treat esophagitis/gastritis with PPIs and avoidance of inciting causes (aspirin, NSAIDs, alcohol, bisphosphonates).

Lower GI Bleed

Bleeding that is distal to the ligament of Treitz. Causes include enteritis, mesenteric ischemia, infectious or ischemic colitis, Meckel diverticulum, angiodysplasia, IBD, carcinoma, diverticulosis, polyps, hemorrhoids, and diverticulosis.

History/PE

- Presents with hematochezia.
- Diarrhea, tenesmus, bright red blood per rectum, and maroon-colored stools are also seen.

- As with upper GI bleeds, check vital signs to assess the severity of the bleed. Obtain orthostatics; perform a rectal exam for hemorrhoids, fissures, or a mass.

Diagnosis

- Bleeding usually stops spontaneously; however, colonoscopy should be performed. If the bleed continues, a nuclear medicine scan (99Tc-tagged RBC scan) can be done to detect bleeding if it is > 1.0 mL/min.
- If the bleed is refractory and significant, arteriography or exploratory laparotomy may be done.

Treatment

Although bleeding generally ceases spontaneously, resuscitative efforts should be initiated until the source is found and the bleeding stops.

KEY FACT

Think diverticulosis with painless lower GI bleeding. Think diverticulitis in the presence of left lower quadrant pain without bleeding.

Pancreatitis

Inflammation of the pancreas that is thought to be caused by the release of excessive pancreatic enzymes. Can be acute or chronic. Etiologies include:

- Acute disease:
  - Gallstones and alcohol: Account for 70–80% of acute cases.
  - Other causes: Obstruction (pancreatic or ampullary tumors), metabolic factors (severe hypertriglyceridemia, hypercalcemia), abdominal trauma, endoscopic retrograde cholangiopancreatography (ERCP), infection (mumps, CMV, clonorchiasis, ascariasis), drugs (thiazides, azathioprine, pentamidine, sulfonamides), smoking, genetic mutations.
- **Chronic disease:** Alcohol, cystic fibrosis, a history of severe pancreatitis, idiopathic causes (excluding gallstones).

MNEMONIC

Causes of acute pancreatitis—

GET SMASHED

Gallstones
Ethanol
Trauma
Steroids
Mumps
Autoimmune
Scorpion bites
Hyperlipidemia
ERCP
Drugs

History/PE

- Pancreatitis presents with abdominal pain—typically mid-epigastric—that radiates to the back. The pain may be relieved by sitting forward.
- Nausea, vomiting, and fever are also common.
- Exam reveals mid-epigastric tenderness, guarding, occasionally jaundice, and fever.
- Cullen sign (periumbilical ecchymoses) and Grey Turner sign (flank ecchymoses) reflect retroperitoneal hemorrhage and severe pancreatitis, although they are often seen long after symptoms manifest and the diagnosis has been made.

Diagnosis

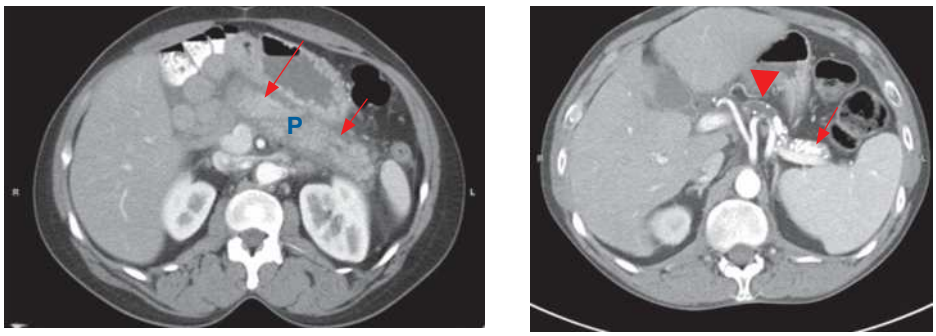
- **Acute pancreatitis:** Often diagnosed by presence by two of the following:
  - Characteristic abdominal pain.
  - Serum lipase and/or amylase > 3X the upper limit of normal.
  - Abdominal imaging with characteristic findings (see Figure 7-7).
- **Chronic pancreatitis:** May not demonstrate lipase/amylase elevation because of diffuse fibrosis.
- ↑ ALT, AST, or alkaline phosphatase levels suggest gallstone pancreatitis.
- Ultrasound may show gallstones, a dilated common bile duct, or sludge in the gallbladder.

Q 1

A 74-year-old woman is transported from a rehabilitation facility where she was being treated for osteomyelitis. She was sent to the hospital after having many foul-smelling bowel movements over the past 2 days. What is the likely cause of her diarrhea, and what is the treatment of choice?

Q 2

A 32-year-old man presents to the ED with sharp abdominal pain. He states that the pain radiates to his back and is constant in nature. He adds that the pain started after he attended a barbecue at which he drank 14 beers. What is your diagnosis, and how should the patient be managed?



A B

FIGURE 7-7. Pancreatitis. Transaxial contrast-enhanced CT images. (**A**) Uncomplicated acute pancreatitis. Peripancreatic fluid and fat stranding can be seen (*arrows*). *P*, pancreas. (**B**) Chronic pancreatitis. Note the dilated pancreatic duct (*arrowhead*) and pancreatic calcifications (*arrow*). (Reproduced with permission from USMLE-Rx.com.)

Treatment

- Acute:
  - Supportive: NPO, IV fluids (patients may need large quantities), and pain management. In the setting of gallstone pancreatitis, ERCP with sphincterotomy is appropriate with common bile duct obstruction or with evidence of cholangitis. If the gallstone has passed, perform a cholecystectomy once the patient is sufficiently stable for surgery.
  - Antibiotics are useful only when there is suspicion for an infected necrotic pancreas (10% of cases; can be seen on CT). Treat with imipenem monotherapy or a fluoroquinolone + metronidazole.
  - Resume diet once pain and nausea have abated. Enteral feeding is preferable to total parenteral nutrition (TPN) if nutritional support is needed in patients with protracted pancreatitis.
- Chronic:
  - Treat malabsorption with pancreatic enzyme and B_{12} replacement.
  - Treat glucose intolerance or diabetes; encourage alcohol abstinence.
  - Manage chronic pain.

KEY FACT

Chronic pancreatitis can result in diabetes and steatorrhea.

Complications

- **Acute:** Pseudocyst, peripancreatic effusions, necrosis, abscess, acute respiratory distress syndrome, hypotension, splenic vein thrombosis.
- **Chronic:** Malabsorption, osteoporosis, diabetes, pancreatic cancer.

1 **A**

This patient was likely receiving long-term antibiotics for osteomyelitis, placing her at risk for *C difficile* infection. She needs to be treated with metronidazole.

Approach to Liver Function Tests

The algorithm in Figure 7-8 outlines a general approach toward the interpretation of LFTs.

2 **A**

The patient likely has alcoholic pancreatitis. Initial management should consist of bowel rest, IV hydration, and pain control.

Gallstone Disease

Gallstones can be symptomatic or asymptomatic. In the United States, they are usually cholesterol stones; hemolytic disorders are associated with pigment stones. Gallstones can provoke cholecystitis (inflammation of the gallbladder) or cholangitis (inflammation of the common bile duct). In trauma patients, burn patients, or those on TPN, acute cholecystitis may occur in the absence of stones (acalculous cholecystitis).

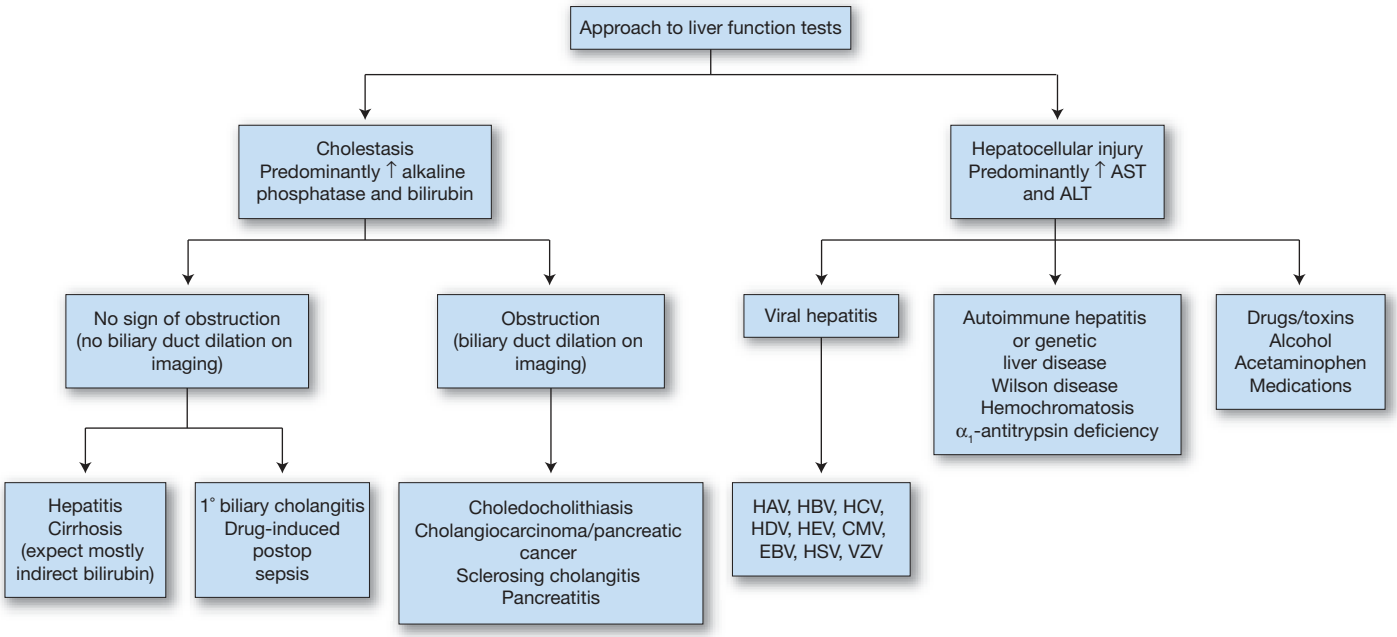


FIGURE 7-8. Abnormal liver function tests.

History/PE

- Most patients with gallstones are asymptomatic.
- May also present as follows:
  - **Biliary colic:** Characterized by episodes of right upper quadrant (RUQ) or epigastric pain that may radiate to the right shoulder. Pain is usually postprandial, lasts about 30 minutes, and is occasionally accompanied by vomiting. Nocturnal pain that awakens the patient is common. Biliary colic is associated with fatty food intolerance and the Murphy sign (inspiratory arrest during deep palpation of the RUQ).
  - **Cholangitis:** Suggested by fever, jaundice (a sign of common bile duct obstruction), and persistent RUQ pain (Charcot triad).
  - **Reynolds pentad:** Charcot triad plus shock and altered mental status may be seen in suppurative cholangitis.

Diagnosis

- Labs reveal leukocytosis and ↑ LFTs.
- Ultrasound is 85–90% sensitive for gallbladder gallstones and cholecystitis (echogenic focus that casts a shadow; pericholecystic fluid = acute cholecystitis). A thickened gallbladder wall and biliary sludge are less specific findings (see Figure 7-9).
- If ultrasound is equivocal and suspicion for acute cholecystitis is high, proceed to a hepato-iminodiacetic acid (HIDA) scan. A ⊖ HIDA indicates no obstruction in the gallbladder. False positives are common.

Treatment

- Acute cholecystitis:
  - IV antibiotics (generally a third-generation cephalosporin plus metronidazole in severe cases), IV fluids, and electrolyte replacement.
  - Early cholecystectomy within 72 hours with an intraoperative cholangiogram to look for common bile duct stones. For patients who are high-risk surgical candidates, elective surgery may be appropriate if the clinical condition allows.

KEY FACT

Symptoms of cholangitis:
- RUQ pain.
- Fever.
- Jaundice.

MNEMONIC

Risk factors for cholecystitis—

The 5 Fs

Fat (BMI ≥ 30)
Female
Forty or older
Fair-skinned
Fertile

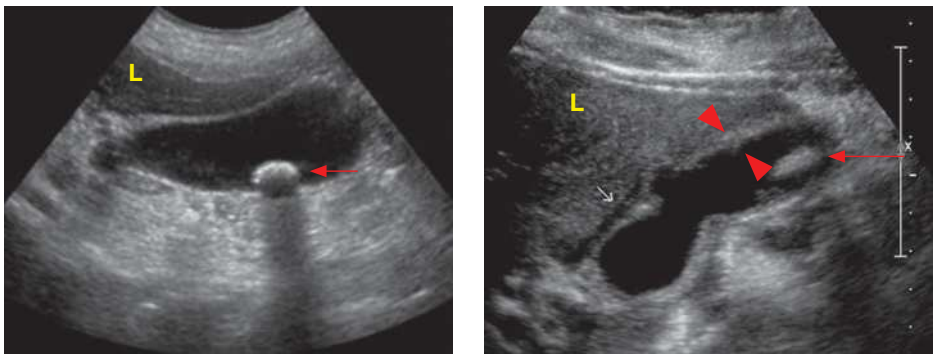


FIGURE 7-9. Gallstone disease. **(A)** Cholelithiasis. Ultrasound image of the gallbladder shows a gallstone (*arrow*) with posterior shadowing. **(B)** Acute cholecystitis. Ultrasound image shows a gallstone (*red arrow*), a thickened gallbladder wall (*arrowheads*), and pericholecystic fluid (*white arrow*). *L*, liver. (Reproduced with permission from USMLE-Rx.com.)

- For patients who are not candidates for surgery, consider a percutaneous biliary drain.
- Cholangitis:
  - Admission, NPO, hydration, pressors if needed, IV antibiotics (ciprofloxacin is preferred).
  - For very ill patients who are not responsive to medical treatment, urgent next-day ERCP with endoscopic sphincterotomy may be needed. Other emergency options include ERCP with stent placement, percutaneous transhepatic drainage, and operative decompression.

Viral and Nonviral Hepatitis

May be acute or chronic, self-limited symptomatic; may not be detected until years after the initial infection.

History/PE

- In acute cases, patients may present with anorexia, nausea, vomiting, malaise, and fever, but are frequently asymptomatic.
- Exam is often normal but may reveal an enlarged and tender liver, dark urine, and jaundice.

Differential

- With a high level of transaminase elevation (> 10–20 times the upper limit of normal), consider acute viral infection as well as ischemia ("shock liver"), acute choledocholithiasis, autoimmune hepatitis, or toxic exposure (acetaminophen).
- With moderate transaminase elevation, consider the most common cause, nonalcoholic fatty liver disease. Also consider chronic viral infection, mononucleosis, CMV, 2° syphilis, drug-induced illness, alcohol, Budd-Chiari syndrome, hemochromatosis, celiac disease, IBD, right-sided heart failure, and muscle damage (eg, rhabdomyolysis).

KEY FACT

Risk of cirrhosis and hepatocellular carcinoma is ↑ with chronic hepatitis B virus (HBV).

Diagnosis

- Clinical presentation in the setting of ↑ transaminases.
- Conduct serology and/or PCR testing to confirm a specific virus (see Figure 10 and Tables 7-4 and 7-5).

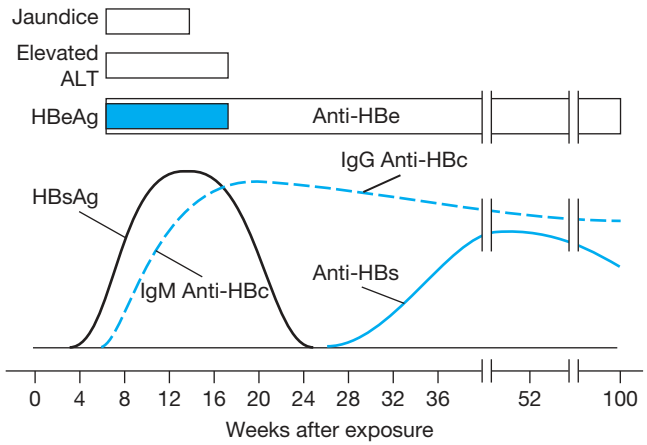


FIGURE 7-10. Natural history of HBV infection. (Reproduced with permission from Stern SD et al. *Symptom to Diagnosis: An Evidence-Based Guide,* 2nd ed. New York: McGraw-Hill, 2010, Fig. 22-2.)

- If the cause cannot be determined, liver biopsy may be helpful.
- RUQ ultrasound may be performed to see if the liver is enlarged in acute hepatitis (vs cirrhotic nodular liver in the advanced disease state).

Treatment

- Treat according to subtype as outlined in Table 7-5.
- Avoid hepatotoxic agents and elective surgery. Use hepatically metabolized drugs with caution (eg, opiates).
- Although most symptoms resolve in 3–16 weeks, LFTs may remain ↑ for much longer.

TABLE 7-4. Viral Hepatitis and Serologic Tests

Type of Viral Hepatitis	⊕ Serology[a]
Acute HAV	Anti-HAV IgM
Previous HAV	Anti-HAV IgG
Acute HBV	HBsAg, HBeAg, HBcAb IgM
Acute HBV, window period	HBcAb IgM only
Chronic active HBV	HBsAg, HBeAg, HBcAb IgG
Recovery HBV	HBsAb IgG, HBcAb IgG, normal ALT
Immunized HBV	HBsAb IgG
Chronic HCV infection	HCV RNA, anti-HCV Ab, elevated/normal ALT
Recovery HCV	Anti-HCV Ab and ⊖ HCV RNA

[a]*Anti-HAV IgM,* anti-hepatitis A IgM antibody; *anti-HAV IgG,* anti-hepatitis A IgG antibody; *HBsAg,* hepatitis B surface antigen; *HBeAg,* hepatitis B core antigen; *HBcAb IgM,* hepatitis B core IgM antibody; *HBcAb IgG,* hepatitis B core IgG antibody; *HBsAb IgG,* hepatitis B surface IgG antibody; *HCV RNA,* hepatitis C RNA (can be quantitative to determine disease severity); *anti-HCV Ab,* hepatitis C antibody

MNEMONIC

Vowels from the Bowels!

Hepatitis A and E are transmitted through the fecal-oral route; B and C are not.

Q 1

A 48-year-old woman with a history of diabetes, obesity, and hyperlipidemia comes to your clinic for a routine physical and lab work. Labs show a normal bilirubin level with an aspartate aminotransferase (AST) and alanine aminotransferase (ALT) of 58 and 72 U/L, respectively; alkaline phosphatase is within normal limits. What is the likely cause of her transaminitis?

Q 2

A 59-year-old man comes to your clinic for a checkup. He lived in Vietnam until age 32 and has not seen a primary care physician since that time. He is concerned that many of the people in his community have had hepatitis B. Which labs should be ⊕ if this patient has chronic hepatitis B?

TABLE 7-5. Etiologies, Diagnosis, and Treatment of Viral Hepatitis

Subtype	Transmission	Clinical/Lab Findings	Treatment and Course
HAV	Fecal-oral transmission	No chronic infection	Supportive; generally no sequelae
HBV	HBV is transmitted by infected blood, through sexual contact, or perinatally HDV can coinfect those with HBV	Prevalence is high in men who have sex with men, prostitutes, and IV drug users Adult acquired infection usually does not become chronic HBV is much more common in Asian countries and among immigrants from that region	Interferon (IFN) and other nucleotide/nucleoside analogs (the goal is to ↓ viral load and improve liver histology; cure is uncommon) Vaccinate against HAV Associated with arthritis, glomerulonephritis, and polyarteritis nodosa; chronic infection can result in HCC even without cirrhosis
HCV	HCV is transmitted through blood transfusion or IV drug use, tattoos, or body piercing	Acute illness is often mild or asymptomatic; more than 70% of infections become chronic Characterized by waxing and waning aminotransferases HCV antibody (not protective) appears 6 weeks to 9 months after infection; if antibody testing is ⊖ but suspicion is high, check HCV RNA	HCV is classically treated with IFN (ie, ribavirin); newer therapies include IFN-free direct-acting antivirals; therapies are tailored to viral genotype, patient characteristics Vaccinate against HAV and HBV Complications include cryoglobulinemia, membranoproliferative glomerulonephritis, and HCC in patients with cirrhosis; check for HIV Screen all people born in the United States between 1945 and 1965 for HCV
HDV	HDV requires a coexistent HBV infection Exposure is percutaneous HDV is usually found in IV drug users and high-risk HBsAg carriers	Anti-HDV IgM is present in acute cases Immunity to HBV implies immunity to HDV	See HBV infection for treatment If acquired as a superinfection in chronic HBV, there is ↑ severity of infection Fulminant hepatitis or severe chronic hepatitis with rapid progression to cirrhosis can occur HDV is associated with an ↑ risk of HCC
HEV	Fecal-oral transmission Endemic to India, Afghanistan, Mexico, and Algeria	Will test ⊕ on serology for HEV	Supportive Self-limited; carries a 10–20% mortality rate in pregnant women

1 A

Nonalcoholic fatty liver disease, a common cause of liver disease in patients with obesity and diabetes. Other causes of liver disease, such as hepatitis and alcoholism, should be excluded.

2 A

Hepatitis B surface antigen (HBsAg), hepatitis B early antigen (HBeAg), and hepatitis B core antibody (HBcAb) IgG.

Cirrhosis and Ascites

Chronic irreversible changes of the hepatic parenchyma, including fibrosis and regenerative nodules. The most common cause in the United States is alcohol abuse, followed by chronic viral hepatitis.

History/PE

- May be asymptomatic for long periods. Symptoms reflect the severity of hepatic damage, not the etiology (see Figure 7-11).
- ↓ Hepatic function leads to jaundice, edema, coagulopathy, hypoglycemia, and metabolic abnormalities.
- Fibrosis and distorted vasculature results in portal hypertension, which leads to esophageal varices and splenomegaly.
- ↓ Hepatic function and portal hypertension result in ascites and hepatic encephalopathy.

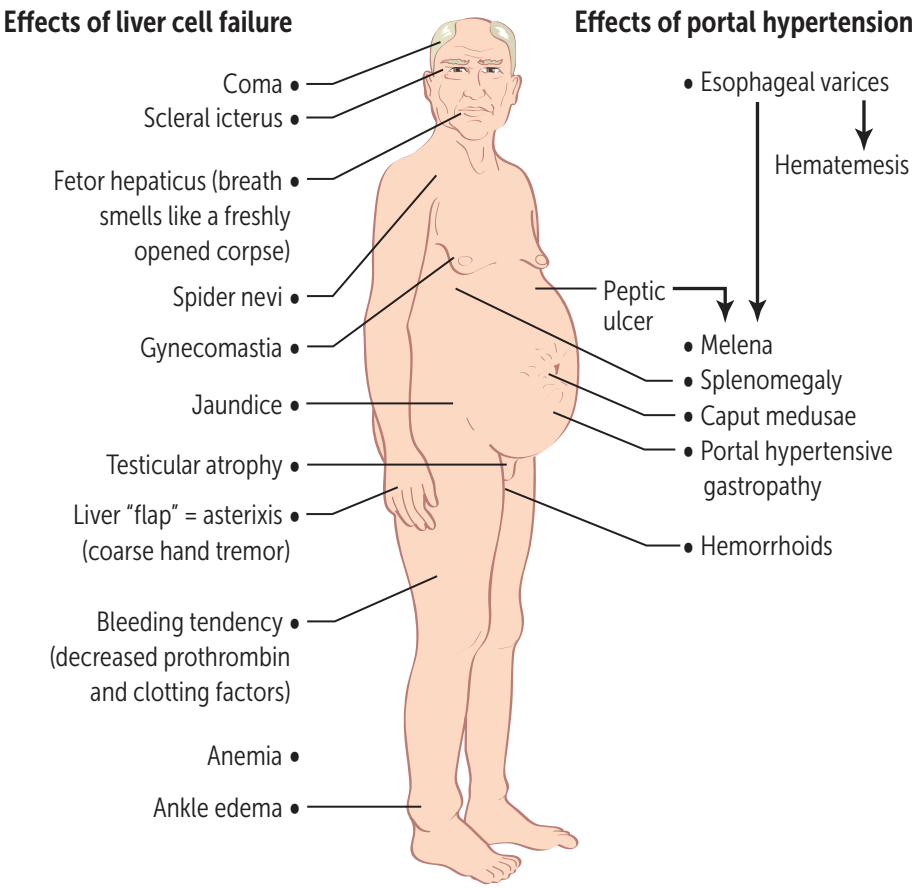


FIGURE 7-11. Clinical effects of cirrhosis. (Reproduced with permission from USMLE-Rx.com.)

Diagnosis

- Cirrhosis, while a tissue diagnosis, is often diagnosed using clinical evidence of disease such as ascites, portal hypertension, esophageal varices, and hepatic encephalopathy. It may be evaluated as follows:
  - Labs: ALT/AST may be elevated or normal as fibrotic tissue eventually replaces normal liver parenchyma. Additional lab findings include pancytopenia, prolonged PT and elevated International Normalized Ratio (INR), hyponatremia, and elevated ammonia.
- Imaging: Ultrasound may be used to evaluate for liver size, nodularity, and echogenicity.
- Ascites, if present, can be evaluated with paracentesis: Check cell count, differential, albumin, and bacterial cultures +/− acid-fast stain and +/− cytology. The etiology of the ascites can be further characterized as follows:
  - Related to portal hypertension (serum-ascites albumin gradient [SAAG] ≥ 1.1): Cirrhosis, heart failure, Budd-Chiari syndrome (hepatic vein thrombosis).
  - Unrelated to portal hypertension (SAAG < 1.1): Peritonitis (eg, TB), cancer, pancreatitis, trauma, nephrotic syndrome.
- If a patient with cirrhosis and ascites presents with worsening ascites, fever, altered mental status, renal dysfunction, or abdominal pain, consider spontaneous bacterial peritonitis (SBP).

KEY FACT

Diagnose spontaneous bacterial peritonitis with ⊕ cultures or a peritoneal fluid neutrophil count > 250 cells/mm^3.

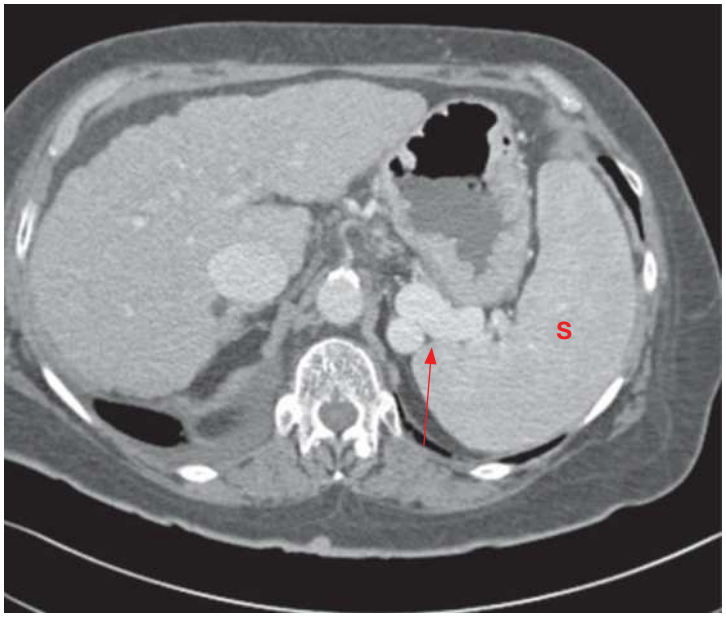


FIGURE 7-12. Cirrhosis. Transaxial image from contrast-enhanced CT shows a nodular liver contour and the stigmata of portal hypertension, including splenomegaly (S) and perisplenic varices (*arrow*). (Reproduced with permission from USMLE-Rx.com.)

Treatment

- Cirrhosis is treated as follows:
  - Abstinence from alcohol.
  - Restriction of fluid intake (1-1.5 L) if hyponatremic.
  - Rifaximin and lactulose with hepatic encephalopathy.
  - Liver transplantation is the definitive treatment in the setting of progressive liver disease.
- Treatment for ascites includes the following:
  - Restrict sodium to < 2 g/day.
  - Treat with diuretics (furosemide and spironolactone).
  - Obtain large-volume paracentesis for ascites refractory to diuretics.
  - TIPS can be used in refractory cases caused by portal hypertension, but this will predispose to encephalopathy.
  - Again, liver transplantation is the definitive treatment.
- Treat SBP with a third-generation cephalosporin (first-line therapy) or a fluoroquinolone. SBP often recurs.

KEY FACT

The MELD score (**m**odel for **e**nd stage **l**iver **d**isease) uses INR, bilirubin, and creatinine to estimate 90-day mortality.

Acetaminophen Toxicity

Early acetaminophen toxicity (< 24 hours) may be asymptomatic or present with nonspecific symptoms such as malaise, nausea, vomiting. This may be followed by RUQ pain and transaminitis, and eventual jaundice, encephalopathy, and multiorgan failure, possibly resulting in death.

Treatment

- Start N-acetylcysteine with a 4-hour acetaminophen level > 150 mcg/mL, any single acute ingestion > 150 mg/kg, or evidence of liver injury.
- Consider activated charcoal with presentation < 4 hours after ingestion.

- Supportive care.
- King's College criteria are used to determine which patients with acetaminophen overdose should be referred immediately for liver transplant.

Hereditary Hemochromatosis

- An autosomal recessive disorder of iron overload affecting predominately those of Northern European descent. Women develop symptoms much later than men 2° to blood loss with menstruation.
- **Hx/PE:** Presents with fatigue, DM, arthritis, ↑ skin pigmentation, infertility, transaminitis, and cardiomyopathy; may develop cirrhosis.
- **Dx:** ↑ Fe saturation↑ ferritin, ↑ transferrin saturation, *HFE* gene mutation.
- **Tx:** Phlebotomy; genetic counseling to assess likelihood of transmission.

Wilson Disease

- An autosomal recessive disorder of impaired copper excretion.
- **Hx/PE:** May present with liver disease, neuropsychiatric symptoms, Kayser-Fleischer rings on exam.
- **Dx:** ↓ Serum copper and ceruloplasmin, increased urinary copper, confirmatory liver biopsy with increased hepatic copper content or genotyping.
- **Tx:** Lifelong chelation (penicillamine, trientine), high-dose oral zinc, liver transplant.

α1-Antitrypsin Disorder

- Consider in a young nonsmoker presenting with panacinar emphysema. In the liver, aberrant α1-antitrypsin (AAT) polymerization leads to hepatocyte damage and cirrhosis.
- **Dx:** Serum AAT levels, genotyping.
- **Tx:** AAT augmentation to slow the progression of disease, lung and liver transplant, with liver transplant being largely curative for both lung and liver disease.

Autoimmune Hepatitis

- More common in women, suspected with transaminitis.
- **Dx:** Elevated IgG, ⊕ ANA, ⊕ ASMAm, ⊕ LKMA. Confirmed by liver biopsy.
- **Tx:** Treated with corticosteroids and azathioprine; relapse likely when therapy is withdrawn and requires chronic therapy.

1° Biliary Cholangitis

- Autoimmune destruction of intrahepatic bile ducts; ↑ risk of cirrhosis and HCC; associated autoimmune disorders including hypothyroidism and arthritis.
- **Hx/PE:** Presents with fatigue, pruritus, jaundice, fat malabsorption, and osteoporosis.

Q

A 46-year-old woman presents to your clinic with scleral icterus, pruritus, and abnormal LFTs. Her AST, ALT, and alkaline phosphatase levels are 48, 56, and 603 U/L, respectively. What lab test will reveal the likely diagnosis?

- **Dx:** Elevated alkaline phosphatase and bilirubin; ⊕ ANA, ⊕ AMA; confirmed by biopsy.
- **Tx:** Ursodeoxycholic acid, cholestyramine, fat-soluble vitamins.

1° Sclerosing Cholangitis

- Intra- and extrahepatic bile duct fibrosis. Affects predominately men with median age of onset 30–40 years. Associated with IBD (usually ulcerative colitis). ↑ risk cholangiocarcinoma, gallbladder cancer, colorectal cancer, HCC.
- **Hx/PE:** Often asymptomatic, but may present with fatigue, pruritus, RUQ pain.
- **Dx:** Elevated alkaline phosphatase and bilirubin; ⊕ ANA, ⊕ anti-smooth muscle antibody, ⊕ perinuclear antineutrophil cytoplasmic antibody (p-ANCA). Can rule out biliary obstruction with U/S or CT; magnetic resonance cholangiopancreatography preferred over ERCP for diagnosis, showing multiple areas of beaded bile duct strictures (see Figure 7-13).
- **Tx:** Ursodeoxycholic acid, cholestyramine, fat-soluble vitamins in more advanced disease, balloon dilation of strictures. More than half will require liver transplant as, unlike 1° biliary cholangitis patients, most 1° sclerosing cholangitis patients will not respond to medical management.

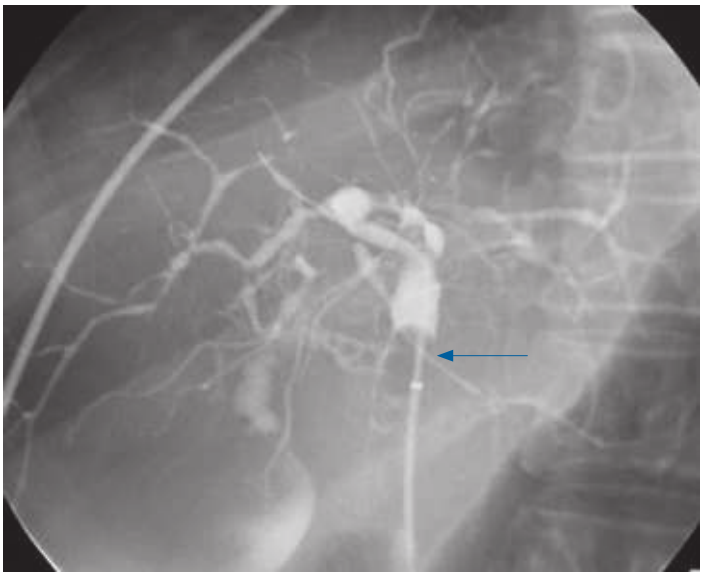


FIGURE 7-13. Primary sclerosing cholangitis. ERCP image following contrast injection through a catheter in the common bile duct with the balloon (*blue arrow*) inflated. Multifocal structuring and dilation of the intrahepatic bile ducts can be seen. (Reproduced with permission from USMLE-Rx.com.)

A

A ⊕ antimitochondrial antibody will reveal the likely diagnosis of 1° biliary cholangitis.

CHAPTER 8

HEMATOLOGY

Hematology Definitions

- **Ferritin:** A measure of iron stores (↓ in iron-deficiency anemia but ↑ in infection and inflammation).
- **Haptoglobin:** A protein that binds free hemoglobin (in intravascular hemolysis, free hemoglobin is released, haptoglobin binds to the hemoglobin, and levels of haptoglobin ↓).
- **Mean corpuscular volume (MCV):** Also known as mean cell volume; a measure of the average volume of the RBCs.
- **Mean corpuscular hemoglobin concentration (MCHC):** Measure of hemoglobin in a given volume of RBCs.
- **Red blood cell distribution width (RDW):** Measure of the variation in volume of the RBCs ("width" refers to the volume curve or distribution width, not the actual width of the individual cells).
- **Reticulocyte count (RC):** Percentage of reticulocytes (or immature blood cells) in the blood.
- **Total iron-binding capacity (TIBC):** Measures the capacity of transferrin to bind with iron (or how much iron is carried throughout the body).
- **Transferrin:** Protein that reversibly binds and carries iron.
- **Direct Coombs test:** An antiglobulin test to determine if antibodies are bound to the RBC membrane; indicative of hemolytic anemia.
- **Indirect Coombs test:** A serum test to determine if there are antibodies to Rh factor in a mother's blood.

Anemia

Defined as a reduction in the amount of circulating red blood cells. Confirmed through testing hematocrit and hemoglobin, which will be low (hemoglobin in anemia will be < 13.5 g/dL in men; < 12.5 g/dL in women). Once anemia is established, look next to the MCV to determine the cause (see Table 8-1).

- **Microcytic anemia** = < normal MCV.
- **Normocytic anemia** = normal MCV, 80–100 fL.
- **Macrocytic anemia** = > normal MCV.

History/PE

Patients present with any of the following:

- Fatigue.
- Weakness.
- Pallor (in skin and conjunctiva).
- Headache.
- Lightheadedness.

TABLE 8-1. Common Causes of Anemia

Microcytic Anemia (MCV < 80 fL)	Normocytic Anemia (MCV 80–100 fL)	Macrocytic Anemia (MCV > 100 fL)
Iron-deficiency anemia	Anemia of chronic disease	Vitamin B_{12} deficiency
Thalassemia	Hemolytic anemia	Folate deficiency
Sideroblastic anemia	Acute blood loss	Liver disease
Anemia of chronic disease		Thyroid disease

- Pica.
- Tachycardia.
- If underlying coronary artery disease, could also present with angina.

Diagnosis

- In determining the etiology, consider bleeding, ↓ production, ↑ destruction.
- Identify a bleeding source.
- Order labs: CBC with differential, RC, and peripheral blood smear.
- Check to see if other cell lines (eg, granulocytes and platelets) are low.

Treatment

- If hemoglobin is < 7 g/dL, transfuse packed red blood cells.
- Determine the etiology of the anemia and treat.

KEY FACT

If granulocytes and platelets are low, consider marrow failure (due to radiation exposure, lupus, vitamin B_{12} deficiency, drug ingestion), leukemia, myelodysplasia, or malignancy metastatic to marrow.

MICROCYTIC ANEMIA

Table 8-2 provides a review of the causes of microcytic anemia.

Iron-Deficiency Anemia

The most common form of anemia in the world. There are three major causes:

- Excessive blood loss (menstruation, GI bleed).
- ↓ Iron absorption (eg, celiac disease, bariatric surgery patients, achlorhydria).
- ↑ Iron demand (as seen in pregnancy).

TABLE 8-2. Causes of Microcytic Anemia

	Iron-Deficiency Anemia	Thalassemia	Sideroblastic Anemia	Anemia of Chronic Disease (late)
Pathology	↓ Iron in marrow, ↓ heme synthesis	↓ Synthesis of α- or β-globin subunits	Defective heme synthesis in RBC precursors	↓ Ability to use iron and response to erythropoietin from an ↑ of inflammatory markers
Serum ferritin[a]	↓[b]	Normal to ↑	↑	↑
Serum iron	↓	Normal to ↑	↑	Slightly ↓
TIBC	↑	Normal to ↑	Normal to ↓	Normal or ↓
Other tests	Wide RDW Thrombocytosis common Peripheral blood smear shows microcytic RBCs with central pallor	Normal RDW Diagnosis confirmed with hemoglobin electrophoresis Presence of basophilic stippling; typically MCV < 70, ↑ MCHC	Smear showing normal and dimorphic RBCs with basophilic stippling Diagnosis confirmed with bone marrow biopsy (shows erythroid hyperplasia and ringed sideroblasts) Check lead levels if suspected	

[a]Ferritin may have to be ordered in addition to an iron panel.

[b]May be normal in inflammatory states and cancer.

History/PE

Look for signs of anemia, as discussed above. Can also present with pica—eating substances that have little to no nutritional value (eg, ice, dirt, clay, paper, or hair).

Diagnosis

- CBC: MCV low; RDW high.
- Iron studies:
  - Serum iron: ↓.
  - Serum ferritin: ↓ (iron stores are depleted).
  - TIBC: ↑ (will rise to bind any iron available).
- Serum transferrin: ↓ (no iron to transport); peripheral blood smear: central pallor in RBCs (see Figure 8-1).
- Workup for GI etiology (IBS, celiac disease, parasites in third world countries).

KEY FACT

RDW is ↑ in iron deficiency anemia but normal in thalassemia.

Treatment

- Iron supplementation: Ferrous sulfate orally.
- Build iron stores by continuing treatment for 3 to 6 months after serum levels have normalized.
- IV iron can be considered for the following:
  - Poor absorption (malabsorption, inflammatory bowel disease [IBD], gastric bypass surgery).
  - Extreme deficiencies of serum iron.
  - Chronic kidney disease.
- Do not give IV iron to patients with active infections (risk of adverse reactions).
- Refer to GI if GI etiology suspected.

Thalassemia

Describes a group of inherited disorders that present as ↓ hemoglobin because of an error in the production of either the α- or β-globin chains of the hemoglobin molecule. Most α-thalassemias are found in Asians and African-Americans; β-thalassemias are found in people of Mediterranean origin, Asians, and African-Americans.

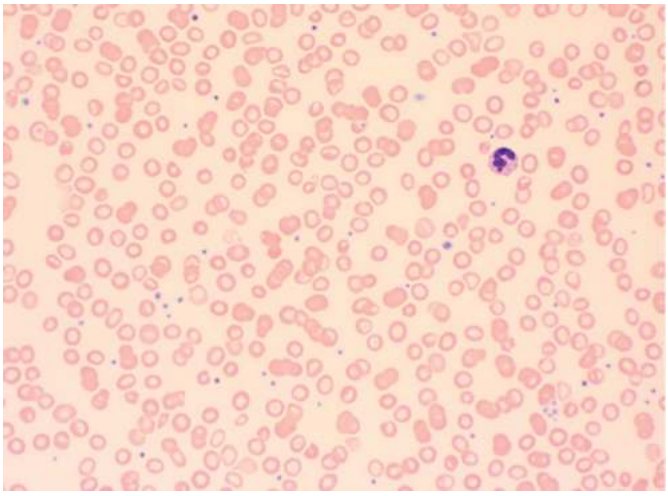


FIGURE 8-1. Iron deficiency anemia. Oil immersion view of a peripheral blood smear demonstrating microcytic RBCs with central pallor. (Reproduced with permission from Dr. Bethany D. Vallangeon, Department of Pathology, East Carolina University.)

History/PE

Presentation is dependent on the type of thalassemia:

- **α-Thalassemia:** Four alleles are responsible for the α-globin chain of hemoglobin.
  - **Single allele mutated:** Patients (silent carriers) will be asymptomatic but may pass the trait to their offspring.
  - **Two alleles mutated (α-thalassemia trait):** This is nearly always asymptomatic but will be mildly anemic and severely microcytic.
  - **Three alleles mutated (α-thalassemia intermedia or hemoglobin H disease):** Patients will have chronic hemolytic anemia and splenomegaly.
  - **Four alleles mutated (hemoglobin Barts disease):** Incompatible with life; it is characterized by hydrops fetalis.
- **β-thalassemia:** Two alleles create the β-globin chain of hemoglobin.
  - **One mutated allele (β-thalassemia minor or β-thalassemia trait)** is asymptomatic.
  - **β-thalassemia intermedia** presents when there is poor production of both β-globin alleles; hemoglobin deficiency is more severe (7–10 g/dL).
  - **β-thalassemia major** is the most severe form (no β-globin chain production; presents with growth retardation, hepatosplenomegaly, jaundice, and bony deformities in the first year of life as production of fetal hemoglobin declines).

Diagnosis

- Peripheral blood smear will show poikilocytosis and nucleated RBCs.
- In α-thalassemia, hemoglobin electrophoresis shows ↑ hemoglobin A_2 and possibly hemoglobin F.
- β-Thalassemia is diagnosed with β-globin gene analysis.

Treatment

- Differs based on type of thalassemia.
- Mild forms (eg, α-thalassemia, β-thalassemia minor) may need no treatment.
- Moderate to severe forms (eg, α-thalassemia intermedia [hemoglobin H disease], β-thalassemia intermedia) require transfusions as needed to keep hemoglobin > 9 g/dL.
- Severe forms (eg, β-thalassemia major) will require repeated transfusions and iron chelation therapy, or even stem cell transplant.
- Consider splenectomy if the patient requires more than 2 units/month.

KEY FACT

Repeated transfusions can lead to iron overload, which can result in:
- Heart failure (HF).
- Hepatic dysfunction.
- Glucose intolerance.
- Secondary hypogonadism.

Chelation therapy delays or prevents these outcomes.

Sideroblastic Anemia

Inherited or acquired disorder caused by abnormal iron metabolism. Acquired via 1° sideroblastic anemia, drug use—specifically ethanol, chloramphenicol, cycloserine, or pyrazinamide—or metal toxicity (lead, zinc, or copper).

Diagnosis

Bone marrow aspirate will show ringed sideroblasts.

Treatment

- **Acquired** types: Remove the causative agent.
- **Inherited** types: Trial of pyridoxine daily.

KEY FACT

Always consider colon cancer in an adult patient with microcytic anemia.

Anemia of Chronic Disease

Caused by multiple factors: poor iron mobilization, erythropoiesis suppression as a response to an inflammatory process, or an impaired response of erythropoietin to anemia. It is also attributable to ↑ hepcidin levels in chronic inflammation.

KEY FACT

Hepcidin is important in regulating iron absorption. When iron is low, hepcidin is normally also low to stimulate iron absorption. Since chronic inflammation raises hepcidin levels, it creates an iron deficiency because of ↓ absorption.

Diagnosis

- Microcytic or normocytic and low RC.
- Iron studies: Low iron; low total iron-binding capacity (TIBC); transferrin normal (versus ↑ in iron-deficiency anemia).
- If ferritin is low (below 30 ng/mL), both anemia of chronic disease and iron-deficiency anemia.

KEY FACT

For anemia of chronic disease, do not give IV iron. Treat the underlying disease.

Treatment

- Focus on treating the underlying disease.
- Remove other factors such as nutritional deficiencies or marrow-suppressing drugs.

NORMOCYTIC NORMOCHROMIC ANEMIA AND HEMOLYTIC ANEMIA

- Anemia with a mean corpuscular volume (MCV) of 80–100 fL, or normocytic normochromic anemia, may be due to blood loss (hemorrhage), hemolysis, or ↓ production.
- Hemolytic anemia is a state of hemolysis in which ↑ erythrocyte production is insufficient to keep up with accelerated RBC destruction. RBC destruction may be extravascular or intravascular. Presentation, diagnosis, and treatment will differ depending upon the type of anemia. Specific hemolytic anemias are outlined below (see also Table 8-3).

History/PE

Look for evidence of acute bleeding. Patients with hemolytic anemia may present with jaundice and dark urine from unconjugated hyperbilirubinemia as well as with pigment gallstones and splenomegaly.

Diagnosis

The initial workup includes RC, creatinine, hemolysis labs, and blood smear.

- **Normal RC:** Anemia of chronic disease or chronic kidney disease.
- **↑ RC with normal hemolysis labs:** Hemorrhage.
- **↑ RC, ↑ LDH, ↑ unconjugated bilirubin, and ↓ haptoglobin:** Hemolysis.

Treatment

- Patients who are hemorrhaging must be resuscitated with RBC transfusions. Identify and treat the cause.
- **Autoimmune hemolytic anemia:** Treatment includes steroids, immunosuppressive agents, intravenous immunoglobulin (IVIG), and, if necessary, splenectomy.
- **Hemolytic-uremic syndrome (HUS):** Usually treated with supportive care only. Prolonged atypical HUS with acute kidney injury (AKI) will require dialysis.
- **Thrombotic thrombocytopenic purpura (TTP):** Treat with rapid plasma exchange. If unavailable, an infusion of fresh frozen plasma (FFP) is indicated, along with glucocorticoids.
  - Platelet transfusion is contraindicated without severe bleeding.
  - 90% remission rate, although relapses can occur years later.

KEY FACT

Distinguish HUS from TTP by the presence of neurologic signs in TTP. The treatment of choice for TTP is plasma exchange; for HUS it is supportive care and dialysis if needed.

Sickle Cell Anemia

An autosomal recessive disease resulting from the substitution of valine for glutamic acid at the sixth position in the globin chain.

TABLE 8-3. Types and Characteristics of Selected Hemolytic Anemias

Subtype	Pathology	Special Features
	Autoimmune Hemolytic Anemia	
Cold agglutinin disease	IgM binds to RBC antigens, causing intravascular lysis	Smear: Spherocytes, ⊕ Coombs test Acrocyanosis in cold; cold agglutinin test ⊕; seen with *Mycoplasma* infection and mononucleosis
Warm autoimmune hemolytic anemia	IgG binds to RBC antigens and is cleared by the spleen	Smear: Spherocytes; ⊕ Coombs test Can present with jaundice/splenomegaly
	G6PD Deficiency	
	Deficiency in G6PD enzyme; hemolysis in the presence of infection or drugs (eg, sulfa)	Smear: Bite cells; G6PD possibly normal during hemolytic episodes but ↓ after
	Microangiopathic Hemolytic Anemia	
	RBC fragments due to shearing through partially coagulated capillaries	Smear: Schistocytes and helmet cells
	Hemolytic Uremic Syndrome	
	Platelet-fibrin aggregates cause microangiopathic hemolytic anemia and organ ischemia	HUS triad: Hemolytic anemia, thrombocytopenia, and AKI Usually occurs with gastroenteritis in children Typical association with *E coli* (O157:H7) production of Shiga-like toxins
	Thrombotic Thrombocytopenic Purpura	
	Platelet-von Willebrand factor (vWF) aggregates cause microangiopathic hemolytic anemia and organ ischemia Results from autoantibody against ADAMTS13, a vWF-cleaving protease	TTP pentad: HUS triad plus fever and fluctuating neurologic signs Can develop sporadically
	Other Normocytic Anemia	
Myelofibrosis	Myeloproliferative disorder with abnormally activated fibroblasts Leads to medullary fibrosis and anemia	Idiopathic or 2° to polycythemia vera; can have splenomegaly Labs: Reticulocytes, teardrop RBCs, ↑ LDH Dx: Bone marrow; see discussion of Myeloproliferative Disorders
Paroxysmal nocturnal hemoglobinuria	Acquired disorder with intravascular hemolysis and hemoglobinuria	Recurrent thrombosis and pancytopenia Dx: Flow cytometry

KEY FACT

Hydroxyurea, a chemotherapeutic agent that reduces sickle hemoglobin and raises fetal hemoglobin, should be considered in patients symptomatic with sickle cell—particularly those with frequent pain crises and a history of strokes or other serious complications.

History/PE

Seen predominantly among African-Americans, who often have a family history. Clinical features include:

- Chronic hemolysis resulting in gallstones, poorly healing ulcers, jaundice, splenomegaly (usually during childhood), and HF.
- Pain due to vaso-occlusion (most commonly musculoskeletal).

Diagnosis

Blood smear shows sickled cells, Howell-Jolly bodies, and evidence of hemolysis (See Figure 8-2). Hemoglobin electrophoresis is the definitive diagnostic test.

Treatment

- Autosplenectomy is common so vaccinate all patients against encapsulated organisms (*S pneumoniae*, *H influenzae*, *N meningitidis*) as well as hepatitis B virus and the influenza virus.
- Consider IV fluids if the patient appears dehydrated, as dehydration may worsen sickling.
- Supplement folic acid to aid erythropoiesis.
- Instruct patients to avoid dehydration, hypoxia, intense exercise, and high altitudes.
- In patients with frequent pain crises, consider hydroxyurea or bone marrow transplantation.

Complications

- **Pain (vaso-occlusive) crisis:**
  - Sickled cells cause occlusion of arterioles, leading to tissue ischemia and/or infarction.
  - Characterized by pain in the back, limbs, abdomen, and ribs; it is precipitated by dehydration, acidosis, infection, fever, or hypoxia.
  - Treat with hydration, analgesia, and supplemental oxygen.
- **Aplastic crisis:** A sudden decrease in hemoglobin and RC caused by parvovirus B19. Support with transfusions.

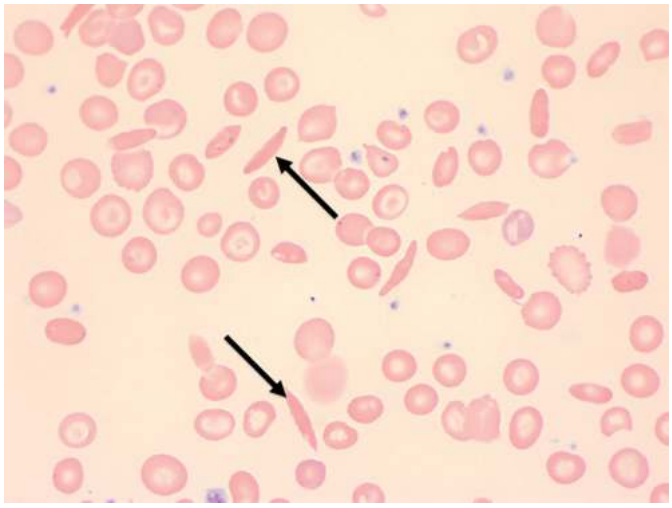


FIGURE 8-2. Sickle cell anemia. Oil immersion of a peripheral blood smear demonstrating sickled RBCs (*arrows*). (Reproduced with permission from Dr. Bethany D. Vallangeon, Department of Pathology, East Carolina University.)

- **Acute chest syndrome:**
  - A combination of factors, including infection, infarction, and pulmonary fat embolism.
  - Clinical findings include fever, chest pain, cough, wheezing, tachypnea, and new pulmonary infiltrate on CXR.
  - Treat with oxygen, analgesia, transfusions, and antibiotics (a second- or third-generation cephalosporin with a macrolide such as erythromycin).
- **Lungs:** Pulmonary infarcts can lead to pulmonary hypertension. This is caused by chronic intravascular hemolysis, which decreases nitric oxide and leads to pulmonary artery vasoconstriction.
- **Heart:** Sickle cell cardiomyopathy may lead to HF.
- **Abdomen:** Cholecystitis, which may lead to cholecystectomy; splenic infarcts.
- **Kidneys:** Sickling of cells can cause infarcts, leading to papillary necrosis and AKI, particularly in sickle cell trait.
- **Genital:** Priapism and impotence in men.
- **Infections:** The absence of a functional spleen predisposes patients to encapsulated organisms, including *S pneumoniae*, *H influenzae*, *N meningitidis*, and gram ⊖ bacterial infections.
- **Bones:** Avascular necrosis; *Salmonella* osteomyelitis.
- **CNS:** Stroke is one of the most devastating complications. Treat with exchange transfusion rather than thrombolytics.
- **Pregnancy:** Patients are at ↑ risk for spontaneous abortions.

KEY FACT

As in thalassemia, patients with sickle cell anemia who receive frequent transfusions need prophylactic treatment of hemosiderosis with iron chelators such as deferasirox or deferoxamine.

Hereditary Spherocytosis

Caused by a defect in the cytoskeleton of RBCs—most commonly ankyrin or spectrin. With defects in cytoskeletons, the cell membranes form blebs, which eventually break off, reducing the volume of the RBC. Cells become spherical instead of their usual disc shape.

Diagnosis

- Spherocytes on blood smear; cells with central pallor.
- ↑ RDW; ↑ MCHC.
- Splenomegaly.
- Jaundice from ↑ indirect (unconjugated) bilirubin.
- Possible aplastic crisis if patients have coexisting infection of Parvovirus B19.
- Confirmed by osmotic fragility test.

Treatment

Splenectomy will resolve anemia, but spherocytes will persist and develop Howell-Jolly bodies. Remember to vaccinate against encapsulated organisms (*Neisseria meningitidis*, *Streptococcus pneumoniae*, *Haemophilus influenzae* type b).

Methemoglobinemia

Occurs when hemoglobin is "stuck" in an oxidized state, which is unable to carry oxygen. May be hereditary or caused by substance exposure (benzocaine, dapsone, sulfonamides).

History/PE

Shortness of breath with no clear etiology. CXR is normal. May also present with dizziness, confusion, headaches, and seizures.

Diagnosis

- Pulse oximetry classically reads 85% due to the color given off by oxidized hemoglobin particles. Diagnose methemoglobinemia with co-oximetry.

- Arterial blood gas (ABG) will have normal O_2 levels.
- Blood is chocolate-brown.
- Obtain a methemoglobin level.

Treatment

- Administer 100% O_2.
- Treat with methylene blue.

MACROCYTIC ANEMIA

Anemia with an MCV of > 100 fL. Characterized by impaired DNA synthesis with normal cytoplasm maturation and delayed nucleus development that results in macrocytosis. The most common etiologies include:

- **Folate deficiency:** Poor dietary intake (including alcoholism) and drugs (eg, phenytoin, zidovudine, TMP-SMX, methotrexate and other chemotherapeutic agents).
- **B_{12} deficiency:** Commonly caused by a strict vegan diet, pernicious anemia (destruction of gastric parietal cells leading to a lack of intrinsic factor and therefore ↓ absorption), gastrectomy, proton pump inhibitors (which inhibit B_{12} absorption), and ileal dysfunction (IBD, surgical resection). B_{12} deficiency can cause neurologic deficits (paresthesias, gait disturbance, and mental status changes).
- **Other:** Liver disease, hypothyroidism, alcohol abuse, myelodysplasia, and fish tapeworm.

Diagnosis

- Check serum B_{12}, folate and obtain a blood smear to look for megaloblastic anemia, which shows oval macrocytes and hypersegmented neutrophils.
- If B_{12} deficiency is suspected, check intrinsic factor antibody and anti–parietal cell antibody for pernicious anemia.
- Homocysteine and methylmalonic acid (MMA) levels can distinguish folate from B_{12} deficiency:
  - **Folate deficient:** ↑ Homocysteine but normal MMA.
  - **B_{12} deficient:** ↑ Homocysteine and ↑ MMA.

Treatment

- Treat B_{12} deficiency with monthly B_{12} shots or oral replacement (in a normal GI tract, oral replacement has been shown to be as effective as IV); treat folate deficiency with oral replacement.
- Discontinue any medications that could be contributing to megaloblastic anemia; minimize alcohol use.

Myeloproliferative Disorders

A group of conditions that arise when the bone marrow overproduces building blocks to maintain hemostasis. Presentation will differ based on the specific disorder. Table 8-4 provides a succinct guide for the basic pathophysiology of each disorder.

POLYCYTHEMIA VERA

- Disorder caused by the production of too many RBCs by the bone marrow. Average age at diagnosis is 65.

TABLE 8-4. Pathophysiology of Myeloproliferative Disorders

Disorder	Overproduction of...
Polycythemia vera	RBCs (and others)
Essential thrombocytosis	Platelets
Primary myelofibrosis	Collagen or fibrous bone tissue
Chronic myelogenous leukemia[a]	Granulocytes

[a]See the Leukemia section of the Oncology chapter.

- **Hx/PE:** Headache, blurry vision, fatigue, itching after a hot shower.
- **Dx:** ↑ Hematocrit (> 52% in men; 48% women) and ↑ platelets (> 400,000/mL), a *JAK2* mutation, and ↓ erythropoietin levels.
- **Tx:** Serial phlebotomy: Goal hematocrit of < 45% in men; 42% in women.

KEY FACT

Hypoxia can also trigger ↑ erythropoietin. Order an ABG to differentiate between polycythemia vera and erythropoiesis triggered by hypoxia.

ESSENTIAL THROMBOCYTOSIS

- An ↑ platelet count with no Philadelphia chromosome (translocation on chromosome 22).
- **Hx/PE:** Visual complaints, headaches, or erythromelalgia (pain in hands and feet).
- **Dx:** Platelet count sustained at levels > 450,000/mL; JAK2 ⊕ in 50% of patients. Bone marrow biopsy: Megakaryocytic hyperplasia and no rise in RBC or WBC (see Figure 8-3).
- **Tx:** Hydroxyurea to reduce platelet count; add aspirin if associated thrombocytosis.

1° MYELOFIBROSIS

- An abnormal myeloid proliferation with impaired marrow function and extramedullary hematopoiesis.
- **Hx/PE:** Presents with fever, sweats, weight loss, and hepatosplenomegaly.

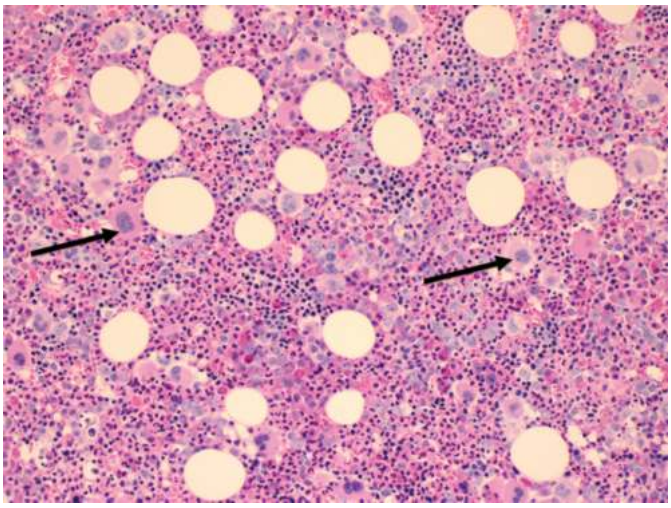


FIGURE 8-3. Essential thrombocytosis. H&E section showing megakaryocytic hyperplasia.
(Reproduced with permission from Dr. Bethany D. Vallangeon, Department of Pathology, East Carolina University.)

- **Dx:** Bone marrow is difficult to aspirate ("dry tap"). Labs ↑ LDH, alkaline phosphatase, and uric acid.
- **Tx:** Asymptomatic patients should be followed. If symptomatic, treat supportively with transfusions, hydroxyurea, and occasionally splenectomy or radiation. Allogeneic stem cell transplantation may be considered in younger patients.

Bleeding Disorders

Disorders in coagulation or platelets that predispose patients to bleed (see Table 8-5).

Diagnosis

- Think thrombocytopenia when the platelet count is < 90,000/μL.
- Think coagulopathy if the prothrombin time (PT) or partial thromboplastin time (PTT) is ↑ (see Figure 8-4 and the discussion of coagulopathies).

MNEMONIC

Petechiae = **P**latelet deficiency
Cavity/joint bleeding = **C**lotting factor deficiency

Treatment

- Patients who are hemodynamically unstable need immediate resuscitation with IV fluids. The source of hemorrhage should be treated.
- Blood transfusions should be given to maintain a hemoglobin level of > 7 g/dL. FFP should be given to normalize PTT and PT. Platelets should be given as needed.

PLATELET DISORDERS

A decrease in the number of platelets (thrombocytopenia) as well as a decrease in the functioning of platelets predisposes patients to bleed (platelet dysfunction). Look for petechiae and easy bruising. In addition to TTP and HUS, common platelet disorders include:

- ↑ **Platelet destruction:**
  - **Idiopathic thrombocytopenic purpura (ITP)/autoimmune thrombocytopenia:** Severe thrombocytopenia due to platelet-associated IgG antibodies; this is a diagnosis of exclusion. Treatment involves prednisone and, if the patient is unresponsive to steroids, splenectomy.
  - **Heparin-induced thrombocytopenia:** Immune-mediated thrombocytopenia occurring 5–14 days after the initiation of heparin (or < 24 hours

TABLE 8-5. Clinical Features of Coagulopathies and Platelet Disorders

Clinical Feature	Platelet Disorders	Coagulopathies
Amount of bleeding after surface cuts	Excessive, prolonged bleeding	Normal to slightly ↑ bleeding
Onset of bleeding after injury	Immediate	Delayed after surgery or trauma Spontaneous bleeding into joints or hematoma
Clinical presentation	Superficial and mucosal bleeding (GI tract, gingival, nasal) Petechiae, ecchymosis	Deep and excessive bleeding into joints, muscles, GI tract, and GU tract

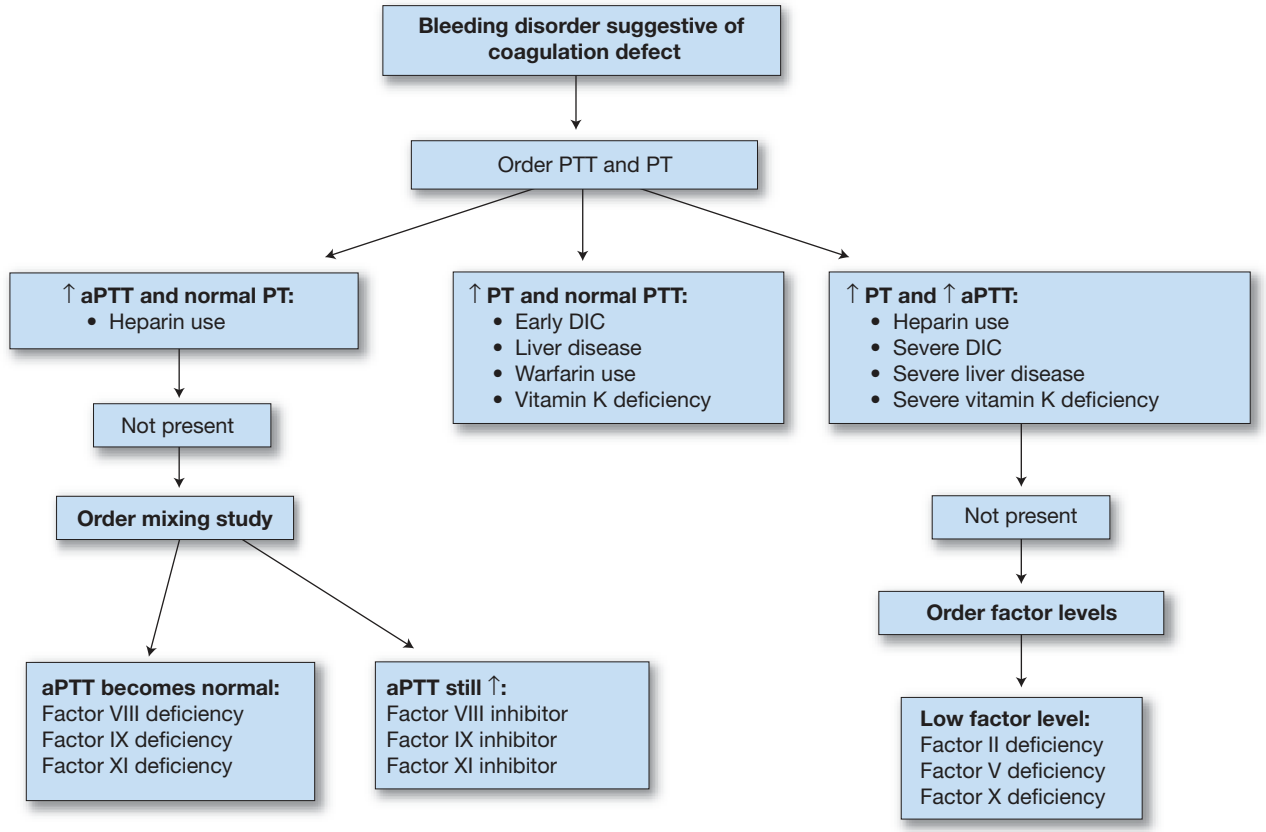


FIGURE 8-4. Approach to patients with bleeding disorders suggestive of a coagulation defect.

if previously exposed). Platelet factor-4 (PF-4) antibodies and the serotonin release assay are used for diagnosis. Stop heparin immediately and start an alternative anticoagulant such as fondaparinux, lepirudin, argatroban, or danaparoid sodium (not warfarin). Do not use a low molecular weight heparin.

- **Platelet dysfunction—acquired:**
  - **Acquired disease:** Platelet function can be impaired as a result of severe liver disease (from splenic sequestration), severe renal disease, or multiple myeloma. Treat with desmopressin, FFP, or cryoprecipitate for major bleeding. Do not use aspirin or NSAIDs as they inhibit platelet function.
  - **Drug-induced thrombocytopenia:** One of the most common causes of mild asymptomatic thrombocytopenia. Common medications include quinine, antibiotics, sulfa drugs, and glycoprotein IIb/IIIa inhibitors. It usually resolves within 1 week of stopping the implicated drug.
- **Platelet dysfunction—inherited:** Includes Bernard-Soulier syndrome (a problem with adhesion), Glanzmann thrombasthenia (a problem with aggregation), and storage pool disease (problems with platelet granule release). Treatment is the same as that for acquired disease.

Diagnosis

- Confirm the presence of thrombocytopenia (ie, recheck platelets in citrated blood).
- Check a peripheral blood smear and a 1-hour post-transfusion platelet count to distinguish ↓ platelet production (pancytopenia, small platelets, ↑ platelet count following platelet transfusion) from ↑ platelet destruction (large platelets, no significant rise in platelet count after platelet transfusion).

KEY FACT

Idiopathic **T**hrombocytopenic **P**urpura: **T**reat with **P**rednisone.

KEY FACT

Generally, treat with platelet transfusion if platelet count is:

- < 100,000 before neurosurgery or if there is active bleeding.
- < 50,000 before a general procedure or symptomatic.
- < 20,000 in an asymptomatic patient who has fever/sepsis, is receiving heparin, or will be outpatient soon.
- < 10,000 in an asymptomatic patient.

- Obtain a bone marrow biopsy in cases of severe thrombocytopenia or if anemia or neutropenia are present.

Treatment

See above.

COAGULOPATHIES

A defective clotting cascade predisposes patients to bleeding. Ask about medications that predispose to bleeding (eg, warfarin, enoxaparin, heparin); note factors that predispose to vitamin K deficiency (eg, liver disease, malnutrition, antibiotic use, alcoholism).

- Recurrent spontaneous bleeding suggests a factor deficiency (eg, factor VIII [hemophilia A] or factor IX [hemophilia B]).
- Delayed bleeding after trauma or surgery (classically after the umbilical cord falls off) suggests factor XIII deficiency.

Diagnosis

- Look for evidence of liver disease on exam and order liver function tests and PT/PTT.
- Defects in the clotting cascade can be due to defects in the intrinsic pathway, the extrinsic pathway, or the common pathway.
  - **Intrinsic pathway:** Involves factors VIII, IX, XI, and XII. Abnormality results in a rise in activated partial thromboplastin time (aPTT). Impaired in patients with hemophilia A (factor VIII) or B (factor IX).
  - **Extrinsic pathway:** Involves factor VII. Abnormality leads to a rise in PT (INR). Prolonged by warfarin.
  - **Common pathway:** Involves factors V, X, and II (prothrombin). An increase is seen in both aPTT and PT (INR).

Treatment

- Coagulopathic patients who are actively bleeding need FFP to normalize their PT and PTT levels. All pharmacologic anticoagulation should be stopped.
- If vitamin K deficiency is suspected, it is reasonable to give oral vitamin K empirically for 3 days to see if PT normalizes.
- Patients with hemophilia A or B require factor VIII (either recombinant factor VIII or as cryoprecipitate) or factor IX replacement, respectively.

von Willebrand Disease

An autosomal dominant condition that is the most common bleeding disorder. Characterized by low levels of vWF, which is involved in the transport of factor VIII and also helps platelets form a hemostatic plug.

History/PE

Clinical features can mimic platelet dysfunction (causing mucocutaneous bleeds and ↑ bleeding time) as well as hemophilia (joint bleeds, ↑ aPTT) depending on the subtype.

Diagnosis

Diagnosed by ↓ levels of:

- vWF (also called factor VIII antigen).
- Ristocetin cofactor level.
- Factor VIII (functional) level.

Treatment

- Generally, no treatment is routinely required except before surgical procedures or in the setting of bleeding.
- Desmopressin (increases endothelial release of vWF) is first-line therapy in symptomatic cases.

KEY FACT

Desmopressin, also known as antidiuretic hormone, increases circulating concentrations of factor VIII and vWF while also improving platelet adhesion. It is used to reverse coagulopathic hemorrhage in vWD and mild hemophilia VIII.

Hypercoagulable State (Thrombophilia)

Thrombophilias are a group of conditions that predispose patients to blood clotting. They may be inherited or acquired (see Table 8-6).

History/PE

Look for possible 1° causes of hypercoagulability in the following patients:

- Those with a history of a first venous thrombotic event before age 50.
- Those with recurrent thrombotic episodes.
- Those who have had a thrombotic event as well as a first-degree relative who experienced a thromboembolic event before age 50.

TABLE 8-6. Inherited vs Acquired Thrombophilias

Condition	Pathology	Diagnosis/Comments
	Inherited	
Factor V Leiden	Mutation disrupts activated protein C (APC), which slows the breakdown of Va and ultimately VIIIa	Most common
Prothrombin G20210A mutation	Mutation stabilizes and thus ↑ prothrombin	DNA testing to confirm; second most common
Protein C or S deficiency	Protein C normally inactivates Va and VIIIa; mutation affects protein C synthesis; protein S is a cofactor for protein C	Warfarin carries a risk of skin necrosis.
Anti–thrombin III deficiency	Antithrombin typically inhibits thrombin and factor Xa	Can result in heparin resistance
Hyperhomocysteinemia	Inherited or acquired	
	Acquired[a]	
Antiphospholipid syndrome	Any thrombosis and > 3 miscarriages before 10 weeks or 1 after 10 weeks	⊕ Anticardiolipin or lupus anticoagulant antibodies
Cancer	Expresses tissue factor on surfaces and leads to a prothrombotic state	Cancer screening

[a]Acquired thrombophilia is associated with prolonged rest, immobilization, smoking, oral contraceptive pill use, pregnancy, nephrotic syndrome, cancer, disseminated intravascular coagulation (DIC), and lupus anticoagulant (antiphospholipid syndrome).

KEY FACT

Factor V Leiden deficiency, the most common inherited hypercoagulable disorder, is screened with an APC resistance assay and is confirmed with DNA testing. Factor V Leiden mutation disrupts the activated protein C cleavage sites.

KEY FACT

The Virchow triad: endothelial damage, venous stasis, and a hypercoagulable state.

KEY FACT

Bridge the initiation of warfarin therapy with IV heparin for at least 5 days until INR rises to the therapeutic goal. (Factor II and X levels require at least 5 days to decline.)

Diagnosis

- Screening should include APC resistance, prothrombin gene mutation, antiphospholipid antibody, plasma homocysteine, antithrombin deficiency, protein C deficiency, and protein S deficiency.
- Protein C, protein S, and antithrombin III are affected by acute thrombosis or anticoagulation. Check levels for at least 2–4 weeks after completing anticoagulation.

Treatment

- Acute thrombosis must be treated with at least 6 months of anticoagulation.
- Indications for lifelong anticoagulation include:
  - > 2 spontaneous thromboses.
  - Antithrombin deficiency.
  - Antiphospholipid syndrome.
  - Spontaneous life-threatening thrombosis.
  - Thrombosis in an unusual site (eg, the mesenteric or cerebral vein).
- Warfarin takes 3–5 days to reach its therapeutic effect, can lead to serious skin necrosis in those with protein C deficiency, and can initially be thrombotic. Thus, bridge with heparin.
- Pregnant women with a history of hypercoagulable state need to be treated with low molecular weight heparin due to warfarin's teratogenic effects.

Transfusion Reactions

Occur when a patient is infused with incompatible blood. The complications of transfusion-related reactions are listed in Table 8-7.

TABLE 8-7. Complications of Transfusion-Related Reactions

Complication	Presentation	Pathology	Diagnosis/Labs	Treatment
Febrile reaction	Fever; chills and malaise possible	Interaction between antibodies in the recipient and cytokines from the donor	Hemolytic reaction or infectious causes of hemolysis must be ruled out	Avoid transfusion when febrile For future transfusions, use leukocyte-reduced RBCs
Hemolytic reaction: Acute (< 24 hours)	Fever, chills, pain at site of reaction, hypotension, flushing	ABO incompatibility between donor and recipient Complications: AKI (from hemoglobinuria) and DIC	⊕ Coombs test, agglutination of RBC on smear, low haptoglobin (best test) Urinalysis for hemoglobinuria (⊕ Urine dip for hematuria in the setting of few RBCs on microscopy)	Stop transfusion Maintain BP and urine output with IV fluids; give furosemide if urine output is < 100 mL/hr Type and cross RBCs just transfused
Hemolytic reaction: Delayed (4–14 days post-transfusion)	Jaundice, anemia, hemoglobinuria, fever	Previous exposure to erythrocyte antigen outside ABO system; can develop alloantibodies after transfusion	↑ LDH, unconjugated hyperbilirubinemia, decreased haptoglobin	Type and screen blood before future transactions Give acetaminophen for fever. Patients with sickle cell disease may have a worsening pain crisis
Allergic reaction	Urticaria, itching, hives; rarely anaphylaxis			Stop transfusion and monitor for anaphylaxis Give diphenhydramine or other antihistamines Resume transfusion at a slower rate when symptoms resolve Provide ventilation (O_2, intubation), diuretics, steroids
TRALI (transfusion-related acute lung injury)	Shortness of breath, hypoxemia, bilateral chest infiltrates Occurs 1-6 hours post-transfusion Like acute respiratory distress syndrome Acute respiratory distress, cyanosis, fever, resolves within 24 hours	Reaction between donor antibodies against recipient neutrophil antigens	CXR shows bilateral pulmonary infiltrates without HF	Stop transfusion Provide ventilation (oxygen, intubation), diuretics, steroids
TACO (transfusion-associated circulatory overload)	Shortness of breath, edema Symptoms similar and hard to distinguish from TRALI	Overload of fluid in patients with CV compromise	Patients will exhibit signs of pulmonary edema and volume overload	Give blood slowly Give furosemide with transfusion

NOTES

CHAPTER 9

ONCOLOGY

Hematologic Malignancies

KEY FACT

- T and B lymphocytes and natural killer cells are derived from a common lymphoid progenitor.
- Megakaryocytes, neutrophils, eosinophils, basophils, monocytes, erythrocytes, and mast cells are derived from a common myeloid progenitor.

KEY FACT

Epstein-Barr Virus (EBV) is associated with aggressive lymphomas (eg, Burkitt) in patients with immune deficiencies such as HIV.

LEUKEMIA

Defined as malignant proliferations of hematopoietic cells. May be myelogenous or lymphocytic and may have an acute or chronic course, but all generally result in marrow failure that produces anemia, infections, and bleeding by reducing red blood cells (RBCs), white blood cells (WBCs), and platelets, respectively (see Table 9-1). Characterized as follows:

- **Acute leukemia:** Immature cells (myeloblasts, lymphoblasts); at least 20% blasts in bone marrow (cases with < 20% blasts are defined as "*myelodysplastic syndrome*"). Typically affects the very young or very old with a short and potentially life-threatening course.
- **Chronic leukemia:** More mature differentiated cells (metamyelocytes/myelocytes and lymphocytes). Affects middle-aged adults and has a more protracted and insidious course.

LYMPHOMA

Results from monoclonal proliferation of cells of lymphocyte lineage. Approximately 90% of lymphomas are derived from B cells, 9% from T cells,

TABLE 9-1. Characteristics of Acute and Chronic Leukemias

	Acute Lymphocytic Leukemia (ALL)	Acute Myelogenous Leukemia (AML)	Chronic Lymphocytic Leukemia (CLL)	Chronic Myelogenous Leukemia (CML)
Epidemiology	Most common in children; ↑ risk in Down syndrome	Median age 65; risk ↑ with age and with previous chemotherapy or radiation	The most common adult leukemia; affects those > 65 years of age	Affects the middle-aged; risk ↑ with previous radiation
Symptoms	Viral-like syndrome; bone pain and bruising	Fever, bruising, fatigue, anemia, or frequent infections	Often asymptomatic; may be an incidental finding on CBC; can present with fatigue and B symptoms (weight loss, night sweats, fever)	Chronic phase: Asymptomatic or presents with fatigue, B symptoms, and splenomegaly Accelerated or blastic phase: Worsening symptoms; bone pain, bleeding (platelet dysfunction), infections
Exam	Pallor, petechiae/purpura (see Figure 9-1), bleeding Adenopathy, hepatomegaly, splenomegaly, testicular and CNS involvement (all rare in AML) T-cell ALL often presents with an anterior mediastinal mass	Petechiae/purpura (see Figure 9-1), lethargy, leukemia cutis (cutaneous infiltration of leukemic cells) Gingival hyperplasia, DIC, or tumor lysis syndrome	Lymphadenopathy and hepatosplenomegaly in addition to leukemic cells	Splenomegaly, early satiety, purpura

(continues)

TABLE 9-1. Characteristics of Acute and Chronic Leukemias *(continued)*

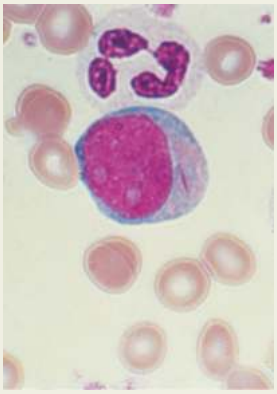
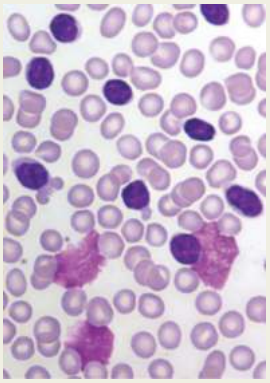
	Acute Lymphocytic Leukemia (ALL)	Acute Myelogenous Leukemia (AML)	Chronic Lymphocytic Leukemia (CLL)	Chronic Myelogenous Leukemia (CML)
Differential	AML	ALL Acute promyelocytic leukemia (AML M3): A different variant of AML; ⊕ (15;17) gene translocation	Mantle cell lymphoma: Typically more aggressive, with extranodal involvement in the small intestine, colon, and bone marrow. ⊕ cyclin D1 and t(11;14) translocation	Hairy cell leukemia: B lymphocytes with hairy cytoplasmic projections (see Figure 9-2); CD11c, TRAP ⊕, CD103 ⊕ In addition to aplastic anemia and myelofibrosis, it is a common cause of a "dry" bone marrow aspiration or tap
Diagnosis	↑ or ↓ leukocytes; ↓platelets ↑ LDH, ↑ uric acid (from tumor lysis) Smear: Lymphoblasts Bone marrow: > 20% lymphoblasts Order CXR, LP to rule out CNS involvement, and CT for mediastinal involvement	↑ uric acid from ↑ cell turnover Smear: Predominance of myeloblasts with Auer rods (Image A)  **A** Bone marrow: > 20% blasts, hypercellular (⊕ myeloperoxidase staining), and cytogenetics	Lymphocytosis Smear: Predominance of small lymphocytes; smudge cells may be present (Image B)  **B** Bone marrow: Lymphocytes, CD5 (T-cell marker), and CD23 ⊕	↑ WBC count (median 150,000 cells/μL) Smear: ↑ WBCs (mature and immature, primarily neutrophils or granulocytes) and basophilia Bone marrow blast count: ■ Chronic: < 10% ■ Accelerated: 10–19% ■ Blastic: > 20% Confirm t(9;22) Philadelphia chromosome bcr-abl gene
Treatment	Chemotherapy induction: To induce remission (destroy all blasts) Consolidation: To kill any residual leukemia Maintenance: Maintain remission	Chemotherapy induction: 7+3 induction involving an anthracycline-based chemotherapy APL treatment: *A*ll-trans-retinoic acid +/− arsenic Allogeneic bone marrow transplantation (BMT): If poor prognostic factors	No treatment indicated for asymptomatic patients; often indolent disease Anemia and thrombocytopenia have ↓ survival. Symptomatic patients are treated with a fludarabine-based regimen. May be associated with autoimmune hemolytic anemia and ITP, which can be treated with splenectomy and/or steroids	Treat even if asymptomatic Imatinib specifically targets and inhibits bcr-abl tyrosine kinase and eliminates the CML clone Allogeneic BMT can be curative in select patients and should be more strongly considered for patients in the accelerated or blast phase

Image A reproduced with permission from Longo DL et al. *Harrison's Principles of Internal Medicine,* 18th ed. New York: McGraw-Hill, 2012, Fig. 109-1B; image B reproduced with permission from Lichtman MA et al. Williams Hematology, 8th ed. New York: McGraw-Hill, 2010, Fig. 94-1A.

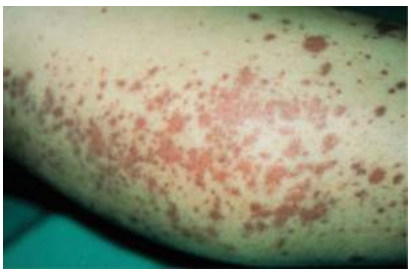


FIGURE 9-1. Scattered nonblanchable petechiae coalescing into purpura on the lower limb. (Reproduced with permission from Lichtman MA et al. *Williams Hematology,* 8th ed. New York: McGraw-Hill, 2010, Fig. 123-5.)

KEY FACT

Stem cell transplantation is used for a variety of hematologic malignancies and has two types:

- Autologous: The patient serves as the source of stem cells (eg, multiple myeloma, lymphoma).
- Allogeneic: Stem cells are acquired from a matched donor (eg, leukemia, aplastic anemia, MDS).

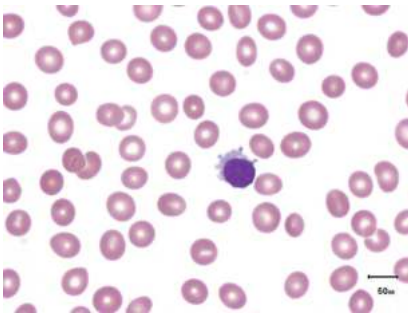


FIGURE 9-2. Hairy cell in peripheral blood with cytoplasmic projections. Note the single neoplastic cell with fine, hairlike projections extending from its surface. (Reproduced with permission from USMLE-Rx.com.)

and 1% from monocytes or natural killer (NK) cells. There are two main types: Hodgkin and non-Hodgkin lymphoma (see Table 9-2).

Hodgkin Lymphoma

A malignancy that is thought to arise from B cells and is associated with neoplastic Reed-Sternberg cells (see Figure 9-3). EBV infection may play a role in its pathogenesis.

History/PE

- Usually presents with cervical or mediastinal lymphadenopathy and spreads in a contiguous manner along the lymph nodes. Enlarged lymph nodes that fail to resolve after 3–4 weeks should be investigated with biopsy. The spleen is the most commonly involved intra-abdominal site.
- B symptoms, which indicate bulky disease and a worse prognosis, are defined as:
  - 10% weight loss in 6 months.
  - Night sweats requiring a change of clothes/sheets.
  - Fever: Temperature > 38.5°C (101.3°F).

Diagnosis

- Excisional lymph node biopsy shows Reed-Sternberg cells.
- Staging is based on anatomic lymph node involvement; prognosis depends on stage and other risk factors. PET/CT of the chest, abdomen, and pelvis is gold standard for staging; bone marrow biopsies should also be considered.

Treatment

Chemotherapy with doxorubicin (Adriamycin), Bleomycin, Vinblastine, and Dacarbazine (ABVD cocktail) +/− radiation of the involved field.

Non-Hodgkin Lymphoma

A proliferation of B and occasionally T cells. Classified as indolent or aggressive by histologic type (see Table 9-3). Extranodal involvement is common. Associated with infections—EBV with Burkitt lymphoma; HIV with central nervous system (CNS) lymphoma; human T-cell lymphotropic virus (HTLV) with T-cell lymphoma; and *H pylori* with gastric MALToma. Diffuse large B-cell lymphoma is the most common type.

History/PE

Symptoms similar to other lymphomas. Lymphadenopathy typically occurs in groups of peripheral nodes, and patients may have fewer B symptoms.

TABLE 9-2. Hodgkin vs Non-Hodgkin Lymphoma

Hodgkin	Non-Hodgkin
Reed-Sternberg cells	No Reed-Sternberg cells
Mediastinal mass/lymph nodes	Peripheral lymph nodes
B symptoms	Fewer B symptoms
Contiguous spread	Typically noncontiguous
Young (but bimodal)	Old/middle-age

TABLE 9-3. Indolent vs Aggressive Non-Hodgkin Lymphoma

Indolent	Aggressive
Follicular	Diffuse large B-cell lymphoma
MALT	Mantle cell
Marginal zone	Peripheral T cell
CLL/small lymphocytic lymphoma	Anaplastic
	Burkitt lymphoma

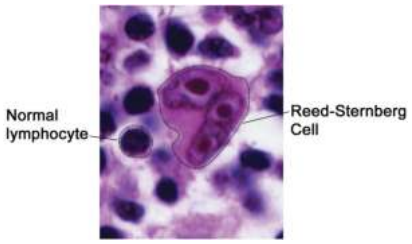


FIGURE 9-3. Hodgkin lymphoma. A Reed-Sternberg cell shows a characteristic "owl's eye" appearance. (Reproduced from the National Cancer Institute.)

Diagnosis

See Hodgkin lymphoma above. Lactate dehydrogenase (LDH) is a prognostic marker. Excisional biopsy is preferred to fine-needle aspiration for the evaluation of lymph node architecture.

Treatment

- Chemotherapy with **R**ituximab (monoclonal anti-CD20) plus **C**yclophosphamide, **H**ydroxy doxorubicin, vincristine (**O**ncovin), and **P**rednisone (**R-CHOP**).
- Treatment of high-grade non-Hodgkin lymphoma may be complicated by tumor lysis syndrome (see below). Treat with aggressive hydration and allopurinol.
- Gastric MALTomas are treated with antibiotics if *H pylori* ⊕.
- All HIV-related non-Hodgkin lymphoma requires initiation of antiretroviral therapy.

KEY FACT

Allogeneic stem cell transplantation can cause graft-versus-host disease (GVHD), in which lymphocytes from the donor mount an immune response to the patient's organs; manifesting most commonly as skin, GI, and/or liver involvement. Prophylactic immunosuppressive agents reduce the risk of GVHD.

KEY FACT

Hodgkin lymphoma: Cervical/mediastinal lymphadenopathy; centrifugal spread.
Non-Hodgkin lymphoma: Non-contiguous spread; can present with diffuse lymphadenopathy.

TUMOR LYSIS SYNDROME

A metabolic disturbance that may follow the initiation of cancer therapy. Most often associated with high-grade lymphomas or ALL. It is an oncologic emergency!

History/PE

- Tumor cell lysis results in severe hyperkalemia, hyperphosphatemia, hyperuricemia, and hypocalcemia. Hyperuricemia results from the release of large amounts of serum nucleic acids, and hypocalcemia is 2° to calcium phosphate deposition. Can quickly lead to renal failure from uric acid crystal and calcium phosphate deposition.
- Clinical manifestations may also include seizure, cardiac arrhythmia, or sudden death.

Treatment

- Prevent with adequate IV hydration and the reduction of uric acid with allopurinol or rasburicase (the drug of choice if uric acid levels are high before the initiation of chemotherapy).
- Correct electrolyte abnormalities using phosphate binders, calcium gluconate, sodium polystyrene sulfonate, insulin, and sodium bicarbonate.
- Consider dialysis if abnormalities are severe or do not respond to therapies.

Q

A 70-year-old man presents with fatigue. His PE is unrevealing, but a routine CBC shows lymphocytosis with a normal hematocrit and platelet count. What is the next step in diagnosis?

MULTIPLE MYELOMA

A malignancy of monoclonal plasma cells within bone marrow, often with unbalanced, excessive production of immunoglobulin protein. Typically seen in older adults.

History/PE

- Often presents with one or more of the four primary manifestations of the disease known by the mnemonic **CRAB.** These can be discovered on routine labs or by the symptoms they can cause. Hyper**C**alcemia ("stones, bones, abdominal groans, and psychiatric overtones"), **R**enal failure, **A**nemia (fatigue), and/or **B**one lesions (bone pain or pathologic fractures). See Table 9-4.
- May also present with frequent infections 2° to dysregulation of antibody production.

Differential

Contains several plasma cell dyscrasias and includes the spectrum myeloma-associated diseases: **M**onoclonal **G**ammopathy of **U**ndetermined **S**ignificance (**MGUS**) and smoldering myeloma (see Table 9-5), along with the related disorders of AL amyloidosis (see below) and Waldenström macroglobulinemia, characterized by ↑ cold agglutinins (can cause autoimmune hemolysis, lymphadenopathy, and hepatosplenomegaly).

Diagnosis

- Can be diagnosed in several different ways, all relating to the primary disorder of plasma cells and importantly distinguishing it from MGUS and smoldering myeloma, as well as Waldenström macroglobulinemia. This includes any of the following scenarios:
  - Bone marrow biopsy showing > 10% clonal plasma cells or extramedullary plasmacytoma + end organ damage (CRAB).
  - Bone marrow biopsy with > 60% clonal plasma cells, regardless of presence of end organ damage.
  - Serum free light chain ratio of > 100:1 of involved to uninvolved light chains.
- A full-body skeletal survey is the test of choice to demonstrate "punched-out" osteolytic lesions of the skull and long bones (see Figure 9-4).

Treatment

- It is important to determine which patients are candidates for high-dose chemotherapy and stem cell transplantation. The latter improves disease-free and overall survival.
- β-Microglobulin, LDH, and albumin are prognostic markers.

TABLE 9-4. Bone Lesions and Associated Malignancies

Bone Lesions	Associated Cancer
OsteoLytic	Myeloma, kidney, lung, breast, GI (can see on plain films)
OsteoBlastic	Prostate, breast (may be mixed), germ cell, ovary, uterus (less likely to be seen on plain films)

A

Obtain a peripheral smear to check for smudge cells. Chronic lymphocytic leukemia is the most common type of leukemia encountered in adults.

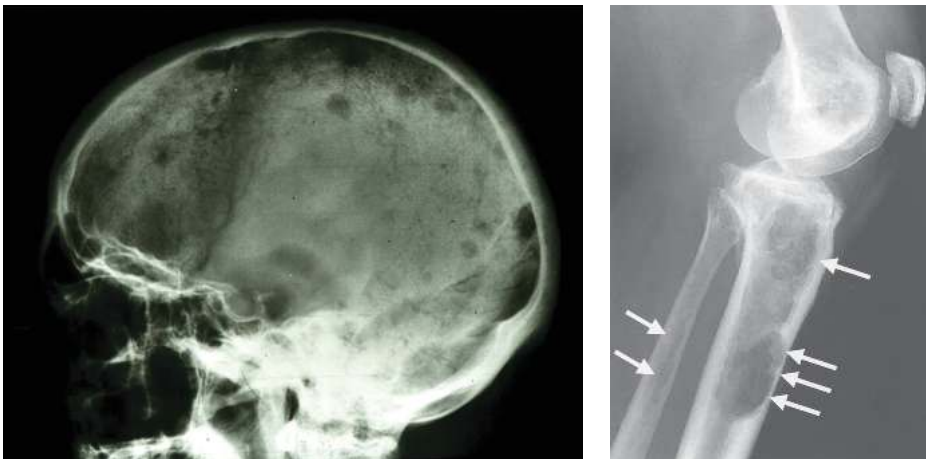
TABLE 9-5. Differential Diagnosis of Multiple Myeloma

	MGUS	Smoldering Myeloma	Multiple Myeloma
Plasma cells in bone marrow	< 10% (always)	> 10% (sometimes)	> 10% (sometimes)
M protein on SPEP	< 3 g/dL (always)	> 3 g/dL (sometimes)	> 3 g/dL (sometimes)
End organ damage	No CRAB (always)	No CRAB (always)	CRAB symptoms (often)

- Bortezomib- or lenalidomide-based regimens must be first-line therapy; three-drug regimens are preferred over two-drug regimens.
- Symptom management:
  - **Hypercalcemia:** Hydration, bisphosphonates, and diuresis.
  - **Bone pain/destruction/fractures:** Bisphosphonates, radiation, and kyphoplasty.
  - **Renal failure:** Hydration to help prevent myeloma cast nephropathy due to high concentration/precipitation in the renal tubules.
  - **Infections:** Vaccinate, diagnose early, and treat appropriately.
  - **Hyperviscosity syndrome:** Characterized by encephalopathy and bleeding; treated with plasmapheresis.
  - **Anemia:** Erythropoietin, transfusions
  - **Thrombosis:** Monitor closely.

AMYLOIDOSIS

There are many types of amyloidosis, but all are characterized by tissue deposition of abnormal protein fibrils. AL amyloidosis, one of the most common types, is a disorder of plasma cells that leads to deposition of monoclonal light chains in organs such as the kidney and heart, resulting in proteinuria and restrictive cardiomyopathy (see Table 9-6).



A B

FIGURE 9-4. Multiple myeloma. (**A**) Radiograph of the skull showing "punched out" osteolytic lesions characteristic of multiple myeloma. (**B**) Lateral view of the tibia and fibula showing focal lytic lesions (*arrows*). (Image A reproduced with permission from Kantarjian HM et al. *The MD Anderson Manual of Medical Oncology,* 2nd ed. New York: McGraw-Hill, 2011, Fig. 11-2. Image B reproduced with permission from Lichtman MA et al. *Williams Hematology,* 8th ed. New York: McGraw-Hill, 2010, Fig. 109-13A.)

Q 1

A 30-year-old man presents with a temperature of 38.7°C (101.7°F), drenching night sweats, and weight loss of 6 months' duration. Exam reveals cervical lymphadenopathy. He is not incarcerated and has no travel history or exposure to sick contacts. What diagnosis do you consider, and what is the next step in diagnosis?

Q 2

A 65-year-old woman presents with back pain and fatigue. Routine lab testing reveals anemia, hypercalcemia, and renal failure. A bone scan shows multiple lytic lesions. What is your diagnosis, and which other tests should you order?

Q 3

A 68-year-old man presents with lower extremity edema, dyspnea on exertion, periorbital bruising, and ↑ tongue size. He is found to have nephrotic-range proteinuria and a low-voltage ECG. What is a possible diagnosis, and which other minimally invasive test can help confirm the diagnosis?

TABLE 9-6. Types of Amyloidosis

	1° Amyloidosis (AL)	2° Amyloidosis (AA)	Familial Amyloidosis (ATTR)
Protein source	Bone marrow, clonal plasma cells	2° inflammatory reaction to an infection or a rheumatologic disorder, creating an abundance of amyloid A (AA) protein	Liver, mutation in the transthyretin (TTR) gene produces abnormal TTR protein
Most common organ involvement	Heart and kidneys	Kidneys	Heart, nerves
Treatment	Chemotherapy, autologous stem cell transplant	Treat the underlying infection or inflammation	Determine whether wild type or hereditary type New drug-stabilizing agents Liver transplant

1 A

Given the patient's history, an infectious etiology such as TB or HIV is unlikely. An excisional lymph node biopsy should be done to rule out lymphoma in a young patient with B symptoms (weight loss, night sweats, fever).

2 A

With renal failure, anemia, hypercalcemia, and lytic bone lesions, think multiple myeloma and order:

- **SPEP:** To quantify M protein (most commonly IgG > 3 g/dL).
- **SIFE:** To identify M protein subtype: immunoglobulin and light chain type; determine monoclonality.
- **SFLC:** To determine serum free light chain levels and ratio (Ratio > 100:1 is diagnostic).
- **UPEP:** To determine the presence of Bence Jones protein in the urine. A standard dipstick only measures albumin and may miss other types of protein.
- **UIFE:** To identify the types of light chains in the urine.

3 A

AL amyloidosis and fat pad aspirate. A fat pad aspirate is highly sensitive and specific for amyloidosis.

Diagnosis

- Fat aspirate: When amyloid proteins are stained with Congo red, they demonstrate an apple-green birefringence under polarized light (see Figure 9-5).
- Without treatment, the prognosis for AL amyloidosis is poor. Timely diagnosis is key, to prevent further organ damage.

Breast Cancer

A malignant neoplasm of ductal or lobular breast tissue. The most commonly diagnosed cancer in women and the second most common cause of cancer death in women in the United States (after lung cancer).

- **Screening:** All organizations recommend screening with mammography at least every 2 years between the ages of 50 and 74, but starting screening earlier may be considered in certain patients (see the Ambulatory Medicine chapter).
- **Risk factors:** Include female gender, older age, obesity, early menarche, late menopause, first childbirth after 30 years, hormone replacement therapy use for > 5 years, ↑ alcohol intake (2–5 drinks per day), breast cancer in first-degree relatives, a history of atypical hyperplasia or carcinoma in situ, BRCA1/2 mutation. Certain risk factors may influence the decision of when to start screening and with what imaging modality.

History/PE

- Often diagnosed in asymptomatic patients on screening imaging. When presenting symptomatically, most masses are hard, irregular, immobile, and painless, possibly with nipple discharge.

- Adolescents may experience breast tenderness that resolves with menses. Solitary masses in adolescent women are often fibroadenomas that fluctuate in size with menses; they may resolve completely.
- Skin changes (dimpling, erythema, ulceration) and axillary adenopathy indicate more advanced disease.

Diagnosis

- When a mass is detected on exam, the first imaging study of choice is a diagnostic mammogram, which may demonstrate microcalcifications, hyperdense regions, and irregular borders.
- Ultrasound is an appropriate initial imaging modality in women < 40 years of age or for confirming suspicious lesions seen on mammography in women > 40 years (ie, to check for cystic vs solid lesions). All abnormal findings on mammogram or ultrasound should be confirmed with a biopsy.
- Obtain biopsies, then determine estrogen/progesterone receptor (ER/PR) and HER2/neu status to help guide treatment strategy.
- Special forms of breast cancer include:
  - **Inflammatory breast cancer:** Highly aggressive and rapidly growing; invades the lymphatics and causes skin inflammation (peau d'orange). Has a poor prognosis.
  - **Paget disease:** Ductal carcinoma in situ or invasive cancer of the nipple with unilateral itching, burning, and nipple erosion. May be mistaken for infection or eczema; associated with another focus of invasive cancer elsewhere in the breast.

Treatment

- **Ductal carcinoma in situ (DCIS):** Preferred treatment modality is lumpectomy +/− radiation therapy. Endocrine therapy for a duration of 5 years reduces the risk of recurrence in ER/PR ⊕ tumors.
- **Lobular carcinoma in situ (LCIS):** Carries a high risk (up to 20%) of developing a subsequent infiltrating breast cancer, including cancer in the contralateral breast. Consider close monitoring, mastectomy, or tamoxifen for prophylaxis.
- **Invasive breast cancer:** Choice of treatment is based on lymph node status, tumor size, and hormone receptor status (see Table 9-7).
- **Adjuvant chemotherapy:** Indicated for larger tumors, those associated with a high risk of recurrence (based on genomic assay), hormone ⊖ tumors, and lymph node involvement. Several regimens are now used (eg, cyclophosphamide or doxorubicin followed by paclitaxel for 4–6 months).

TABLE 9-7. Invasive Breast Cancer Treatment

Infiltrating ductal carcinoma	Treatment
With ⊖ lymph nodes	Lumpectomy, breast-conserving surgery, and radiation may be considered, depending on tumor size Chemotherapy to shrink large tumors preoperatively; adjuvant chemotherapy if ↑ risk of recurrence; endocrine therapy if ER/PR ⊕
With ⊕ lymph nodes	Breast-conserving surgery or modified radical mastectomy, axillary dissection, radiation, adjuvant chemotherapy, and endocrine therapy if ER/PR ⊕

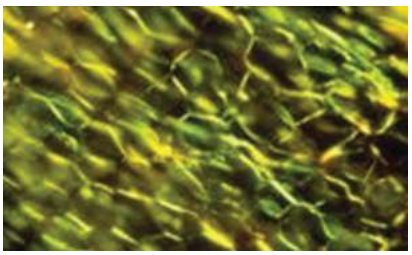


FIGURE 9-5. Subcutaneous fat aspirate in amyloidosis. Note the apple-green birefringence when viewed under polarized light. (Reproduced with permission from Lichtman MA et al. *Williams Hematology,* 8th ed. New York: McGraw-Hill, 2010, Fig. 110-1C.)

KEY FACT

The sensitivity of mammography for breast cancer is only 75–80%, so do not stop workup following a ⊖ mammogram in clinically suspicious cases.

KEY FACT

Sentinel lymph node biopsy, not axillary lymph node dissection, is the current standard of care for nodal staging in patients with breast cancer.

KEY FACT

Breast-conserving surgery is generally as effective as radical mastectomy in patients with a unifocal tumor size of < 5 cm.

KEY FACT

ER/PR ⊕ status is a good prognostic indicator; patients should be treated with hormonal therapy.

MNEMONIC

The 3 Cs of squamous cell carcinoma of the lung:

Central
Cavitary
Hyper**C**alcemia

- **Endocrine therapy:** Some types of breast cancer are dependent on estrogen for growth. Endocrine therapy is indicated for all patients with ER/PR ⊕ tumors.
  - In **premenopausal** women, estrogen is produced by the ovaries. Tamoxifen and raloxifene block estrogen effects on receptors.
  - In **postmenopausal** women, estrogen is produced by fat and muscles. Aromatase peripherally converts androgens to estrogen. Aromatase inhibitors such as anastrozole do not inhibit ovarian production of estrogen and are thus ineffective in premenopausal women.
- **Trastuzumab** (Herceptin) is beneficial for those with HER2-neu ⊕ tumors.
- In BRCA ⊕ patients, prophylactic bilateral mastectomy and/or salpingo-oophorectomy significantly ↓ the risk of breast or ovarian cancer.

Lung Cancer

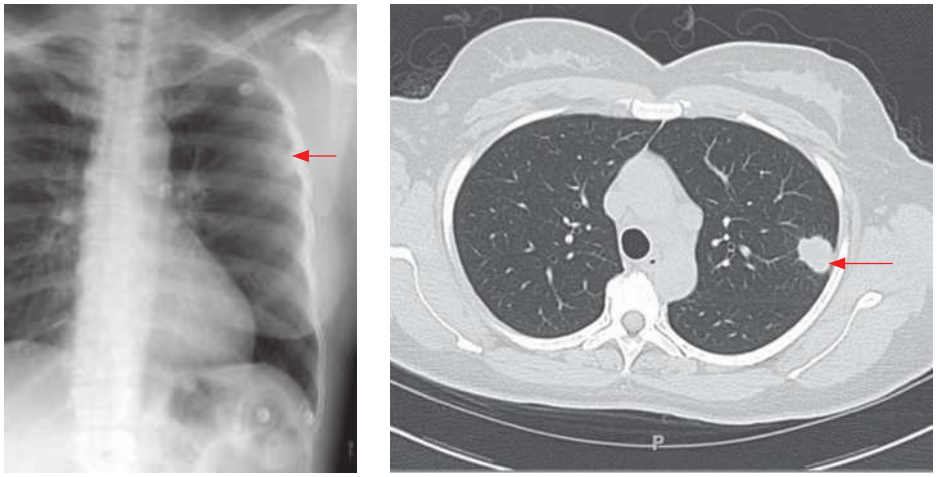
A malignancy of lung tissue (subtypes are described in Table 9-8). It remains the leading cause of cancer death. Tobacco use continues to be the major risk factor, while other risk factors include radon and asbestos. Many societies have begun recommending screening for lung cancer in those with a prolonged history of cigarette smoking. Current US Preventive Services Task Force screening recommendations are covered in the Ambulatory Medicine chapter.

History/PE

- Asymptomatic lesions are discovered incidentally on either CXR or chest CT (see Figure 9-6).
- Most patients develop signs that herald a problem (eg, chronic cough, hemoptysis, weight loss, or postobstructive pneumonia).

TABLE 9-8. Classification and Treatment of Lung Cancers

Subtype	Characteristics	Treatment
Small cell lung cancer (SCLC)	Highly related to cigarette exposure. Usually centrally located; often presents as disseminated disease (Classification system for SCLC uses terms "limited" and "extensive," not "stages")	Extensive-stage disease: Chemotherapy Limited-stage disease: Concurrent chemoradiation
Non–small cell lung cancer (NSCLC)	Adenocarcinoma: The most common lung cancer; has a peripheral location. More common in women than in men Adenocarcinoma, bronchoalveolar subtype: Multiple nodules, bilateral lung infiltrates, and metastases late in the disease course Squamous cell carcinoma: Presents centrally and is often cavitary Large cell carcinoma: Least common	Localized and locally advanced (stage I/II/III) ▪ Surgery + adjuvant chemotherapy (stage II, III) ▪ Concurrent chemoradiation (stage II, III) ▪ Stereotactic body radiation therapy for isolated with ⊖ lymph node disease (stage I) ▪ Surgery alone (stage I) Advanced disease (stage IV) ▪ Palliative chemotherapy or immunotherapy (nivolumab, pembrolizumab) ▪ Palliative radiation therapy (for symptom management, eg, painful bone lesions, brain metastasis)



A B

FIGURE 9-6. Lung cancer. Lung cancer (*arrows*) on (**A**) frontal CXR and (**B**) transaxial CT. (Reproduced with permission from USMLE-Rx.com.)

- Less frequently, patients may present late with complications of a large tumor burden:
  - **Pancoast syndrome:** Presents with shoulder pain, Horner syndrome (miosis, ptosis, anhidrosis), and lower brachial plexopathy.
  - **Superior vena cava syndrome:** Characterized by swelling of the face and arm, most often on the right side, and ↑ jugular venous pressure (JVP); urgent treatment with radiation.
  - **Hoarseness:** Vocal cord paralysis from entrapment of the recurrent laryngeal nerve, most often on the left.

KEY FACT

Adenocarcinoma presents **A**way (peripheral).
Squamous cell presents **C**entrally in **S**mokers and can have hyper**C**alcemia

Differential

- Patients with a history of exposure to asbestos are at ↑ risk of bronchogenic carcinoma and malignant mesothelioma.
- Any lung nodule in a smoker or an ex-smoker should be evaluated for cancer. Serial CXRs are useful for distinguishing benign from malignant lesions. Lesions that remain stable > 2 years are generally not cancerous.
- Other features suggestive of benign lesions include young age, smooth margins, and small size (< 2 cm). Eccentric or heterogeneous calcification and spiculated margins are more typical of malignant lesions, while popcorn or central calcifications are typically more benign.

KEY FACT

If a patient has recurrent pneumonia in the same spot with no improvement on appropriate antibiotics, look for cancer.

Diagnosis

- Biopsy of the lung mass is critical. If there is a palpable lymph node, consider biopsy of the node first. Order a CXR, and in doubtful or suspicious cases, obtain a chest CT and, if necessary, bronchoscopy.
- If mediastinal lymph nodes are enlarged, consider a PET scan and mediastinoscopy for proper staging.
- Centrally located cancers can be diagnosed by bronchoscopy or sputum cytology.
- Staging workup includes chest and abdominal CT with contrast or PET scan, bone scan, and MRI of the brain.

Treatment

See Table 9-8.

Paraneoplastic Syndromes

Disorders or symptoms that result from an immune, hormonal, or cytokine response to a neoplasm. Can present before the diagnosis of cancer.

- **Hypercalcemia:** Most often seen with squamous cell carcinoma from ↑ PTHrP production or bone metastases. Treat with bisphosphonates.
- **SIADH/hyponatremia:** Occurs more frequently with small cell carcinoma, secondary to increased ADH production.
- **Cushing disease:** Results from overproduction of ACTH secreted by small cell carcinoma. ACTH ↑ cortisol levels; can also cause high BP or new-onset DM.
- **Lambert-Eaton syndrome:** Like myasthenia gravis except that muscle fatigue improves with repeated stimulation (vs myasthenia gravis, in which repeated stimulation yields no improvement). Found more often in small cell carcinoma.
- **Erythrocytosis:** Seen in renal cell carcinoma and hepatocellular carcinoma 2° to ectopic erythropoietin production.

MNEMONIC

Paraneoplastic syndromes—

CLASH

Carcinoid
Lambert-Eaton syndrome
ACTH
SIADH
Hypercalcemia

GI Tumors

PANCREATIC CANCER

KEY FACT

Painless jaundice and/or a palpable gallbladder—think pancreatic cancer.

Typically seen in patients > 50 years of age. The most common histology is ductal adenocarcinoma, accounting for 85% of primary tumors; > 60–70% of tumors arise in the head of the pancreas. Risk factors include smoking, chronic pancreatitis, and DM, although patients often have no risk factors. Trousseau syndrome (migratory thrombophlebitis; hypercoagulable state with venous thrombosis associated with pancreatic adenocarcinoma) can occur.

History/PE

Most commonly presenting as painless jaundice (due to obstruction from cancer in the head of the pancreas), pancreatic cancer can be accompanied by a number of symptoms, including nausea, anorexia, weight loss, abdominal and lumbar back pain, new-onset DM, and venous thromboembolism.

Diagnosis

- Laboratory abnormalities may include ↑ bilirubin, ↑ aminotransferases, and normocytic normochromic anemia.
- Ultrasound is useful as an initial diagnostic test. Abdominal/pelvic CT can show the extent of disease (see Figure 9-7) and help determine whether the mass is resectable.
- Endoscopic U/S yields excellent anatomic detail and can help determine whether the tumor is resectable.

Treatment

- Pancreaticoduodenectomy (Whipple procedure) is appropriate for patients with resectable tumors.
- Chemotherapy or radiation is used for palliative care in patients with advanced or unresectable disease.

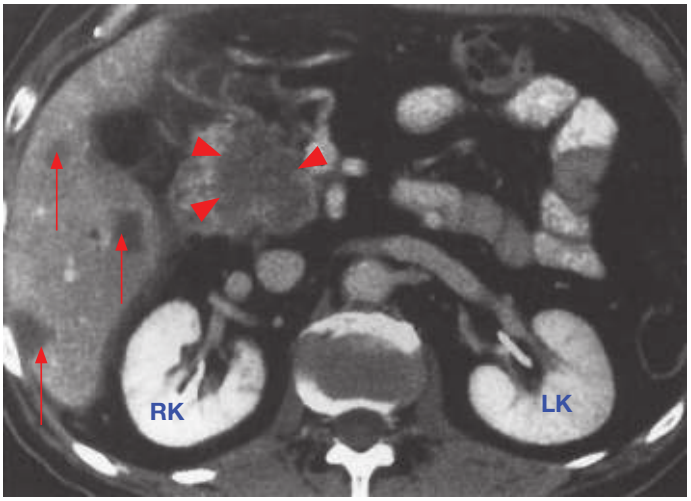


FIGURE 9-7. Pancreatic adenocarcinoma. Transaxial contrast-enhanced CT shows a mass in the head of the pancreas (*arrowheads*) and multiple liver metastases (*arrows*). RK, right kidney; LK, left kidney. (Reproduced with permission from Chen MY et al. *Basic Radiology,* 2nd ed. New York: McGraw-Hill, 2011, Fig. 11-71.)

HEPATOCELLULAR CANCER

Risk factors for hepatocellular cancer (HCC) include viral hepatitis (HBV, HCV), alcoholic cirrhosis, hemochromatosis, and α_1-antitrypsin deficiency. Oral contraceptive pills (OCPs) are associated with benign hepatic adenoma (vs HCC).

History/PE/Diagnosis

Abdominal discomfort with ↑ aminotransferases, ↑ bilirubin, and coagulopathy. Diagnosed on abdominal imaging (see Figure 9-8).

Treatment

- Surgical resection and liver transplantation can yield long-term survival.
- Alternatives for unresectable tumors include percutaneous alcohol injections, transarterial chemoembolization, radiofrequency ablation, and systemic therapy (eg, molecularly targeted agents such as sorafenib, chemotherapy).

KEY FACT

2° liver tumors (metastases) are more common than 1° liver tumors.

COLORECTAL CANCER

Typically occurs after the age of 50 years, although the incidence is currently rising among those under 50 for unknown reasons. The fourth most common cause of cancer and the second leading cause of cancer death in the United States, after lung cancer. Table 9-9 highlights the various risk factors. Screening for colorectal cancer typically begins at age 50 but may begin earlier in patients with affected first-degree relatives, African-American patients, and in those with inflammatory bowel disease (IBD) or certain genetic syndromes (see the Ambulatory Medicine chapter).

History/PE

Symptoms depend on the site of the 1° tumor and may include a change in bowel habits, melena, bright red blood per rectum, weight loss, fatigue, vomiting, or abdominal discomfort.

Q

A 60-year-old woman presents with painless jaundice and weight loss. What is the most likely location of the obstructing mass?

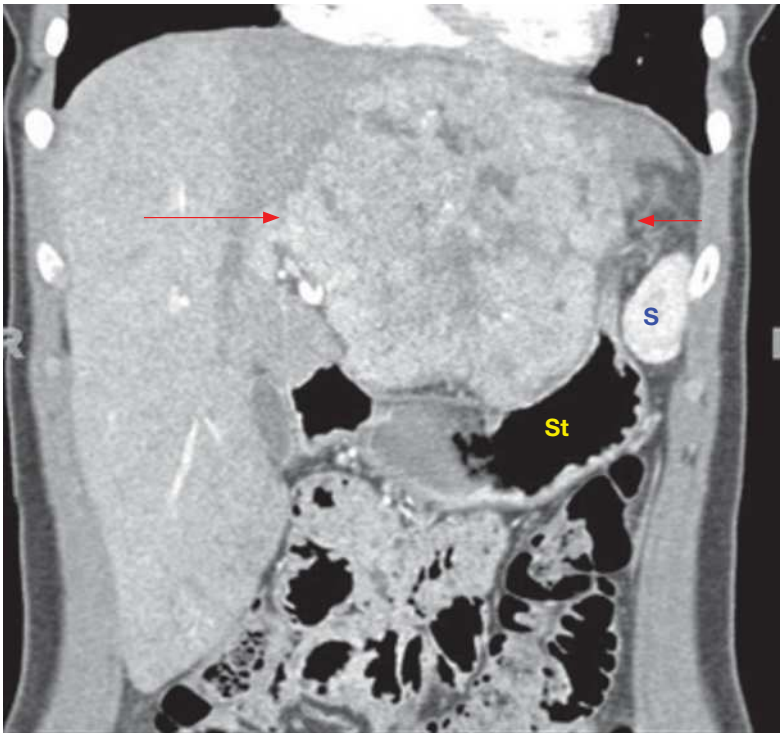


FIGURE 9-8. Hepatocellular carcinoma. Coronal reformation from a contrast-enhanced CT shows a large HCC in the left hepatic lobe (*arrows*). St, stomach; S, spleen. (Reproduced with permission from USMLE-Rx.com.)

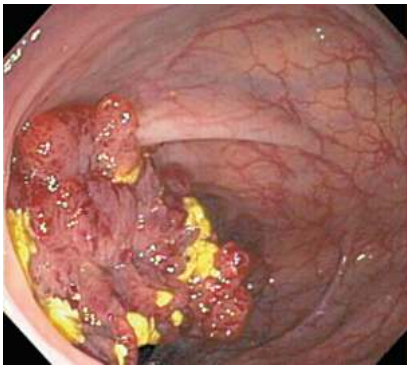


FIGURE 9-9. Colon cancer. View of the lumen via colonoscopy reveals an adenocarcinoma. (Reproduced with permission from Fauci AS et al. *Harrison's Principles of Internal Medicine,* 17th ed. New York: McGraw-Hill, 2008, Fig. 285-6.)

Diagnosis

- Found on screening colonoscopy.
- Diagnosed by a mass palpated by digital rectal examination (DRE) or detected by fecal occult blood test (FOBT).
- Iron-deficiency anemia or ↑ transaminases may be seen.
- Often metastasizes to the liver.
- Confirm the diagnosis via colonoscopy and biopsy (see Figure 9-9).

Treatment

- Influenced by tumor stage at diagnosis. 1° surgical resection involves resection of the bowel segment with adjacent mesentery and regional lymph nodes. Solitary liver/lung metastases can be resected.

TABLE 9-9. Risk Factors for Colorectal Cancer

Patient Age	Personal History	Colorectal Cancer or Adenomatous Polyps	Hereditary Colorectal Cancer Syndromes
> 50 years	Previous colorectal cancer Adenomatous polyp IBD, particularly ulcerative colitis Alcohol abuse	One first-degree relative < 60 years of age or two first-degree relatives of any age	HNPCC (Lynch syndrome) Familial adenomatous polyposis Hamartomatous polyposis syndromes

A

The pancreatic head. A mass at the head of the pancreas obstructs the common bile duct as it runs through the pancreas, causing painless jaundice.

- Stage I patients have an excellent prognosis with surgery alone (90% survival at 5 years).
- Adjuvant chemotherapy (5-FU based) is warranted for patients at stage III and above.

MISCELLANEOUS GI TUMORS

Esophageal Tumors

- Risk factors include:
  - **Lower esophagus:** Obesity, gastroesophageal reflux disease (GERD), and Barrett esophagus (associated with adenocarcinoma).
  - **Upper esophagus:** Tobacco and alcohol use (associated with squamous cell carcinoma).
- **Hx/PE:** Dysphagia in elderly person. Esophageal reflux with Barrett esophagus.
- **Dx:** Esophagogastroduodenoscopy (EGD) with biopsy (see Figure 9-10).
- **Tx:** Resection for localized disease; radiation with chemotherapy for advanced disease.

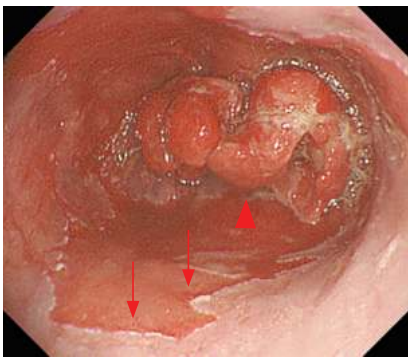


FIGURE 9-10. Esophageal cancer. An esophageal adenocarcinoma (*arrowhead*) is seen on endoscopy against a background of the pink tongues of Barrett esophagus (*arrows*). (Reproduced with permission from Fauci AS et al. *Harrison's Principles of Internal Medicine,* 17th ed. New York: McGraw-Hill, 2008, Fig. 285-3D.)

Gastric Tumors

- Risk factors include *H pylori*, smoking, and a ⊕ family history. More common in Asia and South America.
- **Hx/PE:** Classically presents as iron-deficiency anemia with vague abdominal pain in elderly patients.
- **Dx:** EGD with biopsy (see Figure 9-11).
- **Tx:** Resection for localized disease and radiation therapy with chemotherapy for advanced disease.

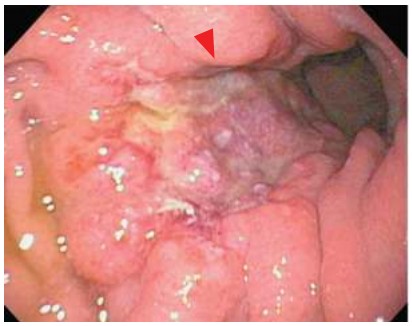


FIGURE 9-11. Gastric cancer. A malignant gastric ulcer (*arrowhead*) involving the greater curvature of the stomach is seen on endoscopy. (Reproduced with permission from Fauci AS et al. *Harrison's Principles of Internal Medicine,* 17th ed. New York: McGraw-Hill, 2008, Fig. 285-2B.)

Carcinoid Tumors (Neuroendocrine Tumors)

- Usually occur in the appendix or small bowel.
- **Hx/PE:** Clinical features include flushing, abdominal pain, diarrhea, and tricuspid regurgitation (carcinoid syndrome; symptoms result from ↑ serotonin). Tumors may also be asymptomatic and may be discovered incidentally.
- **Dx:** Diagnosed by elevated levels of 5-HIAA (the breakdown product of serotonin) or chromogranin A.
- **Tx:** Surgical resection is curative in localized disease. For symptomatic control, consider octreotide, a synthetic somatostatin analog that ↓ the secretion of serotonin. Patients with well-differentiated tumors can be managed with close observation and serial imaging.

Islet Cell Tumors

- **Hx/PE:** Presentation depends on type. Insulinoma presents with the triad of hypoglycemic symptoms, a fasting blood glucose < 40 mg/dL, and immediate relief with glucose. VIPoma (↑ VIP levels): Suspect in profuse, watery diarrhea that causes hypokalemia. Glucagonoma: Persistent hyperglycemia with necrolytic erythema (intertriginous and perioral rash).
- **Dx:** Islet cell tumors and their metastases (liver is most common) can be localized by somatostatin receptor scintigraphy.
- **Tx:** Options vary according to type. Treatment includes surgical resection, debulking, chemotherapy, and somatostatin analogs with glucagonomas and VIPomas.

Q 1

A 60-year-old man with a known diagnosis of colon cancer in remission is found to have a carcinoembryonic antigen (CEA) level that is ↑ from baseline. What does this indicate?

Q 2

A 65-year-old man with a history of GERD presents with a 10-lb weight loss, dysphagia, and epigastric pain. What will biopsy results from EGD most likely reveal?

MNEMONIC

Esophageal cancer risk factors—

ABCDEF

Achalasia
Barrett esophagus
Corrosive esophagitis
Diverticulosis
Esophageal web
Familial

KEY FACT

Low risk: Noninvasive, confined to the bladder mucosa or submucosa.
High risk: Multifocal or recurrent lesions, carcinoma in situ, or invasion of the connective tissue, especially the muscularis mucosa.

1 **A**

Cancer recurrence. CEA is normally produced in GI tissue during fetal development. An ↑ in CEA suggests colorectal cancer recurrence.

2 **A**

Esophageal adenocarcinoma. In the 1960s, most esophageal cancers were squamous cell and were associated with tobacco and alcohol use. Esophageal adenocarcinoma is now the common type in the United States and is thought to be associated with acid reflux (this patient has a history of GERD, Barrett esophagus being the premalignant condition).

Genitourinary Tumors

BLADDER CANCER

The most common malignant tumor of the urinary tract; usually transitional cell carcinoma (now known as Urothelial carcinoma). Risk factors include smoking, exposure to aniline (rubber) dyes, and chronic bladder infections (eg, schistosomiasis).

History/PE

Gross painless hematuria is the most common symptom. Other symptoms, such as frequency, urgency, and dysuria, may also be seen.

Diagnosis

- UA often shows hematuria (macro- or microscopic). Lack of dysmorphic RBCs helps distinguish this from glomerular bleeding. Cytology may show dysplastic cells.
- CT urography or IV pyelography can examine the upper urinary tract as well as defects in bladder filling.
- Cystoscopy with biopsy is diagnostic.

Treatment

Depends on the extent of spread beyond the bladder mucosa.

- **Noninvasive stage I:** Transurethral resection of the bladder tumor (TURBT). If high risk (histologic grade or invasion), treat with intravesical immunotherapy (eg, bacillus Calmette-Guérin). If very low risk, observe or give a single dose of intravesicular chemotherapy.
- **Invasive cancers without metastases:** Aggressive surgery, radiation therapy, or both.
- **Distant metastases:** Chemotherapy alone.

PROSTATE CANCER

The most common cancer in men; 95% are adenocarcinomas. Risk ↑ linearly with age.

History/PE

- Many patients are asymptomatic and are incidentally diagnosed either by DRE or by a prostate-specific antigen (PSA) level that is obtained for screening purposes.
- If symptomatic, patients may present with urinary urgency/frequency/hesitancy and, in late or aggressive disease, with anemia, hematuria, or low back pain (from bone metastases).
- Routine screening in asymptomatic patients with PSA is controversial. Most groups now recommend a shared decision-making process (typically beginning at age 55), in which physician and patient together choose the best screening option. Factors to consider are:
  - Risks: Side effects of additional work-up with prostate biopsy (can lead to incontinence, impotence); anxiety involved with an elevated PSA.
  - Indolent course of some prostate cancers and ability to pursue "watchful waiting" as opposed to treatment.

- Benefits: ↓ in mortality among screened population.
- However, if the patient is symptomatic, test, as you are no longer "screening."

Diagnosis

- Ultrasound-guided needle biopsy of the prostate allows for both diagnosis and staging.
- The Gleason score (6–10) remains the best predictor of clinical behavior. It sums the scores of the two most prevalent differentiation patterns seen on biopsy on a scale of 1–5: well differentiated (low) to poorly differentiated (high).
- Radionuclide bone scan (technetium-99) is the best modality to diagnose bone metastasis in prostate cancer.

Treatment

- Choice is based on the aggressiveness of the tumor and on the patient's risk of dying from the disease.
- Watchful waiting may be the best approach for elderly patients with low Gleason scores.
- Consider radical prostatectomy or radiation therapy (eg, brachytherapy or external beam) for node ⊖ disease. Treatment is associated with an ↑ risk of incontinence and/or impotence. Androgen deprivation therapy is often indicated following radiation therapy even in node (–) disease for high-risk disease.
- Treat node ⊕ and metastatic disease with androgen deprivation therapy (eg, GnRH agonists, orchiectomy, bicalutamide) +/− chemotherapy. Symptomatic bone lesions can be treated with palliative radiation.

KEY FACT

Incidental asymptomatic prostate cancer is especially common among men > 80 years of age and does not always need treatment.

TESTICULAR CANCER

Most common solid malignant tumor in men 20–35 years of age. It is highly treatable and often curable; 95% are germ cell tumors (seminomas or nonseminomas); pure seminomas have a better prognosis. Risk factors: family history, cryptorchid testis, and Klinefelter syndrome.

KEY FACT

Nonseminoma: ↑ α-fetoprotein, ↑ β-hCG.
Seminoma: Normal α-fetoprotein, ↑ β-hCG.

History/PE

- A unilateral painless scrotal mass is testicular cancer until proven otherwise.
- Other symptoms include testicular discomfort or swelling suggestive of orchitis or epididymitis.

KEY FACT

Do not do a scrotal biopsy to diagnose testicular cancer, as this may result in seeding of the biopsy tract.

Diagnosis

- Serum levels of α-fetoprotein (AFP), LDH, and β-hCG should be measured.
- Scrotal ultrasound is useful to differentiate non-neoplastic lesions (eg, hydrocele, spermatocele, infection) (see Figure 9-12).
- Definitive diagnosis is made by radical inguinal orchiectomy.
- Staging evaluation (TNM is widely used) should include serum lactate dehydrogenase (LDH), AFP, β-hCG, and CT of the chest/abdomen and pelvis (the retroperitoneal lymph nodes and thorax are usually the first sites of metastasis).

Treatment

Radical inguinal orchiectomy +/− chemotherapy/radiation therapy.

Q

A 60-year-old man with a 35-pack-year smoking history presents with pink urine. UA reveals RBCs; CT urography reveals no abnormalities of the kidneys or ureters. What is the diagnostic test of choice?

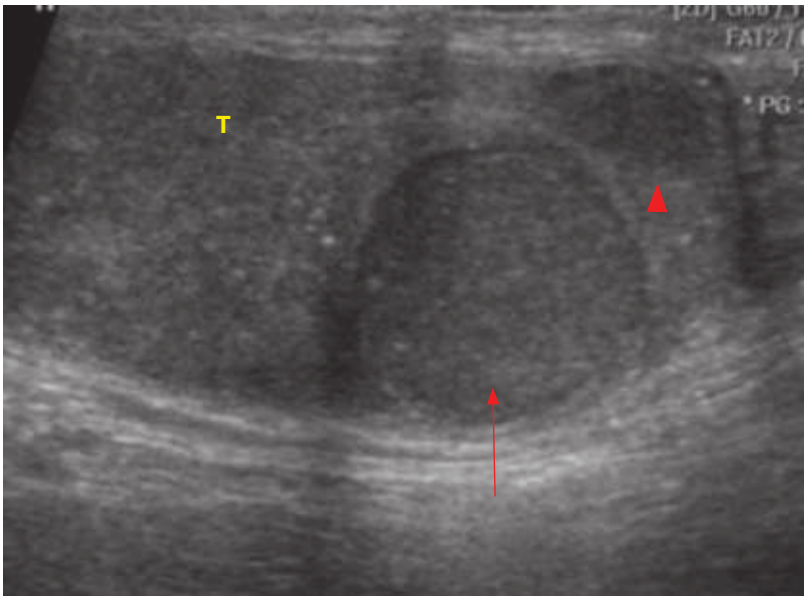


FIGURE 9-12. Seminoma. Longitudinal ultrasound image of testicle (T) shows a homogeneous intratesticular mass (*arrow*) and an additional smaller focus of tumor (*arrowhead*). (Reproduced with permission from USMLE-Rx.com.)

KEY FACT

Biopsy should not be used to diagnose renal cell carcinoma unless disseminated disease or another 1° tumor is suspected. Risks include false negatives, bleeding, and tumor seeding.

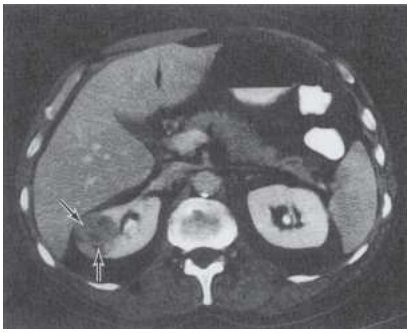


FIGURE 9-13. Renal cell carcinoma (*arrows*). (Reproduced with permission from McAninch JW, Lue TF. *Smith & Tanagho's General Urology,* 18th ed. New York: McGraw-Hill, 2013, Fig. 22-5.)

A

Cystoscopy with possible biopsy.

RENAL CELL CARCINOMA

Malignancies of the kidneys are often diagnosed incidentally but may be associated with various symptoms as noted below. Typically a disease of older age and is more common in men. Like many other malignancies, cigarette smoking is a risk factor, although it is also associated with several conditions, including von Hippel Lindau disease, tuberous sclerosis, and cystic kidney disease. Clear cell is the most common type.

History/PE

- Renal cell carcinoma (RCC) is generally asymptomatic in the early stages, but symptoms can include hematuria, flank pain, a palpable mass, fevers, night sweats, anemia, or symptoms of disseminated disease such as dyspnea and bone pain.
- Paraneoplastic effects such as erythrocytosis, hypercalcemia, and hypertension may be seen.

Diagnosis

- Most cases are found incidentally (see Figure 9-13).
- Renal ultrasound can determine whether the mass is cystic or solid. CT-guided biopsies are usually not performed if the mass fits the appropriate radiographic criteria for RCC.

Treatment

- **Local disease:** Partial vs radical nephrectomy vs cryoablation/radiofrequency ablation.
- Disseminated disease: Vascular endothelial growth factor (VEGF) tyrosine kinase inhibitors (pazopanib, sunitinib), immunotherapy (nivolumab, atezolizumab), chemotherapy, or mammalian target of rapamycin (mTOR) inhibitors (eg, everolimus).

OVARIAN CANCER

Malignancies of the ovary are typically seen in women > 50 years of age and are 95% epithelial in origin. They are associated with several genetic and familial conditions, including hereditary nonpolyposis colorectal cancer (HNPCC) and BRCA1/2, and risk is ↑ by delayed menopause and infertility (while the use of ovulatory agents to treat infertility has not been proven to ↑ the risk of ovarian cancer). On the contrary, OCPs, childbirth, breastfeeding, bilateral tubal ligation, and total abdominal hysterectomy–bilateral salpingo-oophorectomy (TAH-BSO) are all protective.

History/PE

- Usually asymptomatic until the disease has reached an advanced stage.
- Symptoms include abdominal pain, bloating, pelvic pressure, urinary frequency, early satiety, constipation, vaginal bleeding, and systemic symptoms (fatigue, malaise, weight loss).
- Exam reveals a palpable solid, fixed, nodular pelvic mass; ascites; and pleural effusion (Meigs syndrome). Ovarian mass in postmenopausal women is ovarian cancer until proven otherwise.

Diagnosis/Treatment

- Evaluate adnexal masses with pelvic ultrasound and possibly CT; obtain serum CA-125 and a CXR.
- Staging is surgical and includes TAH-BSO, omentectomy, and tumor debulking.

CERVICAL CANCER

While having significantly declined in the United States, cervical cancer is still a leading cause of cancer mortality in the developing world. Compared to other solid tumors, it is a disease of a relatively younger population with mean age at diagnosis in the mid-40s. Human papillomavirus (HPV) is the cause of almost all cases of cervical cancer (see Figure 9-14). Thus, risk factors include multiple sexual partners, early onset of sexual activity, and STDs (along with

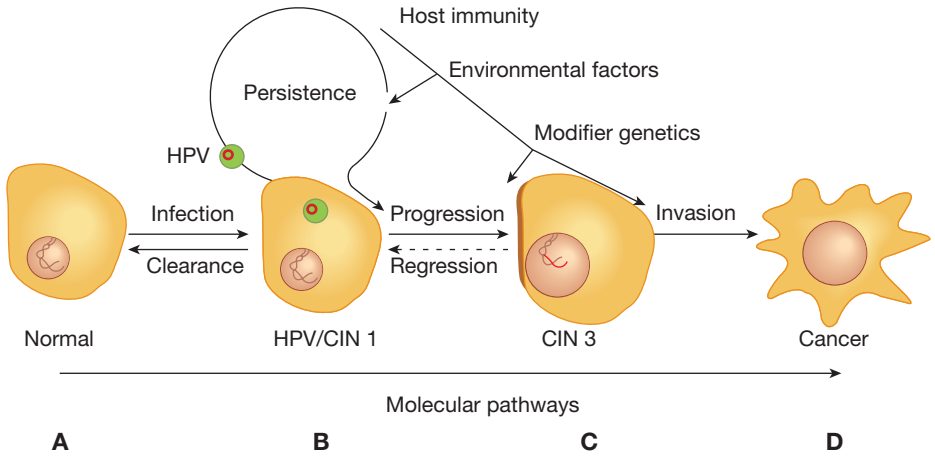


FIGURE 9-14. Genesis of cervical cancer. (**A**) Normal cell. (**B**) Cell at risk from active HPV infection. The HPV genome is a plasmid separate from the host DNA. (**C**) Cervical intraepithelial neoplasia 3 (CIN 3) or carcinoma in situ (CIS). The HPV genome has become integrated into the host DNA. (**D**) Interactive effects between environmental insults, host immunity, and somatic cell genomic variations lead to invasive cervical cancer. (Reproduced with permission from Hoffman BL et al. *Williams Gynecology,* 2nd ed. New York: McGraw-Hill, 2012, Fig. 30-1.)

tobacco abuse and immunocompromise). See the Ambulatory Medicine chapter for screening recommendations.

History/PE

- Usually asymptomatic and diagnosed on routine Pap smear.
- If symptomatic, patients may present with menorrhagia and/or metrorrhagia, postcoital bleeding, pelvic pain, and vaginal discharge.

KEY FACT

In suspicious cases, the Pap smear should be followed by colposcopy and biopsy.

Diagnosis

- Colposcopy and biopsy in patients with an abnormal Pap smear or visible cervical lesions.
- Cervical lesions categorized as cervical carcinoma (depth > 3 mm, width > 7 mm) or cervical intraepithelial neoplasia (CIN).

Treatment

- **CIN I** (mild dysplasia, low-grade squamous intraepithelial lesion): Can be monitored in appropriate settings with further Pap smear testing.
- **CIN II** (moderate dysplasia, classification depends on further testing) **and CIN III** (severe dysplasia or carcinoma in-situ, high-grade squamous intraepithelial lesion): Typically require excision or ablation of transformation zone (T-zone).
- **Invasive cancer:** Early-stage disease can be treated with surgery or radiation therapy; advanced disease can be treated with chemotherapy +/− surgical resection.

Prevention

HPV vaccine: The CDC recommends a two-dose vaccine schedule if started before age 15 years and a three-dose schedule if started between 15 and 26 years. The vaccine targets HPV 6, 11, 16, and 18; HPV 6 and 11 cause most genital warts, HPV 16 and 18 cause most cervical cancers.

CNS Tumors

1° brain tumors make up < 2% of all tumors diagnosed. Meningioma, glioma, vestibular schwannoma, pituitary adenoma, and 1° CNS lymphoma are the most common CNS tumors in adults. There is an ↑ risk in immunocompromised states such as AIDS. Imaging findings can help distinguish the tumor from other intracranial lesions (see Table 9-10).

MENINGIOMA

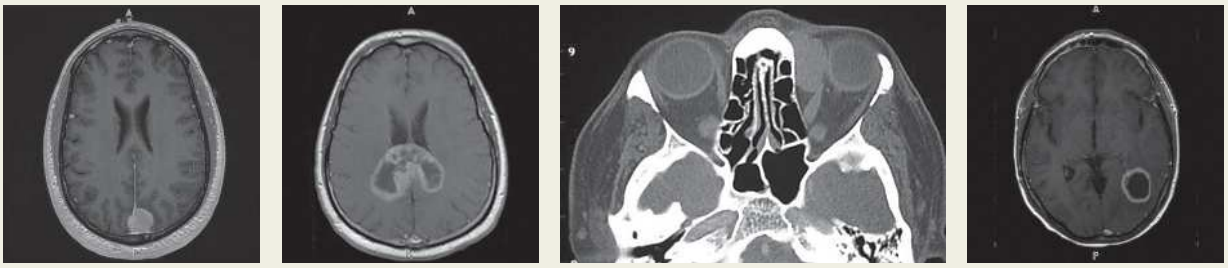
- Accounts for one-third of all 1° brain tumors; the tumors are usually benign.
- **Hx/PE:** Most tumors are small, asymptomatic, and discovered incidentally. When symptoms are present, they usually consist of progressive headache or a focal neurologic deficit reflecting the location of the tumor. Symptoms can also include spastic paresis, urinary incontinence, or new-onset seizures.
- **Dx:** CT or MRI of the head typically demonstrates a partially calcified, homogeneously enhancing extra-axial mass adherent to the dura (see Table 9-10, image A). Craniopharyngioma can cause bitemporal hemianopia.
- **Tx:** Surgical resection is appropriate for large or symptomatic tumors; observation with serial scans is the preferred approach for small or asymptomatic lesions.

KEY FACT

MRI is superior to CT for viewing skull-base/cerebellar lesions but is less reliable for detecting calcifications.

TABLE 9-10. Imaging Findings Associated with Brain Tumors

Tumor	Imaging Finding	Example
Meningioma	Extradural, calcified	Axial T1-weighted CT shows well-circumscribed, homogeneously-enhancing mass within the left aspect of the sagittal sinus with edema of the adjacent brain parenchyma within the left occipital lobe (Image A)
Glioma—glioblastoma multiforme	Multifocal or "butterfly lesions"; possible hemorrhage; centrally necrotic lesion	Transaxial contrast-enhanced image shows an enhancing intra-axial mass with central necrosis crossing the corpus callosum ("butterfly glioma") (Image B)
1° CNS lymphoma	Typically multifocal, diffusely enhancing, periventricular	CT scan shows a soft tissue density mass in the medial anterior left orbit (Image C)
Metastatic tumor	Multifocal; ring enhancement with contrast; located at the gray/white matter junction. (The most common tumors that metastasize to the brain are lung, breast, and melanoma)	Post-contrast axial T1-weighted MRI shows lung adenocarcinoma metastatic to the brain (Image D)



A B C D

Images A–D reproduced with permission from USMLE-Rx.com.

GLIAL TUMORS

- Include astrocytomas, oligodendrogliomas, mixed gliomas, and ependymomas.
- **Hx/PE:** Headache is the most common symptom. It may be generalized or unilateral, often awakens the patient from sleep and induces vomiting, and worsens with the Valsalva maneuver. Tumors are diffusely infiltrating, creating areas of low attenuation on CT or an ↑ T2 signal on MRI. Astrocytomas (specifically glioblastoma multiforme) are the most common 1° brain tumor. Glioblastoma multiforme (see Table 9-10, image B).
- **Dx:** Biopsy is required for definitive diagnosis.
- **Tx:** Surgical resection followed by external beam radiation is used for high-grade tumors. Chemotherapy can be of benefit for some 1° CNS tumors.

Tumor Markers

Usually sensitive but not specific. Thus, they are most useful for monitoring recurrence and disease activity following resection. Tumor markers can also

Q

A 60-year-old woman is involved in a motor vehicle accident in which she sustains head trauma. Her exam, which includes a nonfocal neurologic exam, is unrevealing except for some minor bruising of the forehead. Imaging shows an extradural 9-mm calcified lesion. What is the most likely diagnosis?

be useful in diagnosis if they are supported by clinical evidence. Common tumor markers and associated malignancies include the following:

- **CA-125:** Ovarian cancer.
- **CA 15-3:** Breast cancer.
- **CA 19-9:** Pancreatic cancer.
- **CEA:** GI cancer, particularly of the colon.
- **AFP:** Liver, yolk sac (testicular) cancer.
- **hCG:** Choriocarcinoma (testicular/ovarian).
- **PSA:** Prostate cancer.
- **LDH:** Lymphoma.
- **Calcitonin:** Medullary thyroid carcinoma.
- **Chromogranin A:** Carcinoid tumor.
- **β2 microglobulin:** Multiple myeloma.

Cancer Treatment Side Effects

All chemotherapeutic agents have side effects that are important to be aware of as they can affect pretreatment screening as well as parameters to monitor while on therapy:

- **Anthracyclines, such as Adriamycin (doxorubicin):** Used for the treatment of lymphomas (ABVD for Hodgkin lymphoma and R-CHOP for non-Hodgkin lymphoma), breast cancer, and several other malignancies. Most concerning side effect is dilated cardiomyopathy. Patients should be prescreened with radionuclide ventriculography or echocardiography.
- **Bleomycin:** Used for testicular cancer and non-Hodgkin lymphoma (ABVD) among other malignancies. Most concerning side effect is pulmonary fibrosis. Patients should be prescreened with pulmonary function tests.
- **Cisplatin/Carboplatin/Oxaliplatin:** Used in the treatment of a variety of malignancies. Can cause renal toxicity, ototoxicity, and neuropathy.
- **Cyclophosphamide:** Used for a variety of malignancies. Can cause hemorrhagic cystitis.
- **Methotrexate:** Used for a variety of malignancies. Can cause myelosuppression resulting in pancytopenia. Can induce folate deficiency resulting specifically in macrocytic anemia. Folinic acid (leucovorin) is used to treat this disorder as it bypasses the mechanism by which methotrexate operates.
- **Radiation:** Used for a variety of malignancies. Can cause inflammation (eg, dermatitis, colitis, cystitis, pneumonitis) at any site of treatment. In patients with Hodgkin lymphoma (especially in younger patients), radiation to the chest can cause restrictive cardiomyopathy, valvular disease, or coronary disease.
- **Metoclopramide:** Dopamine antagonist often used to treat nausea associated with chemotherapy. Can cause extrapyramidal symptoms.

A

Benign meningioma. Calcified lesions that are extradural, or outside the brain, are typically benign and rarely limit life expectancy.

CHAPTER 10

INFECTIOUS DISEASE

Soft Tissue Infections

Infections of the epidermis, dermis, subcutaneous fat, and/or fascia. Patients with diabetes, HIV or other immunosuppression, peripheral vascular disease, and edema are at ↑ risk.

IMPETIGO

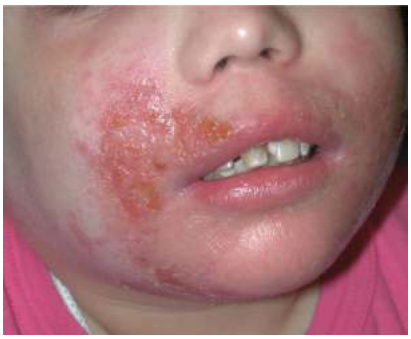


FIGURE 10-1. Impetigo. Classic honey-colored, crusted lesions are shown. (Reproduced with permission from Stern SD et al. *Symptom to Diagnosis: An Evidence-Based Guide,* 3rd ed. New York: McGraw-Hill, 2015, Fig. 29-6.)

An infection of the epidermis, usually caused by *S aureus*, and in some cases β-hemolytic streptococci.

History/PE

Presents with vesicles filled with serous fluid, usually in areas with disrupted epidermal barrier. The vesicles rupture, leaving a honey-colored crust (see Figure 10-1).

Treatment

- Limited infections: Topical mupirocin or retapamulin.
- More extensive infections: Penicillinase-resistant penicillin (such as dicloxacillin) or a first-generation cephalosporin (such as cephalexin).
- Methicillin-resistant *S aureus* (MRSA) coverage: Use trimethoprim-sulfamethoxazole (TMP-SMX) or doxycycline.

ERYSIPELAS

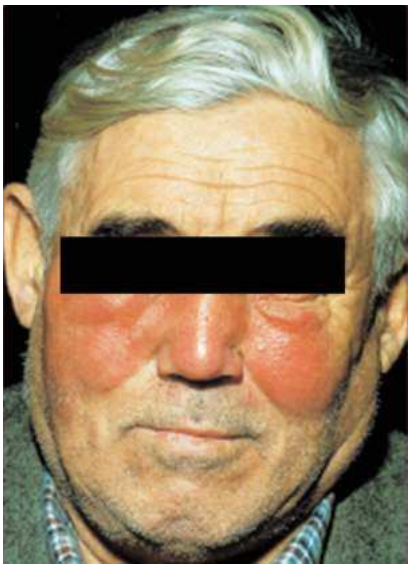


FIGURE 10-2. Erysipelas. Painful, edematous erythema with sharp margination is seen on both cheeks and on the nose. (Reproduced with permission from Goldsmith LA et al. *Fitzpatrick's Dermatology in General Medicine,* 8th ed. New York: McGraw-Hill, 2012, Fig. 178-4.)

Infection of the upper dermis, usually caused by β-hemolytic streptococci or, rarely, by *S aureus.*

History/PE

Presents with a well-demarcated, edematous area of erythema, often on the face (see Figure 10-2). Systemic symptoms, such as fever, are typically present.

Treatment

- Select the antimicrobial in consideration of patient risk factors and clinical severity.
  - **First line:** Penicillin.
  - If *S aureus* is suspected, use a first-generation cephalosporin.
  - For MRSA coverage, use TMP-SMX or doxycycline.

CELLULITIS

Infection of the dermis and subcutaneous fat that may be associated with an identifiable portal of entry (eg, cuts, animal/insect bites, ulcers, or injection sites).

- Most commonly due to *S aureus* or *Streptococcus pyogenes.*
- In diabetics, consider *Pseudomonas aeruginosa* and other gram ⊖ rods (GNRs).
- In human bite infections, consider anaerobes such as *Eikenella* as well; in animal bites, consider anaerobes, *Pasteurella* (cats), and *Capnocytophaga* (dogs). (See the chapter on Emergency Medicine for more on bite types, infecting organisms, and treatment.)

History/PE

- Presents with warm, erythematous, and tender skin (see Figure 10-3).
- Patients may also have fever, chills, regional lymphadenopathy, lymphangitis (seen as red streaks), or associated abscess.

Differential

- Cellulitis in the lower extremities may be difficult to distinguish from stasis dermatitis; look for clues suggesting cellulitis, including new-onset erythema, unilateral findings, and systemic symptoms.
- Consider necrotizing fasciitis if the patient presents with pain out of proportion to the PE findings with or without evidence of systemic inflammatory response syndrome (SIRS).
- May be differentiated from hypersensitivity reactions, which usually present with discrete urticarial lesions (hives) that are pruritic and in the distribution of the suspected allergen (eg, belt buckle).
- Lower extremity cellulitis can be associated with deep venous thrombosis (DVT). If clinically indicated, ultrasound may be useful for evaluation.

Diagnosis

- Cellulitis is primarily a clinical diagnosis.
- Consider obtaining blood cultures, CBC, erythrocyte sedimentation rate (ESR), and radiographs if there is a possibility of deeper infection such as necrotizing fasciitis or osteomyelitis.

Treatment

- **First line:** First-generation cephalosporin (such as cephalexin) or an antistaphylococcal penicillin (such as dicloxacillin) if *S aureus* is suspected (usually associated with an abscess).
- For MRSA coverage: Clindamycin, doxycycline, or TMP-SMX.
- For inpatients: Vancomycin may be used.
- Choose an antibiotic with GNR coverage for patients with diabetes.
- For human or animal bites, choose a penicillin/penicillinase combination (eg, amoxicillin/clavulanate) for coverage of anaerobes, *Pasteurella*, and *Capnocytophaga*; consider tetanus vaccination.
- If associated with abscess, perform incision and drainage.

NECROTIZING FASCIITIS

Rapidly spreading infection of the subcutaneous fat and fascia.

History/PE

- Presents with erythematous, warm, and tender skin that may rapidly progress to dark, indurated skin with bullae. Patients typically appear more toxic than those with simple cellulitis and may have significant pain in the involved area. The presence of subcutaneous gas on examination is also a clue.
- A complication of necrotizing fasciitis is compartment syndrome due to edema, which causes elevated intracompartmental pressure that ultimately leads to hypoperfusion of the muscle. Symptoms of compartment syndrome include pain seemingly out of proportion to the infection, muscle weakness, and paresthesia/numbness.

Differential

May be difficult to distinguish from cellulitis and requires a high degree of suspicion. Pain out of proportion to the PE findings distinguishes necrotizing

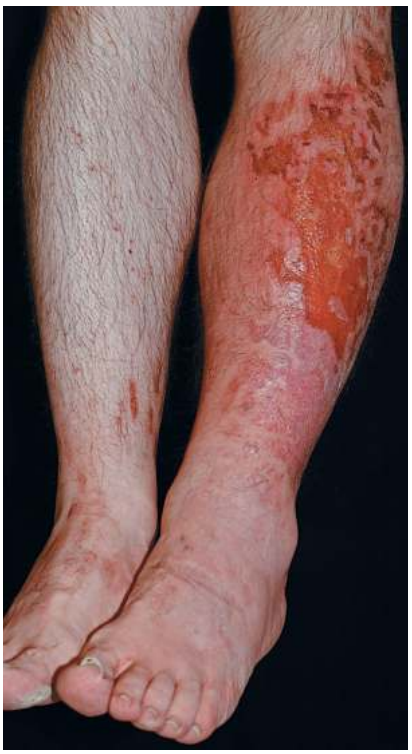


FIGURE 10-3. Cellulitis. Repeated excoriation of extremities led to MRSA cellulitis. Note the unilateral distribution. (Reproduced with permission from Wolff K et al. *Fitzpatrick's Color Atlas and Synopsis of Clinical Dermatology,* 7th ed. New York: McGraw-Hill, 2013, Fig. 25-38.)

KEY FACT

Compartment syndrome can present with a normal or unchanged arterial pulse.

Q

A 43-year-old man with diabetes presents with 1 week of edema, erythema, and warmth of his anterior left lower leg. You start him on IV vancomycin for cellulitis. A few hours later, he complains of 10/10 pain in his left leg. His leg is extremely painful to manipulation, and left foot dorsiflexion is 3/5. His left dorsalis pedis and posterior tibial pulses are 1+, unchanged from baseline. What is the next step?

fasciitis from cellulitis. An ↑ creatine kinase level can suggest the presence of myonecrosis or myositis in addition to necrotizing fasciitis.

Diagnosis

Obtain a CT or an MRI to look for gas and soft tissue involvement.

Treatment

- Obtain a surgery consult for debridement. Fasciotomy may be needed if compartment syndrome develops.
- A penicillin is best for coverage of group A streptococcus; clindamycin may be used to shut down toxin production. Vancomycin can be added for MRSA coverage.
- If mixed infection is possible, a broad-spectrum penicillin with anaerobic coverage (piperacillin/tazobactam) should be used.

KEY FACT

If necrotizing fasciitis is suspected, prompt medical and surgical management is imperative.

Complications

If it is not treated early, the condition may rapidly progress to compartment syndrome, shock, multiorgan failure, and death.

Periorbital/Orbital Infections

- **Hx/PE:** Differentiating between periorbital (preseptal) and orbital infection is critical, as management differs significantly. Although both present with erythema and pain, orbital infections may also present with oculomotor dysfunction, proptosis, chemosis, worsening pain on eye movement, and ↓ visual acuity.
- **Dx:** The diagnosis of preseptal cellulitis is typically clinical. If there is concern or suspicion for orbital infection, obtain a CT of the orbit (see Figure 10-4), blood cultures, and a CBC with differential.
- **Tx:** Preseptal cellulitis can be managed on an outpatient basis with antibiotics that cover skin flora (*S aureus*, *Streptococcus* spp). Orbital cellulitis requires broad-spectrum IV antimicrobials to cover gram-negative

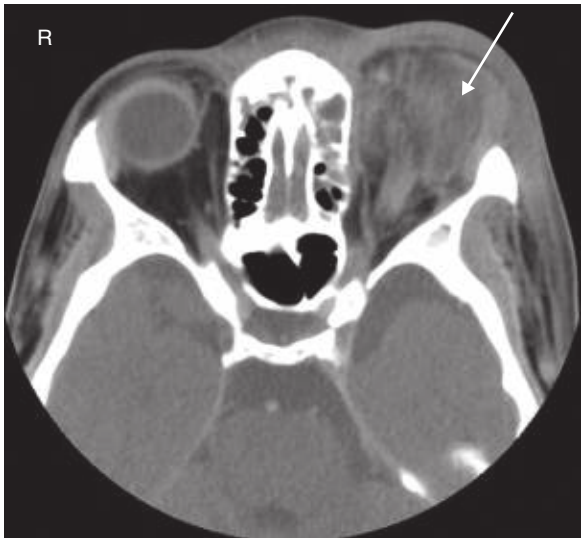


FIGURE 10-4. Left orbital abscess. (Reproduced with permission from Riordan-Eva P, Cunningham E. *Vaughan & Asbury's General Ophthalmology,* 18th ed. New York: McGraw-Hill, 2011, Fig. 13-6.)

A

The patient's presentation raises concern for acute compartment syndrome, which suggests that his soft tissue infection has extended to the muscle fascia (ie, necrotizing fasciitis). Acute compartment syndrome requires immediate surgical consultation for possible fasciotomy.

rods (GNRs) (eg, ceftriaxone, ampicillin/sulbactam) and skin flora, including MRSA (vancomycin). Surgical consultation is an important part of management.
- **Cx:** Because orbital infections involve postseptal structures, they can lead to blindness, meningitis, and cavernous sinus thrombosis.

Acute Osteomyelitis

Infection of the bone that is spread by direct inoculation or, less commonly, through hematogenous dissemination (except in pediatrics where hematogenous osteomyelitis is common). Those with peripheral vascular disease, diabetes, and recent orthopedic surgery are at ↑ risk.

History/PE

Presents with pain with overlying erythema, edema, and tenderness. Patients may have an overlying ulcer or skin interruption. Systemic symptoms include fevers, chills, and fatigue.

Differential

Cellulitis, necrotizing fasciitis.

Diagnosis

- Obtain blood cultures, CBC, and ESR/CRP. ESR and CRP are usually ↑, but blood cultures may remain ⊖.
- Obtain plain films of the suspected area of infection. These may be normal, as infection must have been present for 10–14 days before changes are seen on x-ray. Periosteal elevation is a typical x-ray finding associated with osteomyelitis.
  - If plain films are normal, proceed to MRI. If plain films or MRI/bone scan are abnormal, obtain a bone biopsy with culture for definitive diagnosis.

Treatment

- Start with broad coverage and narrow once the organism has been identified. Treatment duration is 4–6 weeks of oral or IV antimicrobial therapy.
- The most common organism is *S aureus*. Consider *Salmonella* if the patient has sickle cell anemia and consider *Pseudomonas* in the setting of IV drug use or diabetes.
- Axial skeleton osteomyelitis can resolve with antimicrobials alone, but all other cases require surgical debridement for cure.

Septic Arthritis

- Infection of a joint. Risk factors include recent instrumentation of a joint (injection, arthroscopy, arthroplasty), joint damage (osteoarthritis, trauma, RA), a prosthetic joint, gonococcal infection, and bacteremia. Commonly caused by skin flora.
- Think of disseminated gonococcal infections in sexually active young adults.
- *Staphylococcus epidermidis* is common in prosthetic joints.

Q

A 23-year-old female heroin user is diagnosed with osteomyelitis. Her history is significant for sickle cell anemia. While you are awaiting culture results, she needs to begin empiric antibiotic treatment. In addition to *S aureus*, for which additional organisms is this patient at risk?

History/PE

Presents as an erythematous, warm, swollen, and painful joint with ↓ range of motion. Gonococcal septic arthritis may present with multiple infected joints and rash. Systemic symptoms include fever and chills.

KEY FACT

Synovial fluid in septic arthritis will typically have > 50,000 WBCs with > 90% neutrophilic predominance.

Differential

- Trauma, hemarthrosis (spontaneous or traumatic), crystalline arthropathy, and autoimmune disease may all present with a similar joint exam.
- Autoimmune disease may present with systemic symptoms similar to those of septic arthritis.
- Septic arthritis may be concurrent with any of these processes; therefore, diagnosis relies on arthrocentesis.

Diagnosis

- Arthrocentesis is required for definitive diagnosis. Send fluid for Gram stain, culture, cell count/differential, and crystal analysis.
- Obtain blood cultures.

Treatment

- Initiate empiric antibiotics promptly after joint aspiration based on Gram stain. Narrow coverage once the organism has been identified.
- Surgical management with washout and 4–6 weeks of directed antimicrobials are necessary for appropriate management.

Complications

Joint destruction, sepsis, and death.

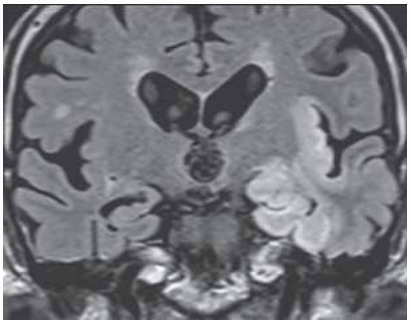


FIGURE 10-5. Herpes encephalitis. Coronal FLAIR MRI in a patient with acute herpes encephalitis shows increased T2 signal within the inferior and medial left temporal lobe. (Reproduced with permission from Ropper AH et al. *Adams & Victor's Principles of Neurology,* 10th ed. New York: McGraw-Hill, 2014, Fig. 33-1A.)

Encephalitis

Involves the brain parenchyma; herpes simplex virus (HSV) is the leading cause. Patients may have nonspecific complaints that are initially consistent with a viral prodrome (eg, fever, malaise, body aches) and may subsequently develop confusion, seizures, and focal neurologic deficits. Headaches, photophobia, and meningeal signs may be seen in meningoencephalitis.

HERPES SIMPLEX VIRUS ENCEPHALITIS

- Most cases are due to HSV-1 reactivation.
- **Hx/PE:** Think of HSV encephalitis when patients present with bizarre behavior, speech disorders, gustatory or olfactory hallucinations, or acute hearing impairment.
- **Dx:** Key cerebrospinal fluid (CSF) studies include HSV polymerase chain reaction (PCR) tests and to a lesser extent HSV culture. MRI (see Figure 10-5) will show a characteristic pattern in the temporal lobes, usually bilaterally.
- **Tx:** Treat empirically with IV acyclovir.

WEST NILE ENCEPHALITIS

A

Her IV drug use puts her at risk for *Pseudomonas* infection, and her sickle cell anemia puts her at risk for *Salmonella*.

- Suspect in anyone presenting with fever and altered mental status in late spring, summer, or early autumn.
- **Hx/PE:** In addition to fever and altered mental status, patients may have extrapyramidal symptoms or flaccid paralysis suggestive of transverse myelitis.

- **Dx:** CSF findings resemble those of viral meningitis. Test serum or CSF by enzyme-linked immunosorbent assay (ELISA) for IgM antibody to West Nile virus.
- **Tx:** Provide supportive care (eg, fluids).

Bacterial Meningitis

Common causative organisms vary with age (see Table 10-1).

History/PE

- Typical symptoms include fever, malaise, headaches, photophobia, and neck stiffness. Patients may also complain of nausea and vomiting.
- Nuchal rigidity, Kernig sign, Brudzinski sign, or "jolt sign."

Diagnosis

- Obtain LP in any patient suspected of having meningitis.
- When clinical features suggest a possible intracranial mass or ↑ intracranial pressure or if the patient has altered mental status or focal neurologic defects, obtain a head CT before LP.
- Obtain blood cultures before administering antibiotics. See Table 10-2 for CSF findings in meningitis.

KEY FACT

Add ampicillin for empiric meningitis coverage (for Listeria) if the patient is > 50 years old or immunocompromised.

Treatment

- Begin empiric therapy immediately after obtaining blood cultures in anyone suspected of having bacterial meningitis, as even a short delay will ↑ mortality. Antimicrobial therapy should not be delayed if LP cannot be performed immediately.
- Consider the patient's risk factors and then choose an antimicrobial regimen that will cover the most likely organisms (see Table 10-3).
- Administer dexamethasone before administering antibiotics if *S pneumoniae* is suspected, as this ↓ mortality.

Upper Respiratory Tract Infections

ACUTE SINUSITIS

- Inflammation of the mucosal lining of the paranasal sinuses. Viruses are the most common cause. The most common bacterial causes are *S pneumoniae*, *H influenzae*, and *Moraxella catarrhalis*. Anaerobes and rhinoviruses may

TABLE 10-1. Common Causes of Bacterial Meningitis by Age

Age Group	Typical Bacterial Pathogen
Neonates (0–4 weeks)	Group B streptococcus, *E coli, Listeria*
Infants (1–23 months)	*Streptococcus pneumoniae, Neisseria meningitidis, H influenzae*
Age 2–50 years	*S pneumoniae, N meningitidis*
Age > 50 years	*S pneumoniae, N meningitidis, Listeria monocytogenes*

TABLE 10-2. Common CSF Findings in Meningitis

CSF Parameter	Bacterial	Viral	TB
Opening pressure (mm H_2O)	200–500	< 250	180–300
Cell type	PMNs	Lymphocytes	Lymphocytes
Glucose (mg/dL)	Low	Normal	Low to normal
Protein (mg/dL)	High	Normal	Normal to high

also be implicated. Think of *Mucor* in diabetics with rapid progression of disease despite antibiotics.

- **Hx/PE:** Look for acute onset of fever, headache, facial pain, or swelling. Most cases involve cough and purulent postnasal discharge. Patients with bacterial sinusitis are typically febrile and have unilateral tenderness over the affected sinus.
- **Dx:** Based on clinical findings. Radiographic imaging or CT may help (air-fluid level, inflammation of tissues).
- **Tx:** Initial treatment is symptomatic. If symptoms persist after 10 days, are severe, or initially improve and then worsen, treat with a 7- to 10-day course of amoxicillin/clavulanate or doxycycline.

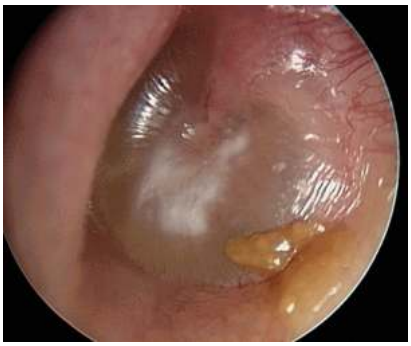


FIGURE 10-6. Acute otitis media. (Reproduced with permission from Brunicardi FC et al. *Schwartz's Principles of Surgery,* 9th ed. New York: McGraw-Hill, 2010, Fig. 18-1.)

OTITIS MEDIA

Same causative agents as acute sinusitis.

History/PE

- Typical features include fever and unilateral ear pain.
- There may also be hearing loss, and children may be irritable or may tug at their ears.
- The tympanic membrane is typically erythematous, lacks a normal light reflex, and is bulging (see Figure 10-6). Look for perforation of the tympanic membrane along with pus in the ear canal.

TABLE 10-3. Antibiotic Regimens for Bacterial Meningitis

Pathogen	Gram Stain	Risk Factors	Treatment of Choice
S pneumoniae	Gram ⊕ cocci in pairs and short chains	All patients	Vancomycin + third-generation cephalosporin + dexamethasone
N meningitidis	Gram ⊖ diplococci	Age < 50 years	Ampicillin or third-generation cephalosporin
L monocytogenes	Gram ⊕ rods	Age > 50 years or immunocompromised	Ampicillin (not cephalosporins)
Streptococcus agalactiae (group B strep)	Gram ⊕ cocci in pairs and short chains	Neonates 0–4 weeks	Ampicillin
H influenzae type b	Gram ⊖ coccobacilli	Unvaccinated patients	Third-generation cephalosporin

Treatment

- **First line:** Amoxicillin. Use amoxicillin/clavulanate if a history of recurrent otitis or if no improvement on amoxicillin.
- Patients who do not respond to antimicrobial therapy or who develop hearing loss should have tympanostomy tubes placed.

OTITIS EXTERNA

- Predisposing factors include swimming, eczema, hearing aid use, and mechanical trauma (eg, cotton swab insertion). In most patients, the causative organism is *Pseudomonas*. *S aureus* is implicated in acute otitis externa.
- **Hx/PE:** Patients have a painful ear along with foul-smelling drainage. The external ear canal is typically swollen and erythematous. There may also be pus. Patients have tenderness upon movement of the pinna or tragus.
- **Tx:** Remove any foreign material from the ear canal and start a topical antimicrobial (typically ofloxacin) with steroids.

KEY FACT

Malignant otitis externa occurs more commonly in patients with diabetes. Antipseudomonal therapy such as ciprofloxacin is first line.

PHARYNGITIS

Typically due to viral causes. Group A streptococcus is implicated in up to 25% of cases. Untreated group A streptococcal infection can result in acute pyogenic complications and rheumatic fever (fever, arthritis, carditis, chorea, rash).

History/PE

Symptoms include sore throat and fever +/− cough. Look for tonsillar exudates and tender anterior cervical adenopathy.

Diagnosis

- Calculate the Centor score to determine the likelihood of streptococcal infection and the need for rapid streptococcal antigen testing (see Table 10-4).
- Rapid streptococcal antigen testing is the best initial test; culture is the most accurate.
- Think about infectious mononucleosis in patients with cervical lymphadenopathy, malaise, and/or splenomegaly.
- In adults with pharyngitis, always consider HIV infection and acute retroviral syndrome.
- In children, think about epiglottitis (febrile patients with complaints of severe sore throat and dysphagia with minimal findings on exam).

Treatment

- Treat group A streptococcal infections with penicillin. Use a macrolide such as azithromycin for patients with penicillin allergy.
- Chronic carriers (ie, those who have a ⊕ throat culture or are asymptomatic) should be treated with clindamycin for eradication.

KEY FACT

Treatment of strep throat with antibiotics helps prevent rheumatic fever but not glomerulonephritis.

TABLE 10-4. Centor Scoring for Streptococcal Infection[a]

Finding	Points
Anterior cervical lymphadenopathy	1
Tonsillar exudate	1
History of fever > 38°C	1
Absence of cough	1

[a] < 3 point: Low risk; no testing or antibiotics are required.

3 points: Test and treat if ⊕.

4 points: High risk; consider empiric treatment with antibiotics; no testing required.

Pneumonia

Pneumonia still ranks as the sixth leading cause of death overall and is the leading cause of death from infection. Etiologies include:

- **Typical pathogens:** *S pneumoniae*, *H influenzae*, *S aureus* (in the setting of influenza virus).
- **Atypical pathogens:** *Mycoplasma*, *Chlamydia*, *Legionella*.

Q

A 55-year-old man with chronic obstructive pulmonary disease (COPD) and hypertension is admitted to the ED with a 12-hour history of fever, photophobia, and headache. LP cannot be performed immediately. Which antibiotics should be started empirically?

History/PE

- Think of pneumonia in any patient with acute onset of fever, productive cough, dyspnea, and/or pleuritic chest pain.
- Atypical organisms may present with low-grade fever, nonproductive cough, and myalgias ("walking pneumonia"). However, they may also present typically as above.
- Look for evidence of consolidation (dullness to percussion, crackles, egophony) on lung exam.

Diagnosis

- There should be radiographic evidence of an infiltrate in all immunocompetent patients (see Figure 10-7) as well as recovery of a pathogenic organism from blood, sputum, or pleural fluid.
- Consider sending urine *Legionella* antigen and urine *S pneumoniae* antigen in patients who require ICU admission, fail outpatient antibiotic therapy, have alcohol use disorder, or have a pleural effusion. Asplenic patients and those with chronic liver disease should also be screened for *S pneumoniae*.
- Remember to check arterial blood gas to determine the acid-base status of patients who appear to be in distress.
- If the patient is hospitalized, check blood cultures.

KEY FACT

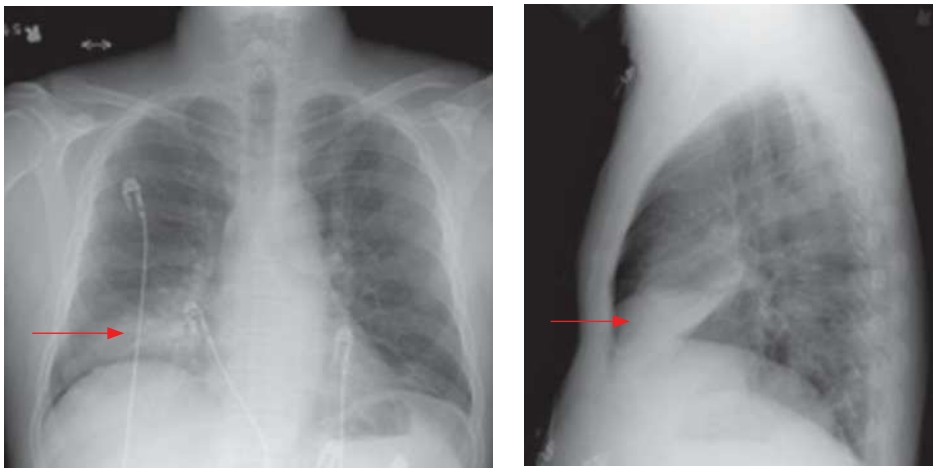
Think of *Legionella* infection in a smoker with pneumonia, diarrhea, hyponatremia, and elevated lactate dehydrogenase.

Treatment

- Use the **CURB-65** score to determine the need for hospital admission. Patients get 1 point for each of the following: **C**onfusion, **U**rea > 19 mg/dL, **R**espiratory rate ≥ 30/min, **B**lood pressure (systolic < 90, diastolic ≤ 60), and age ≥ **65.** Patients with a score of 2 or more should be hospitalized.
- Initiate empiric antimicrobial therapy based on the patient's risk factors (eg, community-dwelling, healthy vs diabetic). Think about MRSA in patients with a history of colonization or in those who have been hospitalized (see Table 10-5).

KEY FACT

Use the CURB-65 score to determine the need for hospitalization in patients with pneumonia.



A B

FIGURE 10-7. Community-acquired pneumonia. Frontal (**A**) and lateral (**B**) radiographs show airspace consolidation in the right middle lobe (*red arrows*) in a patient with community-acquired pneumonia. (Reproduced with permission from USMLE-Rx.com.)

A

After blood cultures are obtained, vancomycin and ceftriaxone should be initiated to cover for *S pneumoniae, N meningitidis,* and *H influenzae.* In patients > 50 years of age, ampicillin should be started to cover for *L monocytogenes.*

TABLE 10-5. Empiric Antibiotic Treatment Strategies for Pneumonia

Patient Profile	Include Coverage For	Empiric Antibiotic Choice
Healthy community members	*S pneumoniae, H influenzae,* atypicals	Macrolide (azithromycin)
Community members with comorbidities (DM, alcoholism, asplenia, malignancies, chronic heart, lung, liver, or renal disease) OR Community members requiring hospitalization	*S pneumoniae, Klebsiella, Legionella*	Respiratory fluoroquinolone (levofloxacin or moxifloxacin) OR Third-generation cephalosporin (ceftriaxone) + macrolide (azithromycin)
Patients at ↑ risk for multidrug-resistant (MDR) organisms[a]	Gram ⊖ rods, *Pseudomonas,* MRSA	Vancomycin or linezolid + cefepime or imipenem or piperacillin/tazobactam + respiratory fluoroquinolone
Patients with cystic fibrosis	*Pseudomonas*	Ceftazidime + respiratory fluoroquinolone + aminoglycoside
Community members with suspected aspiration	Anaerobes in addition to other organisms found in community members	Clindamycin or metronidazole added to the above regimen
Suspicion for influenza		Oseltamivir if within 48 hours of symptom onset or in those who require hospitalization
Ventilated patients	*Pseudomonas, Klebsiella, Legionella, Acinetobacter,* MRSA, other GNRs	Vancomycin or linezolid + cefepime or imipenem or piperacillin/tazobactam + respiratory fluoroquinolone or gentamicin

[a]Defined as patients who have been exposed to antimicrobials within the past 90 days, have been hospitalized for ≥ 5 days, are immunosuppressed, or have health care–associated exposure (hospitalization for ≥ 2 days within the past 90 days, residency in a long-term care facility, hemodialysis, home wound care, or a family member with a known MDR infection).

PNEUMOCYSTIS JIROVECI PNEUMONIA

Formerly known as *Pneumocystis carinii* pneumonia, *P jiroveci* pneumonia is still abbreviated as PCP. Can occur as an opportunistic infection in HIV patients (usually when the CD4 count is < 200) as well as in anyone on immunosuppressive therapies such as high-dose steroids.

History/PE

- Presents with fever, nonproductive cough, and dyspnea on minimal exertion that resolves quickly at rest.
- Patients may have tachypnea or tachycardia with exertion, fever, or diffuse rales on exam.

Diagnosis

- CXR ranges from normal to bilateral interstitial or alveolar infiltrates. The classic appearance is that of "ground-glass" infiltrates (see Figure 10-8). Look for pneumothorax.
- Other findings include ↑ lactate dehydrogenase, often > 500 U/L and ↑ β-D-glucan.

Q 1

A 28-year-old man with a history of IV drug use presents with sore throat, myalgia, fever, and night sweats of 10 days' duration. He has cervical lymphadenopathy. In addition to being screened for group A streptococcal infection, for which condition should this patient be evaluated?

Q 2

A 75-year-old woman with a history of diabetes comes to the ED with shortness of breath and cough. She is breathing at a rate of 35 bpm and has an O_2 saturation of 94% on room air. She has crackles in her right lower base. Should she be admitted to the hospital?

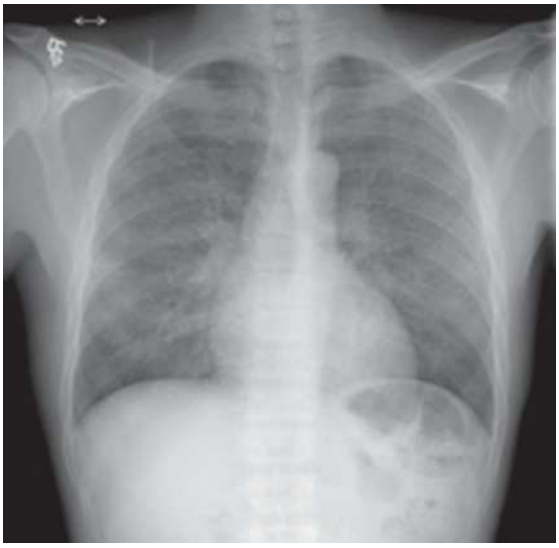


FIGURE 10-8. *Pneumocystis jiroveci* pneumonia. Frontal CXR shows diffuse "ground-glass" lung opacities characteristic of PCP in a patient with AIDS and a CD4 count of 26. (Reproduced with permission from USMLE-Rx.com.)

KEY FACT

Use concomitant prednisone if Pao_2 is < 70 mm Hg or if the patient has an alveolar-arterial oxygen gradient of > 35 mm Hg on room air.

- Obtain a fluorescence stain of sputum or bronchoalveolar lavage to look for *Pneumocystis* organisms.

Treatment

- **First-line:** IV TMP-SMX. Alternatives include IV pentamidine.

Bronchitis

- Infection of the upper airways (bronchi). Most commonly caused by respiratory viruses.
- **Hx/PE:** Presents with cough +/− sputum production. Dyspnea, fever, and chills rarely occur. The lungs are clear with possible upper airway noise.
- **DDx:** URI, pneumonia, allergic rhinitis.
- **Dx:** Often clinical (cough > 5 days), with ⊖ CXR to rule out pneumonia.
- **Tx:** For the vast majority of patients with acute bronchitis, antibiotics are not warranted. Focus is on patient education and supportive therapy.

1 **A**

Acute HIV infection. The symptoms of acute HIV are nonspecific but usually arise 2–4 weeks following exposure.

Tuberculosis

Caused by *Mycobacterium tuberculosis*. May be 1°, latent, extrapulmonary, or reactivation (see Figure 10-9). Only about 10% of those infected with the bacterium develop active disease.

History/PE

- **1° TB:** Symptoms include fevers and a dry cough. 1° TB usually involves the middle or lower lung zones and is associated with hilar adenopathy (Ghon complex) and radiographic abnormalities. The infection usually resolves, but reactivation occurs in 50–60% of patients.
- **Latent TB infection (LTBI):** Inactive and noninfectious, but reactivation occurs in about 10% of patients, typically involving the upper lungs and

2 **A**

Yes. Her clinical presentation is consistent with pneumonia. Her CURB-65 score is 2, indicating that she should be admitted to the hospital and started on a respiratory fluoroquinolone or ceftriaxone and azithromycin.

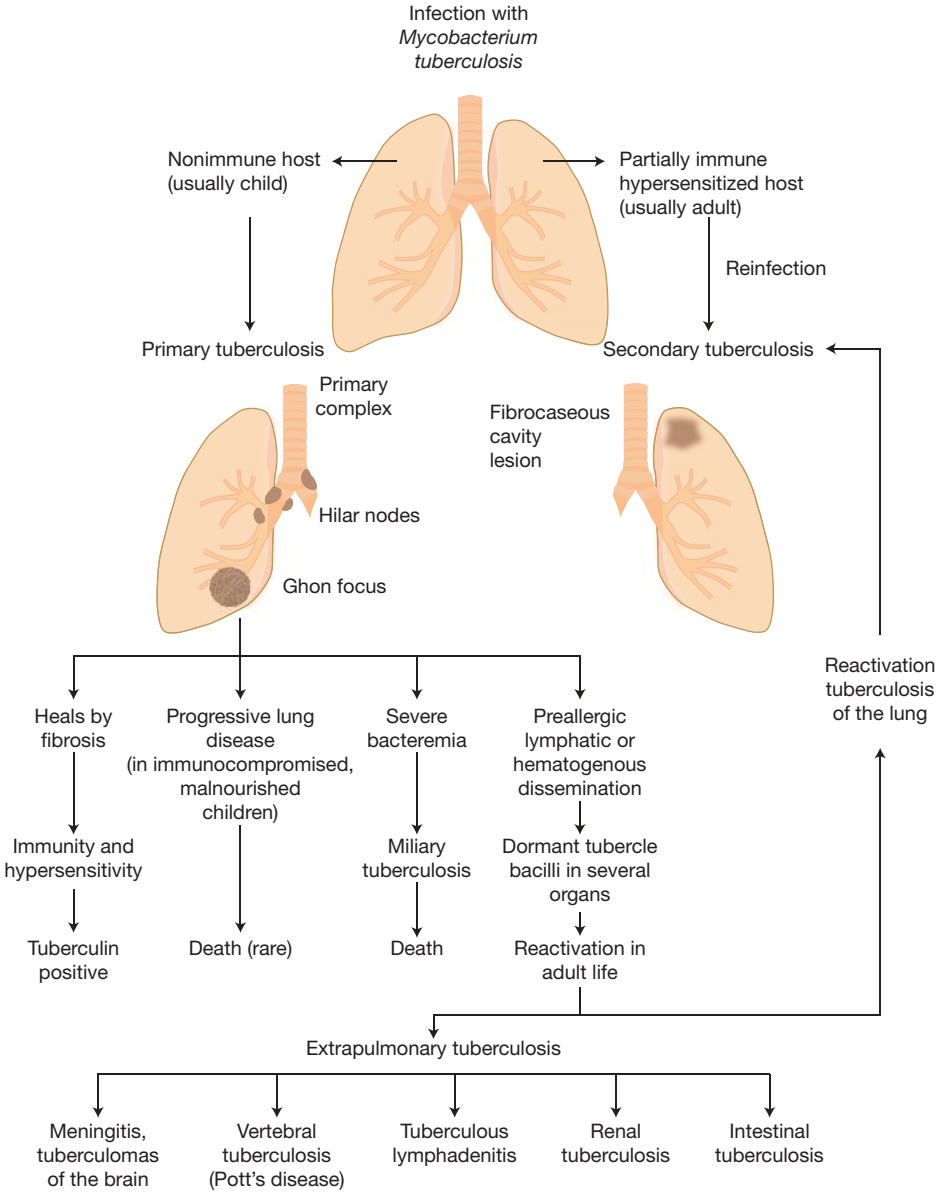
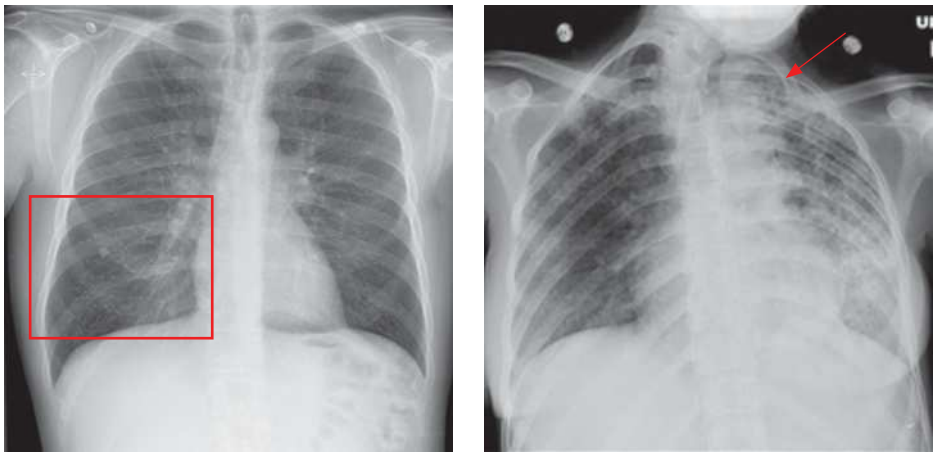


FIGURE 10-9. Evolution of pulmonary tuberculosis. (Modified with permission from Chandrasoma P, Taylor CR. *Concise Pathology,* 2nd ed. Originally published by Appleton & Lange. Copyright © 1995 by The McGraw-Hill Companies, Inc.)

cavitation. Latent infection can be detected by a ⊕ purified protein derivative (PPD) or interferon gamma release assay (IGRA). If the PPD or IGRA is ⊕, the next step is to evaluate for possible active disease with a CXR (see Figure 10-10).

- **Extrapulmonary TB:** Usually associated with HIV. May involve any organ, but areas most commonly affected (in order of frequency) are the lymph nodes, pleura, genitourinary tract, bones and joints, meninges, peritoneum, and pericardium. Symptoms are related to the organ involved. Diagnosis is based on an acid-fast bacilli (AFB) culture of affected tissue.
- **Reactivation TB:** After 1° infection and subsequent latent disease, TB can be reactivated. Symptoms include fevers, productive cough, hemoptysis, night sweats, and weight loss. Reactivation TB is characterized by fibrocaseous cavitary lesions, usually in the upper lobes. Diagnosis is based on an AFB sputum culture.



A B

FIGURE 10-10. Pulmonary tuberculosis. (**A**) Frontal CXR demonstrating diffuse, 1- to 2-mm nodules due to miliary TB. (**B**) Frontal CXR demonstrating left apical cavitary consolidation (*red arrow*) and patchy infiltrates in the right and left lung in a patient with reactivation TB. (Reproduced with permission from USMLE-Rx.com.)

KEY FACT

You should not consider previous BCG vaccination status when interpreting a reactive PPD.

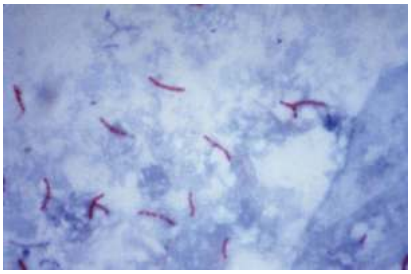


FIGURE 10-11. *Mycobacterium tuberculosis* on AFB smear. (Reproduced from the CDC/Dr. George P. Kubica.)

Diagnosis

- Screening by PPD placement or IGRA (eg, QuantiFERON Gold) should be conducted for latent tuberculosis infection (LTBI) in high-risk groups (see Table 10-6).
- Bacille Calmette-Guérin (BCG) vaccination status should be disregarded in the interpretation of test results. If initial testing is ⊕, obtain a CXR to evaluate for active infection. If CXR is ⊖, treat for LTBI as below.
- Active infection is diagnosed by AFB culture of sputum or tissue involved (see Figure 10-11).

Treatment

- The most commonly used regimen consists of four drugs described by the mnemonic **RIPE**—**R**ifampin, **I**soniazid (INH), **P**yrazinamide, and **E**thambutol—given daily for 8 weeks, followed by INH and rifampin for

TABLE 10-6. PPD Interpretation

Population	⊕ TB Skin Test
Low risk of disease—patients with no risk factors for TB	≥ 15 mm
Exposure risk: Health care workers Immigrants from endemic areas Patients with chronic illness (eg, COPD, CKD, DM, posttransplant, cancer) Homeless persons Injection drug users	≥ 10 mm
HIV patients Immunocompromised Recent contact with TB CXR consistent with previous TB infection	≥ 5 mm

TABLE 10-7. Common Adverse Effects of Tuberculosis Drugs

Drug	Adverse Effects
Rifampin	Red-orange body fluids, hepatitis
Isoniazid	Peripheral neuropathy (consider giving pyridoxine [vitamin B_6] with medication), hepatitis, lupus-like syndrome
Pyrazinamide	Hyperuricemia, hepatitis
Ethambutol	Optic neuritis

an additional 16 weeks. Table 10-7 outlines the common side effects of these drugs.

- Treatment of LTBI requires 6–9 months of INH.

KEY FACT

Give vitamin B_6 to prevent INH-associated neuropathy.

Genitourinary Tract Infections

CYSTITIS

- **Uncomplicated infection of the lower urinary tract** (ie, cystitis): A symptomatic urinary tract infection (UTI) in a patient with normal immunity and a normal GU tract with no prior instrumentation. Infections are common; approximately 10% of US women have at least one uncomplicated UTI each year.
- **Complicated UTIs:** Infections occurring in patients with functional or structural abnormalities of the GU tract, recent instrumentation of the urinary tract, or immune compromise (eg, patients with diabetes, pregnant women, transplant patients). UTIs in which symptoms are present for > 7 days are also considered complicated.
- **Hx/PE:** Dysuria, urgency, and frequency of urination are the most common complaints. Patients usually do not have a fever.
- **DDx:** Think about urethritis/cervicitis in sexually active patients. Renal stones may also present with colicky pain and dysuria.
- **Dx:** Check a UA for the presence of bacteria, WBCs, leukocyte esterase, and nitrites.
- **Tx:** Uncomplicated UTIs: Give a 3-day course of TMP-SMX, a 5-day course of nitrofurantoin, or single-dose fosfomycin. Use fluoroquinolones or β-lactams only if the previous agents are contraindicated. Complicated UTIs: May be treated with oral fluoroquinolones but often require IV antibiotics.

PYELONEPHRITIS

- Infection of the upper urinary tract/kidneys.
- **Hx/PE:** Findings are like those of cystitis, with the addition of back or flank pain, cerebrovascular accident tenderness, and systemic symptoms such as fever/chills.
- **Dx:** Urine specimens usually demonstrate significant bacteriuria, pyuria, and occasional WBC casts. A urine culture and blood culture should be sent on all patients.

KEY FACT

Always obtain blood cultures on admission, as 15–20% of patients will be bacteremic.

- **Tx:** Mild infection may be treated on an outpatient basis with a fluoroquinolone. Otherwise, hospitalization for IV antibiotics is required. If there is no clinical response, order CT or ultrasound to look for an intrarenal or perinephric abscess or an obstruction such as a renal calculus or stricture.

PROSTATITIS

- **Hx/PE:** Presenting symptoms include fevers, chills, dysuria, cloudy urine, and even obstructive symptoms if prostate swelling is significant. In patients with chronic infection, low back pain or perineal/testicular discomfort may be present. The gland is exquisitely tender on prostate digital rectal exam.
- **Dx:** Obtain urine cultures before and after a prostatic massage. In addition to typical organisms like *E coli*, think of atypical organisms such as *Chlamydia trachomatis* and *Neisseria gonorrhoeae*.
- **Tx:** Treat acute bacterial prostatitis with a fluoroquinolone or IV piperacillin/tazobactam or with a third-generation cephalosporin for 14 days. Treat chronic bacterial prostatitis with a fluoroquinolone or TMP-SMX for 4–6 weeks.

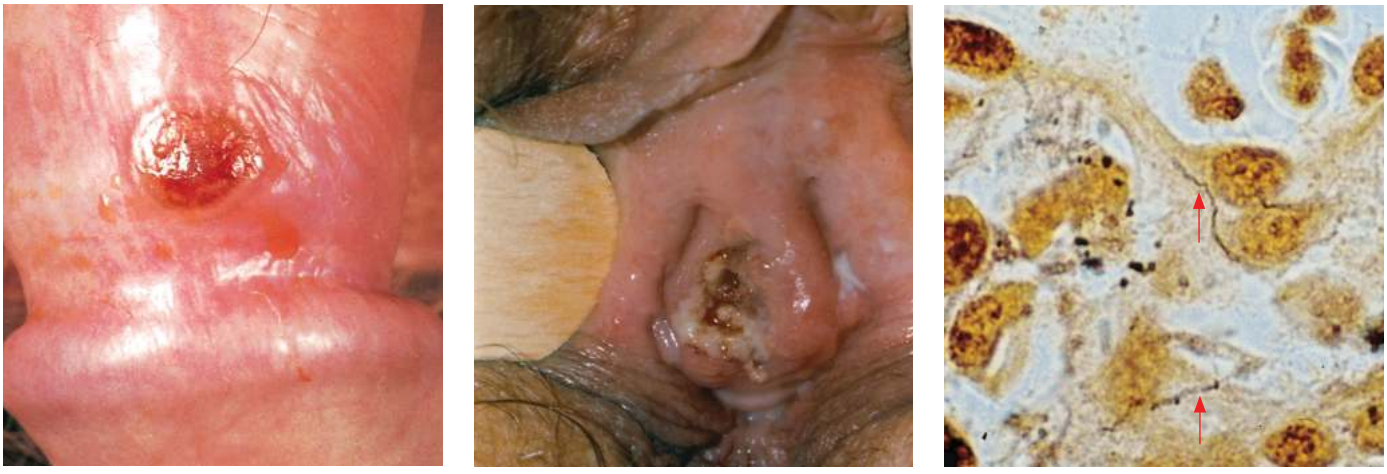
Sexually Transmitted Diseases

SYPHILIS

Caused by *Treponema pallidum*. Transmissible during early disease (1° and 2° syphilis) through exposure to open lesions—loaded with spirochetes!

History/PE

- **1° syphilis:** Develops within several weeks of exposure; involves one or more painless, indurated, superficial ulcerations (chancre; see Figure 10-12).



A B C

FIGURE 10-12. Syphilis. (**A**) Male and (**B**) female genital chancres, respectively, in primary syphilis infection. (**C**) Silver stain of sample from a chancre showing spiral-shaped spirochetes (*arrows*). (Reproduced with permission from Wolff K et al. *Fitzpatrick's Dermatology in General Medicine,* 7th ed. New York: McGraw-Hill, 2008, Figs. 200-2, 200-5, and 200-1.)

- **2° syphilis:** After the chancre has resolved, patients may develop malaise, anorexia, headache, diffuse lymphadenopathy, or rash (involves the mucosal surfaces, palms, and soles).
- **3° syphilis:** Includes cardiovascular, neurologic, and gummatous disease (eg, general paresis, tabes dorsalis, aortitis, meningovascular syphilis).

Diagnosis

- **1°:** Nontreponemal tests (RPR or VDRL) are used for screening. Send a specific treponemal serologic test (FTA-ABS, MHA-TP, or syphilis enzyme immunoassay) for confirmation. Darkfield microscopy of the exudate will show the spirochetes.
- **2°:** Diagnose by the presence of clinical illness and ⊕ serologic tests.
- **3°:** Perform an LP in the presence of neurologic or ophthalmic signs and symptoms, in the setting of treatment failure, or with a VDRL of ≥ 1:32. Correlate with cardiovascular, neurologic, and systemic symptoms.

Treatment

- **1°/2°:** Penicillin G 2.4 MU in a single IM dose. Alternatives include doxycycline or erythromycin for 14 days. If the disease duration is unknown or > 1 year, give three doses of penicillin G IM 1 week apart.
- **Neurosyphilis or syphilis in pregnant patients:** Penicillin G IV. If a patient is penicillin sensitive, desensitization is necessary.

GENITAL HERPES

- Painful grouped vesicles in the anogenital region. Caused by the human HSV, usually type 2.
- **Hx/PE:** Frequently associated symptoms include tender inguinal lymphadenopathy, fever, myalgias, headaches, and aseptic meningitis. Symptoms are usually more pronounced during the initial episode and grow less frequent with recurrences.
- **Dx:** Can be confirmed by viral PCR, by direct fluorescent antibody stain or by culture of the vesicle fluid.
- **Tx:** Acyclovir or valacyclovir for 1° infections. Treatment should begin within 48 hours of symptom onset. Severe recurrences may necessitate repeat treatment with either acyclovir or valacyclovir. Daily suppressive therapy can be used for frequent recurrences.

KEY FACT

Counsel patients regarding safe-sex practices. HSV transmission can occur even in the absence of visible vesicles.

KEY FACT

Painful genital lesions are caused by herpes or chancroid.

CERVICITIS/URETHRITIS

- Chlamydial and gonococcal infections often present as cervicitis or urethritis. *Mycoplasma genitalium* is an emerging pathogen.
- **Hx/PE:** Dysuria, dyspareunia, and a mucopurulent vaginal discharge are frequent complaints in women. In men, dysuria and a purulent penile discharge predominate.
- **Dx:** A ⊕ endocervical or urethral culture or a ⊕ urine PCR for chlamydia/gonorrhea is diagnostic.
- **Tx:** Consists of simultaneous treatment for both infections and for sexual partners. Treat chlamydia with a single PO dose of azithromycin. Treat gonorrhea with a single IM dose of ceftriaxone.

KEY FACT

Always treat for both cervicitis and urethritis simultaneously, and treat sexual partners.

HIV Infection

Acute retroviral syndrome occurs in 50–90% of cases. The incubation period is usually 2–6 weeks. Acute symptoms last 1–4 weeks, with an average of 2 weeks.

History/PE

Patients have a typical viral prodrome (eg, malaise, low-grade fever) followed by the development of adenopathy. Unusual presentations include Bell palsy, peripheral neuropathy, radiculopathy, cognitive impairment, and psychosis.

Diagnosis

- The CDC recommends fourth-generation HIV serology (enzyme immunoassay [EIA]) that detects both antibody to HIV and HIV antigen for HIV screening. Serology becomes ⊕ 2–3 weeks after exposure. A confirmatory Western blot is no longer used.
- For patients with suspected acute retroviral syndrome, check a viral load, as the EIA may not have had time to turn ⊕.

Treatment

- Begin antiretroviral therapy in all patients with HIV regardless of CD4 count. This includes asymptomatic patients and pregnant women.
- Counsel pregnant women with HIV to avoid breastfeeding to ↓ the risk of HIV transmission.
- Start postexposure prophylaxis within 72 hours of a needlestick involving blood or for sexual exposure to individuals with HIV.
- Regimens should include two nucleoside reverse transcriptase inhibitors (NRTIs) and a third drug from a different category (see Table 10-8).

Complications

Complications are numerous and typically involve opportunistic infections and side effects from drugs. See Table 10-9 for prophylaxis indications.

Travel Medicine

FEVER IN THE RETURNED TRAVELER

Patients who present with a fever after international travel must be evaluated for tropical illnesses. Always consider common illnesses such as URI or UTI as causes of fever.

History/PE/Diagnosis

- Obtain a thorough travel history, including location of travel, immunization status, food precautions taken (or not taken), and sexual exposures.
- Look for rashes, lymphadenopathy, hepatosplenomegaly, jaundice, and neurologic status on exam. Altered mental status after travel is considered a medical emergency.
- Initial evaluation should include a CBC with differential, a complete metabolic panel, blood cultures, thin and thick smears for malaria, and a UA and culture.
- See Table 10-10 for a list of possible causes, presentations, and treatment.

TABLE 10-8. Categories of Antiretroviral Drugs

Examples	Common Adverse Effects
Nucleoside Reverse Transcriptase Inhibitors (NRTIs)	
Zidovudine (AZT)	Myopathy and bone marrow suppression
Didanosine (ddI)	Pancreatitis
Abacavir	Hypersensitivity reactions (eg, fever, chills, dyspnea)
Emtricitabine (FTC)	Diarrhea, nausea, and headache
Lamivudine (3TC)	Same as those for emtricitabine
Tenofovir (TNV)	Renal toxicity
Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)	
Efavirenz	CNS toxicity and teratogenicity
Rilpivirine	Depression, headache, insomnia
Nevirapine	Rash and hepatic failure
Protease Inhibitors (PIs)[a]	
Atazanavir	Benign indirect hyperbilirubinemia
Indinavir	Kidney stones
Ritonavir	Potent P-450 inhibitor
Integrase Strand Transfer Inhibitors (INSTIs)	
Raltegravir (RAL)	Hypersensitivity reaction
Dolutegravir (DTG)	Muscle weakness/rhabdomyolysis

[a]All PIs can ↑ lipids, redistribute fat, and cause DM.

MALARIA PROPHYLAXIS

- Tailor prophylaxis to reflect the prevalence of resistant *Plasmodium falciparum* (high mortality) in the area of proposed travel.
- Weekly chloroquine is the mainstay of therapy in chloroquine-sensitive areas.
- Mefloquine is active against chloroquine-resistant *P falciparum* and is also given weekly. Mefloquine resistance is present in Southeast Asia.
- Daily doxycycline or daily atovaquone-proguanil can be used in those who are unable to take mefloquine or who are traveling to mefloquine-resistant areas. Atovaquone-proguanil can be used for short trips.
- **Precautions:**
  - Mefloquine has the potential for serious neuropsychiatric side effects and should not be prescribed to people with recent or active depression, psychosis, schizophrenia, or anxiety disorders.

Q

A 37-year-old man with newly diagnosed HIV presents for routine care. His CD4 count is 35 and viral load 120,000 copies/mL. Which prophylaxis regimens should be started?

TABLE 10-9. Prophylaxis in HIV

Disease	Indication	Prophylaxis
PCP	CD4 < 200 or previous PCP or thrush	TMP-SMX, dapsone, or atovaquone
Mycobacterium avium complex (MAC)	CD4 < 50	Azithromycin weekly
Toxoplasma gondii	CD4 < 100 and *Toxoplasma* IgG ⊕	TMP-SMX or dapsone + leucovorin + pyrimethamine
TB	Recent contact or PPD > 5 mm	INH for 9 months
Pneumococcal pneumonia	All HIV patients	Vaccine; repeat in 5 years
Influenza	All HIV patients	Yearly vaccine
Hepatitis B	All HIV patients	Hepatitis B vaccine

- Other effects of mefloquine include sinus bradycardia and QT-interval prolongation; avoid in patients on β-blockers or in those with known conduction disorders.

Infectious Diarrhea

KEY FACT

Causes of bloody diarrhea:
Yersinia
Campylobacter
Enterohemorrhagic *E coli*
Entamoeba
Shigella
Salmonella

- **Hx/PE:** Diarrhea usually associated with abdominal pain +/− fever. Bloody diarrhea is typically due to enterohemorrhagic *E coli* (EHEC), Campylobacter, Shigella, and occasionally *Salmonella*.
- **DDx:** Inflammatory bowel disease, ischemic bowel, Whipple disease, celiac disease, irritable bowel syndrome, lactose intolerance, neuroendocrine disorders.
- **Dx:** Clinical diagnosis. Because most cases of diarrhea are self-limited, studies are not usually warranted. For patients with blood in the stool, fever, and severe abdominal pain, obtain a stool sample to examine for fecal leukocytes and send for culture. Bloodwork may show leukocytosis, evidence of dehydration, hemolysis, or renal failure.
- **Tx:** The most important treatment is fluid resuscitation; in children, use oral rehydration therapy. Avoid antimotility agents. For travelers, consider an empiric fluoroquinolone or azithromycin if severe. Avoid antimicrobials in EHEC, as this could precipitate hemolytic-uremic syndrome.

A

The patient should be started on TMP-SMX for PCP and toxoplasmosis prophylaxis and should be given azithromycin for MAC prophylaxis. The patient should also be vaccinated against influenza (not the live vaccine), hepatitis B, and pneumococcus.

CLOSTRIDIUM DIFFICILE COLITIS

- Risk factors include recent antimicrobial use (other than metronidazole), recent hospitalization, and proton pump inhibitor use.
- **Hx/PE:** Abdominal pain, diarrhea, nausea/vomiting (if ileus). PE shows diffuse thrombotic thrombocytopenic purpura.
- **Dx:** Stool EIA for toxins A and B followed by confirmatory cell cytotoxic assay/oxygenic culture or PCR. Also check KUB or CT of the abdomen and pelvis for toxic megacolon or associated ileus.

TABLE 10-10. Causes, Diagnosis, and Management of Fever in the Returned Traveler

Cause	High-Risk Areas	Method of Transmission	Incubation Period	Presentation	Diagnosis	Treatment
Chikungunya	West Africa, Asia, Europe, Indian and Pacific Islands, Caribbean Islands	*Aedes* mosquito bite	3–7 days	High-grade fever, bilateral polyarthralgia, maculopapular rash, headache, myalgia, facial edema	RT-PCR (presenting 1–7 days after symptom onset) ELISA or IFA for ≥ 8 days after symptom onset	Acute: Supportive care Chronic: DMARDs (MTX)
Malaria	Africa, South-central and Southeast Asia, Western Pacific, Caribbean islands, Central America, South America	*Anopheles* mosquito bite	7–30 days	Malaise, headache, myalgias, jaundice, anemia, abnormal LFTs, thrombocytopenia, hypoglycemia, cyclical fevers	Serial thin and thick smears, at least × 3, looking for ring forms inside RBCs	Antibiotic treatment varies depending on local resistance patterns; blood products as needed for anemia
Typhoid fever	South-central and Southeast Asia, southern Africa	Fecal-oral	5–21 days	Malaise, abdominal discomfort, diarrhea, hepatosplenomegaly, rose spots	Growth on blood, urine, or stool culture	Fluoroquinolones
Dengue fever	South-central and Southeast Asia, Western Pacific, Africa, Central America, South America, Caribbean islands	*Aedes* mosquito bite	3–10 days	Severe myalgias (also known as "breakbone fever" because of associated pain), headache, retroorbital pain, maculopapular rash, thrombocytopenia, hemorrhage	Primarily clinical; can check titers	Supportive care/ blood products as needed

- **Tx:** Discontinue or minimize all antimicrobials. See Figure 10-13 for a treatment algorithm. Some patients may require fecal transplant or colectomy if symptoms do not resolve with antibiotics.

Tick-Borne Diseases

Lyme disease, Rocky Mountain spotted fever, human monocytic ehrlichiosis, human granulocytic anaplasmosis, and babesiosis are all transmitted to humans via tick bites. They are particularly prevalent in the Northeast. See Table 10-11 for details.

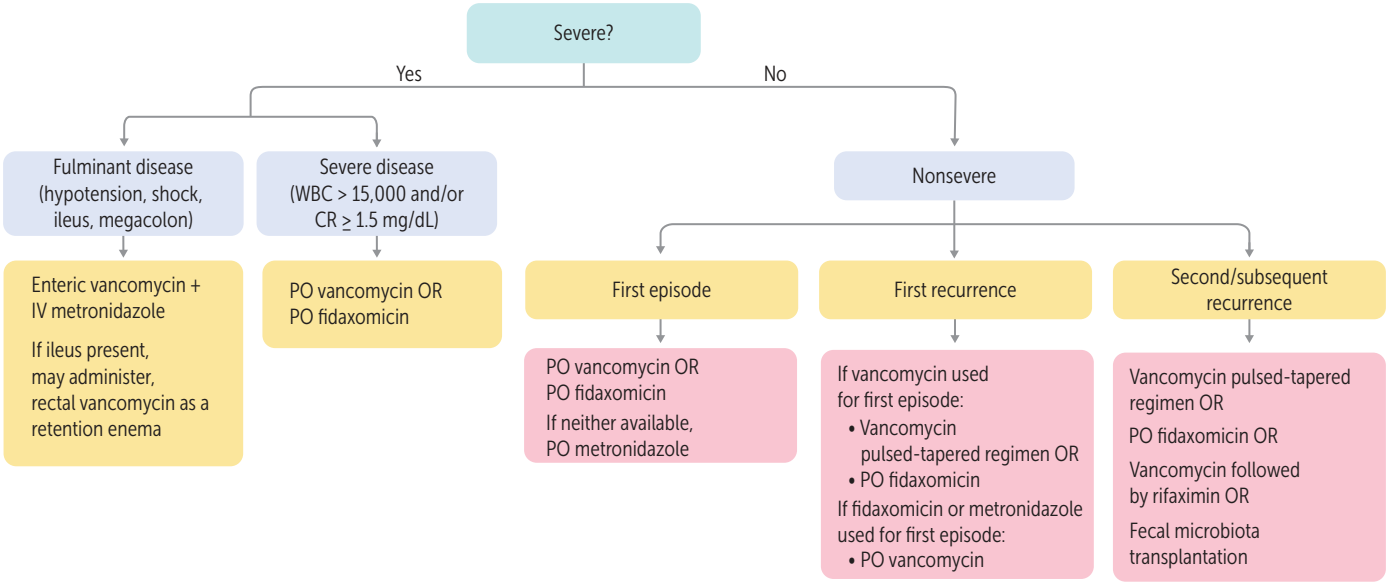


FIGURE 10-13. Algorithm for the treatment of *Clostridium difficile* infection. (Reproduced with permission from USMLE-Rx.com.)

KEY FACT

In a patient with neutropenic fever, do not conduct a digital rectal examination unless perirectal abscess is suspected.

KEY FACT

Elderly patients or those on corticosteroids may not be able to mount a fever that meets the diagnostic criteria for neutropenic fever.

Neutropenic Fever

Most often occurs after chemotherapy. Defined as a single temperature of > 38.3°C (101.3°F) or a sustained temperature of > 38°C (100.4°F) for > 1 hour in a neutropenic patient (absolute neutrophil count [ANC] = polymorphonuclear leukocytes [PMNs] + bands < 500).

History/PE

- The skin should be examined for signs of erythema, rash, cellulitis, ulcers, or line infection.
- All indwelling lines should be carefully examined for subtle signs of infection, as erythema, tenderness, fluctuance, or exudate may be the only evidence of a serious "tunnel infection."

Diagnosis

- Obtain a CBC with differential, a complete metabolic panel, amylase, lipase, and a CXR.
- Obtain at least two sets of blood cultures and urine cultures. Consider sending stool and sputum cultures if clinically indicated. LP is warranted only if CNS symptoms are present.

Treatment

- Empiric antimicrobials should cover *Pseudomonas*. Use cefepime IV or a carbapenem IV.
- Consider vancomycin in patients with a history of MRSA infections, hypotension, persistent fever on empiric therapy, or skin or catheter site infections.
- Think about fungal infections (especially *Candida* and *Aspergillus*) in patients with 4–7 days of persistent fever despite empiric antibiotic therapy, and begin amphotericin B, micafungin, or voriconazole.

TABLE 10-11. Clinical Features of Selected Tick-Borne Diseases

Disease/Causative Pathogen	History/PE	Diagnosis	Treatment
Lyme disease *Borrelia burgdorferi;* transmitted by *Ixodes* deer tick	Early localized: Erythema migrans (see Figure 10-14), fever, arthralgias, myalgias, lymphadenopathy Early disseminated: Myocarditis +/− AV block, Bell palsy, peripheral neuropathy, meningitis Late disseminated: Arthritis, chronic neurologic symptoms	ELISA as initial screen followed by Western blot or PCR as a confirmatory test	Doxycycline (patients > 9 years) or amoxicillin (children < 9 years, pregnant women); ceftriaxone if cardiac or neurologic symptoms are present Doxycycline or amoxicillin if neurologic symptoms are an isolated Bell palsy
Rocky Mountain spotted fever *Rickettsia rickettsii;* transmitted by a variety of ticks (different from those that transmit Lyme disease)	Fever, rash on palms and soles that spreads to the trunk, arthralgias, headache, thrombocytopenia, hyponatremia, ↑ transaminases	Serum antibody titers	Doxycycline regardless of patient age
Human monocytic ehrlichiosis, human granulocytic anaplasmosis *Ehrlichia spp, Anaplasma phagocytophilum;* transmitted by several deer ticks; may be cotransmitted with Lyme disease	Nonspecific (fever, chills, malaise, headache, myalgias) with no PE findings; patients often have thrombocytopenia, leukopenia, and ↑ transaminases	Serology, PCR, or peripheral blood smear to look for intracytoplasmic inclusions (morulae)	Doxycycline
Babesiosis *Babesia spp* (*Babesia* organisms infect RBCs)	Fever, chills, fatigue, myalgias. Bloodwork will reflect hemolytic anemia	Peripheral blood smear looking for organisms inside RBCs (in Maltese cross formation) or PCR	Clindamycin and quinine are preferred. Atovaquone and azithromycin are alternatives Consider plasma exchange in those with severe infection (> 10% parasitemia, significant hemolytic anemia); if symptoms persist, consider coinfection with *Anaplasma/Ehrlichia* or Lyme disease

Sepsis

Defined as two or more SIRS criteria with evidence of infection. Divided into three levels of severity (see Table 10-12). SIRS criteria are as follows:

- **Temperature:** < 36°C (< 96.8°F) or > 38°C (> 100.4°F).
- **HR:** > 90 bpm.
- **Respiratory rate:** > 20 breaths/min or a P_{CO_2} of < 32 mm Hg.
- **Leukocytes:** > 12,000 cells/mm^3, < 4000 cells/mm^3, or > 10% bands on peripheral blood smear.

Q

A 52-year-old man presents to the ED with altered mental status. He has a fever of 39°C (102.2°F), an HR of 130 bpm, and a BP of 100/60. His WBC count is 13,500 cells/mm^3. What are the next most important steps in his management?

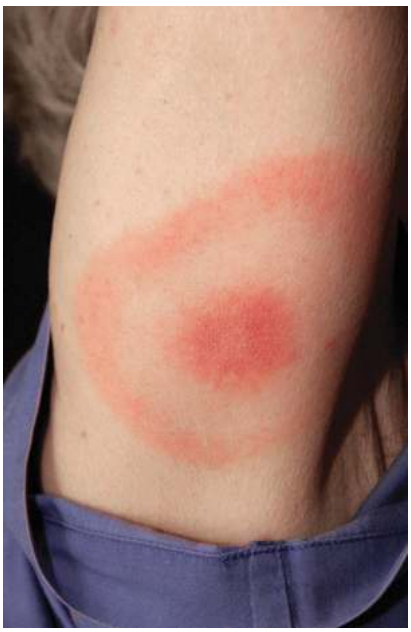


FIGURE 10-14. Erythema migrans. The classic "target" or "bull's-eye" lesion of Lyme disease is shown. (Reproduced from the CDC/Dr. James Gathany.)

KEY FACT

Aggressive fluid resuscitation and early initiation of appropriate antimicrobials is critical in the management of sepsis.

A

This patient is septic. Aggressive IV fluid resuscitation and broad-spectrum antibiotics should be initiated immediately to reduce mortality.

History/PE

- Presents with nonspecific infectious symptoms such as fever, chills, and fatigue.
- Symptoms and signs suggestive of cellulitis, necrotizing fasciitis, meningitis, sinusitis, pneumonia, endocarditis, UTI, or GI infection are seen.
- Vital signs may be abnormal (see the SIRS criteria above).
- Evidence of hypoperfusion includes cool, pale extremities, ↓ pulses, altered mental status, and ↓ urine output.

Diagnosis

- Find the focus of infection based on the history and PE.
- Always obtain blood cultures and sensitivities.
- Obtain a serum lactate to evaluate for end-organ hypoperfusion.

Treatment

- Early antimicrobial therapy and fluid resuscitation have been shown to ↓ mortality and are therefore critical to the management of sepsis.
- The initial choice of antimicrobials should be based on the likely source or should be broad spectrum if the source is unclear. These should be tailored based on culture data.
- Initiate aggressive fluid resuscitation with a goal of 30 mL/kg in the first 6 hours. If this fails to achieve a mean arterial pressure > 65 mm Hg and urine output > 0.5 mL/kg/h, initiation of vasopressors may be necessary.
- Consider central-line access for cardiovascular and pulmonary monitoring as well as administration of high-volume fluid resuscitation, blood products, and/or pressors/inotropes.
- Consider an arterial line for continuous monitoring of BP.

Complications

Can lead to acute respiratory distress syndrome, disseminated intravascular coagulation, multiorgan failure, and death.

Staphylococcal Toxic Shock Syndrome

A systemic response to staphylococcal infection, resulting in shock with multiorgan failure. Caused by toxic shock syndrome (TSS) toxin-1, a staphylococcal exotoxin that acts as a superantigen, activating multiple T cells at once and leading to massive cytokine release.

TABLE 10-12. Severity of Sepsis

Severity	Criteria
Sepsis	Meets at least two of the SIRS criteria with evidence of infection
Severe sepsis	Meets the criteria for sepsis with evidence of end-organ damage
Septic shock	Meets the criteria for sepsis with BP not responding to fluid resuscitation and necessitating the initiation of pressors and/or inotropes

History/PE

- Fever, hypotension, a diffuse macular rash followed by desquamation (1–2 weeks later), and multiorgan failure (eg, diarrhea/vomiting, myalgias/rhabdomyolysis, renal failure, liver failure, thrombocytopenia, altered mental status).
- Think of staphylococcal TSS in menstruating women (tampons can serve as a nidus for infection), in patients with nasal packing for epistaxis, in women with postpartum wounds, and in postsurgical patients with wounds that might serve as a source of infection.

Diagnosis

Check blood, wound, and/or vaginal cultures for *Staphylococcus*.

Treatment

- Aggressive IV fluid resuscitation is essential owing to capillary leak caused by cytokine release.
- Any foreign bodies in the vaginal canal or nose should be removed. If related to an infected wound, fluid collections should be drained.
- Antibiotic treatment should include a penicillinase-resistant penicillin for methicillin-susceptible *S aureus* or vancomycin for MRSA. All patients should be started on clindamycin to stop protein/toxin synthesis.

Fungal Infections

Typically affect immunocompromised patients and should always be considered in this population but may also affect healthy adults. Consider fungal infection in the neutropenic patient with persistent fevers for 4–7 days despite broad-spectrum antibiotic therapy. Fungus morphology may be as a yeast with spores, as a mold with hyphae, or both (see Table 10-13). Fungi that can present with both morphologies are referred to as dimorphic fungi and grow as a mold at room temperature and as a yeast at body temperature.

Antimicrobial Selection

When a pathogen has been definitively identified, it is important to choose an antimicrobial with narrow coverage. Table 10-14 reviews selected antimicrobials and their spectra of coverage, mechanisms of action, and common adverse effects.

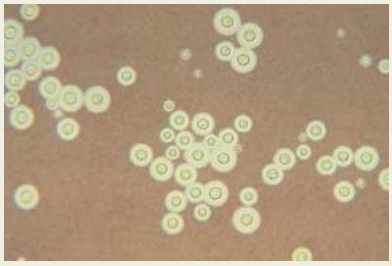
TABLE 10-13. Characteristics, Diagnosis, and Management of Fungal Infections

Infection	Morphology	Geographic Location/Mode of Transmission	History/Symptoms/Exam	Diagnosis	Treatment
Cryptococcosis	Encapsulated yeast (Image A)	Not localized to a particular region Inhalation of pigeon droppings	Self-limited pneumonia in healthy patients Invasive with meningoencephalitis if depressed T-cell function	Antigen testing and culture of infected tissue (blood, sputum, CSF); may be seen with silver stain; India ink test may show a halo 2° to capsule (see Image A)	Mild to moderate disease: Fluconazole x 6–12 months Invasive disease or immuno-compromised hosts: Amphotericin + flucytosine for 2 weeks followed by long-term fluconazole
Histoplasmosis	Dimorphic fungus; narrow-based budding yeast on biopsy (Image B)	Ohio/Mississippi River Valleys Inhalation of bat guano or bird excrement, typically in caves or at construction sites	Respiratory/flu-like illness in healthy host Disseminated disease in immuno-compromised hosts, with palatal ulcerations, fever, weight loss, splenomegaly, and anemia/bone marrow suppression	Silver staining and culture of biopsied infected tissue +/− *Histoplasma* antigen tests of urine and serum	Mild to moderate disease without CNS involvement: Itraconazole Severe/disseminated disease: Amphotericin
Coccidioidomycosis	Dimorphic fungus; spherules with endospores on biopsy (Image C)	Southwestern United States, particularly Arizona or the San Joaquin Valley in California Inhalation of spores from soil	1° disease is usually a self-limited pneumonia with dry cough and fever Disseminated disease affects the CNS (meningitis), skin (erythema nodosum), bones, and joints	Silver stains of culture or biopsy, serologic studies, or antibody detection in CSF if meningitis is present	Fluconazole or itraconazole Amphotericin for severe pneumonia, disseminated infection (including CNS infection), and immuno-compromised patients
Blastomycosis	Dimorphic fungus, broad-based budding yeast on biopsy (Image D)	Ohio/Mississippi River Valleys, states bordering the Great Lakes Inhalation of spores from soil	Most patients present with pneumonia; up to 50% may have disseminated disease with a verrucous-like rash/subcutaneous nodules and/or osteomyelitis	Direct visualization on wet prep and culture of infected tissues With bone involvement, lytic lesions may be seen on plain film	Mild to moderate disease without CNS involvement: Itraconazole Severe/disseminated disease: Amphotericin

(continues)

TABLE 10-13. Characteristics, Diagnosis, and Management of Fungal Infections *(continued)*

Infection	Morphology	Geographic Location/Mode of Transmission	History/Symptoms/Exam	Diagnosis	Treatment
Aspergillosis	Mold, septated branched hyphae on biopsy (Image E)	Not localized to a specific region Inhalation of mold, which is abundant in nature	Invasive aspergillosis may present with the classic triad of fever, pleuritic chest pain, and hemoptysis Chronic pulmonary infection with aspergilloma (fungus ball), nodules, or cavitary lesions	Direct visualization and culture of infected tissues, detection of anti-aspergillus IgG, +/− serum galacto-mannan antigen detection May present with cavitary lesions or nodules with surrounding ground-glass infiltrates representing hemorrhage in invasive aspergillosis; chronic infection can present with nodules or aspergilloma (fungus ball)	Voriconazole +/− surgical resection or embolization if uncontrolled hemoptysis



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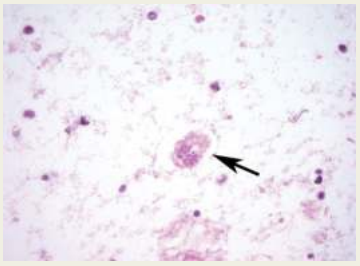

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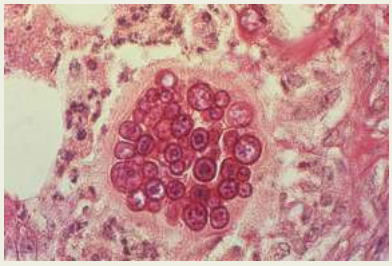

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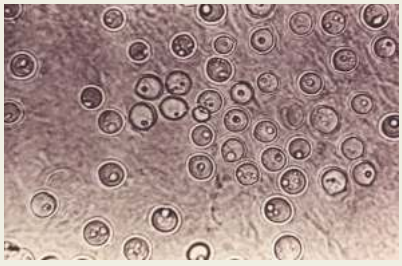

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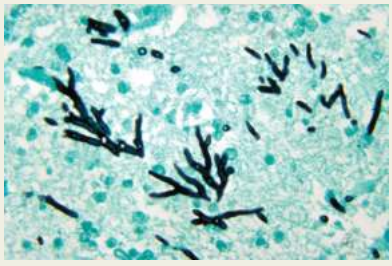


E

Image A reproduced from the CDC/Dr. Leanor Haley; image B reproduced with permission from USMLE-Rx.com; images C–E reproduced from the CDC/Dr. Lucille K. Georg.

TABLE 10-14. Selected Antimicrobials

Antimicrobial Group	Common Examples	Organisms Covered	Mechanism of Action	Common Adverse Effects
Natural penicillins	Penicillin G, penicillin V	*T pallidum*, *Enterococcus*, streptococci, and rare penicillin-sensitive staphylococci	Inhibit bacterial cell wall synthesis	Hypersensitivity reaction
β-lactamase-resistant penicillins	Dicloxacillin, methicillin (no longer used clinically, but important because of methicillin-resistant staphylococci), nafcillin, oxacillin	Used primarily for methicillin-sensitive staphylococci, but do cover some streptococci		
Aminopenicillins	Amoxicillin, amoxicillin/clavulanic acid, ampicillin, ampicillin/sulbactam	Natural penicillin coverage and *E coli, Proteus, H influenzae,* and *Enterococcus.* β-Lactamase inhibitors add coverage for enteric gram ⊖ organisms and anaerobes		
Extended-spectrum penicillins	Piperacillin/tazobactam, ticarcillin/clavulanic acid	Aminopenicillin/β-lactamase inhibitor coverage in addition to resistant gram ⊖ organisms, including *Pseudomonas*		
First-generation cephalosporins	Cefazolin, cephalexin	Staphylococci, streptococci, ***P**roteus, **E** coli,* and ***K**lebsiella* **(PEcK)** Cephalosporins do not cover any enterococci	Inhibit bacterial cell wall synthesis; less susceptible to β-lactamases	Hypersensitivity reaction
Second-generation cephalosporins	Cefaclor, cefuroxime	First-generation cephalosporin coverage and ***H** influenzae,* **E**nterobacteriaceae, ***N**eisseria* **(HEN PEcK)**		
Cephamycins	Cefotetan, cefoxitin	Second-generation cephalosporin coverage and gram ⊕/gram anaerobes		
Third-generation cephalosporins	Cefotaxime, ceftazidime, ceftriaxone	Most gram ⊖ aerobes and gram ⊕ anaerobes; ceftriaxone adds streptococcal coverage and ceftazidime adds *Pseudomonas* coverage		
Fourth-generation cephalosporins	Cefepime	Gram ⊖ aerobes, streptococci, and *Pseudomonas*		
Second-generation quinolones	Ciprofloxacin	Gram ⊖ aerobes and atypicals such as *Legionella, Mycoplasma,* and *Chlamydia;* best *Pseudomonas* coverage of all quinolones	Inhibit DNA synthesis	Tendinopathy, QTc prolongation, myasthenia gravis exacerbation

(continues)

TABLE 10-14. Selected Antimicrobials *(continued)*

Antimicrobial Group	Common Examples	Organisms Covered	Mechanism of Action	Common Adverse Effects
Third-generation quinolones	Levofloxacin	Gram ⊖ aerobes, streptococci, and atypicals		
Fourth-generation quinolones	Moxifloxacin	Gram ⊕ organisms, some anaerobes, weak gram ⊖ coverage, and atypicals		
Carbapenems	Ertapenem, imipenem, meropenem	Gram ⊕ organisms (except resistant *Staphylococcus* and *Enterococcus*); gram ⊖ organisms, including *Pseudomonas* and anaerobes; ertapenem has no *Pseudomonas* or *Enterococcus* coverage	Inhibit bacterial cell wall synthesis; highly resistant to β-lactamases	CNS effects including seizures
Macrolides	Azithromycin, erythromycin, clarithromycin	Gram ⊕ organisms and atypicals; high *S pneumoniae* resistance	Inhibit bacterial protein synthesis	QTc prolongation, cholestasis
Aminoglycosides	Gentamicin, tobramycin	Gram ⊖ aerobes, including *Pseudomonas*	Inhibit bacterial protein synthesis	Hearing loss, renal dysfunction
Monobactams	Aztreonam	Gram ⊖ aerobes, including *Pseudomonas*	Inhibits bacterial cell wall synthesis	Transaminitis, GI upset, neutropenia
Semisynthetic lincosamides	Clindamycin	Gram ⊕ anaerobes, MRSA	Inhibits bacterial protein synthesis	GI upset, rash
Oxazolidinones	Linezolid	MRSA; vancomycin-resistant enterococcus	Inhibits protein synthesis	Bone marrow suppression, peripheral neuropathy, lactic acidosis
Synthetic nitroimidazole	Metronidazole	Anaerobes *(C difficile)*	Inhibits bacterial DNA synthesis	GI upset, peripheral neuropathy, disulfiram-like reaction with EtOH
Combination	TMP-SMX	Gram ⊖ organisms, gram ⊕ organisms, *P jiroveci*	Inhibits bacterial DNA synthesis	Hyperkalemia, thrombocytopenia, ↓ creatinine clearance
Glycopeptides	Vancomycin	MRSA and *C difficile* (PO only)	Inhibits bacterial cell wall synthesis	Red man syndrome, thrombocytopenia; rarely renal toxicity
Tetracyclines	Doxycycline, minocycline, tigecycline	Tick-borne infections, atypical organisms, streptococcus, and MRSA	Inhibit bacterial protein synthesis	Tooth discoloration, skin photosensitivity, drug-induced lupus, GI upset

NOTES

CHAPTER 11

MUSCULOSKELETAL

Systemic Lupus Erythematosus

A multisystem, chronic inflammatory disease resulting from the deposition of autoimmune antibody-antigen complexes into tissues. SLE is generally primary but sometimes occurs secondary to medication use. Secondary lupus is reversible. Risk factors: Young female, Asian, Hispanics, African-Americans.

History/PE

- **Constitutional:** Fatigue, weight loss, fever.
- **Musculoskeletal:** Symmetric, nonerosive arthritis often involving the hands.
- **Skin:** Malar rash (a "butterfly rash" over the cheeks and nose; see Figure 11-1), discoid rash (erythematous plaques with central atrophy), painless oral ulcers, Raynaud phenomenon, and a photosensitive rash.
- **Renal:** Nephritis and nephropathy (membranous most common).
- **Pulmonary:** Pleurisy, pleural effusion, interstitial lung disease (ILD), pulmonary hypertension, pneumonitis, alveolar hemorrhage.
- **Cardiovascular:** Pericarditis, pericardial effusion, verrucous endocarditis (Libman-Sacks), ↑ risk of coronary artery disease (CAD).
- **CNS:** Seizures, headache, peripheral neuropathies, thromboembolic disease, blindness.
- **Psychological:** Delirium, anxiety, depression, psychosis.
- **Hematologic:** Thrombocytopenia, hemolytic anemia, leukopenia, thrombophilia, lymphadenopathy, splenomegaly.
- **GI:** Peritonitis and lupoid hepatitis.

Diagnosis

- Positive antinuclear antibody (ANA) (98% of patients); screening measure not specific.
- Anti–double-stranded DNA (dsDNA) (60% of patients) highly specific.
- Anti-Sm antibodies highly specific for lupus.
- Antihistone antibodies can be seen in drug-related lupus-like symptoms and primary SLE.
- Often false-positive test for syphilis (rapid plasma reagin [RPR]).
- Antiphospholipid (anticardiolipin) antibodies.
- Decreased C3 and C4 (most notable in acute flares).

Treatment

- NSAIDs are used for arthritis and mild serositis.
- Hydroxychloroquine are used to treat skin and renal symptoms.
- Steroids and immunosuppressants (cyclophosphamide, azathioprine), including biologic agents that target B cells (belimumab, rituximab), are used for refractory or serious cases.
- Active flare-ups are treated with steroid tapers.
- Patients with antiphospholipid antibody syndrome need lifelong anticoagulation with warfarin.

Complications

- Pregnant women with SLE have a higher incidence of spontaneous abortion.
- Infants of mothers with anti-SSA (Sjögren syndrome and SLE) may develop neonatal lupus from the transplacental transfer of autoantibodies. This may result in complete heart block.

MNEMONIC

Medications associated with 2° SLE—

SHIPP

Sulfonamides
Hydralazine
Isoniazid
Phenytoin
Procainamide

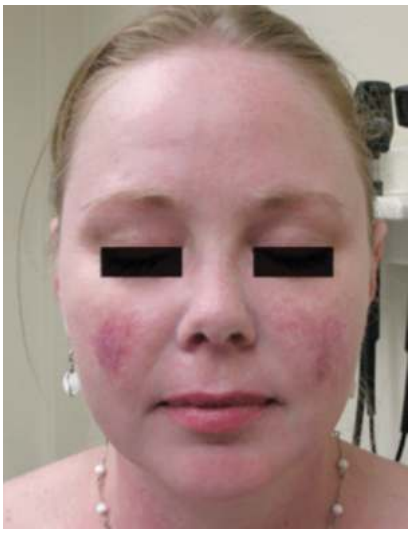


FIGURE 11-1. Malar rash in a butterfly distribution. (Reproduced with permission from Imboden JB et al. *Current Diagnosis & Treatment: Rheumatology,* 3rd ed. New York: McGraw-Hill, 2013, Plate 35.)

KEY FACT

Libman-Sacks endocarditis, also known as verrucous endocarditis, is characterized by noninfectious, granular, pea-sized masses near the edge of a valve or valve ring. It typically affects both surfaces of the valve leaflet.

KEY FACT

Active SLE (flare-up) presents with an ↑ anti-dsDNA titers and a ↓ in complement levels (especially CH50, C3, and C4).

- Thrombosis, embolism, and hypercoagulability (antiphospholipid syndrome) can increase risk of deep venous thrombosis, pulmonary embolism, stroke, and miscarriages.
- Mortality in SLE is frequently due to accelerated atherosclerosis, infections, malignancy, or renal disease.

Rheumatoid Arthritis

A chronic inflammatory disorder that affects peripheral synovial joints symmetrically triggering synovial hypertrophy by replacing synovial cartilage with fibrosing granulation tissue. Extra-articular manifestations include pulmonary fibrosis, serositis, vasculitis, and rheumatoid nodules. Risk factors include middle-aged female and serotype HLA-DR4.

History/PE

- **Constitutional:** Malaise, weight loss, fever, scleritis, episcleritis, Sjögren syndrome.
- **Musculoskeletal:** Morning stiffness, pain and swelling, decreased mobility, Boutonniere (flexed proximal interphalangeal [PIP] joint), Swan neck deformities (flexed distal interphalangeal [DIP] joint with hyperextended PIP), ulnar deviation—typically symmetrical involving metacarpophalangeal (MCP) joint and PIP, sparing the DIP (see Figure 11-2).
- **Skin:** Subcutaneous nodules ("rheumatoid" nodules).
- **Pulmonary/cardiac/vascular:** Pleuritis, pulmonary fibrosis, pericarditis, myocarditis, vasculitis.

Diagnosis

- Requires the presence of four or more of the following criteria for 6 weeks:
  - **Arthritis of 3 or more joint areas,** most commonly the PIP, MCP, wrist, elbow, knee, or ankle.
  - **Rheumatoid nodules,** most commonly found at the elbow.
  - **Labs:** ↑ C-reactive protein (CRP) or erythrocyte sedimentation rate (ESR), rheumatoid factor (RF) ⊕ in 75% of patients, anti-cyclic citrullinated peptide (anti-CCP) (most specific to RA).
  - **Radiographic:** Classic changes are symmetric joint space narrowing; periarticular osteoporosis with erosions around the affected MCP and PIP joints also common features on x-ray (see Figure 11-3).
  - **Joint aspiration:** Inflammatory fluid.

FIGURE 11-2. Ulnar deviation of the MCP joints and swelling of the PIP joints in rheumatoid arthritis. Multiple subcutaneous rheumatoid nodules are also seen. (Reproduced with permission from Goldsmith LA et al. *Fitzpatrick's Dermatology in General Medicine,* 8th ed. New York: McGraw-Hill, 2012, Fig. 160-1A.)

MNEMONIC

SLE Dx requires 4 of 11 criteria—

DOPAMINE RASH

Discoid rash
Oral ulcers
Photosensitive rash
Arthritis
Malar rash
Immunologic criteria (⊕ anti-dsDNA or ⊕ anti-Sm)
NEurologic or psychiatric symptoms
Renal disease
ANA ⊕
Serositis (pleural, peritoneal, or pericardial)
Hematologic disorders (thrombocytopenia, hemolytic anemia, or leukopenia)

Q 1

A 27-year-old woman presents with SLE, and you start her on hydroxychloroquine. What is a potential toxicity associated with the long-term use of this drug?

Q 2

A 58-year-old woman with warm and tender joints at her wrists and the bases of her fingers has failed methotrexate therapy for her rheumatoid arthritis (RA) and wants to try anti-tumor necrosis factor (anti-TNF) therapy. What should she be screened for prior to initiating anti-TNF therapy?

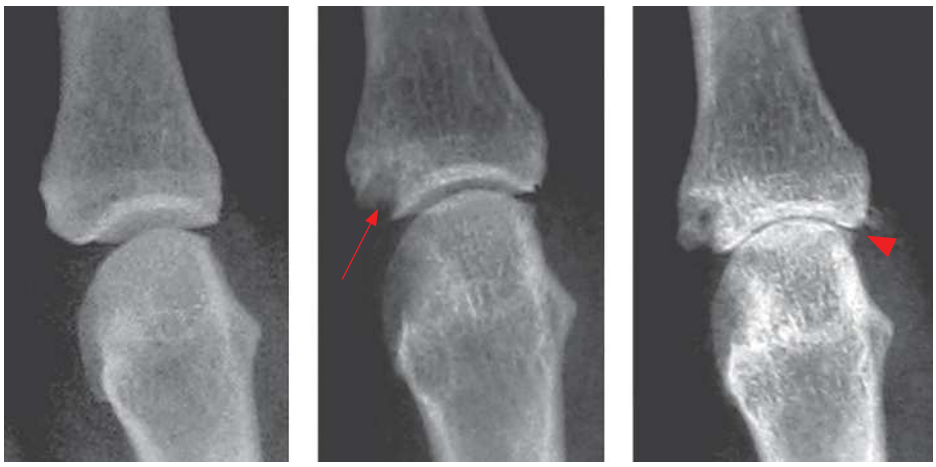


FIGURE 11-3. Progression of radiographic findings in rheumatoid arthritis. (**A**) Normal MCP joint 1 year before the onset of RA. (**B**) Six months following disease onset, there is a bony erosion (*arrow*) adjacent to the joint, along with joint space narrowing. (**C**) After 3 years of disease, diffuse loss of articular cartilage has led to marked joint space narrowing (*arrowhead*). (Reproduced with permission from Imboden JB et al. *Current Rheumatology Diagnosis & Treatment,* 3rd ed. New York: McGraw-Hill, 2013, Fig. 15-3.)

Treatment

- NSAIDs, physical therapy.
- Mild disease: Sulfasalazine, hydroxychloroquine, glucocorticoids.
- Moderate disease: First-line therapy is disease-modifying antirheumatic drugs (DMARDs) such as methotrexate, followed by anti-TNF drugs (infliximab, etanercept, adalimumab) or corticosteroids. Always test for TB prior to the initiation of anti-TNF therapy.
  - Methotrexate for RA is contraindicated in pregnant patients and in those with HIV, liver disease, renal failure, bone marrow suppression, or ILD.
- Severe disease: Anti-TNF plus corticosteroids.
- Acute exacerbations: Corticosteroids.

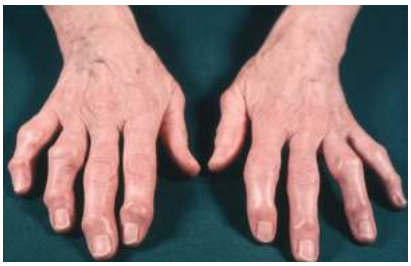


FIGURE 11-4. Osteoarthritis. Severe osteoarthritis of the hands affecting the DIP joints (Heberden nodes) and the PIP joints (Bouchard nodes). (Reproduced with permission from Longo DL et al. *Harrison's Principles of Internal Medicine,* 18th ed. New York: McGraw-Hill, 2012, Fig. 332-2.)

1 A

Retinal toxicity. Monitor the patient with baseline and follow-up ophthalmologic exams.

2 A

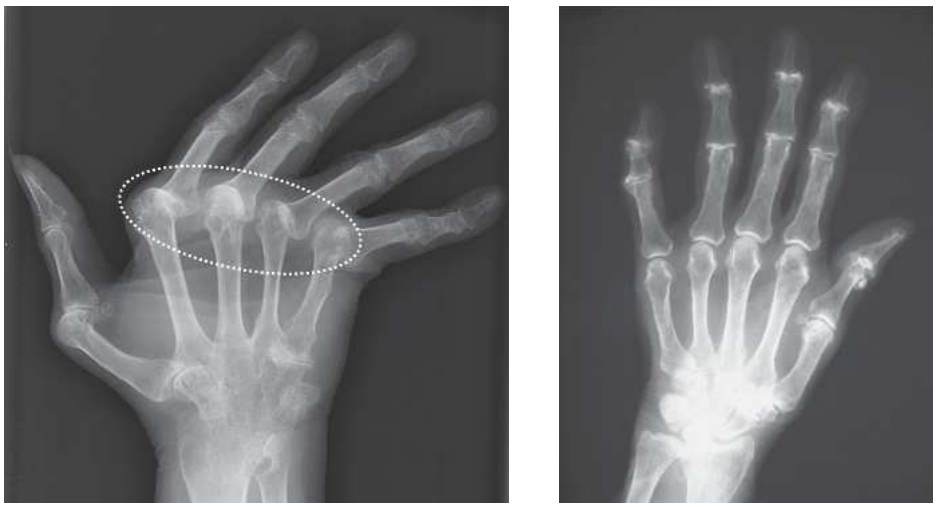
Screen for latent tuberculosis (TB) with a PPD test or QuantiFERON Gold and test for hepatitis B and C antibodies.

Osteoarthritis

A chronic, noninflammatory joint disease characterized by degeneration of the articular cartilage, hypertrophy of the bone margins, and synovial membrane changes. Osteoarthritis (OA) may be 1° or 2° to trauma or a systemic metabolic disorder (hemochromatosis, Wilson disease).

History/PE

- Marked by insidious onset of joint pain without inflammatory signs.
- In contrast to the "morning stiffness" of inflammatory arthritis, OA worsens with activity during the day and improves with rest. Morning stiffness has a duration of < 30 minutes.
- 1° OA usually involves the following joints:
  - **Hands:** DIP, PIP, and first carpometacarpal joints. Heberden nodes (DIP deformities) and Bouchard nodes (PIP deformities) (see Figure 11-4). Compare with ulnar deviation in RA in Figures 11-2 and 11-5.
  - **Feet:** First metatarsophalangeal (MTP) joint.
  - **Knees, hips** (see Figure 11-6).



A B

FIGURE 11-5. Rheumatoid arthritis vs osteoarthritis. (**A**) Classic changes of RA include ulnar deviation at the MCP joints, destruction of carpal bones, and destruction of the radiocarpal and ulnocarpal joints. (**B**) OA changes include severe joint space narrowing at all DIP and PIP joints. Joint space narrowing at the carpometacarpal joint of the first digit is also seen. (Image A reproduced with permission from Brunicardi FC et al. *Schwartz's Principles of Surgery,* 9th ed. New York: McGraw-Hill, 2010, Fig. 44-18B. Image B reproduced with permission from Imboden JB et al. *Current Diagnosis & Treatment: Rheumatology,* 3rd ed. New York: McGraw-Hill, 2013, Fig. 43-1.)

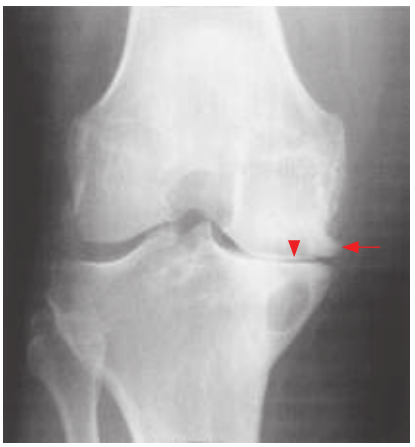


FIGURE 11-6. Radiographic changes in knee osteoarthritis. Anteroposterior (AP) knee radiograph shows a narrowed joint space on the medial side only and subchondral sclerosis (*arrowhead*); a cyst (lucency below the arrowhead) and osteophytes (*arrow*) are also present. (Reproduced with permission from Chen MY et al. *Basic Radiology.* New York: McGraw-Hill, 2004, Fig. 7-40.)

Diagnosis

- Based on clinical and radiographic findings showing joint space narrowing that is frequently asymmetric (see Figure 11-6), subchondral sclerosis, and osteophytes.
- ANA, ESR, RF, and anti-CCP are normal, if no other comorbidities exist. Joint fluid has a leukocyte count of < 2000.

Treatment

- **First line:** Weight loss, physiotherapy, and low-impact exercise.
- **Mild symptoms:** Use acetaminophen or NSAIDs. Intra-articular corticosteroid injections may be added for further pain control.
- **Joint replacement:** For severe OA in patients who have marked limitation of their daily activities and in whom medical management fails.

KEY FACT

OA: Short morning stiffness (< 30 minutes), pain WORSENS with activity.
RA: Long morning stiffness (> 30 minutes), pain IMPROVES with activity.

Gout

Peripheral monoarthritis caused by intra-articular deposition of monosodium urate crystals resulting in inflammatory changes and joint destruction. May be due to hyperuricemia from excessive urate production or from ↓ renal uric acid excretion. Risk factors include male sex, Pacific Islanders, renal disease, obesity, diuretic use, consumption of purine-rich foods, cancer.

History/PE

- **Constitutional:** Fever, chills, malaise.
- **Musculoskeletal:** Typically monoarticular with sudden pain and swelling of first metatarsophalangeal joint (most common), ankle, knee, elbow.
- Patients with long-standing disease may develop tophi that lead to joint deformation.
- **Renal:** Complications of chronic hyperuricemia include nephrolithiasis and chronic urate nephropathy.

Q

A 47-year-old man celebrates his birthday by going out for steak and beer. The following morning, his first MTP joint is red and painful even to light touch. He is on lovastatin, aspirin, hydrochlorothiazide, and niacin. Which of his medications likely contributed to his gout?

TABLE 11-1. Interpretation of Joint Aspiration

	Normal	Noninflammatory	Inflammatory	Infectious	Hemorrhagic
Color	Clear	Xanthochromic	Yellow	Opaque	Bloody
Viscosity	High	High	Low	Low	Variable
WBCs/mm^3	< 200	200–3000	3000–50,000	> 50,000	Variable
% PMNs	< 25	< 25	> 50	> 75	Variable
Crystals	None	None	May be present	None	None
Differential	None	Osteoarthritis, SLE, trauma, aseptic, necrosis, Charcot joint	Gout, pseudogout, RA, SLE, TB, scleroderma, ankylosing spondylitis, psoriatic arthritis	Bacterial, TB	Coagulopathy, trauma

KEY FACT

Monoarthritis? Think:
- Gout
- Septic arthritis
- Lyme disease
- Pseudogout
- Trauma

Differential

Calcium pyrophosphate crystal disease (pseudogout) is often associated with other diseases (DM, hyperparathyroidism, Wilson disease, hemochromatosis) and is typically seen in patients < 65 years of age. Joint aspiration shows positively birefringent, rhomboid crystal. X-ray shows chondrocalcinosis.

Diagnosis

- Acute gout attacks often occur at night between periods of remission. The three stages are acute gouty arthritis, intercritical gout, and chronic recurrent and tophaceous gout.
- Common precipitants of attacks include a high-purine diet (eg, meats, alcohol), dehydration or diuretic use (thiazides), high-fructose corn syrup, stress, severe illness, trauma, and tumor lysis syndrome.
- **Best initial test:** Arthrocentesis. Joint aspiration from warm, swollen joints helps distinguish inflammatory from noninflammatory disease as well as infectious from hemorrhagic processes (see Table 11-1). In gout, joint aspirate is inflammatory with needle-shaped, negatively birefringent (yeLLow when paraLLel to the condenser or axis of polarization) crystals (see Figure 11-7 and Table 11-2).

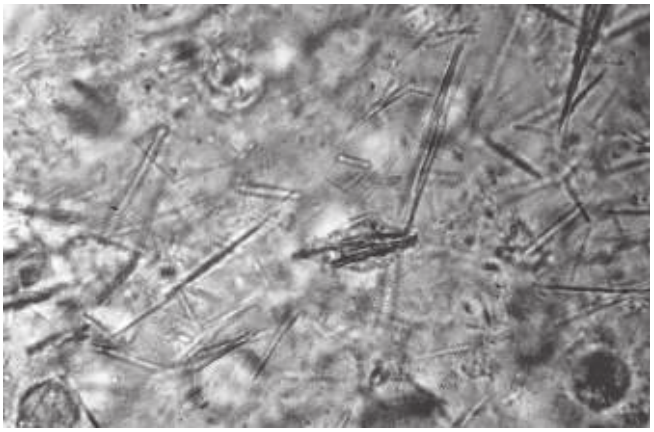


FIGURE 11-7. Gout crystals. (Reproduced with permission from Longo DL et al. *Harrison's Principles of Internal Medicine,* 18th ed. New York: McGraw-Hill, 2012, Fig. 333-1.)

A

Hydrochlorothiazide and other thiazide diuretics interfere with the excretion of uric acid, thereby exacerbating gout.

TABLE 11-2. Differential Diagnosis of Gout and Pseudogout

	Gout Crystals	Pseudogout Crystals
Composition	Urate	Calcium pyrophosphate
Shape	Needle-shaped	Rhomboid-shaped
Refringence	Negatively birefringent	Strongly positively birefringent
Red compensator	YeLLow with paraLLel light	Blue with parallel light, yellow with perpendicular light

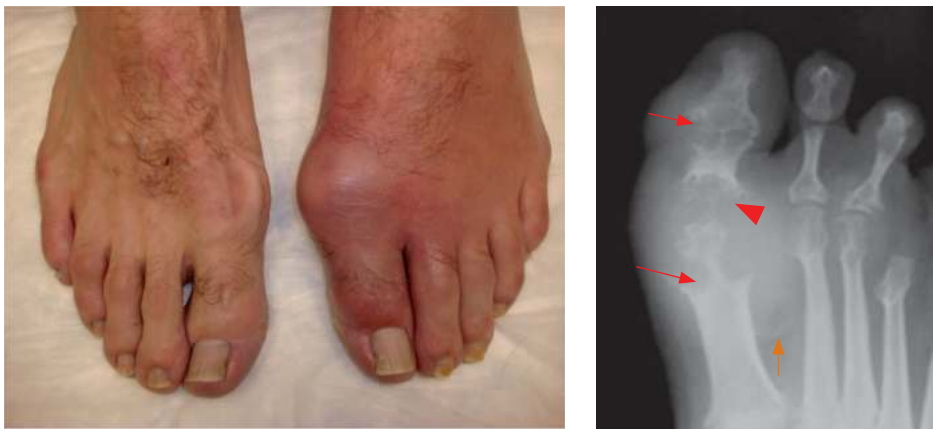
- **Radiographs:** Normal in early gout. Characteristic punched-out erosions with overhanging cortical bone ("rat bites") are seen in advanced disease (see Figure 11-8).

Treatment

- **Acute attacks:** High-dose NSAIDs (eg, indomethacin), corticosteroids (PO, intra-articular) and colchicine are useful if started within the first 24 hours of an attack. Side effects of colchicine include diarrhea, nausea, and bone marrow suppression.
- **Maintenance therapy:** Only begin once the acute attack resolves; start allopurinol to reduce the risk of recurrence by lowering serum uric acid levels. Allopurinol can be continued if patient is already taking it prior to gout attack.
- **Lifestyle changes:** Encourage a low-purine diet (eggs, cheese, fruit, and vegetables). Weight loss and BP control can also prevent flares.

KEY FACT

Remember to **A**void starting **A**llopurinol in **A**cute gout **A**ttacks.



A B

FIGURE 11-8. Gout. (**A**) A swollen left first MTP joint with overlying erythema and warmth, characteristic of an acute gout attack (podagra). (**B**) AP radiograph of the right foot in a different patient showing the severe consequences of long-standing gout, including large, nonmarginal erosions with overhanging edges of bone (*red arrows*), soft tissue swelling, and destruction of the first MTP joint (*arrowhead*). Note the subtle calcification of a gouty tophus (*orange arrow*). (Image A reproduced with permission from LeBlond RF et al. *DeGowin's Diagnostic Examination,* 9th ed. New York: McGraw-Hill, 2009, Plate 30. Image B reproduced with permission from USMLE-Rx.com.)

Low Back Pain

Leading cause of missed work days in the United States. Causes are shown in Table 11-3.

Diagnosis

- **Neurologic exam** to determine if the spinal nerves are affected (see Table 11-4). Suspect spinal cord involvement if the Babinski reflex is upgoing or if there is sphincter laxity. An UPgoing toe is an UPper motor neuron sign.
- **Straight leg raise test:** If ⊕ (in which a supine patient experiences leg, buttock, or back pain in the affected leg at < 30° of elevation of the affected leg) is sensitive for spinal nerve irritation or radiculopathy.

TABLE 11-3. Causes of Low Back Pain

	History/PE	Diagnosis
Cauda equina syndrome	Bowel and bladder incontinence or retention, saddle anesthesia A medical emergency	Order a stat MRI if suspected
Degenerative processes	Chronic and progressive Degeneration of disks, localized pain that can refer to adjacent spinal nerves (eg, pain that radiates down the thigh) Severe facet degeneration can lead to spinal stenosis: "Neurogenic claudication" → LBP worsens with standing and walking but improves with sitting or leaning forward (patients typically find it easier to walk uphill than downhill)	Order a lumbar spine x-ray to rule out other causes of LBP
Neoplastic	1° or metastatic to bone; suspect in elderly patients with unintentional weight loss or a history of cancer	A tumor mass may be seen on lumbar spine x-ray; bone scan or MRI can detect disease not seen on plain film
Traumatic	Acute onset of LBP is temporally associated with a traumatic event Look for local spinal tenderness 2° to a fracture or a herniated disk (pain worsens with cough; L4 or L5 nerve root compression) Paraspinal tenderness indicates myofascial strain	X-ray (first line) or CT (second line) may be necessary to confirm a fracture and to assess the spinal column for stability; myofascial strain and disk herniations cannot be seen
Osteomyelitis	Fever, chills, or IV drug use; ESR is often ↑↑	X-ray is not sensitive but may show disk narrowing and endplate destruction MRI may be needed to aid in diagnosis and to assess for epidural abscess
Ankylosing spondylitis	Typical patient a young man presenting with chronic LBP that is worse in the morning, improving with movement Associated with HLA-B27 in Caucasians Associated with anterior uveitis, ↓ spinal mobility	X-ray may show fusing of sacroiliac joints, squaring of the lumbar vertebrae, development of vertical syndesmophytes; "bamboo spine" in long-standing disease ⊕ HLA-B27
2° to disease from the aorta, kidneys, ureter, or pancreas	Pain is referred	Conduct a thorough abdominal exam

TABLE 11-4. Spinal Nerve Damage and Associated Sensorimotor Deficits

Nerve Roots	Motor Deficits	Sensory Deficit	Reflexes
C5	Deltoid, biceps	Ant shoulder	↓ Biceps reflex
C6	Biceps, wrist extensors	Brachioradialis	↓ Biceps, triceps reflex
C7	Triceps, wrist flexors, finger extensors	Triceps	↓ Triceps reflex
L3, L4	Problems in rising from a chair and heel walking	Over the anterior knee or the medial calf	↓ Knee jerk
L5	Problems with heel walking, extension of the big toe, or dorsiflexion of the ankle	Over the medial aspect of the foot	
S1	Problems with toe walking or plantar flexing the ankle	Over the lateral aspect of the foot	↓ Ankle jerk

- **Crossed straight leg raise test:** If ⊕ (in which a supine patient experiences leg, buttock, or back pain in the affected leg at < 30° of elevation of the unaffected leg) is specific for spinal nerve irritation.
- **Imaging:** Order a lumbar spine x-ray for patients in whom osteomyelitis, cancer, fractures, or ankylosing spondylitis is suspected or for those who fail to improve after 2–4 weeks of conservative therapy. Consider screening for osteoporosis if fractures are seen on x-ray. An MRI should be ordered if cauda equina syndrome is suspected or if the patient has neurologic deficits for which surgery is being considered.

Treatment

- Cauda equina syndrome or spinal nerve involvement require surgical evaluation.
- **Degenerative Low Back Pain (LBP):** Treated with NSAIDs and physiotherapy.
- **Ankylosing spondylitis:** Treated with TNF inhibitors and physiotherapy (see below).
- Most LBP from disk herniation will improve within 6 weeks; surgery should be considered in cases of progressive neurologic deficits.

Spondyloarthropathies

The family of spondyloarthropathies encompasses a group of inflammatory arthritides that sometimes overlap (see Figure 11-9). These include:

- Ankylosing spondylitis.
- Reactive arthritis (formerly known as Reiter syndrome).
- Psoriatic arthritis.
- Spondyloarthritis associated with Crohn disease and ulcerative colitis.
- Juvenile-onset spondyloarthritis (including juvenile RA).

KEY FACT

Order x-rays in geriatric patients with new-onset back pain or if the history and physical are suggestive of malignancy, infection, or inflammatory arthropathy.

KEY FACT

Consider cauda equine syndrome if back pain is associated with incontinence of urine or stool, saddle-distribution anesthesia, decreased reflexes/strength in the lower extremities.

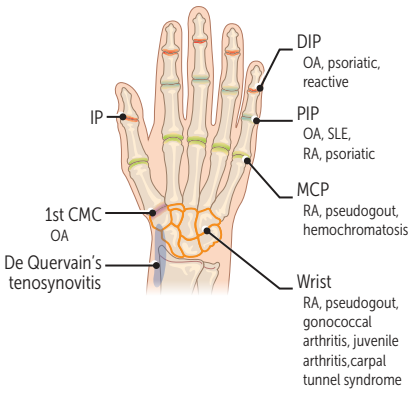


FIGURE 11-9. Diagnosis of rheumatic diseases based on joint distribution. (Reproduced with permission from USMLE-Rx.com.)

Q

A 69-year-old man presents with back pain of more than a year's duration that radiates bilaterally down his lower extremities. He reports that the pain worsens when he walks downhill but is relieved when he pushes his granddaughter's stroller. You diagnose presumed spinal stenosis and order an MRI. You should ask about changes in bowel and bladder function to rule out what complication?

ANKYLOSING SPONDYLITIS

- A chronic inflammatory disease of the axial skeleton that presents with progressive stiffness of the spine that can lead to ascending spinal fusion, hip and shoulder arthritis, enthesitis. Extra-articular involvement includes uveitis, aortitis, psoriasis, and IBD.
- **Hx/PE:** Stiffness of the spine, spinal fusion, and kyphosis. ↓ Chest expansion.
- **Dx:** X-ray of lumbar spine may show fusing of sacroiliac joints, squaring of the lumbar vertebrae, development of vertical syndesmophytes; characteristic "bamboo spine." Associated with HLA-B27.
- **Tx:** First line is NSAIDs, exercise. TNF inhibitors are second line.

MNEMONIC

RF arthritides—

PEAR

Psoriatic arthritis
Enteropathic arthritis (IBD)
Ankylosing spondylitis
Reactive arthritis

REACTIVE ARTHRITIS

- A form of spondyloarthritis that arises following infection, typically of the GI or GU tract, with pathogens such as *Campylobacter, Yersinia, Salmonella, Shigella, Chlamydia trachomatis*, and possibly *C difficile*. Onset occurs days to weeks after infection. Formerly known as Reiter syndrome.
- **Hx/PE:** Musculoskeletal: Asymmetric, typically LE, presenting as monoarthritis or oligoarthritis. Extra-articular symptoms include conjunctivitis, uveitis, and urethritis.
- **Tx:** NSAIDs are first line; intra-articular glucocorticoid injections for patients who are unresponsive to NSAIDs alone. DMARDs if refractory.

PSORIATIC ARTHRITIS

- An inflammatory arthritis associated with psoriasis.
- **Hx/PE:** Presents with pain, swelling, and stiffness in the affected joint, enthesitis), nail pitting, asymmetric oligoarthritis, symmetric polyarthritis (as in RA), and spondyloarthritis, including both sacroiliitis and spondylitis.
- **Tx:** First line: NSAIDS; second line: methotrexate or a TNF inhibitor (infliximab, adalimumab, etanercept).

Vasculitides

Defined by the presence of inflammatory leukocytes in vessel walls with subsequent tissue ischemia or hemorrhage. Vasculitis may occur as a 1° disease or 2° to another underlying pathology. Treatment focuses on management of the underlying disease. It is categorized on the basis of vessel size:

- **Large-vessel vasculitis:** Takayasu arteritis, temporal arteritis.
- **Medium-vessel vasculitis:** Kawasaki disease, polyarteritis nodosa.
- **Small-vessel vasculitis:** Eosinophilic granulomatosis with polyangiitis (Churg-Strauss syndrome), granulomatosis with polyangiitis (Wegener granulomatosis), Henoch-Schönlein purpura, cryoglobulinemic vasculitis.

TEMPORAL ARTERITIS (GIANT CELL ARTERITIS)

Affects older (> 50 years) women more often than men by a ratio of 2:1. Can cause blindness 2° to occlusion of the central retinal artery (a branch of the internal carotid artery). Half of patients also have polymyalgia rheumatica.

A

Cauda equina syndrome, which is a medical emergency and must therefore be ruled out.

History/PE

- Classic symptoms consist of a new headache and scalp tenderness (eg, pain combing the hair) along with temporal tenderness, jaw claudication, and visual symptoms such as monocular blindness.
- It is also associated with weight loss, myalgias/arthralgias, and fever.

Diagnosis

- ESR is elevated (often > 100 mm/hr) but is not specific for diagnosis.
- Gold standard: Temporal artery biopsy.

Treatment

- Treat immediately with high-dose prednisone and continue for 1–2 months before tapering. Do not delay treatment for the temporal artery biopsy, as blindness is permanent.
- Ophthalmologic evaluation.

KEY FACT

Treatment of temporal arteritis should not be delayed while awaiting biopsy results.

POLYARTERITIS NODOSA

A systemic necrotizing vasculitis that involves medium-size muscular arteries. Affects men and women equally. Not associated with the presence of antineutrophil cytoplasmic antibody (ANCA). High association with hepatitis B virus (HBV) and hepatitis C virus (HCV).

History/PE

- Presents with systemic symptoms (fatigue, weight loss, fever, arthralgias); commonly affects the GI tract, skin, joints, nerves, and kidneys (multisystem involvement).
- Frequently presents with mononeuritis multiplex.

Diagnosis

- Diagnosis is primarily clinical; common laboratory features include: ↑ ESR, leukocytosis, thrombocytosis, and anemia.
- Tissue biopsy from muscle and skin (the most accurate test) reveals vasculitis.

Treatment

First line: Glucocorticoid monotherapy. If refractory, consider immunosuppressive medications (eg, cyclophosphamide and rituximab). If associated with HBV or HCV, treat underlying disease.

Polymyalgia Rheumatica

An inflammatory disease that causes severe pain and stiffness in proximal muscle groups without weakness or atrophy. Risk factors include female sex and age > 50. Polymyalgia rheumatica (PMR) is associated with giant cell arteritis, which may precede, coincide with, or follow polymyalgia symptoms.

History/PE

- Typical symptoms include bilateral aching and morning stiffness lasting ≥ 30 minutes for at least 2 weeks.
- Patients present with pain and stiffness of the shoulder and pelvic girdle, along with fever, malaise, weight loss, and minimal joint swelling.

Q

A 73-year-old woman comes to your office complaining of a headache that has developed over the past month, along with pain when combing her hair. She has a palpable tender cord on her right temple, and you strongly suspect temporal arteritis. Should you wait to start systemic corticosteroids until she can get a temporal artery biopsy?

- Patients classically have difficulty getting out of a chair or lifting their arms above their heads but have no objective weakness.

Diagnosis

Look for ↑↑ ESR that occasionally exceeds 100 mm/hr.

Treatment

Treat with low-dose prednisone followed by a long taper. Pain due to PMR responds rapidly to corticosteroids (in 2–4 days). The principal goal of treatment is symptom relief.

KEY FACT

Polymyalgia causes pain but not weakness.

KEY FACT

Long-term steroid use can cause osteoporosis. Screen with DEXA scans, and prevent and treat with calcium, vitamin D, weight-bearing exercise, and, when necessary, bisphosphonates.

Fibromyalgia

A chronic pain disorder characterized by soft tissue and axial skeletal pain in the absence of joint pain. Affects women more often than men, and prevalence ↑ with age.

History/PE

- Presents as a syndrome of myalgias, insomnia, weakness, and fatigue in the absence of inflammation; muscle aches and stiffness with trigger points.
- Associated with depression, anxiety, and irritable bowel syndrome.

Diagnosis

- Lab results are ⊖.
- American College of Rheumatology criteria: Diagnosis is made with widespread pain index (WPI) > 7 and symptom severity (SS) scale score ≥ 5 or WPI 3–6 and SS scale score > 9.

Treatment

- Pregabalin, selective serotonin reuptake inhibitor, gabapentin, low-dose tricyclic antidepressants, progressive physical reconditioning, improvement of restorative sleep, and supportive measures such as heat application.
- Consider hydrotherapy, transcutaneous electrical nerve stimulation, stress reduction, or psychotherapy.

Polymyositis and Dermatomyositis

- **Polymyositis:** A progressive systemic connective tissue disease characterized by muscle inflammation, muscle fiber necrosis, degeneration, and inflammatory cell infiltration.
- **Dermatomyositis:** Characterized by similar muscle weakness but typically with coexisting cutaneous involvement. Systemic manifestations include myocarditis, pulmonary fibrosis, and cardiac conduction deficits. More commonly seen in older women (50–70 years of age).

History/PE

- **Polymyositis:** Presents with symmetric, progressive proximal muscle weakness that is sometimes accompanied by pain, resulting in the classic complaint of difficulty rising from a chair. Patients may have trouble swallowing and speaking and may eventually have difficulty breathing. Dyspnea may be a sign of ILD or pulmonary fibrosis.

A

No. Diagnostic biopsy results may not be accurate weeks to months after starting treatment, but blindness resulting from temporal arteritis is permanent.

- **Dermatomyositis:** May present with a heliotrope rash (a violaceous periorbital rash) and Gottron papules (papules located on the dorsum of the hands over bony prominences); see Figure 11-10. New-onset dermatomyositis requires age-appropriate cancer screening because of its high association with internal malignancy.

Diagnosis

- Look for ↑ CK and aldolase.
- Electromyography demonstrates fibrillations. Muscle biopsy, which is necessary for definitive diagnosis, shows inflammatory cells and muscle degeneration.

Treatment

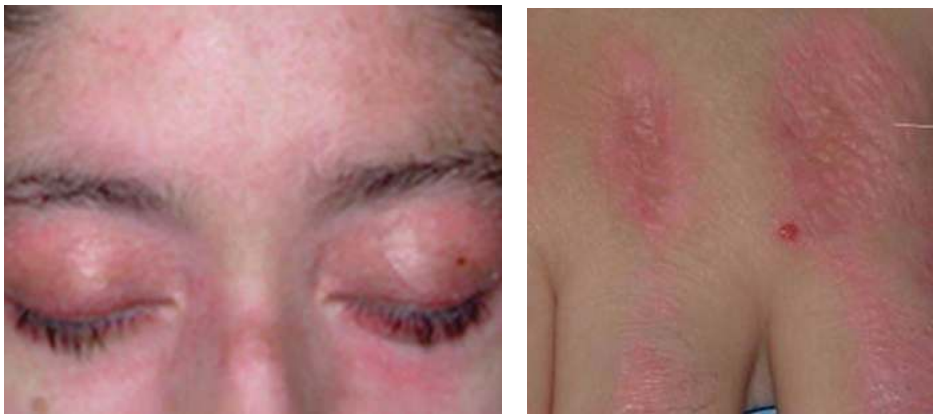
- High-dose corticosteroids generally result in improved muscle strength in 4–6 weeks and are then slowly tapered to the lowest effective dose for maintenance.
- Methotrexate or azathioprine may be used as steroid-sparing therapy or for refractory symptoms.

Systemic Sclerosis (Scleroderma)

A multisystem disease with symmetric thickening of the skin on the face and extremities. It typically affects women 30–65 years of age. Diagnosis is clinical and is supported by biopsy. There are two subtypes: limited and systemic (see Table 11-5).

History/PE

- Presents with prominent symmetrical skin thickening, loss of normal skin that gives the appearance of a tight face, and telangiectasias of the fingers, face, and lips.



A B

FIGURE 11-10. Dermatomyositis. (**A**) Heliotrope rash and (**B**) Gottron papules are hallmark cutaneous features of dermatomyositis and, when combined with nail-fold changes, are pathognomonic for the disease. (Images reproduced from Dhoble A et al. Dermatomyositis and supraventricular tachycardia. *Int Arch Med.* 2008;1:25.)

Q

A 64-year-old woman with diffuse scleroderma and stable angina underwent an echocardiogram and was found to have pulmonary hypertension. What medication, although typically prescribed for other purposes, is a possible treatment for pulmonary hypertension?

TABLE 11-5. Limited vs Diffuse Scleroderma

	Limited (CREST)	Diffuse
Skin involvement	Distal, face only	Generalized
Progression	Slow	Rapid
Immunologic finding	Anticentromere antibody	Anti-Scl-70 antibody
Prognosis	Fair	Poor
Calcinosis	+++	+
Telangiectasias	+++	+
Renal failure	None	++
Pulmonary interstitial fibrosis	Pulmonary hypertension	Pulmonary interstitial fibrosis

MNEMONIC

CREST syndrome

Calcinosis
Raynaud phenomenon
Esophageal dysmotility
Sclerodactyly
Telangiectasias

- Associated with Raynaud phenomenon, an exaggerated vasoconstrictive response to stimuli such as cold temperature and emotional stress; digital ulceration may occur.
- Systemic involvement of diffuse scleroderma includes GI (esophageal hypomotility leading to Barrett esophagus and reflux), pulmonary (ILD, fibrosis), and renal disease (scleroderma renal crisis).

Diagnosis

- In the presence of characteristic clinical findings, consider ANA as a screening test. Other tests include anti-topoisomerase I antibody (anti-Scl-70), which is highly specific but not sensitive.
- Skin biopsy is generally not essential for confirmation of the diagnosis.

A

Sildenafil. Remember that nitrates such as sublingual nitroglycerin are strongly contraindicated for 24 hours after the use of sildenafil or other phosphodiesterase type 5 (PDE-5) inhibitors.

CHAPTER 12

NEPHROLOGY

Acute Kidney Injury

An abrupt impairment in renal function that leads to the accumulation of waste products (eg, urea nitrogen) normally eliminated by the kidneys.

- Defined as a rise in serum creatinine of ≥ 0.3 mg/dL within 48 hours.
- Further classified into prerenal, intrinsic renal, and postrenal injuries (see Table 12-1).

History/PE

- Patients are often asymptomatic but may present with dyspnea, edema/anasarca, uremic symptoms (eg, anorexia, nausea, malaise, hyperpigmented skin, asterixis, pericarditis [listen for a friction rub]), and anemia.
- Exam should include checking blood pressure, weighing daily, and assessing volume status. Other findings are specific to the etiology of the renal failure.

Diagnosis

- Obtain urine sodium (U_{Na}) and urine creatinine (U_{Cr}) to calculate a fractional excretion of sodium (Fe_{Na}). The following Fe_{Na} formula can be used to differentiate the two most common causes of acute kidney injury (AKI)—prerenal injury and acute tubular necrosis (ATN):

$$(U_{Na} \times P_{Cr}) / (U_{Cr} \times P_{Na}) \times 100$$

KEY FACT

Anything that reduces renal blood flow can cause both a prerenal and intrinsic renal injury (eg, ATN caused by renal ischemia).

- Fractional excretion of urea (Fe_{urea}) should be calculated in the place of Fe_{Na} for patients taking diuretics, as these medications raise the concentration of U_{Na}. Fe_{urea} is calculated as follows:

$$(U_{Ur} \times P_{Cr}) / (U_{Cr} \times P_{Ur}) \times 100$$

  - Fe_{urea} of $< 35\%$ suggests a prerenal state.
  - Fe_{urea} of $> 50\%$ suggests intrinsic renal disease.
- Order urine microscopy for sediment and cast analysis.

Treatment

Varies depending on the underlying cause of injury. In general, stop all potentially nephrotoxic medications and those that can contribute to further

TABLE 12-1. Laboratory Findings Associated with Acute Kidney Injury

Class	Cause	Fe_{Na}	UA
Prerenal	↓ Renal blood flow, as in renal artery stenosis, shock, heart failure, hepatorenal syndrome, and NSAID or ACEI/ARB use	< 1%	Usually not helpful but may see hyaline casts
Intrinsic	Acute glomerulonephritis (AGN): Poststreptococcal glomerulonephritis, IgA nephropathy	Variable	AGN: Dysmorphic RBCs and RBC casts
	Acute interstitial nephritis (AIN): Antibiotics (penicillins, cephalosporins), NSAIDs, and PPIs/H_2-receptor blockers	Variable	AIN: Eosinophils and WBC casts
	ATN: See Table 12-2	> 2%	ATN: Pigmented granular ("muddy brown") casts
Postrenal	Any condition that impedes urinary excretion (prostatic hypertrophy)	Variable	Variable

TABLE 12-2. Causes of Acute Tubular Necrosis

Cause	Examples
Exogenous nephrotoxins	Antimicrobials (eg, aminoglycosides, amphotericin) and radiocontrast agents
Endogenous nephrotoxins	Rhabdomyolysis (myoglobin), multiple myeloma (immunoglobulin light chain), tumor lysis syndrome (uric acid)
Ischemia	Shock (eg, hypovolemic, septic, cardiogenic)

damage (eg, NSAIDs). Hemodialysis may be indicated in severe cases (see **AEIOU** mnemonic).

- **Prerenal injury:** Start IV fluids.
- **Intrinsic renal injury:** Highly variable; often supportive care.
- **Postrenal injury:** Relieve obstruction (eg, Foley catheter for benign prostatic hyperplasia).

MNEMONIC

Indications for emergent dialysis—

AEIOU

Acidosis
Electrolytes (hyperkalemia)
Ingestion of toxins (eg, lithium, aspirin)
Overload (volume)
Uremic symptoms (encephalopathy)

Electrolyte Disorders

HYPONATREMIA

Defined as serum sodium (Na^+) concentrations < 135 mEq/L. Acute hyponatremia occurs in < 24 hours. Chronic hyponatremia occurs in > 48 hours. Pseudohyponatremia is seen in patients with hyperlipidemia or hyperproteinemia.

History/PE

Often asymptomatic at Na^+ concentrations > 130 mEq/L, symptoms can progress to nausea, seizures, and coma at lower values.

Diagnosis

Assess volume status and check serum osmolality, urine osmolality, and urine sodium (see Figure 12-1).

Treatment

- **Acute or chronic hyponatremia with severe symptoms** (eg, seizure, coma): Infuse hypertonic saline.
- **Asymptomatic hyponatremia and hyponatremia with mild symptoms:** Correction should occur at a rate of approximately 0.5 mEq/L/hr with a goal increase of 8–10 mEq/L per day. Treatment is based on the patient's fluid status.
  - Hypervolemia: Administer loop diuretic.
  - Euvolemia: Restrict fluid to 1 L/day, administer loop diuretic, high-sodium diet/salt tabs for poor solute intake.
  - Hypovolemia: Infuse isotonic saline.

KEY FACT

Correcting low sodium concentrations too quickly (> 9 mEq/L/day) can result in osmotic demyelination syndrome. This syndrome is characterized by confusion, dysarthria, neuromuscular dysfunction, and coma.

HYPERNATREMIA

Defined as Na^+ concentrations > 145 mEq/L.

KEY FACT

Hypernatremia usually occurs when a patient has no access to free water (eg, when intubated or demented). Envision a salty desert.

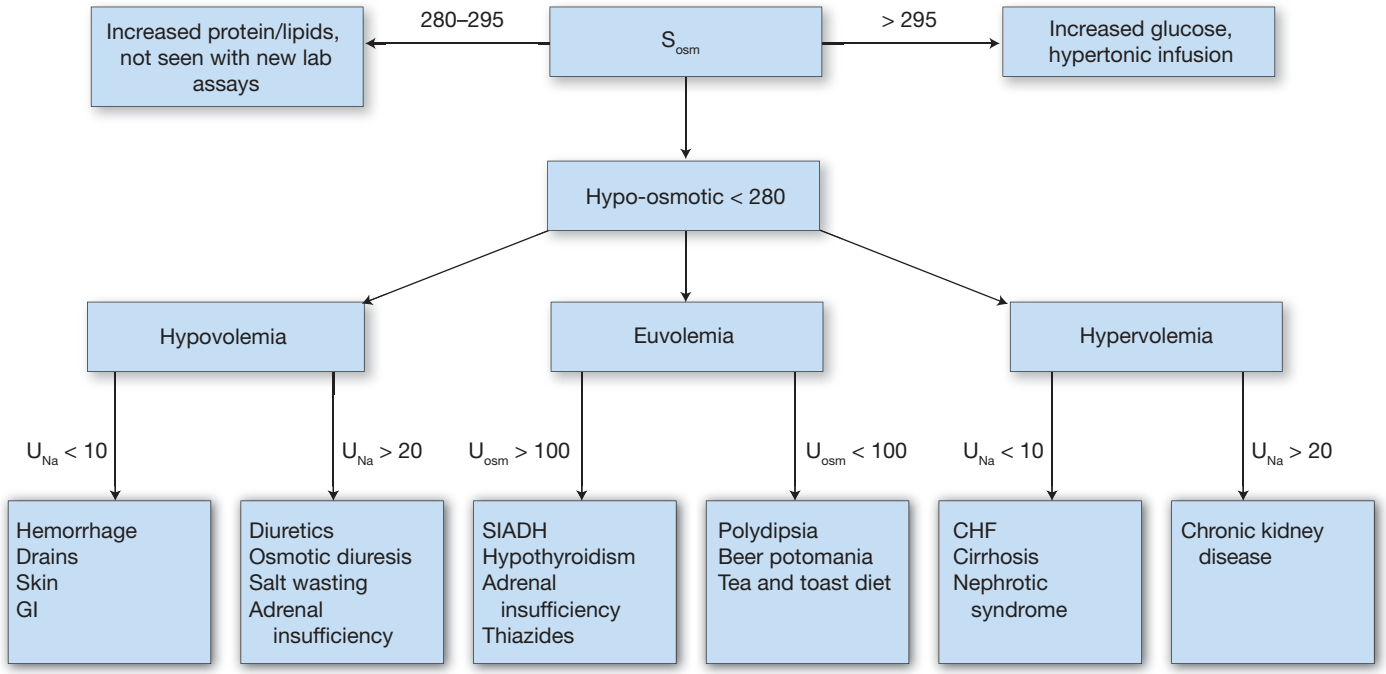


FIGURE 12-1. Evaluation of hyponatremia.

KEY FACT

Do not correct hypernatremia at a rate > 12 mEq/L/day. Correction at faster rates can result in cerebral edema. Compare this to correcting hyponatremia too quickly (> 9 mEq/L/day) which can result in osmotic demyelination syndrome.

History/PE

Often asymptomatic at Na^+ concentrations < 155 mEq/L, symptoms can progress to fatigue, seizures, and coma at higher levels.

Diagnosis

Assess volume status; check urine osmolality and urine sodium (see Figure 12-2).

Treatment

- Correct the free-water deficit with hypotonic saline or oral water.
- For central diabetes insipidus, administer desmopressin.
- For nephrogenic diabetes insipidus, remove offending medication (eg, lithium).

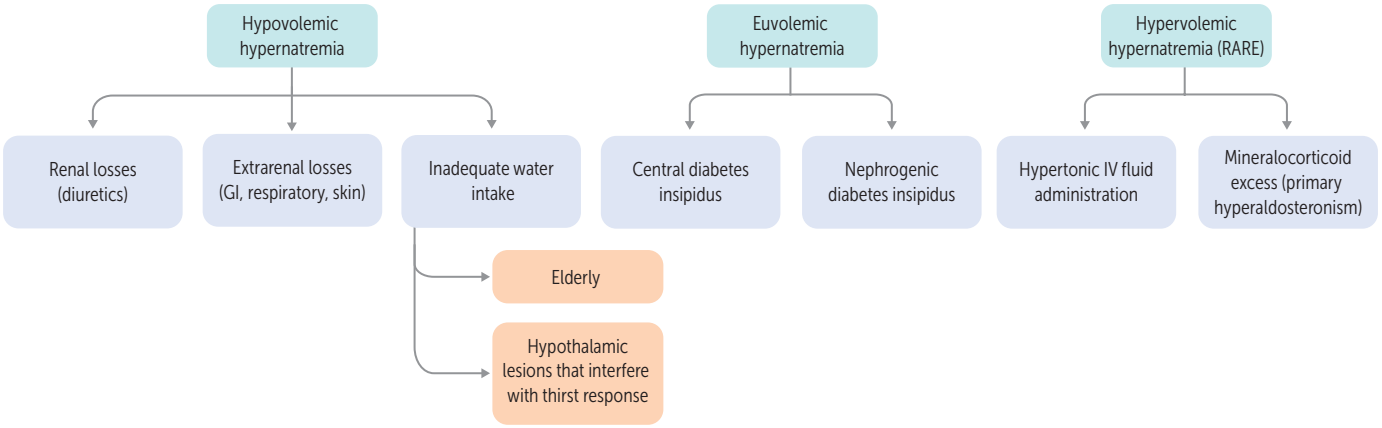


FIGURE 12-2. Evaluation of hypernatremia. (Reproduced with permission form USMLE-Rx.com.)

HYPOKALEMIA

Defined as serum potassium (K^+) concentrations < 3.5 mEq/L.

History/PE

May be asymptomatic or present with muscle weakness/paralysis and cardiac arrhythmias.

Diagnosis

- ECG may show T-wave flattening and U waves (an additional wave after the T wave).
- The underlying cause is often clear based on the history (eg, patient taking loop diuretics).
- If diagnosis is unclear based on history:
  - Check 24-hour urine K^+ or spot urine K^+.
  - Assess acid base status.
- **24-hour urine K^+ > 30 mEq/L:** Indicates that the kidneys are wasting K^+.
  - **Metabolic acidosis:** Type I renal tubular acidosis (RTA), Type II RTA, amphotericin, diabetic ketoacidosis.
  - **Metabolic alkalosis:** 1° hyperaldosteronism (high aldosterone/low renin), Cushing syndrome (check 24-hour urine cortisol), diuretics (loop or thiazide), Bartter syndrome, Gitelman syndrome.
- **24-hour urine K^+ < 20 mEq/L:** Indicates that the kidneys are NOT the source of K^+ loss.
  - **Metabolic acidosis:** Laxative abuse.
  - **Metabolic alkalosis:** Vomiting, NG suctioning.

Treatment

- Manage the underlying disorder (antiemetic therapy).
- Provide oral and/or IV K^+ repletion.

HYPERKALEMIA

Defined as K^+ concentrations ≥ 5 mEq/L.

History/PE

May be asymptomatic or present with muscle weakness/paralysis or cardiac arrhythmias.

Diagnosis

- An ECG may show peaked T-waves (Figure 12-3).
- Assess renal function: Acute and chronic kidney disease are associated with hyperkalemia.
- Medications are often implicated: Spironolactone, eplerenone, amiloride, triamterene, ACEI/ARB, digoxin.
- Assess acid base status: Metabolic acidosis is associated with hyperkalemia.

Treatment

- K^+ > 6.5 mEq/L or ECG changes (peaked T-waves or wide QRS) require emergent treatment (see the mnemonic "**C BIG K Drop**"). Calcium gluconate should be given immediately to prevent cardiac arrhythmias.
- Temporary treatment includes β_2-agonists, insulin with glucose, and sodium bicarbonate.

KEY FACT

Vomiting is associated with hypokalemic hypochloremic metabolic alkalosis. The loss of gastric contents, including hydrochloric acid, results in renal reabsorption of acid (H^+) in place of K^+, which is excreted in the urine.

KEY FACT

Replacement of K^+ is difficult when hypomagnesemia is present. Replete both deficiencies if present.

KEY FACT

In metabolic acidosis, H^+ are shuffled intracellularly in an attempt to reduce the extracellular pH. The movement of H^+ across the cellular membrane requires an exchange with K^+, which moves extracellularly resulting in hyperkalemia.

Q 1

A mother brings her 2-year-old boy to the clinic because his face seems swollen and he "feels heavier." The child recently had a URI, and though his upper respiratory symptoms have improved, he has grown more fatigued. You note dependent edema. UA reveals 3+ protein; light microscopy shows normal-appearing glomeruli. What is your diagnosis?

Q 2

Which secondary cause of nephrotic syndrome appears as apple-green birefringence under polarized light following congo red staining?

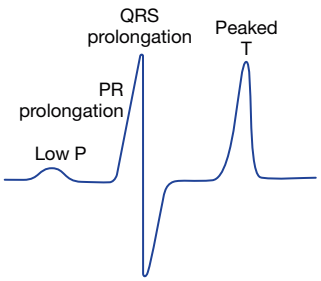


FIGURE 12-3. Effects of hyperkalemia as seen on ECG.

MNEMONIC

Treatment of hyperkalemia—

"C BIG K Drop"

Calcium gluconate
Bicarbonate/β_2-*agonist (albuterol)*
Insulin
Glucose
Kayexalate (sodium polystyrene sulfate)
Diuretic/**D**ialysis

KEY FACT

c-ANCA and p-ANCA are diagnosed by the corresponding antibody staining pattern localized to the cytoplasm or perinuclear area, respectively. The most common antigen target for c-ANCA is PR3 (sometimes referred to as PR3-ANCA). The most common antigen target for p-ANCA is MPO (sometimes referred to as MPO-ANCA).

1 A

Minimal change disease is a common cause of nephrotic syndrome in children that results from effacement of glomerular epithelial foot processes. It is treated with steroids and has an excellent prognosis.

2 A

Renal amyloidosis.

- Permanent elimination requires sodium polystyrene sulfate, a loop diuretic, or hemodialysis.
- Discontinue any medications that may be contributing to the hyperkalemia (eg, angiotensin-converting enzyme inhibitor [ACEI]/angiotensin receptor blocker [ARB]).

Nephrotic and Nephritic Syndromes

Disorders of the glomerulus.

- **Nephrotic syndrome:** Due to loss of glomerular basement membrane (GBM) function; results in loss of large plasma proteins into the urine, which is responsible for many of the manifestations associated with the syndrome.
- **Nephritic syndrome:** Due to inflammation of the glomerulus; results in loss of RBCs and large plasma proteins into the urine.

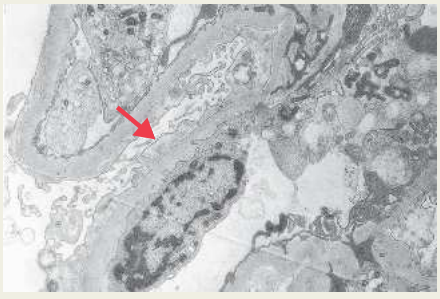
See Table 12-3 for a comparison of nephrotic and nephritic syndromes and Tables 12-4 to 12-6 for various causes of each. Secondary causes of nephrotic syndrome are those that are caused by systemic disease. Examples include diabetic nephropathy, lupus nephritis, and renal amyloidosis (see Table 12-5).

TABLE 12-3. Nephrotic vs Nephritic Syndrome

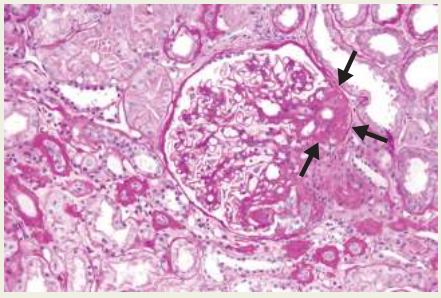
	Nephrotic Syndrome	Nephritic Syndrome
Defining features	Proteinuria (> 3.5 g/day) Edema (loss of serum albumin) Hyperlipidemia Hypercoagulability Immunodeficiency (loss of IgG)	Hematuria Hypertension Proteinuria (usually < 3.5 g/day)
Urine microscopy	Fat vacuoles (Maltese cross pattern)	Dysmorphic RBCs, RBC casts
Diagnosis	Order testing of antinuclear antibody (ANA), complement levels, serum/urine free light chains, rapid plasma reagin, HBV, HCV, and HIV A renal biopsy is often required for definitive diagnosis	Order testing of ANA, complement levels, antineutrophil cytoplasmic antibody (ANCA), anti-GBM antibodies, and anti-streptolysin O antibody A renal biopsy is often required for definitive diagnosis
General treatment	ACEI/ARB (decrease proteinuria) Loop diuretic (decrease edema) Statin therapy (lower lipid levels) Anticoagulation (if thrombosis present) Treat underlying condition (eg, HIV infection)	Treat the underlying condition (can range from supportive therapy to immunosuppressive therapy)

TABLE 12-4. 1° Causes of Nephrotic Syndrome

Pathology	Microscopy	Epidemiology	Treatment
Minimal change disease	Light: Normal Electron: Diffuse podocyte epithelial foot process effacement (Image A, arrow)	More common in children < 10 years of age Idiopathic	First line: Steroids Second line: Cyclophosphamide
Focal segmental glomerulosclerosis	Light: Glomerular sclerosis (Image B, arrows) Electron: Diffuse podocyte foot process effacement	More common in African-American adults Idiopathic HIV Heroin use	First line: Steroids Second line: Cyclosporine
Membranous nephropathy	Light: Capillary wall thickening, "spike and dome" appearance of GBM (Image C, arrows) Electron: Subepithelial deposits	More common in Caucasian adults Idiopathic HBV Malignancy	First line: Steroids + cyclophosphamide/cyclosporine NOTE: Mild presentations can be managed with general treatment strategies alone (eg, ACEI, statin)
Membranoproliferative glomerulonephritis (MPGN)	Light/Electron: Subendothelial (Image D, arrows) or subepithelial deposits	Overall a rare cause of glomerular disease in children and adults HCV Systemic lupus erythematosus (SLE) Idiopathic	Treat the underlying condition (eg, antiviral therapy) NOTE: Some patients may require steroids



A



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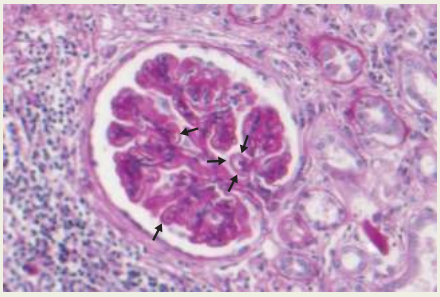
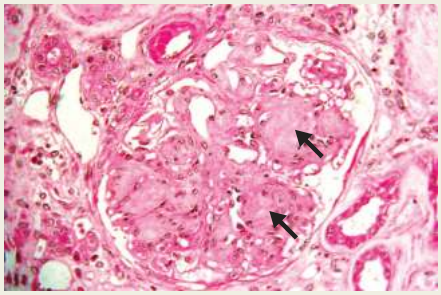


C



D

Image A reproduced with permission from Le T et al. *First Aid for the USMLE Step 1 2018.* New York, NY: McGraw-Hill Education; 2018. Image B courtesy of Dr. Michael Bonert. Images C and D reproduced with permission from USMLE-Rx.com.

KEY FACT

A kidney biopsy is almost always indicated for suspected lupus nephritis as results can help distinguish the class of nephritis that is present. Treatments for lupus nephritis are highly dependent on the class of disease.

TABLE 12-5. 2° Causes of Nephrotic Syndrome

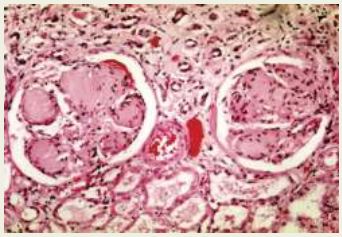
Pathology	Microscopy	Epidemiology	Treatment
Diabetic nephropathy	Light: Nodular glomerulosclerosis (Kimmelstiel-Wilson lesions) 	Common with poorly controlled DM	Glucose control ACEI/ARB
Lupus nephritis	Light: Variable, depending on class of nephritis	More common in African-Americans with SLE	Variable Mycophenolate Steroids + cyclophosphamide
Renal amyloidosis	Light (polarized): Apple-green birefringence following congo red staining	Seen in patients with multiple myeloma (AL amyloidosis) or those with chronic inflammation (AA amyloidosis)	AL: Steroids + melphalan AA: Treatment of underlying condition

Image reproduced from the CDC/Dr. Edwin P. Ewing, Jr.

TABLE 12-6. Causes of Nephritic Syndrome

Pathology	Microscopy	History/PE	Lab findings	Treatment
		ANCA ⊕		
Microscopic polyangiitis	Necrotizing vasculitis without granuloma formation	Hemoptysis Purpura	⊕ p-ANCA Normal complements levels	Steroids + cyclophosphamide/rituximab
Granulomatosis with polyangiitis	Necrotizing vasculitis with granuloma formation	Hemoptysis Oral ulcers Saddle nose	⊕ c-ANCA Normal complement levels	Steroids + cyclophosphamide/rituximab
Eosinophilic granulomatosis with polyangiitis	Necrotizing vasculitis with granuloma formation	Asthma Nasal polyps Skin nodules	⊕ p-ANCA Normal complement levels	Steroids NOTE: May need to add cyclophosphamide if lack of response

TABLE 12-6. Causes of Nephritic Syndrome *(continued)*

Pathology	Microscopy	History/PE	Lab findings	Treatment
		Anti-GBM ⊕		
Goodpasture syndrome	Linear IgG deposits along GBM Crescentic glomerulonephritis	Pulmonary hemorrhage Hematuria	⊕ anti-GBM Normal complement levels	Steroids + cyclophosphamide + plasma exchange
		Immune Complex Mediated		
Poststreptococcal glomerulonephritis	Subepithelial deposits Crescentic glomerulonephritis	Hematuria 3 weeks following URI or skin infection with *S pyogenes*	⊕ Antistreptolysin O antibody ↓ C3	Supportive therapy
IgA nephropathy	Mesangial IgA immune complex deposition	Hematuria 1–2 days following URI or GI tract infection	Normal complement levels	Supportive therapy If proteinuria, ACEI/ARB
		Genetic Mutation		
Alport syndrome	GBM thickening Tubular foam cells	Sensorineural hearing loss Ocular defects Hematuria	None pertinent	If proteinuria, ACEI/ARB

Nephrolithiasis

Kidney stones form when the urine is supersaturated with solutes resulting in solute precipitation and crystal formation. Risk factors include low urinary output, male gender, ⊕ family history, gout, chronic diarrhea, diabetes, and obesity. Additionally, those taking indinavir, acyclovir, or triamterene are at an ↑ risk for drug-induced urinary calculi. See Table 12-7 for the four major types of kidney stones.

History/PE

May present with acute flank pain with radiation to the anterior abdomen or ipsilateral testicle/labium. Gross hematuria is common.

Diagnosis

- Clinical suspicion + imaging—noncontrast CT scan (see Figure 12-4) or ultrasound if pregnant.
- Microscopic urinalysis for crystal visualization.
- Urine culture to evaluate for UTI.
- All urine should be strained and recovered stone should be analyzed for composition.

Q 1

A 38-year-old woman with HIV infection on antiretroviral therapy has a 2-day history of fevers and right flank pain. Exam reveals right costovertebral angle tenderness. UA shows 20–50 RBCs/hpf and 20–50 WBCs/hpf. CT reveals moderate right-sided hydronephrosis along with perinephric and periureteral stranding. Two hours after presentation, her BP goes from 120/75 to 82/50 and her temperature is 40.1°C (104.2°F). What is the next best step in management? Which antiretroviral drug could be implicated in this case?

Q 2

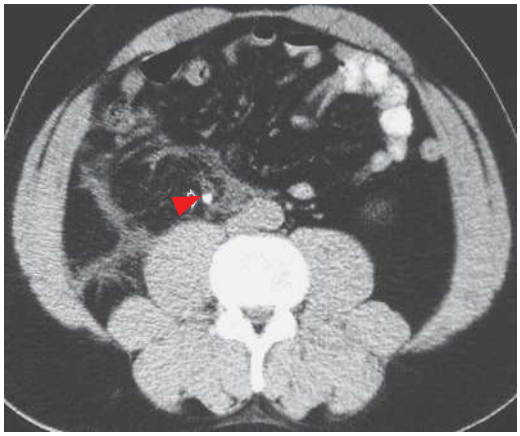
Which type of major kidney stone is not visualized on an x-ray?

TABLE 12-7. Types of Kidney Stones

Type	Urine Microscopy	Radiological Findings	Prevention/Treatment
Calcium oxalate	Envelope-shaped crystals	Radiopaque	Increase fluid intake (goal urinary output 2 L/day) Decrease dietary oxalate and dietary sodium
Struvite ($Mg\text{-}NH_4\text{-}PO_4$)	Coffin-lid shaped crystals	Radiopaque (see Figure 12-4B)	UTI prevention Surgical removal
Uric acid	Diamond-shaped crystals	Radiolucent, visualized on CT	Increase fluid intake Alkalinize urine Administer xanthine oxidase inhibitor
Cystine	Hexagonal shaped crystals	Radiopaque	Increase fluid intake Alkalinize urine Administer penicillamine/tiopronin

Treatment

- **Acute:**
  - Hydration and analgesia; additional management is based on the size of the stone.



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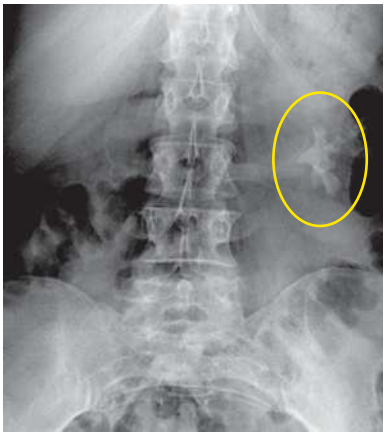


B

FIGURE 12-4. Nephrolithiasis. (**A**) Transaxial CT without IV contrast shows a right ureteral calculus (*arrowhead*) with surrounding inflammatory changes of retroperitoneal fat. (**B**) AXR shows a left staghorn or struvite ($Mg\text{-}NH_4\text{-}PO_4$) stone filling the collecting system of the right kidney. (Image A reproduced with permission from Chen MY et al. *Basic Radiology.* New York: McGraw-Hill, 2004, Fig. 9-31. Image B reproduced with permission from USMLE-Rx.com.)

1 **A**

The patient likely has sepsis 2° to UTI/pyelonephritis. She requires aggressive fluid resuscitation and empiric antibiotics after urine and blood cultures are obtained. Call urology for a presumed indinavir stone, which are not visualized on CT imaging.

2 **A**

Uric acid kidney stones are radiolucent but can be visualized with CT imaging.

- Stones < 5 mm in diameter often pass without surgical intervention.
- Patients presenting with fever and urinary obstruction require immediate urological intervention.

- **Chronic:**
  - In cases where stones are 2° to hypercalciuria, thiazide diuretics can be initiated.
  - Recurrent uric acid stones despite supportive therapy (eg, increasing fluid intake, urine alkalization) require xanthine oxidase inhibitors.
  - Recurrent cysteine stones despite supportive therapy require penicillamine or tiopronin.

Diuretics

Table 12-8 lists commonly used diuretics, their mechanism of action, and their adverse effects. See Figure 12-5 for an illustration of the sites of action of various diuretics.

TABLE 12-8. Mechanism of Action and Adverse Effects of Selected Diuretics

Diuretic Class	Mechanism of Action	Adverse Effects
Osmotic agents (eg, mannitol, urea)	Entire tubule	↑ Tubular fluid osmolarity, ↓ Na^+
Carbonic anhydrase inhibitors (eg, acetazolamide)	Inhibition of carbonic anhydrase in the proximal tubule	Metabolic acidosis, hypokalemia
Loop diuretics (eg, furosemide, torsemide, ethacrynic acid)	Inhibition of the $Na^+/K^+/2Cl^-$ cotransporter in the loop of Henle	Hypokalemia, ototoxicity
Thiazides (eg, hydrochorothiazide, chlorthalidone, metolazone)	Inhibition of the Na^+/Cl^- cotransporter in the distal convoluted tubule	Hypokalemia; hyper **"GLUC":** Hyper**G**lycemia Hyper**L**ipidemia Hyper**U**ricemia Hyper**C**alcemia
K^+ sparing diuretics	Spironolactone/eplerenone: Inhibition of aldosterone receptor in the collection duct Amiloride/triamterene: Inhibition of epithelial sodium channel in the collecting duct	Hyperkalemia, gynecomastia (spironolactone only)

Q 1

A defect in which part of the kidney is responsible for the development of cystinuria?

Q 2

Which bacteria cause struvite kidney stones?

Q 3

A 39-year-old man with a history of major depressive disorder is admitted for altered mental status. His initial labs show a serum HCO_3 of 14 mEq/L and an AG of 22. Arterial blood gas shows a pH of 7.30, a $Paco_2$ of 20 mm Hg, and a Pao_2 of 150 mm Hg. From his acid-base status, what ingestion should you suspect?

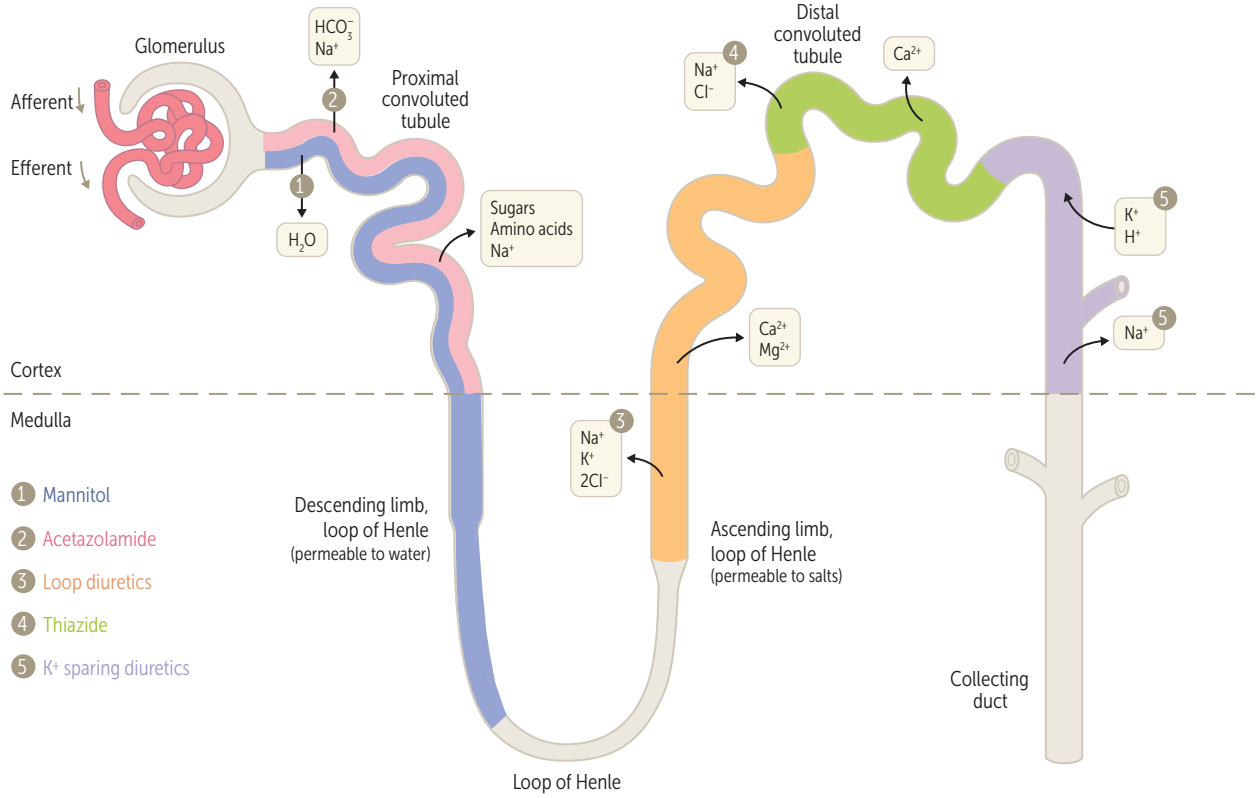


FIGURE 12-5. Diuretics and their site of action. (Reproduced with permission from USMLE-Rx.com.)

Acid-Base Disorders

The algorithm for acid-base disorders is as follows:

1. Identify the 1° disorder:
   - **Metabolic acidosis:** pH < 7.40, HCO_3 < 24.
   - **Metabolic alkalosis:** pH > 7.40, HCO_3 > 24.
   - **Respiratory acidosis:** pH < 7.40, Pco_2 > 40.
   - **Respiratory alkalosis:** pH > 7.40, Pco_2 < 40.
2. Assess compensation:
   - **Expected compensation in metabolic acidosis:**

$$Paco_2 = 1.5 \times [HCO_3] + 8 +/- 2$$

     - If $Paco_2$ is more than expected, it suggests concurrent respiratory acidosis.
     - If $Paco_2$ is less than expected, it suggests concurrent respiratory alkalosis.
   - **Expected compensation in acute respiratory acidosis (onset < 2 days):**
     - ↑ of 1 mEq/L HCO_3 above 24 mEq/L for every 10 mm Hg ↑ in $Paco_2$ above 40 mm Hg.
     - If the change in HCO_3 is more, it suggests concurrent metabolic alkalosis.
     - If the change in HCO_3 is less, it suggests concurrent metabolic acidosis.
   - **Expected compensation in acute respiratory alkalosis (onset < 2 days):**
     - ↓ of 2 mEq/L HCO_3 below 24 mEq/L for every 10 mm Hg ↓ in $Paco_2$ below 40 mm Hg.
     - If the change in HCO_3 is more, it suggests concurrent metabolic acidosis.

1 **A**

A defect in the proximal tubular amino acid cysteine transporters results in high urinary concentrations of the amino acid.

2 **A**

Urease-producing bacteria (eg, *Klebsiella* or *Proteus*).

3 **A**

The patient's findings—a pH < 7.40 and HCO_3 < 24 mEq/L plus a $Paco_2$ that is lower than the expected compensation of $Paco_2$ 27–31 mm Hg—indicate a mixed metabolic acidosis and respiratory alkalosis. This is most commonly seen in aspirin poisoning.

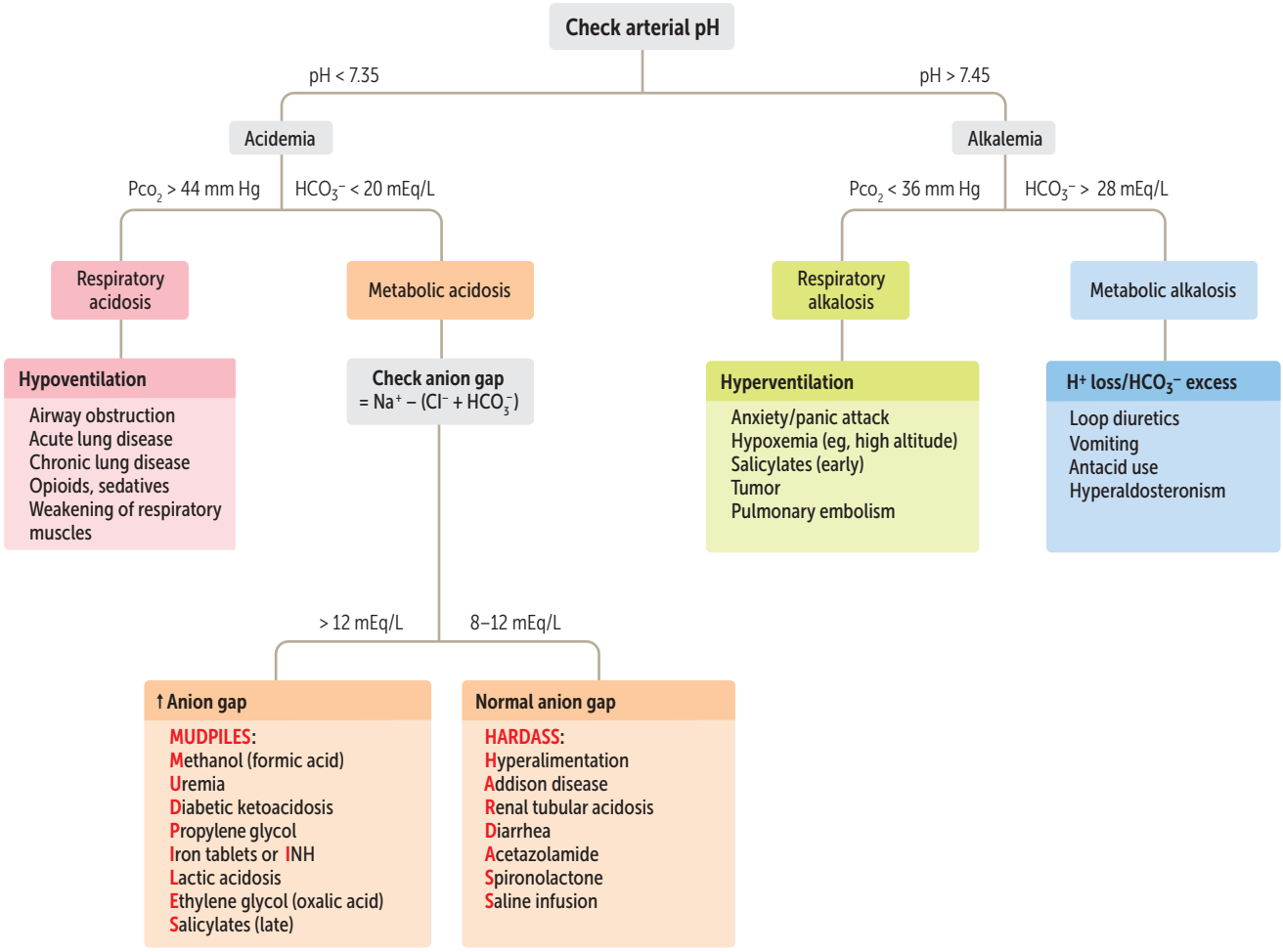


FIGURE 12-6. Acid-base disorders. (Reproduced with permission from USMLE-Rx.com.)

- If the change in HCO_3 is less, it suggests concurrent metabolic alkalosis.

3. Miscellaneous additional calculations for metabolic acidosis:
   - Always calculate the anion gap (AG) using: AG = (Na − [HCO_3 + Cl]).
     - If the AG is ≥ 14, a high AG metabolic acidosis exists (see the mnemonic GOLDMARK).
   - Always calculate the delta ratio for high AG metabolic acidosis using: (AG − 12) / (24 − HCO_3).
     - If the delta ratio is > 2, there is concurrent metabolic alkalosis.
     - If the delta ratio is < 1, there is concurrent non-AG metabolic acidosis.

Figure 12-6 demonstrates a flow chart for evaluating acid-base disorders.

Renal Tubular Acidosis

There are three clinically important types of RTA (see Table 12-9). Each can result in a non-anion gap (AG) metabolic acidosis. Usually asymptomatic. See Figure 12-7 for a diagnostic algorithm.

- Serum K^+ ↓, think type I or II; ↑ think type IV.
- Urine pH > 5.3 suggests type I.
- Urine AG ([Na^+] + [K^+] – [Cl-]) ⊕ indicates type I; ⊖ type II.

MNEMONIC

Common causes of high AG metabolic acidosis—

GOLDMARK

Glycols (ethylene and propylene)
Oxoproline (acetaminophen)
L-lactic acidosis (organ hypoperfusion)
D-lactic acidosis (short bowel syndrome)
Methanol
Aspirin
Renal failure
Ketoacidosis

TABLE 12-9. Types of Renal Tubular Acidosis

Variable	Type I (distal)	Type II (proximal)	Type IV (Impaired Mineralocorticoid Effect)
Defect	H^+ secretion	HCO_3^- reabsorption	Aldosterone deficiency or resistance
Serum K^+	Low	Low	High
Urinary pH	> 5.3	5.3 or high at onset but can be < 5.3 once serum is in its acidotic state	Variable (not typically used to differentiate)
Etiologies (most common)	Autoimmune disorders, hypercalciuria, amphotericin B, ifosfamide, genetic disorders	Multiple myeloma, amyloidosis, all other causes of Fanconi syndrome (eg, genetic and acquired), aminoglycosides, ifosfamide, cisplatin, acetazolamide	Hypoaldosteronism, angiotensin II inhibition (ACEIs/ARBs), urinary tract obstruction, heparin
Treatment	Potassium bicarbonate supplementation	Treat underlying cause; often needs sodium and potassium bicarbonate supplementation	Depending on etiology may need mineralocorticoid replacement, sodium bicarbonate supplementation, or K wasting diuretics
Complications	Nephrolithiasis	Rickets, osteomalacia	

Adapted with permission from Le T et al. *First Aid for the USMLE Step 2 CK,* 10th ed. New York: McGraw-Hill, 2019: 511.

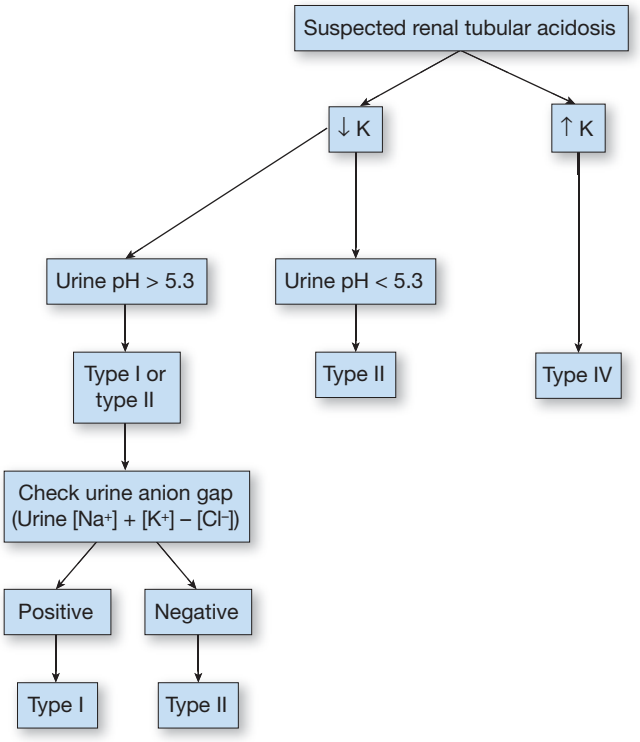


FIGURE 12-7. Diagnosis of renal tubular acidosis.

Chronic Kidney Disease

Kidney dysfunction that occurs for > 3 months. Impairments can be seen in acid-base status, nitrogenous waste excretion, erythropoiesis, and vitamin D metabolism. The most common causes of chronic kidney disease (CKD) in the United States are diabetes mellitus and hypertension.

History/PE

May be asymptomatic but can present with hypertension, pulmonary edema, uremia, or electrolyte disorders (eg, hyperkalemia).

Diagnosis

Look for 3 months of ↓ glomerular filtration rate (GFR) or albuminuria.

Treatment

- Management of underlying cause of CKD (eg, diabetes) to prevent disease progression.
- ACEI/ARB for albuminuria.
- Phosphate binders (eg, sevelamer) for hyperphosphatemia.
- Bicarbonate therapy for acidosis.
- Erythropoietin for anemia.
- Furosemide for volume overload.
- Vitamin D supplementation.
- Preparation for renal replacement therapy, including hemodialysis and transplantation.

KEY FACT

Some causes of ↑ Cr and ↑ BUN without ↓ GFR:

- ↑ Cr without ↓ GFR: Trimethoprim, cimetidine, cefoxitin, ketoacidosis.
- ↑ BUN without ↓ GFR: Steroids, GI bleed, burns/sepsis (high-catabolic states), high-protein diet.

NOTES

CHAPTER 13

NEUROLOGY

Localization

Neurology is all about the ability to localize lesions. Use the neuroaxis to determine the location of a lesion (see Figure 13-1). Findings in the history and PE can help differentiate between central—upper motor neuron (UMN)—lesions and peripheral—lower motor neuron (LMN)—lesions (see Table 13-1).

Brain

STROKE

Occurs when poor blood supply to the brain leads to acute onset of neurologic dysfunction. Can be ischemic (most common) or hemorrhagic (see Table 13-2). Etiology of stroke can be classified into five categories:

- Large vessel atherosclerosis: Embolus, thrombus.
- Small vessel disease: hypertension, hyperlipidemia, DM, smoking.
- Cardioembolic: Atrial fibrillation (AF), endocarditis, recent myocardial infarction (MI), prosthetic valve.
- Cryptogenic: Unknown (but thought to be due to undiagnosed AF in many patients).

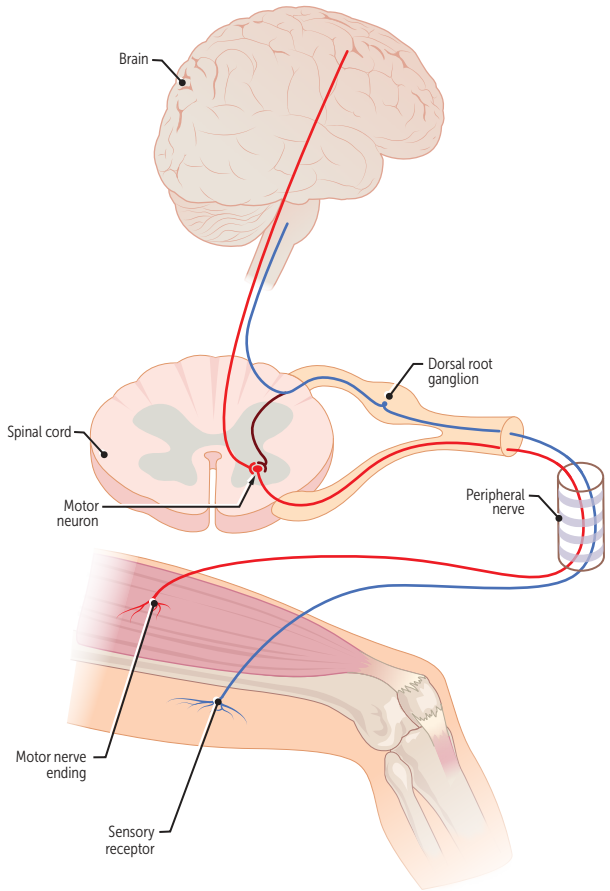


FIGURE 13-1. Neuroaxis. When localizing a lesion, consider all aspects of the neuroaxis, including the brain, spinal cord, anterior horn, nerve roots, peripheral nerves, neuromuscular junctions, and muscles. (Reproduced with permission from USMLE-Rx.com.)

TABLE 13-1. Upper Motor Neuron vs Lower Motor Neuron Lesions

	UMN Lesions	LMN Lesions
Anatomy	Central nervous system (brain and spinal cord)	Peripheral nervous system
Tone	Spasticity	Flaccidity
Wasting	Absent	Present
Deep tendon reflexes	Hyperactive	Hypoactive or absent
Plantar reflexes	Upgoing (⊕ Babinski sign)	Downgoing (normal)
Fasciculations	Absent	Present

- Other: Vasculitis, drug-induced, hypercoagulable state, vertebral or carotid artery dissection, paradoxical stroke secondary to patent foramen ovale.

History/PE

Stroke symptoms can be localized to a particular vascular territory based on knowledge of anatomical structures in the brain (see Table 13-3 and Figure 13-2).

Diagnosis

- The vascular territories affected can be seen on imaging (see CT scans in Table 13-2).
- Further workup to evaluate etiology of stroke:
  - MRI brain to look for stroke distribution and pattern.
  - CTA to look for vessel abnormalities (eg, occlusion) or stenosis.
  - TTE to look for shunt, clot, or valvular AF.
  - Telemetry to look for AF.

Treatment

- **First line** for ischemic stroke: Tissue plasminogen activator (tPA).
- Inclusion criteria:
  - ≥ 18 years of age.
  - Ischemic stroke.
  - Onset < 4.5 hours.
- Absolute contraindications:
  - Current intracerebral hemorrhage (ICH) or subarachnoid hemorrhage (SAH).
  - Prior hemorrhagic stroke.
  - Platelets < 100,000 or Internationalized Normalized Ratio (INR) > 1.7 (or on novel oral anticoagulants).
  - BP > 185/110.
  - Recent major surgery.
  - Active internal bleeding.
- Use caution when giving tPA between 3 and 4.5 hours of ischemic stroke onset in patients with the following:
  - Age > 80.
  - History of stroke + DM.
  - NIH score > 25.
  - Oral anticoagulant use.

KEY FACT

In UPPER motor neuron lesions—everything is INCREASED.
In LOWER motor neuron lesions—everything is DECREASED.

KEY FACT

The biggest modifiable risk factor for stroke is hypertension.

KEY FACT

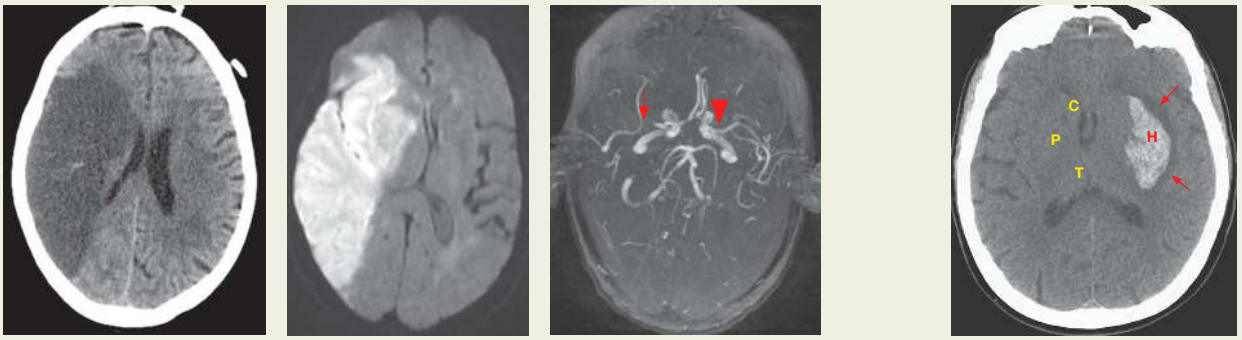
When you highly suspect SAH, order LP even if the head CT is ⊖ (15% of patients with aneurysmal SAH have a ⊖ CT). LP will show high RBCs in all tubes and xanthochromia (yellow cerebrospinal fluid [CSF]).

Q

An 81-year-old woman with a history of hypertension presents with sudden onset of left-sided weakness. She displays left-sided neglect and left facial and arm paralysis with relative sparing of the left leg. Which vessel territory is affected?

TABLE 13-2. Ischemic vs Hemorrhagic Stroke

Ischemic		Hemorrhagic	
Transient ischemic attack	Ischemic stroke	Intracerebral hemorrhage	Subarachnoid hemorrhage
Transient neurologic dysfunction that resolves to baseline in < 24 hours No changes seen on imaging	Blockage of blood flow to the brain from thrombus or embolus resulting in infarction of brain tissue	Bleeding within the brain parenchyma Due to ruptured aneurysm, tumor, arteriovenous malformation (AVM), high blood pressure	Bleeding in the subarachnoid space Can be traumatic or spontaneous Classically presents as "worst headache of life"



A B C D

Acute ischemic stroke. (**A**) Noncontrast transaxial head CT with loss of gray and white matter differentiation and asymmetrically ↓ size of the right lateral ventricle in a right MCA distribution (indicating mass effect). (**B**) Transaxial MRI with reduced diffusion in the same distribution. (**C**) Maximum-intensity projection of a transaxial time-of-flight MRA shows the cause: an abrupt occlusion of the proximal right MCA (*arrow*). Compare with the normal left MCA (*arrowhead*).

Intracerebral hemorrhage. (**D**) Transaxial image from a noncontrast head CT shows an intraparenchymal hemorrhage (H) and surrounding edema (*arrows*) centered in the left putamen, a common location for hypertensive hemorrhage. C, P, and T denote the normal contralateral caudate, putamen, and thalamus.

Images A–C reproduced with permission from USMLE-Rx.com. Image D reproduced with permission from Fauci AS et al. *Harrison's Principles of Internal Medicine,* 17th ed. New York: McGraw-Hill, 2008, Fig. 364-17.

MNEMONIC

LEFT MCA stroke leads to **L**ANGUAGE deficits.

A

The right middle cerebral artery (MCA). This is supported by neglect (a cortical sign) and sparing of the left leg, indicating preservation of the anterior cerebral artery (ACA) territory. The MCA supplies the lateral frontal, parietal, and temporal cortex; the ACA supplies the territory for motor control of the leg.

- If there is evidence of large vessel occlusion on CTA and symptom onset was < 24 hours ago, then patient is a candidate for endovascular thrombectomy.
- **First line** for hemorrhagic stroke:
  - Control BP (typically SBP below 140–160).
  - Insert external ventricular drain to alleviate pressure.
  - If evidence of aneurysm, consider coiling or clipping.
  - If evidence of midline shift, neurologic decline, or impending herniation, consult neurosurgery for decompressive craniectomy.

2° Prevention

- Aspirin daily.
- Atorvastatin daily.
- Smoking cessation.
- BP control.
- Anticoagulation if patient has AF.
- Carotid endarterectomy recommended for patients with symptomatic stenosis 70–99% and should be strongly considered in patients with symptomatic stenosis > 50% or asymptomatic stenosis 60–99%.

TABLE 13-3. Vessels Affected in Stroke and Associated Symptoms

Vessel Affected	Deficit
MCA stroke	Contralateral weakness of the arm and face; contralateral sensory deficits Right side leads to neglect Left side leads to language deficits: Broca (expressive) aphasia: Nonfluent speech, comprehension intact Wernicke (receptive) aphasia: Poor comprehension, speech production intact, "word salad" nonsensical speech
ACA stroke	Contralateral leg weakness and sensory deficits
PCA stroke	Homonymous hemianopia with macular sparing
Brainstem strokes	**Posterior inferior cerebellar artery** (medulla) Wallenberg syndrome: Nystagmus, Horner syndrome, loss of pain and temperature sensation on the ipsilateral face and contralateral body **Anterior inferior cerebellar artery** (pons): Ipsilateral limb ataxia and contralateral hemiplegia and loss of pain and temperature sensation **Posterior cerebral artery (PCA)** (midbrain) Weber syndrome: Ipsilateral cranial nerve III palsy and contralateral arm and leg weakness
Lacunar stroke	Internal capsule: Pure motor stroke Thalamus: Pure sensory stroke Basilar part of pons: Dysarthria (clumsy hand syndrome)

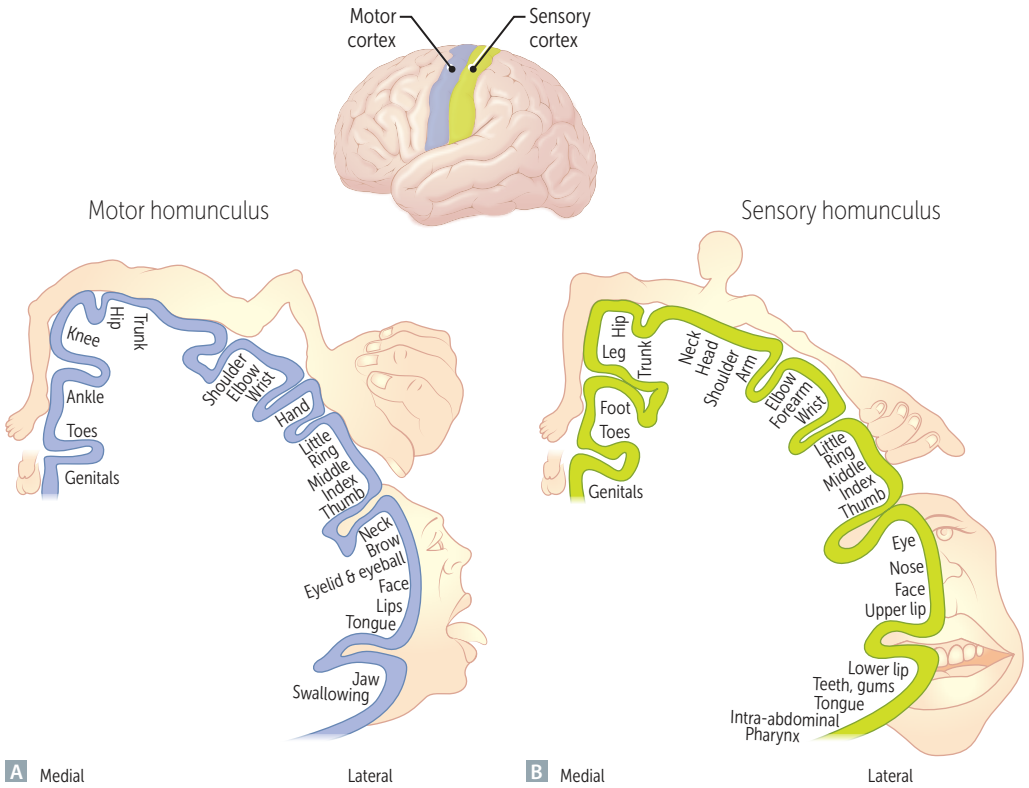


FIGURE 13-2. Motor and sensory homunculus. Note that the medial portion, supplied by the ACA, maps to the leg whereas the lateral section, supplied by the MCA, maps to the face and hand. (Reproduced with permission from USMLE-Rx.com.)

HEMATOMA

An intracranial accumulation of blood. Diagnosis and treatment of epidural hematoma (blood between the skull and the dura) and subdural hematoma (blood between the arachnoid membrane and the dura) are reviewed in Table 13-4.

TABLE 13-4. Epidural vs Subdural Hematoma

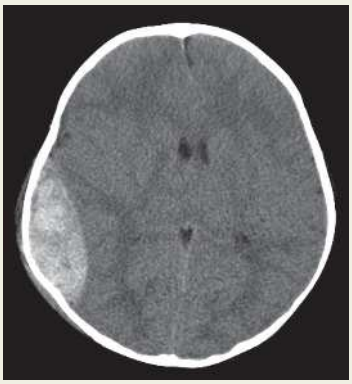
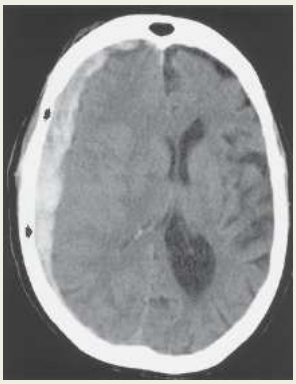
	Epidural Hematoma	Subdural Hematoma
Clinical presentation	Brief loss of consciousness (LOC) followed by "lucid" interval before neurologic deterioration	Usually seen in elderly persons or alcoholics following a single fall or history of many falls Headache, altered mental status, possible hemiparesis
Affected vessels	Middle meningeal artery	Bridging veins
Appearance on imaging	Biconvex hyperdensity, does not cross suture lines	Crescentic hyperdensity, may cross suture lines
Treatment	Surgical evacuation and possible craniotomy	If acute, surgical evacuation If chronic, observation
	 **A** Noncontrast transaxial CT showing a right temporal acute epidural hematoma	 **B** Noncontrast transaxial CT demonstrating a right acute holohemispheric subdural hematoma

Image A reproduced with permission from Doherty GM. *Current Diagnosis & Treatment: Surgery,* 13th ed. New York: McGraw-Hill, 2010, Fig. 36-8.
Image B reproduced with permission from Chen MY et al. *Basic Radiology.* New York: McGraw-Hill, 2004, Fig. 12-32.

HEADACHE

Can be 1° or 2° to an underlying disorder. It is important to differentiate between the two because the underlying cause of a 2° headache is often a neurologic emergency. Table 13-5 summarizes the most common 1° headache syndromes. Table 13-6 lists 2° causes of headache other than traumatic brain injury (TBI) or brain bleeds such as subdural hematoma or SAH.

KEY FACT

Horner syndrome presents with ipsilateral miosis (pupillary constriction), ipsilateral ptosis (eyelid droop), and ipsilateral anhidrosis (lack of sweating) of the face.

Diagnosis

Obtain imaging if you suspect headache is 2° to another underlying disorder:

- A headache that is acute and extremely severe ("thunderclap headache") → think SAH.
- New onset headache in an adult with no headache history.
- Focal neurologic signs or other neurologic sequelae (seizures).
- Papilledema → think ↑ intracranial pressure (ICP).
- A headache in an immunocompromised patient (eg, HIV).

TABLE 13-5. Presentation, Diagnosis, and Treatment of 1° Headache

Type	Symptoms	Exam/Diagnosis	Treatment
Tension	Tight, bandlike pain bilaterally lasting 30 min to 7 days	Normal exam; a clinical diagnosis	NSAIDs/acetaminophen; relaxation techniques
Migraine	Typically unilateral throbbing pain lasting for 4 hours to 3 days; can be associated with photophobia, phonophobia, nausea, vomiting, and aura Aura: Visual disturbance such as scotoma that occurs prior to onset of migraine	Normal exam; a clinical diagnosis that has a familial predisposition; more common in women	Elimination of triggers Prophylaxis: Amitriptyline, topiramate, propranolol, zonisamide Abortive agents: Triptans, NSAIDs Severe requiring hospitalization: IV hydration, antiemetics, and antihistamine; IV steroids; ergotamine
Cluster	Brief, severe, unilateral, periorbital headache; attacks at the same hour each day	Exam reveals ipsilateral lacrimation, conjunctival injection, Horner syndrome, and nasal congestion; more common in men	Abortive: 100% O_2 or injectable triptan Prevention: Verapamil or steroids

SEIZURES

Can be 1° or 2°. Common 2° causes of seizures include:

- **Infectious** (meningitis or any infectious process can lower seizure threshold).
- **Metabolic derangements** (hepatic encephalopathy, hypoglycemia, hyponatremia, hypomagnesemia, hypercalcemia).
- **Toxins** (drug-induced, ethanol withdrawal, medication-induced such as fluoroquinolones, carbapenems, isoniazid [INH], and bupropion).
- **Brain Injuries** (SAH, intraparenchymal hemorrhage, cortical strokes, subdural or epidural hematomas, TBI).
- **Brain tumor or metastasis.**

Q

A 27-year-old woman with a history of epilepsy is planning her first pregnancy. What should you recommend for her prenatal care?

TABLE 13-6. Presentation, Diagnosis, and Treatment of 2° Headaches

Type	Symptoms	Exam/Diagnosis	Treatment
Idiopathic intracranial hypertension (pseudotumor cerebri)	Mimics symptoms of tumor headache or migraine	Young, overweight female with elevated opening pressure on LP and evidence of papilledema on exam, with no evidence of tumor on MRI	Weight loss to reduce headaches, acetazolamide to reduce risk of vision loss, and therapeutic lumbar punctures
Aneurysm	May mimic migraine symptoms; sudden and severe pain with rupture	Family history of aneurysms, CTA reveals vessel abnormality	Surgical repair, BP control
Tumor headache	Progressively worsening headache; worse in the morning, refractory to traditional treatment	May have personality changes or other neurologic sequelae such as seizures	Surgery, radiation, or resection depending on the type and location of the tumor
Giant cell arteritis	Age > 50, pain around the ear and associated with chewing, can have visual loss	Temporal tenderness, jaw claudication, elevated ESR > 50, temporal artery biopsy	Steroids

KEY FACT

Jacksonian march seizure activity presents as progressive jerking that spreads from one limb to the next on the ipsilateral side.

KEY FACT

Postictally, seizure patients may have a focal neurologic deficit that mimics a stroke such as unilateral weakness (eg, Todd paralysis) that resolves within minutes to days.

MNEMONIC

Seizures: Eyes look away from the side with lesion.

StrOkes: Eyes look tOward the side with lesion.

History/PE

- Neurological exam is typically NORMAL interictally.
- **Pre-ictal:** Patient may experience an aura.
- **Ictal period:** May see rhythmic jerking of extremities or ↑ tone with gaze deviation toward the side of the seizure, bowel or bladder incontinence, and tongue biting.
- **Postictal:** Patient may be confused, have slow reaction times, or be very sleepy.

Diagnosis

- To rule out 2° causes of seizures, obtain CBC, BMP, magnesium, ammonia, EtOH level, toxicology screen, antiepileptic drug (AED) level.
- Obtain EEG to establish a baseline, localize the focus, and confirm epileptic vs nonepileptic seizures.
- MRI of the brain is indicated in any new adult-onset seizure to look for a structural abnormality. If central nervous system (CNS) infection suspected and no evidence of ↑ ICP on imaging, obtain LP.
- Seizures can be classified based on seizure focus and symptomology (see Table 13-7). Please note that the current classification system is in flux and will likely no longer be categorized based on "simple vs complex," but you may still see seizures described this way on exam.
- Status epilepticus is defined as continuous seizures for ≥ 5 minutes or discrete seizures with impaired consciousness in the interictal period. It is a medical emergency with up to a 20% mortality rate.

TABLE 13-7. Partial vs Generalized Seizures

Subtype	Presentation
Partial Seizures: involve a specific focus of the brain that can progress to generalized	
Simple	Acute onset of motor, sensory, autonomic, or psychiatric symptoms; no alteration of consciousness
Complex	Same symptoms as simple partial seizures, but with transient loss or alteration of consciousness (may begin with aura)
Generalized Seizures: arise from both hemispheres	
Tonic-clonic ("grand mal")	Acute loss of consciousness; tonic phase (stiffening of body) followed by clonic phase (jerking of body) Postictal period (deep sleep) that presents with incontinence, confusion, low serum HCO_3, and ↑ serum CK and prolactin
Absence ("petit mal")	Acute brief lapses of consciousness that begin in childhood (ages 4–8) No postictal period
Atonic	Acute brief loss of postural control resulting in a fall (1–2 seconds)
Myoclonic	Acute shock-like contraction of muscle groups (jerks)

A

For the pregnant woman with epilepsy, recommend that she stay on her antiepileptic therapy. If she is taking valproate, the most teratogenic antiepileptic, switching to another drug (eg, levetiracetam) is recommended before pregnancy. Taking 4 mg of folic acid daily is also recommended, as are regular checks of serum drug levels.

Treatment

- Acute management of status epilepticus:
  - Check ABCs; intubation may be required to protect the airway.
  - Give lorazepam.
  - If the seizure continues, give loading dose of fosphenytoin.
  - If the seizure persists, consider induction of coma with anesthetic (propofol, midazolam, phenobarbital).
- AEDs: There is no clear first-line agent. Some AEDs are indicated for specific types of seizures (narrow spectrum), whereas others work for a wide variety of both focal and generalized epilepsy (broad spectrum). AEDs are typically selected based on side effect profile and effectiveness for patient on a case-by-case basis. See Table 13-8 for commonly used and tested AEDs.

BRAIN DEATH

Irreversible loss of all functions of the brain, characterized by coma, absence of brainstem reflexes, and apnea.

Diagnosis

- Exclude sedatives, hypothermia, hypotension, metabolic derangements.
- Prerequisite states:
  - Core temperature ≥ 36°C.
  - SBP ≥ 100 mm Hg.
  - Eucapnia ($Paco_2$ 35 to 45 mm Hg).
  - Euvolemia.

KEY FACT

Most AEDs are teratogenic. Rule out pregnancy before starting treatment.

KEY FACT

To diagnose brain death, you must exclude sedative medication. Thus, the patient being off all sedatives is a prerequisite state.

KEY FACT

Common causes of coma include ischemic brain injury, TBI, and metabolic derangements (eg, profound hypoglycemia).

TABLE 13-8. Antiepileptic Drugs for Treatment and Prevention of Seizure

Drug	Uses	Adverse Effect(s)
Levetiracetam	Broad spectrum: All seizure types	↑ Risk of suicidality and mood disturbance
Lamotrigine	Broad spectrum: All seizure types; also a mood stabilizer	Stevens-Johnson syndrome
Valproate	Broad spectrum: All seizure types	Teratogenic, weight gain, hair loss, tremor, liver failure
Topiramate	Broad spectrum: All seizure types; also migraine prophylaxis	Cognitive impairment (why Topamax is nicknamed "Dopamax"), weight loss, kidney stones
Carbamazepine	Narrow spectrum: Focal or 2° generalized; trigeminal neuralgia	Hyponatremia, pancytopenia
Phenytoin	Narrow spectrum: Focal or 2° generalized	Gingival hyperplasia, bone demineralization
Ethosuximide	Narrow spectrum: Absence seizures	Sedation

Q

A 43-year-old woman complains of severe dizziness every time she turns her head abruptly. She states that the episodes make her feel as though the world is moving around her. She denies accompanying symptoms, takes no medications, and says that the episodes usually resolve on their own. What is her diagnosis?

TABLE 13-9. Evaluation for Absent Brainstem Functions

Absent Reflex	Definition	Nerves Involved
Pupillary light	No change in pupil size in response to bright light	CN II, III
Corneal	No blinking when the cornea is touched	CN V, VII
Oculovestibular	No deviation of eyes to stabilize images on retina during simulated head movement ("doll's eyes" reflex)	CN III, IV, VI, VIII
Gag	No response when the posterior pharynx is stimulated	CN IX, X

- Examine for absent brainstem reflexes (see Table 13-9).
- Apnea test: Complete apnea is denoted by no respirations at a $Paco_2$ of 60 mm Hg, or 20 mm Hg above normal values.
- If the prerequisites are met, with no explanation for coma, absent brainstem reflexes, and ⊕ apnea test, brain death can be diagnosed.
- **Confirmatory testing:** May be required if apnea test is inconclusive.
  - **Four-vessel angiography:** Absence of blood flow to the brain.
  - **EEG:** Low amplitude or flat brain wave pattern.
  - **Transcranial Doppler U/S:** Small systolic peaks without diastolic flow.

KEY FACT

In comatose patients, evaluate for nonconvulsive status epilepticus with an EEG.

VERTIGO

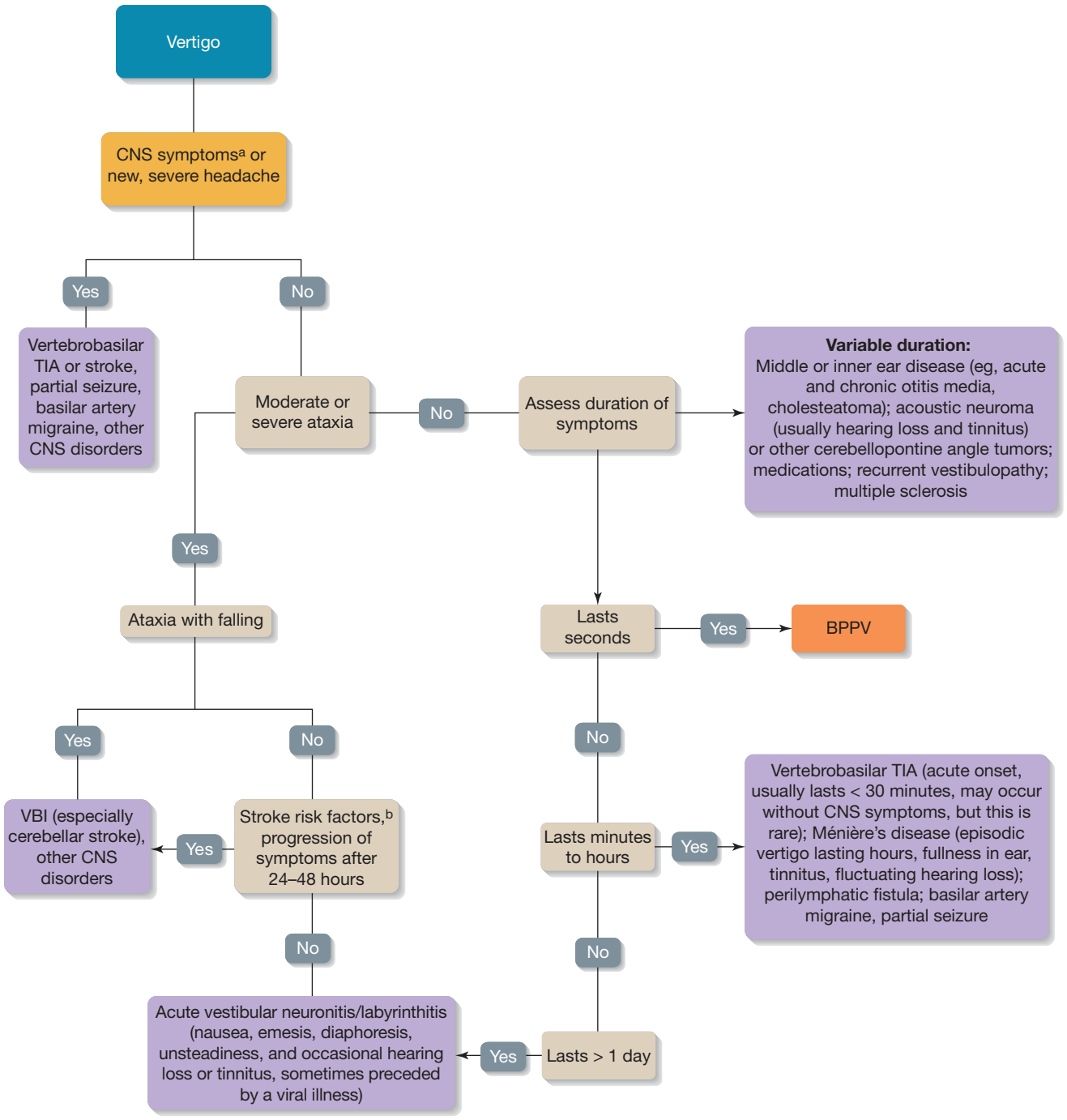
The sensation of the room spinning around, often described as "dizziness." This should be differentiated from lightheadedness, for which the differential includes orthostatic hypotension, cardiac arrhythmia, and presyncope/syncope. Once vertigo is diagnosed, the next step is to determine whether it is peripheral or central (see Table 13-10).

TABLE 13-10. Peripheral vs Central Vertigo

	Peripheral	Central
Pathology	Lesion of the vestibular apparatus of the inner ear or CN VIII	Lesion of brainstem vestibular nuclei or their connections
Symptoms	Vertigo is intermittent, positional and may be associated with tinnitus, hearing loss, and postural unsteadiness Nystagmus is rotary, unidirectional, and fatigable Fixation of gaze or eye closure stops vertigo	Vertigo is not positional and may have accompanying cranial nerve injuries (facial droops, dysarthria, absent corneal reflexes, skew deviation) Nystagmus changes direction with gaze; vertical nystagmus is highly specific for central vertigo Visual fixation does not stop vertigo
Diagnosis	See Figure 13-3	See Figure 13-3
Treatment	Treat by canalith repositioning (Epley maneuver) for benign paroxysmal positional vertigo; physical therapy, antihistamines/benzodiazepines/scopolamine	Treat the underlying cause (brainstem stroke, vertebral dissection, mass or aneurysm)

A

Benign paroxysmal positional vertigo. The woman's symptoms are caused by free-moving canaliths in the vestibular canals.



[a] CNS symptoms = focal or sensory or motor deficits, brainstem findings (eg, dysarthria, diplopia, dysphagia).

[b] Stroke risk factors = advanced age, smoking, dyslipidemia, family history, DM, hypertension, AF, CAD, CHF, peripheral vascular disease.

FIGURE 13-3. Diagnostic approach to vertigo. (Reproduced with permission from Henderson MC et al. *The Patient History: An Evidence-Based Approach to Differential Diagnosis,* 2nd ed. New York: McGraw-Hill, 2012, Fig. 6-2.)

Spinal Cord

COMPRESSION

A neurologic emergency that needs urgent imaging and surgical consultation. Can be caused by anything that puts pressure on the cord, including:

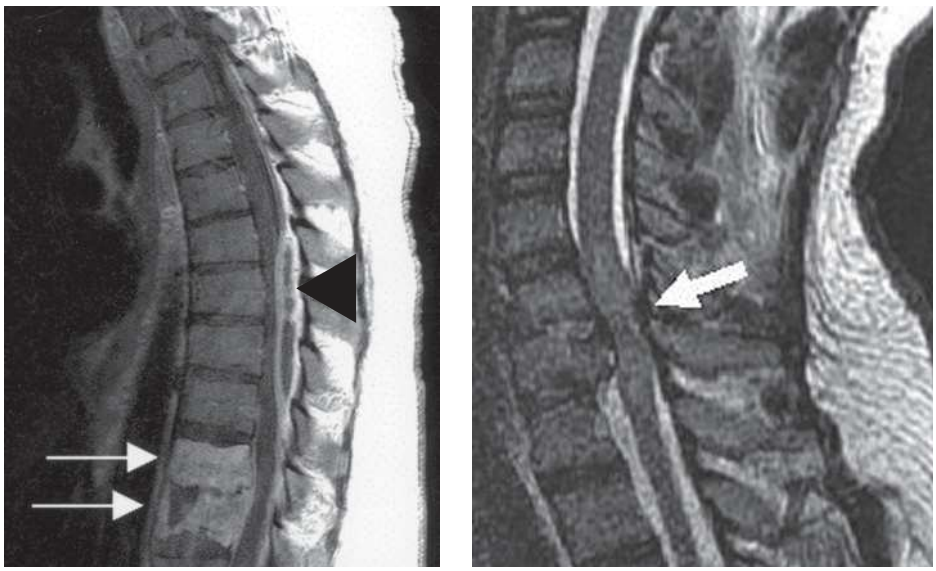
- **Trauma:** Motor vehicle accidents; sports-related injuries.
- **Infection:** Epidural abscess in IV drug users; spinal TB (Pott disease) in immunocompromised patients; vertebral osteomyelitis.
- **Neoplasms:** Metastases most common.
- **Degenerative disease:** Cervical and lumbar disk herniations.
- **Vascular events:** Infarction, epidural and subdural hematomas, and AVMs rare.

KEY FACT

Loss of anal reflex ("anal wink") indicates a lesion at or above S2–S4.

History/PE

- Bilateral pain, numbness, and weakness below the level of the lesion.
- A sensory level (by pinprick).
- Hyperreflexia below the sensory level.
- Saddle anesthesia and loss of anal wink seen in conus medullaris and cauda equina syndrome.
- Severe back pain and fever seen in epidural abscess.
- Spastic paralysis followed by flaccid paralysis ("spinal shock") and seen in complete cord transection (due to loss of UMN inhibition that causes initial spasticity).



A B

FIGURE 13-4. Spinal cord compression. (**A**) Sagittal postcontrast MRI shows diskitis/osteomyelitis (*arrows*) and a rim-enhancing epidural abscess (*arrowhead*) compressing the spinal cord. (**B**) Sagittal T2-weighted MRI in another patient shows a traumatic fracture at C6–C7 compressing the spinal cord. Note the abnormally high signal within the spinal cord (*arrow*). (Image A reproduced with permission from Tintinalli JE et al. *Tintinalli's Emergency Medicine: A Comprehensive Study Guide,* 6th ed. New York: McGraw-Hill, 2004, Fig. 305-5. Image B reproduced with permission from Doherty GM. *Current Diagnosis & Treatment: Surgery,* 13th ed. New York: McGraw-Hill, 2010, Fig. 36-12.)

Diagnosis

STAT MRI of the spine (CT myelography if MRI is contraindicated): shows source of compression (see Figure 13-4).

Treatment

- Dependent on the etiology of the cord compression.
- Noninfectious cause: First line is steroids.
- Consult surgery for decompression.
- For epidural abscess, drain abscess and administer antibiotics (empiric therapy includes third-generation cephalosporin and vancomycin).

KEY FACT

Always look for a sensory level when considering a spinal cord process. The pinprick test is precise and reproducible. T4 is nipple line. T10 is belly button.

SPINAL STENOSIS

Narrowing of the spinal canal that leads to nerve root compression.

History/PE

- Neurogenic claudication (pain relieved with bending over). Classic history: back pain improved when walking uphill.
- Back pain and referred buttock pain.
- ⊖ Straight leg raise sign.

Diagnosis

- X-ray or MRI will show degenerative changes and stenosis of the spinal canal.

KEY FACT

Neurogenic claudication: Exacerbated by spinal extension and standing.
Vascular claudication: Exacerbated by walking.

Treatment

- **First line:** Conservative management with NSAIDs and physical therapy.
- Refractory stenosis: Steroid injections and laminectomy.

TRANSVERSE MYELITIS

- Inflammatory disease of the spinal cord that can lead to motor, sensory, and autonomic dysfunction that localizes to a discrete spinal segment.
- Can be idiopathic or secondary to an autoimmune or infectious process.
- No evidence of compression on imaging.

History/PE

- Weakness, numbness, and autonomic dysfunction below the level of the lesion.

Diagnosis

- MRI spine will show an enhancing region and there will be no sign of a mass lesion.
- Obtain CSF cell count, glucose, and protein to look for infectious source: herpes simplex virus (HSV), varicella-zoster virus (VZV), Lyme.
- Obtain CSF oligoclonal bands and MRI brain to look for evidence of MS.

Treatment

- **First line:** High-dose IV glucocorticoids.
- **Second line:** Plasma exchange.
- If an infectious source is identified, treat the underlying infection.

Q

A 58-year-old woman who is being treated with estrogen presents with an inability to walk or to urinate. Exam shows a distended bladder, ↓ rectal tone, spastic weakness in the bilateral lower extremities, and bilateral ankle clonus. Where is the lesion, and what are the most likely etiologies?

TABLE 13-11. Common Spinal Cord Lesions

Location	Spinal Tracts Affected	Symptoms/Presentation
Syrinx (central cord)	Initially spinothalamic tracts crossing at ventral commissure followed by corticospinal tracts	Loss of pain and temperature sensation in a "cape" distribution followed by weakness of the arms (typically a cervical lesion)
Brown-Sequard syndrome (hemi-section)	Unilateral posterior column, spinothalamic, and cortical spinal tracts	Ipsilateral weakness and loss of light touch, vibration, and proprioception and contralateral loss of pain and temperature sensation
Anterior cord syndrome	Bilateral spinothalamic and corticospinal tracts, often due to infarction of anterior spinal artery	Motor paralysis and loss of pain and temperature sensation below the level of the lesion
Posterior cord syndrome	Posterior columns	Bilateral loss of light touch, vibration, and proprioception; can be seen in vitamin B_{12} deficiency or syphilis ("tabes dorsalis")

CORD SYNDROMES

Spinal cord lesions can arise from traumatic injury, vascular events, infectious or metabolic derangements. The key to identifying these lesions is an understanding of the neuroanatomy, and the most commonly tested lesions are described in Table 13-11.

Anterior Horn Cells

AMYOTROPHIC LATERAL SCLEROSIS

A progressive neurodegenerative motor neuron disease with pure motor symptoms (sensations are intact).

History/PE

- Progressive muscular weakness and wasting, spasticity, respiratory insufficiency, and possible dementia.
- **UMN signs**: Spasticity, ⊕ Babinski sign.
- **LMN signs**: Muscle atrophy, fasciculations.
- **Bulbar signs**: Dysarthria, dysphagia, tongue fasciculations.

Diagnosis

- EMG shows widespread denervation and re-enervation as well as fasciculations.
- Neuroimaging is normal and used to exclude other potential causes.

Treatment

- Mainly supportive, as ALS has no cure.
- Riluzole, which inhibits glutamate release, and edaravone (infusion) can potentially prolong survival in some patients.

KEY FACT

Amyotrophic lateral sclerosis (ALS) classically has a combination of UMN and LMN signs.

KEY FACT

Polio is another motor neuron disease that affects the anterior horn cells.

A

The lesion is likely in the spinal cord at the lumbar level or higher. The most likely etiologies are neoplastic, infectious, inflammatory, vascular, or structural processes (disk herniation).

Nerve Roots

RADICULOPATHIES

Result from compression of the dorsal nerve root, most commonly from degenerative changes.

History/PE

- Acute symptoms are typically caused by a herniated disk.
- Gradual symptoms are typically caused by spondylosis and other degenerative changes.
- Patient may experience neck or back pain at the location of the lesion.
- Spurling maneuver (extending and rotating neck to the side of pain and applying pressure) reproduces the patient's symptoms in cervical radiculopathy.
- Straight-leg raise reproduces the patient's symptoms in lumbosacral radiculopathy.

Diagnosis

- EMG: Abnormalities in the muscles innervated by the affected root.
- Nerve conduction study: Normal study since lesion is at the dorsal root ganglion and sensation not affected.
- MRI: Not diagnostic but may show degenerative changes.

Treatment

- **First line:** Conservative. NSAIDs, low-dose steroids, physical therapy.
- **Second line:** If symptoms do not improve with 6–12 weeks of conservative treatment, can consider surgery.

Peripheral Nerves

BELL PALSY

Idiopathic cranial nerve VII palsy causing facial droop and difficulty with eyelid closure.

History/PE

- Acute onset of facial droop.
- To distinguish Bell palsy from stroke or other central processes, look for involvement of the forehead (see Figure 13-5). There is no involvement of the forehead in central processes.

Diagnosis

- Clinical diagnosis; etiology typically idiopathic.
- Can obtain MRI to look for enhancement if concerned for infectious process or stroke if concerned for central process.
- Can obtain LP to look for Lyme, VZV, or HSV if there is history indicative of an infectious process.

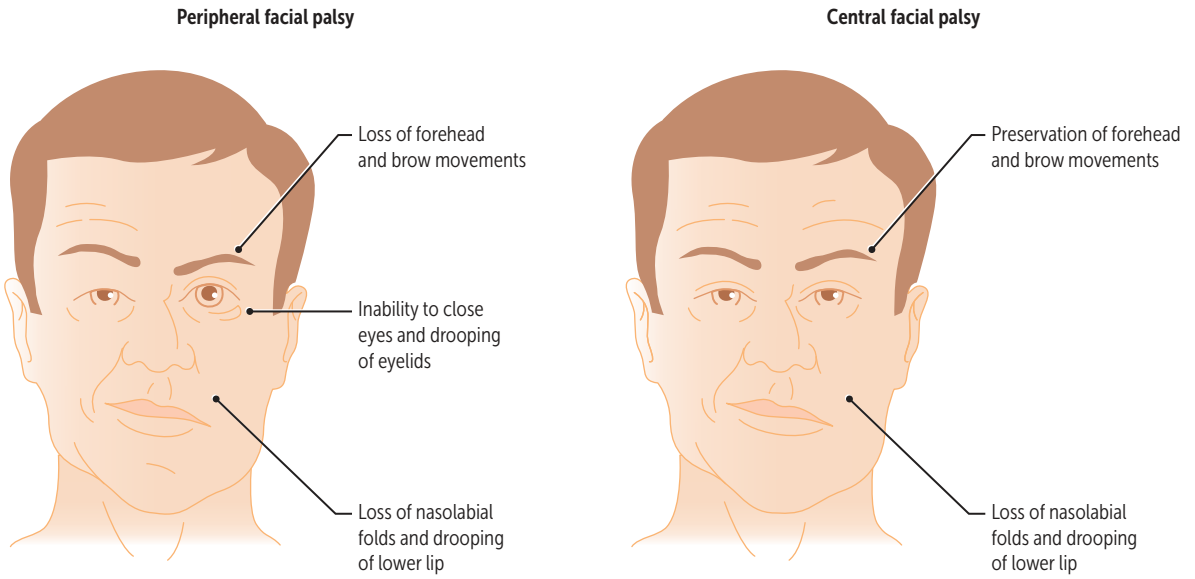


FIGURE 13-5. Peripheral vs central facial palsy. Note that in peripheral facial palsy the mouth droops, the eyelid does not close, and there is loss of wrinkles in the forehead, whereas in central palsy there is no involvement of the forehead.
(Reproduced with permission from USMLE-Rx.com.)

Treatment

- **First line:** Steroids or watchful waiting. Symptoms typically resolve on their own. Valacyclovir is also typically prescribed with steroids due to the suspicion that most cases are caused by VZV.
- Use eye drops and eye patch at night to avoid corneal abrasions due to lack of complete eyelid closure.

CARPAL TUNNEL SYNDROME

Compression of the median nerve in the carpal tunnel of the wrist, leading to numbness/tingling of the hands.

History/PE

- Numbness/tingling in the hand and first three and a half fingers.
- Symptoms typically worse after typing, driving, or upon waking in the morning.
- If severe, can also develop grip strength weakness.
- Tinel sign: Symptoms reproduced when median nerve is percussed at the wrist.
- Phalen sign: Numbness reproduced when wrists are flexed.

Diagnosis

- Mainly clinical.
- Use nerve conduction study (NCS)/EMG to confirm carpal tunnel and rule out coexisting radiculopathies.

Treatment

- **First line:** Wrist splint at night.
- **Second line:** Myofascial release surgery.

Neuromuscular Junction

MYASTHENIA GRAVIS

Autoimmune disorder that affects postsynaptic acetylcholine (ACh) receptors. Bimodal age distribution: early peak 30s–40s (women) and late peak 70s–90s (men).

History/PE

- Ocular myasthenia: Ptosis and diplopia toward the end of the day.
- Generalized myasthenia: Weakness of skeletal muscles throughout the day.
- Myasthenic crisis: Respiratory muscle fatigability leading to potential respiratory failure.

Differential

Lambert-Eaton myasthenic syndrome (see Table 13-12), botulism, drug-induced myasthenia, motor neuron diseases (eg, ALS), generalized fatigue.

Diagnosis

- **Gold standard:** Single-fiber EMG will show "jitter"—defined as an unstable interval between the two action potentials of the same motor unit.
- **Repetitive nerve stimulation** will show a decrement in the motor action potential with repeated stimulation.
- **Edrophonium chloride (Tensilon)** is an acetylcholinesterase inhibitor that prolongs the presence of ACh at the neuromuscular junction. A ⊕ test results in an immediate ↑ in the strength of affected muscles.
- **ACh receptor antibody** ⊕ (if seronegative, test for muscle-specific kinase antibodies).

Treatment

- **First line:** Acetylcholinesterase inhibitors (pyridostigmine).
- **Second line:** Immunomodulating agents, steroids, steroid-sparing agents (cyclosporine, azathioprine, mycophenolate mofetil).
- **Myasthenic crisis:** Plasmapheresis and/or IV immunoglobulin (IVIG).
- **Thymectomy** has been shown to be beneficial in reducing symptoms and exacerbations.

TABLE 13-12. Autoimmune Neuromuscular Junction Disorders

Myasthenia Gravis	Lambert-Eaton Myasthenic Syndrome
Antibody to postsynaptic ACh receptors	Antibody to presynaptic voltage-gated calcium channel receptors
Symptoms worse with physical activity	Symptoms improve with physical activity
Associated with thymoma	Associated with small cell lung cancer producing antibodies
⊕ Edrophonium test	⊖ Edrophonium test

KEY FACT

Neuromuscular blocking agents used during anesthesia can unmask or worsen myasthenia gravis leading to prolonged postoperative weakness and ventilator dependence.

Q

A 31-year-old man complains that when he looks up to catch a baseball, he sees two balls and cannot make the catch. Exam shows ptosis and weakness in all extraocular muscles. He also complains of generalized fatigue. What is the likely diagnosis?

Muscle

MUSCULAR DYSTROPHY

Group of hereditary progressive muscle-based diseases. The most common form is Duchenne muscular dystrophy, which is X-linked and caused by a defect in the gene encoding the dystrophin protein.

History/PE

- Presents between ages 3 and 5; wheelchair bound in childhood; death due to pulmonary complications in adolescence.
- Presents with toe walking, waddling gait, and inability to run or climb stairs.
- Gower Sign: Using arms to climb up the body when standing up.
- Proximal and girdle muscle weakness and pseudohypertrophy of the calves.

Diagnosis

- Gold standard: Genetic testing for dystrophin gene mutation.
- Muscle biopsy shows absence of dystrophin on immunohistochemistry.
- Serum CK levels are ↑ to 20–100 times normal.

Treatment

First line: Prednisone can slow disease progression by up to 3 years.

Movement Disorders

PARKINSON DISEASE

Neurodegenerative disease characterized by loss of substantia nigra neurons leading to ↓ dopamine transmission in the basal ganglia. It typically presents in patients in their early 60s with slowed movements and resting tremor.

History/PE

- Bradykinesia (slow movement) and akinesia (difficulty initiating movement).
- Masked facies.
- Cogwheel rigidity.
- Resting pill-rolling tremor.
- Monotone, hypophonic speech.
- Slowing of thought processes—depression, cognitive impairment, and psychosis.

Diagnosis

- Clinical diagnosis only is based on the PE described above with 2/4 TRAP features present (one must be bradykinesia).
- Diagnosis is "confirmed" if patient's symptoms respond to carbidopa-levodopa.
- Can consider imaging to rule out other causes.
- DAT scan may be helpful in distinguishing Parkinson disease from essential tremor.

MNEMONIC

Parkinson patients feel "TRAPped" inside their bodies

***T**remor*
***R**igidity*
***A**kinesia/bradykinesia*
***P**ostural instability*

A

The most likely diagnosis is myasthenia gravis. The lesion is in the neuromuscular junction isolated to the eyes. These symptoms can also occur in multiple sclerosis (MS), but the latter is accompanied by other symptoms, such as paresthesias.

Treatment

- **First line:** Carbidopa-levodopa.
- Adjunctive therapy:
  - Dopamine agonists: Pramipexole, ropinirole, bromocriptine.
  - MAO inhibitors: Selegiline.
  - COMT inhibitors: Etacapone.
  - Anticholinergics: Benztropine (for tremor).
- Can consider deep brain stimulation or pallidotomy for cases refractory to medication.

HUNTINGTON DISEASE

Autosomal dominant disorder leading to caudate and putamen atrophy. Young adult onset of gradual progressive involuntary movements, dementia, and psychosis.

History/PE

- Choreiform (dancelike) movements.
- Eye movement slowing.
- Hyperreflexia with hypotonia leading to parkinsonism in advanced stages.
- Cognitive decline, dementia, depression/anxiety/psychosis may be present.

Diagnosis

- If there is a family history of Huntington disease, history and physical alone can make the diagnosis.
- In the absence of family history, gold standard is genetic testing for Huntington gene.
  - Genetic anticipation: Disease severity gets worse each generation due to ↑ CAG repeats.
- MRI may show caudate atrophy.

Treatment

Symptomatic; careful follow-up is necessary, as some treatments may worsen symptoms.

- **Chorea:** Benzodiazepines, valproate, or dopamine-depleting agents such as tetrabenazine.
- **Parkinsonian features:** Carbidopa/levodopa or dopamine agonists.
- **Depression:** Selective serotonin reuptake inhibitors.
- **Psychosis:** Atypical (second-generation) antipsychotics preferred to minimize extrapyramidal side effects.

Autoimmune Disorders

GUILLAIN-BARRÉ SYNDROME

Acute ascending motor paralysis with areflexia and sensory deficits. Autoimmune attack on myelin.

- **Inflammatory demyelinating polyneuropathy:**
  - Acute: Symptoms last 2–4 weeks.
  - Chronic: Symptoms last > 8 weeks.
  - Recent history of respiratory or GI tract infection (particularly *Campylobacter jejuni*) is seen in 70% of patients.

KEY FACT

Primary Parkinson disease responds to carbidopa-levodopa.

Parkinsonism (multiple system atrophy, progressive supranuclear palsy, Lewy body dementia, or vascular Parkinson disease) may clinically appear similar but will not respond to the same treatment.

Q

A 65-year-old man presents with tremor of the right hand and a voice that has become softer over the years. Exam shows hypophonia, a 4-Hz resting tremor, mild right-sided rigidity, and micrographia. What is the diagnosis?

History/PE

- Ascending paralysis: Symmetrical muscular weakness seen first in the legs and then in the arms.
- ↓ or absent reflexes.
- Paresthesias in the hands and feet.
- Dysautonomia including orthostatic hypotension, tachy/bradycardia, urinary retention, and ileus.
- Facial palsies and bulbar weakness.

Diagnosis

- Mainly clinical.
- LP shows ↑ protein with normal WBC levels ("albuminocytologic dissociation").
- EMG/NCS can show evidence of demyelination, typically 2 weeks from onset.

KEY FACT

Lung muscles can become paralyzed in Guillain Barré syndrome just like arms and legs. Keep an eye on respiratory status!

Treatment

- Self-limited condition; treatments are to help abate symptoms faster.
- **First line:** IVIG or plasmapheresis; no benefit to using these together.
- Supportive treatment: Monitor negative inspiratory force and functional vital capacity to assess for respiratory compromise requiring intubation.
- Physical therapy and occupational therapy.

MULTIPLE SCLEROSIS

Autoimmune destruction of CNS myelin leading to weakness, numbness, and cognitive deficits. Young adult women in northern latitudes are at higher risk for developing MS. The four clinical courses of MS are relapsing-remitting, 2° progressive, 1° progressive, and progressive/relapsing.

History/PE

- Depending on the location of the lesion, can have weakness, numbness, diplopia, urinary incontinence, and cognitive deficits.
- **Lhermitte sign:** Radiating/shooting pain up or down the spine on flexion or extension.
- **Optic neuritis:** ↓ Visual acuity, pain with eye movements, central scotoma, red desaturation.
- **Afferent pupillary defect (Marcus Gunn pupil):** The pupil paradoxically dilates to a light stimulus as a result of delayed conduction.
- **Internuclear ophthalmoplegia:** Lesion of the medial longitudinal fasciculus causes ipsilateral eye nystagmus with contralateral weakness in adduction on lateral gaze away from the side of the lesion.

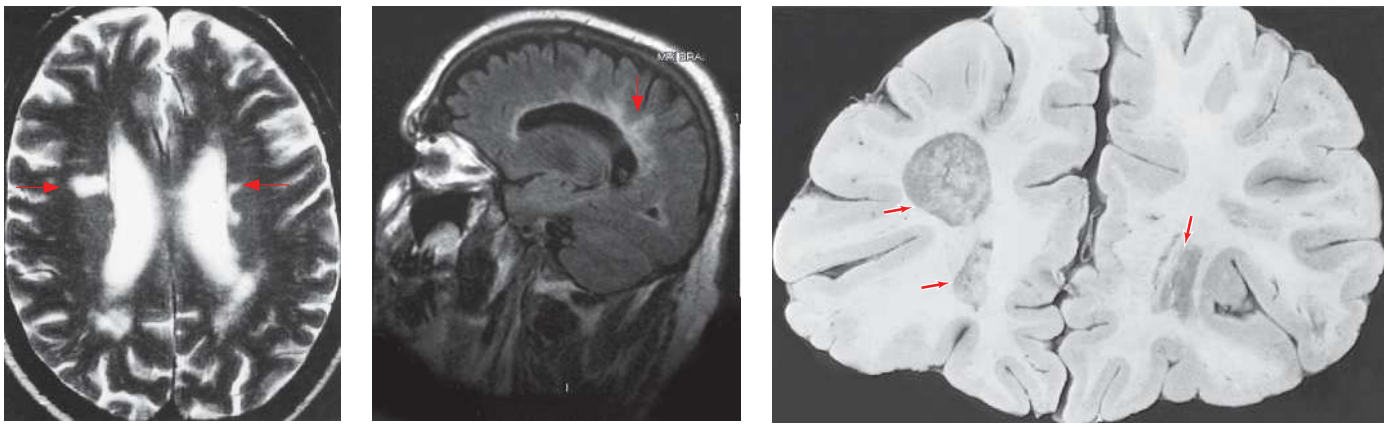
Diagnosis

Gold standard McDonald criteria: Evidence on exam or imaging of at least two CNS lesions disseminated in time and space:

- Brain MRI with gadolinium: Reveals multiple focal periventricular areas of ↑ signal, called Dawson fingers (see Figure 13-6).
- CSF: Shows ↑ protein (myelin basic protein, oligoclonal bands).
- Visual evoked potentials: Demonstrates delayed conduction.

A

Parkinson disease. The lesion is in the left basal ganglia, specifically the substantia nigra, which will show neuronal degeneration and Lewy bodies at autopsy.



A B C

FIGURE 13-6. Multiple sclerosis. Transaxial T2-weighted MRI (**A**) and sagittal FLAIR image (**B**) showing multiple MS plaques (*arrows*) in the periventricular matter oriented radially from the corpus callosum ("Dawson fingers"). (**C**) Areas of demyelination of the white matter (*arrows*) in the frontal lobe of a patient with multiple sclerosis. (Images A and B reproduced with permission from Ropper AH, Samuels MA. *Adams & Victor's Principles of Neurology,* 9th ed. New York: McGraw-Hill, 2009, Fig. 36-1. Image C reproduced with permission from Waxman SG. *Clinical Neuroanatomy,* 27th ed. New York: McGraw-Hill, 2013, Fig. 25-9.)

Treatment

- **First line** for relapsing-remitting MS:
  - Disease-modifying agents: Copaxone or interferon.
- **Second line:** Dimethyl fumarate, natalizumab, and teriflunomide due to side effect profile.
- Acute exacerbation: High-dose steroids.

Neuropsychiatric Disorders

DEMENTIA

Progressive cognitive decline that interferes with the performance of the activities of daily living. It differs from mild cognitive impairment (MCI) in that MCI symptoms are less severe, presenting with memory loss and attention deficits that exceed those of normal aging but do not interfere with activities of daily living. Some commonly tested types of dementia are summarized in Table 13-13.

History/PE

- Impairment of recent memory is typically the first sign.
- Subsequent manifestations include deficits in visuospatial ability (depth perception), language (speech or naming), calculation, or problem solving; behavioral and personality changes; and depression.

Diagnosis

- Always check for reversible causes first:
  - Thyroid-stimulating hormone.
  - Vitamin B_{12} and B_6.
  - Urine drug screen and EtOH levels.
  - Infectious workup.
  - Depression screen.
- Conduct a complete history and exam, a mini-mental status exam, and neuropsychological testing.

Q

A 58-year-old inebriated man presents to the ED. He is uncoordinated, and review of his medical chart shows that he has a significant history of alcoholism. What treatment should the patient be given?

TABLE 13-13. Types of Dementia

Type	Distinguishing Characteristics
Alzheimer disease	Most common type of dementia, β-amyloid plaques and neurofibrillary tangles
Frontotemporal dementia (Pick disease)	Frontal disinhibition, socially inappropriate, poor decision making, Pick bodies found in the cortex
Lewy body dementia	Parkinsonian features on exam associated with visual hallucinations, daily fluctuating cognition, REM sleep behavior disorder, and mood disturbance
Creutzfeldt-Jakob disease	Acute onset of dementia associated with myoclonic jerks and periodic sharp waves on EEG, prion disease
Vascular dementia	Stepwise worsening of symptoms with evidence of lacunar strokes and white matter changes on imaging, may have associated focal deficits

- Review medications.
- Obtain CT and possibly MRI of the brain; may show atrophy or another cause for the cognitive impairment (eg, stroke, mass).

Treatment

- Treat reversible conditions that mimic dementia.
- Alzheimer disease:
  - Acetylcholinesterase inhibitors: Donepezil, rivastigmine, and galantamine early in the disease course.
  - N-methyl-d-aspartate glutamate receptor antagonists: Memantine for more advanced disease.
- Offer social support and assisted-living interventions.

WERNICKE-KORSAKOFF SYNDROME

- A nutritional disorder of the nervous system caused by a deficiency in thiamine (vitamin B_1), resulting in symmetrical lesions in the mammillary bodies. It is a syndrome complex consisting of Wernicke encephalopathy and Korsakoff amnesia, which may be seen separately:
  - **Wernicke encephalopathy:** Characterized by the triad of ataxia, ophthalmoplegia, and confusion.
  - **Korsakoff psychosis (amnesia):** Characterized by impaired short-term memory. Confabulation may be an accompanying symptom.
- **Dx:** A clinical diagnosis. MRI can rule out other causes.
- **Tx:** First line is high-dose thiamine. Give thiamine before glucose! Administering glucose prior to thiamine can lead to permanent brain injury.

A

IV electrolytes and thiamine. He should also be put on watch for signs of alcohol withdrawal. Alcoholics are often malnourished and lack many vitamins, including thiamine, which can subsequently cause Wernicke-Korsakoff syndrome.

CHAPTER 14

OBSTETRICS

KEY FACT

Remember that twins account for 1 pregnancy, 1 delivery, but 2 live children.

MNEMONIC

To remember the order in which parity is presented, use **F**lorida **P**ower **A**nd **L**ight.

Determination of Gravidity and Parity

Gravidity (G) refers to the total number of pregnancies a patient has had. Parity (P) refers to the outcome of these pregnancies and is expressed in the following order:

- **Full term** = Number of deliveries ≥ 37 weeks.
- **Preterm** = Number of deliveries between 20 and 36 6/7 weeks.
- **Aborted** = Number of pregnancies ending before 20 weeks (includes abortion, miscarriage, and ectopic pregnancies).
- **Living** = Number of current living children.

Hence, a woman who is a G3P2012 has had 3 total pregnancies, 2 full-term deliveries, 1 miscarriage or abortion, and 2 living children.

Prenatal Care and Nutrition

All prenatal visits should document weight, BP, extremity edema, urine protein and glucose, fundal height (> 20 weeks), and fetal HR. Further recommendations are as follows:

- **Weight gain:** Women with a normal prepregnancy body mass index should gain a total of 25–35 lbs during the pregnancy; obese women should gain less (11–20 lbs) and underweight women more (28–40 lbs).
- **Nutrition:** Requirements ↑ for total calories, protein, iron, folate, calcium, and zinc. All patients should take prenatal vitamins and continue them while breastfeeding.
- **Caloric intake:** An additional 300 kcal/day is needed during pregnancy and 500 kcal/day during breastfeeding.
- **Folate:** Supplement with 400 μg/day at least 1 month prior to conception to ↓ the risk of neural tube defects (NTDs). Women with multiples, history of a fetus with NTD, or who take antiepileptic medication should receive 4 mg/day.
- **Preventative care:** Pap smear, purified protein derivative, and flu vaccine at first prenatal visit if needed. Give Tdap for all patients at 28 weeks. Defer other vaccinations until postpartum.
- **Smoking, alcohol, and drug cessation.**
- **Screening for domestic violence** (risk ↑ in pregnancy).
- **Prenatal labs:** See Table 14-1 for a testing timeline.

Aneuploidy Screening and Diagnostic Testing

PRENATAL ANEUPLOIDY SCREENING

Should be offered to all patients with careful discussion of possible results, test characteristics, and implications for management of the pregnancy.

- **Cell-free DNA, or NIPT (≥ 10 weeks):** Tests fragments of fetal DNA in maternal blood, and can evaluate risk for aneuploidy, determine fetal gender, and identify an Rh ⊕ fetus if maternal blood is Rh ⊖.
- **First-trimester screen (10–14 weeks):** U/S to measure nuchal translucency (fluid-filled subcutaneous space at the posterior fetal neck) combined with measurement of maternal serum β-hCG and pregnancy-associated plasma protein-A (PAPP-A).

TABLE 14-1. Prenatal Care by Week

Gestational Age (GA)	Recommended Testing and Treatment
Initial visit	Obtain CBC, blood type, Rh-antibody screen, UA with culture, gonorrhea and chlamydia testing, rubella antibody titer, hepatitis B surface antigen, syphilis screen, HIV Offer genetic carrier screening (ie, cystic fibrosis, sickle cell) to all patients Women at risk for gestational diabetes (ie, prior gestational diabetes, obesity, or DM in a first-degree relative) should get HbA_{1c} and/or early glucose tolerance testing
6–11 weeks	Conduct ultrasound to determine GA (more accurate than later scans)
10–14 weeks	Conduct ultrasound to determine nuchal translucency Obtain first-trimester serum aneuploidy screening OR noninvasive prenatal testing (NIPT), also called cell-free fetal DNA Discuss chorionic villus sampling with high-risk patients (based on abnormal NIPT or risk factors)
15–19 weeks	Conduct second-trimester aneuploidy screening (ie, Quad screen) Offer amniocentesis to patients with abnormal screening
18–21 weeks	Conduct screening ultrasound to survey fetal anatomy, placental location, and amniotic fluid
24–28 weeks	Order a 1-hour glucose challenge test; if ≥ 140 mg/dL, follow with a 3-hour glucose tolerance test Repeat hemoglobin/hematocrit
28 weeks	Give Rho(D) immune globulin (eg, RhoGAM) injection for Rh ⊖ patients Start fetal kick counting (the patient should count 10 fetal movements in 2 hours)
35–37 weeks	Screen for group B *Streptococcus* (GBS) with a rectovaginal swab Repeat hemoglobin/hematocrit Repeat gonorrhea and chlamydia testing, rapid plasma reagin, and HIV (in at-risk patients) Assess fetal position with Leopold maneuvers and ultrasound if needed

- **Second-trimester screen (15–19 weeks):** "Quad screen" includes maternal serum α-fetoprotein (MSAFP), unconjugated estriol, hCG, and inhibin A. "Penta screen" increases sensitivity by adding hyperglycosylated hCG (H-hCG). See Table 14-2.

An MSAFP result that is > 2.5 multiples of the mean (MoM) can signify incorrect dating, an open NTD, abdominal wall defect, fetal death or distress, or multiple pregnancy.

KEY FACT

The most common cause of elevated MSAFP is incorrect dating.

PRENATAL DIAGNOSTIC TESTING

- **Chorionic villus sampling:** Diagnoses genetic abnormalities at an earlier GA (10–14 weeks) than amniocentesis with comparable accuracy. Risks include fetal loss (1–5%) and an association with distal limb defects. Preferred test for patients with baseline ↑ risk of aneuploidy (ie, advanced maternal age, history of aneuploid fetus). Largely being replaced by NIPT first, and if normal, may avoid invasive procedure.
- **Amniocentesis:** Aspiration of amniotic fluid, ideally between 15 and 20 weeks' gestation, to diagnose genetic abnormalities. Risks include

Q

A 39-year-old G2P0010 woman at 10 weeks' gestation has a history of a second-trimester pregnancy loss with trisomy 21. What is the next step?

TABLE 14-2. Interpretation of Second Trimester Screening Results

	Neural Tube Defect	Trisomy 18	Trisomy 21
MSAFP	↑	↓	↓
Estriol	↔ Spina bifida ↓ Anencephaly	↓	↓
Inhibin A	↔	↔	↑
hCG	↔	↓	↑
H-hCG	Not used	↓	↑

fetal-maternal hemorrhage (1–2%) and fetal loss (0.5%). Preferred test for patients with abnormal aneuploidy screening. Can also be used for evaluation of fetal blood type or hemolysis, chorioamnionitis, or fetal lung maturity.

Tests of Fetal Well-Being

NONSTRESS TEST

- **Baseline:** Mean fetal HR (110–160 bpm is normal).
- **Variability:** Beat-to-beat change in HR measured from peak to trough.
  - **Absent (undetectable):** Concerning for fetal acidemia.
  - **Minimal (1–5 bpm):** May indicate sleep cycle or drug effect, but consider fetal acidemia if prolonged.
  - **Moderate (6–25 bpm):** Reassuring, indicates normal acid/base status and neurologic function.
  - **Marked (≥ 26 bpm):** Significance is unclear.
- **Acceleration:** Rise in HR ≥ 15 bpm above baseline lasting ≥ 15 seconds (after 32 weeks).
  - **Reactive** nonstress test (NST) includes two accelerations in a 20-minute period (see Figure 14-1).
  - **Nonreactive** NST may be caused by fetal sleep cycle or maternal medications (ie, sedatives, narcotics), but warrants a biophysical profile or a contraction stress test (CST) to rule out uteroplacental insufficiency (see below).

CONTRACTION STRESS TEST

- Used to identify uteroplacental dysfunction and predict how a baby will tolerate labor.
- Fetal HR is monitored during spontaneous or induced (nipple stimulation or oxytocin) contractions with at least three contractions in 10 minutes.
- A normal or "negative" CST has no late or significant variable decelerations and is highly predictive of fetal well-being.
- An abnormal or "positive" CST is defined by late decelerations in conjunction with at least 50% of contractions.

A

This woman's baseline risk is higher for aneuploidy given her history of an affected pregnancy and her advanced maternal age. Therefore, the patient should be offered cell free fetal DNA testing, and if abnormal, a chorionic villus sampling should be offered for diagnosis of aneuploidy from 10–14 weeks.

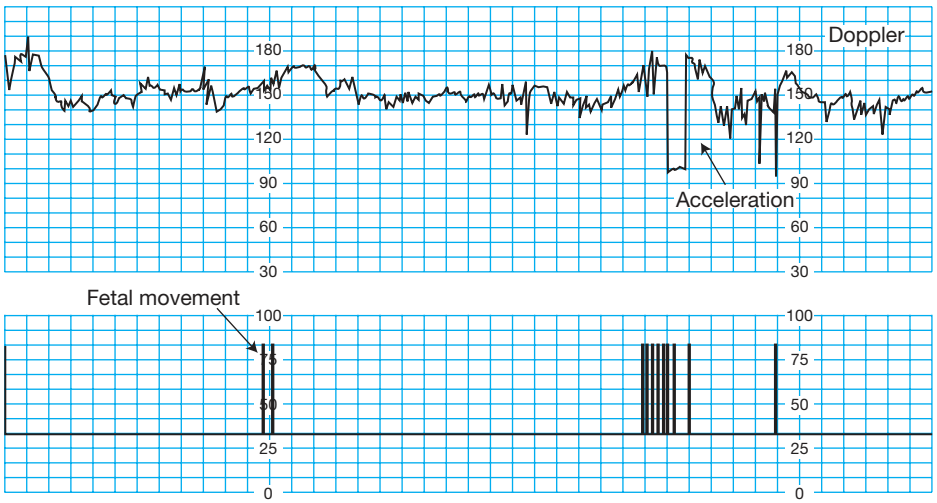


FIGURE 14-1. Reactive nonstress test. (Modified with permission from Cunningham FG et al. *Williams Obstetrics,* 23rd ed. New York: McGraw-Hill, 2010, Fig. 15-7.)

- Any result not satisfying the above criteria is considered equivocal, and the test must be repeated.

BIOPHYSICAL PROFILE

- Ultrasound is used to assess five parameters (see the mnemonic Test the Baby, MAN!).
- A score of 2 (normal) or 0 (abnormal) is given to each of the parameters.
  - A score of 8–10 is reassuring for fetal well-being.
  - A score of ≤ 6) is worrisome for fetal compromise and should prompt delivery or repeat testing depending on score and GA.

MNEMONIC

When performing a BPP, remember to—

Test the Baby, MAN!

Fetal **T**one
Fetal **B**reathing
Fetal **M**ovements
Amniotic fluid pocket
Nonstress test

FETAL HEART RATE DECELERATIONS

Table 14-3 describes the three types of fetal HR deceleration and their causes. Decelerations can be categorized as recurrent (occurring with ≥ 50% of contractions) or nonrecurrent.

Normal Labor and Delivery

DEFINITIONS

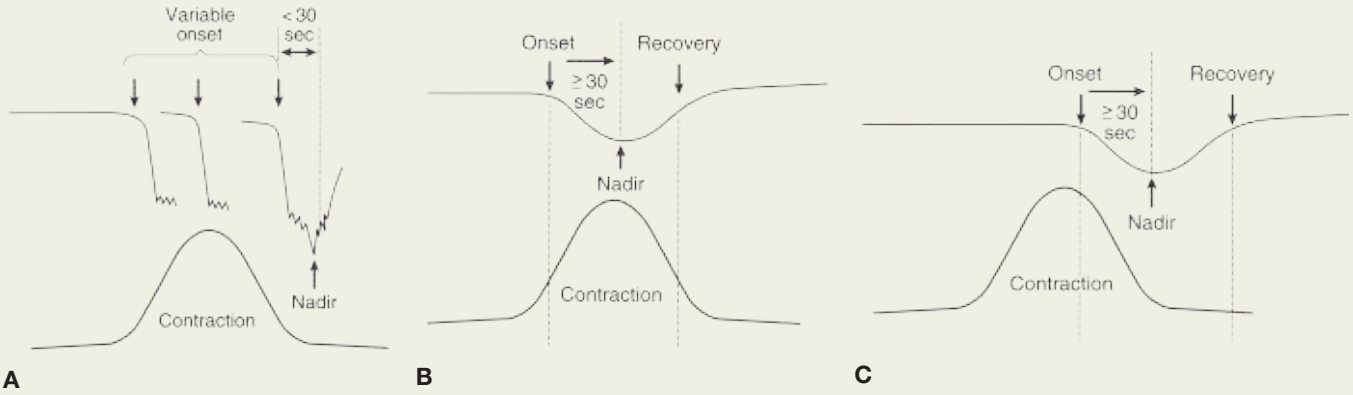
- **Labor:** Defined by painful contractions with cervical change.
- **Term:** Labor and delivery occur between 37 and 41 weeks + 6 days. Labor and/or delivery prior to this time is considered preterm, and after this time is postterm.

STAGES OF LABOR

- First stage: The time from the onset of labor to 10 cm of dilation.
  - **Latent labor:** Slow cervical change, lasting up to 20 hours for nulliparous women and 14 hours for multiparous women.
  - **Active labor:** Rapid cervical change (≥ 1cm/hr), beginning at 6 cm of dilation on average.

TABLE 14-3. Fetal Heart Rate Patterns

Type of Deceleration	Description	Schematic	Common Cause
Variable	Abrupt (< 30 seconds) onset of HR deceleration, which may occur before, with, or after a contraction; return to baseline often similarly abrupt	Image A	Umbilical cord compression
Early	Slow (> 30 seconds) onset of HR deceleration in which the onset and nadir of the deceleration coincide with the onset and peak of the contraction	Image B	Fetal head compression (no fetal distress)
Late	Slow (> 30 seconds) onset of HR deceleration in which the nadir of the deceleration occurs after the peak of the contraction	Image C	Fetal hypoxia and uteroplacental insufficiency (fetal distress)



Images reproduced with permission from Cunningham FC et al. *Williams Obstetrics,* 24th ed. New York: McGraw-Hill, 2014, Figs. 24-14, 24-16, and 24-18.

- **Second stage:** The time from complete dilation (10 cm) to delivery of the baby.
- **Third stage:** The time from delivery of the baby to delivery of the placenta.

MONITORING IN LABOR

- **Cervical exams:** Monitor the progression of labor and identify need for augmentation with oxytocin. Also perform prior to induction of labor to determine need for cervical ripening (ie, with prostaglandins).
  - **Dilation:** Diameter of internal cervical os (0–10 cm).
  - **Effacement:** Length of cervix from internal to external os (0–100% effaced).
  - **Station:** Distance between the presenting part and maternal ischial spine (−5 cm to +5 cm).
- **Fetal heart tracing:** Monitor status of fetus and identify need for resuscitation or cesarean delivery. See Table 14-3 to review decelerations.
  - **Category 1:** Baseline 110–160 bpm, moderate variability, no decelerations; reassuring, no action needed.
  - **Category 3:** Absent variability with recurrent late or variable decelerations, or fetal bradycardia (< 110 bpm); indicative of fetal distress, emergent cesarean delivery necessary.
  - **Category 2:** Any pattern not categorized above; resuscitation of the fetus with maternal repositioning, ↑ IV hydration, or administration of O_2.

Teratogens in Pregnancy

- **Radiation:** Ionizing radiation > 5000 mrads can cause fetal teratogenicity, so preferred imaging modalities during pregnancy are U/S and MRI, as these do not produce radiation. However, no single imaging study will subject the patient to > 5000 mrads, so x-ray and CT scan may be used if clinically indicated. As with all patients, the developing fetus should be exposed to as little radiation for as little time as possible, and the mother should be informed of teratogenic risks.
- **Medications:** See Table 14-4 for safe and teratogenic medications during pregnancy.
- **FDA pregnancy risk categories** are as follows:
  - **Class A:** Safety demonstrated in controlled human studies.
  - **Class B:** Considered safe; no ↑ risk in animal studies, but no adequate studies in humans.
  - **Class C:** Use with caution; fetal adverse effects in animals but no adequate human studies, or no human or animal data are available.
  - **Class D:** Avoid if possible; associated with fetal risks based on human studies, but the benefits may outweigh the risks.
  - **Class X:** Teratogenic; risks outweigh benefits.

TABLE 14-4. Safe vs Teratogenic/Unsafe Medications During Pregnancy

Indication	Safe for Use	Contraindicated
Acne	Benzoyl peroxide	Vitamin A and derivatives (eg, isotretinoin, etretinate) → heart and great vessel defects, craniofacial dysmorphism, and deafness
Antibiotics	Penicillins, cephalosporins, clindamycin; macrolides, metronidazole after first trimester	Tetracycline → tooth discoloration, ↓ bone growth Quinolones → cartilage damage Sulfonamides third trimester → kernicterus Streptomycin → CN VIII damage/ototoxicity Trimethoprim (Bactrim) → neural tube defects (folic acid antagonist)
Bipolar disorder	Assess risks vs benefits	Lithium → Ebstein anomaly (defect of the tricuspid valve and atrialization of right ventricle)
Cancer	Alkylating agents in the second and third trimesters	Folic acid antagonists → abnormalities of the neural tube and cranium
Contrast solution	Indigo carmine	Methylene blue → jejunal and ileal atresia
Depression	Assess risks vs benefits	SSRIs may cause persistent pulmonary hypertension of the newborn, poor feeding, and/or jitteriness
GERD	Calcium carbonate, ranitidine, cimetidine, omeprazole	Alka-Seltzer, bismuth subsalicylate (contains NSAID)
Headache/ migraine	Acetaminophen, codeine, caffeine	NSAIDs may cause oligohydramnios and closure of the ductus arteriosus, especially in the third trimester Ergotamine has abortifacient potential and a theoretical risk of fetal vasoconstriction

(continues)

TABLE 14-4. Safe vs Teratogenic/Unsafe Medications During Pregnancy *(continued)*

Indication	Safe for Use	Contraindicated
Hypertension	Labetalol, hydralazine, nifedipine, methyldopa, clonidine	ACEIs and ARBs → fetal renal damage and oligohydramnios
Hyperthyroidism	Propylthiouracil (PTU) during first trimester Switch to methimazole after first trimester due to risk of maternal liver toxicity from PTU	Methimazole (first trimester) → aplasia cutis
Hypothyroidism	Levothyroxine	
Nausea/vomiting	Pyridoxine (B_6), doxylamine, prochlorperazine, metoclopramide, ondansetron, granisetron, promethazine	
Pain	Acetaminophen, menthol, topical patches, morphine, hydrocodone, propoxyphene, meperidine—should not be used continuously	NSAIDs → oligohydramnios, closure of ductus arteriosus. If needed, may use < 48 hours Long-term use of opioids may lead to neonatal abstinence syndrome
Seizure	Use an anticonvulsant that works best to control maternal seizures; monotherapy at the lowest dose is preferred Folate supplementation (4 mg/day) should be started 3 months before conception	Valproic acid should be avoided if possible → craniofacial defects and NTDs Phenytoin → dysmorphic facies, microcephaly, intellectual disability, hypoplasia of the nails and distal phalanges, and NTDs Carbamazepine → craniofacial defects, intellectual disability, and NTDs Phenobarbital → cleft palate and cardiac defects Trimethadione and paramethadione → intellectual disability, speech difficulty, and abnormal facies
Thromboembolic disease	Heparin, low-molecular-weight heparin; warfarin may be used in cases of highly thrombogenic artificial heart valves	Warfarin → fetal nasal hypoplasia and bony defects (chondrodysplasia) Avoid use of direct thrombin and factor Xa inhibitors, as safety is not well-studied
URI	Guaifenesin, acetaminophen, diphenhydramine, loratadine, nasal sprays	Avoid OTC combination medications, as many include NSAIDs

Abnormal Labor and Delivery

PREMATURE RUPTURE OF MEMBRANES

Defined as spontaneous rupture of membranes before the onset of labor. If this occurs at < 37 weeks, it is termed preterm premature rupture of membranes (PROM), or PPROM. Risk factors for PPROM include low socioeconomic status, young maternal age, smoking, illicit drug use, and infection (UTI, STDs).

History/PE

- Patients may complain of feeling a "gush" or "trickle" of fluid.

Diagnosis

- Sterile speculum exam shows pooling of amniotic fluid in the vaginal vault and/or fluid expressed from cervical os with Valsalva.
- **Nitrazine paper test:** Paper turns blue in alkaline amniotic fluid.
- **Fern test:** A ferning pattern is seen under the microscope after amniotic fluid dries on glass slide.

KEY FACT

The three signs of PROM are pooling of fluid on speculum exam, a ⊕ Nitrazine test, and ferning on microscopy.

Treatment

- If ≥ 37 weeks, induce labor.
- If 34–36 weeks and 6 days, induce labor after betamethasone is given.
- If 24–34 weeks, treat medically to prolong pregnancy and ↓ fetal risks.
  - Betamethasone: Two doses over 24 hours to improve fetal lung maturity.
  - Magnesium sulfate: ↓ Risk of cerebral palsy if delivery likely at < 32 weeks, and for tocolysis to provide time for complete steroid course.
  - Ampicillin and erythromycin: To prolong pregnancy and ↓ infection rate.
- In all PROM patients, suspicion for chorioamnionitis should be high. Treat with ampicillin and gentamicin and deliver regardless of GA if signs of infection are present—maternal fever, ↑ WBC, fetal tachycardia, purulent amniotic fluid.

PRETERM LABOR

Labor (painful contractions with cervical change) between 20 and 37 weeks' gestation.

History/PE

- Patients may complain of menstrual-like cramps, uterine contractions, low back pain, pelvic pressure, new vaginal discharge, or bleeding.

Diagnosis

- Look for regular uterine contractions with concurrent cervical change.
- Fetal fibronectin test may assist in diagnosis of preterm labor before 35 weeks. A ⊕ test indicates ↑ likelihood of preterm delivery but can also be caused by blood, recent intercourse, or recent cervical exam.
- Obtain an ultrasound to verify GA, fetal presentation, and amniotic fluid index.

Treatment

- Begin with hydration.
- If GA is < 37 weeks, administer steroids (to accelerate fetal lung maturity) and tocolytics (commonly nifedipine or magnesium) during steroid dose. Magnesium should be used for neuroprotection < 32 weeks. If GA is 34–36 weeks and 5 days, give steroids, but do not attempt tocolytic therapy.
- Give penicillin or ampicillin for GBS prophylaxis if preterm delivery is likely and GBS status is unknown or ⊕.

KEY FACT

Steroids accelerate the development of type I pneumocytes, which help with gas exchange within the alveoli, and type II pneumocytes, which produce surfactant.

Complications

If preterm labor leads to preterm delivery, it can result in fetal respiratory distress syndrome, intraventricular hemorrhage, retinopathy of prematurity, necrotizing enterocolitis, or fetal death.

FETAL MALPRESENTATION

Defined as any presentation other than cephalic (head down). Breech presentation is the most common fetal malpresentation (affects 3% of all pregnancies).

Diagnosis

- Perform Leopold maneuvers to identify fetal lie (see Figure 14-2).
  - Rock the thumb and index finger above the pubic symphysis to determine if there is a bony head presenting (vs soft tissue).
  - Palpate the remainder of the uterus for feet and the position of the back.
- Check with ultrasound if there is any doubt.

Treatment

- Follow: Up to 75% of cases spontaneously change to cephalic presentation by 38 weeks.
- External cephalic version can be attempted at 37 weeks in the setting of persistent malpresentation.
  - Apply pressure to the maternal abdomen to turn the infant.
  - Risks are placental abruption, cord compression and fetal distress; the infant must be monitored during and after the procedure, and consent must be obtained for emergent cesarean delivery.

KEY FACT

When preparing for external cephalic version, always give Rho(D) immune globulin if patient is Rh ⊖.

SHOULDER DYSTOCIA

Defined as entrapment of the fetal shoulder at the level of the pubic bone. Risk factors include:

- A prior history of a shoulder dystocia.
- Gestational diabetes, fetal macrosomia, or inadequate pelvis.

Diagnosis

- A prolonged second stage of labor with retraction of the head ("turtle sign") back into the vaginal canal after pushing.
- After delivery of the head, there is difficulty delivering the anterior shoulder.

Treatment

- **Best initial step:** Flex and open the maternal hips (McRoberts maneuver) followed by suprapubic (not fundal) pressure.

MNEMONIC

For shoulder dystocia—

ALARMER

Ask for help
Legs up (McRoberts)
Anterior shoulder pressure (suprapubic)
Rotate (internal and external)
Manually remove posterior arm
Episiotomy
Repeat

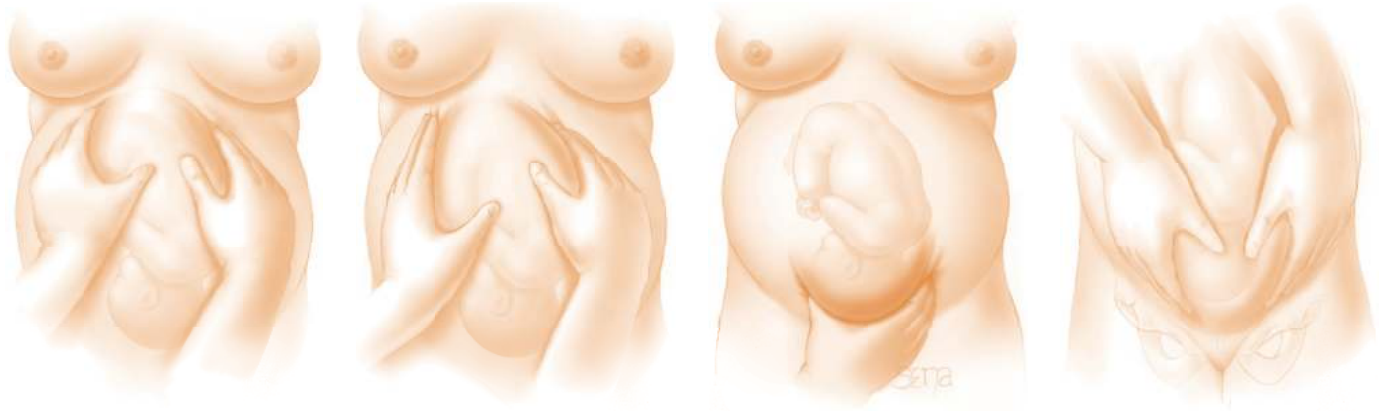


FIGURE 14-2. Leopold maneuvers. Maneuvers are performed with the fetus in a longitudinal lie in the left occiput anterior position.
(Reproduced with permission from Cunningham FG et al. *Williams Obstetrics,* 23rd ed. New York: McGraw-Hill, 2010, Fig. 17-8.)

TABLE 14-5. Indications for Cesarean Delivery

Maternal Factors	Fetal and Maternal Factors	Fetal Factors
> Two prior cesarean deliveries or invasive uterine surgery	Cephalopelvic disproportion or suspected macrosomia	Placenta previa
Active genital herpes infection	Placental abruption	Fetal malposition
Cervical carcinoma	Labor dystocia or failed induction	Fetal distress
HIV infection with high viral load		Cord prolapse

- If the above is unsuccessful, consider the following:
  - Delivery of the posterior fetal arm, internal or external rotation of the fetal shoulders (Rubin or Woods screw maneuver), episiotomy allowing better access for maneuvers, and turning mother to hands and knees (Gaskin Maneuver).

INDICATIONS FOR CESAREAN DELIVERY

Table 14-5 outlines the indications for cesarean delivery.

Postdelivery Care

- Calculate the Apgar score at 1 and 5 minutes postpartum; scores ≥ 7 are considered normal. See Table 14-6.
- Give topical erythromycin for prevention of ophthalmia neonatorum (*Neisseria gonorrhoeae*).
- Administer vitamin K injection to prevent bleeding from vitamin K deficiency.

Medical Complications of Pregnancy

DIABETES MELLITUS

The most common medical complication of pregnancy. See Table 14-7 for a comparison of pregestational and gestational DM.

TABLE 14-6. Apgar Scoring System by Category

	0	1	2
Appearance	All blue or pale	Acrocyanosis	All pink
Pulse	Absent	< 100	≥ 100
Grimace (reflex)	No response	Grimace	Cry
Activity	None	Some flexion	Resists extension
Respiration	None	Irregular gasps	Strong cry

Q

A 36-year-old G3P2002 woman at 10 weeks' gestation presents for her first prenatal visit. She has a history of two previous pregnancies complicated by gestational diabetes. Her last delivery was complicated by shoulder dystocia. Which tests should you order for her?

TABLE 14-7. Pregestational vs Gestational Diabetes Mellitus

	Pregestational	Gestational
Definition	DM present before pregnancy	DM provoked by pregnancy
Risk factors	Family history, autoimmune disorders (type 1), obesity (type 2)	Obesity, family history (in a first-degree relative), prior history of DM in pregnancy
Diagnosis	If not diagnosed prior to conception, may be diagnosed by $HbA_{1C} > 6.4$ in the first trimester	Diagnosed if the 1-hour glucose test is ≥ 140 mg/dL and the follow-up 3-hour glucose test has at least two ↑ levels
Treatment	Strict control of blood glucose levels with diet, exercise, and glycemic agents or insulin Insulin requirements increase drastically during pregnancy Monitor fetal well-being with NSTs and growth scans	ADA diet and regular exercise. If blood sugars are ↑ after 1 week, glyburide can be added If glyburide is not sufficient, initiate insulin therapy Monitor fetal well-being with NSTs and growth scans
Postpartum	Continue glucose monitoring and decrease insulin accordingly, as requirements quickly decrease after delivery	No further BG or insulin required. Perform a 2-hour glucose tolerance test at the postpartum visit to ensure resolution of diabetes
Complications		
Fetus	Congenital malformations, spontaneous abortion (SAB), stillbirth, intrauterine growth restriction (IUGR), polyhydramnios, macrosomia, shoulder dystocia, neonatal hypoglycemia (due to hyperinsulinemia)	Polyhydramnios, macrosomia, shoulder dystocia, neonatal hypoglycemia
Mother	Hypoglycemia, diabetic ketoacidosis, preterm labor, worsening end-organ dysfunction, ↑ risk of preeclampsia	Perineal trauma from macrosomic infant; ↑ lifetime risk of developing DM

KEY FACT

Hypertensive symptoms may occur any time after 20 weeks' gestation and up to 6 weeks postpartum.

KEY FACT

Angiotensin-converting enzyme inhibitors and angiotensin receptor blocker are contraindicated in pregnancy.

A

The patient is at high risk for developing gestational diabetes again in this pregnancy. Order a HbA_{1C} and early 1-hour glucose challenge test.

HYPERTENSIVE DISEASE IN PREGNANCY

Thought to be due to ↓ organ perfusion 2° to vasospasm and endothelial activation. Risk factors include nulliparity, African-American ethnicity, extremes of age (< 18 or > 40 years), multiple gestations, renal disease, systemic lupus erythematosus (SLE), antiphospholipid syndrome, and chronic hypertension. A spectrum of disease is observed, including gestational hypertension, preeclampsia, and eclampsia, see Table 14-8.

Diagnosis

- Based on clinical and laboratory findings described in Table 14-8.
- UA, 24-hour urine for protein and creatinine clearance, CBC, creatinine, uric acid, lactate dehydrogenase (LDH), and AST/ALT.
- PT/PTT, INR, fibrinogen, and a toxicology screen to rule out other causes.

Treatment

- **Definitive:** Delivery, although patients are at risk for seizures up to 6 weeks postpartum. Timing of delivery is dependent on the severity of the disease (see Table 14-8), and any patient at risk for preterm delivery should receive betamethasone for fetal lung maturation.
- **Initial:** For eclampsia and preeclampsia with severe features, give magnesium sulfate. IV antihypertensives should be used for immediate control of BP in severe range.
- **Long-term:** Regimens include β-blockers and calcium channel blockers.

TABLE 14-8. Hypertensive Disorders in Pregnancy

	Diagnosis	Treatment	Complications
Gestational hypertension	Systolic BP (SBP) ≥ 140 or diastolic BP (DBP) ≥ 90 on ≥ two occasions 4 hours apart at ≥ 20 weeks No elevated BP prior to 20 weeks' gestation	Deliver at 37 weeks	Progression to preeclampsia
Preeclampsia	SBP ≥ 140 or DBP ≥ 90 on ≥ two occasions 4 hours apart Proteinuria (≥ 300 mg/24 hours)	Deliver at 37 weeks Magnesium sulfate is no longer recommended for seizure prophylaxis	Fetal growth restriction, preterm delivery, placental abruption, disseminated intravascular coagulation (DIC), cerebral hemorrhage, fetal/maternal death
Preeclampsia with severe features	SBP ≥ 160 or DBP ≥ 110 on ≥ two occasions 4 hours apart Elevated creatinine Impaired liver function (elevated liver function test or right upper quadrant/epigastric pain) Thrombocytopenia Pulmonary edema Headache or vision changes	Deliver at 34 weeks Give hydralazine or labetalol IV for acute BP control Give magnesium sulfate for seizure prophylaxis Continue magnesium sulfate for at least 24 hours after delivery, and watch for magnesium toxicity; treat toxicity with IV calcium gluconate	HELLP syndrome (see mnemonic)
Eclampsia	Preeclampsia + seizure	Magnesium sulfate to control seizures Monitor ABCs closely; when stable, deliver	Injury from falls, maternal and fetal hypoxia

THYROID DISEASE IN PREGNANCY

Hypothyroidism in Pregnancy

- The most common cause is autoimmune (Hashimoto) thyroiditis. Sequelae include ↑ rate of spontaneous abortion, preterm delivery, hypertensive disorders, and placental abruption.
- **Tx:** Levothyroxine. Consider treating women with subclinical hypothyroidism.

Subclinical Hyperthyroidism

Transient condition that can occur in the first trimester when serum thyroid-stimulating hormone falls below the lower limit of normal and serum T_3 and T_4 levels are within their reference range.

Hyperthyroidism in Pregnancy

- Most commonly caused by Graves disease.
- Sequelae include spontaneous abortion, preterm labor, and intrauterine fetal demise. In the fetus, it can cause fetal tachycardia, fetal goiter, and advanced bone age. Thyroid storm can be precipitated by labor, infection, or preeclampsia.
- **Tx:** Radioiodine ablation (contraindicated in pregnancy) may be recommended prior to conception if the pregnancy is planned; β-blockers

MNEMONIC

HELLP syndrome:

Hemolysis (↑ LDH, uric acid; ↓ hemoglobin, hematocrit)
Elevated **L**iver enzymes (AST/ALT)
Low **P**latelets (< 100)

Q

A 32-year-old G1P0 at 34 weeks' gestation with a diagnosis of preeclampsia presents with a refractory headache and nausea. She has a BP of 208/112 and 3+ protein on urine dipstick. Her labs are pending. What is the next step?

(atenolol or propranolol) can be used for the management of symptomatic tachycardia; propylthiouracil (PTU) should be used in the first trimester but then replaced by methimazole in the second trimester, given the ↑ risk of PTU hepatotoxicity; methimazole is avoided in the first trimester because of its teratogenic effects, notably cutis aplasia, and is safer than PTU in the second and third trimesters.

HYPEREMESIS GRAVIDARUM

- Refractory vomiting that leads to weight loss, poor weight gain, dehydration, ketosis from starvation, and metabolic alkalosis. Symptoms peak at 9 weeks but typically improve by 20 weeks.
- Risk factors include nulliparity, multiple gestation, and trophoblastic disease.
- **DDx:** Rule out molar pregnancy, hepatitis, gallbladder disease, reflux, and gastroenteritis.
- **Dx:** Patient reports inability to tolerate PO despite medication. Labs show hyponatremia and a hypokalemic, hypochloremic metabolic alkalosis. Ketonuria suggests starvation ketosis.
- **Tx:** If there is evidence of weight loss, dehydration, or altered electrolytes, hospitalize and give vitamin B_6, metoclopramide or ondansetron, IV hydration, and electrolyte replacement. Advance diet slowly and avoid fatty foods.

KEY FACT

If postpartum uterine bleeding persists after conventional therapy, lifesaving techniques include uterine/internal iliac artery ligation or embolization, uterine balloon tamponade, and hysterectomy.

MNEMONIC

The 7 W's of postpartum fever:

Womb—endometritis
Wind—atelectasis, pneumonia
Water—UTI
Walk—DVT, pulmonary embolism
Wound—incision, lacerations
Weaning—breast engorgement, mastitis, breast abscess
Wonder drugs—drug fever

KEY FACT

The only absolute contraindications to breastfeeding are maternal HIV, human T-cell lymphotropic virus, active herpes simplex virus of the breast, current treatment with chemotherapy or radioactive isotopes, current illicit drug abuse, or infant with galactosemia.

A

The patient is presenting with severe preeclampsia that raises concern for the development of eclampsia. You should administer antihypertensives and magnesium for seizure prophylaxis and prepare for delivery.

Peripartum Complications

POSTPARTUM HEMORRHAGE

- Defined as blood loss of > 500 mL during a vaginal delivery or > 1000 mL during a cesarean delivery. Table 14-9 summarizes common causes.
- Complications include Sheehan syndrome (see below) and DIC.

SHEEHAN SYNDROME (POSTPARTUM HYPOPITUITARISM)

- The most common cause of anterior pituitary insufficiency in women. It occurs 2° to pituitary ischemia, usually as a result of postpartum hemorrhage and hypotension.
- **Hx/PE:** The most common presenting symptom is failure to lactate that results from ↓ prolactin levels. Other symptoms include lethargy, anorexia, weight loss, amenorrhea, and loss of sexual hair, but these may not be recognized for many years.
- **Tx:** Lifelong hormone replacement therapy (corticosteroids, levothyroxine, estrogen and progesterone).

INTRAPARTUM AND POSTPARTUM FEVERS

Most commonly due to infections (see Table 14-10). Remember the 7 W's for the causes of postpartum fever (see the mnemonic).

MASTITIS

- Cellulitis of the periglandular tissue in breastfeeding mothers. It is typically due to *S aureus* and occurs at about 2–4 weeks postpartum.

TABLE 14-9. Common Causes of Postpartum Hemorrhage

	Uterine Atony	Genital Tract Trauma	Retained Placental Tissue
Risk factors	Uterine overdistention (multiple gestation, polyhydramnios), prolonged labor/induction, uterine infection, grand multiparity	Precipitous delivery, operative vaginal delivery, large infant	Placenta accreta/increta/percreta, placenta previa, prior cesarean delivery or curettage, accessory placental lobe
Diagnosis	Palpation of a soft, enlarged, "boggy" uterus	Inspection of the cervix, vagina, and vulva for lacerations or hematoma	Inspection of the placenta and bimanual exam and/or ultrasound of uterine cavity
Treatment	Vigorous bimanual massage with empty bladder Oxytocin infusion Methylergonovine if not hypertensive; PGF_{2a} if not asthmatic; misoprostol	Surgical repair of the defect, which may require additional anesthesia and OR setting	Removal of remaining placental tissue manually or surgically via curettage For placenta accreta/increta/percreta, hysterectomy may be necessary

- **Hx/PE:** Patient presents with breast pain and redness along with a high fever, chills, and flu-like symptoms. Look for focal breast erythema, swelling, and tenderness. Fluctuance points to a breast abscess.
- **DDx:** Distinguish from simple breast engorgement, which can present as a swollen, firm, tender breast with low-grade fever and does not require antibiotics.
- **Dx:** Obtain breast milk cultures and CBC.
- **Tx:** Dicloxacillin or erythromycin. Continue nursing or pumping to prevent milk stasis. If an abscess is present, treat with needle aspiration.

Postpartum Psychiatric Disorders

- **Definitions:**
  - "Postpartum blues": Mild depressive symptoms that develop within a few days of delivery and resolve within 2 weeks.
  - **Postpartum depression:** Major depressive disorder occurring within 12 months of giving birth.
  - **Postpartum psychosis:** Psychotic symptoms that develop within 2 weeks of giving birth.
- **Tx:** Patients with "postpartum blues" should be reassured and offered close follow-up. Patients with depression or psychosis should be screened for suicidal or homicidal ideations and referred to a psychiatrist. **First-line treatment for postpartum depression is an SSRI.** If patients have a history of depression and were previously managed successfully on another medication, that medication should be restarted.

Obstetric Complications of Pregnancy

FIRST-TRIMESTER BLEEDING

The differential diagnosis includes:

- **Ectopic pregnancy:** Pregnancy outside the endometrial cavity. Any woman with a ⊕ pregnancy test and vaginal bleeding should have an ultrasound to confirm intrauterine pregnancy.

Q 1

A 27-year-old G1P1001 delivers an infant weighing 9.5 lbs (4.3 kg). After delivery of the placenta, the patient has brisk vaginal bleeding with an estimated blood loss of 700 mL. What is the most likely cause of her hemorrhage?

Q 2

A 31-year-old healthy woman develops fevers (39.1°C/102.4°F) and severe uterine tenderness 8 hours after cesarean delivery for fetal malposition. The baby is doing well, and the amniotic fluid at delivery was clear. What is the likely source of infection?

Q 3

Two days after an uncomplicated vaginal delivery, a 26-year-old G1P1 tells you that she has developed insomnia. Although she says that she is very happy with the baby, she complains of being anxious and irritable. What is her most likely diagnosis?

TABLE 14-10. Common Infections During Labor and After Delivery

	Chorioamnionitis	Endometritis
Definition	Infection of the chorion, amnion, and amniotic fluid, diagnosed during labor	Infection of the uterus, diagnosed after delivery
Risk factors	Prolonged PROM, GBS, meconium	Cesarean delivery, prolonged PROM, chorioamnionitis
Symptoms/ exam	Intrapartum fever with no other obvious source and one of the following: ▪ Fetal tachycardia ▪ Maternal leukocytosis ▪ Purulent fluid from cervical os	Postpartum fever with fundal tenderness, or fever within 24 hours postpartum without an obvious source
Diagnosis	Treated based on clinical symptoms +/− CBC; diagnosis confirmed by placental pathology	Pelvic exam to rule out hematoma or retained membranes CBC with differential, UA and urine culture, and blood cultures as indicated
Treatment	Antibiotics and delivery of the fetus (not an indication for cesarean delivery) "Cured" by delivery of placenta, but some clinicians recommend additional dose of antibiotics to decrease risk of endometritis	Antibiotics until the patient is afebrile for 24 hours

- **Ectropion:** An endocervical canal that everts to face the vagina. Friable tissue can bleed after intercourse.
- **Subchorionic hemorrhage:** Collection of blood behind the placenta, which may result in vaginal bleeding. Should be evaluated and followed by ultrasound.
- **Spontaneous abortion:** Loss of a pregnancy prior to 20 weeks' gestation, also called miscarriage. Occurs in 10–15% of recognized pregnancies. Risk factors include advanced maternal age, prior SAB, diabetes, antiphospholipid syndrome, thrombophilia, and structural uterine or cervical abnormalities. Symptoms include bleeding and cramping. Diagnosis and treatment depend on the state of the fetus and cervical dilation. See Table 14-11.

1 **A**

The most common cause of postpartum hemorrhage is uterine atony. This patient's risk factor was having a baby large for GA, which caused uterine over-distention and inability to contract well post-delivery.

2 **A**

The uterus (endometritis). This is a rapid postoperative presentation, making the standard causes of postoperative fever less likely.

3 **A**

This patient most likely has "postpartum blues," which typically arise 2–3 days after delivery and resolve within 2 weeks. If her symptoms persist or worsen, she will need evaluation for postpartum depression.

RECURRENT ABORTION

- Defined as three or more consecutive pregnancy losses before 20 weeks' gestation.
- Usually due to chromosomal or uterine abnormalities, but can also result from hormonal abnormalities, infection, or systemic disease.
- **Dx:** Based on clinical, lab, and imaging results.
  - Perform a pelvic exam (to look for anatomic abnormalities).
  - Check cervical cultures for chlamydia and gonorrhea.
  - Perform a maternal and paternal genetic analysis.
  - Obtain a hysterosalpingogram to look for uterine abnormalities.
  - Order thyroid function tests, progesterone, lupus anticoagulant, and anticardiolipin antibody.
- **Tx:** Based on the diagnosis.

TABLE 14-11. Types of Spontaneous Abortions

Type	Exam	Ultrasound	Treatment
Threatened abortion	Cervix closed	Normal ultrasound for GA (shows at least a gestational sac, and may show yolk sac or fetus with HR)	Expectant management; consider pelvic rest for several weeks
Inevitable abortion	Cervix dilated, no products of conception (POC) expelled	Normal ultrasound for GA	Expectant (no intervention) Medical (misoprostol) Surgical (D&C)
Missed abortion	Cervix closed	Absent HR	Expectant Medical (misoprostol) Surgical (D&C)
Incomplete abortion	Cervix open, some POC expelled or visible in cervical canal	No viable pregnancy, but POC visualized in endometrial cavity	Expectant Medical (misoprostol) Surgical (D&C)
Complete abortion	Cervix may be closed or slightly dilated	Empty endometrial cavity	None
Septic abortion	Fever, severe abdominal and cervical tenderness, purulent and malodorous discharge on speculum exam	No viable pregnancy, but POC visualized in endometrial cavity	D&C and IV antibiotics, hospital monitoring, and supportive care until afebrile

INTRAUTERINE GROWTH RESTRICTION

- Defined as an estimated fetal weight at or below the 10th percentile for GA. See Table 14-12 for common causes of IUGR.
- **Hx/PE:** Suspect IUGR clinically if the difference between fundal height and GA is > 2 cm in the second trimester or > 3 cm in the third trimester.
- **Tx:** Assess interval growth by ultrasound every 2–4 weeks. Check umbilical artery Doppler studies to assess for placental dysfunction and deliver by 38 weeks or earlier if studies are abnormal.

KEY FACT

All women with first-trimester bleeding should receive Rho(D) immune globulin if the mother is Rh ⊖.

OLIGOHYDRAMNIOS AND POLYHYDRAMNIOS

Table 14-13 contrasts oligohydramnios with polyhydramnios.

TABLE 14-12. Causes of Intrauterine Growth Restriction

Fetal	Maternal
Chromosomal abnormalities: Trisomy 21 most common, followed by trisomies 18 and 13	Hypertension or preeclampsia
Infection: CMV most common; toxoplasmosis, syphilis, rubella	Drugs: Cigarette smoking most common; alcohol, heroin, methamphetamines, cocaine
Multiple gestation	SLE
Placental or umbilical cord abnormalities	Pregestational diabetes
	Antiphospholipid syndrome
	Ethnic/genetic variation

TABLE 14-13. Oligohydramnios vs Polyhydramnios

	Oligohydramnios	Polyhydramnios
Definition	Amniotic fluid index (AFI) ≤ 5 cm on ultrasound	AFI ≥ 25 cm on ultrasound
Causes	Fetal urinary tract abnormalities (renal agenesis, polycystic kidneys, GU obstruction) Chronic uteroplacental insufficiency, PROM Use of NSAIDs or ACEIs	Uncontrolled maternal DM, multiple gestations, fetal pulmonary or GI anomalies (duodenal atresia, tracheoesophageal fistula)
Diagnosis	Ultrasound for anomalies Fern test and Nitrazine paper to rule out PROM	Ultrasound for fetal anomalies; glucose testing for DM
Treatment	Hydration; consider amnioinfusion during labor to prevent cord compression	Consider therapeutic amniocentesis
Complications	Cord compression → fetal hypoxia Musculoskeletal abnormalities (facial distortion, clubfoot) Pulmonary hypoplasia, IUGR	Preterm labor, placental abruption, fetal malpresentation, cord prolapse on PROM, postpartum hemorrhage due to uterine atony

RHESUS ISOIMMUNIZATION

When fetal Rh ⊕ RBCs leak into Rh ⊖ maternal circulation, maternal anti-Rh IgG antibodies can form. These antibodies can cross the placenta and react with fetal Rh ⊕ RBCs, leading to fetal hemolysis (erythroblastosis fetalis) and hydrops fetalis.

- **Prevention:** Give Rho(D) immune globulin to Rh ⊖ women:
  - If there is concern for SAB, ectopic, abruption, or other opportunity for fetal-maternal hemorrhage including invasive prenatal testing or trauma.
  - Routinely at 28 weeks.
  - After delivery, if the baby is Rh ⊕; the Kleihauer-Betke fetal-maternal hemorrhage test can be used to quantify the number of fetal RBCs mixed with maternal blood and determine the amount of Rho(D) immune globulin needed.
- **Management:**
  - Sensitized Rh ⊖ women with titers > 1:16 should be closely monitored for evidence of fetal hemolysis with serial ultrasound and middle cerebral artery Doppler velocimetry.
  - In severe cases, intrauterine blood transfusion via the umbilical vein or preterm delivery is indicated.

THIRD-TRIMESTER BLEEDING

KEY FACT

For third-trimester bleeding …
With pain → abruption or uterine rupture.
Without pain → placenta previa.

May be benign or pathologic.

- **Benign causes** include bleeding from ectropion. Most commonly, bleeding in the third trimester results from cervical change once labor starts as well as from bloody show (a small amount of bloody mucous).
- **Pathologic causes** include preterm labor, vasa previa, genital tract lesions, and trauma. See Table 14-14.

TABLE 14-14. Life-threatening Causes of Third-Trimester Bleeding

	Placental Abruption	Placenta Previa	Uterine Rupture
Definition	Placental separation from the site of uterine implantation before delivery of the fetus	Abnormal placental implantation covering all of part of the cervical os	A tear in the myometrium, often at the site of a previous scar
Risk factors	Hypertension, abdominal/pelvic trauma, tobacco or cocaine use, uterine distention	Prior Cesarean delivery, grand multiparity, multiple gestations, prior placenta previa	Prior uterine scar from cesarean delivery or myomectomy, uterine anomalies, grand multiparity
Symptoms	Abdominal pain; persistent vaginal bleeding Prolonged or frequent uterine contractions and sudden cervical dilation Fetal distress	Painless vaginal bleeding with or without uterine contractions, which may spontaneously resolve Occurs in the second or third trimester Usually no fetal distress	Severe abdominal pain, usually during labor Change in the shape of the abdomen Loss of fetal station Fetal distress
Diagnosis	Primarily clinical Ultrasound for retroplacental hemorrhage (low sensitivity) KB fetal-maternal hemorrhage test, coagulation tests to assess for DIC	Ultrasound for placental position	Primarily clinical; diagnosis confirmed on cesarean delivery
Treatment	Mild/chronic abruption prior to term: Hospitalization, fetal monitoring, type and cross, bed rest Severe abruption: Stabilization (ABCs), type and cross, immediate delivery	No cervical exam, no vaginal delivery Cesarean at term or with fetal distress or persistent heavy bleeding Pelvic rest Serial ultrasound to assess fetal growth and resolution of previa	Immediate cesarean delivery and repair of the rupture
Complications	Hemorrhagic shock; DIC; fetal death with severe abruption	↑ Risk of placenta accreta Persistent hemorrhage requiring hysterectomy to prevent maternal death	Fetal and maternal death

NOTES

CHAPTER 15

GYNECOLOGY

Review of the Menstrual Cycle

- A normal menstrual cycle is 28 ± 7 days in length with bleeding lasting for 3–7 days.
  - The first day of bleeding = day 1 of the cycle.
  - Ovulation typically occurs at day 10–14 (variable depending on length of the follicular phase).
  - Menstrual cycles are most irregular in the years immediately following menarche and preceding menopause.
  - Menopause is characterized by rises in follicle-stimulating hormone (FSH) and luteinizing hormone (LH).
- Table 15-1 and Figure 15-1 offer an overview of the physiologic changes involved in the menstrual cycle.

Abnormal Uterine Bleeding

Characterized by abnormalities in the frequency, duration, volume, and/or timing of menstrual bleeding. A useful mnemonic for categorizing its causes is **PALM-COEIN** (see Table 15-2).

History/PE

- Take a thorough menstrual history to determine the onset, quantity, and timing of abnormal bleeding.
- Perform a speculum exam to assess for any vaginal or cervical lesions (eg, cervical polyps). Conduct a bimanual exam to assess the size, shape, and contour of the uterus and ovaries.

Diagnosis

- Initial lab work includes beta-human chorionic gonadotropin (β-hCG) (always rule out pregnancy!), CBC, thyroid-stimulating hormone (TSH), and prolactin.
- Conduct pelvic ultrasound to look for structural causes.

TABLE 15-1. Overview of the Normal Menstrual Cycle

Organ	Phase
Ovary	**Follicular phase:** Release of FSH and LH from the pituitary gland stimulates the ovary and results in preantral follicular recruitment within the ovary and eventually development of a dominant follicle for ovulation **Luteal phase:** About 32 hours after the start of the LH surge, ovulation occurs, which releases the ovum (egg) and results in formation of the corpus luteum from the residual follicle
Uterus	**Proliferative phase:** Estradiol, produced by the ovarian follicles, induces growth and proliferation of the endometrium **Secretory phase:** After ovulation, the corpus luteum secretes predominantly progesterone and lower levels of a less potent estrogen, estrone, to maintain the endometrium for implantation. If implantation does not occur, the corpus luteum undergoes involution, which causes an abrupt drop in progesterone and estrogen levels, resulting in shedding of the endometrium (menstruation)

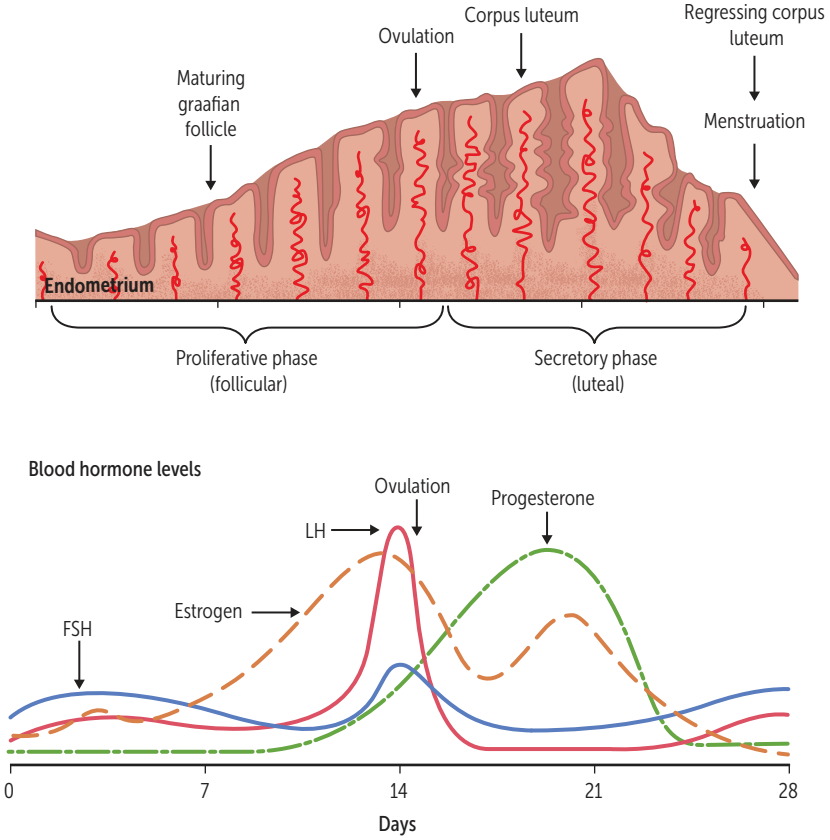


FIGURE 15-1. Normal menstrual cycle. (Reproduced with permission from USMLE-Rx.com.)

- Other testing includes:
  - In adolescents: complete metabolic panel (CMP) to evaluate for renal or hepatic causes of coagulopathy, coagulation studies, and von Willebrand studies.
  - Saline infusion sonohysterography to look for uterine polyps if initial ultrasound suggests intracavitary mass.
  - Endometrial biopsy for women ≥ 45 years of age or younger women with risk factors for endometrial hyperplasia/malignancy (ie, obesity, polycystic ovarian syndrome [PCOS]).
  - Hysteroscopy for direct visualization of the endometrial cavity.
- In older women, consider FSH/LH. An ↑ in both FSH and LH is suggestive of menopause, as the ovaries can no longer respond to hormonal signals by producing estrogen and progesterone.

Treatment

- Treat the underlying cause.
- First-line approaches to managing heavy or irregular menses: NSAIDs, combined contraceptives (pills, patch, vaginal ring), medroxyprogesterone acetate injections, progestin-secreting intrauterine devices (IUDs), and oral tranexamic acid.
- Uterine artery embolization and endometrial ablation can be considered as less invasive surgical management options in patients who have completed childbearing.
- Ultimate management is hysterectomy if medical management is declined, contraindicated, or fails.
- Acute, profuse bleeding can be treated with high-dose oral progesterone, high-dose combined oral contraceptive pills (OCPs), high-dose IV estrogen, dilation and curettage (D&C), uterine artery embolization, uterine

TABLE 15-2. Causes of Abnormal Uterine Bleeding

Structural Causes (PALM)	Nonstructural Causes (COEIN)
Polyps	**C**oagulopathy
Adenomyosis	**O**vulatory dysfunction
Leiomyomas	**E**ndometrial
Malignancies	**I**atrogenic
	Not yet classified

KEY FACT

Women ≥ 45 years of age (or younger with risk factors) with abnormal uterine bleeding should have an endometrial biopsy to rule out malignancy.

balloon tamponade while the underlying cause of abnormal uterine bleeding is determined.

Amenorrhea

KEY FACT

Always rule out pregnancy in a patient with amenorrhea.

Defined as either 1° or 2° amenorrhea.

- **1° amenorrhea:** Absence of menses by age 15 or absence of menses within 5 years of breast development. Differential diagnoses include the following (see Figure 15-2):
  - Pregnancy.
  - Gonadal failure (eg, Turner syndrome, sex chromosome mosaicism).
  - Hypothalamic failure (eg, gonadotropin-releasing hormone [GnRH] deficiency, Kallmann syndrome, central nervous system neoplasm).
  - Pituitary failure (eg, prepubertal hypothyroidism, early mumps infection).
  - Androgen resistance (*46XY*), congenital adrenal hyperplasia disorders.
  - Anatomic anomaly (eg, congenital absence of the uterus or transverse vaginal septum).
- **2° amenorrhea:** Absence of menses for three cycles (if previously regular) or for 6 months (if previously irregular). Differential diagnoses include pregnancy, hypothyroidism, hyperandrogenism (eg, PCOS), hyperprolactinemia, anorexia nervosa, stress, strenuous exercise, uterine outflow defect (intrauterine adhesions), and premature ovarian insufficiency (see Figure 15-3).

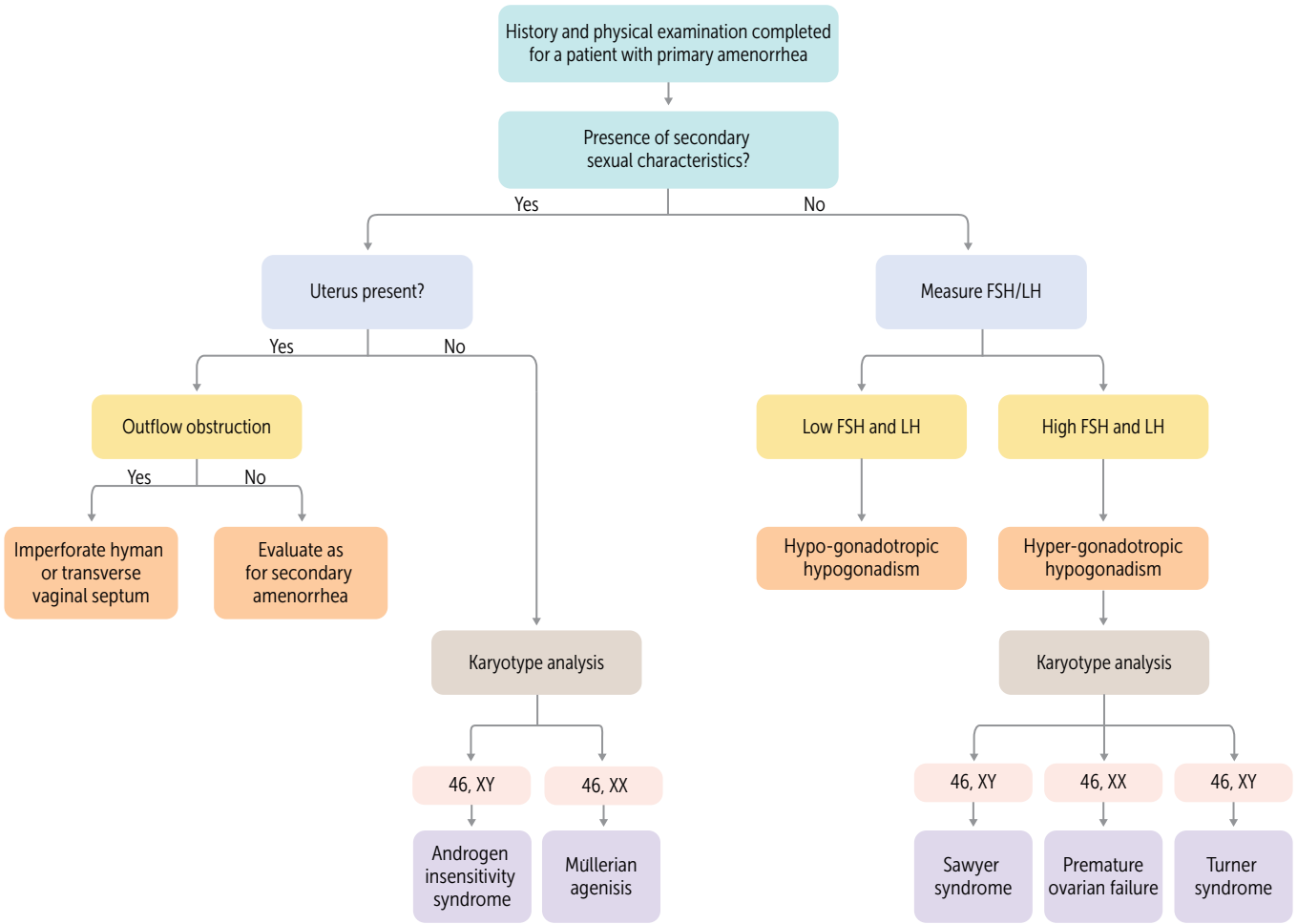


FIGURE 15-2. Workup for patients with 1° amenorrhea. (Reproduced with permission from USMLE-Rx.com.)

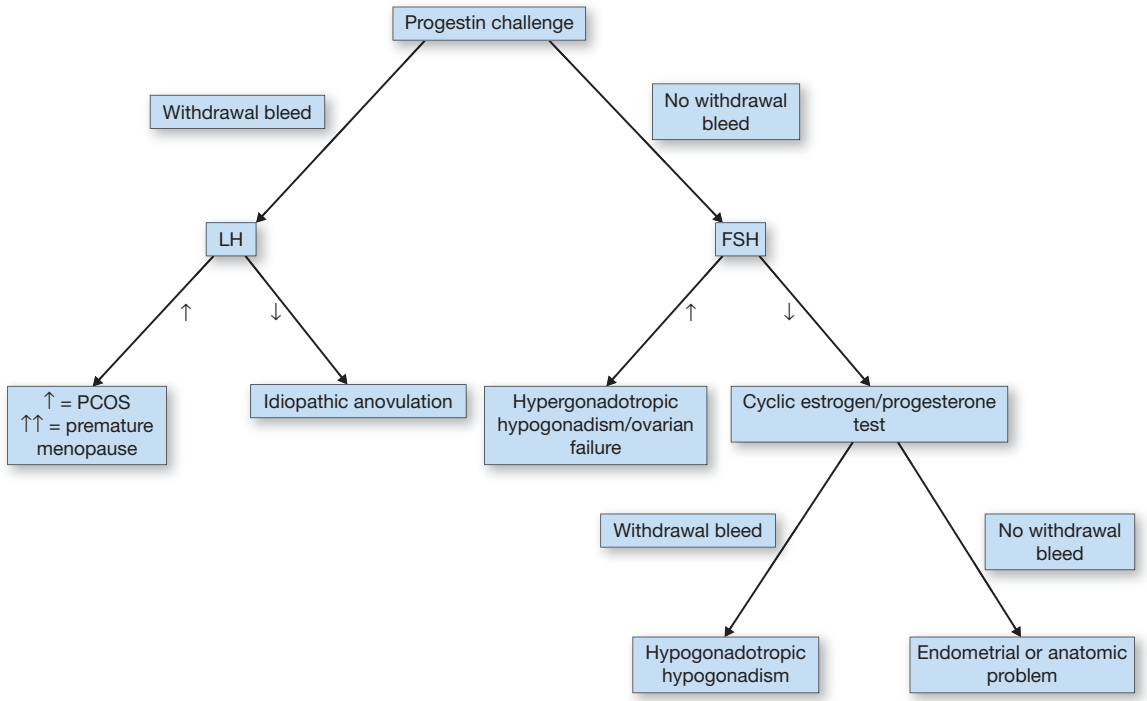


FIGURE 15-3. Workup for patients with 2° amenorrhea.

Diagnosis

- Check β-hCG, prolactin, TSH reflex free T4, LH, and FSH.
- **1° amenorrhea:** See Figure 15-2.
- **2° amenorrhea:** See Figure 15-3.

KEY FACT

Amenorrhea is a symptom, not a diagnosis.

Treatment

Depends on the etiology; it may include surgery or hormonal therapy +/− drug therapy.

Dysmenorrhea

Defined as pain with menstrual periods that requires medication and prevents normal activity. It is defined as either 1° or 2° dysmenorrhea.

- **1° dysmenorrhea:** No clinically detectable pelvic pathology; most likely due to ↑ uterine prostaglandin production.
- **2° dysmenorrhea:** Menstrual pain due to pelvic pathology; most commonly endometriosis, adenomyosis, or leiomyomas.

Q 1

A 46-year-old woman presents to her gynecologist with intermittent and painless noncyclic vaginal bleeding of 6 months' duration. She otherwise feels well and has a normal pelvic exam. What is the next step?

Polycystic Ovarian Syndrome

The most commonly diagnosed cause of hyperandrogenism in women. PCOS often affects adolescent women. The pathogenesis is complex.

History/PE

- Patients often present with a history of infrequent or irregular menstrual bleeding, unwanted hair growth, acne, evidence of insulin resistance (acanthosis nigricans) and/or weight gain.

Q 2

A 23-year-old woman with a history of irregular menses has been unable to conceive for 2 years. Her partner's infertility workup has been ⊖. The patient has diabetes, diagnosed at age 14, but is otherwise healthy. She is 5'2", weighs 165 lbs (74.8 kg), and has acne. What could you expect to find on exam and imaging?

- Pelvic exam may show palpably enlarged ovaries but will most likely be unremarkable.

Diagnosis

- Most commonly diagnosed using the Rotterdam criteria, which requires the presence of two of three of the following:
  - Oligo- or anovulation.
  - Hyperandrogenism (clinical evidence by hirsutism or laboratory by elevated free or total testosterone).
  - Polycystic ovaries on ultrasound.
- Women with PCOS have an ↑ risk of diabetes and cardiac disease. Once PCOS has been diagnosed, order a glucose tolerance test and a lipid panel.
- An ↑ LH/FSH ratio (> 2) is also characteristic.

Treatment

Treat the specific symptoms:

- **Hyperglycemia/diabetes:** Weight loss; hypoglycemic agents like metformin.
- **Infertility:** Symptoms may also improve with diet and exercise. Induce ovulation with clomiphene and/or metformin.
- **Hirsutism:** Start combination OCPs to suppress ovarian steroidogenesis and protect the uterine lining from unopposed estrogen secretion. Spironolactone may also be used.

Endometriosis

Growth of endometrial tissue in locations other than the uterus. The most common location is the ovaries (called endometriomas or "chocolate cysts"), cul-de-sac, and uterosacral ligament. It is associated with premenstrual pelvic pain due to stimulation of endometrial tissue from estrogen and progesterone during the menstrual cycle.

KEY FACT

If a patient presents with dyspareunia and pelvic pain or dyschezia, consider endometriosis as your top differential.

History/PE

- May present with cyclic pelvic pain, dysmenorrhea, dyspareunia, and infertility.
- On pelvic exam, patients may have tender nodularity along the uterosacral ligament +/− a fixed, retroflexed uterus or enlarged ovaries.

Diagnosis

The history and physical can suggest the diagnosis, but the gold standard is direct visualization during laparoscopy with biopsy showing endometrial glands.

Treatment

- Depends on the patient's symptoms, age, desire for future fertility, and disease stage. The extent of pelvic disease does not correlate with the patient's symptoms.
- If a patient has a confirmed diagnosis of endometriosis and tubal occlusion causing infertility, she should be referred to a reproductive endocrinologist. Management options include operative laparoscopy or in vitro fertilization.
- If the patient's main complaint is pain, the objective is to induce a state of anovulation.
  - For mild pain, first-line treatment is NSAIDs and/or continuous OCPs.
  - For moderate to severe pain, options include medical treatment to induce anovulation (GnRH agonists).

1 **A**

Rule out endometrial cancer, which requires sampling the endometrium by performing either an endometrial biopsy or a D&C (the gold standard).

2 **A**

The patient probably has PCOS. You may find enlarged ovaries on bimanual exam and many follicles in her ovaries on ultrasound.

- If medical management fails, consider operative laparoscopy to excise endometrial implants.
- Hysterectomy with bilateral salpingo-oophorectomy is used as a final therapeutic option.

Gestational Trophoblastic Disease

Includes hydatidiform moles, which may be complete or partial (see Table 15-3), and gestational trophoblastic neoplasia (GTN). Hydatidiform mole accounts for approximately 80% of cases of gestational trophoblastic disease.

History/PE

- Patient may present with first-trimester uterine bleeding and excessive nausea and vomiting.
- Pelvic exam might show bleeding from the cervical os and uterine size greater than dates.
- Rarely, it can be associated with preeclampsia or eclampsia at < 20 weeks or thyroid storm.

Diagnosis

- CBC, type and screen, CMP.
- Markedly elevated serum β-hCG.
- A "snowstorm" appearance of grapelike molar clusters on pelvic ultrasound (see Figure 15-4) with or without presence of a fetus.
- Obtain a CXR to rule out metastases.

Treatment

- D&C with preoperative preparation for hemorrhage with two large-bore IVs, crossmatch for blood, and uterotonic medications available.
- **Postsurgical management:**
  - Carefully follow serum β-hCG levels after D&C for possible development of GTN. Check weekly until β-hCG is ⊖ and then monthly for 6 months.
  - Contraceptive plan is essential during time of serum β-hCG monitoring.
  - Subsequent development of GTN is treated with chemotherapy or hysterectomy.

TABLE 15-3. Partial Versus Complete Hydatidiform Mole

Feature	Partial Mole	Complete Mole
Karyotype	Most commonly 69, XXX or 69, XXY	Most commonly 46, XX or 46, XY
Fetal parts	Usually present	Absent
β-hCG level	< 100,000	> 100,000
Theca lutein cysts	Rare	15–25%
Malignancy	< 5%	6–32%

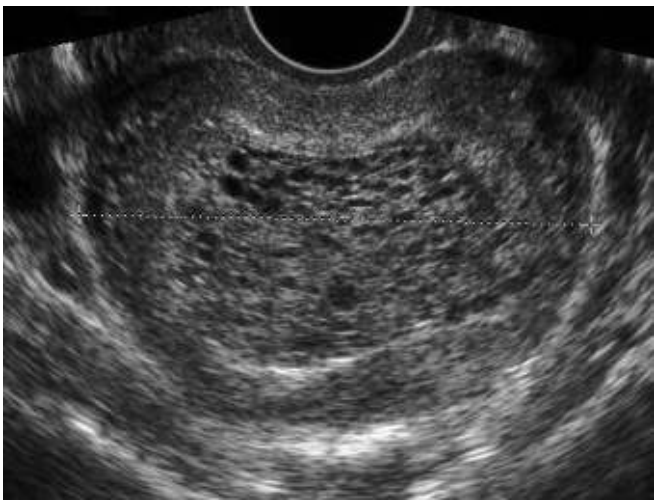


FIGURE 15-4. Gestational trophoblastic disease. The classic "snowstorm" appearance is seen on transverse ultrasound of a patient with gestational trophoblastic disease. The patient has a complete hydatidiform mole. (Reproduced with permission from Hoffman BL et al. *Williams Gynecology,* 2nd ed. New York: McGraw-Hill, 2012, Fig. 37-5.)

Vulvovaginitis

Most commonly caused by bacterial vaginosis (*Gardnerella vaginalis*), fungal infection (*Candida albicans*), or protozoal infection (*Trichomonas vaginalis*). It can also be caused by sexually transmitted infections (STIs) such as gonorrhea or chlamydia (see Table 15-4).

KEY FACT

While the most common cause of vaginal discharge in pediatric patients is retained foreign body, sexual abuse must be considered in any child with vulvovaginitis.

History/PE

- May present with ↑ vaginal discharge, a change in discharge odor, vulvovaginal pruritus, and/or vaginal spotting.
- Perform a complete exam of the vulva, vagina, and cervix. Look for vulvar edema, erythema, and discharge.

Diagnosis/Treatment

Obtain swabs from the vagina to perform a wet mount and cultures for gonorrhea and chlamydia.

Pelvic Inflammatory Disease

An infection of the upper genital tract that may involve uterus, fallopian tubes, and/or ovaries with or without peritonitis. Risk factors include age < 25, multiple sexual partners, lack of condom/barrier use, and a history of pelvic inflammatory disease (PID) or STIs. PID is usually a polymicrobial infection involving aerobic and anaerobic organisms from the lower genital tract. Patients infected with gonorrhea or chlamydia are at ↑ risk of developing PID.

KEY FACT

Tenderness in the right upper quadrant can be a sign of Fitz-Hugh–Curtis syndrome, perihepatic adhesions associated with peritonitis resulting from pelvic infection.

History/PE

Patients often present with abdominal pain, vaginal discharge +/− fevers and malaise. Exam findings may include tachycardia, fever, diffuse abdominal tenderness, and cervical motion tenderness ("chandelier sign") on pelvic exam.

TABLE 15-4. Common Causes of Vulvovaginitis

	Bacterial Vaginosis	Yeast (usually *Candida*)	*Trichomonas vaginalis*
Exam	Can be unremarkable except for discharge	Erythema and inflammation of vulva and vagina	The vagina and cervix may be swollen and red, "strawberry cervix"
Discharge	Grayish or white with a fishy odor	White, thick, curdlike	Yellow-green, frothy, malodorous
Microscopy	Wet mount: > 20% of epithelial cells with indistinct cell margins—"clue cells" (Image A) KOH prep: ⊕ "whiff test," when placed on a slide leads to a fishy odor	Wet mount: No characteristic findings KOH prep: Pseudohyphae and budding yeast cells (spores) of *Candida albicans* (Image B)	Wet mount: Motile, flagellated protozoans (Image C) KOH prep: Nothing
pH	Elevated (> 7)	Normal or < 7	Elevated (> 7)
Treatment			
Nonpregnant	Metronidazole × 7 days	Topical antifungal × 3–7 days or oral fluconazole × one dose	Metronidazole × one dose
Pregnant	Metronidazole × 7 days	Use only topical antifungals × 7 days	Metronidazole × one dose

A B C

Image A reproduced from the CDC/M. Rein; image B reproduced with permission from USMLE-Rx; courtesy of Dr. Kachiu Lee; image C reproduced from the CDC.

Diagnosis

- Diagnosed clinically.
- Otherwise unexplained low abdominal tenderness, adnexal tenderness, or cervical motion tenderness in a sexually active young woman is sufficient for diagnosis.
- Additional supportive findings include fever, mucopurulent discharge, > 10 WBCs/low-power field on Gram stain or vaginal secretions, ⊕ STI testing.
- Vaginal cultures should be obtained to rule out gonorrhea or chlamydia. However, do not delay treatment while awaiting results, as ⊖ results do not rule out PID and delayed treatment may lead to tubal scarring and infertility.

Treatment

- **Inpatient management:**
  - **Indications:** Pregnancy, noncompliance with medication or follow-up, inability to tolerate PO, tubo-ovarian abscess.
  - **Tx:** Give IV agents, eg, cefoxitin + doxycycline OR clindamycin + gentamicin; alternative option is ampicillin-sulbactam + doxycycline. Transition to PO doxycycline 24 hours after clinical improvement.

Q

A 19-year-old woman who is sexually active with multiple partners presents to your clinic with vaginal pruritus and ↑ discharge. A wet mount is ⊕ for protozoans, but KOH prep reveals no organisms. Which organism is likely contributing to her vulvovaginitis?

Treatment duration is 14 days. If the patient does not improve, consider imaging (ultrasound) to evaluate for a tubo-ovarian abscess that requires drainage.

- **Outpatient management:**
  - **Indications:** Mild disease without the above findings.
  - **Tx:** Single IM dose + 14-day PO regimen. Consider IM veftriaxone + PO doxycycline OR IM cefoxitin + PO probenecid + PO doxycycline (either option with or without metronidazole) OR IM cefotaxime or IM ceftizoxime + PO doxycycline.

Ectopic Pregnancy

Defined as any pregnancy that is implanted outside the uterine cavity. The most common location is the fallopian tube (95%). Risk factors include a history of prior ectopic pregnancy, PID, tubal/pelvic surgery, and diethylstilbestrol exposure in utero.

History/PE

KEY FACT

Any woman with abdominal pain needs a urine pregnancy test.

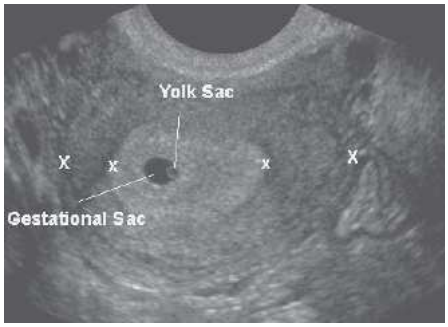
- Patient may report amenorrhea, lower abdominal pain, nausea, vomiting, and/or abnormal vaginal bleeding.
- Patient may have abdominal tenderness to palpation, adnexal mass, or fullness.
- A ruptured ectopic may present with unstable vital signs, diffuse abdominal pain, rebound tenderness, guarding, and shock.

Differential

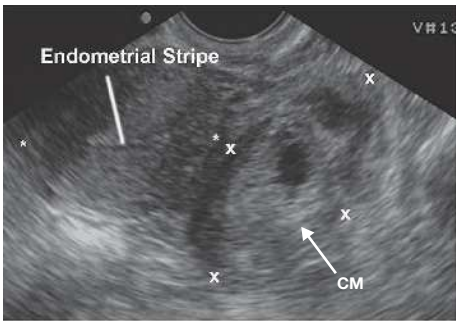
Spontaneous abortion, molar pregnancy, ruptured or hemorrhagic corpus luteum cyst, PID, ovarian torsion, appendicitis, pyelonephritis, diverticulitis, regional ileitis, ulcerative colitis.

Diagnosis

- Highly suspect ectopic in a patient with low abdominal/pelvic pain, ⊕ urine or serum β-hCG, and no intrauterine pregnancy on ultrasound.
- Measure serum β-hCG.
- Ultrasound findings concerning for ectopic include adnexal mass and/or complex free fluid and no intrauterine pregnancy (see Figure 15-5).



A



B

FIGURE 15-5. Normal intrauterine pregnancy and ectopic pregnancy. Transvaginal ultrasound showing **(A)** a normal intrauterine pregnancy with a gestational sac containing a yolk sac within the uterine cavity, and **(B)** a complex mass/ectopic pregnancy adjacent to an empty uterus. (Reproduced with permission from Tintinalli JE et al. *Tintinalli's Emergency Medicine: A Comprehensive Study Guide,* 6th ed. New York: McGraw-Hill, 2004, Figs. 113-15 and 113-22.)

A

Trichomonas vaginalis.

- The gestational sac may be visualized on transvaginal ultrasound when serum β-hCG is approximately 1500–3000 mIU/mL (sometimes referred to as the "discriminatory zone").
- Fetal heart motion of the embryo can be seen after 5–6 weeks' gestational age.
- Definitive diagnosis is made by laparoscopy, laparotomy, or ultrasound visualization of a pregnancy outside the uterus.

Treatment

- **Hemodynamically unstable patients:** Immediate surgery required (eg, salpingectomy or salpingostomy).
- **Pregnancy of unknown location in hemodynamically stable patients:** Serum β-hCG below the discriminatory zone (< 1500), no intrauterine pregnancy or ectopic pregnancy on ultrasound.
  - Expectant management with repeat β-hCG in 48 hrs and repeat ultrasound within a week.
- **Confirmed ectopic pregnancy:**
  - Expectant management for stable, compliant patients with decreasing β-hCG levels or β-hCG < 200 mIU/mL if the risk of rupture is low.
  - Candidates for medical management with methotrexate:
    - No fetal cardiac motion.
    - β-hCG < 5000 mIU/mL.
    - Gestational sac diameter size < 3.5 cm.
    - Patient reliable to follow-up.
  - Surgical intervention: Laparoscopy or laparotomy for removal of ectopic pregnancy.
    - Hemodynamically unstable patients.
    - Noncompliant patients.
    - Contraindications to methotrexate administration.
- Prevention of ectopic pregnancies: Prevention and thorough treatment of STIs.

KEY FACT

A β-hCG of 3000 mIU/mL will not always show an intrauterine pregnancy (eg, in the case of twins). Therefore, it is important to repeat the β-hCG and ultrasound in 48 hours to confirm the abnormal pregnancy before treating the patient.

KEY FACT

All women with ectopic pregnancies should be typed and screened and given RhoGAM if Rh is ⊖.

Contraception

ORAL CONTRACEPTIVES

There are two types of oral contraceptives: combined (estrogen and progesterone) and progesterone only. The long-term effects of combined OCP use include a ↓ in ovarian and endometrial cancers, a ↓ incidence of breast disease (but not breast cancer), ↓ menstrual flow, ↓ acne, and ↓ dysmenorrhea. Contraindications to combined OCPs include:

- Pregnancy.
- Migraines with aura.
- Previous or active thromboembolic disease.
- Smoking in patients > 35 years of age.
- Undiagnosed genital bleeding.
- Estrogen-dependent neoplasms.
- Hepatocellular carcinoma.
- Acute liver dysfunction.
- Poorly controlled hypertension.

OTHER CONTRACEPTIVES

Table 15-5 contrasts hormonal contraceptives with nonhormonal methods.

Q

A 28-year-old woman who is 6 weeks pregnant presents to the ED complaining of vaginal spotting and right lower quadrant (RLQ) pain. Her exam is significant for RLQ tenderness and no cervical motion tenderness. What is the next step?

TABLE 15-5. Hormonal vs Nonhormonal Methods

Method	Indications/Comments
	Hormonal
Progesterone-only contraceptives	Indicated in woman for whom combined OCPs are contraindicated; less effective than combined agents and generally reserved for breastfeeding mothers who have lactational amenorrhea
Injectable	Administered intramuscularly every 3 months; associated with irregular spotting and weight gain, hair thinning, and transient ↓ in bone mineral density
Subdermal progesterone implant	Most effective method; approved for 3 years of use Can be associated with irregular spotting or local irritation at insertion site (erythema, swelling)
Transdermal patch	Applied weekly for 3 weeks followed by a 1-week patch-free interval during which menses occurs Similar indications, contraindications, and side effect profile as combined OCPs May be less effective in obese patients (weight > 90 kg [198 lb])
Vaginal ring	Kept in place for 3 weeks, followed by a 1-week holiday during which menses occurs Contains estrogen and must be used in appropriate candidates Similar indications, contraindications, and side effect profile as combined OCPs
Intrauterine devices	See below
	Nonhormonal
Condoms, male or female	Provide protection against STIs
Cervical diaphragm	Placed intravaginally over the cervix immediately before intercourse and removed within 3 hours afterward
Spermicidal gel	Can be used in combination with condoms or diaphragm; when used alone, it is unreliable
Copper IUD	See below
Fertility awareness method	The "rhythm method"; relies on avoidance of intercourse during the ovulatory period
Male or female sterilization	Either fallopian tube interruption in women (tubal ligation or permanently implanted birth control device) or ligation of the vas deferens in men

A

Obtain quantitative β-hCG and transvaginal ultrasound. If the patient is hemodynamically stable with a hCG level is less than 3000 and no intrauterine pregnancy and no adnexal masses, the patient is diagnosed with a pregnancy of unknown location. Repeat the patient's β-hCG in 48 hours. If the value does not double in 48 hours, suspect ectopic pregnancy. It is also important to consider nongynecologic causes.

INTRAUTERINE DEVICES

Two types of IUDs are approved for use in the United States. Both are highly effective, with > 99% efficacy.

- **Levonorgestrel IUD:** A progesterone-only IUD that causes thickening of the cervical mucus, thinning of the endometrium, and decreased peristalsis of fallopian tubes.
  - Lasts 5 years.
  - ↓ Menstrual bleeding and dysmenorrhea; thus, a good choice for the treatment of women with heavy menstrual bleeding.
  - **Side effects:** Perforation with placement, irregular menstrual bleeding (30–70% of women experience amenorrhea), pelvic cramping, vaginal discharge.

- **Copper IUD:** Causes a sterile inflammatory response that prevents pregnancy implantation.
  - Lasts 10 years.
  - Nonhormonal; a good choice for women who have contraindications to hormone treatment.
  - **Side effects:** Dysmenorrhea and ↑ menstrual bleeding.

KEY FACT

The IUD itself does not ↑ the risk of ectopic pregnancy. However, if a patient has a ⊕ pregnancy test with an IUD, suspect ectopic pregnancy.

EMERGENCY CONTRACEPTION

- Should be taken immediately after unprotected intercourse; can be taken up to 5 days afterward, but with decreasing effectiveness.
- Options include oral levonorgestrel (Plan B) (most effective when used within 3 days but can be used up to 5 days after), oral ulipristal acetate (within 5 days), or placement of a copper IUD (5 days).
- The most effective emergency contraception is copper IUD.

Infertility

Defined as inability of a couple to conceive after 1 year of unprotected intercourse (or 6 months if > 35 years of age). It affects 10–15% of couples. Causes are listed in Table 15-6.

KEY FACT

Endometriosis is one of the leading causes of female infertility, followed by PID.

Diagnosis

- Semen analysis to rule out male factors.
- Assessment of ovulation status with home ovulation predictor kits or measurement of basal body temp, serum testing of androgens, FSH, LH, TSH, prolactin to rule out endocrine dysfunction.
- PE, pelvic ultrasound, and hysterosalpingography to rule out uterine anatomical abnormalities and assess tubal patency.

Treatment

- Treat the underlying cause.
- Fertility rates in endometriosis can be improved through use of operative laparoscopy to lyse scar tissue and endometriomas causing tubal occlusion.
- Ovulation can be induced with clomiphene or letrozole. Caution should be exercised with these medications, as they can lead to ovarian hyperstimulation and multiple gestations.

TABLE 15-6. Causes of Infertility

Female	Male
Ovulatory dysfunction: Ovarian failure, prolactinoma	Congenital disorders: Include Klinefelter syndrome, androgen insensitivity, 5α-reductase deficiency, Kallmann syndrome, and Prader-Willi syndrome
Uterine/tubal factors: Tubal occlusion 2° to endometriosis or PID, myomas that distort the endometrium or fallopian tubes, congenital genital tract abnormalities	Systemic disorders: Obesity, chronic illness
Endocrine dysfunction: Thyroid/adrenal disease, PCOS	Disorders of sperm production and transport: Ejaculatory dysfunction, ↓ sperm count, abnormal morphology, or ↓ motility
Unexplained infertility or rare problems	Unexplained infertility or rare problems

- For refractory cases, assisted reproductive technologies such as in vitro fertilization can be used.

KEY FACT

Premature menopause occurs before age 40 and is often due to idiopathic premature ovarian insufficiency.

Menopause

Cessation of menstruation for 12 consecutive months. Average age of onset is 51. Surgical menopause occurs following removal or irradiation of the ovaries. Postmenopausal women are at ↑ risk for developing osteoporosis and heart disease.

History/PE

- Patients may complain of menstrual irregularities, hot flashes, night sweats, sleep disturbances, mood changes, ↓ libido, and vaginal dryness.
- Exam may reveal vaginal dryness, ↓ breast size, and genital tract atrophy.

Diagnosis

- Requires 1 year without menses with no other known cause.
- ↑↑ Serum FSH (> 30 IU/L) is suggestive.

Treatment

- Hormone therapy with estrogen or combined estrogen and progesterone can be used for short-term symptomatic relief of vasomotor symptoms (hot flushes, night sweats).
- Absolute contraindications to hormone therapy include undiagnosed vaginal bleeding, active liver disease, recent myocardial infarction, recent or active vascular thrombosis, and a history of endometrial or breast cancer.
- Symptoms may be treated with alternatives to hormone therapy:
  - **Vasomotor instability:** Venlafaxine and some selective serotonin reuptake inhibitors, clonidine.
  - **Vaginal atrophy:** Vaginal lubricants or topical estrogens.
  - **Osteoporosis:** Calcium, vitamin D, calcitonin, bisphosphonates (eg, alendronate), selective estrogen receptor modulators (eg, raloxifene), denosumab.
  - **↓ Libido:** Flibanserin ("female Viagra").
- Unopposed estrogen (without progesterone therapy) can lead to endometrial hyperplasia and/or carcinoma.

KEY FACT

Use the lowest possible dose of hormone therapy for the shortest duration to treat menopausal symptoms, as prolonged use ↑ the risk of endometrial carcinoma.

Urinary Incontinence

Involuntary loss of urine that negatively affects a patient's psychological, physical, and social well-being. See Table 15-7 for an outline of stress, urge, and mixed incontinence.

History/PE/Diagnosis

- Voiding diaries can help quantify the frequency and volume of urine lost, the circumstances of leakage (to diagnose type of incontinence), voiding patterns, and the amount and type of fluid taken in.
- If history and exam findings do not clearly demonstrate simple stress urinary incontinence, patients should have a screening neurologic exam to rule out neurologic causes as well as urologic evaluation.
- A standing cough stress test can be used to diagnose stress incontinence; urodynamics/cystometry can be used to diagnose urge incontinence.

TABLE 15-7. Types of Urinary Incontinence

	Stress Incontinence	Urge Incontinence/ Overactive Bladder (Detrusor Instability)	Mixed Incontinence
History	Loss of urine with ↑ intra-abdominal pressure (eg, running, coughing, laughing, sneezing)	Urge incontinence: Loss of urine with urge to void Overactive bladder syndrome: Urgency to void with or without urge incontinence and often with nocturia and frequency	Stress and urge incontinence presenting simultaneously
Mechanism	Poor support or poor function of the urethral sphincter	Involuntary detrusor muscle contractions	A combination of both mechanisms
Etiology	↑ Elasticity of the vagina; loss of muscle mass of vagina, urethral hypermobility Risk factors: Age, genetics, childbirth, obesity, COPD, menopause	Idiopathic, neurologic (Alzheimer disease, diabetes, MS)	As for both conditions
Diagnosis	Patient history Demonstrable leakage with stress (cough) = ⊕ stress test	Patient history Urodynamics/cystometry reveals involuntary detrusor muscle contraction associated with urinary leakage	As for both conditions
Treatment	Pelvic floor strengthening exercises (Kegel exercises) weight loss, biofeedback, pessaries, surgery (suburethral sling) to restore bladder neck support	Behavior modification (eg, limiting fluid intake; avoiding caffeinated or alcoholic beverages) Bladder training Medical therapy (anticholinergic) Surgical therapy (sacral neurostimulators, intravesical Botox injections)	Treat urge incontinence first Geared towards the patient's worst symptom; some treatments overlap (eg, Kegel exercises)

- Urinary retention with overflow can be a cause of urinary incontinence and can be diagnosed with an elevated postvoid residual.

Treatment

Table 15-7 outlines treatment measures for urinary incontinence.

KEY FACT

Urinary tract infection must be ruled out in all women complaining of urinary incontinence.

Benign Breast Disorders

Include fibrocystic change (the most common), fibroadenoma, intraductal papilloma (a common cause of bloody nipple discharge), duct ectasia, fat necrosis, mastitis, and breast abscess. See Table 15-8 for a list of common examples.

- **Nipple discharge:** Most commonly seen in women 20–40 years of age.
  - Should raise concern if bloody, brown, black, unilateral, or persistent; appears spontaneously without manipulation; or is associated with systemic signs.
  - Unilateral discharge is most commonly from intraductal papilloma, which is rare and benign. Discharge is sticky and clear to straw-colored.

TABLE 15-8. Benign Breast Disease

Disease Type	History/PE	Treatment	Associated with Carcinoma
Fibrocystic changes	Mild to moderate pain in the breasts +/− lumps premenstrually; multifocal, bilateral nodularity Most common in women 20–50 years of age	OCPs	Patients are at ↑ risk for breast cancer only in the presence of cellular atypia Cancer must be excluded in high-risk groups
Fibroadenoma	It is the most common tumor in menstruating women < 25 years of age It presents as a small, firm, unilateral, nontender mass that is freely movable and slow growing Ultrasound can be used to differentiate from a cyst	Thirty percent will spontaneously disappear Removal is not necessary, but surgical excision is both diagnostic and curative; biopsy if the patient is in a high-risk group Recurrence is common	Risk is twice as high as that of control patients
Intraductal papilloma	Clear, bloody, or discolored fluid from a single duct opening Milking of the breast shows drainage from one duct opening	Drainage and surgical exploration of the duct A malignant process must always be excluded	Risk is twice as high as that of control patients
Mastitis	Seen mainly in breastfeeding women; presents as a hard, red, tender, swollen area of breast accompanied by fever, myalgias, and general malaise	Continued breastfeeding; NSAIDs and antibiotics to cover common etiologies (*Staphylococcus*, *Streptococcus, E coli*)	None
Abscess	Can develop if mastitis is inadequately treated Exam reveals a fluctuant mass accompanied by systemic symptoms similar to those of mastitis	Needle aspiration or surgical drainage in addition to antibiotics	None
Fat necrosis	Firm, tender, and ill-defined with surrounding erythema; related to trauma/ischemia	Analgesia An excisional biopsy may be done to rule out malignancy	None

KEY FACT

Mammography should be performed for any new breast mass in an older woman even if the patient had a recent ⊖ study.

- Bilateral discharge requires workup for prolactinoma (see Chapter 5 for a more detailed discussion).
- The differential diagnosis includes malignancy and mastitis.

- **Breast lump:**
  - Evaluation includes assessing the general appearance of the breast (inverted nipple, change in size or symmetry) or any skin changes.
  - Determine if related to menses or if it was spontaneously discovered and has not gone away.
  - Exam should include evaluation of the lymph nodes.
  - For young women, it is reasonable to start with a breast ultrasound before mammography. For older women, start with mammography.

CHAPTER 16

PEDIATRICS

Well-Child Care/Routine Health Screening

SCREENING BASICS

Routine health screening includes (1) monitoring of growth and development; (2) prevention of illness and promotion of safety; and (3) anticipatory guidance. Key features of routine screening include the following:

- **Metabolic/genetic diseases:** Newborns are typically screened within the first days of life before leaving the hospital following birth. The exact content of the screen varies by state but includes diseases that can be treated to ↓ morbidity and mortality (eg, thyroid disease, cystic fibrosis [CF], phenylketonuria, galactosemia, and tyrosinemia).
- **Growth parameters/development/behavior:** Screen or monitor at each visit to ensure age-appropriate milestones are being met and growth curves are being followed; otherwise, can start early interventions.
- **Lead/anemia:** Start screening during the developmental period in which children begin to explore their environment via hand-to-mouth interactions (ie, 9–15 months). Repeat at age 2 years, especially in high-risk communities (eg, those with houses built before 1950).
  - Screening blood lead levels > 15 mcg/dL need to be reported to the Health Department.
  - Chelation with dimercaptosuccinic acid, succimer begins at blood lead level > 45 mcg/dL.
- **BMI:** Track starting at 2 years of age.
- **BP:** Screen with every medical exam starting at age 3. Norms are based on sex, age, and height percentile.
- **Vision and hearing:** Objective hearing at birth; objective hearing and vision annually starting at age 3. Subjective visual testing can be done with developmental monitoring in between (eg, visual tracking of eyes to objects or people).

KEY FACT

Absolute contraindications to breastfeeding in the developed world:

- Maternal HIV infection or HTLV infection.
- Untreated TB infection.
- Infant diagnosis of galactosemia.
- Maternal use of illegal substances (not including physician-supervised opioid weaning programs or prescribed medications).
- Active herpes simplex virus (HSV) lesion on breast.
- Maternal exposure to certain medications: chemotherapeutic agents, antimetabolites, lithium, and radioisotopes.

NUTRITION

- **Breastfeeding:**
  - Encouraged as an exclusive feeding source until 6 months of age.
  - Benefits: Confers immunogenic factors (including IgA, T-cells, and antibodies) that ↓ the risk of allergies, necrotizing enterocolitis, and infections of the respiratory and GI tract. Also improves bonding between mother and infant.
- **Formula:**
  - All formulas are mixed to 20 kcal/oz unless concentrated to optimize growth.
  - Milk protein intolerance can be IgE mediated with anaphylaxis or non–IgE mediated; presentations include vomiting, diarrhea, constipation, gastroesophageal reflux disease, and bloody stools 2° to proctocolitis.

NORMAL GROWTH PATTERNS

- **Newborns**: Expected to lose up to 10% of their birth weight in their first several days of life and to regain their birth weight by 2 weeks.
- **Term infants and children**: Typically follow the growth curves they begin on without deviation > 2 percentile curves in either direction.

- **Premature infants**: Have a separate growth curve, and they may exhibit jumping up several curves when they are "catching up" their growth to match what they would have been if they had been born term. However, if all three parameters are not changing somewhat consistently with one another, this may be cause for investigation.

KEY FACT

The "falling off" a curve, especially only one of three growth parameters (length, weight, and head circumference) is a cause for investigation.

ABNORMAL GROWTH PATTERNS

Failure to Thrive

Indicates persistent failure to follow upward trend of a growth curve (weight or length). Often seen when a growth curve of an infant becomes a horizontal or near-horizontal line and transverses several percentile curves. However, some of these patients should be matched to their family members (ie, if an infant is born at the 90th percentile, but both parents are small and short, the patient may be re-equilibrating to true familial genetic stature). Failure to thrive (FTT) has a multitude of causes, including:

- Inadequate Intake: Overdilution of formula, infrequent feeding, mechanical problems.
- Inadequate absorption or ↑ losses: Malabsorption, infectious diarrhea, biliary atresia, intestinal obstruction, necrotizing enterocolitis, short gut.
- ↑ Metabolic demand or ineffective utilization: Inborn errors of metabolism, CF, HIV, endocrine disorders, congenital heart disease (CHD).

History/PE

A good history may reveal diagnosis.

- Nutrition history with possible need for observed feeding of the child. This is especially true for breastfed infants who should have the mother-baby dyad observed feeding by a lactation specialist.
- Elimination history along with quality and frequency of stools.
- Systemic symptoms (such as ↑ work of breathing, cough, vomiting, etc.).
- Family and social history.

Diagnosis

If history and physical are not revealing, consider basic lab workup (CBC, comprehensive metabolic panel, lead level, and UA).

Treatment

Treat the underlying cause.

Constitutional Growth Delay

- In older children where there is concern over short stature.
- **Dx:** Bone scan will show bone age younger than chronological age.
- **Tx:** Reassure the parents and continue to chart growth at annual visits.

DEVELOPMENTAL MILESTONES

Table 16-1 highlights major developmental milestones. Red flags include:

- Persistent primitive reflexes by 6 months.
- Handedness before 1 year.
- No pointing by 18 months.

Q

You are seeing a formerly full-term female infant for a routine well-child checkup. The mother reports that the infant has started crawling, is saying "mama" and "dada," and is waving "bye-bye." If the infant is developmentally on target, how old should she be?

TABLE 16-1. Developmental Milestones

Age[a]	Gross Motor	Fine Motor	Language	Social/Cognitive
2 months	Lifts head/chest when prone	Tracks past midline	Alerts to sound; coos	Recognizes parent; exhibits social smile
4–5 months	Rolls front to back and back to front (4 months)	Grasps rattle	Laughs and squeals; orients to voice; begins to make consonant sounds	Enjoys looking around; laughs
6 months	Sits unassisted	Transfers objects; demonstrates raking grasp	Babbles	Demonstrates stranger anxiety
9–10 months	Crawls; pulls to stand	Uses three-finger (immature) pincer grasp	Says "mama/dada" (nonspecific); says first word at 11 months	Waves "bye-bye"; plays pat-a-cake
12 months	Walks alone; throws object	Uses two-finger (mature) pincer grasp	Uses one to three words	Imitates actions; exhibits separation anxiety Follows one-step commands
2 years	Walks up/down steps with help; jumps	Builds tower of six cubes	Uses two-word phrases	Follows two-step commands; removes clothes
3 years	Rides a tricycle; climbs stairs with alternating feet (3–4 years)	Copies a circle; uses utensils	Uses three-word sentences	Brushes teeth with help; washes/dries hands
4 years	Hops	Copies a cross (square at 4.5 years)	Knows colors and some numbers	Exhibits cooperative play; plays board games
5 years	Skips; walks backward for long distances	Copies a triangle; ties shoelaces; knows left and right; prints letters	Uses five-word sentences	Exhibits domestic role playing; plays dress-up

[a]For premature infants < 2 years of age, chronologic age must be adjusted for gestational age. For example, an infant born at 7 months' gestation (2 months early) would be expected to perform at the 4-month level at the chronologic age of 6 months. However, vaccines should be administered based on chronologic age despite prematurity.

Adapted with permission from Le T et al. *First Aid for the USMLE Step 2 CK*, 10th ed. New York: McGraw-Hill, 2019: 292.

KEY FACT

Mild acute illness is not a contraindication or an indication for delay in vaccination regardless of use of concurrent antimicrobials.

A

Nine months.

IMMUNIZATIONS

Figure 16-1 summarizes the recommended timetable for childhood immunizations. Schedules may vary for children who are behind and require catch-up immunizations. Key considerations before immunization include the following:

- **Severe allergic reaction** (such as anaphylaxis) to a vaccine or its components: A contraindication to that vaccination. Other allergic reactions (even those to egg) are considered precautions, and vaccines may be administered in a controlled setting depending on the reaction.
- **Live virus vaccines** (eg, varicella; measles, mumps, rubella [MMR]; combination vaccines; intranasal influenza): Contraindicated in patients who are immunocompromised, immunosuppressed, or pregnant. Parents should be counseled to monitor for signs of rash in vaccinated family members. If rash

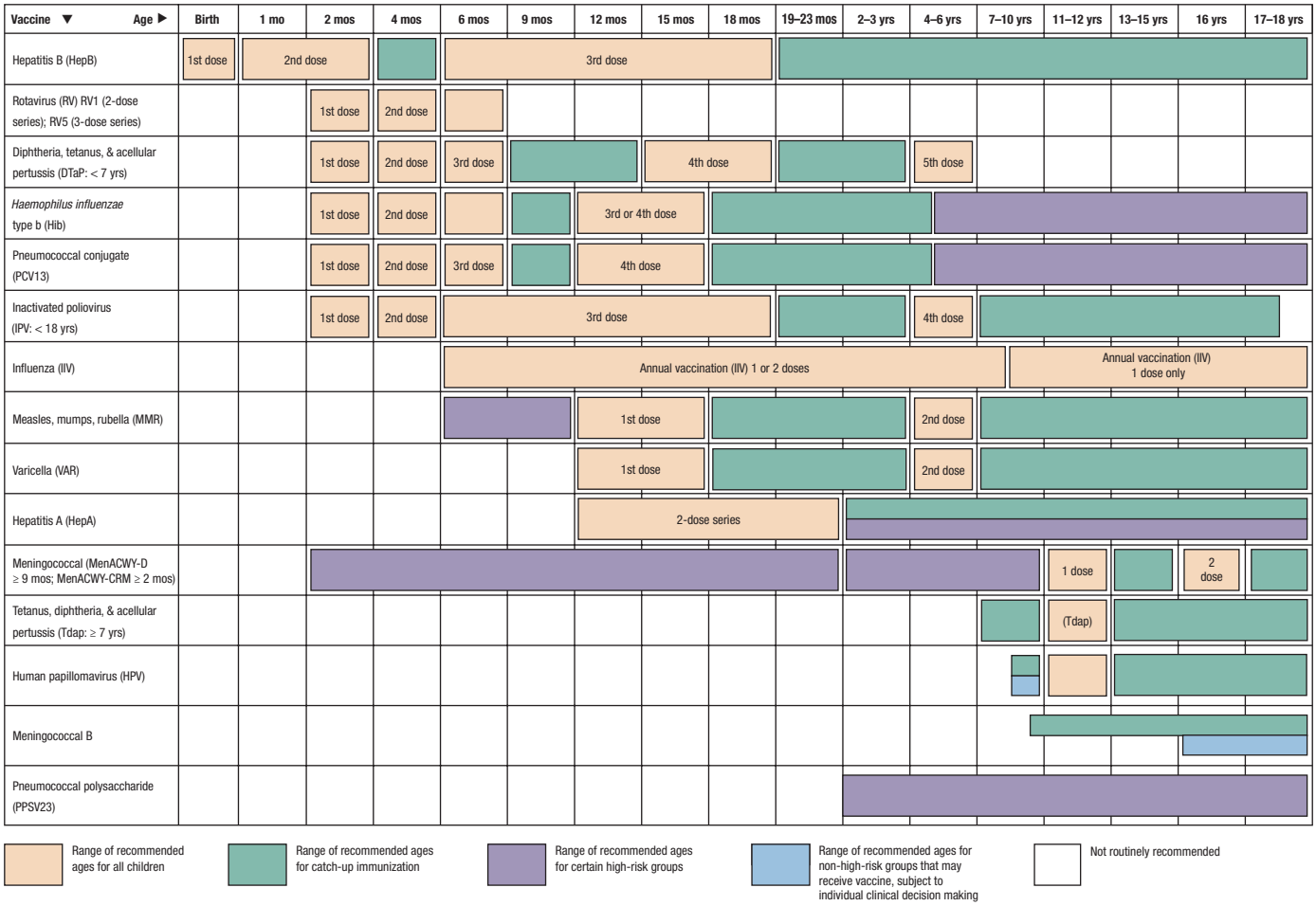


FIGURE 16-1. Recommended vaccinations for children and adolescents 0–18 years. For footnotes, see https://www.cdc.gov/vaccines/schedules/downloads/child/0-18yrs-child-combined-schedule.pdf. (Reproduced from the CDC.)

develops, the vaccinated patient will have to be isolated from the at-risk person immediately.

- **Moderate or severe acute illness:** A delay in vaccination can be considered.
- **Parental refusal of vaccination:** Try to discover why the parent is refusing and create an open dialogue with them. Alternative and customized vaccination schedules are better than no vaccinations. Vaccines do not cause autism.

ANTICIPATORY GUIDANCE

- Provide nutrition, dental hygiene, screen time, injury/violence prevention, and sleep counseling at each health maintenance visit.
- Teenagers should be screened with the **B-HEADSS** interview (see mnemonic) to gauge psychosocial risk in adolescents.

Safety

- Anticipatory guidance should include developmentally significant guidance at the well check prior to development of a new skill—such as parents of children anticipated to begin cruising should be counseled on the proper storage of chemicals, cleaners, and medications; use of plug covers on all electrical outlets; and counseling on helmet use.

KEY FACT

Immunocompromised, immunosuppressed, and pregnant patients should not be given live virus vaccines (eg, intranasal influenza, varicella, and MMR-containing vaccines).

MNEMONIC

Use the B-HEADSS interview for adolescents:

Body image
Home
Education and **E**mployment
Activities
Drugs
Sexuality
Suicidality/depression

MNEMONIC

To reduce the risk of SIDS—

ABCs of safe sleep for infants:

Alone on their **B**ack in their own **C**rib.

MNEMONIC

The 5 S's for soothing crying babies:

Swaddling
Side/**S**tomach position (done under close supervision only)
Shushing sounds
Swinging
Sucking

- **Car safety:**
  - Car seats should be placed in the rear seat of the car, rear-facing, until the child is ≥ 2 years of age or until the height and weight determined by the car seat manufacturer is reached.
  - Car seats should not be placed in seats with active air bags.
  - Children should remain seated in the back seat until age 13 years.

Colic

- Defined as severe, paroxysmal crying for > 3 hours a day, for > 3 days a week, for > 3 weeks in a healthy, well-fed infant. Usually peaks at around 6 weeks of life, with spontaneous resolution by 3–4 months. A diagnosis of exclusion.
- Can contribute to an ↑ risk for child abuse. Parents should be counseled to set the baby safely down using ABCs of safe sleep and walk away if they feel themselves becoming frustrated.
- **Tx:** Consists of providing reassurance and teaching parents soothing techniques such as the **5 S's** (see mnemonic).

CHILD ABUSE

Workup must consider physical, sexual, and emotional abuse/neglect. Diagnosis is based on a history that is discordant with physical findings or developmental history.

KEY FACT

Consider nonaccidental trauma whenever the history of an injury is discordant with physical findings and/or developmental history.

History/PE

Presentation may include:

- Multiple injuries in varying stages of healing.
- Skeletal trauma in the absence of a developmentally plausible mechanism; indicators also include spiral fracture of long bones, multiple/old/posterior rib fractures, or metaphyseal fractures (also known as corner or bucket-handle fractures).
- Pattern injuries (eg, cigarette/immersion burns).
- Oddly situated bruises (not over bony prominences) or bruises on a child who is not yet mobile.
- Retinal hemorrhage in infants.
- Intracranial hemorrhage, especially in the absence of a plausible mechanism.
- Growth failure.
- Signs/symptoms of sexually transmitted infection (STIs) or genital trauma in prepubertal children.

Diagnosis

- **Labs:** Evaluate for underlying disorders that would result in an acute presentation (eg, osteogenesis imperfecta, bleeding diathesis, acute infection).
  - **Bone metabolism:** Calcium, phosphorus, and alkaline phosphatase.
  - **Metabolic disorders:** Liver function tests (LFTs), electrolytes.
  - **Coagulopathy:** CBC, prothrombin time/partial thromboplastin time, INR.
  - **Infection:** CBC, UA.
  - **General:** Consider toxicology and STI evaluation.
- **Imaging:** Skeletal survey to evaluate for fractures in various stages of healing; head CT for intracranial bleeding. If concern for abdominal trauma, consider abdominal CT, LFTs, amylase, lipase, and check urine and stool for gross blood.
- **Consultation:** Consider an ophthalmology evaluation and consultation with a child abuse team.

Treatment

- Physicians are mandated reporters of any suspected abuse or nonaccidental trauma and should immediately notify social services or Child Protective Services. Parents need to be notified when abuse is suspected and a report is made.
- Consider hospitalization to ensure the safety of the child if there is no other safe discharge plan. Be cognizant of other children in the home and their safety in the evaluation. Physicians can get an emergency court order in the event of a parent declining hospitalization.

The Newborn

NEONATAL RASHES

The vast majority of skin findings in the neonatal period are benign. Nonetheless, they are often a cause for concern among new parents. Table 16-2 describes common neonatal rashes.

RESPIRATORY DISTRESS

- Common causes of neonatal respiratory distress and their treatments are outlined in Table 16-3.
- Other causes include:
  - Sepsis (see Neonatal Sepsis).
  - CHD is important to consider if O_2 saturation fails to improve with supplemental O_2. (Refer to the Cardiology chapter for further details.)
  - Anatomic airway anomalies (eg, choanal atresia, in which an NG tube cannot be passed through the nares at birth).
  - Pneumothorax (especially in an infant who suddenly decompensates) and pneumonia.
  - Neurologic abnormalities.

NEONATAL SEPSIS

Serious bacterial infections are rare in the pediatric population but are relatively more common in young infants by virtue of their immature immune systems and waning maternal antibody protection. Risk factors in the immediate perinatal period include maternal Group B *Streptococcus* (GBS) infection or STI, rupture of membranes lasting > 18 hours, maternal fever, chorioamnionitis, premature labor, and limited or no maternal prenatal care.

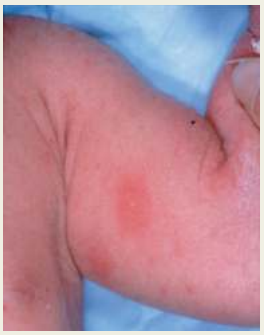
- **Most common pathogens:**
  - **Bacterial:** *E coli;* GBS and other gram ⊖ rods. *Listeria monocytogenes* is rare but is frequently tested on pediatric exams.
  - **Viral:** Mothers with active herpes lesions at the time of delivery or a first-time diagnosis of HSV in the peripartum period carry an ↑ risk of transmitting HSV to the infant. HSV should also be considered in any ill-appearing infant < 28 days of age.

History/PE

Septic infants often present with fever or hypothermia and nonspecific signs such as poor feeding, irritability, rapid breathing, vomiting, or ↓ activity.

TABLE 16-2. Presentation and Treatment of Common Neonatal Rashes

Abnormality	Presentation/Treatment
Erythema toxicum neonatorum	Erythematous macules and papules that progress to pustules (Image A) Lesions usually appear within 24–48 hours after birth and resolve spontaneously in 5–7 days
Transient neonatal pustular melanosis	May present as pustules with a nonerythematous base or erythematous macules with a surrounding scaly area, with hyperpigmented macules Lesions present at birth and resolve spontaneously within weeks to months
Neonatal acne	Papules and pustules appearing on the face and/or scalp (Image B) at 3 weeks of age; generally resolves by 4 months of age Tx: Gentle cleansing with soap and water; avoidance of oils and lotions
Milia	White papules composed of retained keratin and sebaceous material Present at birth; usually found on the cheeks and nose; resolves spontaneously within the first weeks of life
Seborrheic dermatitis	Erythema and greasy scales, usually on the face and scalp (Image C); resolves within weeks to months Tx: Application of emollient overnight followed by massage and shampooing with baby shampoo to loosen scales; use of a soft brush to remove scales Medication: Ketoconazole, selenium sulfide, or hydrocortisone may be tried for persistent scales
Congenital dermal melanocytosis (Mongolian spots)	Dark blue to black birth marks generally present in lumbosacral area, particularly in patients of African or Asian descent patients; can fade by 2 years of age but can persist to adulthood
Port wine stains	Capillary malformation (Image D); presents at birth and generally doesn't resolve, although some variants will



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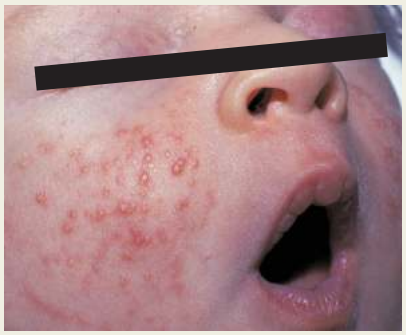

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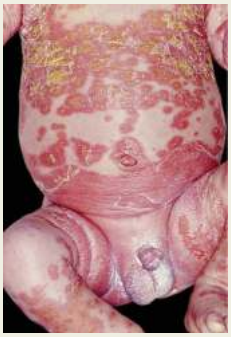

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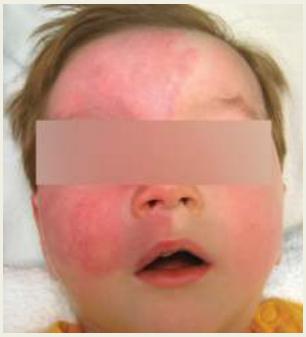

D

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TABLE 16-3. Common Neonatal Respiratory Disorders

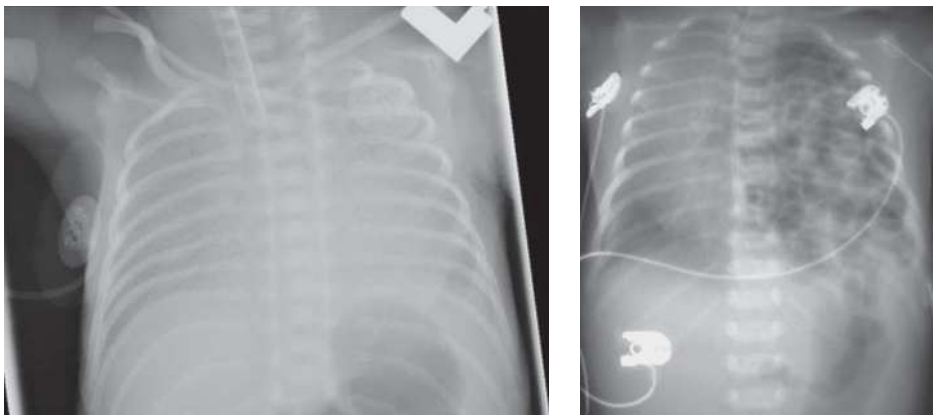
Disorder	Description	History	Exam/CXR Findings	Treatment	Complications
Respiratory distress syndrome/ hyaline membrane disease	Surfactant deficiency leading to poor lung compliance and respiratory failure	Usually occurs in premature infants	Hypoxemia, ↓ air movement; CXR ↓ lung volumes and "ground-glass" appearance (see Figure 16-2A)	Maternal antenatal steroids for prevention; O_2 and CPAP; surfactant administration; respiratory support	Chronic lung disease (BPD), retinopathy of prematurity, intraventricular hemorrhage
Transient tachypnea of the newborn	Retained fetal lung fluid leading to brief, self-resolving, mild respiratory distress; diagnosis of exclusion	Term or near-term infants; nonasphyxiated; born following short labor or via Cesarean delivery without labor	CXR shows perihilar streaking and fluid in interlobar fissures	Usually only a mild to moderate O_2 requirement for support; typically resolves over time	None
Meconium aspiration syndrome	Inhalation of meconium at or near the time of birth leading to aspiration pneumonitis	Term infants; meconium present at the time of delivery	Hypoxia; coarse breath sounds; CXR shows coarse, irregular infiltrates, hyperexpansion (seen by diaphragmatic flattening), and lobar consolidation	Nasopharyngeal suctioning at perineum if vigorous; tracheal suctioning at birth if not vigorous; ventilatory support and antibiotics; nitric oxide if severe pulmonary hypertension	Pulmonary hypertension, pneumothorax, pneumomediastinum; patients can be critically ill, with some even requiring extracorporeal membrane oxygenation (ECMO) support
Congenital diaphragmatic hernia	A defect in the diaphragm leading to herniation of abdominal contents into the chest cavity; limitation of lung growth leading to pulmonary hypoplasia	Severe respiratory distress at birth; may be diagnosed by prenatal ultrasound	Scaphoid abdomen; CXR may show bowel loops in the chest (see Figure 16-2B)	Immediate intubation, placement of NG tube to suction, ventilatory support, and surgical correction after stabilization; patients may require ECMO	Severe pulmonary hypertension; mortality 25–40%

Diagnosis

- All evaluations should include a CBC, a blood culture, a UA and urine culture, and an LP for cerebrospinal fluid (CSF) cell counts, glucose, protein, and culture.
- Workup for HSV should include HSV polymerase chain reaction (PCR) from CSF/skin and LFTs for infants who appear toxic. Workup is also indicated if there is suspicion for first-time HSV infection in a mother during pregnancy.
- Consider a CXR if a patient exhibits hypoxemia, respiratory distress, or clinical findings that raise concern for pneumonia.
- Pneumonia is the most common source of sepsis immediately after birth. Then the chances of meningitis and bacteremia increase after the first 24 hours.

Q

A 3-month-old infant presents to the pediatric ED with a broken left femur. Her parents explain that they had left her alone for only a minute when she "rolled off the living-room couch." In addition to obtaining leg x-rays, what other evaluations would you conduct?



A B

FIGURE 16-2. Neonatal respiratory distress. (**A**) Frontal CXR in a neonate with respiratory distress syndrome showing diffuse fine granular ("ground-glass") opacities and hypoaeration. (**B**) Frontal radiograph in a patient with congenital diaphragmatic hernia, demonstrating air-filled loops of bowel in the left chest and rightward displacement of mediastinal structures. (Image A reproduced with permission from USMLE-Rx.com. Image B reproduced with permission from Brunicardi FC et al. *Schwartz's Principles of Surgery,* 9th ed. New York: McGraw-Hill, 2010, Fig. 39-3.)

KEY FACT

A fever in the first month of life is an indication for a full sepsis workup, admission, and IV antibiotics.

- If the cause of sepsis is a urinary tract infection (UTI), a renal ultrasound and voiding cystourethrography (VCUG) may be obtained to evaluate the infant for hydronephrosis and vesicoureteral reflux.

Treatment

- **Initial treatment:** IV ampicillin to cover *Listeria* plus either gentamicin or a third-generation cephalosporin such as cefotaxime.
- Avoid ceftriaxone in premature infants and infants < 28 days old because it displaces bilirubin from albumin and can cause sequelae of hyperbilirubinemia (eg, kernicterus).
- Consider acyclovir if there is a maternal history of HSV (especially if the mother had her first infection during pregnancy or active lesions at birth) or if the infant appears ill.

KEY FACT

Ampicillin and gentamicin or cefotaxime are generally the antibiotics of choice in neonatal sepsis.

CONGENITAL TORCHES INFECTIONS

Many congenital infections present with jaundice, hepatosplenomegaly, and thrombocytopenia. Table 16-4 outlines the diagnosis and treatment of each.

CONGENITAL ANOMALIES

Table 16-5 outlines the clinical presentation and treatment of common congenital anomalies and malformations.

A

Three-month-old infants rarely roll, and a fall from a couch should not cause a broken femur. Therefore, a full workup should be conducted for medical causes of unusual fractures (eg, osteogenesis imperfecta, nutritional deficiencies) as well as for injuries of abuse. Consider a skeletal survey, an ophthalmologic exam, and head imaging along with hematology labs, liver and pancreatic enzymes, bone labs, electrolytes, and a UA.

TABLE 16-4. ToRCHeS Infections

Infection	Description	Treatment	Prevention
Toxoplasmosis	Hydrocephalus, seizures, chorioretinitis, intracranial calcifications, and ring-enhancing lesions on head CT	Pyrimethamine, sulfadiazine, spiramycin	Avoid exposure to cats and cat feces during pregnancy; avoid raw/undercooked meat; treat women with 1° infection
Rubella	"Blueberry muffin" rash, cataracts, hearing loss, patent ductus arteriosus (PDA) and other cardiac defects, encephalitis	None	Immunize mothers prior to pregnancy
Cytomegalovirus (CMV)	Petechial rash, periventricular calcifications, microcephaly, chorioretinitis	Ganciclovir	Avoid exposure
Herpes simplex (HSV)	Skin, eye, and mouth vesicles; can progress to severe CNS/systemic infection	Acyclovir	Perform Cesarean delivery if birthing mother has active lesions The highest risk is from mothers with 1° infection
Syphilis	Maculopapular skin rash on the palms and soles, lymphadenopathy, "snuffles," osteitis	Penicillin	Treat seropositive mothers with penicillin

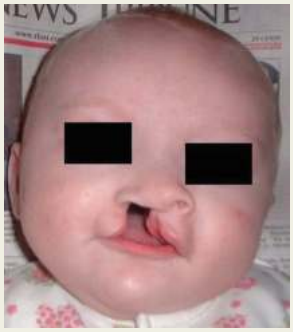
TABLE 16-5. Common Congenital Anomalies and Malformations

Lesion	Description	History/PE	Treatment
Cleft lip/palate	Abnormal ridge/division of the lip and/or palate (Image A)	Presents at birth Poor feeding; aspiration; severe, recurrent otitis media May be associated with other anomalies	Surgical repair of the lip/palate
Tracheoesophageal fistula	Five types; a blind esophageal pouch with a fistula between the distal esophagus and trachea the most common (Image B)	Apparent within first hours of life or presents later in infancy Copious secretions, choking/coughing with feeds, cyanosis, respiratory distress/aspiration "Can't pass NG tube"	Suctioning of the pouch with an NG tube; reflux precautions; supportive care; surgical repair
Abdominal wall defects	Omphalocele (Image C, a membrane-covered herniation of abdominal contents) Gastroschisis (Image D, extrusion of the intestine through the defect)	A visible defect seen antenatally or at birth Associated anomalies are common with omphalocele but are rare in gastroschisis	Coverage of abdominal contents with moist sterile dressing NG decompressions, antibiotics, supportive care, and stabilization followed by 1° or staged closure
Intestinal atresias	Intestinal obstruction With Down syndrome, "double bubble" appearance of the duodenal bulb (1) and stomach (2) in duodenal atresia (Image E)	Present antenatally or at birth Abdominal distention, bilious vomiting, obstipation/failure to pass meconium, polyhydramnios	Surgical resection

(continues)

TABLE 16-5. Common Congenital Anomalies and Malformations *(continued)*

Lesion	Description	History/PE	Treatment
Hirschsprung disease	Absence of ganglion cells in the colon (on rectal suction biopsy) leading to narrowing of the aganglionic segment with dilation of the proximal normal colon; can be a short (75%) or long segment	Usually presents within first 2 years of life Failure to pass meconium, vomiting, abdominal distention, chronic constipation Region of marked dilation superior to the aganglionic segment shown via barium enema	Rectal irrigation for decompression A staged procedure with an initial diverting colostomy followed by resection when the infant is > 6 months of age
Neural tube defects	Include anencephaly (incompatible with life) and spina bifida (eg, myelomeningocele) (Image F, arrowheads indicate nerve roots within the anechoic herniated sac. The arrow shows overlying skin visible above the level of the spinal defect but abruptly stops at the defect)	May be detected prenatally Associated with ↑ maternal age and amniotic fluid α-fetoprotein Varies depending on the type of defect Associated with an ↑ risk of latex allergy	Risk ↓ with folate ingestion during the first trimester Surgical repair
Branchial cleft cysts	Most common congenital neck mass	Presents in late childhood/early adulthood when it becomes infected (often with fistula formation and drainage)	Surgical excision
Thyroglossal duct cysts	Midline lesion of the anterior neck that moves with swallowing	Most present during childhood with acute viral infection	Complete excision, which usually requires part of the hyoid bone; can recur with incomplete excision



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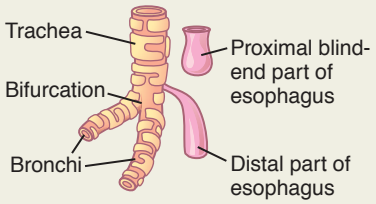

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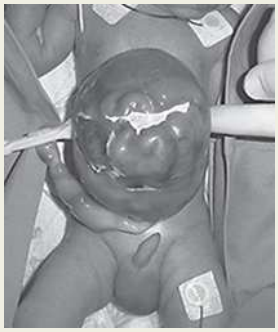

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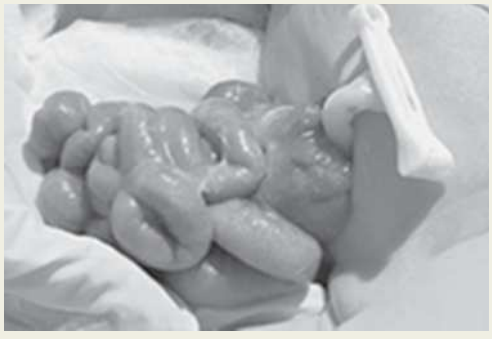

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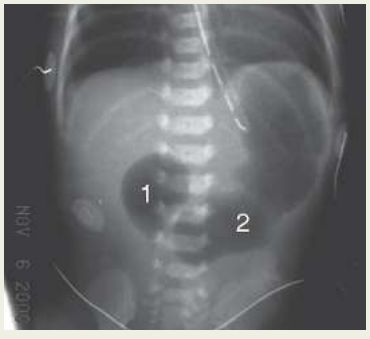

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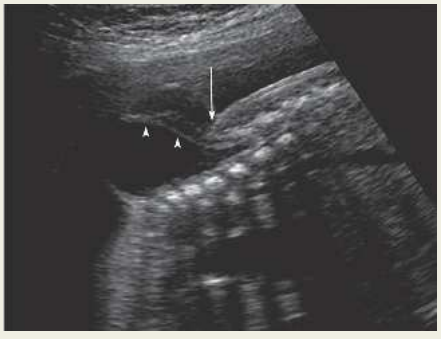

F

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JAUNDICE

Physiologic Jaundice

Nearly all babies have some form of indirect (unconjugated) hyperbilirubinemia, commonly known as physiologic jaundice. Causes include:

- ↑ RBC breakdown.
- ↓ Bilirubin breakdown due to ↓ conjugation in the immature liver and lack of appropriate bacterial components in the intestines.
- ↓ Excretion due to less frequent stooling and urination.

History/PE

- Physiologic jaundice usually presents in the first 36–48 hours of life and reaches peak total bilirubin levels of 10–15 mg/dL at 5–7 days of life.
- Visible jaundice starts at the head (or eyes) and travels down the body as bilirubin levels ↑.
- Initial evaluation should include both total and direct bilirubin to establish whether the hyperbilirubinemia is direct or indirect.
- **Risk factors:** Mother's blood type O negative, birth trauma, Asian descent, preterm.

Treatment

- ↑ **Feeding:** Most normal babies will be able to excrete bilirubin on their own with time, additional intake, and improved intestinal motility from the gastrocolic reflex.
- **Phototherapy:** Modifies the bilirubin molecule into a water-soluble form that can be more easily excreted as long as it is indirect hyperbilirubinemia.
- Exchange transfusion is indicated for severe jaundice.
- Serum bilirubin levels should be trended during treatment for hyperbilirubinemia.

Breastfeeding Failure and Breast Milk Jaundice

Breastfeeding failure jaundice: Occurs in exclusively breastfed newborns as a result of ineffective breastfeeding (poor latch, low maternal milk production).

- **Hx/PE:** Typically presents in the first week of life with bilirubin levels greater than those seen with physiologic jaundice.
- **Dx:** Made with a good history in the setting of an exclusively breastfed newborn. May help to look at degree of weight loss in the infant and to have a lactation specialist observe and evaluate quality of breastfeeding.
- **Tx:** Assistance with improvement of breastfeeding. Preference is to preserve exclusive breastfeeding per mother's desires but may need to supplement with formula if weight loss and jaundice continue. Phototherapy initiated if bilirubin reaches light levels on the phototherapy nomogram.

Breast milk jaundice: Delay in hepatic bilirubin conjugation that can prolong jaundice in newborns.

- **Hx/PE:** Presents after the first 3–5 days of life and peaks at 2 weeks of age. Total bilirubin levels may reach 19–20 mg/dL and may persist for 1–2 months.
- **Dx:** A diagnosis of exclusion.
- **Tx:** Rarely requires phototherapy. Breastfeeding should be encouraged, as the problem will resolve without treatment.

KEY FACT

Breastfeeding failure jaundice occurs chronologically before breast milk jaundice because ineffective breastfeeding typically becomes apparent sooner. In both instances, encourage continuation of breastfeeding.

Pathologic Jaundice

Jaundice is considered pathologic if it is severe or prolonged, occurs within the first 24 hours of life, or is associated with ↑ direct (conjugated) bilirubin. A direct bilirubin of > 10% or 2 mg/dL of the total suggests a hepatobiliary or general metabolic disorder. Very high levels of unconjugated bilirubin (> 30 mg/dL) can cross the blood-brain barrier and deposit in the basal ganglia, causing kernicterus, an irreversible, potentially fatal encephalopathy.

- Causes of pathologic indirect hyperbilirubinemia include:
  - ↑ **Bilirubin production:** Hemolysis, sepsis, severe bruising/hematoma.
  - **Bilirubin conjugation abnormalities:** Hepatic enzyme deficiencies, hepatic dysfunction.
  - **Bilirubin excretion abnormalities:** Intestinal obstruction, poor motility.
- Causes of pathologic direct hyperbilirubinemia include:
  - **Intrahepatic:** Biliary obstruction/atresia (most common), choledochal cysts, neonatal hepatitis, Dubin-Johnson syndrome, Rotor syndrome, Alagille syndrome, α_1-antitrypsin deficiency, total parental nutrition [TPN] cholestasis (affects premature infants on TPN). See also Table 16-6.
  - **Extrahepatic:** Sepsis, UTIs, hypothyroidism, CF, inborn errors of metabolism, RBC abnormalities such as sickle cell disease or hereditary spherocytosis.

KEY FACT

Remember that a direct bilirubin of > 10% or 2 mg/dL of total bilirubin points to a hepatobiliary or general metabolic disorder.

History/PE

- Look for hepatomegaly, acholic (pale to white) stools, signs of anemia or plethora, evidence of sepsis, growth abnormalities, and congenital abnormalities.
- Kernicterus (usually caused by extremely high levels of indirect hyperbilirubinemia) presents with jaundice, lethargy, poor feeding, a high-pitched cry, hypertonicity, and seizures.

KEY FACT

The aim of bilirubin screening is to prevent kernicterus, which results from irreversible deposition of bilirubin in the basal ganglia and brainstem nuclei and requires emergent exchange transfusion.

Diagnosis

- Order a CBC (to assess for anemia), a reticulocyte count, and a peripheral blood smear (to rule out hemolysis).
- A Coombs test can distinguish antibody-mediated disease (eg, ABO incompatibility) from non–immune-related disorders (eg, G6PD deficiency, hereditary spherocytosis).

TABLE 16-6. Common Intrahepatic Causes of Hyperbilirubinemia

	Characteristics	History/PE	Treatment
Gilbert syndrome	The most common inherited disorder of bilirubin glucuronidation (see Figure 16-3); due to a defect in UGT1A1 Presentation in adolescence due to hormonal changes; rarely diagnosed before puberty	Repeated episodes of jaundice with stressors such as illness, fever, dehydration, and fasting Asymptomatic	None
Crigler-Najjar syndrome	Abnormal functioning of the bilirubin-UGT enzyme	↑ Unconjugated bilirubin; normal hepatic enzymes Patients typically have persistent hyperbilirubinemia despite treatment with phototherapy and plasmapheresis	Liver transplantation is the only curative therapy

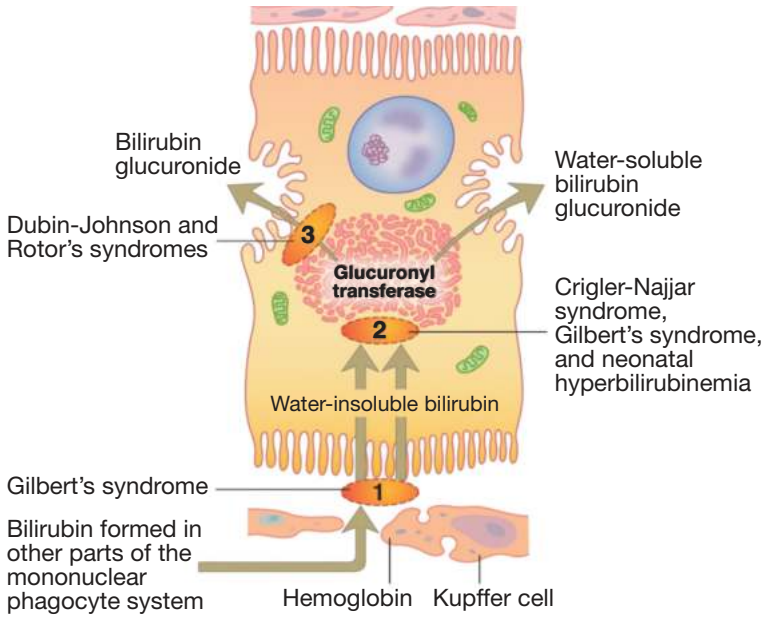


FIGURE 16-3. Bilirubin metabolism. (Reproduced with permission from USMLE-Rx.com.)

- Additional testing should be guided by the patient's history and physical with a focus on maternal pregnancy history, family history, and concerns for infection and feeding.

Treatment

- Phototherapy and, rarely, exchange transfusion.
- Treat associated conditions (eg, hemolysis, sepsis, hypothyroidism, biliary obstruction).

Dermatology

Common dermatologic conditions in children include diaper dermatitis, viral exnthems, and eczema (atopic dermatitis)—discussed in the Ambulatory Medicine chapter.

DIAPER DERMATITIS ("DIAPER RASH")

The skin of the buttocks, groin, and mons pubis is in a moist, warm environment with frequent exposure to bacteria from stool and acidic urine, resulting in skin irritation and barrier disruption. Subtypes include:

- **Irritant diaper dermatitis:** Erythema and skin breakdown where the diaper contacts the skin (classically can avoid skin folds). It generally results from prolonged contact with urine or stool. Treat with frequent diaper changes, cleansing with soap and water, and use of barrier creams or lubricants to protect the skin from contact exposure.
- **Candidal diaper dermatitis:** Bright red, well-demarcated papules and pustules with satellite lesions, often in skin folds. Consider in the presence of antibiotic use, oral thrush, or diaper dermatitis that is unresponsive to symptomatic treatment. Treat with topical antifungals, keeping the area clean and dry, and use of barrier creams.

VIRAL EXANTHEMS

Table 16-7 describes several classic viral exanthems, their infectious agents, and typical presentations and treatment.

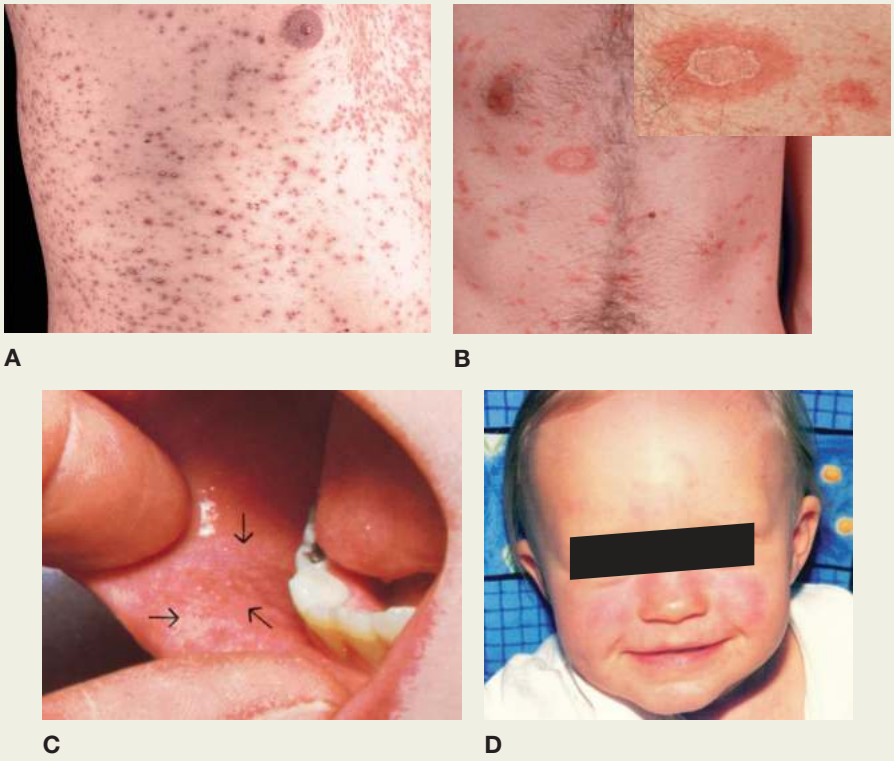
TABLE 16-7. Classic Childhood Viral Exanthems

Exanthem	Presentation	Epidemiology/Complications	Treatment
Varicella-zoster virus (VZV)	Typically appear as pruritic vesicles on an erythematous base in multiple stages of eruption and healing (Image A)	VZV is uncommon owing to vaccination; it most often occurs in immunosuppressed and unvaccinated patients Complications: Systemic viremia or bacterial superinfection can occur	Consider VZIG for immunocompromised patients who are exposed Prevent with vaccination
Pityriasis rosea	Often begins with a "herald patch," a large, salmon-colored, scaly lesion (Image B), followed 5–10 days later by lesions, especially on the trunk running along Blaschko lines in a "Christmas tree" distribution		Supportive care; may improve more rapidly with UV light Resolves in weeks to months
Rubeola (measles virus)	Fever with the 3 C's—Cough, Coryza, and Conjunctivitis—and Koplik spots (Image C) Erythematous papules start 2–4 days later on the face and spread downward	Complications: Pneumonia, gastroenteritis, myocarditis, and encephalitis	Consider vitamin A supplementation in patients with malnutrition or malabsorptive states as measles can increase risk of deficiency Prevent with vaccination
Erythema infectiosum, also called fifth disease (Parvovirus B19)	Presents with fever, chills, and headache followed 2–3 days later by the development of a "slapped cheek" appearance with a flat, erythematous rash on the cheeks (Image D); evolves to a lacy rash on the trunk and legs lasting 2–3 weeks		Provide supportive care
Roseola (HHV-6 or -7)	Begins as poorly defined erythematous macules and papules on the chest and spreads outward Classic presentation includes high, spiking fevers lasting 3–5 days, followed by a rash developing after fever has resolved or is resolving	Complications: The first febrile seizures may be associated with infection; encephalitis	Provide supportive care
Mumps (Mumps virus)	Fever, malaise, headache, and anorexia; affects glands and neural tissue Commonly recognized by parotid swelling	May result in orchitis or meningoencephalitis	Provide supportive care Prevent with vaccination

(continues)

TABLE 16-7. Classic Childhood Viral Exanthems *(continued)*

Exanthem	Presentation	Epidemiology/Complications	Treatment
Hand-foot-and-mouth disease (Coxsackievirus)	Begins with fever, malaise, and ↓ appetite followed 1–2 days later by painful oval vesicles on an erythematous base in the mouth and on the palms and soles of the feet		Provide supportive care; it resolves in 7–10 days



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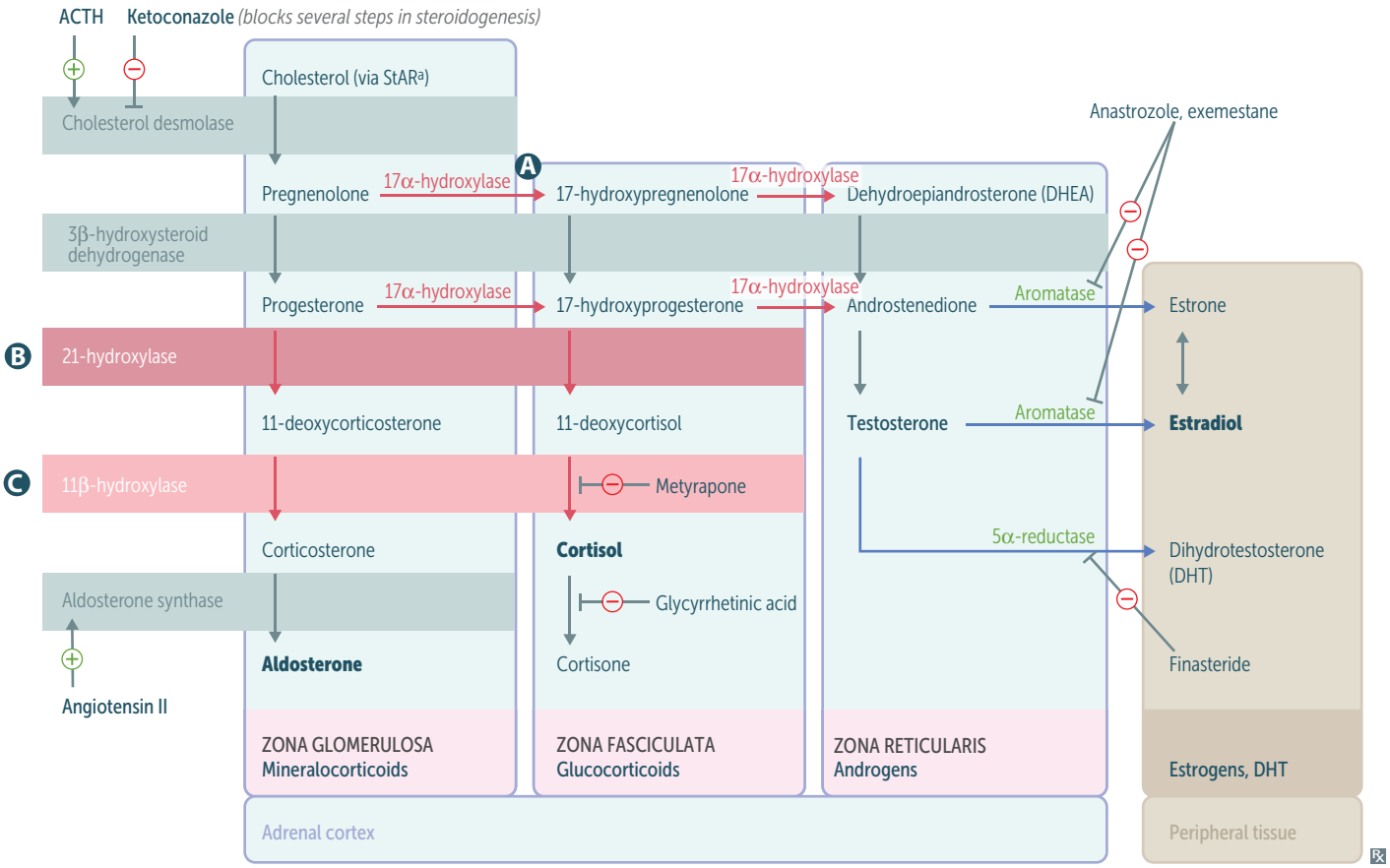
Endocrinology

CONGENITAL ADRENAL HYPERPLASIA

A group of disorders caused by a defect in one or more of the enzymes required for glucocorticoid, mineralocorticoid, and androgen synthesis. These defects lead to overproduction of the precursors in the pathway and to an excess of adrenocorticotropic hormone (ACTH) as the body attempts to stimulate the adrenal gland. The most common defect, which accounts for 90–95% of all cases, is in the 21-hydroxylase enzyme (see below). Deficiency in the 21-hydroxylase enzyme classically causes buildup of 17-hydroxyprogesterone (17-OHP). Defects in 11β-hydroxylase and 17α-hydroxylase, as well as other enzymes in the pathway for adrenal steroid synthesis, are less common (see Figure 16-4).



[a]Rate-limiting step.

FIGURE 16-4. Congenital adrenal hyperplasia. (Reproduced with permission from USMLE-Rx.com.)

History/PE

- **Classic form of 21-hydroxylase deficiency:** More severe than the nonclassic form. Has two variants—salt-losing (secondary to aldosterone deficiency) and non–salt-losing congenital adrenal hyperplasia (CAH).
  - **Girls with either variant:** Present as infants with ambiguous genitalia.
  - **Boys with the salt-losing variant:** Present in the first 1–2 weeks of life with hyponatremia, hyperkalemia, dehydration, and FTT.
  - **Boys with the non–salt-losing variant:** Present at 2–4 years of age with early virilization (development of pubic hair, adult body odor, and a growth spurt).
- **Nonclassic (mild) form of 21-hydroxylase deficiency:** Typically presents later in life with signs of excess androgen production—hirsutism, acne, early pubarche, irregular menses, and premature closure of the physes.

KEY FACT

Children with CAH can have an adrenal crisis with any stressor, including illness or surgery. Presenting symptoms can be fatigue, altered mental status, poor feeding, vomiting, abdominal pain, hypothermia, hypotension, or electrolyte abnormalities. Crisis is treated with stress-dose steroids.

Treatment

- **Symptom control:**
  - **Glucocorticoid replacement:** Hydrocortisone in infants and younger children; dexamethasone or prednisone in older adolescents.
  - **Mineralocorticoid replacement:** Fludrocortisone.
- **Monitoring:**
  - Serum levels of 17-OHP, androstenedione, and plasma renin activity.
  - Bone-age films and growth/development (especially height).

PUBERTY AND ABNORMAL PUBERTAL DEVELOPMENT

Normal Puberty

- **Boys:** Physical pubertal changes mostly begin at 10–13 years of age. Enlargement of testes → pubic hair and penile growth → growth spurt.
- **Girls:** Physical pubertal changes begin at 9–12 years of age. Breast development → growth spurt → menarche.

Delayed Puberty

The delay or absence of the physical pubertal changes mentioned above by age 14 in boys and age 13 in girls. Axillary and pubic hair development may be noted despite delay because it is not associated with the hypothalamic-pituitary-gonadal (HPG) axis.

- Puberty delay in boys:
  - **Constitutional delayed puberty:** More common in boys. Has genetic component. Concomitant with bone-age delay—will undergo puberty, but later in adolescence (15–17 years of age).
  - **Other causes:** Rare, generally present after 17 years of age, include isolated gonadotropin deficiency (low to nonexistent levels of gonadotropin-releasing hormone [GnRH], luteinizing hormone [LH], and follicle-stimulating hormone [FSH]); primary gonadal failure (hypergonadotropic hypogonadism) suspected with history of prior testicular malignancy with radiation, cryptorchidism, or testicular torsion, ↑ GnRH; and Klinefelter syndrome.
- **Puberty delay in girls:**
  - **Constitutional delayed puberty:** Suspect if one parent with history of pubertal delay in an otherwise healthy 13–15-year-old girl with no pubertal development; concomitant with bone-age delay.
  - **Functional gonadotropin deficiency:** ↓ GnRH, LH, and FSH; seen with anorexia nervosa, excessive exercise, as part of the athletic triad, and in girls who have very little body fat for other reasons (ie, chronic disease).
  - **Primary ovarian failure (hypergonadotropic hypogonadism):** ↑ GnRH; always consider Turner syndrome, autoimmune disorder affecting the ovaries, or treatment for malignancy including radiation and chemotherapy.

Precocious Puberty

Defined as the development of 2° sex characteristics before age 8 in girls and age 9 in boys.

- **Gonadotropin-dependent precocious puberty (GDPP):** Presents as normal development but early puberty 2° to early activation of the HPG axis. ~ 80% of cases are idiopathic. Other etiologies include CNS lesions; therefore, GDPP patients require brain imaging (CT or MRI).
- **Gonadotropin-independent precocious puberty (GIPP):** Interruption of normal sequence of development 2° to the presence of sex hormones outside of HPG axis sequence. Possible causes include exogenous estrogen/testosterone, CAH, and McCune-Albright syndrome. Hormone-secreting tumors are also a possibility: ovarian tumors, Leydig cell tumors, adrenal androgen-secreting tumors, pituitary gonadotropin-secreting tumors.

Q

A 10-day-old male infant is brought to the clinic because he is "acting funny." He is lethargic with poor skin turgor, a sunken fontanelle, and dry lips. His growth curve reveals that he is < 10% below his birth weight despite frequent breastfeeding with good latch. Labs show hyponatremia and hyperkalemia. Beyond evaluating for sepsis, which labs should you consider?

Diagnosis

Determine bone age with x-rays of the hand and wrist.

- **General diagnosis:** Determine serum estradiol or testosterone level; 17-hydroxyprogesterone (17-OHP); basal and GnRH-stimulated LH; dehydroepiandrosterone.
  - **GDPP** would show prepubertal LH and FSH levels with appropriate pubertal response to GnRH stimulation test.
  - **GIPP** would show low FSH and LH from feedback inhibition from steroids outside of HPG axis. Similarly, GnRH stimulation would produce suppressed response.
- **Specific diagnosis** with GIPP can be sought with other labs (estradiol in ovarian tumors, ↑ androgen metabolites in CAH and androgen-secreting tumors, etc.).

Treatment

- **GDPP:** GnRH agonists used to ensure patients reach the projected height or rate of development.
- **GIPP:** Does not respond to GnRH agonists; treatment depends on the etiology.

Infectious Disease

FEVER WITHOUT A SOURCE

Approximately 20% of children with fever do not have signs or symptoms of a bacterial or viral infection on history or exam. Fever without a source (FWS) is a concern because it may represent an occult serious bacterial infection (SBI).

Diagnosis

- The concern for SBI, and therefore the recommended workup for FWS, is age dependent.
  - **0–90 days:** See the discussion of neonatal sepsis.
  - **3–36 months:** If infants in this age group have been vaccinated and appear well, the risk of bacteremia and/or meningitis is low. Consider a UA and urine culture. If unvaccinated, obtain a CBC and a blood culture. Obtain a blood culture and treat with ceftriaxone if the WBC count is > 15.
- UTI is the most common bacterial cause of FWS. In infants < 3 months of age, uncircumcised boys are at highest risk. Among infants > 3 months of age, Caucasian girls are at highest risk.
- Children < 2 months of age with their first UTI do not require VCUG unless renal and bladder ultrasounds show abnormal findings, eg, those suggestive of vesicoureteral reflux (see Figure 16-5).
- Significant debate exists in the literature and in practice regarding the utility of VCUG in the setting of a first febrile UTI in children > 2 months of age.

A

In this setting, congenital adrenal hyperplasia must be considered, and 17-hydroxyprogesterone and androstenedione levels must be sent. The newborn screen should also be reviewed to ensure that other metabolic disorders are not missed.

MENINGITIS

Inflammation of the meninges. May be bacterial, viral, or fungal. Most children are infected with viruses; however, it is estimated that > 75% of bacterial

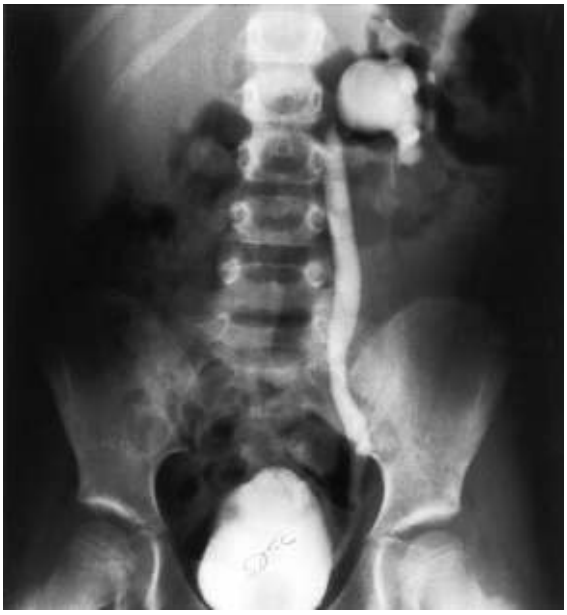


FIGURE 16-5. Vesicoureteral reflux. Frontal radiograph from a voiding cystourethrogram shows reflux to the left ureter and intrarenal collecting system with hydronephrosis. Note the absence of reflux on the normal right side. (Reproduced with permission from Doherty GM. *Current Diagnosis & Treatment: Surgery,* 13th ed. New York: McGraw-Hill, 2010, Fig. 38-7.)

meningitis cases occur in children < 5 years of age. More than 90% of bacterial etiologies are 2° to *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae*.

History/PE

- Infants and children < 1 year of age may present with nondistinct symptoms such as irritability, vomiting, poor feeding, hypo- or hyperthermia, apnea, lethargy, and seizure activity.
- Older children may demonstrate similar symptoms but may also present with photosensitivity, headache, and neck stiffness, although these symptoms may be difficult to elicit depending on the child's age and cooperation with the examiner. Older children may also exhibit signs and symptoms commonly seen in adults, including ⊕ Kernig and Brudzinski signs.
- Children with Lyme and bacterial meningitis may demonstrate cranial nerve palsies.

Diagnosis

- Depending on the clinical presentation and history, consider a CT scan if there is concern for intracranial bleeding, ↑ intracranial pressure, or trauma.
- Blood tests include a CBC, a chemistry panel that includes serum sodium and glucose levels, a blood culture, and a UA and urine culture. Serum sodium is important in view of risk of hyponatremia 2° to syndrome of inappropriate secretion of antidiuretic hormone (SIADH). Serum glucose is used as a direct comparison to CSF glucose measurement. Consider full-panel sepsis labs.
- Additional tests include lumbar puncture (LP) with CSF analysis to examine the color of the supernatant, cell counts with differential, protein, glucose, microscopic evaluation, and bacterial culture. Table 16-8 describes

TABLE 16-8. CSF Findings in Normal, Infectious, and Inflammatory Conditions

CSF	Initial Pressure (mm H_2O)	Appearance	Cells/μL	Protein (mg/dL)
Normal	< 160	Clear	0–5 lymphocytes; first 3 months, 1–3 polymorphonuclear leukocytes (PMNs); neonates, up to 30 lymphocytes, rare RBCs	15–35 (lumbar), 5–15 (ventricular); up to 150 (lumbar) for a short time after birth; to 6 months up to 65
Bloody tap	Normal or ↓	Bloody (sometimes with clot)	One additional WBC/700 RBCs[b]	One additional milligram per 800 RBCs[b]
Bacterial meningitis, acute	200–750+	Opalescent to purulent	Up to thousands, mostly PMNs; early, few cells	Up to hundreds
Bacterial meningitis, partially treated	Usually ↑	Clear or opalescent	Usually ↑; PMNs usually predominate	↑
Tuberculous meningitis	150–750+	Opalescent; fibrin web or pellicle	250–500, mostly lymphocytes; early, ↑ PMNs	45–500; parallels cell count; ↑ over time
Fungal meningitis	↑	Variable; often clear	10–500; early, ↑ PMNs; then mostly lymphocytes	Elevated and increasing
Aseptic meningoencephalitis	Normal or slightly ↑	Clear unless cell count > 300/μL	None to a few hundred, mostly lymphocytes; PMNs predominate early	20–125
Parainfectious encephalomyelitis	80–450, usually ↑	Usually clear	0–50+, mostly lymphocytes; lower numbers, even 0, in MS	15–75
Polyneuritis	Normal and occasionally ↑	Early: normal; late: xanthochromic if protein ↑	Normal; occasionally slight ↑	Early: normal; late: 45–1500

[a]*CSF-IgG index*, (CSF IgG/serum IgG)/(CSF albumin/serum albumin).

[b]Many studies document pitfalls in using these ratios due to WBC lysis. Clinical judgment and repeat LPs may be necessary to rule out meningitis in this situation.

[c]*CSF WBC* (predicated), CSF RBC × (blood WBC/blood RBC); *O:P ratio*, (observed CSF WBC)/(predicted CSF WBC). Also do WBC:RBC ratio. If O:P ratio ≤ 0.01 and WBC:RBC ratio ≤ 1:100, meningitis is absent.

Adapted with permission from Stone CK, Humphries RL. *Current Diagnosis & Treatment: Emergency Medicine,* 7th ed. New York: McGraw-Hill, 2011, Table 50-14.

Glucose (mg/dL)	Other Tests	Comments
50–80 (two-thirds of blood glucose); may be ↑ after seizure	CSF-IgG index < 0.7[a]; LDH 2–27 U/L	CSF protein in the first month may be up to 170 mg/dL in small-for-date or premature infants; no ↑ in WBCs due to seizure
Normal	RBC number should ↓ between the first and third tubes; wait 5 minutes between tubes	Spin down fluid; supernatant will be clear and colorless[c]
↓; May be none	Smear and culture are mandatory; LDH > 24 U/L; lactate, IL-8, TNF ↑, correlate with prognosis	Very early, glucose may be normal; PCR meningococci and pneumococci in plasma; CSF may aid diagnosis
Normal or ↓	LDH usually > 24 U/L; PCR may still be ⊕	Smear and culture may be ⊖ if antibiotics have been used
↓; May be none	Smear for acid-fast organisms; CSF culture and inoculation; PCR	Consider AIDS, a common comorbidity of TB
↓	India ink preparations, cryptococcal antigen, PCR, culture, inoculations, immunofluorescence tests	Often superimposed in patients who are debilitated or on immunosuppressive therapy
Normal; may be ↓ in mumps, HSV, or other viral infections	CSF, stool, blood, throat washings for viral cultures; LDH < 28 U/L; PCR for HSV, CMV, EBV, enterovirus, etc	Acute and convalescent antibody titers for some viruses; in mumps, up to 1000 lymphocytes; serum amylase often ↑; up to 1000 cells present in enteroviral infection
Normal	CSF-IgG index, oligoclonal bands variable; in MS, moderate ↑	No organisms; fulminant cases resemble bacterial meningitis
Normal	CSF-IgG index may be ↑; oligoclonal bands variable	Try to find cause (eg, viral infections, toxins, lupus, diabetes)

Q

An 11-month-old, fully immunized girl presents to urgent care with a fever of 39.2°C (102.6°F). She is non–toxic appearing and, although irritable, is consolable with an otherwise unremarkable exam. What workup, if any, should be performed for this child?

common characteristics of CSF findings in various infectious and inflammatory states.
- Consider viral PCR testing (including HSV and enteroviruses), encephalitis panels, and fungal cultures depending on clinical presentation and risk factors.

Immunology

IMMUNODEFICIENCY SYNDROMES

Present as recurrent or severe infections. In general, the frequency is roughly 1 in 10,000. Table 16-9 outlines the clinical presentation, diagnosis, and treatment of common pediatric immunodeficiency disorders.

KAWASAKI DISEASE (MUCOCUTANEOUS LYMPH NODE SYNDROME)

A relatively common medium-vessel vasculitis of childhood that predisposes to coronary artery aneurysms and to the subsequent development of myocardial ischemia. It is more common in children < 5 years of age and among those of Asian, particularly Japanese, ethnicity.

History/PE

Presents as an acute illness characterized by the symptoms outlined in the **CRASH and BURN** mnemonic. Children tend to be highly irritable.

Diagnosis

- Diagnosis is clinical.
- Patients must have fever for > 5 days and meet four to five of the following criteria: Conjunctivitis, rash, at least one cervical node > 1 cm, oropharyngeal mucosal changes, hand/foot swelling, and/or desquamation.
- Occasional findings include arthritis, scrotal swelling, pericarditis, and gallbladder inflammation.
- Labs may reveal sterile pyuria on clean-catch urine (catheterization bypasses the urethral origin of pyuria), ↑ erythrocyte sedimentation rate (ESR)/C-reactive protein (CRP), thrombocytosis, ↑ transaminases, hypoalbuminemia, and hyponatremia.
- Echocardiography may reveal coronary artery aneurysms.

Treatment

- Give high-dose aspirin during the acute phase for its anti-inflammatory properties and to ↓ the risk of thrombosis.
- Administer intravenous immunoglobulin (IVIG) to prevent coronary artery aneurysms (given as a single infusion within the first 7–10 days of illness; repeat if the patient is still febrile 24 hours later).
- During the convalescent phase, switch to low-dose aspirin for its antiplatelet effect.
- Follow patients with repeated echocardiography and cardiology follow-up.

Complications

Myocarditis, pericarditis, coronary artery aneurysm predisposing to myocardial ischemia.

MNEMONIC

Kawasaki symptoms—

CRASH and BURN

Conjunctivitis (bilateral, limbic sparing, nonpurulent)
Rash
Adenopathy (at least one cervical node > 1 cm)
Strawberry tongue (or any change in oropharyngeal mucosa, including an injected pharynx or lip fissuring)
Hand/foot swelling and/or desquamation
BURN (fever for > 5 days)

KEY FACT

Aspirin is typically avoided in children due to the risk of Reye syndrome; however, Kawasaki syndrome is an important exception where aspirin's benefits outweigh the risks.

A

Aside from her fever and irritability, the child is asymptomatic (ie, she has a fever without an obvious source). In this age group, UTI must be considered. Labs include a UA with culture, a CBC with differential, and a blood culture. LP with CSF analysis should be considered if the patient appears ill or exhibits changes in mental status.

TABLE 16-9. Pediatric B-Cell and T-Cell Deficiencies

Disorder	Description	Infection Risk/Type	Diagnosis/Treatment
		B-Cell Disorders	
Bruton agammaglobulinemia	An X-linked recessive B-cell deficiency found only in boys Symptoms beginning after 6 months of age, when maternal IgG (transferred transplacentally) is no longer active	Life-threatening; characterized by encapsulated *Pseudomonas, S pneumoniae,* and *Haemophilus* infections after 6 months of age	Quantitative Ig levels: if low, confirm with B- and T-cell subsets (B cells are absent; T cells are often high) Absent tonsils and other lymphoid tissue may provide a clue Treat with prophylactic antibiotics and IVIG
Common variable immunodeficiency (CVID)	Usually a combined B- and T-cell defect All Ig levels low (in the 20s and 30s) Normal B-cell numbers; ↓ plasma cells Symptoms usually present later in life (15–35 years of age)	↑ Pyogenic upper and lower respiratory infections ↑ Risk of lymphoma and autoimmune disease	Quantitative Ig levels; confirm with B- and T-cell subsets Treat with IVIG
IgA deficiency	Mild; the most common immunodeficiency ↓ IgA levels only	Usually asymptomatic; patients may develop recurrent respiratory or GI infections (*Giardia*) Anaphylactic transfusion reaction due to anti-IgA antibodies is a common presentation	Quantitative IgA levels; treat infections Be careful giving IVIG, as it can lead to the production of anti-IgA antibodies and cause severe allergic reactions; if IVIG is necessary, give IgA-depleted IVI
Hyper-IgM Syndrome	Absence of CD40 ligand that allows class-switching from IgM to other Ig classes ↑ IgM levels, low levels of all other Ig, and normal numbers of lymphocytes	Severe, recurrent sinopulmonary infections due to impaired Ig	↑ Treat with antibiotic prophylaxis and IVIG
		T-Cell Disorders	
Thymic aplasia (DiGeorge syndrome)	See the mnemonic CATCH 22 Presents with tetany (2° to hypocalcemia) in the first days of life Autosomal dominant	Variable risk of infection ↑↑↑ Infections with viruses, fungi, and PCP pneumonia X-ray film may show absent thymic shadow	Absolute T-lymphocyte count; mitogen stimulation response; delayed hypersensitivity skin testing Treat with bone marrow transplantation and IVIG for antibody deficiency; give PCP prophylaxis. Thymus transplantation is an alternative

(continues)

TABLE 16-9. Pediatric B-Cell and T-Cell Deficiencies *(continued)*

Disorder	Description	Infection Risk/Type	Diagnosis/Treatment
		Combined Disorders	
Ataxia-telangiectasia	Progressive cerebellar ataxia and oculocutaneous telangiectasias Caused by an autosomal recessive mutation in gene responsible for repair of dsDNA breaks	↑ Incidence of malignancies, including non-Hodgkin lymphoma, leukemia, and gastric carcinoma	No specific treatment; may require IVIG depending on the severity of the Ig deficiency
Severe combined immunodeficiency (SCID)	Most commonly X-linked recessive Severe lack of B and T cells due to a defect in stem cell maturation and ↓ adenosine deaminase Referred to as "bubble boy disease," because children are confined to an isolated, sterile environment	Severe, frequent bacterial infections; chronic candidiasis; opportunistic organisms	Bone marrow or stem cell transplantation and IVIG for antibody deficiency Requires PCP prophylaxis
Wiskott-Aldrich syndrome	An X-linked recessive disorder seen only in male patients Symptoms usually present at birth ↑ IgE/IgA, ↓ IgM, and thrombocytopenia The classic presentation involves bleeding, eczema, and recurrent otitis media Remember the mnemonic **WIPE:** **W**iskott-Aldrich **I**nfections **P**urpura (thrombocytopenic) **E**czema	↑↑ Risk of atopic disorders, lymphoma/leukemia, and infection from *S pneumoniae, S aureus,* and *H influenzae* type b (encapsulated organisms; think back to how IgM functions)	Treatment is supportive (IVIG and antibiotics) Patients are at higher risk for developing autoimmune diseases and malignancies Patients rarely survive to adulthood Patients with severe infections may be treated with bone marrow transplantation

Adapted with permission from Le T et al. *First Aid for the USMLE Step 2 CK,* 10th ed. New York: McGraw-Hill, 2019:416.

Rheumatology

JUVENILE IDIOPATHIC ARTHRITIS

Diagnosed after > 6 weeks of arthritis symptoms after all other etiologies of childhood arthritides (eg, inflammatory bowel disease) have been excluded. Classified on the basis of several factors:

- Age of symptom onset.
- Number and type of joints involved.
- The presence of other systemic symptoms.
- Clinical course for 6 months after diagnosis.

There are three main categories: systemic, pauciarticular, and polyarticular.

Systemic Juvenile Idiopathic Arthritis

Presents with intermittent fever, rash (macular and salmon-pink), and arthritis (usually of the knees, wrists, and ankles, but can affect other joints as well). Diagnosed in patients < 16 years of age; after this age, it is considered adult-onset Still disease. Affects boys and girls equally.

Diagnosis

- Generally involves workup for infectious processes and leukemia.
- WBC count, ESR, CRP, and platelets are ↑.
- In order for the diagnosis of systemic juvenile idiopathic arthritis (JIA) to be made, the patient must have a daily fever for 2 weeks, typically > 38.5°C (101.3°F), and arthritis. Arthritis may develop after the initial fever and rash.

Treatment

- **First line:** NSAIDs.
- **Second line:** Corticosteroids; nonbiologic disease-modifying antirheumatic drugs (DMARDs) such as methotrexate; biologic DMARDs, including IL-1 and IL-6 inhibitors.
- **Other:** Agents such as thalidomide, IVIG, hydroxychloroquine, sulfasalazine, cyclosporine, and tumor necrosis factor (TNF) inhibitors have been used with varying degrees of success.
- **Course:** The initial episode of JIA may last 4–6 months. Some children will continue to have fever and rash for years. The long-term sequelae vary from none at all to severe destruction requiring joint replacement.

Pauciarticular Juvenile Idiopathic Arthritis

The most common form of JIA; affects girls more often than boys. Also called oligoarticular arthritis. Involves < 5 joints (generally large joints); usually presents at age 2–3.

Diagnosis

Workup for systemic JIA (see above). Patients exhibit antinuclear antibody (ANA) ⊕.

Treatment

- **First line:** NSAIDs and/or glucocorticoids injected into affected joints.
- **Second line:** Methotrexate, TNF inhibitors (rarely used).
- **Course:** Usually resolves within 6 months. More than 50% of patients will not have relapses; however, severe destructive arthritis may occur.

KEY FACT

Patients with pauciarticular or polyarticular JIA are at risk for uveitis and require screening by an ophthalmologist.

Polyarticular Juvenile Idiopathic Arthritis

Involves > 4 joints; affects girls more often than boys. Age of onset is 2–5 years and 10–14 years.

Diagnosis

Workup for systemic JIA (see above). Patients may be positive for ANA and/or rheumatoid factor (RF); lab findings may include anemia, ↑ ESR, and hypergammaglobulinemia.

Treatment

- **First line**: NSAIDs but this is unlikely to yield long-term control when used as a single agent.
- DMARDs such as methotrexate, leflunomide, sulfasalazine, TNF inhibitors, cyclosporine, azathioprine, rituximab, corticosteroids (systemic and injected), and gold compounds should be added early in the course of treatment.
- **Course:** The prognosis is generally better for RF-seronegative patients than for those who are seropositive. RF-seronegative patients often respond to NSAID therapy, whereas seropositive patients require treatment with DMARDs.

Q

A 2-year-old girl presents with fever and cough. She is found to have right lower lobe pneumonia both on exam and on CXR. She has been hospitalized twice—once with mastoiditis at 6 months and again with left-sided pneumonia with empyema and bacteremia at 15 months. Her weight is less than the third percentile for age. In addition to an acute workup, what tests would you consider?

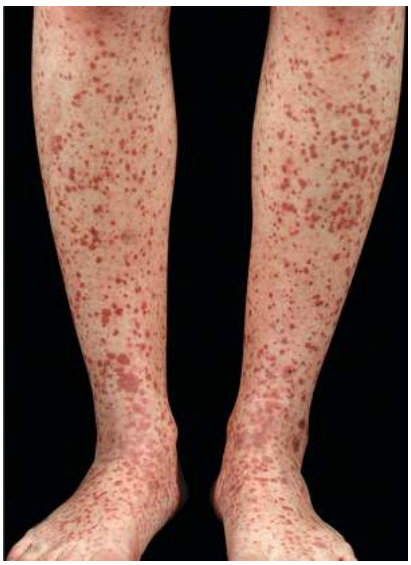


FIGURE 16-6. Classic palpable purpura in Henoch-Schönlein purpura. (Reproduced with permission from Wolff K, Johnson RA. *Fitzpatrick's Color Atlas & Synopsis of Clinical Dermatology,* 6th ed. New York: McGraw-Hill, 2009, Fig. 14-35.)

HENOCH-SCHÖNLEIN PURPURA

The most common small-vessel vasculitis of childhood. It is typically preceded by upper respiratory infection (URI) a few weeks before symptom onset.

History/PE

- **Palpable purpura** (see Figure 16-6).
- **Fever.**
- **Arthritis/arthralgia**: Usually migratory, affecting the large joints of the lower extremities more often than the upper extremities.
- **Glomerulonephritis:** If renal involvement occurs, it is usually seen within 4 weeks of presentation and is typically self-limited.
- **Abdominal pain**: Results from bowel wall edema and inflammation and may be treated with systemic corticosteroids if severe.

Diagnosis

- Based on clinical presentation. If unclear, a skin or kidney biopsy with evidence of IgA deposits can confirm the diagnosis.
- Labs may show thrombocytosis, leukocytosis, anemia; ↑ ESR, IgA, IgM; UA with RBCs and leukocytes; anticardiolipin or antiphospholipid antibodies.

Treatment

Acetaminophen or NSAIDs for pain control +/− glucocorticoids. This is another situation where aspirin may be given if there is concern that the patient is at ↑ risk for thrombotic events.

Complications

- Intussusception due to bowel wall edema and inflammation can occur.
- Recurs in roughly one-third of cases.

MNEMONIC

Causes of cyanotic CHD (right-to-left shunts):

The 5 Ts

Truncus arteriosus (one common artery off of both ventricles)
Transposition of the great arteries (two vessels switched)
Tricuspid atresia (three leaflets not well formed)
Tetralogy of Fallot (four problems present)
Total anomalous pulmonary venous return (five words)

A

A healthy child is unlikely to have multiple severe infections in different anatomic locations. Therefore, 1° immunodeficiency and other chronic diseases should be considered. Accordingly, a CBC, immunoglobulin levels, antibody titers to vaccinations, and a CH50 should be ordered. More specific tests (eg, HIV, CF) can be ordered if indicated.

Cardiology

The most common congenital heart lesion is ventricular septal defect (VSD), followed by atrial septal defect (ASD). The most common cyanotic lesion is transposition of the great arteries (TGA).

VENTRICULAR SEPTAL DEFECT

A hole in the ventricular septum. Can be membranous (least likely to close spontaneously), perimembranous, or muscular (most likely to close spontaneously).

History/PE

- May be asymptomatic at birth if the lesion is small.
- Cardiac exam may reveal a holosystolic, vibratory murmur at the left lower sternal border without radiation to the axilla.
- May become symptomatic between 2 and 6 months of age. Symptoms result from flow across the defect, usually from the left to the right ventricle.
- If the lesion is large, it may present with symptoms of heart failure (HF), including shortness of breath, pulmonary edema; frequent respiratory infection; FTT; and exercise/feeding intolerance (sweating with feeds).
- Look for cardiomegaly and crackles on exam (signs of right HF).

Diagnosis

- ECG shows right ventricular hypertrophy (RVH) and left ventricular hypertrophy.
- CXR may show pulmonary edema.
- Echocardiography is definitive.

Treatment

- Treat HF if present.
- Follow small, asymptomatic VSDs.
- Surgically repair large or membranous VSDs to prevent subsequent development of HF and pulmonary hypertension. Also repair VSDs in patients exhibiting FTT.

Complications

If left untreated, VSD may lead to irreversible Eisenmenger syndrome (pulmonary hypertension, RVH, and reversal of left-to-right shunt).

ATRIAL SEPTAL DEFECT

A hole in the atrial septum.

History/PE

- Typically asymptomatic until late childhood or early adulthood.
- Cardiac exam may reveal a systolic murmur at the left upper sternal border.
- A loud S1 with a wide and fixed, split S2 and a heaving cardiac impulse at the left lower sternal border are characteristic signs.
- Progression to HF and cyanosis may occur in the second or third decade of life and depends on the size of the lesion.

Diagnosis

- ECG may show left-axis deviation.
- CXR reveals cardiomegaly and ↑ pulmonary vascularity (if the defect is large).
- Echocardiography is definitive.

Treatment

- Treat HF if present; follow small ASDs.
- Surgically repair large ASDs in patients with HF and repair before the third decade to prevent symptoms.
- Patient will also need surgery if there is a history of paradoxical embolic event.

Complications

Eisenmenger syndrome, dysrhythmias, and pulmonary hypertension.

PATENT DUCTUS ARTERIOSUS

- Failure of the ductus arteriosus (the connection between the pulmonary artery and aorta) to close in the first few days of life. Usually results in a left-to-right shunt (from the aorta to the pulmonary artery). Risk factors include prematurity, high altitude, and maternal first-trimester rubella infection.
- **Hx/PE:** Presentation ranges from asymptomatic to HF. Cardiac exam may reveal a wide pulse pressure; a continuous "machinery" murmur at the left upper sternal border; and bounding peripheral pulses.

KEY FACT

Patients with CHD no longer require prophylactic antibiotics before dental work. Antibiotic prophylaxis is required for:

- Unrepaired or incompletely repaired cyanotic CHD.
- Repaired CHD with a residual defect at or adjacent to the site of a prosthetic patch or device.
- Repaired CHD with prosthetic patches or devices within the first 6 months following the procedure.
- Patients with a history of infective endocarditis.
- Patients with prosthetic valves or valves repaired using prosthetic materials.

Q

An 8-year-old boy comes to the ED for evaluation of abdominal pain and nausea. Three days earlier he had a fever, and a purpuric rash appeared on his lower extremities. Over the past few hours, his abdominal pain has worsened. What is your concern, and which studies should be ordered for further evaluation?

- **Dx:** Echocardiography is definitive, showing shunt flow as well as left atrial and left ventricular enlargement.
- **Tx:** If diagnosed within days of birth, use indomethacin to close the patent ductus arteriosus (PDA). Surgical repair is indicated if indomethacin fails or the infant is > 6–8 months of age.
- **Cx:** In pulmonary hypertension of the newborn (eg, meconium aspiration syndrome), flow may be right to left across a PDA, resulting in persistent cyanosis/hypoxia. A reduction of pulmonary hypertension is required to reduce the right-to-left flow. Do not close the PDA in ductal-dependent cyanotic heart lesions (eg, TGA). To keep the ductus open, prostaglandin E1 may be indicated until definitive repair can be performed.

TETRALOGY OF FALLOT

- Consists of 4 lesions (see the mnemonic **PROVe**).
- **Hx/PE:** Presentation ranges from acyanotic ("pink tet") to profound cyanosis. Most patients have some cyanosis depending on the severity of pulmonary stenosis and the relative right and left ventricular pressures (which determine the direction of flow across the VSD). Cardiac exam may reveal a systolic ejection murmur at the left sternal border along with right ventricular lift and possible thrill along the left sternal border.
- **Dx:** Echocardiography is definitive. CXR shows a boot-shaped heart.
- **Tx:** If a newborn with this condition is cyanotic, administer prostaglandin E to maintain the PDA. Cyanotic "tet spells" may occur in a child who is crying or overheated. These children should be calmed and given O2; squatting or other measures (fluids, morphine, propranolol, and phenylephrine if severe) can be used to ↑ systemic vascular resistance and restore left-to-right flow across the VSD. Surgical repair is necessary.

MNEMONIC

Anatomy of tetralogy of Fallot—

PROVe

Pulmonary stenosis (right ventricular outflow obstruction)
RVH
Overriding aorta
VSD

TRANSPOSITION OF THE GREAT ARTERIES

The aorta arises from the right ventricle and the pulmonary artery from the left ventricle. TGA will present shortly following delivery.

History/PE

- Presents with extreme cyanosis from birth.
- There may be no murmur.
- A single, loud S2 is characteristic.

Diagnosis

- Echocardiography is definitive.
- CXR shows an "egg on a string."
- An O_2 saturation monitor on the right arm (measuring "preductal" saturation) will show a lower O_2 saturation than the one on the lower extremity ("postductal" saturation).

Treatment

- Administer prostaglandin E1 to maintain the PDA.
- If necessary, a "balloon septostomy" (Rashkind procedure) may be performed to rupture the atrial septum, thereby improving the mixing of venous and arterial blood and ensuring that adequately saturated blood enters the aorta.
- Surgical repair is necessary.

A

The patient's history of Henoch-Schönlein purpura raises concern for intussusception. An abdominal ultrasound is the study of choice for initial evaluation.

COARCTATION OF THE AORTA

- Narrowing of the lumen of the aorta leads to ↓ blood flow below the obstruction and ↑ flow above it, resulting in upper extremity hypertension and cardiomegaly. Risk factors include Turner syndrome and male gender. Coarctation of the aorta is also associated with bicuspid aortic valve.
- **Hx/PE:** Presents with dyspnea with exertion, systemic hypoperfusion/shock, and syncope. Cardiac exam may reveal hypertension in the upper extremities and a lower BP in the lower extremities. ↓ Femoral and distal lower extremity pulses are characteristic.
- **Dx:** Echocardiography or catheterization is definitive. CXR shows rib notching due to collateral circulation through the intercostal arteries.
- **Tx:** Surgical repair or balloon angioplasty +/− stent placement.
- **Cx:** Often recurs and carries an ↑ risk of intracranial hemorrhage due to cerebral aneurysms.

Gastroenterology

PYLORIC STENOSIS

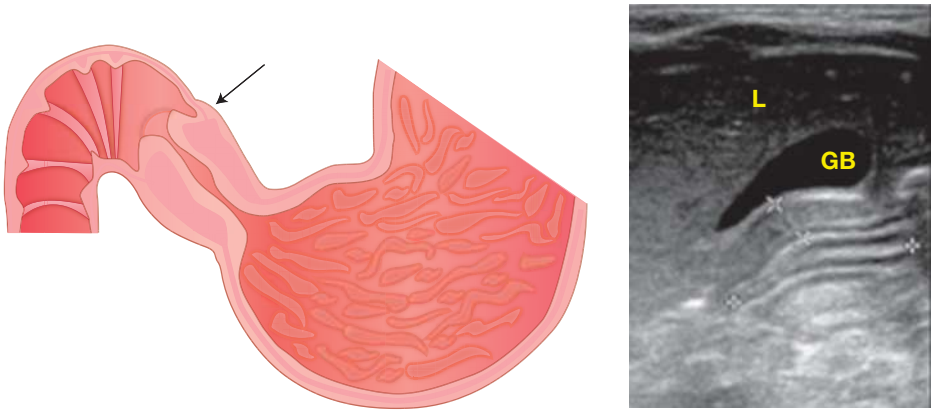
Hypertrophy of the pylorus leading to gastric outlet obstruction.

History/PE

- Occurs at 3–4 weeks of life (range 2 weeks to 4 months), predominantly in term, firstborn male infants.
- Presents with projectile, nonbilious emesis in a well-appearing infant.
- Exam may reveal an olive-shaped mass in the epigastrium along with visible peristaltic waves.

Diagnosis

- **Best initial test:** Ultrasound of abdomen will reveal a hypertrophied pylorus (see Figure 16-7).



A B

FIGURE 16-7. Hypertrophic pyloric stenosis. (A) Schematic representation of a hypertrophied pylorus. The arrow denotes protrusion of the pylorus into the duodenum. (B) Longitudinal ultrasound of the pylorus showing a thickened pyloric musculature (Xs) over a long pyloric channel length (plus signs). L, liver; GB, gallbladder. (Image A adapted with permission from Doherty GM. *Current Diagnosis & Treatment: Surgery,* 13th ed. New York: McGraw-Hill, 2010, Fig. 43-9. Image B reproduced with permission from USMLE-Rx.com.)

Q

A 12-hour male infant in the nursery develops fussiness, ↑ work of breathing, diaphoresis, and pallor. Exam shows scattered crackles in the lungs and no evidence of murmur. However, his femoral pulses are difficult to appreciate with lower extremity mottling, and brachial-femoral pulse delay is noted. What simple test can you perform to confirm your suspected diagnosis?

KEY FACT

In the vomiting infant, think pyloric stenosis. Rehydrate and correct electrolyte abnormalities before surgery.

- Electrolytes show hypochloremic, hypokalemic metabolic alkalosis due to emesis.
- Barium studies show a "string sign" (a narrow pylorus) or a pyloric beak.

Treatment

- First manage dehydration and electrolyte abnormalities.
- Surgical repair consists of pyloromyotomy.

INTUSSUSCEPTION

Telescoping of a bowel segment into itself (see Figure 16-8). May lead to edema, arterial occlusion, gut necrosis, and death. Intussusception is the most common cause of bowel obstruction in the first 2 years of life. It is usually idiopathic in children < 2 years of age and often has an identifiable "lead point" (eg, a lymph node) in children > 5 years of age.

KEY FACT

If paroxysmal abdominal pain and palpable sausage-shaped mass on abdominal exam in a young child, think intussusception.

History/PE

- The classic presentation consists of paroxysmal abdominal pain. The child is often comfortable between paroxysms. Vomiting and heme ⊕ stools may be seen. "Currant jelly" stool (reddish-purple stool mixed with mucus and blood) is a late finding.
- May present with altered mental status (lethargy or even obtundation) and may be preceded by a viral illness.
- Abdominal exam may reveal a palpable sausage-shaped mass.

Diagnosis

- Abdominal ultrasound is the initial step for workup.
- An air-contrast enema or a water-soluble contrast enema is both diagnostic and therapeutic for ileocecal intussusceptions.

KEY FACT

Intussusception may be associated with Henoch-Schönlein purpura, cystic fibrosis, and ongoing viral infections.

Treatment

- Following reduction via enema, treat with supportive care.
- If reduction fails or if perforation is suspected, surgical intervention may be required.

MALROTATION/VOLVULUS

Distinguished as follows:

- **Malrotation:** Failure of gut rotation in the abdominal cavity during the tenth week of gestation. Results in abnormal location of intestinal contents as well as incomplete fixation to the posterior abdominal wall. May predispose to intestinal obstruction or volvulus.
- **Volvulus:** A complication of malrotation in which the malrotated gut twists on the axis of the superior mesenteric artery, resulting in intestinal obstruction and ischemia.

A

You strongly suspect coarctation of the aorta, for which four-extremity blood pressures are performed. A significant gradient is noted between upper and lower extremity blood pressures, and upper extremity hypertension is noted, confirming your diagnosis.

History/PE

- **First 3 weeks of life:** Volvulus presents as acute onset of bilious emesis, small bowel obstruction, or bowel necrosis.
- **Later in infancy/early childhood:** Malrotation may present as acute or intermittent intestinal obstruction, malabsorption, protein-losing enteropathy, or diarrhea.

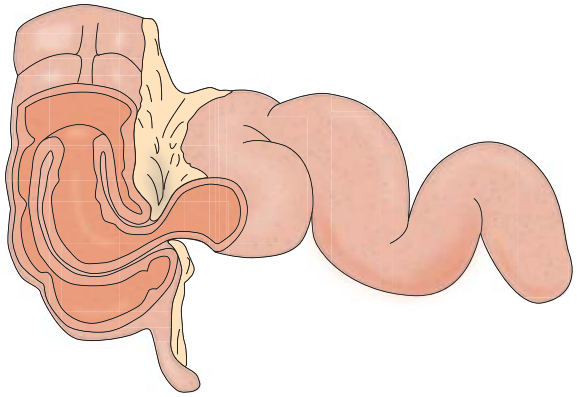


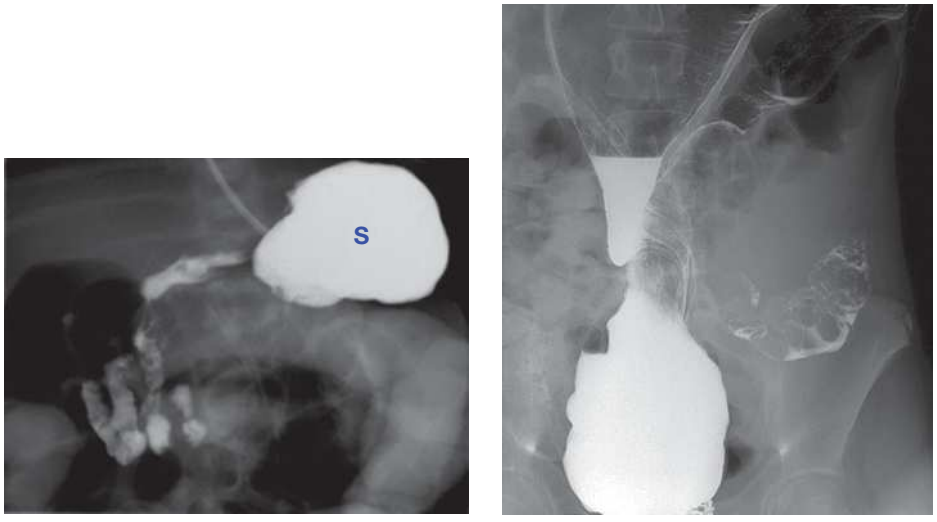
FIGURE 16-8. Intussusception.

Diagnosis

- **Malrotation:** An upper GI series shows the duodenojejunal junction on the right side of the spine (see Figure 16-9A). Barium enema shows a mobile cecum that is not in the RLQ.
- **Volvulus:** Contrast studies show a "bird's beak" where the gut is twisted (see Figure 16-9B).

Treatment

Volvulus is a surgical emergency requiring repair because vascular occlusion may result in tissue ischemia and necrosis. Asymptomatic patients require surgical repair in view of the risk of volvulus and associated complications.



A B

FIGURE 16-9. Midgut malrotation vs volvulus. (**A**) Frontal radiograph from an upper GI study shows a spiral pattern of duodenal and proximal jejunal loops in the right abdomen, consistent with midgut malrotation. The duodenal-jejunal junction should normally be to the left of the patient's spine. *S*, stomach. (**B**) Contrast enema shows a markedly dilated sigmoid colon with the contrast medium passing to the sigmoid colon, which indicates incomplete obstruction. The twist of the colon is clearly seen. (Image A reproduced with permission from USMLE-Rx.com; image B reproduced from Haider F et al. Sigmoid volvulus in children: a case report. *J Med Case Rep.* 2017;11:286.)

Complications

- The 1° complication following surgical bowel resection is short bowel syndrome, which occurs when < 30 cm of short bowel is left, resulting in poor intestinal absorption.
- If a large segment of bowel is lost as a result of bowel ischemia or surgery, the condition may also lead to malnutrition, TPN dependence, and liver failure.

MECKEL DIVERTICULUM

A remnant of the omphalomesenteric duct that persists as an outpouching of the distal ileum. It can contain ectopic (usually gastric or pancreatic) mucosa.

History/PE

- Often asymptomatic.
- Patients may present with painless rectal bleeding or intussusception (with Meckel diverticulum as the lead point).

Diagnosis

- Order a technetium radionuclide scan ("Meckel scan") to detect gastric mucosa.
- The gold standard is tissue obtained surgically.

Treatment

- Stabilize the patient with IV fluids; transfuse if needed.
- Surgical exploration is indicated if the patient is symptomatic.
- Bowel resection may be required with resection of diverticula depending on the location and complexity of the lesion.

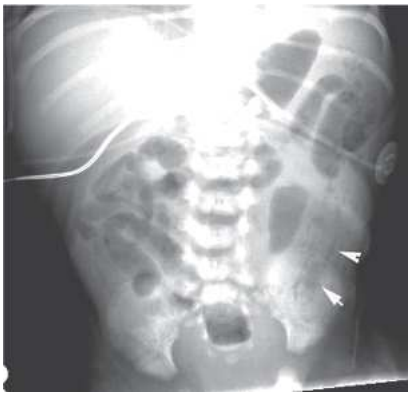


FIGURE 16-10. Necrotizing enterocolitis. Short arrows highlight pneumatosis intestinalis on an abdominal radiograph. (Reproduced with permission from Brunicardi FC et al. *Schwartz's Principles of Surgery,* 10th ed. New York: McGraw-Hill, 2015, Fig. 39-19.)

NECROTIZING ENTEROCOLOTIS

Intestinal necrosis occurring primarily in a watershed distribution. It is the most common GI emergency of newborns. Risk factors include prematurity and congenital heart disease.

History/PE

- Presents with abdominal distention, retention of gastric contents and feeds, abdominal wall tenderness and discoloration, and bloody stools.
- Nonspecific symptoms include apnea, respiratory failure, lethargy, poor feeding, temperature instability, thrombocytopenia, hypoglycemia, and hypotension/shock.

Diagnosis

AXR shows pneumatosis intestinalis and possibly portal venous gas and free intraperitoneal air (see Figure 16-10).

Treatment

- **Medical management:** With IV fluids (no enteral feeds) and antibiotics if the patient is hemodynamically stable and/or too small or sick to go to the OR.
- **Surgical management (resection of necrotic bowel):** Necessary in the setting of extensive disease and/or hemodynamic instability.

MALABSORPTION

The inability or deficiency in absorbing nutrients from food. It can be present at birth or develop when introducing new foods. Three different types involve fat, protein, and vitamin/mineral.

History/PE

- Patients will present with chronic diarrhea; most will have normal height.
- In celiac disease (also known as celiac sprue, see Chapter 7), infants will present with failure to thrive, and children will present with small stature, chronic diarrhea, iron deficiency anemia, and a rash.

Diagnosis

- **Fat malabsorption:** Conduct a Sudan black test initially; 72-hour stool test for fecal fat is confirmatory.
- **Protein malabsorption:** Conduct a stool α-1 antitrypsin test. To confirm celiac disease, start with antitransglutaminase antibodies; intestinal biopsy showing blunted villi is most specific.
- **Vitamin/mineral malabsorption:** Obtain typical vitamin screen (folate, vitamin B_{12}, vitamin D, vitamin A, calcium, zinc, magnesium, and iron).

Treatment

Includes diet modification or vitamin/mineral replacement as needed.

Pulmonology

CROUP (LARYNGOTRACHEOBRONCHITIS)

An acute viral inflammatory disease of the larynx/subglottic space (see Table 16-10). Most common in children 3 months to 3 years of age. Commonly caused by parainfluenza virus (PIV) type 1 but may also be caused by other PIVs as well as by respiratory syncytial virus (RSV), influenza, rubeola, adenovirus, and *Mycoplasma pneumoniae*.

History/PE

- Typically has a 1- to 2-day viral prodrome with URI symptoms.
- Also presents with low-grade fever, mild dyspnea, and inspiratory stridor that worsens with agitation and may improve with cool air or a warm shower.
- Listen for the characteristic barking cough.

Diagnosis

- Based on clinical findings.
- A "steeple sign" formed by subglottic narrowing may be seen on frontal neck x-ray (see Figure 16-11A).

Treatment

- Mist therapy (for mild croup only); oral or IM/IV dexamethasone (for mild or moderate croup); nebulized racemic epinephrine if stridor is present at rest.
- Order heliox and ICU admission for severe croup.
  - Heliox is typically administered at a ratio of 70% helium to 30% O_2 to ↓ the resistance of airflow through a narrowed airway by replacing nitrogen with helium.

Q

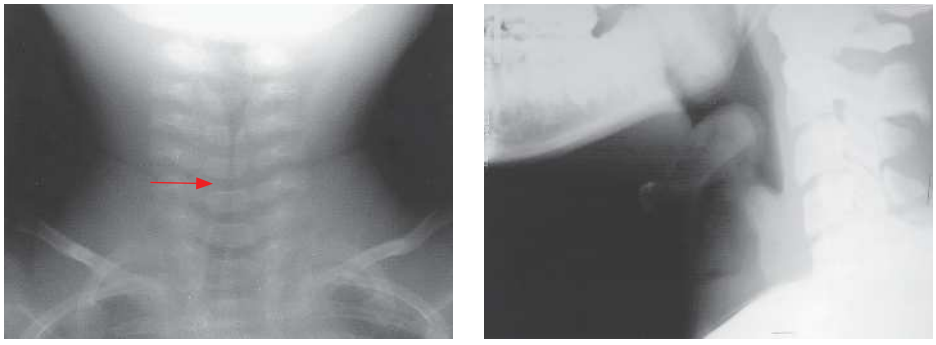
A 3-week-old infant born at 28 weeks' gestation is at his goal feeds. This evening he developed emesis with heme ⊕ stools and an ↑ in abdominal girth. You obtain blood and stool cultures and abdominal x-rays (AXRs). Pneumatosis is noted in the bowel wall and portal venous system. What are the next steps in management?

TABLE 16-10. Characteristics of Tracheitis, Croup, and Epiglottitis

	Tracheitis	Croup	Epiglottitis
Age group	3 months to 2 years	3 months to 3 years	3–7 years
Incidence in children presenting with stridor	2%	88%	8%
Pathogen	Often *S aureus*	PIV	Formerly *H influenzae;* now *S pneumoniae* and *S aureus*
Onset	Prodrome (3 days) leading to acute decompensation (within 24 hours)	Prodrome (1–7 days)	Rapid (4–12 hours)
Fever severity	Intermediate grade	Low grade	High grade
Associated symptoms	Variable respiratory distress	Barking cough, inspiratory stridor, hoarseness	Respiratory distress, acute decompensation, toxic appearance, inspiratory stridor, muffled voice, drooling
Position preference	None	None	Seated, neck extended
Response to racemic epinephrine	None	↓ in stridor	None
CXR findings	May see subglottic narrowing on lateral film	"Steeple sign" on AP film	"Thumbprint sign" on lateral film

Adapted with permission from Le T et al. *First Aid for the USMLE Step 2 CK*, 10th ed. New York: McGraw-Hill, 2019:422.

- This can act as an intermediary step before intubation for children who show evidence of airway compromise and risk progression to respiratory failure.
- Hospitalize patients with stridor at rest or those needing > 1 dose of racemic epinephrine.



A

This patient has necrotizing enterocolitis, which is an emergency! The pediatric surgical team should be consulted and the patient made NPO. Intermittent nasogastric (NG) suctioning should be started, IV antibiotics administered (piperacillin + tazobactam or ampicillin + gentamicin), electrolytes monitored, and TPN or IV fluids initiated.

FIGURE 16-11. Croup vs epiglottitis. (**A**) Croup. X-ray shows marked subglottic narrowing of the airway (*arrow*). (**B**) Epiglottitis. The classic swollen epiglottis ("thumbprint sign") and obstructed airway are seen. (Reproduced with permission from Stone CK, Humphries RL. *Current Diagnosis & Treatment: Emergency Medicine,* 7th ed. New York: McGraw-Hill, 2011, Fig. 32-10A and 50-4.)

EPIGLOTTITIS

A serious and rapidly progressive infection of the epiglottis and contiguous structures that can lead to life-threatening airway obstruction. It is increasingly rare because of the Hib vaccine to prevent *H influenza* infection and is now most commonly caused by *S pneumoniae* or *S aureus*.

History/Exam

- Maintain a high index of suspicion in children with sudden-onset high fever, dysphagia, drooling, a muffled voice, inspiratory retractions, cyanosis, and soft stridor.
- Patients may be in the "sniffing" position, with the neck hyperextended and the chin protruding. These patients should be identified and stabilized rapidly, as the disease can quickly progress to complete airway obstruction and respiratory arrest.

Diagnosis

- Based on the clinical picture.
- Do not attempt to examine the throat unless the patient is in the OR with an anesthesiologist present.
- Lateral neck films show the characteristic "thumbprint sign" of a swollen epiglottis (see Figure 16-11B).

KEY FACT

In epiglottitis, throat examination may cause laryngospasm and airway obstruction.

Treatment

- Keep the patient calm, call anesthesia and otolaryngology immediately, and transfer to the OR. If the patient is unstable, do not delay treatment by getting a neck film.
- Treat with endotracheal intubation and IV antibiotics.

PERTUSSIS

Commonly known as "whooping cough." The causative agent is *Bordetella pertussis* or *Bordetella parapertussis*.

History/PE

The disease has three stages:

- **Catarrhal:** Presents with nasal congestion, sneezing, and low-grade fever.
- **Paroxysmal:** Presents with intense coughing paroxysms followed by a "whoop" in young children. Neonates and infants may experience cyanosis and apnea after coughing fits.
- **Convalescent:** Characterized by a chronic cough that may last for weeks (also known as "hundred-day cough"). Patients are no longer shedding the organism during this phase.

Diagnosis

Nasopharyngeal swab that is ⊕ by PCR or culture for *B pertussis*.

Treatment

- Erythromycin or azithromycin is recommended if the diagnosis is made before the convalescent phase, when the patient is still contagious.
- Vaccination is key to preventing asymptomatic family members from spreading the infection to children.

BRONCHIOLITIS

The most common lower respiratory illness in childhood and a leading cause of hospitalization in infants and young children. Peak incidence is at 2–8 months of age, from October to March. Symptoms are due to virally induced inflammation of the small airways, resulting in edema, mucous plugging, and sloughing of epithelial cells, causing bronchiolar obstruction.

History/PE

- Infants present with fever, nasal congestion, and varying degrees of hypoxemia, tachypnea, retractions, and loud rhonchi on lung exam.
- Wheezing can occur, especially in children with no personal or family history of wheeze.

Diagnosis

- Clinical diagnosis is based on the characteristic age, history, and exam findings.
- Can be caused by many viruses; RSV, influenza, human metapneumovirus, and rhinovirus are common viral causes and are tested by nasopharyngeal swab.
- CXR shows nonspecific bilateral perihilar infiltrates as well as hyperinflation and peribronchial cuffing.

Treatment

- Provide supportive care with nasal suctioning, nebulized hypertonic saline, and O_2. Because infants and young children are obligate nose breathers, feeding difficulties may occur when they are in respiratory distress, necessitating close management of hydration and nutrition.
- Patients may or may not respond to albuterol, racemic epinephrine, and/or systemic corticosteroids. Use of these medications is not routinely recommended.
- Ribavirin can be used for immunocompromised patients and/or severe cases. Endotracheal intubation is indicated for respiratory failure.

PNEUMONIA

Will be either viral or bacterial; presentation will differ based on etiology. The most common bacterial organisms are *S pneumoniae*, *M pneumoniae*, or *C pneumoniae*.

History/PE

- **Viral:** Tachypnea, low-grade fever, URI symptoms.
- **Bacterial:** High fever, chills, pleuritic pain, diminished breath sounds.

Diagnosis

- **CXR:** Hyperinflation with interstitial infiltrates (viral) or lobar consolidation (bacterial).
- **CBC:** WBC count normal or mildly ↑ in viral pneumonia; very ↑ in bacterial pneumonia.
- **Viral antigens:** IgM titers (for *M pneumoniae*).
- **Blood cultures.**

Treatment

- **Ambulatory setting:** Amoxicillin.
- **Hospital setting:** Cefuroxime (addition of vancomycin if *S aureus* is the suspected cause).
- *Chlamydia* or *Mycoplasma*: Erythromycin.

CYSTIC FIBROSIS

A mutation of the *CFTR* gene in which an abnormal CFTR protein functions as a cAMP-regulated chloride channel and other ion channels, resulting in multisystem dysfunction.

- Frequently diagnosed in childhood; only ~5% of cases are diagnosed in adulthood.
- Most often affects the lungs, resulting in chronic bacterial infections and bronchiectasis, exocrine pancreatic dysfunction, abnormal sweat production, intestinal dysfunction, and urodynamics (see Chapter 18 for more detailed coverage).

Neurology

FEBRILE SEIZURES

Benign, self-limited seizures that occur in children 6 months to 6 years of age at the onset of a febrile illness. A ⊕ family history is common. Febrile seizures may be simple or complex:

- **Simple:** A generalized seizure characterized by a short duration (< 15 minutes), one seizure per 24-hour period, and a quick return to normal function with no residual focal neurologic deficit.
- **Complex:** A seizure associated with a febrile illness that does not meet the above criteria. The seizure may be focal; may have a longer duration (> 15 minutes); may recur in a 24-hour period; or may result in incomplete or slow return to normal neurologic status.

Diagnosis/Treatment

- **Simple:** Treatment is focused on determining the source of the fever and providing supportive care, but no further neurologic evaluation is needed.
- **Complex:** Depending on the history, the severity of the seizure, and exam findings, consider performing laboratory or radiologic workup for other etiologies of seizure, such as electrolyte abnormalities, toxic ingestion, sepsis, CNS infection, or CNS trauma.
- Strongly consider LP in patients < 12 months of age with complex febrile seizures as well as in any child who has focal neurologic deficits before or after the seizure.
- EEG and MRI are not routinely recommended for children with febrile seizures. They may be considered on an outpatient basis in a child with a complex febrile seizure, especially a focal seizure or one resulting in prolonged neurologic defects.
- Family education and anticipatory guidance are essential. Although febrile seizures are benign, 30–50% of children with a febrile seizure will have another one before they outgrow the syndrome.
- Febrile seizures cannot be prevented with the use of antipyretics, and anticonvulsants are not routinely recommended. Complications from anticonvulsant use typically outweigh their utility.

KEY FACT

Signs and symptoms of bacterial meningitis may be minimal or absent in infants; in a child with complex febrile seizure, it is important to consider LP.

KEY FACT

Hypsarrhythmia on EEG is characterized by slow, high-amplitude waves with random spikes that originate in all cortical areas with no identified pattern or rhythm.

EPILEPSY SYNDROMES

Table 16-11 outlines the presentation and treatment of common epilepsy syndromes affecting the pediatric population.

Oncology

Hematologic malignancies (leukemia and lymphoma) are the most common form of malignancy in children. Solid tumors in pediatrics most commonly occur in the CNS, bone, and kidneys. These topics are covered in Chapter 9.

WILMS TUMOR

An embryonal tumor of renal origin. Wilms tumor is the most common renal tumor in children and is usually seen in those 1–4 years of age. Risk factors include a ⊕ family history and certain genetic syndromes/birth defects, eg, WAGR syndrome (Wilms tumor, Aniridia, Genitourinary anomalies, intellectual disability, formerly referred to as mental Retardation), Beckwith-Wiedemann syndrome, and Denys-Drash syndrome.

TABLE 16-11. Common Pediatric Epilepsy Syndromes

Syndrome	History/PE	Diagnosis	Treatment
Absence seizures	Multiple, brief staring episodes	A generalized 3-Hz spike-and-wave pattern on EEG	Ethosuximide; valproic acid
Infantile spasms (West syndrome)	Affects infants < 1 year of age, presenting with "jackknife" spasms and psychomotor arrest/developmental regression	Hypsarrhythmia on EEG Associated with tuberous sclerosis	ACTH; vigabatrin Treatment resistant: Topiramate, zonisamide, valproic acid, lamotrigine, ketogenic diet
Lennox-Gastaut syndrome	First seizure between 1 and 7 years of age Presents with multiple, progressive, difficult-to-treat seizure types, including generalized tonic-clonic seizures (GTCS) and drop attacks	An atypical spike-and-wave pattern, primarily in the frontal region, on EEG Progressive intellectual disability Associated with refractory infantile spasms and tuberous sclerosis	Difficult to treat Topiramate, ethosuximide, felbamate, levetiracetam, zonisamide, valproate, clonazepam, rufinamide, clobazam, ketogenic diet, vagus nerve stimulation
Juvenile myoclonic epilepsy	Affects healthy adolescents, presenting with myoclonic jerks or generalized tonic-clonic seizures (GTCS) in the early morning hours/upon awakening	May have a genetic basis; patients often have a ⊕ family history Spike-and-wave sequences or multispike-and-wave complexes on EEG	Antiepileptic medications such as lamotrigine, valproic acid, topiramate, levetiracetam, zonisamide
Benign partial epilepsy	Affects healthy children, presenting with partial seizures during wakefulness (oral, vocal, upper extremity symptoms); may spread to GTCS during sleep	Spikes or sharp waves from the centrotemporal (rolandic) region	Seizures usually disappear by adolescence; often no medication is necessary

Data from Hay WW et al. *Current Diagnosis & Treatment: Pediatrics,* 23rd ed. New York: McGraw-Hill, 2016: Table 25-5.

History/PE

- Patients may have abdominal pain or may present with a painless abdominal or flank mass.
- Hematuria and hypertension are commonly seen.
- Systemic symptoms include weight loss, nausea, emesis, bone pain, dysuria, and polyuria.

Diagnosis

- **Best initial test:** Abdominal CT or ultrasound.
- CXR, chest CT, CBC, LFTs, and blood urea nitrogen (BUN)/creatinine can be used to assess severity and spread.
- Definitive diagnosis confirmed histologically after biopsy or surgical resection.

Treatment

- Transabdominal nephrectomy followed by postoperative chemotherapy.
- Flank irradiation is of benefit in some higher-stage cases.
- The prognosis is usually very good but depends on staging and tumor histology.

NEUROBLASTOMA

A tumor of neural crest cell origin that most commonly affects children < 5 years of age; it is the most common solid tumor during infancy. Risk factors include neurofibromatosis, tuberous sclerosis, pheochromocytoma, and Hirschsprung disease.

History/PE

- Presentations include abdominal mass/distention/hepatomegaly, anorexia, weight loss, bone pain, respiratory distress, fatigue, fever, diarrhea, irritability, or neuromuscular symptoms (if paraspinal). Patient will often appear systemically ill (differentiates from Wilms tumor).
- Soft tissue and bony lesions can appear anywhere in the body (eg, the skin or skull).
- Other symptoms include leg edema (abdominal tumors compress venous or lymphatic drainage), hypertension, and periorbital bruising ("raccoon eyes").

Diagnosis

- Definitive diagnosis is based on a tumor tissue sample with or without ↑ urine catecholamines (vanillylmandelic acid and homovanillic acid) or on metastases to bone marrow with ↑ urine catecholamines.
- The initial workup generally includes a CBC, electrolytes, lactate dehydrogenase, ferritin, LFTs, a coagulation screen, urine catecholamines, and BUN/creatinine.
- To stage and assess severity, obtain bone marrow biopsies, an abdominal CT or MRI, a CXR, bone radiographs, and a technetium radionuclide scan or ^{131}I-metaiodobenzylguanidine scan.

Treatment

- Localized, low-risk tumors are usually cured with excision.
- Chemotherapy includes cyclophosphamide, carboplatin or cisplatin, etoposide or teniposide, vincristine, and doxorubicin.

- Radiation can be used as an adjunct.
- Autologous bone marrow transplants and immunotherapy are used in high-risk cases.
- The prognosis is improved if the diagnosis is made before age 18 months. Staging is based on the International Neuroblastoma Staging System.

RETINOBLASTOMA

The most common intraocular malignancy in children and is usually diagnosed before age 2. One-quarter of cases are bilateral.

History/PE

- Usually presents with leukocoria and/or strabismus.
- Can be sporadic or inherited; the inherited form is associated with an ↑ risk of additional malignancies, including osteogenic sarcoma, soft tissue sarcomas, and malignant melanoma.
- Generally begins to metastasize within 6 months, so early diagnosis is critical.

Diagnosis

Made by indirect ophthalmoscopic exam (with dilated pupils).

Treatment

- Determined by the size and location of the tumor.
- Options include enucleation, external beam radiation therapy, radioactive plaque therapy (^{125}I brachytherapy), cryotherapy with laser photocoagulation, and chemotherapy.

MNEMONIC

Trisomies—

21—**D**rinking age (**D**own syndrome)
18—**E**lection age (**E**dwards syndrome)
13—**P**uberty age (**P**atau syndrome)

Genetics

COMMON GENETIC DISORDERS

Table 16-12 outlines the presentation and diagnosis of genetic syndromes.

TABLE 16-12. Common Genetic Syndromes

Syndrome	Presentation	Associated Conditions	Diagnosis	Prognosis
Trisomy 21 (incidence 1:700)	Hypotonia, brachycephalic head, slanted palpebral fissures, dysplasia of the midphalanx of the fifth finger, single transverse palmar crease	Cognitive delay, cardiac defects, thyroid disease, GI atresias, atlantoaxial instability, leukemia	Karyotype, baseline echocardiogram, TFTs, LFTs, CBC	One-third to one-half of children have congenital heart defects; thyroid dysfunction, visual issues, hearing loss, obstructive sleep apnea, celiac disease, atlanto-occipital instability, and autism may develop; leukemia is common

(continues)

TABLE 16-12. Common Genetic Syndromes *(continued)*

Syndrome	Presentation	Associated Conditions	Diagnosis	Prognosis
Trisomy 18 (Edwards syndrome) (incidence 1:4000; 3:1 female predominance)	Clenched hand/overlapping fingers, intrauterine growth retardation, cardiac defects, rocker-bottom feet	Profound cognitive delay	Karyotype with fluorescence in situ hybridization (FISH) analysis	Death often from HF or pneumonia generally occurs in infancy or early childhood
Trisomy 13 (Patau syndrome) (incidence 1:12,000)	CNS malformations, polydactyly, seizures, deafness, sloping forehead, aplasia cutis, cleft lip/cleft palate, microphthalmia/eye defects, cardiac defects	Profound cognitive delay	Karyotype with FISH analysis	Death typically from HF or infection generally occurs between 3 months and 24 months of life
22q11 syndrome (DiGeorge syndrome, velocardiofacial syndrome) (incidence 1:4000)	Congenital heart disease, palatal abnormalities, prominent/squared nose, thymic hypoplasia/immune deficiency, absent parathyroid glands/hypocalcemia	Mild to moderate cognitive delay (mostly speech and language), learning disabilities, and feeding difficulties; psychotic symptoms are common	FISH analysis for 22q11.2 deletion Serum calcium, absolute lymphocyte count, renal ultrasound, baseline echocardiogram	Parents should be tested for being carriers of the deletion
Turner syndrome (45,XO) (incidence 1:10,000)	Short female with shield chest, widely spaced nipples, a webbed neck, and congenital lymphedema	Cognitive delay, gonadal dysgenesis, renal anomalies, cardiac defects (coarctation of the aorta), hearing loss	Karyotype for diagnosis Baseline echocardiogram, renal ultrasound, BP, hearing screen	Infertility; normal life span
Fragile X syndrome (incidence 1:1500 males)	Boys present with macrocephaly, large ears, macroorchidism, and tall stature Girls may present only with learning disabilities	Mild to profound cognitive delay, autism	DNA analysis shows expansion of a CGG nucleotide repeat in the *FMR1* gene; the size of the repeat correlates with disease severity	Normal life span
Klinefelter syndrome (47, XXY) (1:1000)	Hypogonadism, additional X chromosome inactivated (Barr body)	Testicular atrophy, gynecomastia, tall with long extremities	Karyotype for diagnosis	↑ Risk of breast cancer; males require testosterone replacement therapy
Marfan syndrome (incidence 1:10,000)	Tall stature, low upper-to-lower-segment ratio, arachnodactyly, joint laxity, scoliosis, pectus excavatum or carinatum, lens dislocation, retinal detachment, dilation of the aortic root, mitral valve prolapse, lumbosacral dural ectasia, high-arched palate	Normal intelligence	Slit-lamp examination, echocardiography, genetic evaluation Clinical diagnosis	Normal life span with treatment/corrective surgery of aortic root dilation

Data from Hay WW et al. *Current Diagnosis & Treatment: Pediatrics,* 23th ed. New York: McGraw-Hill, 2016: Chapter 37.

NOTES

CHAPTER 17

PSYCHIATRY

Pharmacotherapy

ANXIOLYTICS AND SEDATIVE-HYPNOTICS

Benzodiazepines

KEY FACT

If a patient develops autonomic instability and becomes restless, agitated, confused, and psychotic a few days in hospitalization, consider alcohol or benzodiazepine withdrawal.

- **Applications:** Used for anxiety, agitation, catatonia, alcohol withdrawal, insomnia, anesthesia, seizures, and muscle spasms.
  - Rapid onset of action; augment sedation and respiratory depression from other CNS depressants (eg, alcohol, opiates).
  - When possible, use only on a short-term basis (eg, no more than 2–3 months) or PRN.
- **Interactions:** P-450 inhibitors (eg, cimetidine, fluoxetine) ↑ levels; inducers (carbamazepine and rifampin) ↓ levels.
- **Relative contraindications:** Disadvantages include a risk of abuse, tolerance, dependence, and withdrawal (can be life-threatening).
  - May also induce delirium in the elderly and/or critically ill patients.
  - Avoid in patients who are at high risk for falling.
  - Avoid in patients on chronic opiate therapy due to the risk of respiratory suppression, death, and overdose. Can cause neonatal withdrawal syndrome if taken in pregnancy.

KEY FACT

Shorter-acting benzodiazepines (such as lorazepam) are preferred in older adults due to lower risk of accumulation and sedation.

Zolpidem

A nonbenzodiazepine used for insomnia. ↓ Sleep latency and ↑ total sleep time. Has rapid onset and can be habit forming and lead to problematic or dangerous sleep behaviors (eg, "sleep driving," "sleep eating"). Withdrawal is uncommon.

Buspirone

- **Mechanism of action:** A 5-HT_{1A} (serotonin receptor) partial agonist.
- **Applications:** Used for generalized anxiety disorder (GAD) and chronic anxiety; and for patients with a history of substance abuse. Unlike benzodiazepines, it has no anticonvulsant or muscle relaxant properties. Also has few side effects and no tolerance, dependence, or withdrawal.
- **Relative contraindications:** Has slow onset of action and lower efficacy than benzodiazepines. Should not be used with monoamine oxidase inhibitors (MAOIs). Not effective as a PRN anxiolytic.

Antihistamines

Used for the short-term management of insomnia and for preoperative sedation. Can be used PRN for anxiety. Diphenhydramine can be used to treat acute extrapyramidal symptoms.

ANTIDEPRESSANTS

Selective Serotonin Reuptake Inhibitors

KEY FACT

Antidepressant use during pregnancy carries the risk of abstinence syndrome, though most SSRIs are generally thought to be safe except for paroxetine (category D). Untreated depression carries a risk of low birth weight.

- Include fluoxetine, sertraline, paroxetine, citalopram, escitalopram, and fluvoxamine.
- **Applications:** First-line therapy for depression, obsessive-compulsive disorder (OCD) (generally requires high doses), and many anxiety disorders.
  - Well tolerated, effective, and relatively safe in overdose.
  - Combine with psychotherapy for synergistic effect.

- Continue treatment at therapeutic dose for 6 months following remission in patients with first episode of depression then consider tapering and discontinuing. More severe, chronic, frequent episodes of depression may require lifelong treatment.
- Medications that a family member responded to are often a good first choice.

- **Interactions:** Can ↑ warfarin levels because of P-450 interactions.
- **Side effects:** Sexual dysfunction, which often persists. GI upset, bruising, headache, anxiety, weight gain or loss, and sleep disturbance often resolve with time. An adequate trial is at least 6 weeks. If side effects are intolerable, switch agents. Black box warning: Selective serotonin reuptake inhibitors (SSRIs) may lead to ↑ suicidal thoughts and behaviors in those < 24 years.

KEY FACT

All antidepressants can provoke mania in patients with undiagnosed bipolar disorder. Stop treatment immediately if manic symptoms emerge.

Atypical Antidepressants

- **Bupropion:**
  - **Mechanism of action:** Dopamine and norepinephrine reuptake inhibition.
  - **Applications:** First-line therapy for depression and smoking cessation. Effective for patients who have had sexual side effects from other antidepressants. Can be used as augmentation if fatigue, weight gain, low energy, or apathy are persistent.
  - **Side effects:** Anxiety, agitation, and insomnia can occur. Can worsen tics. Lowers seizure threshold, especially in high doses. Not associated with weight gain.
  - **Relative contraindications:** A history of seizure disorder, active eating disorders, or head trauma.
- **Venlafaxine/Desvenlafaxine and Duloxetine:**
  - **Mechanism of action:** 5-HT and NE reuptake inhibition.
  - **Applications:** Used for major depression, social anxiety, and GAD.
  - **Side effects:** Adverse effects include hypertension (monitor BP), insomnia, nervousness, sedation, constipation, sexual dysfunction, and nausea.
- **Mirtazapine:**
  - **Mechanism of action:** An α_2-antagonist that enhances NE and 5-HT. Does not affect the P-450 system.
  - **Side effects:** Sedation (worse in lower doses) and weight gain. Has little effect on sexual function.
- **Trazodone:**
  - **Mechanism of action:** 5-HT2A antagonism. At lower doses, may be helpful in insomnia.
  - **Side effects:** Sedation, priapism.

KEY FACT

Antidepressants can initially be anxiogenic.

KEY FACT

Duloxetine has a profile like venlafaxine but has a less pronounced effect on BP and is also approved for the treatment of neuropathic pain.

Tricyclic Antidepressants

- Include nortriptyline, desipramine, imipramine, amitriptyline, clomipramine, and doxepin. Tricyclic antidepressants (TCAs) are considered to be second-line agents owing to their side effect profile, along with the risk of dysrhythmias and death in overdose.
- **Mechanism of action:** Block the reuptake of NE and 5-HT.
- **Applications:** Useful for chronic pain and migraines. OCD responds to clomipramine. Consider imipramine for enuresis and amitriptyline for neuropathic pain.
- **Interactions:** Levels ↑ when used with SSRIs because of P-450 inhibition.
- **Side effects:** Anticholinergic effects (dry mouth, blurry vision, constipation, urinary retention). Sedation, weight gain. Orthostatic hypotension;

Q

A 24-year-old man being treated for depression reports that his depressive symptoms have greatly diminished on fluoxetine 80 mg, but he is now having "intimacy issues," specifically erectile dysfunction. What are options for treatment?

cardiac conduction delays with prolonged PR and QRS intervals. Contraindicated in patients with a history of severe heart disease and in those at high risk for suicide. Use with caution in elderly persons.

Monoamine Oxidase Inhibitors

- Include phenelzine, selegiline, and tranylcypromine. MAOIs are second-line agents owing to their side effect profile and dietary restrictions.
- **Side effects:**
  - Orthostatic hypotension, insomnia, weight gain, edema, and sexual dysfunction are common.
  - May lead to tyramine-induced hypertensive crisis. Culprits are aged cheese, chocolate, certain alcohol, pickled foods.
  - Potentially fatal serotonin syndrome can occur if MAOIs are combined with SSRIs, TCAs, meperidine, fentanyl, or indirect sympathomimetics (eg, those found in some over-the-counter [OTC] cold remedies). Can be prevented with washout period when switching to MAOIs from other antidepressants—fluoxetine has the longest half-life and requires at least a 5-week washout.

KEY FACT

TCAs may be lethal in an overdose. Be sure to check ECG for arrhythmia. Treat TCA cardiotoxicity with sodium bicarbonate.

KEY FACT

If monotherapy with an SSRI is insufficient in controlling symptoms, consider adding bupropion, mirtazapine, buspirone (if anxiety prominent), aripiprazole, triiodothyronine, or lithium. May choose agent based on side effect profile.

St. John's Wort

OTC herbal supplement used for mild cases of depression. Use caution as it induces P450 and has multiple drug interactions.

ANTIPSYCHOTICS

First-Generation ("Typical") Antipsychotics

- **Mechanism of action:** Act through dopamine receptor blockade.
- **Applications:** Used for psychotic disorders and acute agitation. Haloperidol can be used to treat dangerous agitation in delirium. Examples include:
  - **High-potency agents** (haloperidol, fluphenazine): ↓ Only positive symptoms of psychosis. Associated with more extrapyramidal symptoms.
  - **Low-potency agents** (thioridazine, chlorpromazine): Associated with more sedation, anticholinergic effects, and hypotension.
- **Side effects:** Extrapyramidal symptoms from excessive cholinergic effect (see Table 17-1), hyperprolactinemia (amenorrhea, gynecomastia, galactorrhea), anticholinergic effects, neuroleptic malignant syndrome, cardiac arrhythmias, weight gain, sedation.

KEY FACT

Haloperidol is safe and effective for acute mania or psychosis in pregnancy.

KEY FACT

Long-acting injectable formulations of antipsychotics can be used in noncompliant patients. Both first and second generations are available. Choose based on tolerability and efficacy following an oral trial.

Second-Generation ("Atypical") Antipsychotics

- Risperidone, olanzapine, quetiapine, ziprasidone, and aripiprazole are commonly used. Lurasidone, iloperidone, and paliperidone are newer agents. Clozapine is reserved for treatment-refractory psychosis; it is highly effective and reduces risk of suicide but requires intensive monitoring.
- **Mechanism of action:** Act through 5-HT_2 and dopamine antagonism.
- **Applications:** Currently first-line therapy for schizophrenia. Benefits are fewer extrapyramidal symptoms and anticholinergic effects than first-generation agents. Also used for severe tic disorders. Can treat acute mania; may be required as augmentation with mood stabilizer.
- **Side effects:**
  - May cause sedation, weight gain, metabolic syndrome, anticholinergic effects, and QT prolongation. Obtain baseline values and monitor the patient's weight, lipid profile, and glucose levels.

A

Rule out medical causes of erectile dysfunction. Reduce the high dose of SSRI, change to non-SSRI antidepressant, augment with bupropion, or add sildenafil.

TABLE 17-1. Extrapyramidal Symptoms and Treatment

Symptom	Description	Treatment
Acute dystonia	Involuntary muscle contraction or spasm (eg, torticollis, oculogyric crisis); more likely in young men; occurs acutely (often days to weeks after initiation)	Give an anticholinergic (benztropine) or diphenhydramine To prevent, give prophylactic benztropine with an antipsychotic
Dyskinesia	Parkinsonism (eg, shuffling gait, cogwheel rigidity, bradykinesia); onset within weeks of therapy initiation	Give an anticholinergic (benztropine) or a dopamine agonist (amantadine) ↓ The dose of neuroleptic or discontinue (if tolerated) Older adults are at increased risk
Akathisia	Subjective/objective restlessness	↓ Neuroleptic and try β-blockers (propranolol) Benzodiazepines or anticholinergics may help
Tardive dyskinesia	Stereotypic oral-facial movements; likely from dopamine receptor sensitization; often irreversible (50%); more common in older women; generally occurs after long-term use	Discontinue or ↓ the dose of neuroleptic; consider changing neuroleptic (eg, to clozapine or quetiapine) Giving anticholinergics or decreasing neuroleptics may initially worsen tardive dyskinesia

- Olanzapine and clozapine cause the most weight gain and carry the risk of diabetogenesis.
- Clozapine may also cause sialorrhea (drooling), agranulocytosis, myocarditis, severe constipation, and seizures (requires CBCs weekly during the first 6 months, followed by biweekly for 6 months, then monthly monitoring for the remainder of treatment).

MOOD STABILIZERS

Lithium

- **Applications:** Used for long-term maintenance or prophylaxis of bipolar disorder and for both depression and mania. ↓ Suicidal behavior/risk in bipolar disorder. Has a narrow therapeutic index and requires monitoring of serum levels.
- **Side effects:**
  - Thirst, polyuria, fine tremor, weight gain, diarrhea, nausea, acne, and hypothyroidism.
  - Lithium toxicity presents with a coarse tremor, ataxia, vomiting, confusion, seizures, and arrhythmias.
  - Teratogenic. Risk of Ebstein anomaly in pregnancy, particularly in first trimester (though this is rare and safer than valproate in pregnancy).

Valproic Acid

- **Applications:** First-line agent for acute mania and bipolar disorder; effective in rapid cyclers (those with four or more episodes per year).
- **Side effects:**
  - Sedation, weight gain, hair loss, tremor, ataxia, GI distress.
  - Pancreatitis, thrombocytopenia, and fatal hepatotoxicity can occur. Do not use in patients with cirrhosis or severe hepatitis.
  - Monitor platelets, liver function tests (LFTs), and serum drug levels. All mood stabilizers are associated with highest risk of teratogenicity (neural tube defects).

KEY FACT

When using lithium, monitor renal and thyroid function. Long-term use can lead to hypothyroidism, diabetes insipidus, and nephrotoxicity.

KEY FACT

Dehydration, diuretics, NSAIDs, angiotensin-converting enzyme inhibitor, and hyponatremia can increase lithium levels dangerously. Severe toxicity may require hemodialysis.

Q

An 86-year-old woman with vascular dementia in a nursing home is becoming more agitated and experiencing distressing hallucinations of animals chasing her. You feel that treatment with a low-dose antipsychotic may benefit the patient. What risk of treatment is critical to discuss prior to initiation and how will you manage this?

Carbamazepine

- **Applications:** Second-line agent for acute mania and bipolar disorder.
- **Side effects:**
  - Common: Nausea, sedation, rash, and ataxia.
  - Rare: Hepatic toxicity, syndrome of inappropriate secretion of antidiuretic hormone (leading to hyponatremia), bone marrow suppression (leading to life-threatening dyscrasias such as aplastic anemia), and Stevens-Johnson syndrome.
  - Monitor blood counts, transaminases, and electrolytes. Drug interactions complicate its use (eg, cannot be used with MAOIs). Lowers levels of other drugs due to cytochrome P450 induction.
  - Teratogenic.

Other Anticonvulsants Used in Bipolar Disorder

- Include oxcarbazepine, lamotrigine, gabapentin, and topiramate.
- Efficacy is not as well documented.
- Do not require blood level monitoring and do not cause weight gain.
- Lamotrigine is associated with Stevens-Johnson syndrome and toxic epidermal necrolysis. Used in bipolar depression, not effective for mania.

Diagnostic and Statistical Manual of Mental Disorders

Psychiatric disorders affect (but do not always limit) a person's ability to handle daily living and/or social or occupational situations. The American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders*, Fifth Edition (DSM-5), provides diagnostic criteria useful for guiding treatment in psychiatric disorders.

Neurodevelopmental Disorders

KEY FACT

Fetal alcohol syndrome is the main preventable cause of intellectual disability; fragile X is the most common inherited cause. Down syndrome is not inherited but is caused by a chromosome disorder (trisomy 21).

AUTISM SPECTRUM DISORDERS

More common in males. Symptoms are usually recognized by age 2 and are characterized by lack of social interaction. It likely has a genetic component.

History/PE

- Characterized by abnormal social interaction; deficits in nonverbal communication (eg, eye contact, facial expressions); and restricted, repetitive, and stereotyped patterns of behavior, interests, and activities.
- Children may or may not have intellectual and language impairment.

Differential

- **Fragile X syndrome:** A trinucleotide CGG repeat disorder. Children have long faces, a large body size, and macro-orchidism. It is the most common inherited cause of intellectual disability.
- **Rett disorder:** An X-linked genetic disorder that affects only girls. It is characterized by normal development until 6–18 months with arrest or deterioration of mental (especially language) and motor skills; progressive microcephaly; and purposeless, stereotyped hand movements. Epilepsy is comorbid in 70–90% of cases.

A

Increased risk of death from all causes. Use the lowest dose for the shortest period possible and frequently re-evaluate necessity.

Treatment

- **Early intervention** to treat speech delays and help with socialization.
- **Applied behavioral analysis** helps reinforce positive behaviors. Other forms of therapy, including occupational, speech, and sensory integration, may be helpful as well.
- **Irritability and aggression** can be treated with antipsychotics, including risperidone and aripiprazole.

KEY FACT

Always do a hearing test in a child who shows poor language development or does not respond to his name.

ATTENTION-DEFICIT/HYPERACTIVITY DISORDER

The most common childhood psychiatric disorder.

History/PE

- Attention-deficit/hyperactivity disorder (ADHD) presents before age 12.
- It involves six or more symptoms for 6 months of either inattention (eg, easy distractibility, difficulty following instructions/finishing tasks, disorganization) or hyperactivity/impulsivity (eg, fidgeting/interrupting others/difficulty waiting) in two or more settings (school, work, home).
- Many children will continue to have symptoms through adulthood.

Treatment

- Pharmacotherapy is generally first line except in young children (< 6 years) for whom behavior modification is preferred and in patients with contraindications to medication (eg, severely underweight).
- Pharmacologic approaches include stimulants (eg, amphetamines, methylphenidate) or nonstimulant medications (eg, atomoxetine, α_2-agonists, bupropion).
- Stimulants have not been shown to lead to substance use disorders. However, if there is a history of substance abuse, a nonstimulant may be preferable.

KEY FACT

Complete a cardiac history and PE and measure vitals and weight prior to initiating treatment with stimulants.

TIC DISORDERS

Distinguished as follows:

- **Tic:** A sudden, rapid, recurrent, nonrhythmic motor movement or vocalization. Common but often transient.
- **Tourette syndrome:** Multiple motor and vocal tics such as blinking, grimacing, or grunting that occur many times a day for > 1 year and cause functional impairment. It is associated with ADHD and OCD. Treat with dopamine receptor antagonists (eg, haloperidol, pimozide), clonidine, and behavioral therapy. Stimulants can worsen or precipitate tics.

Psychotic Disorders

SCHIZOPHRENIA

A disorder of dopamine (↑ in the limbic system—positive symptoms—and ↓ in the frontal cortex—negative symptoms). Lifetime prevalence is 1%, with peak onset in the late teens to 30s. A ⊕ family history ↑ risk.

- Few patients have a complete recovery; social/occupational dysfunction can be significant.
- Associated with ↑ risk of substance abuse and suicide. It is important to rule out substances as a cause prior to making the diagnosis.

Q

A mother brings her 18-month-old son to the pediatrician because he is nonverbal. He was born full term and met all milestones. He rarely gestures or points at things and always plays alone. On exam, he does not respond to his name or make eye contact. A hearing test was normal. What is the most likely diagnosis?

History/PE

- Two or more positive or negative symptoms must be present for at least 1 month and must result in impairment of functioning. Of these, delusions, hallucinations, or disorganized speech must be present. Continuous signs of the disturbance must persist for at least 6 months.
  - **Positive symptoms:** Bizarre delusions, hallucinations, disorganized thoughts/speech/behavior. Hallucinations are usually auditory (eg, running commentary/monologues or conversations between two voices) but may also be visual, tactile, or, rarely, olfactory.
  - **Negative symptoms:** Affective flattening, avolition, apathy, alogia.

KEY FACT

A bizarre delusion is an absurd, implausible, fixed false belief that is not shared by other members of the society or culture—eg, the conviction that Martians have implanted electrodes into one's brain.

Differential

- **Brief psychotic disorder:** Symptoms are of < 1 month's duration; onset often follows a psychosocial stressor.
- **Postpartum psychosis:** A psychiatric emergency due to ↑ risk of infanticide. Some clinical features of delirium; more likely in mothers who have bipolar disorder. Treat with lithium and antipsychotics.
- **Schizophreniform disorder:** Diagnostic criteria are the same as those for schizophrenia, but symptoms have a duration of 1–6 months. Estimated 60–80% will progress to schizophrenia.
- **Schizoaffective disorder:** Mood symptoms are present for a significant portion of the illness, but psychotic symptoms have been present for at least 2 weeks without a mood episode.
- **Delusional disorder:** Nonbizarre delusions for 1 month or more in the absence of other psychotic symptoms; often chronic, typically responds poorly to antipsychotics.
- **Other:** Schizotypal personality disorder; mood disorder with psychotic features (contrast with schizoaffective disorder); substance-induced psychosis (eg, dopaminergic medications, including carbidopa-levodopa or illicit drugs such as amphetamines) or drug withdrawal (eg, alcoholic hallucinosis); psychosis due to a general medical condition (eg, brain tumor); delirium or dementia; shared psychotic disorder.

KEY FACT

Good prognostic signs in schizophrenia include later age of onset, female gender, acute onset of symptoms, social support, more positive than negative symptoms, no family history.

Diagnosis

- Rule out medical causes such as metabolic disorders, thyroid dysfunction, and intoxication.
  - Check thyroid-stimulating hormone (TSH), electrolytes, drug screen.
  - In selected patients, may also consider checking VDRL to rule out syphilis and EEG to look for epilepsy.

KEY FACT

People with schizophrenia are more likely to attempt and complete suicide. Screen patients carefully and hospitalize if needed.

Treatment

- Hospitalize if the patient is a danger to self or to others.
- Treat with antipsychotic medications (neuroleptics).
- Provide psychosocial treatments, social skills training (particularly for negative symptoms), individual supportive psychotherapy, and family therapy for relapse prevention.

KEY FACT

Negative symptoms are less responsive to pharmacotherapy.

Mood (Affective) Disorders

MAJOR DEPRESSIVE DISORDER

A

Autism spectrum disorder.

Average age of onset is in the mid-20s. Often associated with a life stressor and a high (15%) incidence of suicide; it is important to complete a suicide risk assessment. Hospitalize (involuntarily if necessary) if there is suicidal ideation

with plan and/or intent. If there are passive suicidal thoughts (eg, "I wish it were all over"), outpatient treatment is usually sufficient.

History/PE

Symptoms (**SIG E CAPS**) last 2 or more weeks and must lead to significant dysfunction or impairment.

Differential

- **Persistent depressive disorder (dysthymia):** A milder (two symptoms of major depressive disorder [MDD]), chronically depressed state of 2 or more years' duration.
- **Bereavement:** Does not involve severe impairment, anhedonia, or suicidality; usually improves within 2 months (but can last up to 1 year). Symptoms may vary with cultural norms. For example, visual and auditory hallucinations (eg, seeing or speaking with the deceased) are common and considered normal. Feelings of grief around anniversaries and other special events beyond the 1-year period are also common.
- **Adjustment disorder with depressed mood:** Does not meet full criteria for a mood episode (eg, MDD); occurs within 3 months of a stressor and lasts < 6 months.
- **Bipolar disorder:** Patients can present with depression, so carefully screen for a history of a manic episode. Use caution with SSRIs, as they can precipitate a manic episode.
- **Other mood disorder:** Substance-induced (eg, illicit drugs, β-blockers, oral contraceptives) or due to a medical condition (eg, hypothyroidism, stroke); dementia.

Diagnosis

Requires either or both depressed mood (irritability in children/adolescents) and anhedonia and at least five of the following symptoms during a 2-week period:

- Insomnia or hypersomnia.
- Feelings of worthlessness or excessive guilt.
- Fatigue or loss of energy.
- ↓ Ability to concentrate or indecisiveness.
- Significant weight loss or weight gain/change in appetite.
- Psychomotor agitation or retardation.
- Recurrent thoughts of death or suicide.

Treatment

- **Pharmacotherapy:**
  - Most antidepressants have equal efficacy.
  - If there is co-occurring depression and insomnia, treating the depression will often improve sleep.
  - SSRIs (eg, fluoxetine, paroxetine), serotonin-norepinephrine reuptake inhibitors (SNRIs) (eg, venlafaxine), and bupropion are the main treatments; SSRIs are generally first line.
  - Generally takes 6 weeks for full effect; this is minimum for an "adequate trial" of an antidepressant.
  - Generally safe, but common side effects include GI upset, akathisia, sexual dysfunction (most common with SSRIs; add or use bupropion instead).
  - Abrupt discontinuation can lead to uncomfortable withdrawal symptoms that resolve and are not life-threatening.

KEY FACT

Untreated depression may worsen morbidity and mortality of cardiovascular disease and vice versa.

MNEMONIC

Symptoms of depression—

SIG E CAPS

Sleep (↓/↑)
Interest (↓)
Guilt
Energy (↓)
Concentration
Appetite (↓/↑)
Psychomotor agitation or retardation
Suicidal ideation

KEY FACT

Depression-related cognitive dysfunction "pseudodementia" may present similarly to dementia in older adults. Emphasizing one's own failures, a lack of effort on cognitive testing, and significant subjective deficits incongruent with exam suggest depression.

- **Electroconvulsive therapy (ECT):**
  - ECT is safe and effective. It is best for psychotic or catatonic depression but may also be used for acute mania or psychosis as well as for patients who refuse to eat or drink (eg, severely depressed elderly person) or are suicidal.
  - Side effects include postictal confusion, arrhythmias, headache, and retrograde amnesia (inability to recall memories before the event).
  - Relative contraindications include intracranial mass, aneurysm, and recent myocardial infarction/stroke. Pregnancy is not a contraindication.
- Psychotherapy combined with antidepressants is more effective than either modality alone.

KEY FACT

Severe MDD can present with psychotic symptoms, in which case an antipsychotic in addition to an antidepressant may be required.

KEY FACT

Seasonal affective disorder, typified by fall/winter depression, carbohydrate craving, and hypersomnia, is treated with bright-light therapy (phototherapy).

KEY FACT

Catatonia may be observed in both schizophrenia and mood disorders.

BIPOLAR DISORDER

Prevalence is 1–2%. A family history of bipolar illness significantly ↑ risk. The male-to-female ratio is 1:1. Symptoms usually appear around age 20. About 10–15% of those affected die by suicide.

History/PE

- A manic episode is defined as follows:
  - One week of an abnormally and persistently elevated ("euphoric"), expansive, or irritable mood.
  - At least three of the symptoms (four if the mood is irritable) in the mnemonic **DIGS FAR.**
- A mixed episode characterized by full manic or hypomanic criteria and three major depressive symptoms.
- If psychotic features are present or hospitalization is required due to the severity of symptoms, the episode meets criteria for full mania.

MNEMONIC

Symptoms of a manic episode—

DIGS FAR

Distractibility
Insomnia (↓ need for sleep)
Grandiosity (inflated self-esteem)
Pressured **S**peech
Flight of ideas (racing thoughts)
Psychomotor **A**gitation/↑ Goal-directed Activity
Recklessness/pursuit of pleasurable but risky behaviors (eg, gambling, sexual indiscretions)

Differential

- **Hypomania:** Symptoms last for at least four days, do not cause the same degree of functional impairment of a manic episode (eg, do not usually require hospitalization).
- **Cyclothymic disorder:** Periods of hypomanic symptoms over 2 or more years that never meet full criteria for hypomania/mania, and depressive symptoms that never meet criteria for a major depressive episode.
- **Other:** Substance-induced mood disorder, schizophrenia, schizoaffective disorder, personality disorders, medical conditions (eg, temporal lobe epilepsy, hyperthyroidism), ADHD.

Diagnosis

- **Bipolar I disorder:** Diagnosis made after just one manic episode. Depressive episodes are common but are not required for diagnosis.
- **Bipolar II disorder:** Characterized by at least one hypomanic (rather than manic) episode alternating with at least one major depressive episode.

Treatment

- **Acute mania:** Lithium, anticonvulsants, antipsychotics, benzodiazepines, ECT.
- **Bipolar depression:** Mood stabilizers (lithium or lamotrigine are first line). Monotherapy with an antidepressant is not recommended. If the patient does not respond to first-line treatment, the next step may include adding lamotrigine (if started with lithium). In severe cases, consider ECT.

Anxiety Disorders

PHOBIA

Defined as persistent, excessive, or unreasonable fear and/or avoidance of an object or situation that leads to significant distress or impairment. The three categories of phobia are agoraphobia, social phobia, and specific phobia.

History/PE

- Exposure to the object or stimulus may precipitate panic attacks.
- **Social phobia (social anxiety disorder)** is characterized by unreasonable, marked, and persistent fear of scrutiny and embarrassment in social or performance situations. It usually begins in adolescence.
- **Specific phobia** is immediately cued by an object or a situation (eg, spiders, animals, heights). It usually begins in childhood.

Diagnosis

- Symptom duration is 6 or more months for all ages.
- As in OCD, symptoms interrupt the patient's life, but patients no longer must recognize that their fears are excessive.

Treatment

- Cognitive-behavioral therapy (CBT) and pharmacotherapy (eg, SSRIs, benzodiazepines, β-blockers) are effective for social phobias.
- Behavioral therapy that uses exposure and desensitization is best for specific phobia.

PANIC DISORDER

More common in women, with a mean age of onset of 25. Often accompanied by agoraphobia, a fear of being in places or situations from which escape is difficult; of being outside the home alone; or of being in public places.

History/PE

- Characterized by discrete periods of intense fear or discomfort.
- Attacks are sometimes brought about by an identifiable trigger, but often not.
- There is excessive worry about having recurrent panic attacks.
- At least four of the symptoms in the **PANICS** mnemonic develop abruptly and peak within 10 minutes (may also include depersonalization).

Differential

Medical conditions (eg, angina, hyperthyroidism, hypoglycemia), substance-induced anxiety disorder, other anxiety disorders.

Diagnosis

- Characterized by recurrent, unexpected panic attacks.
- At least 1 month of worry about and/or behavioral change to avoid subsequent attacks.

Treatment

- CBT and pharmacotherapy with SSRIs, either alone or in combination with benzodiazepines.

MNEMONIC

Symptoms of panic disorder—

PANICS

Palpitations
Abdominal distress
Numbness, Nausea
Intense fear of death
Choking, **C**hills, **C**hest pain
Sweating, **S**haking, **S**hortness of breath

- Benzodiazepines (eg, alprazolam, clonazepam) are effective for immediate relief but have abuse potential.

GENERALIZED ANXIETY DISORDER

Can be associated with panic attacks, but they are expected and triggered by an identifiable stressor (vs unexpected panic attacks in panic disorder). Clinical diagnosis is usually made in the early 20s.

History/PE

- Characterized by excessive and pervasive worry about many activities or events, leading to significant impairment or distress.
- Patients may seek medical care for somatic complaints.

Differential

Substance-induced anxiety disorder, anxiety disorder due to a general medical condition (eg, hyperthyroidism), other anxiety disorders (eg, panic disorder, social phobia).

Diagnosis

Diagnostic criteria are as follows:

- Anxiety/worry on most days for at least 6 months.
- Three or more somatic symptoms, including restlessness, fatigue, difficulty concentrating, irritability, muscle tension, and sleep disturbance.

Treatment

- Venlafaxine, SSRIs, benzodiazepines, and buspirone; second-line treatment with TCAs is appropriate if other antidepressants are ineffective or are not tolerated.
- Benzodiazepines are useful for acute relief and as a bridge to long-term treatment with SSRIs.
- Psychotherapy (eg, CBT) and relaxation training are important adjuncts.

Obsessive-Compulsive and Related Disorders

OBSESSIVE-COMPULSIVE DISORDER

Typically presents in late adolescence or early adulthood; it can lead to severe functional impairment.

History/PE

- Obsessions are persistent, intrusive thoughts, impulses, or images that lead to anxiety/distress and interfere with daily life. Common themes are contamination and fear of harm to oneself or to others (eg, recurrent worry that you will harm someone close to you).
- Compulsions are conscious, repetitive behaviors (eg, hand washing) or mental acts (eg, counting) that patients feel driven to perform to neutralize anxiety from obsessions.

KEY FACT

In general, OCD is ego dystonic (manifestations cause distress), whereas OCPD is ego syntonic (does not cause distress).

Differential

Obsessive-compulsive personality disorder (OCPD), other anxiety disorders, medical conditions (eg, brain tumor, temporal lobe epilepsy, pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections).

Diagnosis

Patients recognize that their obsessions and/or compulsions are excessive, unreasonable productions of their own minds (rather than thought insertion). Nonetheless, their behaviors cause marked distress and are time consuming (take > 1 hour/day).

Treatment

Pharmacotherapy (eg, SSRIs, clomipramine, fluvoxamine) and psychotherapy (eg, exposure and response prevention).

BODY DYSMORPHIC DISORDER

Preoccupation with an imagined defect in appearance.

- **Hx/PE:** Multiple visits to surgeons and dermatologists are common; cosmetic procedures and interventions almost never help. Associated with depression.
- **Tx:** CBT and SSRIs.

HOARDING

Persistent difficulty discarding or parting with possessions, regardless of actual value, to save the items and avoid distress associated with discarding them. The items cause clogging and congestion in main areas of the home. Hoarding with excessive acquisition affects 80% of cases.

- **Hx/PE:** Hoarding behavior causes distress and impairment.
- **Tx:** CBT and address comorbid diagnoses. Difficult to treat, with a low response rate.

Trauma- and Stressor-Related Disorders

POSTTRAUMATIC STRESS DISORDER

Results from exposure to a traumatic event that involved actual or threatened death or serious injury and evoked intense fear, helplessness, or horror.

History/PE

- Examples of traumatic events include war, torture, natural disasters, assault, rape, and serious accidents.
- Patients may have experienced the trauma personally, or they may have witnessed the event in a way that leads them to feel personally threatened, helpless, and horrified (eg, a child witnessing a parent being assaulted).
- Nightmares and flashbacks are common.
- Watch for survival guilt, personality change, substance abuse, depression, and suicide.

Differential

- **Acute stress disorder:** Symptoms are like those of posttraumatic stress disorder (PTSD) but last < 1 month and occur within 1 month of a trauma.
- **Adjustment disorder with anxiety:** Emotional or behavioral symptoms occurring within 3 months of a stressor and lasting < 6 months.
- **Other:** Depression, OCD, acute intoxication or withdrawal, factitious disorders, malingering, borderline personality disorder.

Q

A 30-year-old high school guidance counselor presents to her dermatologist for irritation of her hands. She states that she washes her hands under hot water about 20 times a day and uses a variety of alcohol-based hand sanitizer products to avoid picking up germs. What is the best treatment for her disorder?

Diagnosis

Symptoms persist for > 1 month and include:

- Reexperiencing the event (eg, nightmares, flashbacks).
- Avoidance of trauma-related stimuli or numbing of general responsiveness.
- Hyperarousal (eg, hypervigilance, exaggerated startle, irritability, difficulty falling or staying asleep).

Treatment

- **First line:** SSRIs; if not tolerated or if ineffective, use TCAs or MAOIs. α_2-Adrenergic agonists (prazosin, clonidine), or β-blockers (propranolol) may be helpful for some patients.
- CBT, exposure therapy, and group therapy are also effective.

ADJUSTMENT DISORDER

The development of emotional or behavioral symptoms in response to an identifiable stressor occurring within 3 months of the stressor.

- **Dx:** Distress is out of proportion to the severity of the stressor. Symptoms do not meet the criteria for MDD or other disorders and resolve by 6 months once the stressor passes.
- **Tx:** Supportive therapy, CBT, or medication management of distinct symptoms (eg, sleep aids for insomnia); if symptoms become more severe or meet the criteria for another mood or anxiety disorder, antidepressants or anxiolytics may be indicated.

Dissociative Disorders

DISSOCIATIVE IDENTITY DISORDER

Formerly known as multiple personality disorder.

- **Hx/PE:** Patients present with two or more distinct personalities (aka "alters"). Often associated with severe and prolonged abuse and/or neglect in childhood. Comorbid PTSD is common.

DISSOCIATIVE AMNESIA

Temporary amnesia for one's own identity. It typically lasts hours to days. Like other dissociative disorders, it cannot be attributed to the ingestion of illicit substances or to other psychiatric conditions (eg, delirium).

- **Hx/PE:** Usually precipitated by acute stressors. It can be accompanied by a fugue involving travel to a different city or state and having established a new identity. Upon recovery, the individual is amnestic to the fugue episode as well as for the original stressor that caused it.

Somatic Symptoms and Related Disorders

The following disorders consist primarily of somatic symptoms without obvious medical diagnoses that cause significant impairment and distress. Because somatic symptom disorders often accompany medical diagnoses, a medical cause of symptoms must be ruled out before a diagnosis of somatic disorder is made.

A

SSRIs and CBT.

SOMATIC SYMPTOM DISORDER

Defined as somatic symptoms that are highly distressing and/or result in significant disruption of function. It affects women more than men, with a peak onset at 40–50 years of age.

- **Hx/PE:** Symptoms are accompanied by disproportionate thoughts, feelings, or behaviors regarding symptoms. The patient's suffering is authentic even if no medical cause is identified. It presents with predominant pain (formerly pain disorder)—pain intensity or a pain profile that is inconsistent with physiologic processes.
- **Tx:** Psychotherapy and SSRIs for comorbid depression/anxiety. Provide consistent follow-up with the primary care physician and/or psychiatric providers. Minimize unnecessary interventions.

ILLNESS ANXIETY DISORDER

Preoccupation for > 6 months with fear of having a serious disease based on misinterpretation of symptoms (rather than delusions). Formerly known as hypochondriasis.

- **Hx/PE:** Symptoms are exacerbated by or related to psychological factors, especially depression.
- **Tx:** Physical therapy, psychotherapy, and antidepressants. Analgesics rarely provide relief.

KEY FACT

Medical students are prone to thinking they have the symptoms of whatever disease they are studying. This may be nosophobia, or fear of contracting disease, rather than true hypochondriasis.

CONVERSION DISORDER

Characterized by alterations in voluntary motor or sensory function.

- **Hx/PE:** Symptoms are not volitionally produced and cannot be explained by a known organic etiology. Relation to a stressful event suggests association with psychological factors (eg, a mother who has paralysis of the right arm after hitting her child).
- **Tx:** Provide reassurance, psychotherapy, and close monitoring and follow-up. Symptoms usually subside spontaneously.

FACTITIOUS DISORDER

Falsification of physical or psychological symptoms, or inducing injury or illness (eg, a patient who injects himself with insulin) that is associated with identified deception. It is more common among health care workers than in the general population.

- **Hx/PE:** Symptoms are consciously produced, but the reason may be unconscious (eg, wanting to assume the sick role or be taken care of) and can be produced on oneself or on others (eg, a mother who gives her child nuts to induce anaphylactic shock).
- **Tx:** Provide therapy to resolve underlying issues; medication for comorbid diagnoses.

KEY FACT

All forms of factitious disorder were once called Munchausen syndrome, but now the term is reserved for only the most severe cases. Munchausen syndrome by proxy refers to symptoms and illness being feigned by a parent inflicting illness on a child.

MALINGERING

Conscious and deliberate feigning of symptoms for anticipated external rewards (eg, money, food, shelter).

Feeding and Eating Disorders

PICA

- Eating nonnutritive, nonfood substances (eg, ice, clay, sand, chalk, soil) over a period of at least a month.
- Possibly attributed to deficiencies in vitamins/minerals.
- More common with intellectual disability.

ANOREXIA NERVOSA

Females account for 90% of cases. Peak incidence is at age 14 and age 18. Risk factors include a ⊕ family history, higher socioeconomic status, poor self-esteem, psychiatric comorbidities (eg, major depression, OCD, anxiety), and body-conscious careers/activities such as modeling, ballet, and wrestling. Mortality from suicide or medical complications is 10%.

History/PE

KEY FACT

Amenorrhea is no longer required for the diagnosis of anorexia.

- Classified as restricting type (excessive dieting or exercising) or binge-eating/purging type (vomiting, laxatives, diuretics). It presents with the following:
  - Refusal to maintain normal body weight (ie, the patient is < 85% of ideal body weight).
  - Intense fear of weight gain.
  - Distorted body image.

Diagnosis

- Measure height and weight. Check CBC, electrolytes (including phosphate and magnesium), TSH/FT_4, and an ECG.
- Look for lanugo (fine body hair), dry skin, lethargy, bradycardia, hypotension, and peripheral edema.

Treatment

- Hospitalize if there is concern for refeeding syndrome, significant orthostasis, bradycardia, or electrolyte abnormalities.
- Patients often deny the health risks of their behavior. Monitor caloric intake and focus on slow weight gain. Individual, family, and group psychotherapy is crucial.
- Pharmacotherapy is generally not helpful, although SSRIs (fluoxetine) and atypical antipsychotics (olanzapine) have been used with limited success.
- Avoid bupropion, considering the risk of seizure.

BULIMIA NERVOSA

Affects 1–3% of young women. The prognosis is more favorable than that of anorexia nervosa. It is associated with an ↑ frequency of affective disorders, substance abuse, and borderline personality disorder.

History/PE

Patients have normal weight or are overweight but engage in the following behaviors at least once a week for 3 or more months:

- **Binge eating** with a sense of lack of self-control.
- **Compensatory behavior** to prevent weight gain (eg, self-induced vomiting, laxatives, diuretics, overexercise).

Diagnosis

- Look for poor dentition, enlarged parotid glands, scars on the dorsal hand surfaces (from finger-induced vomiting), electrolyte imbalances, and metabolic alkalosis.
- In contrast to anorexia nervosa, patients are typically distressed about their symptoms and behaviors and are consequently easier to treat.

Treatment

- Restore the patient's nutritional status and electrolytes.
- CBT is the most effective treatment. Antidepressants are useful even in nondepressed patients. Avoid bupropion, considering its seizure risk.

BINGE-EATING DISORDER

Occurs in normal-weight/overweight or obese individuals. It begins in adolescence or young adulthood and is common in those who are college-age.

Differential

- **Anorexia, binge-purge type:** Differentiated by weight; patients are underweight in anorexia but are of normal weight or overweight in binge eating.
- **Bulimia nervosa:** Patients with binge-eating disorder do not have compensatory behaviors such as purging, as seen in bulimia nervosa.
- Patients who seek treatment are usually older than those with anorexia or bulimia.

Diagnosis

- **Recurrent episodes of binge eating:** Episodes are characterized by eating, in a discrete period, more than most people would eat in similar situation, with a sense of lack of control over eating.
- **Binge eating is associated with three (or more) of the following:** Eating more rapidly than normal; eating until feeling uncomfortably full; eating large amounts of food when not feeling physically hungry; eating alone because of feeling embarrassed by how much one is eating; feeling disgusted with oneself, depressed, or guilty afterward.

Treatment

- **First line**: CBT and interpersonal psychotherapy. Lisdexamfetamine is approved to treat moderate to severe binge eating.
- In general, binge-eating disorder has a better rate of remission than bulimia nervosa or anorexia nervosa.

Elimination Disorders

ENURESIS

Not a clinical disorder until > 5 years of age as the child may not feel/understand neurologic impulses until then. Primary enuresis is when a child has never achieved continence. Secondary enuresis is when a child achieves nighttime continence for 6 months but then begins bedwetting again. Primary nocturnal enuresis often resolves spontaneously and does not require treatment.

- **Tx:** If necessary, treat initially with behavioral therapy (eg, bed alarms); desmopressin acetate or imipramine should be reserved for refractory cases.

Q

A 15-year-old boy presents to the pediatrician. He states that he has been exercising more and eating less so that he can make the school wrestling team. His growth curve has dropped from the 50th to the 15th percentile for weight. Which psychiatric diagnosis should be considered?

Sleep-Wake Disorders

INSOMNIA DISORDER

Defined as significant difficulty falling or staying asleep. It can have early-morning awakening and is associated with nonrestorative sleep.

- **Hx/PE:** The disorder cannot be attributed to physical or mental conditions but is often precipitated by anxiety. Symptoms occur three or more times a week for at least 3 months.
- **Tx:** CBT is the treatment of choice with best efficacy and durability, particularly in frail or elderly patients who may have side effects from sedatives. Sleep hygiene, hypnotics.

MNEMONIC

Hallucinations are:

Hypna**GO**gic—occur when you **GO** to sleep
Hypno**P**ompic—occur when you wake u**P**

NARCOLEPSY

Usually presents before age 30. It may be familial and is often associated with mood disorders, substance abuse, and GAD.

- **Hx/PE:** Presents with excessive daytime sleepiness and daytime sleep attacks characterized by ↓ rapid eye movement (REM) sleep latency. Symptoms occur at least three times per month for 3 or more months. It may involve hypnagogic (just before sleep) or hypnopompic (just before awakening) hallucinations and hypocretin deficiency, as measured by cerebral spinal fluid (CSF).
- **Tx:** First-line therapy is nonamphetamine stimulants (modafinil). Amphetamine stimulants (methylphenidate) can be added if needed.

KEY FACT

Cataplexy is sudden loss of muscle tone leading to collapse, usually in the setting of strong emotions or excitement. It is treated with SSRIs.

CIRCADIAN RHYTHM SLEEP-WAKE DISORDER

Discrepancy between when the patient would like to sleep and when he or she actually does so. It is often 2° to jet lag or shift work.

PARASOMNIAS

Non-REM Sleep Arousal Disorders

- **Sleepwalking:** Repeated episodes of rising from bed during sleep and walking about. Not responsive to efforts of others to communicate.
- **Sleep terrors:** Abrupt terror arousals from sleep, often starting with a panicky scream. The individual cannot be comforted by others. Resolve spontaneously in most cases.

REM Sleep Disorders

- **Nightmare disorder:** Repeated occurrence of extended, frightening, and well-remembered dreams. If comorbid with PTSD, treat with α-blockers. Systematic desensitization and relaxation may be helpful.
- **REM sleep behavior disorder:** Acting out dreams—arousal from sleep with vocalizations and complex motor behaviors, such as running, kicking, and punching. It can cause injury to the bed partner. Neurodegenerative disease such as Parkinson's develops in 50% of affected persons. Treat with clonazepam and melatonin.
- **Restless leg syndrome:** An urge to move legs that begins or worsens during periods of rest or inactivity, particularly at night, and is partially relieved by movement. It can be associated with iron deficiency, so check

A

Anorexia nervosa. Eating disorders are less common in males than in females but do occur.

serum ferritin level and is often comorbid with depression. Treat with dopamine agonists (eg, pramipexole, ropinirole).

Disruptive, Impulse Control, and Conduct Disorders

- **Oppositional defiant disorder:** Angry, irritable mood with hostile and defiant attitude toward authority figures of ≥ 6 months' duration. Patients easily lose their temper and are vindictive. May lead to conduct disorder. The most effective treatments are parent management training, family therapy, and CBT.
- **Conduct disorder:** A disorder in which a patient repeatedly and significantly violates societal norms and the rights of others (eg, bullies, tortures animals, steals/destroys property) for 1 or more years. Treatment usually involves behavioral therapy. It is considered a precursor to antisocial personality disorder.

Substance-Related and Addictive Disorders

SUBSTANCE USE DISORDER

The lifetime prevalence of using one or more illicit substances in the United States is roughly 40%. Comorbid psychiatric disorders are common.

History/PE

The signs, symptoms, and physical findings of acute intoxication and withdrawal are outlined in Table 17-2.

Diagnosis

- Check urine and serum toxicology. Offer human immunodeficiency virus (HIV) testing; check LFTs and consider hepatitis testing.
- Patients display loss of control over substance use, continued use despite knowledge of harm, and accumulating consequences from use (eg, arrest, job loss). These lead to clinically significant impairment and, in general, to an overall worsening of the situation.

Treatment

- Group therapy, 12-step programs, recovery housing. Hospitalization may be necessary for acute withdrawal. Provide methadone or buprenorphine maintenance for opiate use disorder.
- Treatment for tobacco use disorder includes counseling/physician advice, nicotine replacement, and bupropion or varenicline.

OPIATE USE DISORDER

Epidemic. Dangerous co-ingestions (benzodiazepines, alcohol, other CNS depressants) and potent formulations (eg, fentanyl) have contributed to overdose deaths.

- **Tx:** Replacement opiate agonist therapy is the gold standard for treatment (methadone or buprenorphine). Check QTc if treating with methadone. Treat acute symptoms of withdrawal with clonidine (α_2-antagonist), low dose benzodiazepines, comfort medications (treat GI distress, aches and pains, insomnia).

KEY FACT

DSM-5 no longer distinguishes substance abuse from substance dependence. Rather, it now uses modifiers—mild, moderate, or severe—to define severity of use.

MNEMONIC

MyDriasis: Pupil is Dilated.
MIosis: Pupil is pInpoint.
Alternatively: "Mydriasis" being the longer word "fits" in a larger pupil.

KEY FACT

Avoid varenicline in patients with unstable/untreated psychiatric conditions (severe depression, psychosis, suicidal ideation) due to ↑ likelihood of exacerbating symptoms.

MNEMONIC

Withdrawal from any of the three "**Bs**" may be fatal: "**B**ooze, **B**arbs, and **B**enzos."

TABLE 17-2. Signs and Symptoms of Intoxication and Withdrawal

Drug	Intoxication	Withdrawal
Alcohol	Disinhibition/impaired judgment, emotional lability, slurred speech, ataxia, aggression, hypoglycemia, blackouts (retrograde amnesia), coma	Tremor, tachycardia, diaphoresis, hypertension, malaise, nausea, seizures, delirium tremens (DTs), agitation, hallucinations; may be life-threatening and require hospitalization
Opioids	Euphoria leading to apathy, CNS depression, nausea, vomiting, constipation, pupillary constriction (miosis), respiratory depression (life-threatening in overdose) Naloxone/naltrexone will block opioid receptors and reverse effects (beware of the antagonist clearing before the opioid, particularly with long-acting opioids such as methadone)	Anxiety, insomnia, anorexia, diaphoresis, dilated pupils (mydriasis), fever, rhinorrhea, piloerection, nausea, stomach cramps, diarrhea, yawning, myalgias; extremely uncomfortable, but rarely life-threatening
Amphetamines, cocaine	Psychomotor agitation, impaired judgment, tachycardia, pupillary dilation, fever, diaphoresis, hypertension, paranoia, angina, arrhythmias, seizures, hallucinations, sudden death. Treat with sedatives and benzodiazepines for severe agitation and with symptom-targeted medications	Post-use "crash" with hypersomnolence, dysphoria/nightmares, depression, malaise, severe craving, suicidality
Phencyclidine hydrochloride (PCP)	Belligerence, psychosis, violence, impulsiveness, psychomotor agitation, fever, tachycardia, vertical/horizontal nystagmus, ataxia, seizures, delirium Give benzodiazepines or haloperidol for severe symptoms; otherwise, provide low sensory surroundings & reassurance	Recurrence of intoxication symptoms due to reabsorption in the GI tract; sudden onset of severe, random violence
LSD	Marked anxiety or depression, delusions, visual hallucinations, pupillary dilation. Flashbacks a possible long-term consequence Treat by providing reassurance and a low-stimulation environment. Give benzodiazepines for severe symptoms	
Marijuana (THC)	Euphoria, slowed sense of time, impaired judgment, "heightened senses," social withdrawal, ↑ appetite, dry mouth, diaphoresis, conjunctival injection, hallucinations, anxiety, paranoia, tachycardia, hypertension, amotivation	Rare but can occur in long-time heavy users; irritability, nausea/vomiting, depression, insomnia
Barbiturates	Low safety margin; respiratory depression	Anxiety, seizures, delirium, life-threatening cardiovascular collapse
Benzodiazepines	Interactions with alcohol, amnesia, ataxia, somnolence, mild respiratory depression	Rebound anxiety, seizures, tremor, insomnia, hypertension, tachycardia. Some similarities with alcohol withdrawal
Caffeine	Restlessness, insomnia, diuresis, muscle twitching, arrhythmias, psychomotor agitation	Headache, lethargy, depression, weight gain, irritability, craving
Nicotine	Restlessness, insomnia, anxiety	Irritability, headache, anxiety, weight gain, craving

- **Px:** Opiate-dependent patients will likely require higher doses of pain medications in acute injuries, surgery, etc. Do not undertreat acute pain. Discuss testing for hepatitis C virus and HIV with the patient used injection drugs.

ALCOHOL USE DISORDER

More common in men than in women. Evidence of a problem usually begins to surface between 18 and 25 years of age. A ⊕ family history ↑ risk. Common causes of death include suicide, cancer, heart disease, and hepatic disease.

Diagnosis

- Screen with the **CAGE** questionnaire (see mnemonic) or single-item screener: Check for number of days with > five drinks for men and > four drinks per women in the past year.
- Monitor vital signs for tachycardia and ↑ BP associated with withdrawal; look for stigmata of liver disease such as palmar erythema or spider angiomata.
- Labs may reveal macrocytosis and an ↑ aspartate aminotransferase (AST) and gamma-glutamyl transferase (GGT).

Treatment

- Rule out medical complications; correct electrolyte abnormalities and hydrate.
- Start a benzodiazepine taper (eg, chlordiazepoxide, lorazepam) for withdrawal symptoms (ie, the CIWA protocol).
- Give multivitamins and folic acid; administer thiamine before glucose to prevent Wernicke encephalopathy.
- Individual or group counseling, 12-step programs, disulfiram, naltrexone, or acamprosate may be of benefit.

Complications

- **GI bleeding** (eg, gastritis, varices, Mallory-Weiss tears), pancreatitis, liver disease, DTs, alcoholic hallucinosis, peripheral neuropathy, cerebellar degeneration.
- **Wernicke encephalopathy:** Acute and usually reversible ataxia accompanied by confusion and ophthalmoplegia.
- **Korsakoff syndrome:** A chronic and often irreversible condition marked by anterograde amnesia +/− confabulation.

MNEMONIC

CAGE questions:

1. Have you ever felt the need to **C**ut down on your drinking?
2. Have you ever felt **A**nnoyed by criticism of your drinking?
3. Have you ever felt **G**uilty about your drinking?
4. Have you ever had a morning **E**ye opener?

A total score of 2 or more "yes" answers is clinically significant and should be explored further.

KEY FACT

A**S**T and ALT in a ratio of 2:1 or greater suggests alcoholism. Think **S**cotch.

KEY FACT

Alcohol use is related to 50% of all homicides and automobile fatalities.

KEY FACT

DTs are a medical emergency with an untreated mortality rate of up to 40%. Treat aggressively with IV benzodiazepines.

Neurocognitive Disorders

DELIRIUM

Common in hospitalized medical or surgical patients and is a medical, not a psychiatric, disorder. May mimic psychosis or depression.

History/PE

- Acute onset of disturbances of consciousness (eg, lethargy, agitation) and/or perception (hallucinations) that "wax and wane" during the day and are punctuated by lucid intervals.
- Altered cognition (memory, orientation, language)—eg, diminished attention span, impaired short-term memory, or unclear speech.

MNEMONIC

Causes of delirium—

I WATCH DEATH

Infectious (encephalitis, meningitis, UTI)
Withdrawal (alcohol, benzodiazepines)
Acute metabolic disorder (electrolyte imbalance)
Trauma (head injury, postoperative)
CNS pathology (stroke, hemorrhage, tumor)
Hypoxia (anemia, cardiac failure)
Deficiencies (vitamin B_{12}, folic acid, thiamine)
Endocrinopathies (thyroid, glucose)
Acute vascular (shock, vasculitis, hypertension)
Toxins, substance use, medications
Heavy metals (arsenic, lead, mercury)

- A history suggesting a probable medical cause of delirium, though the etiology is often undetermined.

Differential

In contrast to delirium, dementia usually has an insidious onset; it includes chronic memory and executive function deficits and is characterized by symptoms that tend not to fluctuate during the day (see Table 17-3).

Diagnosis

- Evaluate for recent medication changes, hypoglycemia, hepatic encephalopathy, or UTI.
- Workup may include a CBC, electrolytes, blood urea nitrogen (BUN)/creatinine, glucose, LFTs, UA, urine toxicology, vitamin B_{12}/folate, TSH, VDRL, HIV, blood culture, serum calcium/phosphorus/magnesium, pulse oximetry, arterial blood gas (ABGs), CSF, or serum drug screening.
- The mnemonic **I WATCH DEATH** lists common etiologies of delirium.

Treatment

- Treat the underlying medical condition.
- Minimize or discontinue delirium-inducing drugs (eg, benzodiazepines, anticholinergics) and simplify medication regimens if possible. Provide reorientation techniques (eg, clocks or wall calendars) and an environment that will facilitate healthy sleep/wake cycles.
- Pharmacotherapy may be beneficial and includes low-dose antipsychotics (haloperidol, risperidone, olanzapine, quetiapine), usually for short-term use. Physical restraints may be necessary to prevent physical harm to self/others.

DEMENTIA

- General deterioration of function 2° to chronic, progressive cognitive decline with intact attention and consciousness.
- Most common among the elderly (those > 85 years of age) and most often caused by Alzheimer disease (50%) or multi-infarct/vascular dementia (25%).
- Refer to the Dementia section of Chapter 13 for further details.

TABLE 17-3. Delirium vs Dementia

	Delirium	Dementia
Course	Acute (abrupt onset); lasting hours to days; usually reversible	Chronic (progressive degradation); lasting months to years; usually irreversible
Functionality	Fluctuating ability to focus and shift attention; clouded consciousness	Alert; intact consciousness
Cognition	Like dementia, but more likely to include perceptual disturbances (hallucinations) and paranoia	Disrupted memory, orientation, and language; hallucinations present in ~ 30% of those with advanced disease
Causes	Evidence of a general medical condition causing the problem (seizures, postictal state, infections, thyroid disorders, urinary tract infection (UTI), vitamin deficiencies); substances (eg, cocaine, opioids, PCP); head trauma, kidney disease, sleep deprivation	Insidious processes such as Alzheimer disease, Huntington disease, vascular dementia, AIDS dementia, and MDD in elderly patients

DEPRESSION AND ANXIETY DUE TO A GENERAL MEDICAL CONDITION

- Depression can be 2° to drug intoxication (alcohol or sedative-hypnotics; antihypertensives such as methyldopa, clonidine, and propranolol) or to stroke, hypothyroidism, multiple sclerosis, or systemic lupus erythematosus (SLE).
- Anxiety may be caused by drugs (caffeine, sympathomimetics, steroids), endocrinopathies (pheochromocytoma, hypercortisolism, hyperthyroidism, hyperparathyroidism), metabolic disorders (hypoxemia, hypercalcemia, hypoglycemia), or SLE.

Personality Disorders

Defined as enduring patterns of inner experience and behavior that deviate from cultural standards. They are pervasive and inflexible; begin in adolescence or early adulthood; are stable and predictable over time; and they lead to distress or impairment (see Table 17-4). In some cases (eg, OCPD), however, personality disorders are more noticeable and bothersome to others than the person affected. Treat with psychotherapy. Pharmacotherapy is generally used only if psychiatric comorbidities exist.

TABLE 17-4. Signs and Symptoms of Personality Disorders

Disorder	Characteristics	Clinical Dilemma/Strategies
	Cluster A: "Weird"	
Paranoid	Distrustful and suspicious; interprets others' motives as malevolent; litigious	Patients are suspicious and distrustful of doctors and rarely seek medical attention Be clear, honest, noncontrolling, and nondefensive. Avoid humor. Maintain emotional distance
Schizoid	Think "D" for distant. Isolated, detached "loners"; have restricted emotional expression	
Schizotypal	Think "T" for thoughts. Odd behavior/appearance; exhibit cognitive or perceptual distortions (eg, magical thinking, ideas of reference)	
	Cluster B: "Wild"	
Borderline	Unstable mood/relationships and feelings of emptiness; impulsive; high risk of suicidal ideation or self-harm	Patients change the rules, demand attention, and feel that they are special Patient will manipulate staff and doctor ("splitting") Be firm: Stick to the treatment plan Be fair: Do not be punitive or derogatory Be consistent: Do not change the rules
Histrionic	Excessively emotional and attention seeking; sexually provocative	
Narcissistic	Grandiose; need admiration; have sense of entitlement; lack empathy	
Antisocial	Violate the rights of others, social norms, and laws; impulsive; lack remorse; may have a criminal history; begins in childhood as conduct disorder	

(continues)

TABLE 17-4. Signs and Symptoms of Personality Disorders *(continued)*

Disorder	Characteristics	Clinical Dilemma/Strategies
	Cluster C: "Worried and Wimpy"	
Obsessive-compulsive	Preoccupied with perfectionism, order, and control; miserly; have inflexible morals and values	Patients are controlling and may sabotage their treatment. Words may be inconsistent with actions Avoid power struggles. Give clear recommendations, but do not push patients into decisions
Avoidant	Socially inhibited; sensitive to rejection; fear being disliked or ridiculed	
Dependent	Submissive, clingy, need to be taken care of; have difficulty making decisions; feel helpless	

Psychiatric Emergencies

SUICIDE RISK ASSESSMENT

Suicide is the tenth leading cause of death in the United States. Protective factors include religious affiliation, social support, and responsibility to children. Risk factors include the following:

- **Gender:** Men complete suicide three times more often than do women, whereas women attempt suicide three times more frequently. Men tend to use violent methods (eg, hanging, firearms).
- **Age:** Those > 75 years of age account for 25% of completed suicides. Suicide is also the third leading cause of death in 15- to 24-year-olds, after homicides and accidents.
- **Ethnicity:** Two thirds of completed suicides are done by Caucasian men.
- **Psychiatric illness:** MDD, bipolar disorder, psychotic disorder, substance abuse or dependence.
- **Other risk factors:** Divorced or separated, recent stressors, unskilled/low education status, unemployment or job dissatisfaction; chronic, debilitating illness, substance use, hopelessness, impulsivity; a history of prior suicide attempts; and a family history of suicide.

KEY FACT

In a suicide risk assessment, access to firearms should always be assessed and is a risk factor for completed suicide.

NEUROLEPTIC MALIGNANT SYNDROME

A life-threatening complication of antipsychotic treatment. May also be precipitated in patients with Parkinson disease following the abrupt withdrawal of the dopamine precursor levodopa. Mortality is 10–20%.

History/PE

- Can occur at any time during treatment with antipsychotics.
- Presents with muscular rigidity and dystonia, akinesia, mutism, obtundation, and agitation.
- Autonomic symptoms include high fever, diaphoresis, hypertensive episodes, and tachycardia.
- Look for ↑↑ CK and ↑ liver enzymes. May progress to rhabdomyolysis and/or renal dysfunction.

Treatment

Stop the offending medication; give dantrolene, bromocriptine, or amantadine.

SEROTONIN SYNDROME

Typically emerges shortly after a medication addition, change, or increased dose, usually with multiple serotonergic agents. These can include MAOIs with SSRIs or SNRIs. Less commonly, it may involve lithium, levodopa, metoclopramide, ondansetron, tramadol, or illicit drugs.

History/PE

- Presents with delirium, agitation, tachycardia, diaphoresis, and diarrhea.
- Exam reveals myoclonus and hyperreflexia. In severe cases, patients may present with hyperthermia, seizures, rhabdomyolysis, renal failure, cardiac arrhythmias, and disseminated intravascular coagulation.

Treatment

Stop the offending medications; give supportive care. Administer a serotonin antagonist or cyproheptadine.

KEY FACT

Neuroleptic malignant syndrome is characterized by rigidity, whereas serotonin syndrome is characterized by myoclonus and hyperreflexia. Both can result in fever but are due to different offending agents.

NOTES

CHAPTER 18

PULMONARY

Pulmonary Function Testing

The measurements most often used in pulmonary function tests (PFTs) are forced expiratory volume in 1 second (FEV_1), forced vital capacity (FVC), total lung capacity (TLC), and diffusing capacity of the lungs for carbon monoxide (DLCO) (see Figure 18-1). Three major patterns of pulmonary diseases can be identified in PFTs: obstructive, restrictive, and normal.

- **Obstructive pattern** (asthma, chronic obstructive pulmonary disease [COPD], chronic bronchitis, and bronchiectasis): In all cases of obstruction, there will be a reduction in expiratory flow as noted on the spirogram. The FEV_1 will be reduced. However, this value might also be reduced in restrictive lung disease. Markers for airway obstruction include:
  - An FEV_1/FVC ratio of < 0.8 predicted for age and gender. Severe obstruction is designated by an FEV_1/FVC ratio of < 0.5.
  - An ↑ in the residual volume (RV), referred to as air trapping.
  - With more severe obstruction, increases in functional residual capacity (FRC) and total lung capacity (TLC) can also be seen.
- **Restrictive pattern** (obesity, kyphosis, inflammatory/fibrosing lung disease, interstitial lung disease):
  - The defining factor for restrictive lung disease is ↓ TLC. TLC, RV, vital capacity (VC), and FRC all tend to be reduced, though not in all cases.
  - Measurements of expiratory flow tend to be preserved, including the FEV_1/FVC.
  - Restrictive processes that are parenchymal in origin tend to also decrease the DLCO, whereas processes external to the lung usually have a preserved DLCO.
  - Although FEV_1 and FVC are low, the FEV_1/FVC ratio is normal or ↑.
  - An FVC of $< 80\%$ is suggestive of restriction when the FEV_1/FVC ratio is normal.

KEY FACT

FVC is ↓ in obstructive and restrictive disease; FEV_1/FVC is normal in restrictive disease and ↓ in obstructive disease.

KEY FACT

Although obstructive in nature, asthma is a reversible condition. It usually has a normal DLco because the alveoli are unaffected. By contrast, COPD is characterized by a ↓ DLco because some alveoli are destroyed and unavailable for gas exchange.

Table 18-1 outlines PFT findings in the setting of common lung conditions.

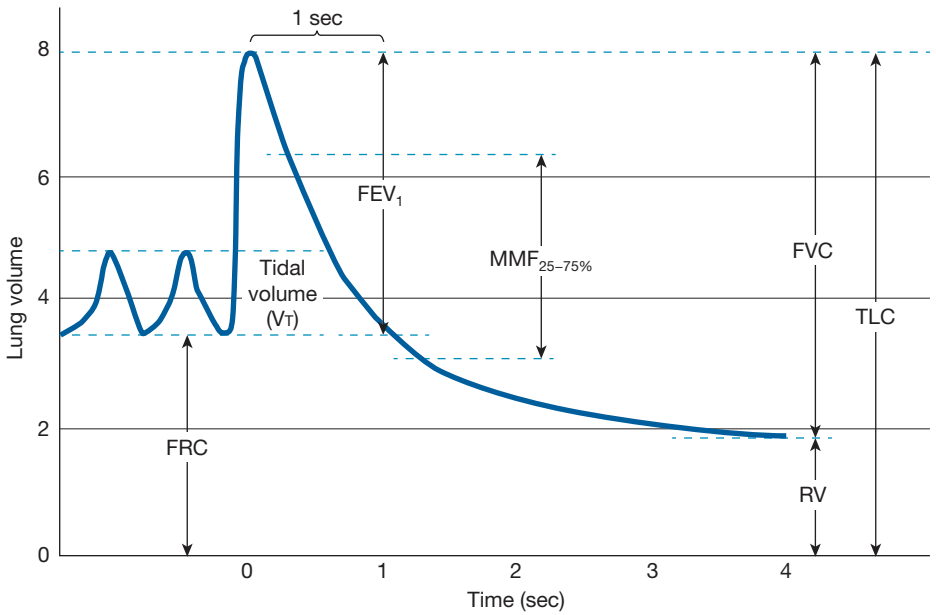


FIGURE 18-1. Normal forced exhalation curve. *FRC*, volume of air in the lungs remaining after passive expiration; $MMF_{25–75\%}$, flow between 25% and 75% of the FVC (mean maximal flow) flow rate; *RV*, volume of air in the lungs remaining after maximum expiratory effort.
(Reproduced with permission from USMLE-Rx.com.)

TABLE 18-1. Pulmonary Function Tests in Common Settings

Setting	FEV_1/FVC	TLC	DLco
Asthma	Normal/↓	Normal/↑	Normal/↑
COPD	↓	↑	↓
Fibrotic disease	Normal/↑	↓	↓
Extrathoracic restriction	Normal	↓	Normal

Asthma

An obstructive disease characterized by intermittent airway inflammation and hyperreactivity. Asthma is one of three most common causes of chronic cough along with postnasal drainage and gastroesophageal reflux disease (GERD).

History/PE

- Presents with intermittent wheezing, most commonly expiratory.
- Symptoms may be seasonal, follow exposure to triggers (eg, upper respiratory infections, dust, pet dander, cold air), or occur with exercise.
- Cough-variant asthma is triggered by exercise, cold, or forced exhalation.
- **Acute asthma exacerbations:**
  - During attacks, patients classically demonstrate a prolonged expiratory phase that is sometimes accompanied by wheezing or cough.
  - Determine severity by assessing mental status, the ability to speak in full sentences, use of accessory muscles, and vital signs. A normal or ↓ respiratory rate suggests respiratory fatigue.
  - Patients with severe exacerbations may have ↓ wheezing and may need prompt assessment of their gas exchange (with arterial blood gas [ABG] analysis) along with aggressive treatment, but don't let this delay care!
- **Chronic intermittent asthma:** Exam may be normal if the patient is not having an exacerbation.

Differential

- Rule out foreign body aspiration, endobronchial mass, vocal cord dysfunction or irritation, and heart failure (HF).
- In patients with chronic cough, think about asthma as well as allergic rhinitis, postnasal drip, or GERD.

Diagnosis

- Definitive diagnosis is made with an obstructive pattern on PFTs supported by reversibility with bronchodilators, as demonstrated by an 12% ↑ in FEV_1 and/or FVC and ≥ 0.20 L.
- If PFTs are normal but suspicion for asthma remains high, a methacholine challenge can be used to provoke symptoms in a monitored setting, or an exhaled nitric oxide level can be measured; a level > 50 ppb (> 35 ppb in children) may be used to indicate that eosinophilic inflammation and, in symptomatic patients, responsiveness to corticosteroids are likely.
- CXR is usually normal but can exclude other causes.

KEY FACT

Be wary of a normal/decreased respiratory rate, decreased breath sounds, or normal/increased partial pressure of carbon dioxide (PCO_2) in an asthma exacerbation—it can indicate impending respiratory failure!

KEY FACT

Not all that wheezes is asthma!

Q

A patient with a history of asthma that was previously controlled with once-monthly albuterol states that he has been using his albuterol inhaler four to five times a week. He denies any nighttime symptoms. How would you adjust his treatment regimen?

Treatment

- **Chronic asthma:** See Table 18-2.
- **Acute asthma exacerbations:**
  - Short-acting β-agonist (albuterol) therapy (nebulizer or MDI): β-Agonists activate β_2 receptors, leading to smooth muscle relaxation of the bronchial passages and thus dilation of the airways.
  - Systemic corticosteroids such as methylprednisolone or prednisone + inhaled corticosteroids (ICS).
  - A single 2-g dose of magnesium sulfate can be administered intravenously in severe exacerbations.
- Follow patients closely with peak flows and tailor therapy to the response. A peak flow that is < 50% of baseline flow suggests a medical emergency. Consider noninvasive positive-pressure ventilation or intubation if necessary (but try to avoid intubation at all costs).
- Antibiotics (in the absence of infection), anticholinergics, cromolyn sodium, and leukotriene antagonists are generally of no utility.

KEY FACT

ICS are safe for use in pregnancy.

Chronic Obstructive Pulmonary Disease

Defined as a chronic airflow obstruction that is not fully reversible. It is often accompanied by chronic cough and sputum production. Subtypes include emphysema and chronic bronchitis. COPD generally involves the destruction of lung parenchyma. This results in ↓ elastic recoil, which leads to air

TABLE 18-2. Medications for the Treatment of Chronic Asthma

Type	Symptoms (Day/Night)	FEV_1	Medications
Mild intermittent	≤ 2 days/week ≤ 2 nights/month	≥ 80%	**Step 1:** ■ No daily medications ■ SABA (albuterol) PRN
Mild persistent	> 2 times/week but < 1 time/day > 2 nights/month	≥ 80%	**Step 2:** ■ Daily low-dose ICS ■ SABA (albuterol) PRN
Moderate persistent	Daily > 1 night/week	60–80%	**Step 3:** ■ Low-dose ICS + LABA **or** Medium-dose ICS ■ SABA (albuterol) PRN
Severe persistent	Continual, frequent	≤ 60%	**Step 4:** Medium dose ICS + LABA **Step 5** (if unable to control symptoms): High-dose ICS + LABA **Step 6** (if still unable to control symptoms): High-dose ICS + LABA + PO SABA (albuterol) PRN for all steps

ICS, inhaled corticosteroids; LABA, long-acting β-agonist such as salmeterol; SABA, short-acting β-agonist.

Reproduced with permission from Le T et al. *First Aid for the USMLE Step 2 CK,* 10th ed. New York: McGraw-Hill, 2019: 480.

A

Add a low-dose ICS, as the patient now has mild persistent asthma.

trapping. TLC ↑ as a result of rising RV. Chronic bronchitis is defined as a chronic productive cough for 3 or more months in each of 2 consecutive years.

History/PE

- Patients complain of cough, excessive sputum production, dyspnea, and wheezing. Dyspnea is usually progressive.
- Look for a history of smoking.
- Exam may show ↓ breath sounds, cough (productive and nonproductive), pursed-lip breathing, barrel chest, rhonchi, or wheezing.
- Hypercarbia/hypoxia and weight loss are seen in later stages.
- Patients may show evidence of cor pulmonale (right HF from pulmonary hypertension).

KEY FACT

Think α1-antitrypsin deficiency in young COPD patients whose emphysematous changes have an apical predominance.

Diagnosis

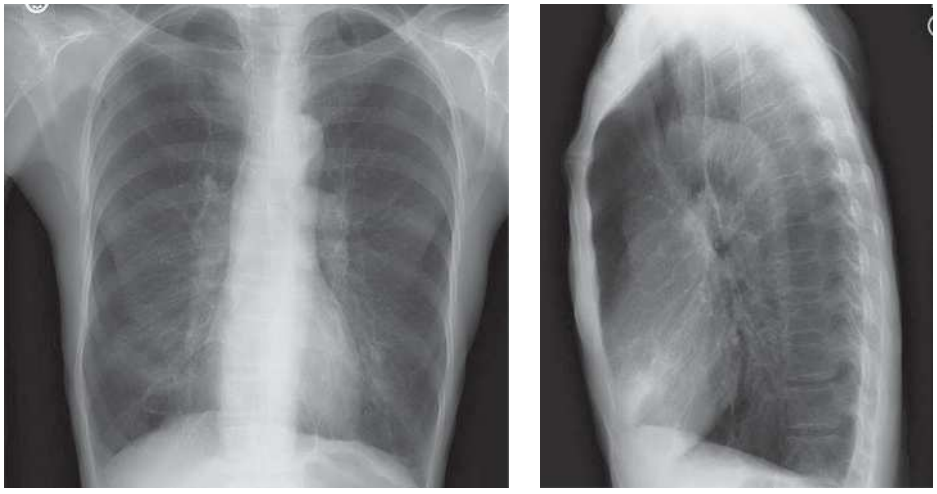
- The post-bronchodilator FEV_1/FVC is < 0.7 and $FEV_1 < 80\%$ of predicted. TLC is usually ↑.
- The condition is not fully reversible with bronchodilators.
- DLco tends to be ↓.
- CXR may show hyperlucent, hyperinflated lungs with flattened diaphragms (see Figure 18-2).

KEY FACT

Decreasing pH on ABG may indicate acute respiratory compromise.

Treatment

- **Stable COPD management:**
  - LABAs and long-acting muscarinic antagonists (eg, ipratropium) are preferred over short-acting agents except for patients with only occasional dyspnea.
  - Patients may be started on single LABA or dual long-acting bronchodilator therapy.
  - Theophylline is not recommended unless other long-term treatment bronchodilators are unavailable or unaffordable.
  - Long-term monotherapy with ICS is not recommended, nor is long-term treatment with oral corticosteroids.
  - O_2 therapy is indicated for patients with an $SaO_2 < 88\%$, a partial pressure of arterial oxygen (PaO_2) of < 55 mm Hg, or a PaO_2 of 55–60 mm Hg with right HF or erythrocytosis. Titrate O_2 to keep $SaO_2 > 90\%$.



A B

FIGURE 18-2. Chronic obstructive pulmonary disease. PA (**A**) and lateral (**B**) radiographs of a patient with emphysema show hyperinflation with large lung volumes, flattening of the diaphragm, and minimal peripheral vascular markings. (Reproduced with permission from USMLE-Rx.com.)

Q

You order PFTs for a patient with worsening shortness of breath. Which of the following values would be consistent with a diagnosis of COPD?

(A) Low FEV_1, low FVC, low FEV_1/FVC, high TLC, low DLco.
(B) Low FEV_1, low FVC, high FEV_1/FVC, low TLC, low DLco.

- Influenza vaccination is recommended for all patients with COPD.
- Pneumococcal vaccination (PCV13 and PPSV23) is recommended for all patients > 65 years of age and in younger patients with significant comorbid conditions including chronic heart or lung disease.
- Lung volume reduction surgery should be considered in selected patients with upper lobe emphysema.

- **Acute COPD exacerbations**: Defined as ↑ dyspnea, a change in cough or sputum production or increased oxygen requirements from baseline.
  - Check a CXR to look for causes of the exacerbation (eg, pneumonia, HF).
  - Hypoventilation leading to acute hypercarbia (an ↑ in PCO_2) may necessitate noninvasive positive pressure ventilation or mechanical ventilation.
  - Administer O_2 to maintain a SaO_2 90–95%.
  - Administer short-acting β-agonists with or without short-acting anticholinergics (eg, ipratropium).
  - Systemic corticosteroids can improve lung function (FEV_1) and oxygenation and shorten recovery time and hospitalization duration. Duration of therapy should not be more than 5–7 days for routine cases.
  - Antibiotics, when indicated, can shorten recovery time, reduce the risk of early relapse, treatment failure, and hospitalization duration. They should cover *Streptococcus*, *H influenzae*, and *Moraxella*, and duration of therapy should be 5–7 days. Appropriate options include any broad-spectrum antibiotics (eg, amoxicillin/clavulanate, trimethoprim-sulfamethoxazole, doxycycline, azithromycin, clindamycin, a respiratory fluoroquinolone, or a third-generation cephalosporin).

KEY FACT

O_2 therapy and smoking cessation have been shown to improve survival in patients with COPD.

Hypoxia and Hypoxemia

Hypoxia is a condition in which the body or a region of the body is deprived of adequate O_2 supply at the tissue level. Hypoxemia is ↓ PaO_2. Both conditions can be caused by multiple processes, outlined below.

Diagnosis

Determine the alveolar-arterial (A-a) oxygen gradient, calculated as $PAO_2 - PaO_2$.

- **Normal gradient** (5–10 mm Hg): Consider a low FiO_2 state or high altitude. Corrects with supplemental O_2.
- **Increased gradient:**
  - **Shunt physiology:** Does not correct with supplemental O_2. Causes may be pulmonary processes (alveolar collapse [atelectasis], lobar pneumonia, acute respiratory distress syndrome [ARDS]) or extrapulmonary processes (patent ductus arteriosus, patent foramen ovale).
  - **Ventilation-perfusion (V/Q) mismatch:** Corrects with supplemental O_2. Causes include asthma, COPD, pneumonia, interstitial lung disease, and pulmonary embolism (PE).

Hypoxia can also be accompanied by hypercarbia (↑ $PaCO_2$). Causes include:

- Hypoventilation from neuromuscular disorder or CNS disorder (opiates, stroke, central sleep apnea).
- COPD or obstructive lung disease (generally ↑ A-a gradient).

KEY FACT

Think of methemoglobinemia in patients with clinical cyanosis but a normal PaO_2. Treat with methylene blue, which restores the iron in hemoglobin to its normal (reduced) oxygen-carrying state.

Treatment

Always treat hypoxic patients with adequate amounts of O_2 to maintain saturations of > 90% or a PaO_2 of > 60 mm Hg.

A

The answer is A. Choice B describes a restrictive pattern.

Pleural Effusion

Characterized as either transudative or exudative by their composition.

History/PE

- Patients may be asymptomatic or present with shortness of breath, fatigue, or chest discomfort.
- Exam reveals ↓ breath sounds, dullness to percussion, and ↓ tactile fremitus on the affected side.

Diagnosis

- **CXR** (see Figure 18-3).
- **Ultrasound**: Can assist with thoracentesis.
- **CT**: Can better visualize fluid and characterize loculations.
- **Thoracentesis:** Determine whether the effusion is exudative or transudative by applying the Light criteria. Check serum protein, pleural fluid protein, and lactate dehydrogenase (LDH). Fluid is exudative if one of the following Light criteria is present (see Table 18-3):
  - Pleural fluid protein/serum protein ratio > 0.5.
  - Pleural fluid LDH/serum LDH ratio > 0.6.
  - Pleural fluid LDH level > 2/3 the upper limit of the laboratory's reference range of serum LDH.
- **Cell count with differential, Gram stain and culture, and glucose:** pH may be a helpful adjunct if you are concerned about infectious or rheumatologic etiology. Acid-fast bacilli (AFB) may be helpful if suspecting TB. Triglycerides may be helpful if suspecting a thoracic duct injury.

Treatment

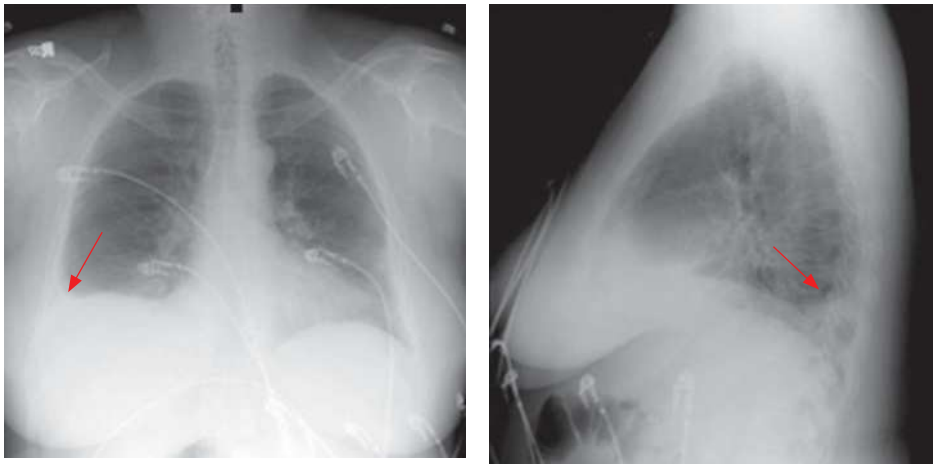
- **Thoracentesis** for an effusion > 10 mm thickness on lateral decubitus CXR may be both therapeutic and diagnostic.
  - If the fluid is transudative, focus on treating the underlying cause (ventriculoperitoneal shunt, HF, hypoalbuminemia, hepatic hydrothorax, nephrotic syndrome, peritoneal dialysis, urinothorax, atelectasis).
  - If the fluid is exudative, refer to Table 18-4 to help determine the cause.

KEY FACT

Consider a pleural biopsy if you suspect TB. Send the fluid for cytology if you suspect malignancy.

TABLE 18-3. Transudative vs Exudative Pleural Effusions

Pleural Fluid/Serum Protein (Ratio)	
Transudative	< 0.5
Exudative	> 0.5
Pleural Fluid/Serum LDH (Ratio)	
Transudative	< 0.6
Exudative	> 0.6
Pleural Fluid LDH	
Transudative	< ⅔ upper limit of normal (ULN) for reference laboratory
Exudative	> ⅔ ULN for reference laboratory



A B

FIGURE 18-3. Pleural effusion. PA (**A**) and lateral (**B**) CXRs show blunting of the right costophrenic sulcus (*arrows*). (Reproduced with permission from USMLE-Rx.com.)

Q

A 33-year-old man presents with cough, night sweats, and pleuritic chest pain. CXR shows a left pleural effusion. PPD demonstrates 16 mm of induration. Thoracentesis reveals a glucose level of 50 mg/dL, LDH 340 U/L, pleural fluid protein 4.6 g/dL, and serum protein 3.0 mg/dL. A sputum culture for AFB is ⊖. What is the next step?

TABLE 18-4. Exudative Pleural Effusion Differential Diagnosis

Pleural Assay	Value	Differential
Glucose	< 60	Empyema, parapneumonic, TB, rheumatologic, malignancy
WBCs	> 10,000	Empyema, parapneumonic, rheumatoid arthritis, malignancy
RBCs	> 100,000	Traumatic tap, hemothorax, PE, malignancy
Cellular differential		
Lymphocytes	85–95% of total nucleated cells	TB, sarcoid, malignancy, chylothorax
Polymorphonuclear leukocytes	Nonspecific	Empyema, PE
Eosinophils	>10% total nucleated cells	Bleeding, pneumothorax
pH	< 7.20	Complicated effusion, empyema, rheumatologic
Triglycerides	> 110	Diagnostic of chylothorax

- **Thoracostomy tube indications:** Empyema, hemothorax, malignant effusion, recurrent effusion, chylothorax, pneumothorax, hemopneumothorax.

Complications

- An untreated pleural effusion in the setting of pneumonia may become infected and turn into an empyema.
- Over time, exudative effusions may become loculated and require drainage by video-assisted thoracoscopy (VATS) or surgical decortication.
- Complications of thoracentesis include pneumothorax and bleeding (remember, the neurovascular bundle runs along the inferior side of the rib). Use ultrasound during the procedure to minimize the risk of pneumothorax and obtain a CXR afterward.

Pneumothorax

Abnormal collection of air in the pleural space between the lung and the chest wall.

KEY FACT

Suspect pneumothorax with shortness of breath and chest pain plus underlying COPD, cystic fibrosis (CF), chest procedures (eg, central lines), trauma, or smoking history. A 1° pneumothorax may be seen in young adults with a tall, thin body habitus.

History/PE

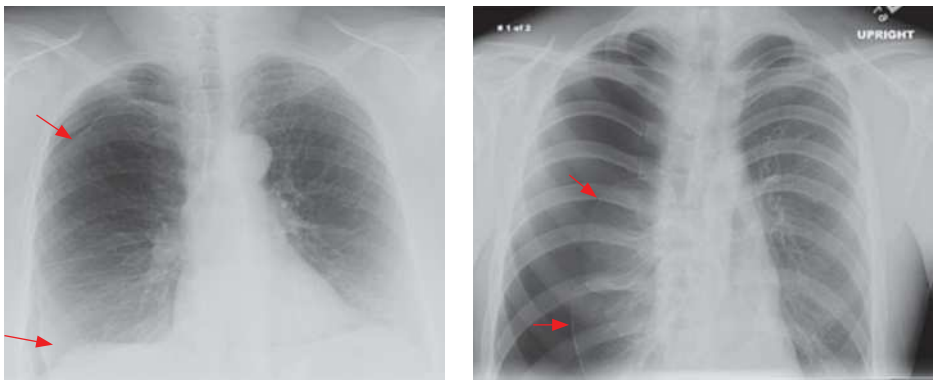
- May present with acute shortness of breath with or without pleuritic chest pain.
- Exam reveals tachypnea, ↓ tactile fremitus, ↓ breath sounds, tympany on percussion on the affected side, and tracheal deviation toward the opposite side (if tension pneumothorax).

Diagnosis

- The main feature on CXR is a white visceral pleural line, which is separated from the parietal pleura by a collection of gas. In most cases, no pulmonary vessels are visible beyond the visceral pleural line (see Figure 18-4).
- Tracheal deviation away from the side of the pneumothorax suggests tension pneumothorax (see below).

A

This patient has an exudative pleural effusion with suspected TB. He will need a pleural biopsy to confirm the diagnosis of TB despite having a ⊖ sputum culture.



A B

FIGURE 18-4. Pneumothorax. (**A**) Small right pneumothorax. (**B**) Right tension pneumothorax with collapse of the right lung and shifting of mediastinal structures to the left. Arrows denote pleural reflections. (Reproduced with permission from USMLE-Rx.com.)

Treatment

- **Minimal pneumothorax** (< 15–20% by Light Index; 2–3 cm from apex to cupola by alternate criteria): Simple observation is appropriate for asymptomatic patients with close follow-up to ensure no enlargement.
- Needle aspiration is safe and effective.
- **Large pneumothorax** (eg, mediastinal shift, cardiovascular collapse): Tube thoracostomy should be performed in any symptomatic patient.
- **First-time 2° spontaneous pneumothorax** (COPD, trauma): Typically requires the approach above for minimal or large.

TENSION PNEUMOTHORAX

- Occurs when air enters the pleural cavity and is trapped during expiration. The intrathoracic pressure compresses the lung and displaces the mediastinum and its structures toward the opposite side, causing cardiopulmonary impairment.
- **Dx:** Look for a pneumothorax along with tachycardia, hypotension, ↑ O_2 requirements, and ↑ jugular venous pressure (JVP). The trachea deviates away from the side with tension.
- **Tx:** If you suspect that the patient has a tension pneumothorax, don't wait for imaging! Insert a large-bore needle with a syringe superior to the second or third rib at the midclavicular line on the side of ↓ breath sounds. Be sure to leave the needle or catheter in the pleural space while placing the chest tube or tension may recur.

Pulmonary Embolism

The factors that contribute to the formation of thrombi are remembered with the Virchow triad:

- **Stasis:** Immobility, HF, obesity, ↑ JVP.
- **Endothelial injury:** Trauma, surgery, recent fracture, prior deep venous thrombosis (DVT).
- **Hypercoagulable state:** Pregnancy, oral contraceptive pill use, coagulation disorders, malignancy, burns.

KEY FACT

The differential for shortness of breath/chest pain includes pneumothorax, myocardial infarction, PE, pleuritis, and aortic dissection.

Q 1

A 64-year-old man with COPD comes to the ED with sudden-onset shortness of breath that requires high levels of supplemental O_2. PE reveals ↓ breath sounds on the left side and tracheal deviation to the right along with hypotension. What is your next step?

Q 2

A 72-year-old patient who was admitted to the hospital for a hemorrhagic stroke develops shortness of breath. Imaging reveals a pulmonary embolus and a left lower extremity DVT. How do you proceed?

History/PE

- Chest pain, shortness of breath, syncope.
- Patients may have hemoptysis or a low-grade fever.
- Consider PE in patients who have risk factors for DVT/PE or leg pain and swelling.
- Exam shows tachypnea, tachycardia, cyanosis, a loud P2 or S2, ↑ JVP, and signs of right HF.

KEY FACT

Risk factors for thrombus include recent immobilization or surgery, malignancy, trauma and coagulation disorders.

Differential

Acute MI, pneumonia, pneumothorax, HF, aortic dissection.

Diagnosis

Initial assessment should include the following (see Figure 18-5):

- **ABGs:** May show a 1° respiratory alkalosis and an ↑ A-a gradient.
- **CXR:** Usually normal but may show atelectasis or the following:
  - A wedge-shaped infarct (Hampton hump).
  - Oligemia in the affected lobe (Westermark sign).
  - Pleural effusion.
- **ECG:** Most commonly demonstrates sinus tachycardia. The S1Q3T3 pattern of an S wave in lead I, a Q wave in lead III, and T-wave inversion in lead III may also be present, but this is neither sensitive nor specific.
- **Chest CT with contrast:** Has largely replaced V/Q scanning as the 1° diagnostic modality unless it is contraindicated by renal insufficiency (chronic kidney disease, not end stage renal disease), pregnancy, or contrast allergy. It will show filling defects in the affected vasculature (see Figure 18-6).
- **Pulmonary angiography:** Rarely necessary but can be considered and may be needed if other testing is intermediate.

KEY FACT

In patients with PEs, elevated cardiac troponins are associated with higher mortality.

KEY FACT

Submassive PE: hemodynamically stable with evidence of RV dysfunction (**S**ubmassive = **S**table).
Massive PE: hemodynamically unstable (ie, with hypotension).

Treatment

- ABCs are #1! Resuscitation should begin with stabilization and oxygenation.
- Treat venous thromboembolism (VTE) patients with anticoagulation to prevent recurrent VTE. Without anticoagulation, the risk of recurrent PE is 25%.
- Initially use IV heparin or low-molecular-weight heparin. Patients who are not adequately anticoagulated within 24 hours have a high rate of recurrence.

KEY FACT

The most common CXR finding in PE is atelectasis.

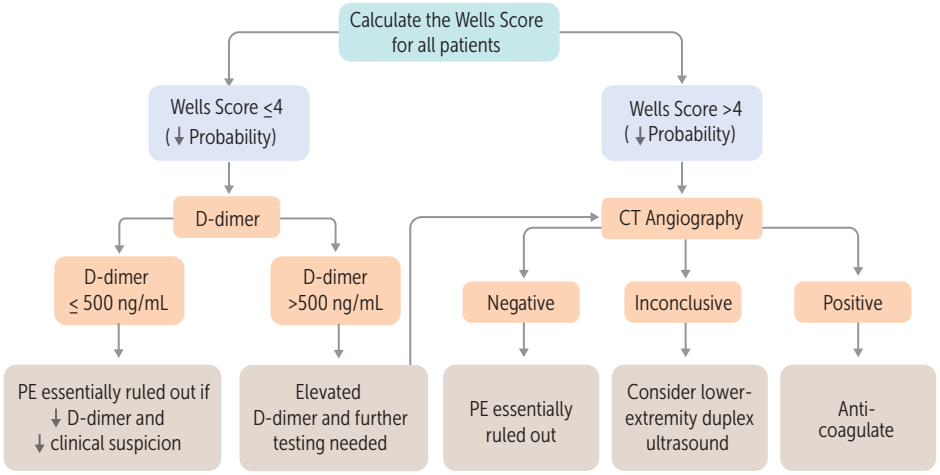


FIGURE 18-5. Diagnostic algorithm for pulmonary embolism using the modified Wells Criteria. (Reproduced with permission from USMLE-Rx.com.)

1 A

Needle decompression for presumed left-sided tension pneumothorax.

2 A

Place an inferior vena cava (IVC) filter. This patient is not a candidate for anticoagulation as she currently has a hemorrhagic stroke. Future PEs should be prevented with an IVC filter.

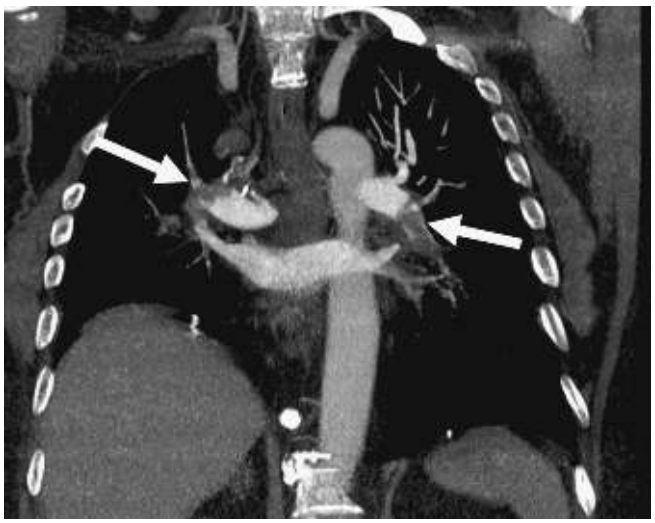


FIGURE 18-6. Bilateral pulmonary emboli. CT angiogram shows filling defects in the main and segmental pulmonary arteries (*arrows*) of a lung cancer patient who developed sudden shortness of breath and chest heaviness. (Reproduced with permission from Longo DL et al. *Harrison's Principles of Internal Medicine,* 18th ed. New York: McGraw-Hill, 2012, Fig. 262-3.)

- Patients can then be transitioned to warfarin therapy (with a goal INR of 2.0–3.0) or a novel anticoagulant (eg, apixaban or rivaroxaban).
- In patients with PE and hypotension or shock, consider administering tissue plasminogen activator (tPA) along with heparin. The duration of anticoagulation therapy will vary with risk factors.
- For patients with a first event and reversible or time-limited risk factors (eg, surgery, pregnancy), treat for at least 3–6 months.
- Consider lifelong anticoagulation in patients with chronic risk factors (eg, malignancy, paraplegia, genes for hypercoagulable conditions, recurrent DVTs, PEs).
- If contraindication to anticoagulation exists, or if the patient develops another thrombus while on anticoagulation, an IVC filter should be considered. Although these filters can ↓ the risk of PE, they are associated with a higher risk of recurrent DVT.

KEY FACT

tPA is currently only indicated in the treatment of MASSIVE pulmonary embolism. No hypotension = no tPA.

KEY FACT

Don't forget to order DVT prophylaxis for all your high-risk hospitalized patients to prevent a PE!

Acute Respiratory Distress Syndrome

Characterized by noncardiogenic pulmonary edema, resulting in bilateral, diffuse alveolar damage and hypoxia. It can be caused by a range of pulmonary and nonpulmonary conditions, including:

- Sepsis.
- Aspiration (usually massive aspiration of gastric contents).
- Pneumonia.
- Trauma (particularly trauma to the chest or massive tissue injury).
- Transfusion-related lung injury.
- Pancreatitis.

History/PE

Look for a patient with risk factors, usually in an ICU setting. Patients will have acute onset of hypoxia along with diffuse rales on exam and will be difficult to oxygenate. Intubation is usually required to maintain an acceptable PaO_2.

Diagnosis

- The Berlin definition of ARDS: Onset within 1 week of clinical insult or worsening of respiratory symptoms; radiographic changes (bilateral opacities not fully explained by effusions, consolidation, or atelectasis; see Figure 18-7); origin of edema not fully explained by cardiac failure or fluid overload; and severity based on the PaO_2/FiO_2 ratio on 5 cm of continuous positive airway pressure (CPAP).
- The 3 categories of ARDS are:
  - Mild (PaO_2/FiO_2 200–300).
  - Moderate (PaO_2/FiO_2 100–200).
  - Severe ($PaO_2/FiO_2 \leq 100$).

Treatment

- Patients typically require intubation and mechanical ventilation for the management of hypoxia.
- **Low tidal volumes** (4–6 mL/kg) and associated permissive hypercapnia may improve the risk of barotrauma.
- **Positive end-expiratory pressure (PEEP)** improves oxygenation and thus ↓ the FiO_2 requirement and associated O_2 toxicity.
- **Look for the underlying cause** and focus treatment on that as you stabilize the patient and treat hypoxia.

KEY FACT

Remember—use low tidal volumes and PEEP for the treatment of ARDS.

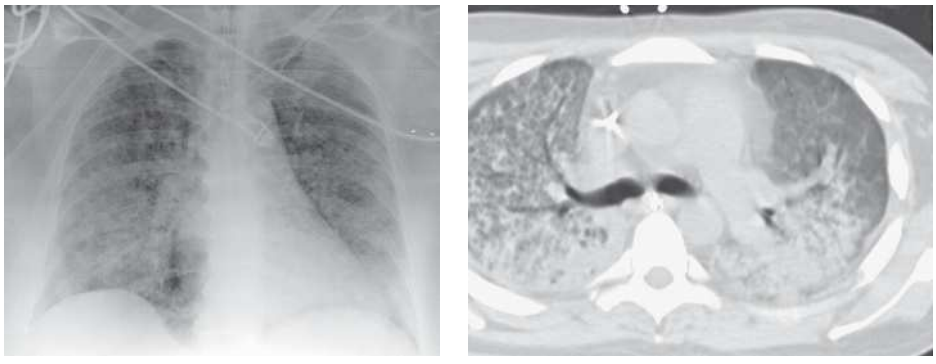
Solitary Pulmonary Nodule

Defined as a radiodense lesion seen on chest imaging that is < 3 cm in diameter and is not associated with infiltrates, adenopathy, or atelectasis.

History/PE

Most solitary pulmonary nodules (SPNs) are detected on routine CXR in patients who are otherwise asymptomatic. Nonmalignant and malignant lesions can be distinguished as follows:

- **Nonmalignant lesions** (eg, histoplasmosis, coccidioidomycosis, TB, hamartoma):
  - No growth on serial imaging 2 years apart.
  - A diffuse, dense and central, popcorn-like, or concentric "target" calcification pattern.



A **B**

FIGURE 18-7. Acute respiratory distress syndrome. (**A**) Frontal CXR showing patchy areas of airspace consolidation in a patient with ARDS. (**B**) Transaxial CT showing ground-glass opacity anteriorly and consolidations dependently in a patient with exudative-phase ARDS. (Reproduced with permission from Longo DL et al. *Harrison's Principles of Internal Medicine,* 18th ed. New York: McGraw-Hill, 2012, Figs. 262-2 and 268-4.)

- Occurrence in patients who are lifelong nonsmokers, are < 30 years of age, and have no history of malignancy.
- **Malignant lesions** (ie, lung cancer or metastases):
  - Size > 2 cm.
  - Spiculation (ie, ragged edges).
  - Sunburst pattern.
  - Upper lobe location.
  - Occurrence in patients who are smokers, are > 40 years of age, or have a prior diagnosis of cancer.

Diagnosis/Treatment

- Start by examining old radiographs to determine age and change in size. Lesions with > 1 malignant feature should be further evaluated with CT imaging.
- If imaging points to a malignancy, biopsy should be performed via bronchoscopy, needle aspiration, or VATS. If the probability of malignancy is low, evaluate with serial CXRs or CTs every 3 months for 1 year and then every 6 months for 1 year.
- For patients who lack previous imaging, follow the Fleischner Society guidelines (see Table 18-5).

KEY FACT

The appearance of "popcorn" calcification within an SPN likely represents a benign hamartoma.

Sarcoidosis

An idiopathic illness characterized by the formation of noncaseating granulomas in various organs. Most patients have pulmonary involvement.

History/PE

Sarcoidosis is a very heterogeneous disease, both in terms of presentation and severity. Common features include fever, cough, malaise, weight loss, dyspnea, and arthritis, particularly of the knees and ankles.

Differential

Sarcoidosis is a diagnosis of exclusion, so be sure to rule out other diseases that present similarly, such as TB, lymphoma, fungal infection, idiopathic pulmonary fibrosis, HIV, and berylliosis.

Diagnosis

- Labs:
  - CBC may show leukopenia, anemia, thrombocytopenia, or pancytopenia.
  - Liver enzymes, alkaline phosphatase, and immunoglobulins may be elevated.

MNEMONIC

Features of sarcoidosis—

GRUELING

Granulomas
Rheumatoid arthritis
Uveitis
Erythema nodosum
Lymphadenitis
Interstitial fibrosis
Negative PPD
Gammaglobulinemia

TABLE 18-5. Guidelines for the Diagnosis of Solitary Pulmonary Nodules

	Follow-up	
Nodule Size	**Low Risk**	**High Risk**
< 6 mm	No routine follow-up	Optional CT at 12 months
6–8 mm	CT at 6-12 months	CT at 6–12 and 18–24 months
> 8 mm	Serial CT, PET scan, or excision based on radiographic characteristics	

Q 1

A chest CT of a 61-year-old patient with no smoking history reveals a noncalcified 1.7-cm nodule. What is your next step?

Q 2

A 46-year-old African-American woman presents with chronic dyspnea and a mild cough with clear sputum. Exam reveals raised, painful lesions on her legs. Labs show a serum calcium level of 9.6 mg/dL, and CXR demonstrates hilar adenopathy. What will confirm the diagnosis of sarcoidosis?

- Hypercalciuria, defined as urinary calcium/Cr ratio of > 0.2 (men > women) and an elevated urinary calcium/Cr ratio is more common than hypercalcemia.
- Elevated angiotensin-converting enzyme is not diagnostic due to false-positives.

- Conduction abnormalities may be seen on ECG.
- Lung involvement may be staged according to radiographic presentation.
  - Features of Stage I include hilar adenopathy without other opacities (see Figure 18-8).
  - Hilar adenopathy with reticular opacities are seen in Stage II disease.
  - Stage III findings include resolving hilar adenopathy but persistent reticular opacities.
  - In Stage IV disease, there is no hilar adenopathy, but reticular opacities and evidence of volume loss can be seen.
  - In Stage V disease, CXR and CT scan show bilateral lung nodules that may be mistaken for metastases, as well as air bronchograms on CT images.
- PFTs show a restrictive or mixed restrictive-obstructive pattern.
- Tissue biopsy shows noncaseating granulomas without organisms.

Treatment

Includes systemic corticosteroids for acute flares or disease suppression in severe cases. Steroid-sparing agents (eg, methotrexate) may be beneficial as maintenance therapy.

Sleep Apnea

The term sleep-disordered breathing encompasses a range of disorders, with most falling into the categories of obstructive sleep apnea (OSA), central sleep apnea (CSA), and sleep-related hypoventilation.

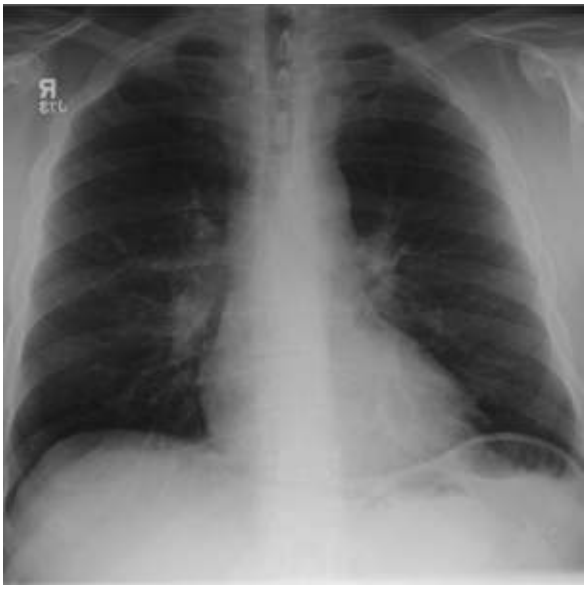


FIGURE 18-8. Bilateral hilar lymphadenopathy in a patient with sarcoidosis. (Reproduced with permission from Imboden JB et al. *Current Diagnosis & Treatment: Rheumatology,* 3rd ed. New York, McGraw-Hill, 2013, Fig. 54-1B.)

1 **A**

Compare the CT scan with an old CXR.

2 **A**

An endobronchial biopsy revealing a noncaseating granuloma is confirmatory. A biopsy specimen of erythema nodosum will not show granulomatous involvement and is not diagnostically helpful.

- **OSA:** Upper airway collapse during sleep (↓ airflow but normal effort).
- **CSA:** Diminished central ventilatory drive (↓ airflow and effort); may be 1° (idiopathic) or 2° (stroke, HF, CNS depressants).

History/PE

- Presents with neurocognitive impairment, morning headache, poor sleep, or impotence.
- With OSA, the patient may report snoring, choking, or gasping during sleep.
- Patients with OSA are typically obese and hypertensive. They may also have a large neck circumference. Look for micrognathia/retrognathia, a large tongue, or large tonsils.

Diagnosis

The *International Classification of Sleep Disorders* (ICSD-3) defines OSA as a polysomnography-determined obstructive respiratory disturbance index (RDI) ≥ 5 events/hour associated with the typical symptoms of OSA (eg, unrefreshing sleep, daytime sleepiness, fatigue or insomnia, awakening with a gasping or choking sensation, loud snoring, or witnessed apneas), or an obstructive RDI ≥ 15 events/hour (even in the absence of symptoms).

Differential

Rule out other causes of excessive daytime sleepiness, including obesity hypoventilation syndrome, narcolepsy, and restless leg syndrome.

Treatment

- The most effective treatment for both CSA and OSA is CPAP or bilevel positive airway pressure ventilation to keep the airways open during sleep.
- For OSA, other treatment options include weight loss, oral appliances to relieve the obstruction, and surgery such as uvulopalatopharyngoplasty (effective in 40–50% of cases).
- For CSA, treat the underlying condition whenever possible (eg, HF, excessive opiates).

Complications

Patients with OSA are at ↑ risk of hypertension, left ventricle dysfunction, cardiac dysrhythmias, pulmonary hypertension, and insulin resistance.

MNEMONIC

Screen for OSA with STOP BANG

Snoring loudly
Tiredness
Observed apnea
High B**P**
BMI > 35
Age > 50
Neck circumference >16 inches
Gender is male

KEY FACT

Central sleep apnea with Cheyne-Stokes breathing—which is characterized by deep, rapid breathing followed by ↓ ventilation and apnea—is often caused by stroke or HF.

Cystic Fibrosis

An autosomal recessive disorder with mutations located in the *CFTR* gene, leading to abnormal transfer of sodium and chloride. Multiple exocrine glands and cilia in various organs become dysfunctional. It is the most common genetic disease in the United States and among Caucasians, affecting 1 in 3200.

History/PE

- Patients typically present in childhood or adolescence.
- Look for recurrent pulmonary infections, sinusitis, or bronchiectasis.
- Infants may present with meconium ileus or intussusception.
- It also presents with pancreatic insufficiency characterized by steatorrhea and poor weight gain due to malabsorption.
- Adult men may present with infertility.

KEY FACT

Historically, causative organisms in patients with CF with signs of pulmonary infection have been *Pseudomonas* (typically in those > 18 years of age), *Staphylococcus* (typically in those < 18 years of age), or *Haemophilus*. More recently, researchers have realized these infections are polymicrobial.

- Patients may have short stature and nasal polyps.
- Lung exam often reveals wheezing, crackles, or squeaks. Clubbing may be present.
- Hyperinflation is seen early and is followed by peribronchial cuffing, mucous plugging, and bronchiectasis (see Figure 18-9).

Diagnosis

- Sweat chloride test of ≥ 60 mEq/L (must be confirmed on two different days).
- Genetic testing can confirm the presence of many of the genetic mutations (ΔF508 is the most common genetic mutation).

Treatment

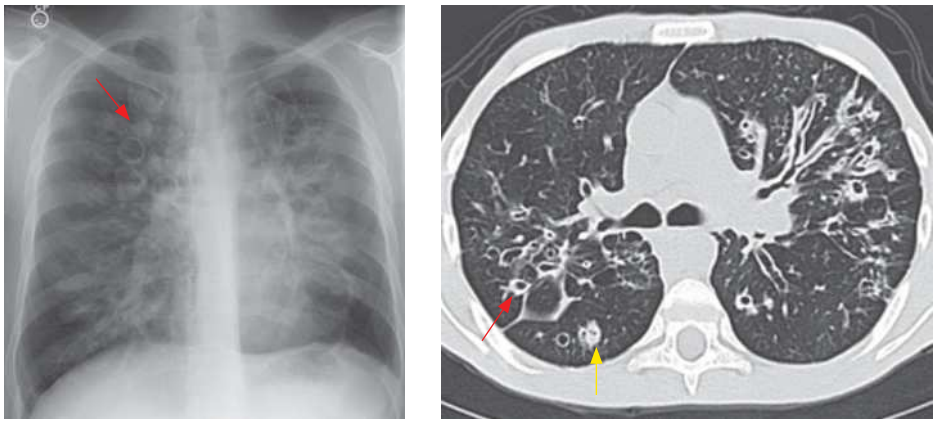
- Pulmonary symptoms are treated with chest physiotherapy, bronchodilators, and mucolytics (DNase).
- Patients need supplemental pancreatic enzymes, fat-soluble vitamins (A, D, E, K) to address fat malabsorption, and stool softeners (fiber).
- Long-term and long-term intermittent oral antibiotics (azithromycin) or inhaled antibiotics (tobramycin) may also be beneficial. *Pseudomonas aeruginosa* is common; therapies are tailored to treat the infecting organism.
- In severe end-stage pulmonary disease, bilateral lung transplantation is the only definitive treatment.

Occupational Lung Disease

Lung diseases caused by occupational exposure to dust, smoke, fumes, or other biologic agents. These include pneumoconiosis (silicosis), occupational asthma, asbestosis, and mesothelioma, among others.

History/PE

- Patients present with cough, dyspnea, pleuritic chest pain, and sometimes fever and weight loss.
- Lung examination findings are usually nonspecific but may reveal crackles or rhonchi.



A **B**

FIGURE 18-9. Cystic fibrosis. (**A**) Frontal CXR showing central cystic bronchiectasis (*arrow*) in a patient with CF. (**B**) Transaxial CT image showing cystic bronchiectasis (*red arrow*), with some bronchi containing impacted mucus (*yellow arrow*). (Reproduced with permission from USMLE-Rx.com.)

- Cardiac examination is usually benign except in the more advanced stages of disease, when pulmonary hypertension and cor pulmonale are more prevalent.
- Extremities may reveal clubbing of the digits.

Diagnosis

- Predominately based on history of exposure:
  - Coal workers pneumoconiosis: Work in coal mines.
  - Asbestosis: Work in ship building, roofing, plumbing.
  - Silicosis: Work in sandblasting or mining.
  - Berylliosis: Work in aerospace or nuclear industry.
- CXR most commonly shows a reticular pattern but can show nodular or mixed patterns.

Treatment

- Avoid exposures.
- Steroids may be used to reduce inflammation.
- Lung transplant may be the best option for some patients.

NOTES

CHAPTER 19

HIGH-YIELD CCS CASES

How to Use This Section

In this section are 100 **minicases** reflecting the types of clinical situations encountered on the actual CCS. Each case consists of **columns** that start on the left-hand page and end on the right-hand page with the **Final Diagnosis.** As you read each column, ask yourself what you should do and/or think next (see Table 19-1). If no results are given for a test, assume that it is **normal.** To get the most out of these minicases, we **strongly** recommend that you do at least a few of the CCS cases on the USMLE website to get a feel for the case flow and key decision points. This will allow you to place the minicases in context.

TABLE 19-1. Approaching the CCS Minicases

When Reading . . .	Ask Yourself . . .
History	What should I be looking for on vital signs (VS) and physical examination (PE)?
	Do I need to stabilize the patient or perform an emergency procedure before conducting a PE?
Physical exam	What are the most likely diagnoses that explain the patient's presentation?
Differential	What are the initial diagnostic tests and treatments that should be done?
	Does the patient need to be transferred to another location (eg, from the ED to the ICU)?
	Does the clock need to be advanced?
Initial management	What additional workup and management should occur?
	Can the patient be discharged or transferred to another setting?
Continuing management	What should be done in follow-up, including long-term disease management, health maintenance, and patient counseling?
	Should any treatment or monitoring be stopped?
Follow-up	What is the final diagnosis?

HEADACHE

CASE 1

HX	PE	DDX
21 yo F presents with a severe headache. She has a history of throbbing left temporal pain that lasts for 2–3 hours. Before these episodes start, she sees flashes of light in her right visual field and feels weakness and numbness on the right side of her body for a few minutes. The headaches are often associated with nausea and vomiting. She has a family history of migraine.	VS: T 37°C (99.2°F), P 70, BP 120/80, RR 15, O_2 sat 100% room air Gen: NAD Lungs: WNL CV: WNL Abd: WNL Ext: WNL Neuro: WNL	▪ Migraine (hemiplegic) ▪ Migraine (complicated) ▪ Cluster headache ▪ Intracranial neoplasm ▪ Partial seizure ▪ Pseudotumor cerebri ▪ Tension headache ▪ Trigeminal neuralgia

CASE 2

HX	PE	DDX
29 yo F presents with daily episodes of bilateral band-like throbbing pain in her frontal-occipital region that last between 30 minutes and a few hours. She usually experiences these episodes when she is either tired or under stress. She denies any associated nausea, vomiting, phonophobia, photophobia, or aura. She also feels pain and stiffness in her neck and shoulder.	VS: Afebrile, P 70, BP 120/80, RR 15 Gen: NAD Lungs: WNL CV: WNL Abd: WNL Ext: WNL Neuro: WNL, vision normal	▪ Tension-type headache ▪ Cluster headache ▪ Intracranial neoplasm ▪ Meningitis ▪ Migraine ▪ Pseudotumor cerebri ▪ Sinusitis

CASE 3

HX	PE	DDX
65 yo F presents with a severe intermittent headache in the right temporal lobe together with blurred vision in her right eye and pain in her jaw during mastication.	VS: T 37°C (99°F), P 85, BP 140/85, RR 18, O_2 sat 100% room air Gen: NAD HEENT: Tenderness on temporal artery palpation Neck: No rigidity Lungs: WNL CV: WNL Abd: WNL Ext: WNL Neuro: WNL	▪ Cluster headache ▪ Glaucoma ▪ Intracranial neoplasm ▪ Meningitis ▪ Migraine ▪ Temporal (giant cell) arteritis ▪ Tension-type headache ▪ Trigeminal neuralgia

INITIAL MGMT	CONTINUING MGMT	F/U
ED W/U ■ CT–head ■ CBC ■ Chem 8 ■ ESR **Rx** ■ IV normal saline ■ IV promethazine, prochlorperazine, or metoclopramide ■ Aspirin, NSAIDs, or acetaminophen ■ Caffeine ■ IM sumatriptan or ergotamine (if the patient does not improve)		■ Follow up in 1 month ■ Prophylactic therapy if patient experiences four or more migraines per month—β-blockers (propranolol), calcium-channel blockers, TCAs, SSRIs, valproic acid, topiramate, or gabapentin

Final Dx: Migraine (hemiplegic)

INITIAL MGMT	CONTINUING MGMT	F/U
Office W/U ■ CBC ■ Chem 8 ■ ESR **Rx** ■ Cold compresses ■ Acetaminophen +/− caffeine (preferred in pregnancy) ■ Aspirin +/− caffeine ■ NSAIDs +/− caffeine		■ Follow up in 1 month ■ Nonpharmacologic therapies (acupuncture, biofeedback, relaxation exercises)

Final Dx: Tension-type headache

INITIAL MGMT	CONTINUING MGMT	F/U
Emergency room STAT ■ IV normal saline ■ Prednisone **Emergency room W/U** ■ CBC ■ Chem 8 ■ MRI/MRA—brain: ⊖ ■ CXR: ⊖ ■ ESR: ↑↑ ■ CRP: ↑↑	**Ward W/U** ■ Ophthalmology consult ■ Temporal artery biopsy: ⊕ for temporal arteritis ■ ESR every morning ■ Screen for polymyalgia rheumatica **Rx** ■ Continue high-dose glucocorticoid for 2–4 weeks and then taper	■ Discharge home ■ Continue low-dose maintenance prednisone with slow taper ■ ESR in 2 weeks ■ Adequate dietary calcium and vitamin D if glucocorticoids are to be used chronically

Final Dx: Temporal (giant cell) arteritis

CASE 4

HX	PE	DDX
22 yo M presents with a high fever, severe headache, and photophobia; lives in college dorms.	VS: T 39°C (103°F), P 95, BP 150/85, RR 18, O_2 sat 100% room air Gen: Moderate distress Neck: Nuchal rigidity Lungs: WNL CV: WNL Abd: WNL Ext: WNL Neuro: ⊕ Kernig and Brudzinski signs	▪ Encephalitis ▪ Intracranial or epidural abscess ▪ Meningitis ▪ Migraine ▪ Sinusitis ▪ Subarachnoid hemorrhage

CASE 5

HX	PE	DDX
60 yo M with a medical history of hypertension presents with severe headache, nausea, and vomiting. The patient states that he stopped taking his metoprolol because he thought that he did not need it anymore.	VS: T 37°C (99.3°F), P 100, BP 220/120, RR 20, O_2 sat 95% room air Gen: Severe distress HEENT: Fundoscopy reveals papilledema Lungs: WNL CV: WNL Abd: WNL Ext: WNL Neuro: WNL	▪ Cluster headache ▪ Hypertensive emergency (malignant hypertension) ▪ Intracranial hemorrhage ▪ Intracranial neoplasm ▪ Migraine

INITIAL MGMT	CONTINUING MGMT	F/U
ED STAT ■ IV normal saline ■ Blood culture ■ CT—head (before LP) ■ Ceftriaxone and vancomycin ■ Adjunctive IV steroids (dexamethasone) ■ LP-CSF: ↑ WBCs, ↑ protein, ↓ CSF/blood glucose ratio, gram ⊕ cocci, ↑ opening pressure **ED W/U** ■ CBC: ↑ WBC count ■ Chem 8 ■ CT—head: ⊖ ■ CXR: ⊖ **Rx** Acetaminophen	**Ward W/U** ■ CSF culture: ⊕ for *S pneumoniae* ■ Blood culture: ⊖ **Rx** ■ Continue ceftriaxone + vancomycin + dexamethasone (continued only when culture ⊕ for *S pneumoniae*)	■ Improved within 48 hours ■ Discharge home ■ Follow up in 1 month ■ Screen for IV drug use

Final Dx: Meningitis (pneumococcal/bacterial)

INITIAL MGMT	CONTINUING MGMT	F/U
ED STAT ■ Supplemental O_2 ■ IV β-blocker (labetalol) ■ BP in both arms ■ CT—head: White matter changes consistent with hypertension ■ ECG: Left ventricular hypertrophy ■ CXR **ED W/U** ■ Cardiac/BP monitoring ■ CPK-MB, troponin × 3: ⊖ ■ CBC ■ Chem 8 ■ UA ■ UTOX	**ICU W/U** ■ Continuous cardiac monitoring ■ Lipid profile ■ Echocardiography: EF < 45% **Rx** ■ Switch to oral agents after first 24 hours; labetalol or metoprolol if good control previously ■ ACEIs (low EF) ■ HCTZ	■ Transfer to the floor ■ Counsel patient re: medication compliance ■ Discharge home ■ Follow up in 1 week

Final Dx: Hypertensive emergency

ALTERED MENTAL STATUS/LOSS OF CONSCIOUSNESS

CASE 6

HX	PE	DDX
84 yo F brought in by her son complains of forgetfulness (eg, forgets phone numbers, loses her way home) along with difficulty performing some of her daily activities (eg, bathing, dressing, managing money, answering the phone). The problem has gradually progressed over the past few years.	VS: Afebrile, P 90, BP 120/60, RR 12 Gen: NAD Lungs: WNL CV: WNL Abd: WNL Ext: WNL Neuro: On mini-mental status exam, patient cannot recall objects, follow three-step commands, or spell "world" backward; cranial nerves intact; strength and sensation intact	▪ Alzheimer disease ▪ Cobalamin (vitamin B_{12}) deficiency ▪ Chronic subdural hematoma ▪ Hypothyroidism ▪ Intracranial tumor ▪ Major depressive disorder ▪ Neurosyphilis ▪ Normal pressure hydrocephalus ▪ Vascular dementia

CASE 7

HX	PE	DDX
79 yo M is brought in by his family complaining of a 7-week history of difficulty walking accompanied by memory loss and urinary incontinence. Since then, he has had increased difficulty with memory and more frequent episodes of incontinence.	VS: Afebrile, P 92, BP 144/86, RR 14 Gen: NAD Lungs: WNL CV: WNL Abd: WNL Ext: WNL Neuro: Difficulty with both recent and immediate recall on mini-mental status exam; spasticity and hyperreflexia in upper and lower extremities; problem initiating gait (gait is shuffling, broad-based, and slow)	▪ Alzheimer disease ▪ Chronic subdural hematoma ▪ Cobalamin (vitamin B_{12}) deficiency ▪ Frontal lobe syndromes ▪ Huntington disease ▪ Intracranial tumor ▪ Meningitis ▪ Normal pressure hydrocephalus ▪ Parkinson disease ▪ Vascular dementia

INITIAL MGMT	CONTINUING MGMT	F/U
Office W/U ■ CBC ■ Chem 14 ■ TSH ■ Serum vitamin B_{12} level ■ Serum folic acid level ■ VDRL/RPR ■ CT—head: Diffuse symmetrical atrophy **Rx** ■ Cholinesterase inhibitor (donepezil, rivastigmine, and galantamine) or memantine (NMDA antagonist)		■ Patient counseling—adequate nutrition, limit alcohol use, safety (eg, driving) ■ Consider referral to cognitive rehabilitation ■ Support group ■ Advance directives ■ Family counseling

Final Dx: Alzheimer disease

INITIAL MGMT	CONTINUING MGMT	F/U
ED W/U ■ CBC ■ Chem 8 ■ LFTs ■ TSH ■ CT—head: Enlarged lateral ventricles with no prominence of cortical sulci (out of proportion to sulcal enlargement) ■ LP ■ Serum vitamin B_{12} level ■ Serum folic acid level	**Ward W/U** ■ Neurosurgery consult ■ Neurology consult ■ Ventriculoperitoneal shunt	■ Advance directives ■ Family counseling ■ Supportive care

Final Dx: Normal pressure hydrocephalus

CASE 8

HX	PE	DDX
The on-call physician is called to see a 46 yo M patient because of seizures. The patient was admitted to the surgical ward 2 days ago, after emergency trauma surgery. The nurse reports that the patient was anxious, agitated, irritable, and tachycardic last night. Later on, the nurse noted nausea, diarrhea, sweating, and insomnia. The patient had tremors, exhibited a startle response, and was hallucinating earlier tonight.	VS: T 37°C (99°F), P 133, BP 146/89, RR 22, O_2 sat 92% room air Gen: Sweating; cigarette burns on hands; multiple tattoos and rings Chest: WNL Abd: Hepatomegaly Ext: Evidence of recent surgery Neuro: Tremor, confusion, delirium, clouded sensorium, and evidence of peripheral neuropathy	▪ Alcohol withdrawal ▪ Amphetamine psychosis ▪ Delirium ▪ Sedative withdrawal ▪ SLE

CASE 9

HX	PE	DDX
24 yo M is brought to the ED in a drowsy state. His wife reports that he was working at home when he suddenly stiffened, fell backward, and lost consciousness. While he was lying on the ground, he was noted to have no respiration for about 1 minute, followed by jerking of all 4 limbs for about 5 minutes. He was then unconscious for another 5 minutes.	VS: T 37°C (98.2°F), P 90, BP 120/80, RR 12 Gen: NAD, evidence of tongue biting Lungs: WNL CV: WNL Abd: WNL Ext: WNL GU: wet underpants from bladder incontinence Neuro: Oriented, but in a state of confusion; no focal neurologic deficits	▪ Acute ischemic or hemorrhagic stroke ▪ Migraine ▪ Nonepileptic psychogenic seizure ▪ Seizure ▪ Subarachnoid hemorrhage ▪ Subdural hematoma ▪ Substance intoxication (eg, cocaine, methamphetamines, amphetamine ▪ Substance withdrawal (eg, alcohol, benzodiazepines) ▪ Syncope ▪ Transient ischemic attack (TIA)

INITIAL MGMT	CONTINUING MGMT	F/U
Ward W/U ■ CBC: MCV 110 fL ■ Chem 8: Hypokalemia, hypomagnesemia ■ UTOX: WNL ■ LFTs: GGT 40 U/L ■ ECG: Sinus tachycardia ■ CT—head: Cerebral atrophy, no subdural hematoma **Rx** ■ NPO to prevent aspiration ■ IV fluids (D_5W NS) ■ Nutritional supplementation: Thiamine (vitamin B_1) before IV D_5W NS, folic acid, and multivitamin ■ IV benzodiazepines ■ Replete K and Mg	**Ward W/U** ■ Chem 8: Corrected hypokalemia, hypomagnesemia **Rx** ■ IV fluids (NS) ■ IV benzodiazepines (CIWA-Ar scale/ protocol)	■ Addiction unit consult ■ Social work consult ■ Nutritional/dietary supplements ■ Referral to outpatient group therapy (eg, Alcoholics Anonymous) ■ Follow up in 4 weeks ■ Patient counseling ■ Consider naltrexone, acamprosate, or disulfiram

Final Dx: Alcohol withdrawal

INITIAL MGMT	CONTINUING MGMT	F/U
ED W/U ■ CBC ■ Chem 7 ■ Calcium, magnesium, phosphate ■ LFTs ■ ABG ■ ECG ■ EEG ■ CT—head ■ MRI—brain ■ UA ■ UTOX	**Rx** ■ Neurology consult	■ Follow up in 4 weeks ■ Patient education—seizure precautions: avoid unsupervised activities that may be dangerous with seizure or sudden loss of consciousness ■ Driving restriction—avoid driving until follow-up ■ Consider anti-seizure drug therapy

Final Dx: Generalized tonic-clonic (grand mal) seizure

CASE 10

HX	PE	DDX
72 yo M is brought to the ED complaining of syncope. He underwent a coronary artery bypass graft (CABG) 3 years ago. He reports fatigue and dizziness over the past 5 days. The patient's fall was broken by his wife, and as a result he has no head trauma. His wife reports loss of consciousness for about 3 minutes. Before this episode, the patient recalls a prodrome of lightheadedness. His medications include propranolol, digoxin, and diltiazem.	VS: T 37°C (98.1°F), P 35, BP 114/54, RR 15 Gen: NAD Lungs: WNL CV: Bradycardia, irregular S_1 and S_2 Abd: WNL Ext: WNL Neuro: Alert and oriented; CN II–XII intact; 5/5 motor strength in all extremities	▪ Aortic stenosis ▪ Asystole ▪ Atrial fibrillation ▪ Dilated cardiomyopathy ▪ Heart block ▪ MI ▪ Myocarditis ▪ Myopathy ▪ Restrictive cardiomyopathy ▪ Vasodepressor/vasovagal response ▪ VT/VF ▪ Medication related (β-blocker, CCB, digoxin overdose/toxicity)

CASE 11

HX	PE	DDX
25 yo F with no significant medical history is brought to the ED after having been found unresponsive with an empty prescription bottle lying next to her.	VS: T 38°C (99.8°F), P 50, BP 110/50, RR 9, O_2 sat 92% room air Gen: Lethargic HEENT: Miotic (pinpoint) pupils Lungs: Decreased inspiratory effort CV: Bradycardia Abd: Decreased bowel sounds Ext: WNL Neuro: Minimally responsive to vocal stimuli, opens eyes in response to noxious stimuli Limited PE with ABCs	▪ Metabolic disturbances (eg, hypoglycemia) ▪ Non-convulsive status epilepticus ▪ Overdose—eg, benzodiazepines, opioids, psychotropics

INITIAL MGMT	CONTINUING MGMT	F/U
ED W/U ■ IV fluids (NS) ■ CBC ■ Chem 8 ■ LFTs ■ ECG: Third-degree AV block ■ Cardiac enzymes ■ Serum calcium, magnesium, phosphate, digoxin level ■ CXR ■ UA ■ Supplemental O_2 ■ Continuous cardiac/BP monitoring **Rx** ■ Temporary transvenous cardiac pacemaker ■ Hold AV nodal agents	**ICU W/U** ■ Continuous cardiac/BP monitoring ■ ECG ■ Lipid profile ■ Echocardiography **Rx** ■ Lipid-lowering agents ■ Cardiology consult ■ Cardiac catheterization, angiocardiography ■ Permanent cardiac pacemaker	■ Cardiac rehabilitation program ■ Smoking cessation ■ Counsel patient to limit alcohol intake ■ Counsel patient not to drive ■ Low-fat, low-sodium diet

Final Dx: Complete heart block

INITIAL MGMT	CONTINUING MGMT	F/U
ED STAT ■ Airway protection ■ IV thiamine ■ Fingerstick blood glucose ■ IV fluids (NS) ■ IV naloxone: Patient responded ■ ABG **ED W/U** ■ CBC ■ Chem 7 ■ Calcium, magnesium, and phosphorus levels ■ Acetaminophen and salicylate levels ■ Lactate level ■ PT/PTT or INR ■ ECG ■ CXR ■ UA ■ UTOX, EtOH level ■ UPREG	**ICU W/U** ■ Gastric lavage: Pill fragments ■ Continuous monitoring: Patient started to become drowsy again (monitor events) **Rx** ■ IV naloxone: Patient responded ■ Suicide precautions ■ Psychiatry consult ■ Collateral information from patient's family	■ Monitor for at least 24 hours ■ Transfer to inpatient psychiatry upon medical clearance

Final Dx: Intentional opioid overdose

CASE 12

HX	PE	DDX
60 yo M was found unconscious by his wife, who called rescue. She left him in bed at 7 AM to go to her volunteer job. When she returned for lunch at 1 PM, she found an empty bottle of amitriptyline next to him. When paramedics arrived, he was noted to be in respiratory distress and was taken to the ED.	VS: T 38°C (101°F), P 110, BP 95/45, RR 35, O_2 sat 89% on 100% face mask Gen: Acute distress; shallow, rapid breathing HEENT: Dilated pupils, dry mucous membranes Lungs: WNL CV: Tachycardia Abd: Decreased bowel sounds Neuro: Opens eyes to noxious stimuli Limited PE	▪ Anticholinergic toxicity ▪ Overdose—TCA

FATIGUE/WEAKNESS

CASE 13

HX	PE	DDX
68 yo M with a history of hypertension, diabetes, and heavy smoking presents following a 20-minute episode of slurred speech, right facial drooping and numbness, and weakness of the right hand. His symptoms had totally resolved by the time he got to the ED.	VS: T 37°C (98°F), P 75, BP 150/90, RR 16, O_2 sat 100% room air Gen: NAD Neck: Left carotid bruit Lungs: WNL CV: WNL Abd: WNL Ext: WNL Neuro: WNL	▪ Intracranial mass ▪ Migraine with aura ▪ Seizure ▪ Stroke ▪ Subdural or epidural hematoma ▪ Transient ischemic attack

INITIAL MGMT	CONTINUING MGMT	F/U
ED STAT ■ Intubate **ED W/U** ■ Cardiac/BP monitoring ■ ABG ■ CBC ■ Chem 14 ■ Fingerstick blood glucose ■ Serum lactate ■ Serum osmolality ■ Serum/blood ketones ■ Cardiac enzymes ■ Serum acetaminophen and salicylate levels ■ UTOX: ⊕ TCAs ■ ECG: Widening of the QRS interval ■ CXR ■ CT—head **Rx** ■ IV fluids (NS) ■ IV sodium bicarbonate ■ Central line placement ■ Activated charcoal	**ICU W/U** ■ Continuous cardiac/BP monitoring ■ Continuous monitoring of urine output every hour ■ Neuro checks **Rx** ■ Cardiology consult ■ Psychiatry consult ■ Lidocaine for refractory TCA-induced arrhythmias ■ Benzodiazepines for TCA-induced seizures ■ Suicide precautions	■ Transfer to inpatient psychiatry upon medical clearance ■ Discontinue TCAs on discharge

Final Dx: TCA intoxication

INITIAL MGMT	CONTINUING MGMT	F/U
ED STAT ■ Assess ABCs ■ Supplemental O_2 ■ Fingerstick glucose ■ IV fluids (NS) ■ CT—head **ED W/U** ■ Continuous cardiac/BP monitoring ■ ECG ■ CBC ■ Chem 8 ■ PT/PTT or INR ■ Neurology consult **Rx** ■ Aspirin	**Ward W/U** ■ Interval neurologic exam ■ Continuous cardiac/BP monitoring ■ Telemetry ■ Lipid panel, Hb_{A1c} ■ Echocardiography: EF 60% ■ Carotid duplex: > 75% stenosis in left carotid artery ■ Brain MRI **Rx** ■ Vascular surgery consult ■ Patient is scheduled for elective carotid endarterectomy ■ Holter (cardiac) monitoring on discharge for 30 days	■ Counsel patient—smoking cessation, diet (low-fat, low-sodium, diabetic), exercise; diabetic teaching ■ Discharge on aspirin and statin for secondary prevention ■ Pharmacologic management as indicated for hypertension, diabetes, and hyperlipidemia

Final Dx: Transient ischemic attack (TIA)

CASE 14

HX	PE	DDX
40 yo F presents with numbness, lower extremity weakness, and difficulty walking. She reports having had a URI approximately 2 weeks ago. She says that her weakness spread from her lower limbs to her hip and then progressed to her upper limbs. She also complains of lightheadedness on standing and shortness of breath.	VS: Afebrile, P 115, BP 130/80 with orthostatic changes, RR 16 Gen: NAD Lungs: WNL CV: WNL Ext: WNL Neuro: Loss of motor strength in lower limbs; absent DTRs in patella and Achilles tendon; sensation intact	▪ Functional neurological symptom disorder (conversion disorder) ▪ Guillain-Barré syndrome ▪ Myasthenia gravis ▪ Paraneoplastic syndrome ▪ Poliomyelitis ▪ Polymyositis ▪ Multiple sclerosis ▪ Transverse myelitis

CASE 15

HX	PE	DDX
40 yo F presents with fatigue, weight gain, daytime somnolence, cold intolerance, constipation, and dry skin.	VS: T 36°C (97°F), BP 100/60, HR 60 Gen: Obese Skin: Dry HEENT: Scar on neck from previous thyroidectomy Lungs: WNL CV: WNL Neuro: Delayed relaxation of DTRs	▪ Anemia ▪ Diabetes mellitus ▪ Hypothyroidism ▪ Major depressive disorder

CASE 16

HX	PE	DDX
16 yo M complains of fatigue, myalgia, dysphagia. He also complains of decreased appetite and nausea without vomiting. He reports that his girlfriend recently had similar symptoms that lasted a few weeks.	VS: T 38°C (101°F), P 85, BP 125/80, RR 18 Gen: Maculopapular rash HEENT: Posterior and auricular lymphadenopathy; pharyngeal inflammation with diffuse tonsillar exudates as well as palatal petechiae Lungs: WNL CV: WNL Abd: Soft, nontender; mild hepatosplenomegaly Ext: WNL Neuro: WNL	▪ Cytomegalovirus infection ▪ Hepatitis ▪ Infectious mononucleosis ▪ Primary/acute HIV infection ▪ Streptococcal pharyngitis ▪ Toxoplasmosis

INITIAL MGMT	CONTINUING MGMT	F/U
ED W/U ■ CBC ■ Chem 8 ■ TSH ■ ESR ■ CRP ■ RF ■ VDRL ■ Serum B_{12} ■ Serum folic acid ■ ECG ■ Serum CPK ■ CXR ■ LP: ↑ CSF protein ■ HIV testing, ELISA	**Ward Rx** ■ Immunoglobulins ■ Plasmapheresis ■ Rehabilitative medicine consult ■ Neurology consult ■ Immunology consult ■ Measure forced vital capacity or negative inspiratory force	■ Follow up in 3–4 weeks ■ Patient counseling ■ Family counseling ■ Advise patient to use seat belts

Final Dx: Guillain-Barré syndrome

INITIAL MGMT	CONTINUING MGMT	F/U
Office W/U ■ CBC ■ Chem 14 ■ TSH: ↑ ■ FT_4: ↓ ■ ECG ■ Lipid profile ■ PHQ-2 depression screen **Rx** ■ Levothyroxine		■ Check TSH with reflex T4 after 1 month

Final Dx: Hypothyroidism

INITIAL MGMT	CONTINUING MGMT	F/U
Office W/U ■ CBC: ↑ WBC count ■ Peripheral smear: Atypical lymphocytes ■ Chem 14: ↑ AST and ↑ ALT ■ ESR ■ CRP ■ Monospot test: ⊕ ■ Serum EBV titer: ↑ ■ Rapid strep **Rx** ■ Acetaminophen or NSAIDs ■ Encourage adequate hydration		■ Follow up in 2 weeks with CBC ■ Advise patient to avoid contact sports for at least 4 weeks from acute illness

Final Dx: Infectious mononucleosis

CASE 17

HX	PE	DDX
40 yo F reports depressed mood and feelings of hopelessness and worthlessness. She also reports low energy and difficulty sleeping. She has been calling out of work. She denies any suicidal or homicidal thoughts and denies having audiovisual hallucinations. She has no history of alcohol or drug abuse and has not lost a loved one within the last 12 months. She is married and has one child and a supportive husband.	VS: Afebrile, P 70, BP 120/60, RR 12 Gen: NAD Lungs: WNL CV: WNL Abd: WNL Ext: WNL Neuro: WNL	▪ Anemia ▪ Chronic fatigue syndrome ▪ Major depressive disorder ▪ Hypothyroidism ▪ Obstructive sleep apnea ▪ Occult malignancy

COUGH/SHORTNESS OF BREATH

CASE 18

HX	PE	DDX
2 yo M is brought in by his mother because of sudden-onset shortness of breath and cough. He had a URI 4 days ago. Earlier in the day he was playing with peanuts with his brother. His immunizations are up to date.	VS: T 37°C (98°F), P 110, BP 80/50, RR 38, O_2 sat 99% room air Gen: Respiratory distress; using accessory muscles HEENT: WNL Neck: WNL Lungs: Inspiratory stridor; ↓ breath sounds in right lower base CV: Tachycardia Abd: WNL	▪ Angioedema ▪ Asthma ▪ Croup ▪ Epiglottitis ▪ Allergic reaction/anaphylaxis ▪ Foreign-body aspiration ▪ Laryngitis ▪ Peritonsillar abscess ▪ Pneumonia ▪ Retropharyngeal abscess

CASE 19

HX	PE	DDX
75 yo F presents with pleuritic chest pain and shortness of breath. She reports having fallen 5 days ago and suffered a femoral fracture. She has a long cast in place on her right leg.	VS: Afebrile, BP 120/75, HR 100, RR 24 Gen: Respiratory distress HEENT: WNL Lungs: Rales, wheezing, ↓ breath sounds in left lower base CV: Loud P_2 and splitting of S_2 Abd: WNL	▪ CHF ▪ Fat embolism ▪ Lung cancer ▪ MI ▪ Pericarditis ▪ Pneumothorax ▪ Pulmonary embolism ▪ Syncope ▪ Pneumonia

INITIAL MGMT	CONTINUING MGMT	F/U
Office W/U ■ CBC ■ Chem 14 ■ TSH ■ UTOX **Rx** ■ Antidepressant (eg, SSRI) ■ Referral for psychotherapy ■ Counsel patient on safety precautions, specifically if starting to feel suicidal present to nearest ED or call 911		■ Follow up in 1 week ■ Supportive psychotherapy ■ Encourage healthy lifestyle (sleep hygiene, exercise)

Final Dx: Major depressive disorder

INITIAL MGMT	CONTINUING MGMT	F/U
ED STAT ■ CXR, PA and lateral ■ X-ray—neck, abdomen ■ Bronchoscopy: Foreign body is removed, and patient improves **Rx** ■ Consider IV methylprednisolone before removal of the foreign body		■ Follow up in 2 weeks

Final Dx: Foreign body aspiration

INITIAL MGMT	CONTINUING MGMT	F/U
ED W/U ■ IV normal saline ■ NPO ■ CBC ■ Chem 14 ■ ABG: Hypoxia and hypocapnia ■ CXR: Left lower lobe atelectasis, Hampton humps ■ CT—chest: Pulmonary embolism ■ ECG ■ DVT U/S: Venous DVT ■ IV heparin, bridge to warfarin	**Ward W/U** ■ Continuous cardiac/BP monitoring ■ Pulmonary medicine consult ■ PT/PTT, INR **Rx** ■ Discontinue heparin 2 days after INR is therapeutic ■ Warfarin	■ Follow up in 2 weeks with PT/INR ■ Chest physical therapy ■ Warfarin ■ Rehabilitative medicine consult

Final Dx: Pulmonary embolism

CASE 20

HX	PE	DDX
5 yo M is brought to the ED with a harsh barking cough. He has a history of URIs with coryza, nasal congestion, and sore throat. His symptoms have been present for about a week.	VS: T 38°C (101°F), BP 110/65, HR 100, RR 22, O_2 sat 100% room air Gen: Pallor and mild respiratory distress with intercostal retraction and nasal flaring HEENT: WNL Lungs: Stridor, hoarseness, barking cough CV: WNL Abd: WNL	▪ Bacterial tracheitis ▪ Diphtheria ▪ Epiglottitis ▪ Foreign-body aspiration ▪ Laryngitis ▪ Laryngotracheitis (croup) ▪ Measles ▪ Peritonsillar abscess ▪ Retropharyngeal abscess ▪ Upper airway injury

CASE 21

HX	PE	DDX
75 yo M presents with shortness of breath on exertion along with cough and blood-streaked sputum. He reports progressive malaise and weight loss together with loss of appetite over the past 6 months. He has a 40 pack-year history of tobacco use.	VS: Afebrile, BP 130/85, HR 90, RR 15 Gen: WNL Chest: Barrel-shaped chest, gynecomastia Lungs: Rales, wheezing, ↓ breath sounds, dullness to percussion in left upper lobe CV: WNL Abd: Mild RUQ tenderness with mild hepatomegaly Ext: Finger clubbing; dark-colored, pruritic rash on both forearms	▪ Lung cancer ▪ Lymphoma ▪ Leukemia ▪ Sarcoidosis ▪ Tuberculosis

INITIAL MGMT	CONTINUING MGMT	F/U
ED W/U ■ Supplemental O_2 ■ CBC ■ Chem 8 ■ Throat culture ■ X-ray—neck: Subglottic narrowing	**Ward Rx** ■ Humidified air ■ Nebulized epinephrine ■ Systemic corticosteroids (eg, IM, IV, or oral dexamethasone)	■ Follow up in 1 month ■ Family counseling

Final Dx: Croup

INITIAL MGMT	CONTINUING MGMT	F/U
Office W/U ■ CBC: ↓ hemoglobin ■ Chem 8 ■ LFTs: ↑ AST, ↑ ALT ■ ABG ■ ESR: ↑ ■ CXR: Infiltrate and nodules in left upper lobe ■ Sputum cytology: Adenocarcinoma ■ Sputum culture: Negative ■ PPD: ⊖ ■ CT—chest: Left upper lobe mass	**Office W/U** ■ PFTs ■ Oncology consult ■ Surgery consult ■ Dietary consult ■ Bronchoscopy with biopsy ■ CT—abdomen and pelvis ■ CT—head ■ Antiemetic medication	■ Smoking cessation ■ Patient counseling ■ Family counseling ■ Follow up in 3–4 weeks with CXR and CBC ■ Counsel patient to limit alcohol intake

Final Dx: Lung cancer

CASE 22

HX	PE	DDX
60 yo M with a history of COPD, active smoker, presents with ↑ dyspnea, sputum production, and a change in the color of his sputum to yellow over the past 3 days.	VS: T 38°C (100.6°F), P 90, BP 130/70, RR 28, O_2 sat 92% on 2L NC Gen: Moderate respiratory distress Lungs: Rhonchi at left lower base; diffuse wheezing, prolonged expiratory phase CV: WNL Abd: WNL Ext: WNL	▪ Bronchitis ▪ CHF ▪ COPD exacerbation ▪ Lung cancer ▪ Pneumonia ▪ URI

CASE 23

HX	PE	DDX
50 yo M, Mexican immigrant, presents with productive cough with bloody sputum accompanied by night sweats, weight loss, and fatigue for the last 3 months.	VS: T 38°C (100°F), BP 130/85, HR 90, RR 22, O_2 sat 99% room air Gen: Pallor Lungs: ↓ breath sounds in upper lobes of both lungs CV: WNL Abd: WNL	▪ Bronchiectasis ▪ Fungal lung infection ▪ Lung cancer ▪ Lymphoma ▪ Sarcoidosis ▪ TB ▪ Vasculitis

INITIAL MGMT	CONTINUING MGMT	F/U
ED STAT ■ Supplemental O_2 with target SpO_2 88–92% ■ IV fluids (NS) ■ IV corticosteroids ■ Inhaled short-acting β-agonist (albuterol) by nebulizer ■ Inhaled short-acting anticholinergic agent (ipratropium) by nebulizer ■ Sputum Gram stain and culture ■ Blood culture **ED W/U** ■ CBC: ↑ WBC count ■ CXR: Left lower lobe infiltrate ■ ECG ■ ABG ■ Peak flow: < 200 L/min ■ Sputum Gram stain: Gram ⊕ cocci ■ Chem 8 **Rx** Third-generation cephalosporin + azithromycin vs levofloxacin or gatifloxacin IV	**Ward W/U** ■ Peak flow: 300 L/min ■ FEV_1: 2 L ■ Sputum culture: ⊕ for *S pneumoniae* sensitive to levofloxacin ■ Blood culture: ⊖ **Rx** ■ Change to PO levofloxacin ■ Change to PO prednisone	■ PO prednisone ■ Smoking cessation ■ Consider pneumococcal vaccine and flu shot

Final Dx: Chronic obstructive pulmonary disease (COPD) exacerbation/pneumonia

INITIAL MGMT	CONTINUING MGMT	F/U
ED W/U ■ CXR: Infiltrate/nodules in upper lobes ■ AFB sputum/culture × 3 days: ⊕ stain ■ Sputum Gram stain and culture ■ PPD: 16 mm ■ CBC ■ Chem 14 ■ HIV testing ■ CT—chest: Infiltrates and cavity consistent with TB **Rx** ■ Respiratory isolation ■ Transfer to the ward	**Ward W/U** ■ Social worker consult **Rx** ■ INH + rifampin + pyrazinamide + ethambutol ■ Vitamin B_6	■ Sputum culture and smear at 3 months ■ LFTs ■ Ophthalmology consult ■ Family education ■ Family PPD placement ■ Report case to the local public health department

Final Dx: Tuberculosis (TB)

CASE 24

HX	PE	DDX
55 yo M smoker presents with a history of hypertension, hyperlipidemia, and a MI 5 years ago with cough that worsens when he lies down at night and improves when he props his head up on 3 pillows. He also reports worsening exertional dyspnea for the past 2 months, and now has dyspnea at rest. He has gained 25 pounds since the onset of his symptoms.	VS: Afebrile, P 70, BP 120/70, RR 28, O_2 sat 86% room air Gen: Moderate respiratory distress Neck: JVD Lungs: Bibasilar crackles CV: S1/S2/S3, RRR, 3/6 systolic murmur at apex Abd: WNL Ext: +2 bilateral pitting edema	■ CHF ■ COPD exacerbation ■ MI ■ Pericardial tamponade ■ Pulmonary embolism ■ Pulmonary fibrosis ■ Renal failure

CASE 25

HX	PE	DDX
5 yo F presents with shortness of breath. She has a history of recurrent pulmonary infection and fatty, foul-smelling stools. She has also shown failure to thrive and has a history of meconium ileus.	VS: T 38°C (101°F), BP 110/65, HR 110, RR 24 Gen: Pallor, mild respiratory distress, low weight and height for age, dry skin HEENT: Nasal polyps Lungs: Barrel-shaped chest, rales, dullness and ↓ breath sounds over lower lung fields CV: WNL Abd: Abdominal distention, hepatosplenomegaly	■ Asthma ■ Cystic fibrosis ■ Failure to thrive ■ Malabsorption syndrome ■ Sinusitis

INITIAL MGMT	CONTINUING MGMT	F/U
ED STAT ■ Supplemental O_2 ■ IV furosemide ■ CXR: Pulmonary edema ■ ECG: Old Q wave in anterior leads **ED W/U** ■ Continuous cardiac/BP monitoring ■ CPK-MB, troponin every 8 hours ■ CBC ■ Chem 8: K 3.4 ■ Serum magnesium, phosphorous **Rx** ■ IV KCl ■ Daily weight ■ SQ heparin ■ Low-fat, low-sodium diet	**Ward W/U** ■ TSH ■ Lipid profile ■ HbA_{1c} ■ Echocardiography: Hypokinesia in anterior wall; EF 20% ■ Chem 8: K 3.7 **Rx** ■ Fluid restriction ■ Lisinopril ■ Atorvastatin ■ Aspirin ■ Digoxin ■ Spironolactone ■ Change IV furosemide ■ Start β-blocker when euvolemic	■ Cardiac rehabilitation ■ Counsel patient re: smoking cessation, hypertension, exercise, relaxation, and lipids ■ Follow up in 1 week ■ Repeat echocardiogram at 3–6 months ■ Refer to cardiology; with ischemic cardiomyopathy and EF $<$ 30%, patients may benefit from an automatic implantable cardiac defibrillator

Final Dx: CHF exacerbation

INITIAL MGMT	CONTINUING MGMT	F/U
ED W/U ■ CBC: ↓ hemoglobin ■ Chem 14: ↑ glucose, ↓ albumin ■ ABG: Hypoxia ■ CXR: Hyperinflation ■ Sputum Gram stain and culture ■ Supplemental O_2	**Ward W/U** ■ PFTs ■ Sweat chloride test: ⊕ ■ Pancreatic enzymes ■ 24-hour fecal fat ■ Dietary consult ■ Genetics consult ■ Cystic fibrosis specialist ■ Pulmonary medicine, pediatrics consults **Rx** ■ IV fluids (NS) ■ Supplemental O_2 ■ IV piperacillin ■ Inhaled albuterol	■ Follow up in 2 months ■ Chest physical therapy ■ Regular multiple vitamins ■ Influenza vaccine ■ Pneumococcal vaccine ■ Family counseling

Final Dx: Cystic fibrosis (CF)

CASE 26

HX	PE	DDX
65 yo F with a history of hypertension and diabetes mellitus presents with LUQ pain accompanied by fever and a productive cough with purulent yellow sputum.	VS: T 38°C (101°F), P 105, BP 130/75, RR 22, O_2 sat 95% room air Gen: NAD Neck: WNL Lungs: left-sided ↓ breath sounds and rhonchi CV: Tachycardia Abd: Tenderness to palpation in LUQ	▪ Bronchitis ▪ Infectious mononucleosis ▪ Lung abscess ▪ Lung cancer ▪ Pneumonia ▪ Pleural/Parapneumonic effusion ▪ Pyelonephritis ▪ Splenic abscess

CASE 27

HX	PE	DDX
25 yo HIV-⊕ M presents with shortness of breath, malaise, dry cough, fatigue, and fever.	VS: T 38°C (101°F), BP 110/65, HR 110, RR 24 Gen: Pallor, mild respiratory distress, generalized lymphadenopathy HEENT: Oral thrush Lungs: Intercostal retraction; rales and ↓ breath sounds bilaterally CV: WNL Abd: Soft, nontender; hepatosplenomegaly Ext: Reddish maculopapular rash	▪ Cytomegalovirus (CMV) ▪ Interstitial pneumonia ▪ Kaposi sarcoma ▪ *Legionella* pneumonia ▪ *Mycobacterium avium* complex lung infection ▪ *Pneumocystis jiroveci* pneumonia ▪ TB

INITIAL MGMT	CONTINUING MGMT	F/U
Office W/U ■ CBC: ↑ WBC count ■ Chem 8 ■ UA ■ Sputum Gram stain: Gram-⊕ cocci ■ Sputum culture: Pending ■ CXR: Left lower lobe infiltrate ■ U/S—abdomen	**Ward W/U** ■ Sputum culture: ⊕ for *S pneumoniae* **Rx** ■ IV fluids (NS) ■ PO levofloxacin ■ Chest physiotherapy ■ SQ heparin	■ Discharge home ■ Continue PO levofloxacin × 14 days

Final Dx: Pneumonia

INITIAL MGMT	CONTINUING MGMT	F/U
Office W/U ■ CBC ■ CD4: 200 ■ Chem 8 ■ ABG: Hypoxia ■ Sputum Gram stain and culture ■ Sputum AFB smear ■ Bronchial washings—*Pneumocystis* stain (bronchoscopy is a prerequisite along with thoracic surgery consult): ⊕ ■ CXR: Bilateral interstitial infiltrate ■ PPD: ⊖	**Office W/U** ■ LFTs ■ VDRL ■ Anti-HCV ■ HBsAg ■ Anti-HBc ■ Serum *Toxoplasma* serology ■ HIV viral load **Rx** ■ TMP-SMX or pentamidine (if patient cannot tolerate TMP-SMX) ■ Prednisone (If $PaO_2 < 70$ mm Hg or A-a gradient > 35 mm Hg on room air) ■ Begin antiretroviral therapy within 2 weeks	■ Regular follow-up visits ■ LFTs ■ Influenza vaccine ■ Pneumococcal vaccine after acute event ■ Counsel patient re: safe sex practices ■ HIV support group ■ Patient counseling ■ Family counseling

Final Dx: *Pneumocystis jiroveci* pneumonia

CHEST PAIN

CASE 28

HX	PE	DDX
40 yo F smoker with a history of hypertension and hyperlipidemia presents with sudden onset of 8/10 substernal chest pain that began at rest, has lasted for 20 minutes, and radiates to the jaw. The pain is accompanied by nausea.	VS: Afebrile, P 80, BP 130/60, RR 14, O_2 sat 99% room air Gen: Moderate distress, diaphoretic Lungs: WNL CV: WNL Abd: WNL Ext: WNL	▪ Angina ▪ Aortic dissection ▪ Costochondritis ▪ GERD ▪ MI ▪ Pericarditis ▪ Pneumothorax ▪ Pulmonary embolism

CASE 29

HX	PE	DDX
58 yo M with a history of asthma and emphysema was working in his office 30 minutes ago when he suddenly developed right-sided chest discomfort and shortness of breath.	VS: Afebrile, P 123, BP 101/64, RR 28, O_2 sat 91% room air Gen: Cyanotic, severe respiratory distress Trachea: Deviated to left Lungs: No breath sounds on right side with hyperresonance on percussion CV: Tachycardia; apical impulse displaced to the left Abd: WNL	▪ Angina ▪ Aortic dissection ▪ Asthma exacerbation ▪ Pneumothorax ▪ Pulmonary embolism ▪ Tension pneumothorax

INITIAL MGMT	CONTINUING MGMT	F/U
ED STAT ■ Supplemental O_2 ■ Chewable aspirin ■ Sublingual nitroglycerin ■ IV fluids (NS) ■ IV morphine ■ ECG: T-wave inversions **ED W/U** ■ Continuous cardiac/BP monitoring ■ CPK-MB, troponin: ⊖ ■ CBC ■ Chem 14 ■ PT/PTT ■ CXR ■ Cardiac catheterization	**ICU W/U** ■ ECG ■ Lipid panel ■ TSH ■ Echocardiography: 60% ■ Cardiac catheterization ■ Stress test (if cardiac catheterization is unavailable) **Rx** ■ Enoxaparin ■ Aspirin ■ Clopidogrel ■ β-blocker ■ ACEI (enalapril) ■ Statin (eg, atorvastatin) ■ Cardiology consult	■ Cardiac rehabilitation ■ Counsel patient re: smoking cessation, hypertension, exercise, relaxation, and lipids ■ Advise patient to rest at home ■ Low-fat, low-sodium diet

Final Dx: Unstable angina

INITIAL MGMT	CONTINUING MGMT	F/U
ED STAT ■ IV fluids (NS) ■ Supplemental O_2 ■ Needle thoracostomy ■ Chest tube ■ CXR: Collapsed right lung, mediastinal shift to left ■ IV morphine **ED W/U** ■ Continuous cardiac/BP monitoring ■ ECG: Sinus tachycardia ■ CBC ■ Chem 14 ■ PT/PTT	**Ward W/U** ■ Thoracic surgery consult ■ CXR: Inflated right lung **Rx** ■ Morphine ■ Chest tube to water seal and vacuum device	■ Pleurodesis if indicated

Final Dx: Tension pneumothorax

CASE 30

HX	PE	DDX
34 yo F presents with stabbing retrosternal chest pain that radiates to the back. The pain improves when she leans forward and worsens with deep inspiration. She had a URI 1 week ago.	VS: T 37°C (99.2°F), P 80, BP 130/70, RR 16, O_2 sat 98% room air Gen: NAD Neck: WNL Lungs: WNL CV: S_1/S_2, pericardial friction rub Abd: WNL Ext: WNL	■ Angina ■ Aortic dissection ■ Costochondritis ■ Esophageal rupture ■ GERD ■ Pericarditis ■ Pneumothorax ■ Pulmonary embolism

CASE 31

HX	PE	DDX
48 yo F presents with anxiety. She reports palpitations, hand tremors, and heat intolerance, feeling as though she has to run to the air conditioner all the time. She has lost 10 pounds over the past few months despite no changes in her appetite.	VS: Afebrile, P 113, BP 145/85, RR 20 Gen: Mild respiratory distress, sweaty palms and face, warm skin, hand tremor HEENT: Exophthalmos with lid lag, generalized thyromegaly, thyroid bruit Lungs: WNL CV: Tachycardia Abd: WNL Ext: Edema over the tibia bilaterally	■ Anxiety ■ Atrial fibrillation ■ Early menopause ■ Hyperthyroidism ■ Mitral valve prolapse ■ Panic attack ■ Withdrawal syndrome

INITIAL MGMT	CONTINUING MGMT	F/U
ED W/U ■ Continuous cardiac/BP monitoring ■ Stat ECG: Diffuse ST elevation, PR depression ■ CPK-MB, troponin × 3 ■ CBC ■ Chem 8 ■ CXR: No cardiomegaly ■ ESR **Rx** ■ IV access ■ Supplemental O_2 ■ NSAIDs	**Ward W/U** ■ Discontinue continuous monitoring ■ Echocardiography: Minimal pericardial effusion **Rx** ■ Reassure patient ■ NSAIDs, colchicine	■ Discharge home ■ Follow up in 2 weeks ■ Restrict physical activity until symptoms have resolved

Final Dx: Pericarditis

INITIAL MGMT	CONTINUING MGMT	F/U
Office W/U ■ CBC ■ BMP ■ Thyroid studies (T_4, T_3RU, T_3, TSH): ↑ T_3/T_4, ↓ TSH ■ Serum thyroid autoantibodies: ⊕ ■ ECG ■ CXR ■ Nuclear scan—thyroid: ↑ uptake **Rx** ■ Propranolol ■ Methimazole or PTU (if pregnant)	**Office W/U** ■ Endocrinology consult	■ Check thyroid studies in 1 month ■ Patient counseling

Final Dx: Hyperthyroidism

CASE 32

HX	PE	DDX
65 yo M with a long-standing history of hypertension presents with sudden onset of severe tearing anterior chest pain that radiates to the back. He is anxious and diaphoretic.	VS: T 36°C (97°F), BP 195/110 right arm, 160/80 left arm, HR 100, RR 30, O_2 sat 98% room air Gen: Acute distress Lungs: WNL CV: Tachycardia, S4, diastolic decrescendo heard best at left sternal border Abd: WNL Ext: Asymmetric radial pulses Limited PE	■ Aortic dissection ■ MI ■ Pericarditis ■ Pulmonary embolism ■ Pneumothorax

CASE 33

HX	PE	DDX
34 yo F is brought to the ED after a car accident. She is gasping for air and complains of weakness, chest pain, and dizziness.	VS: Afebrile, BP 100/50, HR 115, RR 22, pulsus paradoxus Gen: Confusion, cyanosis, respiratory distress Neck: ↑ JVP, engorged neck veins, Kussmaul sign Lungs: WNL CV: Muffled heart sounds, ↓ PMI Abd: WNL Ext: WNL	■ Aortic dissection ■ Cardiogenic shock ■ MI ■ Pericardial tamponade ■ Pericarditis ■ Pneumothorax ■ Pulmonary embolism

INITIAL MGMT	CONTINUING MGMT	F/U
ED STAT ■ Supplemental O_2 ■ IV fluids (NS) ■ NPO ■ CXR: Widened mediastinum ■ IV β-blockers ■ ECG: Left ventricular hypertrophy ■ IV morphine **ED W/U** ■ Continuous cardiac/BP monitoring ■ CPK-MB, troponin × 3: ⊖ ■ CBC ■ Chem 8 ■ TEE: Aortic dissection ■ CT—chest with IV contrast: Aortic dissection **Rx** ■ Thoracic surgery consult	**ICU W/U** ■ Continuous cardiac/BP monitoring ■ Blood type and cross-match ■ PT/PTT, INR **Rx** ■ Continue IV β-blockers ■ Emergent thoracic surgery	■ Diet and lifestyle modifications ■ Lipid/BP management

Final Dx: Aortic dissection

INITIAL MGMT	CONTINUING MGMT	F/U
ED W/U ■ Supplemental O_2 ■ IV fluids ■ NPO ■ Pulse oximetry ■ ECG: Tachycardia, low voltage, nonspecific ST- and T-wave changes ■ CPK-MB ■ CBC ■ Chem 8 ■ ABG ■ Coagulation profile ■ Blood type and crossmatch ■ CXR: Cardiomegaly ■ Echocardiography: Tamponade ■ Pericardiocentesis or pericardial window	**ICU W/U** ■ Continuous cardiac/BP monitoring ■ ECG ■ Echocardiography ■ CXR ■ Cardiac surgery consult ■ ABG **Rx** ■ Advance diet from NPO to liquids as tolerated ■ Continue supplemental O_2 ■ Follow up in 2 weeks	■ CXR ■ Echocardiography ■ Patient counseling

Final Dx: Pericardial tamponade

CASE 34

HX	PE	DDX
28 yo F presents with chest pain, palpitations, nausea, and dizziness that lasted for about 5–6 minutes. She has had several such episodes over the past few weeks. During these episodes, she becomes diaphoretic and occasionally has diarrhea. In the course of some of her episodes, she describes feeling as if she might die.	VS: P 90, BP 125/75, RR 20 Gen: Mild respiratory distress, dehydration, sweating, cold hands HEENT: WNL Lungs: WNL CV: WNL Abd: WNL Ext: WNL	■ Anxiety disorder ■ Asthma attack ■ Atrial fibrillation ■ Early menopause ■ Hyperthyroidism ■ Hyperventilation ■ Hypoglycemia ■ Mitral valve prolapse ■ Panic attack vs panic disorder ■ Pheochromocytoma ■ Pulmonary embolus ■ Substance abuse

CASE 35

HX	PE	DDX
32 yo F presents with new-onset chest pain, palpitations, and dizziness. Her symptoms are intermittent and occur 3–4 times a day. She also reports shortness of breath and chest tightness during her attacks.	VS: P 90–200 (variable), BP 125/75, RR 20 Gen: Mild cyanosis HEENT: WNL Lungs: Bibasilar crackles CV: Irregularly irregular, tachycardia Abd: WNL Ext: WNL	■ Anxiety disorder ■ Atrial fibrillation with variable ventricular rate ■ Hyperthyroidism ■ Hyperventilation ■ Mitral valve prolapse ■ Panic attack vs panic disorder

INITIAL MGMT	CONTINUING MGMT	F/U
Office W/U ■ CBC ■ Chem 8 ■ UA ■ UTOX: ⊖ ■ Thyroid studies ■ ECG ■ CXR **Rx** ■ Reassure patient ■ First-line treatment: SSRI ■ May consider short-course of benzodiazepines		■ Outpatient follow-up in 4 weeks ■ Psychiatry consult ■ Patient counseling ■ Behavioral modification program ■ Relaxation exercises

Final Dx: Panic disorder

INITIAL MGMT	CONTINUING MGMT	F/U
ED W/U ■ Supplemental O_2 ■ IV fluids (NS) ■ CBC ■ Chem 8 ■ Thyroid studies ■ ECG: Atrial fibrillation ■ CXR: Pulmonary vascular congestion ■ Echocardiography: Enlarged left atrium **Rx** ■ Synchronous cardioversion ■ Propranolol ■ Heparin with bridge to warfarin ■ Alternate other oral anticoagulant	**ICU W/U** ■ ECG ■ Continuous cardiac/BP monitoring ■ Aspirin ■ Warfarin ■ Discontinue heparin after therapeutic INR for 2 days	■ Follow up in 2 weeks ■ PT/PTT, INR and warfarin dose adjustment as necessary to target INR 2-3 ■ Patient counseling

Final Dx: Atrial fibrillation

ABDOMINAL PAIN

CASE 36

HX	PE	DDX
38 yo M presents with RUQ abdominal pain for the last 48 hours. The pain radiates to his right groin and scrotum and comes in waves of severe intensity that prevent him from finding a comfortable resting position.	VS: T 36°C (96°F), BP 130/85, HR 110, RR 22 Gen: Acute distress Lungs: WNL CV: Tachycardia Abd: Soft, nontender, non-distended, tenderness in right flank, no peritoneal signs, normal BS GU: No scrotal swelling, symmetric cremasteric reflexes Rectal exam: WNL, guaiac ⊖	▪ Gastroenteritis ▪ Nephrolithiasis ▪ Pancreatitis ▪ Perforated duodenal ulcer ▪ Retrocecal appendicitis ▪ Testicular torsion

CASE 37

HX	PE	DDX
60 yo M presents with generalized weakness, left flank discomfort, nausea, and constipation for the last 2 weeks. He has lost 20 lb over the past 4 months.	VS: T 37°C (99.2°F), P 90, BP 120/60, RR 18 Gen: NAD Lungs: WNL CV: WNL Abd: ↓ BS, left flank tenderness with deep palpation Rectal exam: WNL Ext: WNL Neuro: WNL	▪ Colorectal cancer ▪ Recurrent small bowel obstruction ▪ Renal abscess ▪ Renal mass/cancer ▪ Adrenal mass ▪ Splenic mass ▪ Lymphoma

CASE 38

HX	PE	DDX
32 yo F presents with 2 days of progressively worsening flank pain, urinary frequency, and a burning sensation during urination. She also reports a subjective fever and chills.	VS: T 38.1°C (100.6°F), BP 130/85, HR 86, RR 18 Gen: Mild discomfort with exam Lungs: WNL CV: WNL Abd: ⊕ BS, mild suprapubic tenderness, no peritoneal signs Back: Mild CVA tenderness on the left Pelvic: WNL Rectal exam: WNL, guaiac ⊖	▪ Acute cervicitis ▪ Acute cystitis ▪ Acute pelvic inflammatory disease ▪ Acute pyelonephritis ▪ Acute urethritis ▪ Ectopic pregnancy ▪ Nephrolithiasis

INITIAL MGMT	CONTINUING MGMT	F/U
ED W/U ■ CBC: Normal WBC count ■ Chem 8 ■ Serum amylase, lipase ■ UA: Microscopic hematuria ■ Urine culture ■ KUB: Radiopaque 3-mm stone ■ CT—kidney: Stone visualized in distal ureter **Rx** ■ Analgesia: Opioids and NSAIDs ■ Counsel patient re: oral hydration	■ Serum calcium, magnesium, phosphate ■ Serum uric acid ■ Urine strain ■ Stone analysis: Calcium oxalate	■ ↑ fluid intake ■ Follow up in 4 weeks ■ Patient counseling ■ Counsel patient re: smoking cessation and limiting alcohol and caffeine intake

Final Dx: Nephrolithiasis

INITIAL MGMT	CONTINUING MGMT	F/U
Office W/U ■ CBC: Hemoglobin 9.0 ■ Chem 14: Ca 15, BUN 40, creatinine 2.0 ■ UA: ⊕ for RBCs ■ CXR ■ U/S—complete abdominal: Left renal mass ■ Admit to ward **Rx** ■ IV fluids (NS) ■ Bisphosphonate (pamidronate)	**Ward W/U** ■ Intact PTH: ↓ ■ Chem 7: Ca 10, BUN 20, creatinine 1.5 ■ CT—abdomen and chest: Left renal mass ■ Renal mass biopsy ■ Bone scan ■ CT—head ■ Ferritin, TIBC, serum iron **Rx** ■ Oncology consult ■ Surgery consult	

Final Dx: Renal cell carcinoma

INITIAL MGMT	CONTINUING MGMT	F/U
Office W/U ■ CBC: ↑ WBC count ■ Chem 8 ■ UA: WBC, bacteria, nitrite ⊕ ■ Urine culture: Pending ■ Urinary β-hCG: ⊖ ■ U/S—renal **Rx** ■ Ciprofloxacin (fluoroquinolone) ■ Encourage oral rehydration	**Office W/U** ■ Urine culture: ⊕ for *E coli*	■ Follow up in 3–5 days ■ Patient counseling ■ Counsel patient re: medication compliance ■ Counsel patient to limit alcohol intake

Final Dx: Pyelonephritis

CASE 39

HX	PE	DDX
10 yo African-American M presents with sudden onset of jaundice, dark-colored urine, back pain, and fatigue. He was started on TMP-SMX for an ear infection a few days ago. He has a family history of blood disorders.	VS: T 38°C (99.8°F), P 90, BP 110/50, RR 14 Gen: NAD Skin: Jaundice HEENT: Scleral icterus, pallor Lungs: WNL CV: WNL Abd: WNL Ext: WNL Neuro: WNL	▪ Autoimmune hemolytic anemia ▪ DIC ▪ G6PD deficiency ▪ Sickle cell anemia ▪ Spherocytosis ▪ Thalassemia ▪ TTP

CASE 40

HX	PE	DDX
58 yo M with history of alcoholism presents with a 1-day history of sharp epigastric pain that radiates to his back. He is nauseous and has vomited several times. He also complains of anorexia. He reports heavy alcohol use over the past 2–3 days. He has no previous history of peptic ulcer disease.	VS: T 38.2°C (101°F), BP 138/68, HR 110, RR 22 Gen: WD/WN but agitated, lying on bed with knees drawn up Lungs: ↓ breath sounds over left lower lung CV: Tachycardia Abd: Tender and distended with ↓ BS	▪ Acute alcoholic hepatitis ▪ Acute cholecystitis ▪ Acute gastritis ▪ Acute pancreatitis ▪ Aortic dissection ▪ Cholelithiasis ▪ Intestinal perforation ▪ MI ▪ Perforated gastric or duodenal ulcer ▪ Pneumonia

INITIAL MGMT	CONTINUING MGMT	F/U
Office W/U ▪ CBC stat and q 12 h: ↓↓ hemoglobin, ↓↓ hematocrit ▪ Peripheral smear: Bite cells, fragment cells ▪ Chem 14: ↑ indirect bilirubin ▪ PT/PTT, INR **Rx** ▪ Discontinue TMP-SMX	**Ward W/U** ▪ Reticulocyte count: ↑ ▪ LDH: ↑ ▪ Haptoglobin: ↓ ▪ UA: Hemoglobinuria ▪ G6PD assay: Consistent with G6PD deficiency ▪ Type and cross **Rx** ▪ Start IV ▪ IV fluids (NS) ▪ Transfuse 2 units of packed RBCs	▪ Discharge home ▪ Follow up in 2 months ▪ Educate patient/family (including consideration of genetic counseling)

Final Dx: G6PD deficiency

INITIAL MGMT	CONTINUING MGMT	F/U
ED W/U ▪ IV fluids (NS) ▪ NPO ▪ Continuous BP monitoring ▪ NG tube placement, set to suction ▪ ECG: No evidence of ischemia ▪ CBC ▪ Chem 14 ▪ Serum amylase, lipase: ↑ ▪ ABG ▪ Supplemental O_2 ▪ Pulse oximetry ▪ X-ray—abdomen, upright ▪ CXR **Rx** ▪ NG tube ▪ IV meperidine for pain control ▪ Check for alcohol withdrawal ▪ May need folic acid and thiamine if chronic alcohol use is concerning	**Ward W/U** ▪ Continuous BP monitoring ▪ Continue NPO ▪ U/S—liver, gallbladder and bile duct, pancreas ▪ PT/PTT ▪ CT—abdomen ▪ Surgery consult (should patient become unstable) ▪ GI consult ▪ Advance diet as tolerated ▪ Patient needs pharmacologic and mechanical DVT prophylaxis due to high risk for DVT with pancreatitis ▪ Watch magnesium and phosphorus level as patients with EtOH abuse have high risk for electrolyte abnormality and refeeding syndrome	▪ Follow up in 7 days ▪ Patient counseling ▪ Counsel patient re: abstinence from alcohol ▪ Social work consult for alcohol abuse ▪ Referral to inpatient detoxification or outpatient group therapy (eg, Alcoholics Anonymous) if amenable ▪ Smoking cessation

Final Dx: Acute pancreatitis

CASE 41

HX	PE	DDX
1-day-old M born at home is brought to the ED because of bilious vomiting, irritability, poor feeding, lethargy, and an acute episode of rectal bleeding.	VS: T 38°C (100°F), P 170, BP 69/44, RR 43, O_2 sat 89% room air Skin: Evidence of poor perfusion Chest: WNL CV: WNL Abd: Distention; evidence of intestinal obstruction Limited PE	▪ Duodenal web ▪ Intestinal atresia ▪ Intussusception ▪ Malrotation with volvulus ▪ Meconium plug/ileus ▪ Necrotizing enterocolitis

CASE 42

HX	PE	DDX
21-month-old M is brought to the ED because of intermittent abdominal pain that causes him to become still while drawing up his legs. He also presents with irritability and vomiting that was initially clear but has become bilious. He seems lethargic between pain episodes. In the ED, he passes some dark red stool.	VS: T 38.5°C (101°F), P 157, BP 81/59, RR 35, O_2 sat 93% room air Skin: No evidence of purpura Chest: WNL CV: WNL Abd: Soft, mildly tender; examination of RUQ fails to identify presence of bowel; ill-defined mass in the RUQ Limited PE	▪ Bacterial colitis ▪ Gastroenteritis ▪ Intoxications ▪ Intussusception ▪ Metabolic derangements ▪ Malrotation with midgut volvulus ▪ Meckel diverticulum ▪ Neurologic disease ▪ Small bowel obstruction

INITIAL MGMT	CONTINUING MGMT	F/U
ED STAT ■ IV fluids (NS) ■ Supplemental O_2 ■ ABG: Metabolic acidosis **ED W/U** ■ CBC: ↑ WBC count, mildly ↓ hemoglobin ■ Chem 8 ■ AXR: Airless rectum; large gastric bubble ■ CXR: No evidence of diaphragmatic hernia **Rx** ■ NG tube placement, set to suction ■ IV bicarbonate (to correct acidosis if pH < 7.0) ■ Pediatric surgery consult—Ladd procedure	**Ward W/U** ■ Upper GI series: Bird's beak, corkscrew appearance of proximal jejunum ■ Barium enema: Cecum in RUQ **Rx** ■ NG tube, set to suction ■ IV fluids (NS)	■ Follow up in 48 hours ■ Family counseling

Final Dx: Malrotation with volvulus

INITIAL MGMT	CONTINUING MGMT	F/U
ED STAT ■ IV fluids (NS) ■ Supplemental O_2 **ED W/U** ■ CBC: ↑ WBC count ■ Chem 14 ■ ABG: Metabolic acidosis ■ AXR: Distended bowel with air-fluid levels; mass in right abdomen ■ U/S—abdomen: Compatible with intussusception **Rx** ■ NG tube placement, set to suction ■ Barium enema: Coiled-spring appearance; disorder is relieved by air insufflation ■ Pediatric surgery consult	**Ward W/U** ■ AXR: Gastric bubble; no air-fluid levels ■ ABG: Metabolic derangements resolved **Rx** ■ D/C NG tube ■ IV fluids (NS) ■ Advance diet as tolerated	■ Follow up in 48 hours ■ Family counseling

Final Dx: Intussusception

CASE 43

HX	PE	DDX
27-month-old M presents to the ED with seizures, irritability, anorexia, altered sleep patterns, emotional lability, and vomiting. His mother states that the family has been living for about 1 year in an old, poorly maintained building that has only recently begun to undergo renovation. Since she was laid off at the battery plant, the family has been considering moving out of town.	VS: T 37°C (99°F), P 129, BP 89/61, RR 20, O_2 sat 92% room air Neuro: Lethargy, ataxia, seizures. Remainder of physical examination is noncontributory (except for some conjunctival pallor)	▪ Lead toxicity ▪ Metabolic disease ▪ Neurologic disease ▪ Nonmetal intoxication ▪ Other heavy metal toxicity

CASE 44

HX	PE	DDX
7-day-old alert M presents to a clinic with jaundice that started 2 days ago. The baby was born at term via an uneventful vaginal delivery and started breastfeeding after some delay. The mother states that she took the baby to the doctor's office at that time and that the baby's bilirubin was 14 mg/dL. The mother does not take any medications. She is very concerned that the baby's jaundice is not improving and asks if the baby has kernicterus.	VS: T 37°C (99°F), P 129, BP 80/51, RR 29, O_2 sat 94% room air PE: WNL except for jaundice Neuro: WNL	▪ Breastfeeding jaundice ▪ Hereditary spherocytosis ▪ Physiologic hyperbilirubinemia ▪ Unconjugated hyperbilirubinemia (Gilbert/Crigler-Najjar)

CASE 45

HX	PE	DDX
31 yo M comes to the office complaining of midepigastric pain that usually begins 1–2 hours after eating and sometimes awakens him at night. He also has occasional indigestion. He is taking an antacid for his problem. He denies melena or hematemesis.	VS: T 37.1°C (99°F), BP 130/75, HR 100, RR 16 Gen: No distress Lungs: WNL CV: WNL Abd: Epigastric tenderness Rectal exam: WNL	▪ Acute gastritis ▪ Diverticulitis ▪ Dyspepsia ▪ GERD ▪ Mesenteric ischemia ▪ Pancreatitis ▪ Peptic ulcer disease ▪ Non-ulcer dyspepsia

INITIAL MGMT	CONTINUING MGMT	F/U
ED W/U ■ CBC: Hemoglobin 9 g/dL, MCV 75, blood smear reveals coarse basophilic stippling in RBCs ■ Chem 8 ■ Serum lead: 80 mg/dL ■ UA: Glycosuria ■ Free erythrocyte protoporphyrin: ↑ ■ Serum toxicology: ↑ lead levels ■ X-ray—abdomen ■ CT—head **Rx** ■ IV fluids (NS) ■ IM EDTA	**Ward Rx** ■ IV fluids (NS) ■ Serum lead ■ IM EDTA (if necessary) ■ Family counseling	■ Follow up in 7 days ■ Family counseling ■ Lead paint assay in home

Final Dx: Lead toxicity with encephalopathy

INITIAL MGMT	CONTINUING MGMT	F/U
Office W/U ■ CBC: WNL, smear WNL ■ Direct Coombs test: Noncontributory ■ Serum bilirubin: ↑ indirect bilirubin ■ TSH: WNL	**Office W/U** ■ Breastfeeding suppression test: Bilirubin levels ↓ on cessation of breastfeeding; levels ↑ again when breastfeeding restarted **Rx** ■ Continue breastfeeding ■ Consider phototherapy (if bilirubin levels do not ↓)	■ Follow up in 7 days ■ Family counseling

Final Dx: Breastfeeding neonatal jaundice

INITIAL MGMT	CONTINUING MGMT	F/U
Office W/U ■ CBC ■ Chem 8 ■ Serum amylase, lipase ■ Serum *H pylori* antibody: ⊕ ■ Stool *H pylori* antibody: ⊕ **Rx** ■ Proton pump inhibitor ■ Clarithromycin ■ Metronidazole		■ Follow up in 4 weeks; patient reports that he is feeling better (if symptoms persist or if *H pylori* is still present, may proceed to endoscopy) ■ Patient counseling ■ Counsel patient to limit alcohol intake ■ Counsel patient to avoid NSAID ■ Smoking cessation

Final Dx: Gastritis (*H pylori* infection)

CASE 46

HX	PE	DDX
45 yo M presents with a 6-week history of jaundice, pale stools, tea-colored urine, and epigastric pain that radiates to the back. He also reports that he has bilateral lower extremity swelling.	VS: T 37°C (98°F), BP 130/70, HR 90, RR 16 Gen: Jaundice Lungs: WNL CV: WNL Abd: Palpable epigastric mass Ext: Lower extremity swelling with pain on dorsiflexion of ankle	▪ Cholangiocarcinoma ▪ Colon/stomach cancer with metastases in the porta hepatis region causing biliary obstruction ▪ Pancreatic cancer ▪ Viral hepatitis

CASE 47

HX	PE	DDX
60 yo F G0 presents with a 2-month history of ↑ abdominal girth, ↓ appetite, and early satiety. She also has mild shortness of breath.	VS: T 36°C (97°F), BP 140/60, HR 90, RR 23 Gen: Pallor Breast: WNL Lungs: WNL CV: WNL Abd: Distended, nontender, normal BS, no palpable hepatosplenomegaly Pelvic: Solid right adnexal mass Rectal exam: Solid right adnexal mass; no involvement of rectovaginal septum	▪ CHF ▪ Colon cancer ▪ Liver cirrhosis ▪ Ovarian cancer ▪ Ovarian cyst

CASE 48

HX	PE	DDX
32 yo F presents with sudden onset of left lower abdominal pain that radiates to the scapula and back and is associated with vaginal bleeding. Her last menstrual period was 5 weeks ago. She has a history of pelvic inflammatory disease and unprotected intercourse.	VS: T 37°C (99°F), P 90, BP 120/50, RR 14 Gen: Moderate distress Lungs: WNL CV: WNL Abd: RLQ tenderness with rebound and guarding GU: Slightly enlarged uterus with small amount of dark bloody discharge from cervix; right adnexal tenderness	▪ Ectopic pregnancy ▪ Ovarian torsion ▪ Pelvic inflammatory disease ▪ Ruptured ovarian cyst ▪ Fitz-Hugh–Curtis syndrome

INITIAL MGMT	CONTINUING MGMT	F/U
Office W/U ■ CBC ■ Chem 14 ■ CT—abdomen: Large necrotic mass in head of pancreas with evidence of vascular involvement ■ ERCP/EUS: Biopsy to obtain histology	**Ward Rx** ■ Medical oncology consult ■ Palliative care consult ■ Surgery is not an option owing to advanced disease	

Final Dx: Pancreatic cancer

INITIAL MGMT	CONTINUING MGMT	F/U
Office W/U ■ CBC ■ Chem 14 ■ CA-125: 900 ■ CT—abdomen and pelvis: 10- × 12-cm right complex ovarian cyst; severe ascites ■ CXR: Right moderate pleural effusion ■ ECG ■ Pap smear ■ Mammogram ■ Colonoscopy ■ Gynecology consult	**Ward W/U** ■ Blood type and crossmatch ■ PT/PTT, INR **Rx** ■ Exploratory laparotomy with TAH-BSO and staging (includes ascites collection for peritoneal cytology) ■ Paracentesis for ascites collection	■ Carboplatin ■ CA-125 ■ CBC ■ Chem 14

Final Dx: Ovarian cancer

INITIAL MGMT	CONTINUING MGMT	F/U
ED W/U ■ Urinary β-hCG: ⊕ ■ Quantitative serum β-hCG: 2500 ■ CBC ■ Chem 8 ■ Cervical Gram stain and G&C culture ■ U/S—transvaginal: 2-cm right adnexal mass, no intrauterine pregnancy, free fluid in cul-de-sac **Rx** ■ IV fluid (NS)	■ Blood type and crossmatch ■ PT/PTT, INR ■ Gynecology consult ■ Laparoscopy ■ Rh IgG (RhoGAM) if Rh-⊖	■ Counsel patient re: safe sex practices and contraception

Final Dx: Ectopic pregnancy

CASE 49

HX	PE	DDX
74 yo M presents with LLQ pain, fever, and chills for the past 3 days. He also reports recent-onset of alternating diarrhea and constipation. He consumes a low-fiber, high-fat diet.	VS: T 38°C (101°F), BP 130/85, HR 100, RR 22 Gen: Pallor, diaphoresis Lungs: WNL CV: Tachycardia Abd: LLQ tenderness, no peritoneal signs, sluggish BS Rectal exam: Guaiac ⊖	■ *Clostridium difficile* colitis ■ Colon cancer ■ Crohn disease ■ Diverticular abscess ■ Diverticulitis ■ Gastroenteritis ■ Ulcerative colitis

CASE 50

HX	PE	DDX
41 yo F presents with sudden-onset RUQ pain for the last 6 hours associated with nausea and vomiting. The pain started after lunch and has become more severe and constant. She reports that deep breathing exacerbates her pain and her pain radiates to her shoulder. She had a similar episode almost 1 year ago. She is taking OCPs and has 3 children.	VS: T 39.0°C (102°F), BP 130/82, HR 80, RR 16 Gen: WD, slightly obese, moderate distress Lungs: WNL CV: WNL Abd: Obesity, tenderness and guarding to palpation on RUQ, ⊕ Murphy sign, ↓ BS Rectal exam: WNL, guaiac ⊖	■ Acute appendicitis ■ Acute cholangitis ■ Acute cholecystitis ■ Acute hepatitis ■ Acute pancreatitis ■ Acute peptic ulcer disease with or without perforation ■ Cholelithiasis or choledocholithiasis ■ Fitz-Hugh–Curtis syndrome (gonococcal perihepatitis) ■ Gastritis ■ MI ■ Renal colic ■ Right-sided pneumonia ■ Small bowel obstruction

INITIAL MGMT	CONTINUING MGMT	F/U
ED W/U ■ CBC: ↑ WBC count ■ Chem 14 ■ Serum amylase, lipase ■ UA ■ Urine culture: Pending ■ Blood culture: Pending ■ Stool culture and sensitivity ■ Stool for ova and parasites ■ *C difficile* toxin ■ CXR ■ KUB ■ CT—abdomen: Diverticulitis **Rx** ■ NPO ■ IV fluids (NS) ■ IV metronidazole + ciprofloxacin	**Ward W/U** ■ Urine culture: Pending ■ Blood culture: Pending **Rx** ■ GI consult ■ NPO, advance to clear liquid diet as tolerated ■ Metronidazole + ciprofloxacin × 7–10 days ■ Discharge home in 3–4 days	■ High-fiber diet ■ Colonoscopy 4 weeks after recovery

Final Dx: Diverticulitis

INITIAL MGMT	CONTINUING MGMT	F/U
ED W/U ■ IV fluids (NS) ■ NPO ■ Continuous BP monitoring ■ ECG ■ CBC ■ Chem 14 ■ Serum amylase, lipase ■ Blood/urine cultures ■ X-ray—abdomen ■ CXR ■ Urine pregnancy test ■ U/S—abdomen: Gallstones with gallbladder edema **Rx** ■ IM prochlorperazine ■ IV hydromorphone ■ IV cefuroxime	**Ward W/U** ■ Blood type and crossmatch ■ PT/PTT, INR ■ Surgery consult for cholecystectomy ■ Vitals q 4 h ■ CBC next day ■ Chem 8 next day **Rx** ■ NPO, advance diet as tolerated ■ Continue antibiotic therapy	■ Follow up in 2 weeks ■ Patient counseling ■ Counsel patient to limit alcohol intake

Final Dx: Acute cholecystitis

CASE 51

HX	PE	DDX
24 yo F presents with bilateral lower abdominal pain that started with the first day of her menstrual period. The pain is associated with fever and a thick, greenish-yellow vaginal discharge. She has had unprotected sex with multiple sexual partners.	VS: T 38°C (100.4°F), P 90, BP 110/50, RR 14 Gen: Moderate distress Lungs: WNL CV: WNL Abd: Diffuse tenderness (greatest in the lower quadrants), no distention, no rebound or guarding, ↓ BS Pelvic: Purulent, bloody discharge from cervix; cervical motion and bilateral adnexal tenderness Rectal exam: WNL Ext: WNL	▪ Cervicitis ▪ Dysmenorrhea ▪ Endometriosis ▪ Pelvic inflammatory disease ▪ Pyelonephritis ▪ Vaginitis

CASE 52

HX	PE	DDX
25 yo M is brought to the ED because of abdominal pain and ↓ appetite for 4 days. This episode was preceded by nausea, vomiting, and ↑ urinary frequency.	VS: T 37°C (98°F), P 120, BP 100/60, RR 25 Gen: Moderate distress Skin: Poor skin turgor HEENT: Dry mucous membranes, sweet-smelling breath Lungs: WNL CV: Tachycardia Abd: Generalized tenderness Ext: WNL Neuro: WNL Limited PE	▪ Acute intestinal obstruction ▪ Alcoholic ketoacidosis ▪ Appendicitis ▪ Diabetic ketoacidosis ▪ Drug intoxication ▪ Gastroenteritis ▪ Pancreatitis ▪ Pyelonephritis

INITIAL MGMT	CONTINUING MGMT	F/U
ED W/U ▪ Urinary β-hCG: ⊖ ▪ CBC: ↑ WBC count ▪ Chem 14 ▪ Cervical Gram stain and G&C culture ▪ U/S—pelvis ▪ UA and urine culture **Rx** ▪ IV fluids (NS) ▪ IV ceftriaxone + PO doxycycline or PO azithromycin ▪ Acetaminophen	**Ward W/U** ▪ Cervical culture: ⊕ *N gonorrhoeae* **Rx** ▪ Discontinue **IV** ceftriaxone when symptoms improve (usually in 24–48 hours) ▪ Switch to PO doxycycline or clindamycin	▪ Counsel patient re: safe sex practices ▪ Treat partners

Final Dx: Pelvic inflammatory disease

INITIAL MGMT	CONTINUING MGMT	F/U
ED STAT ▪ Glucometer: 480 mg/dL ▪ IV fluids (NS) **ED W/U** ▪ Continuous monitoring ▪ Chem 14: Normal K, normal Na, ↑ anion gap ▪ CBC: ↑ WBC count ▪ Serum amylase, lipase ▪ UA and urine culture: ⊕ glucose, ⊕ ketones ▪ Urine/serum toxicology ▪ Phosphate: ↓ ▪ ECG ▪ ABG: Metabolic acidosis (pH = 7.1) ▪ Quantitative serum ketones: ↑ ▪ Serum osmolality: Normal ▪ X-ray—abdomen ▪ CXR **Rx** ▪ IV regular insulin, continue ▪ Phosphate therapy as needed	**ICU W/U** ▪ Continuous monitoring ▪ Random glucose q 1 h ▪ Chem 8 q 4 h: ↓ K, glucose < 250 **Rx** ▪ Switch IV NS to D_5W ▪ IV potassium ▪ SQ insulin NPH ▪ SQ insulin regular ▪ Discontinue IV insulin 2 hours after starting long-acting insulin (NPH or insulin glargine injection)	▪ Diabetic diet ▪ Diabetic teaching ▪ Hb_{A1c} q 3 months ▪ Follow up in 2 weeks in the office ▪ Diabetic foot care ▪ Ophthalmology consult ▪ Lipid profile ▪ Instruct patient in home glucose monitoring ▪ Home glucose monitoring, glucometer

Final Dx: Diabetic ketoacidosis

CONSTIPATION/DIARRHEA

CASE 53

HX	PE	DDX
67 yo M presents with constipation, ↓ stool caliber, and blood in his stool for the past 8 months. He also reports unintentional weight loss. He is on a low-fiber diet and has a family history of colon cancer.	VS: P 85, BP 140/85, RR 14, O_2 sat 98% room air Gen: NAD HEENT: Pale conjunctivae Lungs: WNL CV: WNL Abd: WNL Pelvic: WNL Rectal exam: Guaiac ⊕	▪ Angiodysplasia ▪ Colorectal cancer ▪ Diverticulosis ▪ GI parasitic infection (ascariasis, giardiasis) ▪ Hemorrhoids ▪ Hypothyroidism ▪ Inflammatory bowel disease ▪ Irritable bowel syndrome

CASE 54

HX	PE	DDX
28 yo M presents with diffuse abdominal pain, loose stools, perianal pain, mild fever, and weight loss over the past 4 weeks. He denies any history of travel or recent use of antibiotics.	VS: T 37°C (99°F), BP 130/65, HR 70, RR 14 Gen: NAD Lungs: WNL CV: WNL Abd: WNL Rectal exam: Perianal skin tags, guaiac ⊕	▪ Crohn disease ▪ Diverticulitis ▪ Gastroenteritis ▪ Infectious colitis ▪ Irritable bowel syndrome ▪ Ischemic colitis ▪ Lactose intolerance ▪ Pseudomembranous colitis ▪ Small bowel lymphoma ▪ Ulcerative colitis

INITIAL MGMT	CONTINUING MGMT	F/U
Office W/U ■ CBC: ↓ hematocrit, ↓ MCV ■ Chem 8: Normal ■ Ferritin: ↓ ■ Serum iron: ↓ ■ TIBC: ↑ ■ TSH: Normal ■ Stool for ova and parasites ■ ESR: Normal ■ Stool guaiac: ⊕	**Office W/U** ■ GI consult ■ Colonoscopy: Polyp with adenocarcinoma ■ CT—abdomen and pelvis with contrast ■ CEA **Rx** ■ Iron sulfate ■ General surgery consult ■ Plan partial colectomy	

Final Dx: Colorectal cancer

INITIAL MGMT	CONTINUING MGMT	F/U
Office W/U ■ CBC ■ Chem 14 ■ Iron studies ■ Serum folate ■ Serum vitamin D ■ Serum amylase, lipase ■ Stool for ova and parasites ■ Stool *C difficile* ■ X-ray—abdomen ■ Colonoscopy: Crohn disease **Rx** ■ Oral steroids ■ Immunomodulator therapy (eg azathioprine) or biologic therapy (eg anti-TNF such as infliximab)		■ Follow up in 2 weeks ■ Counsel patient re: smoking cessation, NSAID avoidance, medication compliance and adherence ■ Gastroenterology consult

Final Dx: Crohn disease

CASE 55

HX	PE	DDX
30 yo F presents with periumbilical pain cramping in nature for the last 6 months. The pain is relieved by defecation and worsens when she is upset; her pain never awakens her from sleep. She has alternating constipation and diarrhea but no nausea, vomiting, weight loss, or anorexia.	VS: Afebrile, P 85, BP 130/65, RR 14 Gen: NAD Lungs: WNL CV: WNL Abd: WNL Pelvic: WNL Rectal exam: Guaiac ⊖	■ Celiac disease ■ Chronic pancreatitis ■ Colorectal cancer ■ Crohn disease ■ Diverticulosis ■ Endometriosis ■ GI parasitic infection (ascariasis, giardiasis) ■ Hypothyroidism ■ Inflammatory bowel disease ■ Irritable bowel syndrome

CASE 56

HX	PE	DDX
8 yo M is brought to the clinic by his mother for intermittent diarrhea alternating with constipation together with vomiting and cramping abdominal pain. His mother also reports that he has had progressive anorexia.	VS: T 37°C (98°F), BP 110/65, HR 90, RR 16 Gen: Pale and dry mucosal membranes; lack of growth Lungs: WNL CV: WNL Abd: WNL Ext: Muscle wasting, especially in gluteal area	■ Bacterial gastroenteritis ■ Celiac disease ■ Food allergy ■ Giardiasis ■ Protein intolerance ■ Viral gastroenteritis

INITIAL MGMT	CONTINUING MGMT	F/U
Office W/U ■ CBC ■ Chem 14 ■ TSH ■ Stool for ova and parasites ■ Stool for WBCs ■ Stool culture and sensitivity ■ Transglutaminase antibody **Rx** ■ Educate patient ■ Reassurance ■ High-fiber diet ■ Consider antidepressant therapy (TCA)		■ Follow up in 4 weeks ■ Call with questions

Final Dx: Irritable bowel syndrome (IBS)

INITIAL MGMT	CONTINUING MGMT	F/U
Office W/U ■ CBC ■ Chem 14 ■ UA ■ Stool for ova and parasites ■ Stool occult blood ■ Stool Gram stain ■ Stool fat stain ■ Barium enema ■ CT—abdomen ■ Iron studies ■ Serum folate ■ Serum B_{12} ■ Serum vitamin D ■ Serum transglutaminase antibody: ⊕ titers	**Ward W/U** ■ CXR: Normal ■ KUB: Normal ■ D-xylose tolerance test: Carbohydrate malabsorption ■ Peroral duodenal biopsy: Villi are atrophic or absent ■ Dietary consult **Rx** ■ Gluten-free diet ■ Vitamin D supplementation ■ Calcium supplementation	■ Follow up in 1 week ■ Patient counseling ■ Pneumococcal vaccine

Final Dx: Celiac disease

CASE 57

HX	PE	DDX
28 yo M reports intermittent episodes of vomiting and diarrhea along with cramping abdominal pain for the past 2 days. He describes his stool as watery. He returned from Mexico 3 days ago.	VS: T 39°C (101.9°F), BP 135/85, HR 100, RR 22 Gen: Mild dehydration Lungs: WNL CV: WNL Abd: Mild tenderness, no peritoneal signs, hyperactive BS Rectal exam: WNL, guaiac ⊖	▪ *Campylobacter* infection ▪ Cholera ▪ *C difficile* colitis ▪ Crohn disease ▪ Gastroenteritis ▪ Giardiasis ▪ Salmonellosis ▪ Shigellosis

CASE 58

HX	PE	DDX
40 yo F presents with fever, anorexia, nausea, profuse and watery diarrhea, and diffuse abdominal pain. Last week she was on antibiotics for a UTI.	VS: T 38°C (100.4°F), BP 100/50, HR 100, RR 22, orthostatic hypotension Gen: WNL Lungs: WNL CV: Tachycardia Abd: Diffuse tenderness, no peritoneal signs, ⊕ BS Rectal exam: Guaiac ⊕	▪ Amebiasis ▪ Food poisoning ▪ Gastroenteritis ▪ Giardiasis ▪ Hepatitis A ▪ Infectious diarrhea (bacterial, viral, parasitic, protozoal) ▪ Inflammatory bowel disease ▪ Pseudomembranous (*C difficile*) colitis ▪ Traveler's diarrhea

CASE 59

HX	PE	DDX
33 yo M presents with foul-smelling, watery diarrhea together with diffuse abdominal cramps and bloating that began yesterday. He also vomited once. He was recently in Mexico.	VS: T 37°C (98°F), BP 110/50, HR 85, RR 22, no orthostatic hypotension Gen: WNL Lungs: WNL CV: WNL Abd: No tenderness, no peritoneal signs, active BS Rectal exam: Guaiac ⊖	▪ Amebiasis ▪ Food poisoning ▪ Gastroenteritis ▪ Giardiasis ▪ Hepatitis A ▪ Infectious diarrhea (bacterial, viral, parasitic, protozoal) ▪ Inflammatory bowel disease ▪ Pseudomembranous (*C difficile*) colitis ▪ Traveler's diarrhea

INITIAL MGMT	CONTINUING MGMT	F/U
ED W/U ■ CBC ■ Chem 14 ■ Fecal leukocyte stain ■ Stool for *C difficile* ■ Stool Gram stain ■ Stool culture ■ Stool for ova and parasites ■ Stool fat stain ■ UA and urine culture	**ED W/U** ■ Stool culture: ⊕ for *E coli* ■ Stool Gram stain: ⊕ for gram ⊖ rods and ↑ leukocytes **Rx** ■ Oral hydration ■ Ciprofloxacin	■ Follow up in 1 week ■ Patient counseling ■ Counsel patient to limit alcohol intake ■ Smoking cessation

Final Dx: Gastroenteritis

INITIAL MGMT	CONTINUING MGMT	F/U
ED W/U ■ Stool culture ■ Stool *Giardia* antigen ■ Stool for ova and parasites ■ Stool WBCs: ⊕ ■ Stool for *C difficile:* ⊕ ■ CBC: ↑ WBC count ■ Chem 14 **Rx** ■ IV fluids (NS) ■ Metronidazole	**Ward W/U** ■ No orthostatic hypotension **Rx** ■ Send home on metronidazole (when diarrhea improves); no diphenoxylate and atropine/loperamide	■ Counsel patient re: oral hydration

Final Dx: Pseudomembranous (*C difficile*) colitis

INITIAL MGMT	CONTINUING MGMT	F/U
Office W/U ■ Stool culture ■ Stool *Giardia* antigen: ⊕ ■ Stool for ova and parasites ■ Stool WBCs ■ Stool for *C difficile* ■ CBC ■ Chem 8 **Rx** ■ Metronidazole		■ Counsel patient re: oral hydration

Final Dx: Giardiasis

GI BLEEDING

CASE 60

HX	PE	DDX
38 yo M presents with intermittent hematemesis for the last 2 weeks. He has a history of epigastric pain for almost 2 years that occasionally worsens when he eats food or drinks milk. He also reports melena for the last 3 weeks. His social history is significant for alcohol and tobacco use.	VS: T 37°C (98.9°F), BP 90/65, HR 110, RR 24 Gen: Pallor Lungs: WNL CV: WNL Abd: No tenderness, no peritoneal signs, normal BS Rectal exam: WNL, guaiac ⊕ Limited PE	▪ Duodenal ulcer ▪ Esophageal etiologies: tear, varices, esophagitis ▪ Gastric etiologies: angiodysplasia carcinoma, ulcer, gastritis ▪ Intestinal angiodysplasia ▪ Portal hypertension

INITIAL MGMT	CONTINUING MGMT	F/U
ED STAT ■ Placement of two large bore IV ■ IV fluids (NS) ■ Supplemental O_2 ■ NPO ■ Orthostatic vitals: Drop on standing ■ Type and screen, crossmatch **ED W/U** ■ CBC: Hematocrit 24 ■ Chem 14 ■ KUB: No evidence of free air ■ STAT GI consult/endoscopy: Gastric antral lesion with adherent clot ■ PT/PTT, INR ■ CXR ■ ECG **Rx** ■ NPO ■ Blood transfusion if hemoglobin $<$ 7 or active ongoing bleeding ■ NG tube with low intermittent suction to avoid aspiration ■ IV pantoprazole	**ICU W/U** ■ CBC q 4 h until hematocrit is stable; then frequency can be ↓ **Rx** ■ GI consult ■ Combination therapy with epinephrine injection followed by thermal coagulation (or endoscopic clipping) ■ Octreotide for varices ■ Advance diet as tolerated ■ Pantoprazole ■ Transfer to wards if patient remains stable ■ *H pylori* serology and eradication if ⊕	■ Follow up in 1 week ■ Patient counseling ■ Counsel patient to cease alcohol intake ■ Smoking cessation ■ Dietary consult ■ Counsel re: avoidance of NSAID

Final Dx: Bleeding gastric ulcer

CASE 61

HX	PE	DDX
67 yo F presents with acute crampy abdominal pain, weakness, and black stool. She reports diffuse abdominal pain for the last 3 months that worsens when she eats. She has had a 5-lb weight loss over the last 3 months.	VS: T 37°C (98.9°F), BP 90/65, HR 100, RR 24 Gen: Mild dehydration Lungs: WNL CV: WNL Abd: Tender and mildly distended; no rigidity or rebound tenderness Rectal exam: WNL, guaiac ⊕ Limited PE	▪ Colon cancer ▪ Crohn disease ▪ Diverticular bleed ▪ Infectious colitis ▪ Ischemic colitis ▪ Peptic ulcer disease ▪ Small bowel malignancy ▪ Ulcerative colitis

CASE 62

HX	PE	DDX
30 yo M presents with loose, watery stools that are streaked with blood and mucus. He has also had colicky abdominal pain and weight loss over the past 3 weeks. He denies any history of travel, radiation exposure, or recent medication use (antibiotics, NSAIDs).	VS: T 37°C (99°F), BP 130/65, HR 70, RR 14 Gen: NAD Lungs: WNL CV: WNL Abd: WNL Rectal exam: Blood-stained stool	▪ Crohn disease ▪ Diverticulitis ▪ Gastroenteritis ▪ Infectious colitis ▪ Hemorrhoids ▪ Ischemic colitis ▪ Pseudomembranous (*C difficile*) colitis ▪ Ulcerative colitis

INITIAL MGMT	CONTINUING MGMT	F/U
ED STAT ■ IV fluids (NS) ■ Supplemental O_2 **ED W/U** ■ CBC ■ Chem 14 ■ Serum amylase ■ Serum lipase ■ LDH: ↑ ■ PT/PTT ■ CXR ■ ECG ■ AXR ■ CT—abdomen: Pneumatosis coli ■ Blood type and crossmatch **Rx** ■ NPO ■ Surgery consult (for bowel resection) ■ Broad-spectrum antibiotics ■ NG tube placement, set to suction	**Ward W/U** ■ Hemoglobin and hematocrit q 4 h **Rx** ■ Advance diet as tolerated ■ Monitor carefully for persistent fever, leukocytosis, peritoneal irritation, diarrhea, and/or bleeding	■ Follow up in 4 weeks ■ Patient counseling ■ Counsel patient to cease alcohol intake ■ Smoking cessation ■ Dietary consult

Final Dx: Ischemic colitis

INITIAL MGMT	CONTINUING MGMT	F/U
Office W/U ■ CBC: Mild anemia ■ Iron studies ■ Serum folate ■ Serum vitamin D ■ Chem 14 ■ Serum amylase, lipase ■ Stool culture ■ Stool for ova and parasites ■ Stool WBCs ■ PT/PTT ■ Colonoscopy and rectal biopsy: Consistent with ulcerative colitis involving rectum and distal sigmoid colon **Rx** ■ IV steroids (for attack) ■ 5-ASA enema/suppositories ■ Sulfasalazine ■ Immunomodulator therapy (eg, azathioprine) or biologic therapy (eg, anti-TNF such as infliximab)		■ Follow up in 2 weeks ■ Counsel patient re: medication compliance and adherence ■ Gastroenterology referral

Final Dx: Ulcerative colitis

CASE 63

HX	PE	DDX
58 yo M presents with painless bright red blood in his stool. He reports that his diet is low in fiber.	VS: T 37°C (98°F), BP 130/85, HR 90, RR 20 Gen: Pallor, diaphoresis Lungs: WNL CV: WNL Abd: Soft, nontender, no peritoneal signs, ⊕ BS Rectal exam: Bloody stool	▪ Angiodysplasia ▪ Colon cancer ▪ Crohn disease ▪ Diverticulitis ▪ Diverticulosis ▪ Ischemic colitis ▪ Ulcerative colitis

HEMATURIA

CASE 64

HX	PE	DDX
71 yo Asian M with a history of BPH presents with a 3-month history of persistent low back pain that is 3/6 in severity with no radiation. He denies any history of trauma.	VS: T 37°C (98.5°F), P 76, BP 140/75, RR 14 Gen: NAD Neck: WNL Back: Tenderness along lumbar spine (L4, L5) Lungs: WNL CV: WNL Abd: WNL Rectal exam: Irregular, enlarged prostate; guaiac ⊖ Ext: WNL Neuro: WNL	▪ Disk herniation ▪ Lumbar muscle strain ▪ Muscular spasm ▪ Osteoporosis ▪ Prostate cancer ▪ Sciatic irritation ▪ Spinal stenosis ▪ Tumor in the vertebral canal

CASE 65

HX	PE	DDX
40 yo M complains of a slow-onset dull pain in his left flank and blood in his urine. His father died of a stroke.	VS: T 37°C (98°F), P 98, BP 150/95, RR 18 Gen: WD/WN HEENT: WNL Lungs: WNL CV: WNL (no pericardial rub) Abd: Palpable, nontender mass on both flanks Ext: WNL	▪ Polycystic kidney disease ▪ Renal cell carcinoma ▪ Renal dysplasia ▪ Simple renal cyst ▪ Tuberous sclerosis ▪ Wilms tumor

INITIAL MGMT	CONTINUING MGMT	F/U
ED W/U ■ NPO ■ IV fluids (NS) ■ CBC: ↓ hemoglobin ■ Chem 14 ■ PT/PTT ■ Serum amylase, lipase ■ UA ■ CXR ■ CT—abdomen: Diverticulosis	**Ward W/U** ■ Colonoscopy: Diverticulosis, no other source **Rx** ■ Advance diet as tolerated ■ GI consult	■ Follow up in 4 weeks ■ Patient counseling ■ Counsel patient to cease alcohol intake ■ Smoking cessation ■ Dietary consult ■ High-fiber diet

Final Dx: Diverticulosis

INITIAL MGMT	CONTINUING MGMT	F/U
Office W/U ■ CBC ■ Chem 14 ■ UA: Hematuria ■ ESR: ↑ ■ PSA: ↑↑ ■ X-ray—spine: Metastatic lesions in L4 and L5 ■ CT—lumbar spine: Mets to L4 and L5 ■ Transrectal US with biopsy: Multinodular enlarged prostate, biopsy pending **Rx** ■ Acetaminophen ■ Morphine or codeine if pain persists	**Office W/U** ■ Bone scan: Diffuse metastases ■ Prostate biopsy: Adenocarcinoma ■ CT—abdomen and pelvis: ⊕ for lymphatic involvement above aortic bifurcation **Rx** ■ Androgen deprivation therapy ■ Urology consult ■ Radiation oncology consult	■ Patient counseling

Final Dx: Prostate cancer

INITIAL MGMT	CONTINUING MGMT	F/U
Office W/U ■ CBC ■ Chem 8 ■ UA: Hematuria ■ U/S—renal or CT—abdomen: Bilateral renal cysts, enlarged kidneys, no liver cysts ■ MRA—brain: No berry aneurysms **Rx** ■ ACEI (eg, captopril, enalapril, lisinopril)	**Office W/U** ■ Nephrology consult (to look for evidence of renal insufficiency)—creatinine > 2 mg/dL ■ Urology consult (for nephrectomy, cyst decompression, or unroofing)	■ Follow up in 8 weeks with blood testing and ultrasound ■ Patient counseling ■ Counsel patient to cease alcohol intake ■ Smoking cessation ■ Dietary consult ■ Low-sodium diet ■ Counsel patient to avoid sports

Final Dx: Polycystic kidney disease

CASE 66

HX	PE	DDX
10 yo M presents with tea-colored urine and periorbital edema. He had a fever and sore throat 1 week ago. He also complains of malaise, weakness, and anorexia.	VS: T 36°C (97.5°F), BP 140/85, HR 88, RR 18 Gen: Periorbital edema, pallor Lungs: WNL CV: WNL Abd: WNL Ext: Edema around ankles	▪ Cryoglobulinemia ▪ IgA nephropathy ▪ Membranoproliferative glomerulonephritis ▪ Poststreptococcal glomerulonephritis

OTHER URINARY SYMPTOMS

CASE 67

HX	PE	DDX
70 yo M complains of waking up four to five times per night to urinate. He also has urinary urgency, a weak stream, and dribbling, and he needs to strain to initiate urination. He denies any weight loss, fatigue, or bone pain. He also has a sensation of incomplete evacuation of urine from the bladder.	VS: T 37°C (98.5°F), P 78, BP 140/85, RR 14 Gen: NAD Neck: WNL Lungs: WNL CV: WNL Abd: WNL Rectal exam: Enlarged, nodular, non-tender, rubbery prostate gland Ext: WNL	▪ BPH ▪ Bladder cancer ▪ Bladder stones ▪ Bladder trauma ▪ Chronic pelvic pain ▪ Cystitis ▪ Neurogenic bladder ▪ Prostate cancer ▪ Prostatitis ▪ Urethral strictures ▪ UTI

CASE 68

HX	PE	DDX
39 yo M complains of sudden-onset fever and chills, urgency and burning on urination, and perineal pain. His symptoms started after he underwent urethral dilation for stricture.	VS: T 37.3°C (99°F), P 65, BP 101/64, RR 16 Gen: No acute distress Lungs: WNL CV: WNL Abd: Suprapubic tenderness GU: Genitalia WNL Rectal exam: Asymmetrically swollen, firm, markedly tender, hot prostate	▪ Acute cystitis ▪ Anal fistulas and fissures ▪ Epididymitis ▪ Obstructive calculus ▪ Orchitis ▪ Prostatitis ▪ Pyelonephritis ▪ Reiter syndrome ▪ Urethritis

INITIAL MGMT	CONTINUING MGMT	F/U
ED W/U ■ CBC ■ Chem 8 ■ UA: Hematuria, proteinuria, RBC casts ■ 24-hour urine protein: Proteinuria ■ ASO titer: Normal ■ Throat culture: Pending ■ Total serum complement: ↓ **Rx** ■ Furosemide ■ Captopril ■ Penicillin	**Office W/U** ■ U/S—renal ■ Throat culture: ⊕ **Rx** ■ Furosemide ■ ACEI (captopril) ■ Nephrology consult	■ Follow up in 3 weeks with UA and periodic BP and BUN/Cr monitoring ■ Family counseling ■ Dietary consult ■ Low-sodium diet ■ Restrict fluid intake

Final Dx: Poststreptococcal glomerulonephritis

INITIAL MGMT	CONTINUING MGMT	F/U
Office W/U ■ CBC ■ BMP: Elevated creatinine ■ UA and urine culture ■ U/S—prostate ■ ESR ■ Total serum PSA ■ Residual urinary volume **Rx** ■ Finasteride ■ Prazosin (selective short-acting α-blockers)	**Office W/U** ■ Urology consult if refractory to treatment ■ Urodynamic studies	■ Follow up in 6 months with digital rectal examination and PSA ■ Patient counseling ■ Dietary consult

Final Dx: BPH

INITIAL MGMT	CONTINUING MGMT	F/U
Office W/U ■ UA ■ Urine Gram stain and culture ■ CBC ■ Chem 8 ■ VDRL, G/C testing **Rx** ■ TMP-SMX or fluoroquinolone	**Office W/U** ■ Urology consult ■ Cystoscopy	■ Follow up in 4 weeks ■ Patient counseling ■ Counsel patient to cease alcohol intake ■ Smoking cessation ■ Counsel patient re: safe sex practices ■ Treat sexual partner(s)

Final Dx: Prostatitis

CASE 69

HX	PE	DDX
21 yo M complains of a burning sensation during urination and urethral discharge. He recently began having unprotected sex with a new partner. He denies urinary frequency, urgency, fever, chills, sweats, or nausea.	VS: T 37.3°C (98.9°F), P 65, BP 101/64, RR 14 Gen: NAD Lungs: WNL CV: WNL Abd: Mild suprapubic tenderness GU: Erythema of urethral meatus, no penile lesions, pus expressed from urethra	▪ Chemical irritation ▪ Cystitis ▪ Epididymitis ▪ Orchitis ▪ Prostatitis ▪ Reiter syndrome ▪ Urethritis

CASE 70

HX	PE	DDX
20 yo F presents with a 2-day history of dysuria, ↑ urinary frequency, and suprapubic pain. She is sexually active only with her husband. She has no flank pain, fever, or nausea.	VS: Afebrile, P 65, BP 101/64, RR 16 Gen: NAD Lungs: WNL CV: WNL Abd: Mild suprapubic tenderness Pelvic: WNL	▪ Acute cystitis ▪ Nephrolithiasis ▪ Pelvic inflammatory disease ▪ Pyelonephritis ▪ Urethritis ▪ Vaginitis

INITIAL MGMT	CONTINUING MGMT	F/U
Office W/U ■ UA and urine culture ■ Urethral Gram stain: Many WBCs/hpf without bacteria ■ Urethral G&C culture (for *Neisseria gonorrhoeae* and *Chlamydia trachomatis*) ■ CBC ■ VDRL **Rx** ■ PO azithromycin (single dose) ■ IM ceftriaxone (single dose)		■ Follow up in 4 weeks ■ Patient counseling ■ Treat partner ■ Counsel patient re: safe sex practices ■ Repeat testing with nucleic acid amplification testing in 3–6 months

Final Dx: Urethritis

INITIAL MGMT	CONTINUING MGMT	F/U
Office W/U ■ UA: ↑↑ WBCs, +4 bacteria, ⊕ nitrites, ⊕ leukocyte esterase ■ Urine culture ■ CBC ■ Chem 8 ■ Urine pregnancy test **Rx** ■ TMP-SMX × 3 days	**Office W/U** ■ Urine culture: ⊕ for *E coli* sensitive to TMP-SMX **Rx** ■ TMP-SMX	

Final Dx: Acute cystitis

AMENORRHEA

CASE 71

HX	PE	DDX
21 yo F complains of irregular menstrual periods every 3–5 months since menarche at age 15. She also complains of facial hair, weight gain, acne, and darkening of the skin in her axillae.	VS: T 36°C (97°F), P 80, BP 120/80, RR 14 Gen: Obese Skin: Thick hair on face, chest, and buttocks; thickened skin in axillae Lungs: WNL CV: WNL Abd: WNL Pelvic: WNL	▪ Adrenal tumor ▪ Cushing syndrome ▪ Idiopathic hirsutism ▪ Late-onset congenital adrenal hyperplasia ▪ Ovarian neoplasm ▪ Polycystic ovarian syndrome

CASE 72

HX	PE	DDX
50 yo F presents with hot flashes and dyspareunia. Her last menstrual period was 6 months ago.	VS: T 36°C (97°F), BP 120/60, HR 70, RR 13 Gen: NAD HEENT: WNL Breast: WNL Lungs: WNL CV: WNL Abd: WNL Pelvic: Atrophy of vaginal mucosa	▪ Hyperthyroidism ▪ Hypothyroidism ▪ Menopause ▪ Pregnancy ▪ Prolactinoma

INITIAL MGMT	CONTINUING MGMT	F/U
Office W/U ■ DHEAS ■ Testosterone: ↑ ■ Serum 17-hydroxyprogesterone ■ LH/FSH: ↑ ■ Prolactin ■ TSH/free T_4 ■ Insulin/fasting glucose **Rx** ■ Weight loss ■ Exercise program ■ OCPs ■ Spironolactone ■ Smoking cessation		■ Follow up in 6 months

Final Dx: Polycystic ovarian syndrome

INITIAL MGMT	CONTINUING MGMT	F/U
Office W/U ■ Urine pregnancy test ■ Prolactin ■ TSH ■ FSH: ↑ ■ Wet mount ■ Pap smear ■ Mammogram ■ DEXA scan ■ PHQ-2 depression screen **Rx** ■ Calcium supplementation ■ Vitamin D supplementation ■ Hormone therapy for vasomotor symptoms ■ Vaginal estrogen cream ■ Vaginal jelly for lubrication		■ Follow up in 12 months ■ Counsel patient re: HRT—not recommended unless only short-term treatment is planned and if the patient has no CAD, breast cancer, or thromboembolic risk factors ■ Counsel patient re: increased risk of mood symptoms and depression in postmenopausal women

Final Dx: Menopause

CASE 73

HX	PE	DDX
14 yo F is brought into the office by her mother, who is concerned because her daughter is considerably shorter than her classmates and has not yet had her menses. The girl's parents are of normal height, and her sisters had their menses at age 13.	VS: Afebrile, BP 110/70, HR 70, RR 12 Gen: Short stature HEENT: Low posterior hairline, high-arched palate Neck: Short and wide Lungs: Widely spaced nipples CV: Tachycardia, irregular	■ Constitutional growth delay ■ Familial short stature ■ Hypopituitarism ■ Hypothyroidism ■ Turner syndrome

VAGINAL BLEEDING

CASE 74

HX	PE	DDX
21 yo F complains of prolonged and excessive menstrual bleeding and increased menstrual frequency for the past 6 months.	VS: T 36°C (97°F), P 65, BP 120/60, RR 14 Gen: NAD HEENT: WNL Lungs: WNL CV: WNL Abd: WNL GU: WNL	■ Adenomyosis ■ Bleeding disorder/coagulopathy ■ Endometrial hyperplasia/malignancy ■ Endometrial polyp ■ Hyperthyroidism ■ Hypothyroidism ■ Leiomyoma ■ Ovulatory dysfunction ■ Pregnancy ■ Uterine fibroid ■ Uterine polyp

INITIAL MGMT	CONTINUING MGMT	F/U
Office W/U ■ TSH ■ FSH: ↑ ■ LH: ↑ ■ Karyotyping: Consistent with Turner syndrome ■ Lipid panel ■ Fasting glucose **Rx** ■ Growth hormone therapy ■ Estrogen + progestin ■ Psychiatry/social work consult for educational and psychosocial evaluations ■ Orthodontic evaluation ■ Vitamin D supplementation ■ Calcium supplementation	**Office W/U** ■ 2D echocardiography ■ U/S—renal ■ U/S—pelvis: Streaked ovaries ■ Skeletal survey: Short fourth metacarpal ■ Chem 13 ■ CBC ■ UA ■ Lipid profile ■ Hearing test **Rx** ■ Continue growth hormone therapy until epiphysis is closed ■ Combination estrogen and progestin ■ Encourage weight-bearing exercises	■ Stop growth hormone when bone age > 15 years ■ Audiogram every 3–5 years ■ Monitor blood pressure yearly ■ Liver and thyroid studies yearly ■ Monitor aortic root diameter every 3–5 years ■ Referral to support group for patients with Turner syndrome

Final Dx: Turner syndrome

INITIAL MGMT	CONTINUING MGMT	F/U
Office W/U ■ Urine pregnancy test ■ TSH ■ CBC: Hypochromic microcytic anemia ■ Bleeding time ■ PT/PTT, INR ■ U/S—pelvis ■ Pap smear **Rx** ■ Iron sulfate ■ NSAIDs ■ OCPs		■ Follow up in 6 months ■ Counsel patient re: safe sex practices

Final Dx: Abnormal uterine bleeding due to uterine fibroid

CASE 75

HX	PE	DDX
27 yo F presents with lower abdominal cramping and heavy vaginal bleeding. Her last menstrual period was 7 weeks ago.	VS: T 36°C (97°F), BP 120/60, HR 80, RR 12 Gen: NAD Lungs: WNL CV: WNL Abd: Suprapubic tenderness with no rebound or guarding Pelvic: Active bleeding from cervix, cervical os open, 7-week-size uterus, mildly tender, no cervical motion tenderness, no adnexal masses or tenderness	▪ Cervical or vaginal pathology (polyp, infection, neoplasia) ▪ Ectopic pregnancy ▪ Menstrual period with dysmenorrhea ▪ Spontaneous abortion

CASE 76

HX	PE	DDX
60 yo F G0 with a history of hypertension, diabetes mellitus and infertility who had her last menstrual period 10 years ago presents with mild vaginal bleeding for the last 2 days.	VS: T 36°C (97°F), BP 120/60, HR 80, RR 14 Gen: NAD HEENT: WNL Lungs: WNL CV: WNL Abd: WNL Pelvic: WNL	▪ Atrophic endometritis ▪ Cervical cancer ▪ Endometrial cancer ▪ Endometrial polyp

CASE 77

HX	PE	DDX
32 yo F G2P1011 presents with vaginal bleeding after intercourse for the last month. She has no history of abnormal Pap smears or STDs and has had the same partner for the last 8 years. She uses OCPs.	VS: WNL Gen: NAD Abd: WNL Pelvic: Visible cervical lesion Rectal exam: Guaiac ⊖	▪ Cervical cancer ▪ Cervical polyp ▪ Cervicitis ▪ Ectropion ▪ Vaginal cancer ▪ Vaginitis ▪ Pregnancy

INITIAL MGMT	CONTINUING MGMT	F/U
ED W/U ■ Urine pregnancy test: ⊕ ■ Quantitative serum β-hCG: 3000 ■ CBC: Hemoglobin 9 ■ Blood type and screen, crossmatch ■ Rh factor ■ U/S—pelvis: Intrauterine pregnancy sac, fetal pole, no fetal heart tones ■ Gynecology consult **Rx** ■ IV fluids (NS) ■ D&C	**Ward W/U** ■ hCG ■ CBC **Rx** ■ Methylergonovine ■ Doxycycline ■ Anti-D immunoglobulin if Rh(D) ⊖ ■ Counsel patient re: birth control ■ Grief counseling ■ Pelvic rest for 2 weeks	■ Follow up in 3 weeks

Final Dx: Spontaneous (inevitable) abortion

INITIAL MGMT	CONTINUING MGMT	F/U
Office W/U ■ CBC ■ Chem 14 ■ PT/PTT, INR ■ Bleeding time ■ Pap smear ■ Endometrial biopsy: Poorly differentiated endometrioid adenocarcinoma ■ U/S—pelvis: 10-mm endometrial stripe ■ Gynecology consult	**Ward W/U** ■ CXR ■ ECG ■ CA-125 **Rx** ■ Exploratory laparotomy ■ TAH-BSO ■ Depending on staging, patient may benefit from adjuvant therapy (radiation vs chemotherapy vs hormonal therapy)	

Final Dx: Endometrial cancer

INITIAL MGMT	CONTINUING MGMT	F/U
Office W/U ■ UA ■ Urine hCG ■ Pap smear: HGSIL ■ Pelvic: Visible cervical lesion ■ G&C culture or PCR ■ Wet mount ■ Gynecology consult	**Office W/U** ■ Colposcopy ■ Cervical biopsy: Invasive squamous cell carcinoma of cervix	■ Radical hysterectomy vs radiation therapy ■ +/− adjuvant chemoradiotherapy

Final Dx: Cervical cancer

MUSCULOSKELETAL PAIN

CASE 78

HX	PE	DDX
28 yo F complains of multiple facial and bodily injuries. She claims that she fell on the stairs. She was hospitalized for some physical injuries 7 months ago. She denies any abuse.	VS: Afebrile, P 90, BP 120/64, RR 22, O_2 sat 95% room air Gen: Moderate distress with shallow breathing HEENT: 2.5-cm bruise on forehead; 2-cm bruise on left cheek Chest/lungs: Severe tenderness on left fifth and sixth ribs; CTA bilaterally CV: WNL Abd: WNL Ext: WNL Neuro: WNL	▪ Accident proneness ▪ Intimate partner violence ▪ Substance abuse

CASE 79

HX	PE	DDX
28 yo F presents with joint pain and swelling along with a butterfly-like rash over her nasal bridge and cheeks that worsens after exposure to the sun. She also reports pleuritic chest pain, shortness of breath, myalgia, and fatigue over the past few months. She says that her joint pain tends to move from joint to joint and primarily involves her hands, wrists, knees, and ankles. She also has weight loss, loss of appetite, and night sweats.	VS: T 38°C (101°F), BP 140/95, HR 80, RR 18 Gen: Pallor, fatigue HEENT: Oral ulcers, malar erythema Lungs: CTA, pleural friction rub CV: WNL Abd: WNL Ext: Maculopapular rash over arms and chest; effusion in knees, wrists, and ankles	▪ Cutaneous lupus erythematosus ▪ Dermatomyositis ▪ Drug reaction ▪ Mixed connective tissue disease ▪ Photosensitivity ▪ Polymyositis ▪ Rheumatoid arthritis ▪ SLE

INITIAL MGMT	CONTINUING MGMT	F/U
ED W/U ■ X-ray—ribs: Fracture of left 5th and 6th ribs ■ Urine toxicology ■ CT—head ■ Skeletal survey: Old fracture in forearm **Rx** ■ Ibuprofen ■ Oxycodone PRN ■ Splint ■ Counsel patient re: intimate partner violence ■ Assess for child endangerment ■ Social work consult for victim resources ■ Safety assessment and plan		■ Individual/group counseling referral

Final Dx: Intimate partner violence

INITIAL MGMT	CONTINUING MGMT	F/U
Office W/U ■ CBC: ↓ hemoglobin ■ BMP ■ PT/PTT ■ ESR/CRP: ↑ ■ Serum ANA: ⊕ ■ UA: Proteinuria ■ CXR ■ Total complement: ↓ C3 and C4 **Rx** ■ NSAIDs	**Office W/U** ■ Anti-dsDNA or antichromatin antibodies; anti-RNP antibodies; anti-Smith antibodies; anti-SS-A antibodies; anti-SS-B antibodies; rheumatoid factor: ⊕ ■ Bone densitometry **Rx** ■ Prednisone ■ NSAIDs ■ Rheumatology consult ■ Nephrology consult ■ Chloroquine or hydroxychloroquine ■ Ophthalmology consult if using antimalarials (eg, chloroquine)	■ Follow up in 4 weeks with UA ■ Patient counseling ■ Alcohol abstinence counseling ■ Smoking cessation counseling ■ Sunblock

Final Dx: SLE

CASE 80

HX	PE	DDX
35 yo M with a history of hypertension presents with pain and swelling in his left knee for the last 3 days. He was recently started on HCTZ for his hypertension. He is sexually active only with his wife and denies any history of trauma or IV drug abuse.	VS: T 38°C (100.7°F), P 80, BP 130/60, RR 12 Gen: In pain Skin: WNL HEENT: WNL Lungs: WNL CV: WNL Abd: WNL Ext: Left knee is swollen, erythematous, and tender with limited range of motion and effusion	▪ Bacterial arthritis ▪ Gout ▪ Lyme disease ▪ Pseudogout ▪ Psoriatic arthritis ▪ Reiter arthritis

CASE 81

HX	PE	DDX
40 yo M with a history of diabetes mellitus presents with pain, swelling, and discoloration of his right leg for the last week. He denies any trauma.	VS: T 38°C (100.5°F), P 70, BP 120/60, RR 12 Gen: NAD Lungs: WNL CV: WNL Abd: WNL Ext: +2 edema in right lower extremity; warmth, erythematous discoloration of skin, 20-cm ulcer	▪ Calf tear or pull ▪ Cellulitis ▪ Deep venous thrombosis ▪ Lymphedema ▪ Osteomyelitis ▪ Popliteal (Baker) cyst ▪ Venous insufficiency

CASE 82

HX	PE	DDX
50 yo M with a history of hyperlipidemia started on simvastatin 1 year ago complains of a single episode of steady, diffuse, aching pain that affected his skeletal muscles and made it difficult for him to climb stairs. He states that he has never experienced anything like this before. No family history of any similar episodes.	VS: T 37°C (99°F), P 85, BP 127/85, RR 20, O_2 sat 94% room air HEENT and neck: No dysarthria, dysphagia, diplopia, or ptosis; exam WNL Chest: WNL CV: WNL Abd: WNL Ext: Proximal muscle weakness that is more obvious in lower limbs; no evidence of myotonia	▪ Inclusion body myositis ▪ Myopathy due to drugs/toxins (eg, statin-induced myopathy) ▪ Myotonic dystrophy ▪ Polymyositis ▪ Polymyalgia rheumatica

INITIAL MGMT	CONTINUING MGMT	F/U
Office W/U ▪ CBC: ↑ WBC count ▪ Chem 14 ▪ ESR: ↑ ▪ PT/PTT, INR ▪ X-ray—left knee ▪ Joint aspiration fluid analysis: Gram stain ⊖, culture ⊖, ⊖ birefringent and needle-shaped crystals, WBC 8,000 ▪ Urethral Gram stain: ⊖ **Rx** ▪ NSAIDs or corticosteroids ▪ Discontinue HCTZ and start losartan	**Ward W/U** ▪ Blood culture: ⊖ ▪ Urethral culture: ⊖ ▪ Lyme serology: ⊖ ▪ CBC: WBC is trending down **Rx** ▪ Continue NSAIDs and corticosteroids until patient improves ▪ Low-purine diet	▪ Follow up in 2 weeks in the clinic ▪ Uric acid ↑ ▪ Low-purine diet ▪ Start allopurinol or colchicine (to prevent an attack if serum uric acid > 12 or if the patient has tophaceous gout)

Final Dx: Gout

INITIAL MGMT	CONTINUING MGMT	F/U
ED W/U ▪ CBC: ↑ WBC count ▪ Chem 14 ▪ PT/PTT ▪ U/S—left lower extremity: ⊖ for deep venous thrombosis ▪ ESR ▪ X-ray ▪ Blood culture: Pending **Rx** ▪ IV ampicillin-sulbactam ▪ Surgical consult: Debridement of ulcers	**Ward W/U** ▪ Blood culture: ⊖ ▪ Blood glucose: Controlled on insulin regimen ▪ CBC: WBC downtrending **Rx** ▪ Leg elevation ▪ Switch to amoxicillin when patient is afebrile and symptoms improve (usually in 3–5 days) ▪ Discharge home	▪ Two weeks later his leg is back to normal ▪ Amoxicillin is discontinued after a course of 14 days

Final Dx: Cellulitis

INITIAL MGMT	CONTINUING MGMT	F/U
ED W/U ▪ IV fluids (NS) ▪ CBC ▪ BMP ▪ TSH ▪ Serum CPK: ↑ ▪ LDH: ↑ ▪ Vitamin D level ▪ EMG: Muscle injury ▪ UA: Myoglobinuria **Rx** ▪ Counsel patient re: medication side effects ▪ NSAIDs	**Ward W/U** ▪ CPK, LDH: ↑ ▪ UA: ⊕ for myoglobin **Rx** ▪ Discontinue simvastatin	▪ Follow up in 4 weeks ▪ Patient counseling ▪ Switch to alternative statin with less intrinsic muscle toxicity (pravastatin or fluvastatin)

Final Dx: statin-induced myopathy

CASE 83

HX	PE	DDX
21 yo F complains of hot, swollen, painful knee joints following an asymptomatic dermatitis that progressed from macules to vesicles and pustules. She admits to using IV drugs, binge drinking, and having sex with multiple partners. She states that about 3 weeks ago, during a trip to Mexico, she had dysuria, frequency, and urgency during her menses, followed a few days later by bilateral conjunctivitis.	VS: T 39°C (102°F), P 122, BP 138/82, RR 28, O_2 sat 96% room air HEENT and neck: WNL Chest: Four vesicles on thoracic skin CV: WNL Abd: Three vesicles and 1 pustule on abdominal skin Ext: Knee joints are hot, swollen, and tender; ↓ ROM due to severe pain	▪ *Chlamydia trachomatis* infection ▪ *Neisseria gonorrhoeae* infection ▪ Reactive arthritis ▪ *S aureus* infection ▪ *Streptococcus* infection

CASE 84

HX	PE	DDX
25-month-old M is brought to the ED because of sudden respiratory distress. His mother does not remember the boy's immunization, developmental, or nutritional history. She calmly states that her son fell from a sofa a few days ago, and that this accident explains the boy's reluctance to walk. She adds that her son has been exposed to sick children lately and that she has used coin rubbing and cupping as folk medicine practices.	VS: T 37°C (99°F), P 129, BP 82/59, RR 40, O_2 sat 89% room air Gen: Undernourished HEENT: Circumferential cord marks around neck Lungs: Clear; pain with exam CV: Tachycardia; I/VI systolic murmur Abd: Bruising over nipples Ext: Circumferential burns of both feet and ankles with a smooth, clear-cut border; light brown bruises; pain on palpation of right lower limb Neuro/psych: Withdrawn, apprehensive	▪ Accidental injury/trauma ▪ Deliberate criminal violence (home invasion) ▪ Nonaccidental trauma (child abuse)

INITIAL MGMT	CONTINUING MGMT	F/U
ED W/U ■ CBC: ↑ WBC count ■ GC culture assay: ⊕ ■ Blood culture: ⊖ ■ Arthrocentesis ■ Joint fluid analysis ■ Joint fluid culture: Pending ■ Throat culture: Pending ■ Anorectal culture: Pending ■ Urine β-hCG: ⊖ **Rx** ■ NSAIDs ■ Antibiotics: Azithromycin (for *C trachomatis*), penicillin (if susceptible), ceftriaxone (if not resistant), or fluoroquinolones (if not resistant)	**Ward W/U** ■ Joint fluid analysis and culture: 60,000 leukocytes/mL, ⊕ for *N gonorrhoeae* ■ Throat culture ■ Anorectal culture **Rx** ■ Azithromycin (for *C trachomatis*), penicillin (if susceptible), ceftriaxone (if not resistant), or fluoroquinolones (if not resistant) ■ Joint drainage and irrigation (if indicated) ■ Arthroscopy (if indicated)	■ Follow up in 1 week ■ Patient counseling ■ Counsel patient re: safe sex practices ■ Treat sexual partner ■ Counsel patient to cease illegal drug use ■ Counsel patient to cease alcohol abuse ■ Smoking cessation counseling ■ Rest at home

Final Dx: Septic arthritis secondary to *N gonorrhoeae* infection

INITIAL MGMT	CONTINUING MGMT	F/U
ED W/U ■ CBC ■ PT/PTT ■ Chem 7 ■ CXR: Posterior rib fractures ■ Skeletal survey: Posterior rib fractures; obliquely oriented callus formation in right femur ■ CT—head: Short-length skull fractures; small subdural hemorrhages ■ Ophthalmologic exam: Bilateral retinal hemorrhages **Rx** ■ Admission to hospital ■ IV fluids (NS) ■ Neurosurgery consult ■ Ventilator (if necessary)	**Ward W/U** ■ Mandatory reporting of suspected child abuse ■ Child Protective Services evaluation ■ Ventilator (if necessary) ■ IV fluids (NS)	■ Child Protective Services ■ Evaluation of children sharing the household with patient

Final Dx: Nonaccidental trauma (child abuse)

CASE 85

HX	PE	DDX
36 yo F complains of malaise, anorexia, unintended weight loss, and morning stiffness together with swollen and painful wrist, knee, and ankle joints for the last 2 years. Initially, she disregarded her symptoms, as they were insidious. However, over time they persisted and have worsened in severity. An acute disabling episode prompted her to visit the office.	VS: T 38°C (100°F), P 95, BP 132/86, RR 20, O_2 sat 95% room air HEENT and neck: Cervical lymphadenopathy Chest: WNL CV: WNL Ext: Symmetric wrist, knee, and ankle joint swelling with tenderness and warmth; subcutaneous nodules over both olecranon prominences; no ulnar deviation of fingers, boutonnière deformity, or swan-neck deformity; no evidence of carpal tunnel syndrome; knee valgus is observed	▪ Gout ▪ Lyme disease ▪ Osteoarthritis ▪ Paraneoplastic syndrome ▪ Rheumatoid arthritis ▪ Sarcoidosis

CASE 86

HX	PE	DDX
45 yo F bus driver comes to the clinic complaining of pain radiating down the leg that followed back pain. The pain is aggravated by coughing, sneezing, straining, or prolonged sitting.	VS: T 37°C (99°F), P 86, BP 128/86, RR 20, O_2 sat 93% room air Trunk: Lumbar spine mobility ↓ due to pain Ext: ⊕ straight leg raising (Lasègue) sign; ⊕ crossed straight leg sign Neuro: Weak plantar flexion of foot; loss of Achilles tendon reflex; no saddle anesthesia	▪ Cauda equina syndrome ▪ Compression fracture ▪ Diabetic amyotrophy ▪ Disc herniation ▪ Epidural abscess ▪ Sciatica ▪ Facet joint degenerative disease ▪ Neoplasm ▪ Spinal stenosis

INITIAL MGMT	CONTINUING MGMT	F/U
Office W/U ■ CBC: Hypochromic normocytic anemia, thrombocytosis ■ ESR: ↑ ■ X-ray—joints: Soft tissue swelling, juxta-articular demineralization, joint space narrowing, erosions in juxta-articular margin ■ RF: High titer **Rx** ■ Ibuprofen or celecoxib ■ Intraarticular triamcinolone (for acute disabling episodes)	**Office W/U** ■ RF: High titer ■ Joint fluid analysis: Abnormalities suggesting inflammation **Rx** ■ Hydroxychloroquine for mild disease ■ Methotrexate (if unresponsive to NSAIDs) ■ Etanercept (if unresponsive to methotrexate); place PPD; review vaccination history; check hepatitis titers	■ Follow up in 4 weeks ■ Patient counseling ■ Physical therapy ■ Occupational therapy ■ Rest at home ■ Exercise program ■ Splint extremity ■ Ophthalmologic consult if using hydroxychloroquine

Final Dx: Rheumatoid arthritis

INITIAL MGMT	CONTINUING MGMT	F/U
Office W/U ■ None initially **Rx** ■ Conservative treatment ■ Pain control (NSAIDs, may consider a short course of opioids for severe pain)	**Office W/U** ■ MRI—lumbar spine: Disc herniation at L5–S1 level (MRI is not routinely ordered for a disk herniation; it is ordered if conservative treatment fails) **Rx** ■ Conservative treatment ■ Orthopedic surgery consult (if conservative treatment fails)	■ Follow up in 2 weeks ■ Patient counseling ■ Rest at home ■ Physical therapy

Final Dx: Lumbosacral radiculopathy secondary to disc herniation

CHILD WITH FEVER

CASE 87

HX	PE	DDX
40-day-old M is brought to the ED because of irritability and lethargy, vomiting, and ↓ oral intake for the last 3 days. Today, his parents noted that he had a fever of 101.5°F, and he subsequently had a seizure. The baby's weight at delivery was 2500 grams, and he had previously been well.	VS: T 39°C (102°F), P 160, BP 77/50, RR 40, O_2 sat 92% room air Gen: Irritable Lungs: Clear CV: Tachycardia; I/VI systolic murmur Abd: WNL Neuro/psych: Bulging fontanelle, ↓ responsiveness	▪ CNS fungal infection (in immunocompromised patients) ▪ HIV infection (in immunocompromised patients) ▪ Meningitis (viral or bacterial) ▪ Osteomyelitis ▪ Pneumonia ▪ Sepsis ▪ UTI

CASE 88

HX	PE	DDX
4-month-old M is brought to the ED because of apneic episodes following a runny nose, cough, labored breathing, wheezing, and fever for the last 2 days. His asthmatic mother was diagnosed with rubella infection during her pregnancy. He was delivered prematurely at 28 weeks. He has a history of respiratory difficulty and tachycardia, and he has missed several of his health maintenance appointments.	VS: T 39°C (102°F), P 160, BP 77/50, RR 40, O_2 sat 88% room air Gen: Irritable Lungs: Tachypnea, intercostal retractions, nasal flaring, expiratory wheezing, bilateral crackles CV: Tachycardia; continuous II/VI murmur Abd: WNL Neuro/psych: Fontanelle is soft and flat; irritable	▪ Asthma ▪ CHF ▪ Cystic fibrosis ▪ Pneumonia ▪ RSV bronchiolitis

INITIAL MGMT	CONTINUING MGMT	F/U
ED W/U ■ CBC ■ Chem 7: Hyponatremia ■ Blood cultures ■ CXR ■ UA and urine culture ■ LP: Cell count, differential, bacterial culture, viral PCR pending ■ ABG: Metabolic acidosis **Rx** ■ Admission to hospital ■ Empiric IV antibiotics (ampicillin and cefotaxime) ■ IV fluid bolus ■ IV fluids with dextrose	**Ward W/U** ■ Serum glucose: 75 mg/dL ■ Urine culture: ⊖ ■ Blood culture: ⊕ for *S pneumoniae* ■ Ventilator (if necessary) **Rx** ■ IV fluids, ($D_{5½}NS$) ■ IV antibiotics × 10–14 days	■ Follow up in 48 hours of discharge from hospital ■ Family counseling

Final Dx: Bacterial meningitis

INITIAL MGMT	CONTINUING MGMT	F/U
ED W/U ■ CBC: WBC 14,000 ■ Blood culture ■ Chem 7 ■ CXR: Hyperinflation, bilateral patchy interstitial infiltrates, ↑ pulmonary blood flow, prominent left atrium and ventricle ■ UA and urine culture ■ ABG: Hypoxemia ■ RSV PCR: Pending **Rx** ■ Admission to the ICU ■ Empiric IV antibiotics ■ IV fluid bolus ■ Supplemental O_2 ■ Nebulized albuterol trial	**ICU W/U** ■ Serum glucose: 70 mg/dL ■ Urine culture: ⊖ ■ CXR: No change ■ Blood culture: ⊖ ■ RSV PCR ⊕ ■ Ventilator (if necessary) ■ Echocardiogram: Patent ductus arteriosus **Rx** ■ IV fluids ($D_{5½}NS$) ■ Supplemental O_2 ■ Nebulized albuterol (if effective) ■ Cardiology consult	■ Follow up in 48 hours of discharge from hospital ■ Family counseling

Final Dx: Bronchiolitis with patent ductus arteriosus (PDA)

CASE 89

HX	PE	DDX
8-month-old F is brought to the urgent care clinic because of abrupt onset of fever that lasted a couple of days with one seizure episode (the girl and her parents were camping in a remote area). The fever resolved after a rash appeared on the girl's chest and abdomen. Her parents did not notice any lethargy, poor feeding, or vomiting. She has no history of seizures.	VS: T 37°C (100°F); other vital signs WNL HEENT and neck: Bilateral cervical lymphadenopathy, ears WNL, ophthalmologic exam WNL Trunk: Macular rash Neuro: Alert and active; no abnormalities	▪ Fifth disease ▪ Measles ▪ Meningitis ▪ Roseola infantum ▪ Rubella

CASE 90

HX	PE	DDX
3-day-old M presents to the ED with ↑ temperature, lethargy, respiratory distress, and poor feeding for the past 24 hours. His Apgar scores at birth were 6 and 8. His mother had a prolonged rupture of membranes (30 hours).	VS: T 39°C (102°F), P 170, BP 74/51, RR 70, O_2 sat 90% room air Lungs: Grunting respiration, chest indrawing with breathing, ↓ air entry CV: No murmurs or rubs Abd: Distended; ⊖ BS Neuro: Lethargy	▪ *Bordetella* lung infection ▪ *Chlamydia* lung infection ▪ Complicated congenital lung abnormalities (eg, sequestration) ▪ Foreign body causing obstruction ▪ Group B streptococcus bacterial pneumonia

INITIAL MGMT	CONTINUING MGMT	F/U
Office W/U ■ CBC: WNL **Rx** ■ Oral hydration ■ Acetaminophen		■ Follow up in 7 days or as needed ■ Family counseling

Final Dx: Roseola infantum (exanthem subitum)

INITIAL MGMT	CONTINUING MGMT	F/U
ED W/U ■ CBC: ↑ WBC count ■ Random serum glucose: 60 mg/dL ■ CXR: Patchy infiltrates, pleural effusion, gastric dilation ■ Blood cultures: Pending ■ Viral culture ■ ABG: Po_2 50 mm Hg, Pco_2 55 mm Hg **Rx** ■ Supplemental O_2 ■ IV Fluids, $D_{5¼}NS$ ■ Empiric IV antibiotics ■ Respiratory and hemodynamic support (if necessary)	**Ward W/U** ■ Random serum glucose: 65 mg/dL ■ Blood cultures: ⊕ Group B streptococcus ■ ABG: Po_2 60 mm Hg, Pco_2 50 mm Hg **Rx** ■ Antibiotics ■ Ventilatory and hemodynamic support (if necessary) ■ Antiviral drugs (if appropriate) ■ Bronchoscopy (if indicated)	■ Follow up in 48 hours ■ Family counseling

Final Dx: Pneumonia secondary to group B streptococcal infection

FEVER

CASE 91

HX	PE	DDX
49 yo F presents to the ED with fever for the last 3 days. Since she turned 49 (about 7 months ago), she has had recurrent infections that have been treated with antibiotics. She has also been treated with anthracyclines and alkylating agents for another disease for the past 18 months. However, she has not seen a doctor lately. She works in a manufacturing plant that produces cosmetics.	VS: T 39°C (102°F), P 132, BP 108/77, RR 29, O_2 sat 88% room air Lungs: No evidence of consolidation CV: WNL Abd: WNL Ext: WNL Neuro: WNL	▪ Deep abscess (unknown location) ▪ Pneumonia ▪ Pyelonephritis ▪ Sepsis ▪ Severe infection (unknown location)

CASE 92

HX	PE	DDX
43 yo F with a history of diabetes mellitus and mitral valve prolapse with mitral regurgitation presents to the ED with fever, fatigue, malaise, and diffuse musculoskeletal pain for the past 2 days. She also complains of difficulty moving her right eye.	VS: T 40°C (104°F), P 134, BP 113/83, RR 31, O_2 sat 93% room air Ophthalmology: Visual field defects, conjunctival hemorrhage Funduscopy: Abnormal spots Lungs: WNL CV: Regurgitant murmur Abd: WNL Ext: Petechiae on feet Neuro: CN III palsy	▪ Complicated pyelonephritis ▪ Infectious process (undetermined location) ▪ Infective endocarditis ▪ Intracranial infection ▪ Sepsis

INITIAL MGMT	CONTINUING MGMT	F/U
ED W/U ▪ CT—abdomen: WNL ▪ CBC: Neutropenia ▪ CXR: Bilateral infiltrates in both lungs ▪ Sputum cultures: ⊕ for several bacterial species, including *Klebsiella* ▪ Blood cultures: ⊕ for *Klebsiella* ▪ UA: WNL ▪ Urine cultures: ⊖ **Rx** ▪ IV fluids (NS) ▪ IV antibiotics (empiric cefepime or fluoroquinolone) ▪ Acetaminophen	**Ward W/U** ▪ Bone marrow biopsy, needle: Low myelogenous progenitor cell lines ▪ CT—chest, spiral: Widespread bilateral infiltrates in both lungs **Rx** ▪ IV antibiotics (appropriate for *Klebsiella*); tailor antibiotics to sensitivities ▪ IV fluids (NS) ▪ G-CSF (for neutropenia)	▪ Follow up in 4 weeks ▪ Patient counseling ▪ Counsel patient to cease alcohol intake ▪ Smoking cessation ▪ Chest physical therapy

Final Dx: Multilobar pneumonia in a neutropenic patient

INITIAL MGMT	CONTINUING MGMT	F/U
ED W/U ▪ ESR: 59 mm/h ▪ CBC: ↑ WBC ▪ CXR: Some areas of patchy consolidation ▪ Blood cultures: Pending ▪ Echocardiography: Mobile mass attached to a valve ▪ ECG: RBBB ▪ UA: Microscopic hematuria **Rx** ▪ IV fluids (NS) ▪ Supplemental O_2 ▪ Empiric IV antibiotics (vancomycin, oxacillin/gentamicin) ▪ Acetaminophen	**Ward W/U** ▪ Blood cultures: ⊕ for viridans streptococci **Rx** ▪ IV antibiotics ▪ Acetaminophen ▪ IV fluids (NS)	▪ Follow up in 4 weeks ▪ Patient counseling ▪ Counsel patient to cease alcohol intake ▪ Smoking cessation

Final Dx: Infective endocarditis

CASE 93

HX	PE	DDX
60 yo M presents with fever and altered mental status 8 hours after undergoing a diverticular abscess drainage.	VS: T 39°C (102°F), P 110, BP 60/35, RR 22, O_2 sat 92% on 2-L NC Gen: Acute distress HEENT: WNL Lungs: WNL CV: Tachycardia Abd: Lower abdominal tenderness Neuro: WNL	▪ Alcohol withdrawal ▪ Cardiogenic shock ▪ Delirium ▪ Hypovolemic shock ▪ Septic shock

CASE 94

HX	PE	DDX
17 yo F G0 whose last menstrual period was 2 days ago presents with fever, vomiting, myalgia, and a generalized skin rash.	VS: T 39°C (102°F), BP 75/30, HR 120 Gen: NAD Skin: Diffuse macular erythema; hyperemic mucous membranes Lungs: WNL CV: WNL Pelvic: Menstrual flow; foul-smelling tampon Limited PE	▪ Meningococcemia ▪ Rocky Mountain spotted fever ▪ Streptococcal toxic shock syndrome ▪ Toxic shock syndrome ▪ Typhoid fever

INITIAL MGMT	CONTINUING MGMT	F/U
ED STAT ■ Supplemental O_2 ■ IV fluids (NS)/central line placement ■ Blood culture: Pending ■ Wound culture ■ UA and urine culture **ED W/U** ■ CBC: ↑ WBC count ■ Chem 14 ■ ABG: Metabolic acidosis ■ ECG ■ Serum amylase, lipase ■ Serum lactate: 6 ■ Cardiac enzymes ■ CXR ■ CT—abdomen: Persistent diverticular abscess **Rx** ■ Ampicillin-gentamicin-metronidazole or piperacillin-tazobactam or ticarcillin-clavulanate	**ICU W/U** ■ Urine output q 1 h ■ 2D echocardiography ■ Blood culture: ⊕ for *E coli* sensitive to gentamicin and ceftriaxone ■ Wound culture: ⊕ for *E coli* sensitive to gentamicin and ceftriaxone **Rx** ■ Tailor antibiotics to sensitivities ■ Surgery consult	

Final Dx: Septic shock

INITIAL MGMT	CONTINUING MGMT	F/U
ED STAT ■ Supplemental O_2 ■ IV fluids (NS) ■ Pelvic exam: Retained tampon identified and removed **ED W/U** ■ CBC with differential ■ Chem 14 ■ UA ■ Urine culture: Pending ■ Blood culture: Pending **Rx** ■ Admit to ICU ■ IV fluids (NS) ■ Vasopressors (if necessary) ■ Empiric IV clindamycin + vancomycin	**ICU W/U** ■ Blood culture: ⊖ ■ Urine culture: ⊖ **Rx** ■ Continue IV clindamycin and vancomycin ■ Wound care	

Final Dx: Toxic shock syndrome

OUTPATIENT POTPOURRI

CASE 95

HX	PE	DDX
50 yo F presents with a painless lump in her right breast. She first noted this lump 1 month ago. There is no nipple discharge.	VS: Afebrile, P 70, BP 110/50, RR 12 Gen: NAD Skin: WNL HEENT: WNL Lymph nodes: ⊖ Breast: 3-cm, hard, immobile, nontender mass with irregular borders; no nipple discharge Lungs: WNL CV: WNL Abd: WNL	▪ Breast cancer ▪ Fibroadenoma ▪ Fibrocystic disease ▪ Mastitis ▪ Papilloma

CASE 96

HX	PE	DDX
62 yo F complains of vaginal itching, painful intercourse, and a clear discharge.	VS: WNL Gen: NAD Lungs: WNL CV: WNL Pelvic: Vulvar erythema, thin and pale mucosa with areas of erythema, clear discharge, mucosa bleeds easily during exam	▪ Atrophic vaginitis ▪ Bacterial vaginosis ▪ Candidal vaginitis ▪ Cervicitis (chlamydia, gonorrhea) ▪ Trichomonal vaginitis

CASE 97

HX	PE	DDX
33 yo G1Po Rh-negative F at 36 weeks' gestation who currently lives in a battered-women's shelter calls the on-call physician because she noticed ↓ fetal movements. She states that fetal growth has been normal and that her obstetric ultrasound at 18 weeks showed a single normal fetus. The patient has no known preexisting diseases and denies smoking, drinking alcohol, or taking medications or illicit drugs. She received a dose of anti-D at 28 weeks.	VS: T 37°C (99°F), P 96, BP 141/91, RR 26, O_2 sat 93% room air Gen: No jaundice Eyes: Normal vision Lungs: No rales CV: No gallops or murmurs Pelvic: Fundal height in centimeters is appropriate for gestational age; cephalic presentation; speculum exam reveals unripe cervix, no ferning, nitrazine ⊖ Ext: Slight pedal edema	▪ Fetal death ▪ Fetal sleep ▪ Preeclampsia ▪ Pregnancy-induced hypertension

INITIAL MGMT	CONTINUING MGMT	F/U
Office W/U ■ Mammography: Suspicious of tumor ■ FNA biopsy: Malignancy **Rx** ■ Surgery consult for breast conservative therapy or mastectomy with axillary lymph node dissection		■ Regular follow up with annual mammogram (in cases of breast conservative therapy)

Final Dx: Breast cancer

INITIAL MGMT	CONTINUING MGMT	F/U
Office W/U ■ Vaginal pH: 6 ■ Chlamydia PCR ■ Gonorrhea PCR ■ Wet mount ■ Pap smear **Rx** ■ Vaginal jelly for lubrication ■ Counsel patient re: local HRT ■ Vaginal estrogen cream		■ Follow up as needed

Final Dx: Atrophic vaginitis

INITIAL MGMT	CONTINUING MGMT	F/U
Office W/U ■ BMP ■ Chem 14 ■ UA: ⊕ protein ■ Random serum glucose ■ Serum uric acid **Rx** ■ Monitor, continue BP cuff ■ Fetal monitoring	**Ward W/U** ■ UA: Protein 0.3 g/L/24 hrs; normal sediment ■ LFTs: WNL **Rx** ■ Monitor, continue BP cuff ■ Fetal monitoring	■ Patient counseling ■ Obstetric consult

Final Dx: Pregnancy-induced hypertension

CASE 98

HX	PE	DDX
30 yo F presents for her regular checkup. She denies any complaints but is concerned about her BP, as it has been high on both of her previous visits over the past 2 months.	VS: P 75, BP 160/90 (no difference in BP between both arms), RR 12 Gen: WNL HEENT: WNL Breast: WNL Lungs: WNL CV: WNL Abd: WNL Pelvic: WNL Ext: WNL Neuro: WNL	▪ Cushing disease ▪ Essential hypertension ▪ Hyperaldosteronism ▪ Hyperthyroidism ▪ Renal artery stenosis ▪ White coat hypertension

CASE 99

HX	PE	DDX
6 yo M is brought by his mother with continuous oozing of blood from the site of a tooth extraction he underwent 2 days ago. The bleeding initially stopped but restarted spontaneously a few hours later. His mother denies any history of epistaxis, easy bruising, petechiae, or bleeding per rectum. The patient's mother has a brother with hemophilia.	VS: Afebrile, P 80, BP 80/50, RR 14 Gen: NAD Skin: WNL HEENT: Blood oozing from site of extracted tooth Lungs: WNL CV: WNL Abd: WNL Ext: WNL	▪ DIC ▪ Hemophilia ▪ ITP ▪ Liver disease ▪ TTP ▪ Vitamin K deficiency ▪ von Willebrand disease

CASE 100

HX	PE	DDX
27 yo F complains of pain during intercourse. She has a long history of painful periods.	VS: WNL Gen: NAD Lungs: WNL CV: WNL Pelvic: Normal vaginal walls, normal cervix, mild cervical motion tenderness; uterus tender, retroverted, and fixed; right adnexa slightly enlarged and tender	▪ Endometriosis ▪ Pelvic inflammatory disease ▪ Vaginismus ▪ Vaginitis

INITIAL MGMT	CONTINUING MGMT	F/U
Office W/U ■ Lipid profile ■ Chem 14 ■ CBC ■ UA: +1 protein ■ ECG: LVH ■ Echocardiography: LVH ■ TSH **Rx** ■ ACE inhibitor (eg, lisinopril) ■ Exercise program ■ Low-sodium diet	**Office W/U** ■ Consider workup for secondary hypertension given the patient's young age (MRI/MRA renal arteries, urine catecholamines, urine cortisol)	■ Follow up in 1 month

Final Dx: Essential hypertension

INITIAL MGMT	CONTINUING MGMT	F/U
Office W/U ■ CBC ■ Peripheral smear ■ Bleeding time ■ PTT: Prolonged ■ PT, INR ■ Plasma factor VIII: 3% ■ Plasma factor IX **Rx** ■ Factor VIII therapy ■ Genetics consult ■ Counsel parents		■ Console and reassure patient ■ Patient counseling ■ Family counseling

Final Dx: Hemophilia (factor VIII deficiency)

INITIAL MGMT	CONTINUING MGMT	F/U
Office W/U ■ Wet mount ■ Chlamydia DNA probe ■ Gonorrhea DNA probe ■ U/S—pelvis: Retroverted uterus of normal size; 2- × 3-cm cyst on right adnexa that may represent a hemorrhagic corpus luteum or endometrioma **Rx** ■ NSAIDs ■ OCPs		■ If initial treatment with OCPs and NSAIDs does not relieve pain, refer to a gynecologist for a trial of GnRH analogs, progestins, or danazol. ■ Follow up as needed

Final Dx: Endometriosis

NOTES

APPENDIX

ACRONYMS AND ABBREVIATIONS

Abbreviation	Meaning
A-a	alveolar-arterial (oxygen gradient)
AAA	abdominal aortic aneurysm
ABC	airway, breathing, circulation
Abd	abdominal
ABG	arterial blood gas
ACA	anterior cerebral artery
ACE	angiotensin-converting enzyme
ACEI	angiotensin-converting enzyme inhibitor
ACh	acetylcholine
ACL	anterior cruciate ligament
ACLS	advanced cardiac life support (protocol)
ACM	Advanced Clinical Medicine
ACTH	adrenocorticotropic hormone
ADA	American Diabetes Association
ADH	antidiuretic hormone
ADHD	attention-deficit/hyperactivity disorder
AF	atrial fibrillation
AFB	acid-fast bacillus
AFI	amniotic fluid index
AFP	α-fetoprotein
AG	anion gap
AHI	apnea-hypopnea index
AICD	automatic implantable cardiac defibrillator
AIDS	acquired immunodeficiency syndrome
AKI	acute kidney injury
ALL	acute lymphocytic leukemia
ALS	amyotrophic lateral sclerosis
ALT	alanine aminotransferase
AMA	antimitochondrial antibody
AML	acute myelogenous leukemia
ANA	antinuclear antibody
ANC	absolute neutrophil count
ANCA	antineutrophil cytoplasmic antibody
AP	anteroposterior
APC	activated protein C
APL	acute promyelocytic leukemia
ARB	angiotensin receptor blocker
ARDS	acute respiratory distress syndrome
ARR	absolute risk reduction
ART	antiretroviral therapy
5-ASA	5-aminosalicylic acid
ASCA	anti–*Saccharomyces cerevisiae* antibody
ASCVD	atherosclerotic cardiovascular disease
ASD	atrial septal defect

Abbreviation	Meaning
ASMA	anti–smooth muscle antibody
AST	aspartate aminotransferase
ATN	acute tubular necrosis
ATRA	*all*-transretinoic acid
AV	arteriovenous, atrioventricular
AVM	arteriovenous malformation
AVNRT	atrioventricular nodal reentrant tachycardia
AXR	abdominal x-ray
AZT	zidovudine
BB	β-blocker
BCG	bacille Calmette-Guérin
BiPAP	bilateral positive airway pressure
BMI	body mass index
BMP	basic metabolic panel
BMT	bone marrow transplantation
BP	blood pressure
BPH	benign prostatic hyperplasia
BPP	biophysical profile
BS	bowel sounds
BSA	body surface area
BSO	bilateral salpingo-oophorectomy
BUN	blood urea nitrogen
CABG	coronary artery bypass graft
CAD	coronary artery disease
CAH	congenital adrenal hyperplasia
CBC	complete blood count
CBT	cognitive-behavioral therapy
CCB	calcium channel blocker
CCP	cyclic citrullinated peptide
CCS	Computer-based Case Simulations
CD	cluster of differentiation
CEA	carcinoembryonic antigen
CF	cystic fibrosis
CGD	chronic granulomatous disease
CH50	total hemolytic complement
Chem #	chemistry panels
CI	confidence interval
CIN	Candidate Identification Number, cervical intraepithelial neoplasia
CK	creatine kinase
CKD	chronic kidney disease
CK–MB	creatine kinase–MB fraction
CLL	chronic lymphocytic leukemia
CML	chronic myelogenous leukemia

Abbreviation	Meaning
CMV	cytomegalovirus
CN	cranial nerve
CNS	central nervous system
COBI	cobicistat
COMT	catechol-O-methyltransferase
COPD	chronic obstructive pulmonary disease
CPAP	continuous positive airway pressure
CPK-MB	creatine kinase-muscle/brain
CPR	cardiopulmonary resuscitation
CrCl	creatinine clearance
CRP	C-reactive protein
CRT	cardiac resynchronization therapy
CSA	central sleep apnea
CSF	cerebrospinal fluid
CST	contraction stress test
CT	computed tomography
CV	cardiovascular
CVA	costovertebral angle
CVID	common variable immunodeficiency
CXR	chest x-ray
D&C	dilation and curettage
DBP	diastolic blood pressure
DCIS	ductal carcinoma in situ
DDAVP	desmopressin acetate
ddI	didanosine
DDX	differential diagnosis
DES	diethylstilbestrol
DEXA	dual-energy x-ray absorptiometry
DFA	direct fluorescent antibody
DHEA	dehydroepiandrosterone
DI	diabetes insipidus
DIC	disseminated intravascular coagulation
DIP	distal interphalangeal (joint)
DKA	diabetic ketoacidosis
DLCO	diffusing capacity of carbon monoxide
DM	diabetes mellitus
DMARD	disease-modifying antirheumatic drug
DNA	deoxyribonucleic acid
DNR	do not resuscitate
DPoA	durable power of attorney
DPP	dipeptidyl peptidase
DRE	digital rectal examination
dsDNA	double-stranded DNA
DSM-5	*Diagnostic and Statistical Manual of Mental Disorders*, Fifth Edition
DTG	dolutegravir
DTRs	deep tendon reflexes
DTs	delirium tremens
DVT	deep venous thrombosis
Dx	diagnosis
EBV	Epstein-Barr virus
ECFMG	Educational Commission for Foreign Medical Graduates
ECG	electrocardiography
ECMO	extracorporeal membrane oxygenation
ECT	electroconvulsive therapy
ED	emergency department, erectile dysfunction
EEG	electroencephalography
EF	ejection fraction
EGD	esophagogastroduodenoscopy
EHEC	enterohemorrhagic *E coli*
ELISA	enzyme-linked immunosorbent assay
EM	erythema multiforme
ENT	ear, nose, and throat
EPS	extrapyramidal symptoms
ER	estrogen receptor
ERCP	endoscopic retrograde cholangiopancreatography
ESR	erythrocyte sedimentation rate
ESWL	extracorporeal shock-wave lithotripsy
EtOH	ethanol
EUS	endoscopic ultrasound
EVG	elvitegravir
Ext	extremities
FAP	familial adenomatous polyposis
FAST	focused abdominal sonography for trauma
Fe_{Na}	fractional excretion of sodium
Fe_{urea}	fractional excretion of urea
FEV_1	forced expiratory volume in one second
FFP	fresh frozen plasma
FIP	Foundations of Independent Practice
FISH	fluorescence in situ hybridization
FNA	fine-needle aspiration
FOBT	fecal occult blood test
FSH	follicle-stimulating hormone
FSMB	Federation of State Medical Boards
FT_4	free thyroxine
FTA-ABS	fluorescent treponemal antibody absorption
FTC	emtricitabine
FTT	failure to thrive
5-FU	5-fluorouracil
F/U	follow up
FVC	forced vital capacity
FWS	fever without a source
G&C	gonorrhea and chlamydia (culture)
G6PD	gluciose-6-phosphate dehydrogenase
GA	gestational age
GAD	generalized anxiety disorder
GBM	glomerular basement membrane
GBS	group B *Streptococcus*, Guillain-Barré syndrome
GCS	Glasgow Coma Scale
G-CSF	granulocyte colony-stimulating factor
GDPP	gonadotropin-dependent precocious puberty
GERD	gastroesophageal reflux disease
GFR	glomerular filtration rate
GGT	gamma-glutamyl transferase
GI	gastrointestinal
GIPP	gonadotropin-independent precocious puberty

Abbreviation	Meaning
GLP	glucagon-like peptide
GNR	gram-negative rod
GnRH	gonadotropin-releasing hormone
GTCS	generalized tonic-clonic seizure
GTD	gestational trophoblastic disease
GU	genitourinary
H&P	history and physical
HAV	hepatitis A virus
HbA_{1c}	gylcated hemoglobin
HbH	hemoglobin H
HBcAb	hepatitis B core antibody
HBeAg	hepatitis B early antigen
HBIG	hepatitis B immune globulin
HBsAb	hepatitis B surface antibody
HBsAg	hepatitis B surface antigen
HBV	hepatitis B virus
HCC	hepatocellular cancer
hCG	human chorionic gonadotropin
HCTZ	hydrochlorothiazide
HCV	hepatitis C virus
HD	Huntington disease
HDL	high-density lipoprotein
HDV	hepatitis D virus
HEENT	head, eyes, ears, nose, and throat
HEV	hepatitis E virus
HF	heart failure
HFpEF	heart failure with preserved ejection fraction
HGSIL	high-grade squamous intraepithelial lesion
HHS	hyperglycemic hyperosmolar state
HHV	human herpesvirus
5-HIAA	5-hydroxyindoleacetic acid
HIDA	hepato-iminodiacetic acid (scan)
HIPAA	Health Insurance Portability and Accountability Act
HIT	heparin-induced thrombocytopenia
HIV	human immunodeficiency virus
HLA	human leukocyte antigen
HMG-CoA	hydroxymethylglutaryl coenzyme A
HNPCC	hereditary nonpolyposis colorectal cancer
HPA	hypothalamic-pituitary-adrenal (axis)
hpf	high-power field
HPV	human papillomavirus
HR	heart rate
HRIG	human rabies immune globulin
HRT	hormone replacement therapy
HSP	Henoch-Schönlein purpura
HSV	herpes simplex virus
5-HT	5-hydroxytryptamine
HTLV	human T-cell lymphotropic virus
HUS	hemolytic-uremic syndrome
HVA	homovanillic acid
IBD	inflammatory bowel disease
IBS	irritable bowel syndrome
ICH	intracerebral hemorrhage
ICP	intracranial pressure
ICU	intensive care unit
IE	infective endocarditis
Ig	immunoglobulin
IM	intramuscular
IMG	international medical graduate
INH	isoniazid
INR	International Normalized Ratio
INSTI	integrase strand transfer inhibitor
IPT	interpersonal psychotherapy
ITP	idiopathic thrombocytopenic purpura
IUD	intrauterine device
IUGR	intrauterine growth restriction
IV	intravenous
IVC	inferior vena cava
IVIG	intravenous immunoglobulin
IVP	intravenous pyelography
IVS	interventricular septum
JIA	juvenile idiopathic arthritis
JVD	jugular venous distention
JVP	jugular venous pressure
K	potassium
KOH	potassium hydroxide
KUB	kidney, ureter, bladder (study)
LAD	left anterior descending (artery)
LBBB	left bundle branch block
LBP	low back pain
LCIS	lobular carcinoma in situ
LDH	lactate dehydrogenase
LDL	low-density lipoprotein
LEEP	loop electrosurgical excision procedure
LES	lower esophageal sphincter
LFT	liver function test
LGSIL	low-grade squamous intraepithelial lesion
LH	luteinizing hormone
LKMA	liver/kidney microsomal antibody
LLQ	left lower quadrant
LMN	lower motor neuron
LMP	last menstrual period
LMWH	low-molecular-weight heparin
LP	lumbar puncture
LTBI	latent tuberculosis infection
LUQ	left upper quadrant
LV	left ventricle
LVEF	left ventricular ejection fraction
LVH	left ventricular hypertrophy
MAC	*Mycobacterium avium* complex
MAOI	monoamine oxidase inhibitor
MAT	multifocal atrial tachycardia
MCA	middle cerebral artery
MCHC	mean corpuscular hemoglobin concentration
MCI	mild cognitive impairment
MCP	metacarpophalangeal (joint)
MCV	mean corpuscular volume
MDD	major depressive disorder
MDI	metered-dose inhaler, multiple daily injection

Abbreviation	Meaning
MDR	multidrug-resistant
MDRD	Modification of Diet in Renal Disease (equation)
MEN	multiple endocrine neoplasia
MGUS	monoclonal gammopathy of undetermined significance
MHA-TP	microhemagglutination assay for *Treponema pallidum*
MI	myocardial infarction
MIBG	^{131}I-metaiodobenzylguanidine (scan)
MLF	medial longitudinal fasciculus
MMA	methylmalonic acid
MMR	measles, mumps, rubella (vaccine)
MoM	multiple of the mean
MPGN	membranoproliferative glomerulonephritis
MRA	magnetic resonance angiography
MRI	magnetic resonance imaging
MRSA	methicillin-resistant S *aureus*
MS	multiple sclerosis
MSAFP	maternal serum α-fetoprotein
MTP	metatarsophalangeal (joint)
MuSK	muscle-specific kinase
MVA	motor vehicle accident
NAD	no acute distress
NBME	National Board of Medical Examiners
NBT	E nonbacterial thrombotic endocarditis
NCS	nerve conduction study
NE	norepinephrine
NEC	necrotizing enterocolitis
Neuro	neurological
NG	nasogastric
NK	natural killer (cells)
NMDA	*N*-methyl-d-aspartate
NNRTI	non-nucleoside reverse transcriptase inhibitor
NNT	number needed to treat
NPH	neutral protamine Hagedorn (insulin)
NPO	nil per os (nothing by mouth)
NPV	negative predictive value
NRTI	nucleoside reverse transcriptase inhibitor
NS	normal saline
NSAID	nonsteroidal anti-inflammatory drug
NSCLC	non–small cell lung cancer
NST	nonstress test
NSTEMI	non-ST-segment-elevation MI
NTD	neural tube defect
O_2	oxygen
O&P	ova and parasites
OA	osteoarthritis
OCD	obsessive-compulsive disorder
OCP	oral contraceptive pill
17-OHP	17-hydroxyprogesterone
OR	odds ratio, operating room
OSA	obstructive sleep apnea
OTC	over the counter
P	pulse
PA	posteroanterior
PAC	plasma aldosterone concentration, premature atrial contraction
PAN	polyarteritis nodosa
p-ANCA	perinuclear antineutrophil cytoplasmic antibody
Pao_2	partial pressure of oxygen in arterial blood
$Paco_2$	partial pressure of carbon dioxide in arterial blood
PAPP-A	pregnancy-associated plasma protein A
PCA	posterior cerebral artery
PCL	posterior cruciate ligament
Pco_2	partial pressure of carbon dioxide
PCOS	polycystic ovarian syndrome
PCP	phencyclidine hydrochloride, *Pneumocystis carinii* (now *jiroveci*) pneumonia
PCr	plasma creatinine
PCR	polymerase chain reaction
PCV	polycythemia vera
PCWP	pulmonary capillary wedge pressure
PD	Parkinson disease
PDA	patent ductus arteriosus, posterior descending artery
PDE-5a	phosphodiesterase type 5a
PE	physical examination, pulmonary embolism
PEA	pulseless electrical activity
PEEP	positive end-expiratory pressure
PEG	polyethylene glycol
PET	positron emission tomography (scan)
PF	platelet factor
PFT	pulmonary function test
$PGF_{2\alpha}$	prostaglandin F2-α
PI	protease inhibitor
PID	pelvic inflammatory disease
PIP	proximal interphalangeal (joint)
PIV	parainfluenza virus
PMI	point of maximal impulse
PMN	polymorphonuclear (leukocyte)
PMR	polymyalgia rheumatica
PNa	plasma sodium
PNH	paroxysmal nocturnal hemoglobinuria
PNS	peripheral nervous system
PO	per os (by mouth)
POC	product of conception
Posm	plasma osmolarity
PPD	purified protein derivative (of tuberculin)
PPI	proton pump inhibitor
PPROM	preterm premature rupture of membranes
PPV	positive predictive value
PR	progesterone receptor
PRA	plasma renin activity
PRN	pro re nata (as needed)
PROM	premature rupture of membranes
PSA	prostate-specific antigen
PSGN	poststreptococcal glomerulonephritis

Abbreviation	Meaning
PT	prothrombin time
PTH	parathyroid hormone
PTHrP	parathyroid hormone–related peptide
PTSD	posttraumatic stress disorder
PTT	partial thromboplastin time
PTU	propylthiouracil
PUD	peptic ulcer disease
PUVA	psoralen and ultraviolet A
PVC	premature ventricular contraction
PVS	persistent vegetative state
RA	rheumatoid arthritis
RAA	renin-angiotensin-aldosterone (system)
RAI	radioactive iodine
RAIU	radioactive iodine uptake
RAL	raltegravir
RAST	radioallergosorbent testing
RBBB	right bundle branch block
RBC	red blood cell
RC	reticulocyte count
RCA	right coronary artery
RCT	randomized controlled trial
RDS	respiratory distress syndrome
RDW	red cell distribution width
REM	rapid eye movement
RF	rheumatoid factor
RLQ	right lower quadrant
ROM	rupture of membranes
RPR	rapid plasma reagin
RR	relative risk, respiratory rate
RRR	regular rate and rhythm, relative risk reduction
RSV	respiratory syncytial virus
RTA	renal tubular acidosis
RUQ	right upper quadrant
RV	residual volume, right ventricle
RVH	right ventricular hypertrophy
SA	sinoatrial
SAAG	serum-ascites albumin gradient
SAB	spontaneous abortion
SAD	seasonal affective disorder
SAH	subarachnoid hemorrhage
SBFT	small bowel follow-through
SBI	serious bacterial infection
SBP	spontaneous bacterial peritonitis, systolic blood pressure
SCID	severe combined immunodeficiency
SCLC	small cell lung cancer
SERM	selective estrogen receptor modulator
SES	socioeconomic status
SIADH	syndrome of inappropriate secretion of antidiuretic hormone
SIDS	sudden infant death syndrome
SIFE	serum immunofixation electrophoresis
SIRS	systemic inflammatory response syndrome
SLE	systemic lupus erythematosus
SMA	superior mesenteric artery
SNRI	serotonin-norepinephrine reuptake inhibitor
SPEP	serum protein electrophoresis
SPN	solitary pulmonary nodule
SQ	subcutaneous
SSRI	selective serotonin reuptake inhibitor
STD	sexually transmitted disease
STEMI	ST-segment-elevation MI
SVO_2	mixed venous oxygen saturation
SVR	systemic vascular resistance
SVT	supraventricular tachycardia
T_3	triiodothyronine
T_4	thyroxine
TAH	total abdominal hysterectomy
TB	tuberculosis
3TC	lamivudine
Tc	technetium
TCA	tricyclic antidepressant
Td	tetanus and diphtheria toxoid
TdT	terminal deoxynucleotidyl transferase
TEE	transesophageal echocardiography
TENS	transcutaneous electrical nerve stimulation
TGA	transposition of the great arteries
TIA	transient ischemic attack
TIBC	total iron-binding capacity
TIG	tetanus immune globulin
TIPS	transjugular intrahepatic portosystemic shunt
TLC	total lung capacity
TMP-SMX	trimethoprim-sulfamethoxazole
TNF	tumor necrosis factor
TNV	tenofovir
tPA	tissue plasminogen activator
TPN	total parenteral nutrition
TPO	thyroperoxidase
TRALI	transfusion-related acute lung injury
TSH	thyroid-stimulating hormone
TSS	toxic shock syndrome
TSS-T	toxic shock syndrome toxin
TTE	transthoracic echocardiography
TTP	thrombotic thrombocytopenic purpura
TURP	transurethral resection of the prostate
Tx	treatment
UA	urinalysis
U_{Cr}	urine creatinine
UIFE	urine immunofixation electrophoresis
UMN	upper motor neuron
U_{Na}	urine sodium
U_{osm}	urine osmolarity
UPEP	urine protein electrophoresis
URI	upper respiratory tract infection
U/S	ultrasound
USMLE	United States Medical Licensing Examination
USPSTF	United States Preventive Services Task Force
UTI	urinary tract infection

Abbreviation	Meaning
UTOX	urine toxicology screen
UV	ultraviolet
VCUG	voiding cystourethrography
VDRL	Venereal Disease Research Laboratory
VF	ventricular fibrillation
VIP	vasoactive intestinal peptide
VMA	vanillylmandelic acid
V/Q	ventilation-perfusion (ratio)
VRE	vancomycin-resistant enterococcus
VS	vital signs
VSD	ventricular septal defect
VT	ventricular tachycardia
VTE	venous thromboembolism
vWD	von Willebrand disease
vWF	von Willebrand factor
VZV	varicella-zoster virus
WBC	white blood cell
WD/WN	well developed, well nourished
WNL	within normal limits
W/U	workup

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About the Authors

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Tao developed a passion for medical education as a medical student. He currently edits more than 15 titles in the *First Aid* series. In addition, he is founder and chief education officer of USMLE-Rx for exam preparation and ScholarRx for undergraduate medical education. As a medical student, he was editor-in-chief of the University of California, San Francisco (UCSF) *Synapse*, a university newspaper with a weekly circulation of 9000. Tao earned his medical degree from UCSF in 1996 and completed his residency training in internal medicine at Yale University and fellowship training at Johns Hopkins University. Tao subsequently went on to cofound Medsn, a medical education technology venture, and served as its chief medical officer. He is currently chief of adult allergy and immunology at the University of Louisville.

Kachiu Cecilia Lee, MD, MPH

Kachiu received her medical degree and master's degree in public health from Northwestern University and then served as chief resident in her dermatology residency at Brown University. While at Brown, she received the Haffenreffer House Staff Excellence Award, presented yearly to the top five residents/fellows from all training programs. After completing her residency, she completed fellowship training in laser surgery at Massachusetts General Hospital's Wellman Center for Photomedicine (Harvard Medical School). Kachiu currently works as an Assistant Professor of Dermatology in the Department of Dermatology at Brown University. She has contributed to several projects in the *First Aid* series, including the *USMLE-Rx* test bank, *First Aid for the USMLE Step 1*, and *First Aid for the USMLE Step 2 CS*. In her leisure time, she enjoys photography, playing piano, and exploring New England with her husband and children.

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Marina was born in Cairo, Egypt, and has since lived all over the world. She graduated from Penn State College of Medicine in 2016. She is currently testing the limits of her program director's patience working at the Vidant Medical Center in Greenville, North Carolina as a third-year and chief resident in the East Carolina University–Brody School of Medicine Emergency Medicine Residency program. Her passions include critical care, microbiology, and academic medicine. She has contributed to *First Aid for the USMLE Step 1* and other projects in the *First Aid* series. In her free time, Marina enjoys being overly competitive at board games and finding new ways to drive her (very supportive) husband crazy.

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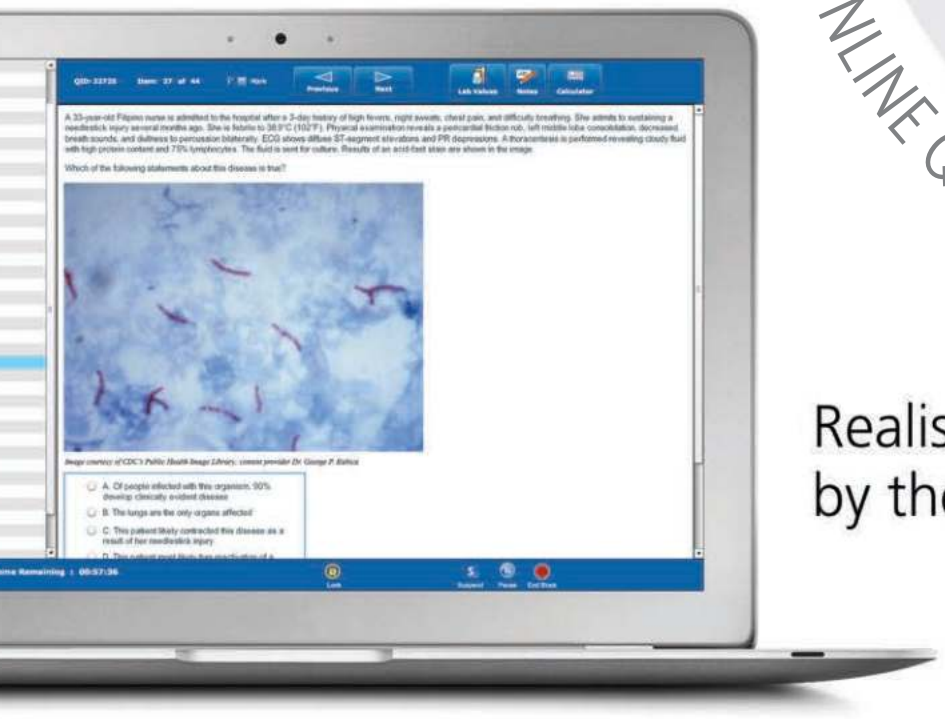

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