STEP-UP to USMLE STEP 2 CK

5TH EDITION

- Focus on what you need to know with a SUCCINCT OUTLINE FORMAT
- Identify key facts with nearly 500 QUICK HITS and MNEMONICS
- BOARD-STYLE QUESTIONS with accurate and insightful explanations

Latha Ganti
David Lebowitz
Javier Rosario
Ariel Vera

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Step-Up SERIES

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5TH EDITION

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Prepress Vendor: Aptara, Inc.

Fifth Edition

9 8 7 6 5 4 3 2 1

Printed in China

978-1-975106-28-7
Library of Congress Cataloging-in-Publication Data
available upon request

shop.lww.com

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PREFACE

In this fifth edition of *Step-Up to Step 2 CK*, we are delighted to bring you high-yield material for one of the most important examinations of your medical education. The Step 2 CK examination is geared mainly at testing your primary care medical knowledge. The authors of this book are all experts of primary care and emergency medicine, the most frequently tested topics on this examination.

We clearly recall the days of endless studying, needing to purchase multiple review books and question banks or question books. What if you had access to a book that could give you both a high-yield review and access to a series of test relevant questions? We wanted to give you that book!

The authors worked together to produce the most high-yield content that you may encounter during your examination. Our main goal was to provide medical students with the core content necessary to not only pass a medical board examination, but to improve patient care. A second goal was to make this as painless as possible for the reader with short and precise content. Each chapter was carefully reviewed several times to provide the most up-to-date and relevant content. For easier reading we worked hard to maintain the same chapter structure throughout the book, but we relish the fact that each chapter has its own expertise and voice. This makes it easy for the reader to pick up the book and read cover to cover, or simply pick up any chapter and read it independently.

Knowing that many students love questions and answers to test themselves, we have added full-length USMLE style questions at the end of each chapter. We encourage you to go through each and every single one of the high-yield knowledge questions. You can choose to answer these questions in test style or Q&A style or as it best meets your needs.

We welcome and encourage your comments, suggestions, and criticism. The authors and editors have gone through great effort to verify these topics, questions, and answers. Please make us aware of any errors that you find. We hope to make continuous improvements to this book and would greatly appreciate any input to make it truly exceptional. You can reach us at StepUpStep2CK@gmail.com

Keep learning! We wish you luck on your exam and future endeavors!

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1
Cardiovascular Disorders

I. Rapid Review

A. Cardiac Output (CO)

1. Heart rate (HR)
   a. Number of cardiac contractions per unit time; expressed as beats per minute (bpm)
2. **Stroke volume (SV)**
   a. SV is the **change in blood volume from immediately before initiation of contraction to completion of contraction** (i.e., SV = end-diastolic volume to end-systolic volume).
   b. It is determined by **contractility** (i.e., SV = [end-diastolic volume] − [end-systolic volume]), **preload** (amount of myocardial stretch at end of diastole), and **afterload** (resistance ventricles must overcome to empty their contents).
   c. **SV increases** with catecholamine release, an increase in intracellular Ca, a **decrease** in extracellular Na, digoxin use, anxiety, pregnancy, and exercise.
   d. **SV decreases** with β-blockers, heart failure (HF), acidosis, and hypoxia.
3. **Fick principle:** $CO = SV \times HR = \frac{(\text{rate of } O_2 \text{ use})}{(\textit{arterial } O_2 \text{ content}) - (\textit{venous } O_2 \text{ content})}$
   a. Rate of O_2 use can be determined by comparing O_2 content in expired air to that in inhaled air; arterial and venous O_2 content can be measured directly from the corresponding vasculature.
   b. CO increases during exercise, initially by increasing SV and later by increasing HR.
4. **Mean arterial pressure** (MAP) = CO × total peripheral resistance (TPR) = diastolic arterial pressure + 1/3 pulse pressure
5. **Pulse pressure** = systolic arterial pressure − diastolic arterial pressure

Quick HIT

In 70% of patients, the posterior descending artery (PDA) derives from the right coronary artery. In 10%, the PDA derives from the circumflex, and in 20%, the PDA derives from an anastomosis of the right coronary and the circumflex.

B. Cardiac and Coronary Anatomy (See Figures 1-1 and 1-2)

C. Electrocardiogram (ECG) (See Figure 1-3)

1. Measures flow of electrical impulses through the heart to provide information regarding **cardiac function**
2. Reviewing an ECG (a consistent order of analysis is useful for picking up abnormalities)
   a. Check calibration on tracing
   b. Rhythm (regular vs. irregular)
      (1) A regular rhythm is seen as a P wave followed by a QRS on every beat. This indicates the impulse originates from the sinus node.
      (2) An irregular rhythm shows absence of clear P waves and an irregular beat pattern.
   c. HR (normal or tachycardia vs. bradycardia)
      (1) Normal adult **HR is 60 to 100 bpm**
      (2) HR <**60 bpm is bradycardia**
      (3) HR >**100 bpm is tachycardia**

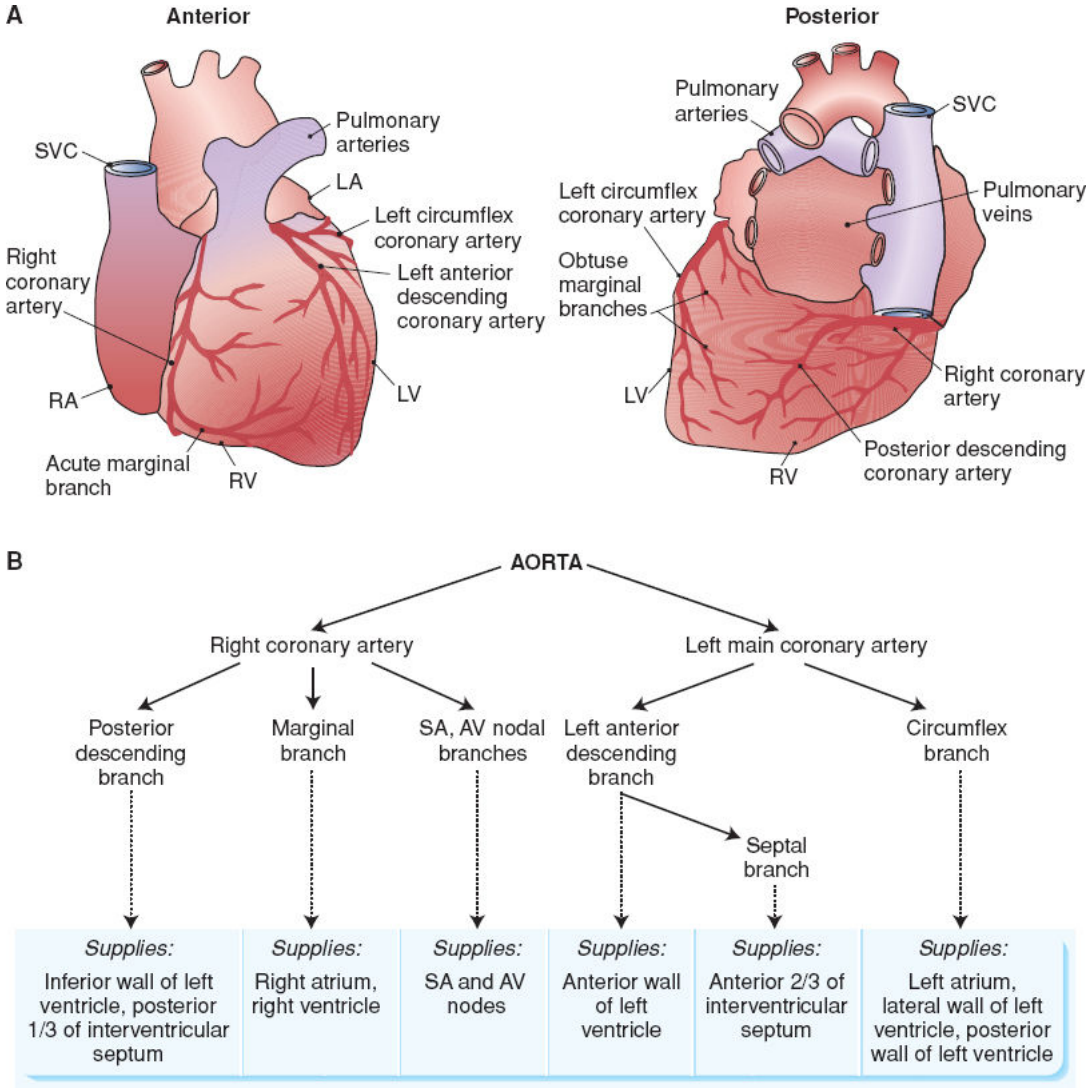


FIGURE 1-1
Coronary artery anatomy.
A: Anterior and posterior views of the heart. **B:** Coronary artery hierarchy and regions of the heart supplied by branches. AV, atrioventricular; LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle; SA, sinoatrial; SVC, superior vena cava.
(Modified from Lilly, L. S. [2011]. *Pathophysiology of Heart Disease* [5th ed.]. Baltimore, MD: Lippincott Williams & Wilkins, with permission.)

d. Intervals (PR, QRS, QT)
(1) PR interval is **normal at 0.12 to 0.20 seconds. A short PR (<0.12 seconds)** could represent fast conduction system. **A prolonged PR (>0.2 seconds)** may represent an AV block
(2) QRS interval is **normal at 0.8 to 0.12 seconds.** A longer QRS may represent a bundle branch block or ventricular conduction delay
(3) QT (or QTc when corrected for extremes in HR) interval is **normal at <0.44 seconds.** A **prolonged QT (>0.44 seconds)** reflects hypokalemia, hypocalcemia, or drug-induced prolongation, and can lead to ventricular dysrhythmias

e. QRS axis (normal vs. deviated to left or right)
(1) Normal axis shows a positive QRS in leads **I** and **aVF**
(2) Left axis shows a positive QRS in lead **I** and a negative QRS in lead **aVF**
(3) Right axis shows a negative QRS in lead **I** and a positive QRS in lead **aVF**

f. P wave (normal vs. abnormal)
(1) Right atrial abnormalities can cause peaked P waves (**P pulmonale**)
(2) Left atrial abnormalities cause a double notch on P waves (**P mitrale**)

g. QRS complex (normal, hypertrophy)
(1) Left ventricular hypertrophy (**LVH**) is met when the amplitude of the **S wave in V_1 + R in V_5 or V_6 is >35 mm** or when the amplitude of the R wave in lead I + S wave in lead III >25 mm
(2) Right ventricular hypertrophy (**RVH**) is met when there is **right axis deviation and an R wave in V_1 >7 mm**

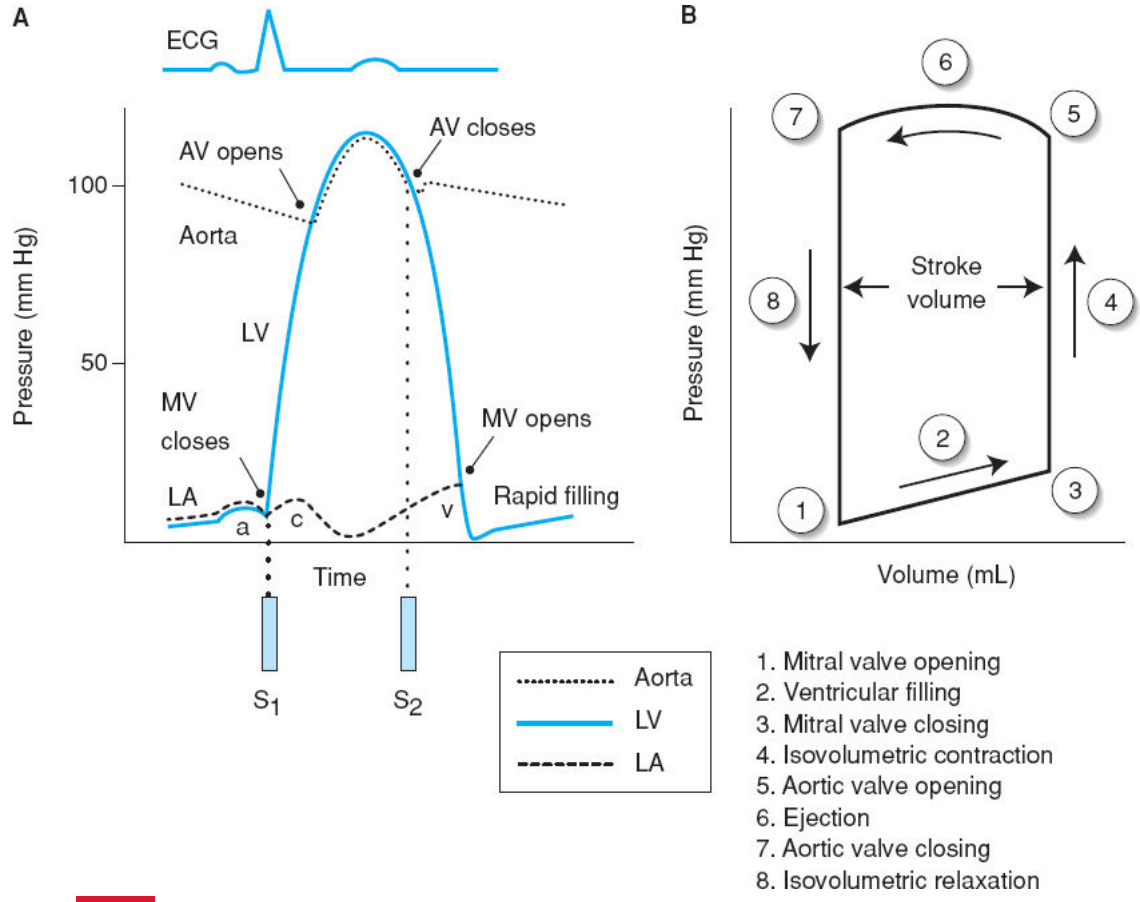


FIGURE 1-2

A: Pressure relationships between left-sided heart chambers and timing with normal heart sounds and the electrocardiogram for one full cardiac cycle. B: Normal left ventricular pressure–volume loop for one full cardiac cycle.

AV, aortic valve; ECG, electrocardiogram; LA, left atrium; LV, left ventricle; MV, mitral valve.

(Modified from Lilly, L. S. [2011]. *Pathophysiology of Heart Disease* [5th ed.]. Baltimore, MD: Lippincott Williams & Wilkins, with permission.)

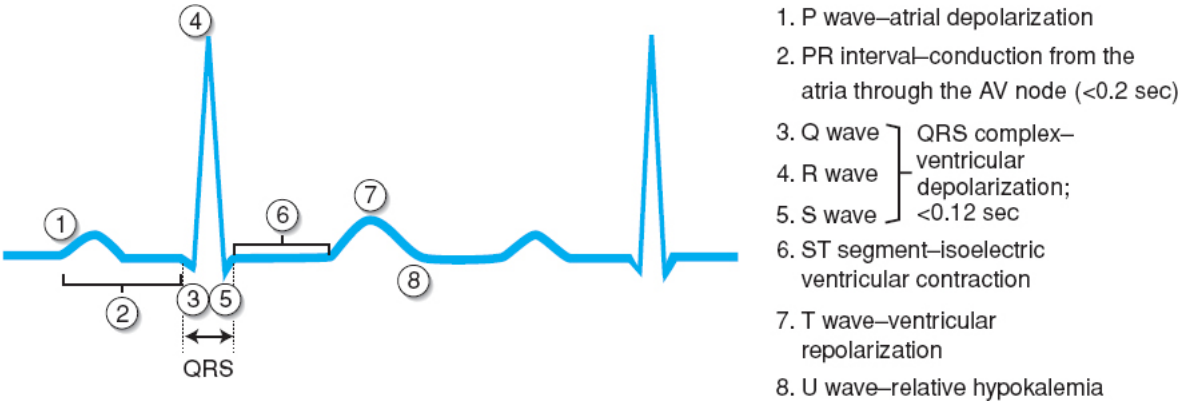


FIGURE 1-3

General structure of the electrocardiogram tracing and significance of specific regions.

AV, atrioventricular.

(Modified from Lilly, L. S. [2011]. *Pathophysiology of Heart Disease* [5th ed.]. Baltimore, MD: Lippincott Williams & Wilkins.)

h. ST-segment and T-wave changes (normal, peaked, depressed, elevated, inverted)

(1) The ST segment is normally isoelectric. T-wave inversion is an early finding of ischemia which can then progress to ST-segment changes (elevation or depression)

(2) Other late findings may include appearance of Q waves (>40 msec or >1/3 of QRS amplitude)

3. Morphology of action potentials varies with location in the heart (see Figure 1-4)

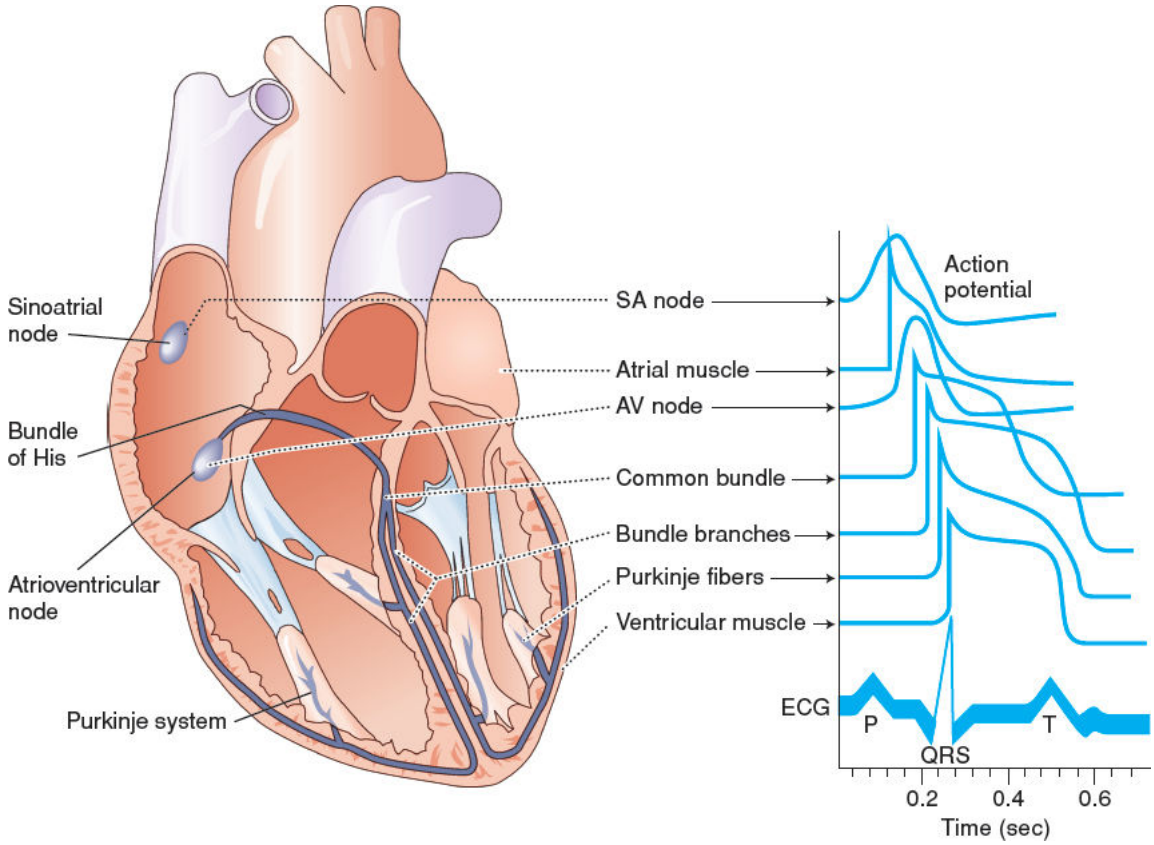


FIGURE **1-4**

Morphology of action potentials at different locations along the conduction pathways of the heart and their relation to the electrocardiogram.

AV, atrioventricular; ECG, electrocardiogram; SA, sinoatrial.

Quick HIT

The patient should be sitting quietly for 5 minutes before blood pressure is measured to minimize **false-high readings.**

NEXT
STEP

If patient has been normotensive in the past and now systolic blood pressure is >140 mm Hg or diastolic blood pressure >90 mm Hg, recheck in 2 months.

Quick HIT

Renal diseases are the most common cause of secondary HTN.

II. Hypertension

A. Primary (Essential) Hypertension (HTN)

1. Cause is idiopathic or no identifiable cause
2. Accounts for 95% of all cases of HTN
3. Diagnosed when systolic blood pressure ≥140 mm Hg and/or diastolic blood pressure ≥90 mm Hg, as measured in three readings taken at three separate appointments
4. **Risk factors** = family history of HTN, high-salt diet (especially if salt sensitive), tobacco use, obesity, increased age; blacks > whites
5. **H/P** = asymptomatic until progression, then headache may be the only symptom until complications develop; blood pressure ≥140/90 mm Hg; arteriovenous nicking (i.e., apparent retinal vein narrowing secondary to arterial wall thickening), cotton-wool spots, or retinal hemorrhages (i.e., **flame hemorrhages**) on funduscopic examination; loud S_2, possible S_4
6. **Treatment** = do not start medications until three consecutive high readings have been recorded
   a. Initially, prescribe weight loss, exercise, salt restriction, smoking cessation, and alcohol reduction.

b. A thiazide diuretic, calcium channel blocker, ACE-I, or ARB is typically the first drug prescribed unless comorbid condition indicates otherwise (see Tables 1-1 and 1-2).
c. **Complications** = untreated or poorly treated disease increases risk of CAD, stroke, aortic aneurysm, aortic dissection, congestive heart failure (CHF), kidney disease, and ophthalmologic disease

B. Secondary HTN

1. HTN due to an identifiable cause (see Table 1-3)
2. Some causes can be reversible, whereas others are progressive

Table 1-1 Common Antihypertensive Agents

Class of Medication	Examples	Mechanism of Action	Prescription Strategy	Side E
Diuretics	Thiazides (HCTZ, etc.); K^+-sparing (spironolactone, etc.); loop diuretics too potent for regular anti-HTN use	Reduce circulatory volume to decrease CO and mean arterial pressure	Early; particularly effective in blacks and salt-sensitive patients	Increas cholest hypoka hypona
Ca^{2+} channel blockers	Dihydropyridines (nifedipine, amlodipine)	Reduce influx of calcium in vascular smooth muscle to cause vasodilation	Second-line; dihydropyridines mainly affect vascular smooth muscle and are utilized more often for HTN	Hypote constip reflux,
	Nondihydropyridines (diltiazem, verapamil)	Reduce influx of calcium in coronary arteries, slows automaticity and conduction of AV node	Nondihydropyridines are less frequently used for HTN	Bradyca headac reflux,
ACE-I	Lisinopril, captopril, enalapril	Block conversion of angiotensin I to angiotensin II and increase circulating bradykinin to decrease angiotensin II vasopressor activity and aldosterone secretion, causing decrease in total peripheral resistance	First or second line; important cardiac and renal uses; more effective in young white patients	Dry cou azotem teratog
ARB	Losartan, valsartan, irbesartan	Block binding of angiotensin II to second-line receptors to inhibit vasopressor activity and decrease aldosterone secretion	First or second line	Azotem teratog
β-Blockers	Nonselective (propranolol, timolol); β_1-selective (metoprolol, atenolol, esmolol)	Decrease HR, contractility, CO, and decrease renin secretion to decrease total peripheral resistance	Early; many important cardiac uses (e.g., CAD, CHF); more effective in white patients	Bronch β_1 sele increas
α-Blockers	Prazosin, doxazosin, terazosin	Block α-adrenergic receptors (primary controllers of vascular tone) to decrease total peripheral resistance	Adjunct to other medications; less commonly used	Postura headac stoppe
Vasodilators	Hydralazine, minoxidil, nitroprusside	Direct relaxation of vascular smooth muscle	Adjunct to other medications; less commonly used	Reflex adverse inciden

ACE-I, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; CAD, coronary artery disease; CHF, congestive heart failure; C
GI, gastrointestinal; HCTZ, hydrochlorothiazide; HDL, high-density lipoprotein; HR, heart rate; HTN, hypertension.

C. Hypertensive Urgency

1. Blood pressure ≥180/120 mm Hg (nonpregnant patient) without symptoms and without evidence of end-organ damage
2. **H/P** = by definition, hypertensive urgency is asymptomatic; no signs of end-organ damage
3. **Hypertensive emergency** (malignant HTN) = BP ≥180/120 mm Hg with evidence of end-organ damage (e.g., progressive renal failure, pulmonary edema, aortic dissection, encephalopathy, papilledema)

4. **Treatment** = for hypertensive emergency, the goal blood pressure varies by the systemic effects seen; drugs used may include intravenous (IV) nitroprusside, nitroglycerin, labetalol, nicardipine; once blood pressure is controlled, convert to oral drugs for further blood pressure reduction and maintenance therapy

Quick HIT

ACE inhibitors are contraindicated in cases of **bilateral renal artery stenosis** because they can accelerate renal failure by impeding sufficient renal perfusion and lowering glomerular filtration rate.

Quick HIT

In a hypertensive emergency, the **initial decrease** (first 2 hours) in mean arterial pressure **should not exceed 25%** of the presenting pressure to avoid triggering an ischemic event.

Table 1-2 Recommendations and Contraindications for Antihypertensive Drug Selection

Comorbid Condition	Recommended Antihypertensive	Reason for Recommendation	Contraindicated Antihypertensive	Reaso Contra
DM	ACE-I	Delays renal damage	±Thiazide diuretic ±β-Blocker	Impaire Can ma cemia
CHF	ACE-I/ARB Aldosterone antagonist β-Blocker	Improves mortality Improves mortality Improves mortality	Ca^{2+} channel blocker	Reduce can exa
Post-MI	β-Blocker ACE-I/ARB Aldosterone antagonist	Improves mortality Improves mortality Improves mortality		
Benign prostatic hypertrophy	Selective α_1-blocker	Reduces symptoms		
Migraine headache	Verapamil, β-blocker	May reduce symptoms		
Osteoporosis	Thiazide diuretic	Maintains normal/high serum calcium		
Asthma/COPD			Nonselective β-blocker	Exacerb striction
Pregnancy	Hydralazine Methyldopa Labetalol Nifedipine		±Thiazide diuretic ACE-I ARB	Increas during maintai Teratog Teratog
Gout			Diuretic	Increas
Depression			β-Blocker	May wo

ACE-I, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blocker; CHF, congestive heart failure; COPD, chronic obstructive pulmo diabetes mellitus; MI, myocardial infarction.

Table 1-3 Causes of Secondary HTN

Condition	Common Patient Group	Signs/Symptoms	Diagnosis	Trea
Renal diseases (various)		Depends on disease identity	Depends on disease identity	ACE-I
Renal artery stenosis	<25 yr of age (fibromuscular dysplasia) or >50 yr of age (atherosclerosis)	Renal artery bruit, hypokalemia	Arteriography, MRA, CT, renal artery duplex scan	Angio ment, surgic
OCP (combination pill)	Women >35 yr of age, obese women, long-term OCP use		History	Stop proge intrar geste
Pheochromocytoma	Young patients; patients with history of endocrine tumors	Episodic HTN, diaphoresis, headaches; symptoms occur suddenly	Increased 24-hr urinary fractionated metanephrines; CT, MRI	Surgi with trol o of sur
Primary hyperaldosteronism (Conn syndrome)		Headache, hypokalemia, metabolic alkalosis	High ratio of plasma aldosterone to plasma renin activity (high PAC:PRA ratio)	Surgi aldos
Excess glucocorticoids (Cushing syndrome)		Central obesity, hirsutism, buffalo hump, striae, and glucose intolerance	Serum cortisol, dexamethasone suppression test	Treat reduc
Coarctation of the aorta	Male > female; Turner syndrome, aortic valve pathology, PDA	HTN in arm but not in legs, weak femoral pulse	Possible LVH on ECG; echocardiogram can localize defect	Surgi
Hyperparathyroidism (hypercalcemia)		Confusion, nephrolithiasis, constipation	Increased serum calcium and PTH level, decreased serum phosphates	Hydra
Hyperthyroidism		Tachycardia, diaphoresis, tremor, weight loss, heat intolerance	Decreased TSH, high free T_4	Radio tion,

ACE-I, angiotensin-converting enzyme inhibitors; CT, computed tomography; ECG, electrocardiogram; HTN, hypertension; LVH, left ventricular hyper
resonance imaging; OCP, oral contraceptive pill; PDA, patent ductus arteriosus; TSH, thyroid-stimulating hormone.

III. Dyslipidemia

A. Introduction

1. Abnormal serum cholesterol levels (**high** low-density lipoprotein [**LDL**] and/or **low** high-density lipoprotein [**HDL**]) that are associated with increased risk of ischemic heart disease
2. Can result from a congenital disorder (less common) or an **acquired condition (most common)**
3. **Normal cholesterol physiology**
   a. Cholesterols and triglycerides are carried by lipoproteins.
   b. Increased LDL leads to increased CAD risk; increased HDL is protective.
   c. Increased LDL and decreased HDL result from a diet high in fatty foods, tobacco use, obesity, alcohol use, diabetes mellitus (DM), and certain medications (e.g., oral contraceptive pills [OCPs], diuretics).
4. **H/P** = usually asymptomatic; extremely high triglycerides and LDL lead to xanthomas (i.e., lipid deposits in tendons), xanthelasmas (i.e., lipid deposits in eyelids), and cholesterol emboli in retina (visible on funduscopic examination); symptoms are more severe and appear earlier in life in primary disorders compared with acquired conditions
5. **Workup** = increased total cholesterol and LDL; possible decreased HDL; total cholesterol may be >300 to 600 mg/dL in primary disorders; screening for hyperlipidemia is performed in men >35 years of age and women >45 years of age (younger if patient has other risk factors for CAD)

6. **Treatment** = focuses on **prevention** of cardiovascular disease and includes tobacco cessation, exercise, and dietary restrictions (e.g., low fat, low cholesterol); guidelines published in 2013 by the American College of Cardiology (ACC) and American Heart Association (AHA) recommend starting **moderate- or high-intensity statin therapy** in patients who meet specific criteria (see Figure 1-5), without specific target values for LDL, HDL, or other lipid parameters; the guidelines do not specifically recommend other cholesterol-lowering medications due to lack of sufficient evidence, although these other medications are often used in patients who do not tolerate moderate- or high-intensity statin therapy (see Table 1-4)

Quick HIT

Most cases of hypercholesterolemia are **acquired.**

Quick HIT

Blood for serum cholesterol levels should be collected from a **fasting** patient (12 to 14 hours) to minimize postprandial influence.

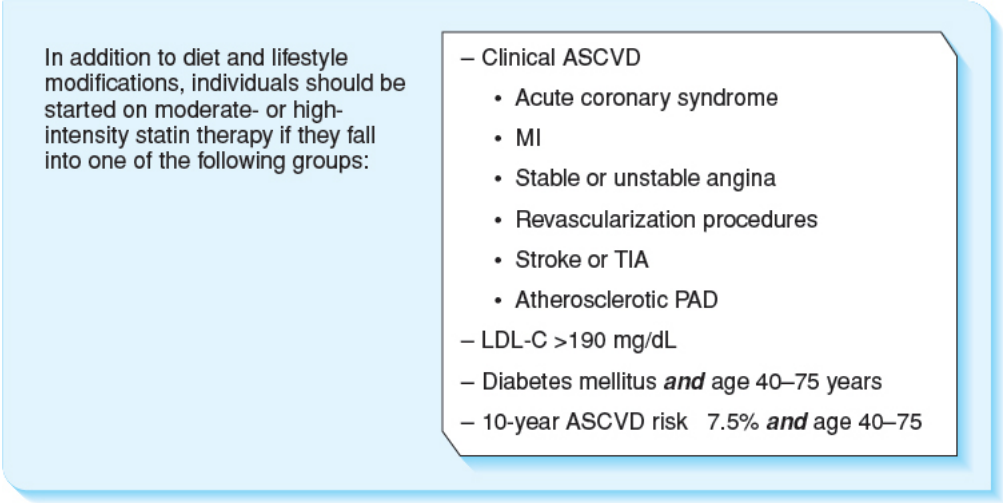


FIGURE 1-5
Recommendations for statin therapy for ASCVD prevention.
ASCVD, atherosclerotic cardiovascular disease; LDL-C, low-density lipoprotein cholesterol; MI, myocardial infarction; PAD, peripheral arterial disease; TIA, transient ischemic attack.

Table 1-4 Lipid-Lowering Agents

Drug	Site of Action	Effect on LDL	Effect on HDL	Effect on Triglycerides	Side Effects
HMG-CoA reductase inhibitors (lovastatin, pravastatin, simvastatin)	Liver	↓↓	↑	↓	Myositis, increase starting medicatic
Cholesterol absorption inhibitors (ezetimibe)	Intestines	↓	No change	No change	Myalgias, possibl
Fibrates (gemfibrozil, fenofibrate)	Blood (all stimulate lipoprotein lipase)	↓	↑	↓↓↓	Myositis, increase starting medicatic
Bile acid sequestrants (cholestyramine, colestipol, colesevelam)	GI tract	↓	No change	—/↑	Bad taste, GI upse
Niacin	Liver	↓	↑↑	↓	Facial flushing, na pruritus, increase ance, exacerbates

GI, gastrointestinal; HDL, high-density lipoprotein; LDL, low-density lipoprotein; LFT, liver function tests; ↑, increased; ↑↑, more increased; ↑↑↑, n change or increased.

Quick HIT

The **left anterior descending artery** is the most common site of coronary artery occlusion.

IV. Ischemic Heart Disease

A. Introduction

1. **Inadequate** supply of O_2 for a given myocardial demand leads to **myocardial hypoxia** and an accumulation of waste products.
2. Most cases of ischemic heart disease arise **from atherosclerosis of the coronary arteries (coronary artery disease [CAD]).**
3. Manifestations of ischemic heart disease can vary in presentation from myocardial infarction (MI), stable angina, unstable angina, dyspnea on exertion, shortness of breath, HF, or sudden death. Any combination of these is also possible in acute or chronic ischemic heart disease.
4. Coronary arteries fill during diastole, thus conditions or drugs that increase HR or reduce diastolic filling allow less coronary perfusion which can lead to more ischemia in an already atherosclerotic heart.

Quick HIT

Risk factors for CAD: age (>45 M, >65 F), male gender, HTN, DM, FHx of CAD (<55 M, <65 F), smoker, dyslipidemia (elev. LDL), obesity.

B. Atherosclerosis

1. Gradual narrowing of arteries caused by endothelial dysfunction, progressive formation of plaques (which consist of lipids and smooth muscle), and the associated inflammatory response
2. Plaques can calcify, rupture, and thrombose, which leads to further narrowing of arteries and progressive occlusion of blood flow
3. **H/P** = asymptomatic for most of disease progression; later sequelae include angina, claudication, progressive HTN, retinal changes, extra heart sounds, MI, and stroke
4. **Workup** = stress testing, echocardiography, nuclear studies, or angiography can be used to detect coronary ischemia
   a. Exercise stress test—patient exercises on an aerobic fitness machine at increasingly strenuous workloads; HR and ECG are constantly monitored; test is continued until patient achieves 85% of predicted maximal HR (predicted

maximal HR = 220 − age) or patient develops angina or signs of ischemia as seen on ECG; ischemic heart disease is diagnosed with signs of **reproducible angina** or obvious signs of **ischemia at low workloads**
   b. Nuclear exercise test—thallium-201 or technetium-99m sestamibi is injected during exercise testing, and scintigraphy (e.g., planar or single-positron emission computed tomography [SPECT]) is performed to assess myocardial perfusion; used in cases of suspected ischemic heart disease in which results of regular exercise stress testing are equivocal
   c. Exercise stress test with echocardiography—exercise stress testing performed in conjunction with echocardiography to increase sensitivity of detecting myocardial ischemia
   d. Pharmacologic stress testing—administration of cardiac inotrope (e.g., dobutamine) in place of exercise to increase myocardial demand; frequently performed in conjunction with SPECT or performed in patients for whom comorbidities interfere with the ability to perform exercise
   e. Positron emission tomography (PET) myocardial imaging—injection of positron- emitting isotopes with subsequent three-dimensional detection imaging to evaluate heart for perfusion defects and tissue viability
   f. Coronary angiography—gold standard for identifying CAD but more invasive than other techniques
5. **Treatment** = management is primarily intended to minimize risk factors (e.g., tobacco use, HTN, hyperglycemia, hypercholesterolemia); diet low in fats and cholesterol and high in antioxidants (e.g., vitamins E and C, β-carotene) is helpful in preventing disease

Quick HIT

Nitroglycerin may also reduce the effects of esophageal spasm.

Quick HIT

A stress test is positive if a chest pain is reproduced or if there is hypotension, ST changes, or a significant arrhythmia.

C. Angina Pectoris

1. Etiology
   a. **Temporary** (10 to 15 minutes) **myocardial ischemia** during exertion that causes chest pain.
   b. Most commonly caused by **CAD;** also occurs secondary to arterial vasospasm (Prinzmetal angina) and valvular disease.
   c. Gastroesophageal reflux disease (GERD) and esophageal spasm can mimic symptoms.
2. **H/P** = **substernal chest pain** that may radiate to left shoulder, arm, jaw, or back
3. **Workup** = stress testing or nuclear studies used for diagnosis
   a. Important in assessment of chest pain
   b. Seeks to increase cardiac workload to assess myocardial ischemia
   c. Accomplished either through exercise or pharmacologic testing
4. **Treatment** = **sublingual nitroglycerin** and cessation of intense activity until completion of workup; full workup (including stress testing or nuclear studies) for cause is needed to define long-term treatment

NEXT
STEP

Use a formal stress test to rule out a cardiac cause for chest pain before considering alternative diagnoses.

Quick HIT

Myocardial ischemia can be asymptomatic in patients with DM because of **sensory neuropathy.**

MNEMONIC

For acute treatment of MI, remember the mnemonic "**MONA** had **Hep B**":

- **M**orphine
- **O**$_2$
- **N**itroglycerin
- **A**SA
- **Hep**arin (or LMWH)
- **B**eta blocker

D. Unstable Angina

1. **Worsening angina** that occurs at rest
2. Frequently caused by **plaque rupture,** hemorrhage, or thrombosis in coronary arteries
3. One-third of patients have an MI within 3 years
4. **H/P** = angina with worse pain and increased frequency than in prior episodes; **symptoms occur at rest;** less responsive to prior treatment regimens
5. **ECG** = **ST depression,** T-wave flattening or inversion
6. **Workup** = any patient suspected of having an MI must have a workup in a hospital setting with an **ECG** and **serial cardiac enzymes.** Any patient with unstable angina should not undergo stress testing
7. **Treatment** = seeks to relieve cause of ischemia and decrease myocardial O_2 demand
   a. **Pharmacotherapy** = IV morphine, supplemental O_2, nitroglycerin, aspirin, β-blockers (to reduce cardiac workload), a statin (preferably before percutaneous coronary intervention [PCI]); if no PCI planned, use clopidogrel or ticagrelor for antiplatelet therapy; if PCI, use glycoprotein (GP) IIb/IIIa inhibitor (abciximab, tirofiban, or eptifibatide) for antiplatelet therapy; anticoagulate with unfractionated heparin (if PCI planned) or low–molecular-weight heparin (if no PCI planned) to help prevent further thrombus formation; administer potassium and magnesium to keep K^+ levels >4 mEq/L and Mg^{2+} levels >2 mEq/L
   b. **Percutaneous transluminal coronary angioplasty (PTCA)**
      (1) Suggested in cases that are nonresponsive to medications
      (2) Catheter inserted through femoral or brachial artery and maneuvered through heart to stenotic vessel
      (3) Balloon on catheter inflated to dilate stenosis
      (4) Catheters can also be used for atherectomy (i.e., plaque is shaved by burr on catheter) or stent placement (i.e., intravascular support structure)
   c. **Coronary artery bypass graft (CABG)**
      (1) Considered for left main stenosis >50%, three-vessel disease, or history of CAD and DM
      (2) Donor vessel grafted to coronary artery to bypass obstruction
      (3) Saphenous vein and internal mammary artery are most commonly used

NEXT
STEP

Reversible myocardial ischemia is an indication for cardiac catheterization to assess the need for percutaneous transluminal coronary angioplasty (PTCA) or coronary artery bypass graft (CABG).

Quick **HIT**

Because general CK will be increased with significant muscular trauma or degradation, CK-MB is a better indicator of cardiac muscle damage.

Quick **HIT**

Since MI happens after plaque rupture into a moderate lesion, a stress test can be negative and the patient still have an MI later. This is because stress tests detect high-grade flow-limiting lesions.

NEXT
STEP

Troponin is the best choice to detect MI. CK-MB is less sensitive and less specific.

E. Myocardial Infarction

1. **Tissue death** resulting from ischemia caused by **occlusion of coronary vessels** or **vasospasm;** often secondary to thrombus formation following plaque rupture
2. **Risk factors** = increased age, HTN, hypercholesterolemia, family history of CAD, DM (highest), and tobacco use; males > females; postmenopausal females > premenopausal females
3. **H/P** = chest pain ("**elephant on chest**") in distribution similar to episodes of angina; possible shortness of breath, diaphoresis, nausea, and vomiting; examination findings can include tachycardia, decreased blood pressure, pulmonary rales, new S_4, and new systolic murmur
4. **ECG** = **ST-elevation** and T-wave changes; possible new arrhythmia, left bundle branch block (LBBB), or Q-wave changes (see Figure 1-6; Table 1-5)
5. **Workup** = serial cardiac enzymes and ECGs
   a. Changes in enzymes in the initial **24 hours** after MI are helpful for making a diagnosis of acute infarction, so enzymes are measured every 8 hours in the first 24 hours after presentation (three sets total).
   b. Creatine kinase muscle/brain (CK-MB) increases in 2 to 12 hours post-MI, peaks in 12 to 40 hours, and decreases in 24 to 72 hours.
   c. Lactase dehydrogenase (LDH) increases in 6 to 24 hours and peaks in 3 to 6 days (rarely used for diagnosis).

d. **Troponin I increases in 2 to 3 hours, peaks in 6 hours,** and gradually decreases over 7 days. Newly FDA-approved more sensitive troponins have recently been approved that may help diagnose MI up to 1 hour earlier.

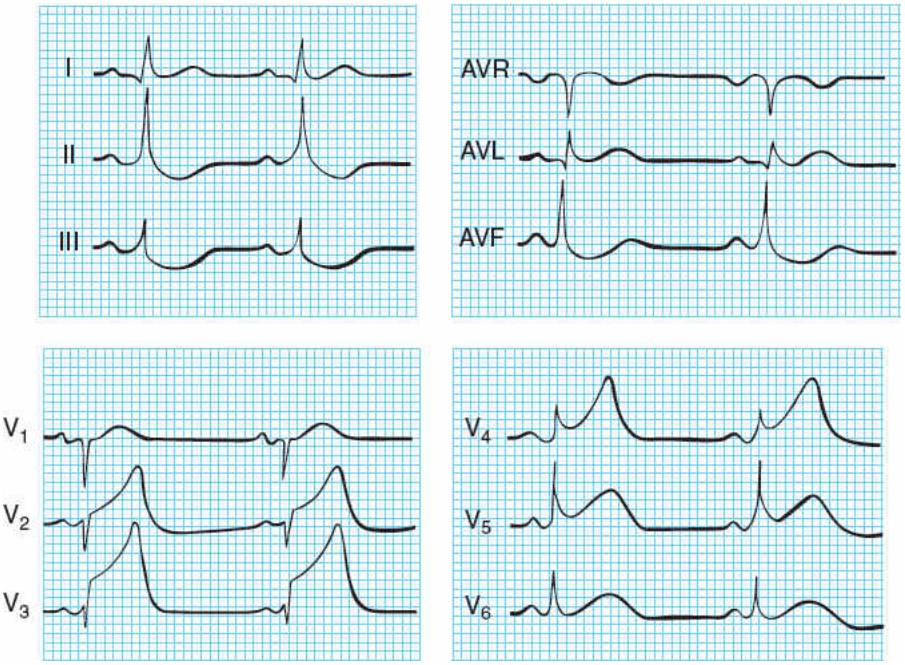


FIGURE **1-6**
Acute myocardial infarction shown on electrocardiogram.
Note the ST elevation in leads V_2 to V_5, suggesting anterior wall involvement.
(From Thaler, M. S. [2015]. *The Only EKG Book You'll Ever Need* [8th ed., p. 260]. Philadelphia, PA: Wolters Kluwer, with permission.)

Table 1-5 Relation of ECG Changes to Location of Infarct

ECG Leads With Changes	Area of Infarct	Coronary Artery Branch
V_2, V_3, V_4	Anterior	Left anterior descending
V_1, V_2, V_3	Septal	Left anterior descending
II, III, aVF	Inferior	Posterior descending or marginal branch
I, aVL, V_4, V_5, V_6	Lateral	Left anterior descending or circumflex
V_1, V_2 (frequent comorbid inferior MI)	Posterior	Posterior descending

ECG, electrocardiogram; MI, myocardial infarction.

6. **Treatment**
   a. Acutely, give IV morphine, supplemental O_2, nitroglycerin, aspirin, heparin (unfractionated heparin for patients undergoing PCI, low–molecular-weight heparin for patients not managed with PCI), β-blocker, a statin, and antiplatelet therapy (clopidogrel or ticagrelor).
   b. For ST-elevation MI (STEMI), perform PCI if possible; patients undergoing PCI should also receive a GP IIb/IIIa inhibitor (abciximab, tirofiban, or eptifibatide). If PCI is not available within 12 hours of presentation, consider fibrinolysis with tPA (only for STEMIs).
   c. If patient is hypotensive, stop nitroglycerin and give IV fluids; give amiodarone for stable patients with ventricular tachycardia (Vtach).
   d. If emergent cardiac catheterization was not performed, perform cardiac catheterization to measure vessel patency and consider possible PTCA or CABG if significant stenosis is found.
   e. Long-term treatment = risk reduction medications should include **low-dose acetylsalicylic acid (ASA) or clopidogrel, a β-blocker, an angiotensin-converting enzyme inhibitor (ACE-I),** an aldosterone antagonist, and a statin (HMG-CoA reductase inhibitor); exercise, smoking cessation, and dietary modifications are also important for risk reduction (see Table 1-6).

Quick HIT

The greatest risk of sudden cardiac death is in the first few hours post-MI from **Vtach, ventricular fibrillation (Vfib),** or **cardiogenic shock**.

++++++++++++++++++++++++

Table 1-6 Common Medications Used in Ischemic Disease

Drug	Indications	Cardiovascular Benefits	Contrain
ASA	MI prevention; during and after MI	Decreases thrombosis risk	High risk c
Clopidogrel	During angina and MI; after PTCA	Decreases thrombosis risk	High risk c
GP IIb/IIIa inhibitor (abciximab, eptifibatide)	During angina or NSTEMI; after PTCA or thrombolysis	Decreases thrombosis risk	High risk c cytopenia
Nitroglycerin	During angina and MI	Decreases venous pressure, causing decrease in preload and end-diastolic volume; as a result, blood pressure, ejection time, and O_2 consumption decrease while contractility and heart rate increase	Significan
β-Blocker	MI prevention; during angina; during and post-MI	Decreases blood pressure, contractility, heart rate, and O_2 consumption; increases end-diastolic volume and ejection time; **decreases mortality** following MI	Long-term COPD, DM mia), and symptoms
ACE-I (or ARB)	Post-MI	Decreases afterload, leading to decreased O_2 consumption and blood pressure; **decreases mortality** following MI; particularly helpful with comorbid CHF or DM	Pregnancy
HMG-CoA reductase inhibitors (e.g., statins)	Post-MI	Decreases risk of atherosclerosis progression by lowering LDL level	Use of mu medicatio
Heparin	Immediately post-MI, inpatient setting	Decreases risk of thrombus formation	Active her
Morphine	During and immediately post-MI	No direct cardiac benefit but decreases pain during MI, leading to decreased heart rate, blood pressure, and O_2 consumption	Respirator
Thrombolytics (tPA, urokinase)	Immediately post-STEMI, inpatient setting	Breaks up thrombus; **decreases mortality** if used within 12-hr post-MI	High bleed

ACE-I, angiotensin-converting enzyme inhibitors; ASA, acetylsalicylic acid; CHF, congestive heart failure; COPD, chronic obstructive pulmonary d tus; GI, gastrointestinal; MI, myocardial infarction; PTCA, percutaneous transluminal coronary angioplasty; PVD, peripheral vascular disease.

7. **Complications** = infarct extension, arrhythmias (2 to 4 days), HF (first 24 hours), papillary muscle necrosis, ventricular wall rupture (5 to 10 days), aneurysm (weeks to months), mural thrombus, pericarditis (2 to 4 days), **Dressler syndrome** (fever, pericarditis, and increased erythrocyte sedimentation rate [ESR] 2 to 8 weeks post-MI)
8. Poor prognosis = left ventricular ejection fraction <50% (normal >50%), multiple-vessel (≥2) disease, left main disease (2/3 of heart supply)

Quick HIT

The greatest risk of ventricular wall rupture is 4 to 8 days post-MI.

V. Arrhythmias

A. Heart Block

1. Impaired myocardial conduction that occurs when electrical impulses encounter tissue that is electronically inexcitable, resulting in an arrhythmia
2. First degree; ECG = **PR >0.2** seconds (see Figure 1-7A)
   a. **Caused** by increased vagal tone or functional conduction impairment
   b. **H/P** = asymptomatic

c. **Treatment** = outpatient observation; none necessary

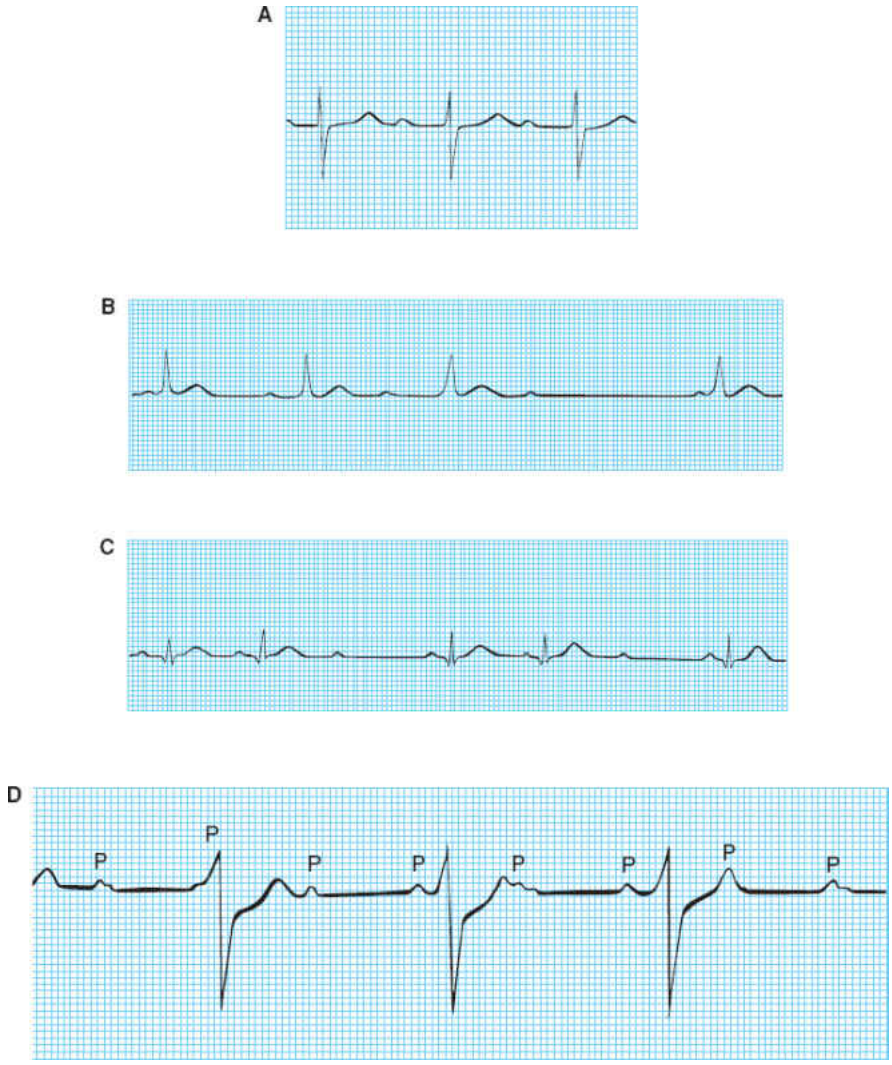


FIGURE 1-7
A: Primary heart block: regular PR prolongation without skipped QRS. B: Secondary Mobitz I heart block: progressive lengthening of PR until QRS is skipped. C: Secondary Mobitz II heart block: regular PR with random skipped QRS. D: Tertiary heart block: no relationship between P and QRS.
(From Thaler, M. S. [2015]. *The Only EKG Book You'll Ever Need* [8th ed., pp. 170–172, 176]. Philadelphia, PA: Wolters Kluwer, with permission.)

3. Second degree—Mobitz I (Wenckebach); **ECG** = **progressive PR lengthening** until skipped QRS; PR progression, then resets and begins again (see Figure 1-7B)
   a. Caused by **intranodal** or His bundle conduction defect, drug effects (e.g., β-blockers, digoxin, calcium channel blockers), or increased vagal tone
   b. **H/P** = asymptomatic
   c. **Treatment** = adjust doses of medications associated with heart block; treatment usually not necessary unless symptomatic bradycardia is present (pacemaker indicated)
4. Second degree—Mobitz II; **ECG** = **randomly skipped QRS** without changes in PR interval (see Figure 1-7C)
   a. Caused by an **infranodal** conduction problem (bundle of His, Purkinje fibers)
   b. **H/P** = usually asymptomatic
   c. **Treatment** = ventricular pacemaker
   d. **Complications** = can progress to third-degree heart block
5. Complete or third-degree heart block; **ECG** = no relationship between P waves and QRS (see Figure 1-7D)
   a. Cause is **absence** of conduction between atria and ventricles
   b. **H/P** = syncope, dizziness, hypotension
   c. Treatment = avoid medications affecting atrioventricular (AV) conduction; ventricular pacemaker

B. Paroxysmal Supraventricular Tachycardia (PSVT)

1. Tachycardia (HR >100 bpm) arising in atria or AV junction
2. Occurs mostly in **young patients** with **healthy hearts**
3. Caused frequently by abnormal reentry pathways
   a. **AV nodal reentry** (see Figure 1-8)—presence of both slow and fast conduction pathways in AV node; conduction proceeds quickly through fast pathway and progresses up slow pathway in retrograde fashion; conduction loop is created, resulting in reentrant tachycardia

b. **AV reentry** in **Wolff–Parkinson–White (WPW) syndrome** (see Figure 1-9) similar to AV nodal reentry, but instead of fast and slow pathways existing in the AV node, a separate accessory conduction pathway exists between the atria and ventricles that returns a conduction impulse to the AV node to set up a reentry loop; ECG shows a delta wave (i.e., slurred upstroke of the initial portion of the QRS) and shortened PR

4. **H/P** = sudden tachycardia; possible chest pain, shortness of breath, palpitations, syncope
5. **ECG** = P waves hidden in T waves; 150 to 250 bpm HR; normal QRS (see Figure 1-10)
6. **Treatment** = carotid massage, Valsalva maneuver, or IV adenosine may halt an acute arrhythmia, but cardioversion or calcium channel blocker is required in cases of hemodynamic instability; pharmacologic therapy (e.g., β-blocker or calcium channel blocker for AV nodal reentrant tachycardia and type IA or IC antiarrhythmic for WPW syndrome) or **catheter ablation** of accessory conduction pathways is frequently used for long-term control in symptomatic patients

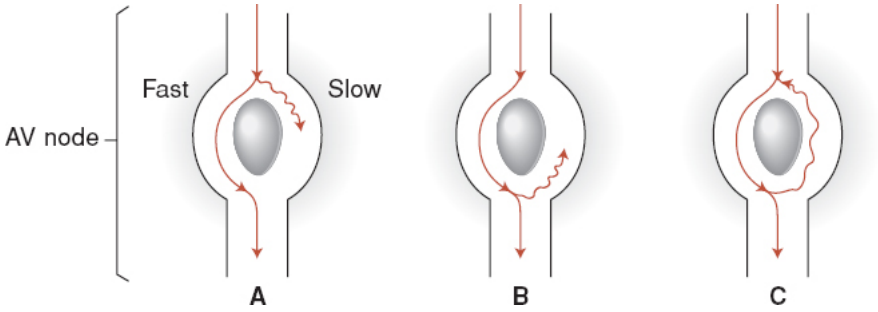


FIGURE 1-8
Mechanism of atrioventricular nodal reentry tachycardia.
A: Action potential reaches division in conduction pathway with both fast and slow fibers. **B:** Conduction proceeds quickly down fast pathway to reach distal fibers and also proceeds up slow pathway in retrograde fashion. **C:** Impulse returns to original division point after fibers have repolarized, allowing a reentry conduction loop and resultant tachycardia. AV, atrioventricular.

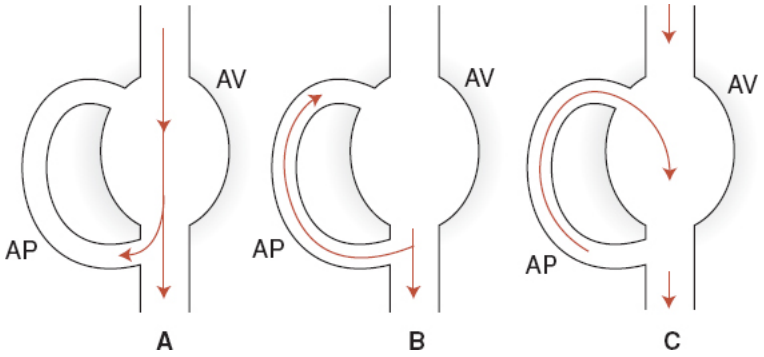


FIGURE 1-9
Mechanism of atrioventricular reentry tachycardia as seen for Wolff–Parkinson–White syndrome.
A: Action potential passes through AV node and encounters accessory pathway during conduction to ventricles. **B:** Accessory pathway conducts action potential back to AV node. **C:** Return of secondary action potential to AV node completes reentry loop and results in tachycardia. AV, atrioventricular node; AP, accessory pathway.

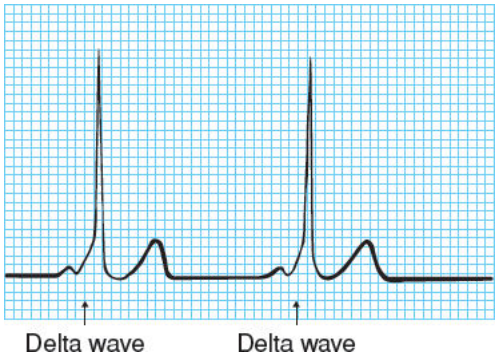


FIGURE 1-10
Wolff–Parkinson–White syndrome on electrocardiogram.
Note the presence of delta waves, slurred upstrokes preceding each QRS that are characteristic of the condition.
(From Thaler, M. S. [2015]. *The Only EKG Book You'll Ever Need* [8th ed., p. 212]. Philadelphia, PA: Wolters Kluwer, with permission.)

C. Multifocal Atrial Tachycardia (MAT) (See Figure 1-11)

1. Caused by several ectopic foci in the atria that discharge automatic impulses (multiple pacemakers), resulting in tachycardia
2. **H/P** = usually asymptomatic, seen in patients with chronic lung disease (commonly in chronic obstructive pulmonary disease [COPD])
3. **ECG** = **variable morphology of P waves** (usually three or more); HR >100 bpm

4. **Treatment** = calcium channel blockers or β-blockers acutely; catheter ablation or surgery to eliminate abnormal pacemakers

MNEMONIC

Treatment of Afib: ABCCD

- **A**nticoagulation
- **B**eta blockers
- **C**ardioversion/**C**a^+ Chn blockers
- **D**igoxin

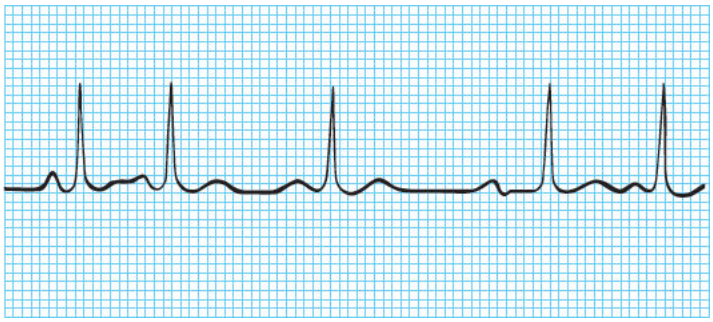


FIGURE 1-11
Multifocal atrial tachycardia (MAT).
Note the variety in shape of P waves and PR intervals and the irregular ventricular rate.
(From Thaler, M. S. [2015]. *The Only EKG Book You'll Ever Need* [8th ed., p. 312]. Philadelphia, PA: Wolters Kluwer, with permission.)

D. Bradycardia

1. HR <60 bpm
2. Caused by increased vagal tone or nodal disease, could also be related to medications
3. **Risk factors** = elderly, history of CAD
4. **H/P** = frequently asymptomatic; possible weakness, syncope
5. Predisposition to development of ectopic beats
6. **Treatment** = stop precipitating medications; pacemaker if severe

E. Atrial Fibrillation (Afib) (See Figure 1-12)

1. Lack of coordinated atrial contractions with independent sporadic ventricular contractions
2. Caused by rapid, disorderly firing from a second atrial focus
3. **Risk factors** = pulmonary disease, CAD, HTN, anemia, valvular disease, pericarditis, hyperthyroidism, rheumatic heart disease (RHD), sepsis, alcohol use
4. **H/P** = possibly asymptomatic; shortness of breath, chest pain, palpitations, irregularly irregular pulse
5. **ECG** = **no discernible P waves,** irregular QRS rate
6. **Treatment** = **anticoagulation** when indicated; **rate control** via calcium channel blockers, β-blockers, or digoxin; electric or chemical (i.e., class IA, IC, or III antiarrhythmics) cardioversion if presenting within initial 2 days; cardioversion can be performed in delayed presentation if absence of thrombi is confirmed by transesophageal echocardiogram (TEE); if presenting after 2 days or if thrombus is seen on echocardiogram, then anticoagulate and wait 3 to 4 weeks before cardioversion; AV nodal ablation can be considered for recurrent cases
7. **Complications** = increased risk of **MI,** HF; poor atrial contraction causes blood stasis, which leads to mural thrombi formation and a risk of embolization

NEXT
STEP

In a patient with Afib >2 days, TEE should be performed **before** cardioversion to rule out mural thrombus formation.

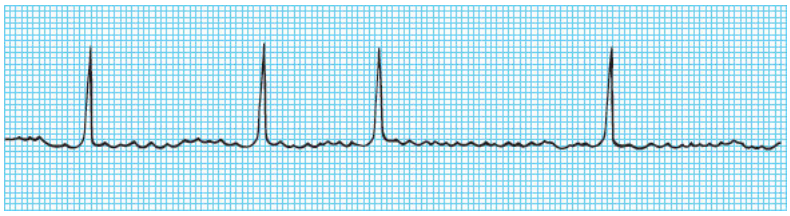


FIGURE 1-12
Atrial fibrillation—irregular QRS rate and no discernable P waves.
(From Thaler, M. S. [2015]. *The Only EKG Book You'll Ever Need* [8th ed., p. 133]. Philadelphia, PA: Wolters Kluwer, with permission.)

F. Atrial Flutter (Aflutter) (See Figure 1-13)

1. Caused by rapid firing of an ectopic focus in the atria
2. **Risk factors** = CAD, CHF, COPD, valvular disease, pericarditis
3. **H/P** = possibly asymptomatic; palpitations, syncope
4. **ECG** = regular tachycardia >150 bpm with occasionally set ratio of P waves to QRS; **sawtooth pattern of P waves**
5. **Treatment** = **rate control** with calcium channel blockers, β-blockers; electrical or chemical (class IA, IC, or III antiarrhythmics) cardioversion if unable to be controlled with medication; catheter ablation to remove ectopic focus may be possible in some cases
6. **Complications** = may degenerate into Afib

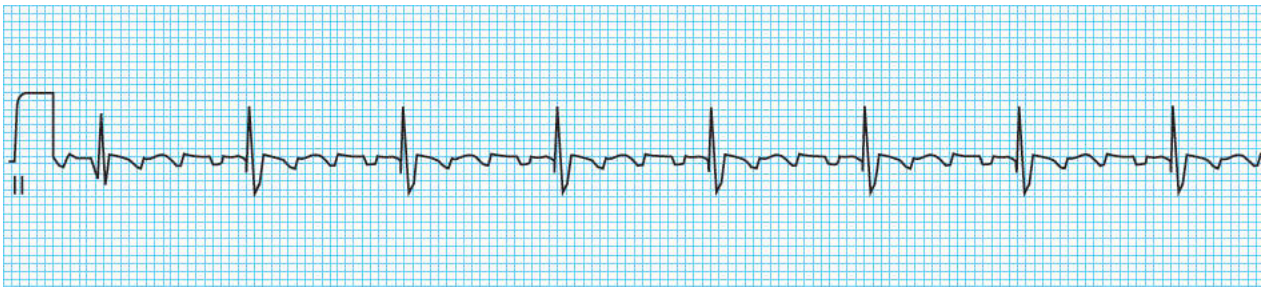


FIGURE 1-13
Atrial flutter—rapid sawtooth P waves preceding QRS.
(From Thaler, M. S. [2015]. *The Only EKG Book You'll Ever Need* [8th ed., p. 331]. Philadelphia, PA: Wolters Kluwer, with permission.)

Quick HIT

PVCs become concerning for the development of other ventricular arrhythmias if there are >3 PVCs/min.

G. Premature Ventricular Contraction (PVC)

1. Caused by ectopic beats from a ventricular origin
2. Common, frequently benign; can also be caused by hypoxia, abnormal serum electrolyte levels, hyperthyroidism, caffeine use
3. **H/P** = usually asymptomatic; possible palpitations, syncope
4. **ECG** = early and wide QRS without preceding P wave followed by brief pause in conduction
5. **Treatment** = none if patient is healthy; β-blockers in patients with CAD
6. **Complications** = associated with increased risk of sudden death in patients with CAD

Quick HIT

Torsades de pointes is Vtach with a sine wave morphology; it carries a poor prognosis and can rapidly convert to Vfib; Mg may be useful in treatment.

H. Ventricular Tachycardia (See Figure 1-14)

1. Series of **3+ PVCs** with HR 160 to 240 bpm
2. **Risk factors** = CAD, history of MI
3. **H/P** = possibly asymptomatic if brief; palpitations, syncope, hypotension

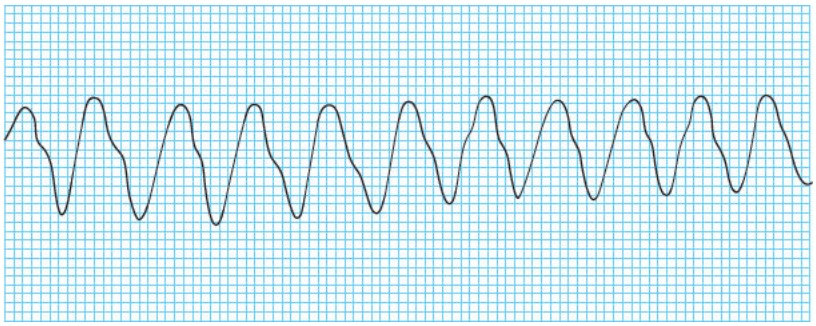


FIGURE 1-14
Ventricular tachycardia—wide, rapid QRS with no discernable P waves.
(From Thaler, M. S. [2015]. *The Only EKG Book You'll Ever Need* [8th ed., p. 141]. Philadelphia, PA: Wolters Kluwer, with permission.)

4. **ECG** = series of regular, wide QRS complexes independent of P waves
5. **Treatment** = electrical cardioversion followed by antiarrhythmic medications (class IA, IB, II, or III); for recurrent Vtach, internal defibrillator may be necessary (senses ventricular arrhythmia and automatically releases electric pulse to restore normal rhythm)
6. **Complications** = sustained Vtach can quickly deteriorate into ventricular fibrillation (Vfib) if not corrected

Quick HIT

Amiodarone also functions as a Na channel blocker.

I. Ventricular Fibrillation (See Figure 1-15)

1. Lack of ordered ventricular contraction leads to **no CO** and is rapidly fatal
2. Frequently occurs after severe MI, post-Vtach

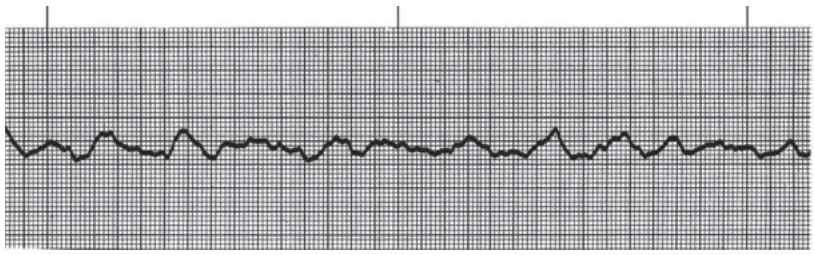


FIGURE 1-15
Ventricular fibrillation.
Ventricular fibrillation (coarse deflections present). Ventricular fibrillation: identifying ECG features; rhythm: none (P wave and QRS are absent); rate: none (P wave and QRS are absent); P waves: wavy, irregular deflection representative of ventricular quivering; deflections may be small (fine ventricular fibrillation) or coarse (coarse ventricular fibrillation); PR interval: not measurable; QRS complex: absent.
(From Kline-Tilford, A. M., & Haut, C. [2016]. *Lippincott Certification Review: Pediatric Acute Care Nurse Practitioner* [1st ed., p. 150]. Philadelphia, PA: Lippincott Williams & Wilkins, with permission.)

Table 1-7 Classes of Antiarrhythmic Medications

Class	General Mechanism of Action	Examples	Potential
IA	Na^+ channel blockers (prolong action potential)	Quinidine, procainamide	PSVT, Afib, A
IB	Na^+ channel blockers (shorten action potential)	Lidocaine, tocainide	Vtach
IC	Na^+ channel blockers (no effect on action potential)	Flecainide, propafenone	PSVT, Afib, A
II	β-Blockers	Propranolol, esmolol, metoprolol	PVC, PSVT, A
III	K^+ channel blockers	Amiodarone, sotalol, bretylium	Afib, Aflutte
IV	Ca^{2+} channel blockers	Verapamil, diltiazem	PSVT, MAT, A
Other	K^+ channel activation, decrease in intracellular cAMP	Adenosine	PSVT

Afib, atrial fibrillation; Aflutter, atrial flutter; cAMP, cyclic adenosine monophosphate; MAT, multifocal atrial tachycardia; PSVT, paroxysmal supra
PVC, premature ventricular contraction; Vtach, ventricular tachycardia.

3. **Risk factors** = CAD, MI

4. **H/P** = syncope, hypotension, pulselessness
5. **ECG** = **totally erratic tracing;** no P waves or QRS
6. **Treatment** = CPR, immediate electric cardioversion

J. Antiarrhythmic Medications (See Table 1-7)

VI. Heart Failure

A. Heart Physiology

1. Principles of contraction
   a. Increases in diastolic ventricular volume cause increases in cardiac muscle fiber stretching; this increased stretching leads to increased contraction force—the Frank–Starling relationship (i.e., increased **preload** causes increased ventricular output).
   b. Pressure generated by ventricles and end-systolic volume is dependent on load-opposing contraction (i.e., **afterload,** approximated at the MAP) but independent of stretch on fibers before contraction.
   c. Increasing **contractility** (force of contraction independent of preload and afterload) leads to greater tension at isometric contraction for a given preload.
2. Ejection fraction $(\text{EF}) = \dfrac{\text{SV}}{\text{end-diastolic volume}}$ (**normal EF = 55% to 75%**)
3. Changes in volume–pressure relationship determines compliance of heart
4. Insufficient CO for systemic demand results from progressive heart dysfunction (i.e., CHF)

Quick HIT

The heart does well in adjusting to changes in blood volume and work demands, but persistently high demands placed on it will cause it to gradually fail.

B. Systolic Dysfunction

1. Inadequate CO for systemic demand
2. Caused by decreased contractility, increased preload, increased afterload, HR abnormalities, or high output conditions (e.g., anemia, hyperthyroidism)

C. Diastolic Dysfunction

1. Decreased ventricular compliance leads to decreased ventricular filling, increased diastolic pressure, and decreased CO
2. Caused by hypertrophy or restrictive cardiomyopathy

Quick HIT

COPD leads to right-side hypertrophy that ends in right-sided failure (i.e., **cor pulmonale**).

Quick HIT

S_3 is the most frequent sign of CHF.

D. Congestive Heart Failure

1. Left side of heart
   a. Left ventricle (LV) **unable to produce adequate CO**
   b. Blood backs up, leading to pulmonary edema, which eventually causes pulmonary HTN
   c. Progressive **LVH** to compensate for poor output causes eventual failure because the heart is unable to keep pace with systemic need for CO
2. Right side of heart
   a. Increased pulmonary vascular resistance leads to **RVH** and systemic venous stasis
   b. **Most commonly caused by left-sided failure;** also can result from unrelated pulmonary HTN, valvular disease, or congenital defects
3. **Risk factors** = CAD, HTN, valvular disease, cardiomyopathy, COPD, drug toxicity, alcohol use
4. **H/P** = fatigue, dyspnea on exertion, orthopnea, paroxysmal nocturnal dyspnea, cough; displaced point of maximal impulse, S_3, jugular vein distention (JVD), rales, peripheral edema, hepatomegaly; symptoms and signs are more severe during exacerbations
5. **Workup** = plasma brain natriuretic peptide (BNP) and N-terminal pro-BNP will be increased with LV dysfunction and expansion

6. **Radiology** = chest x-ray (CXR) shows cardiac enlargement, **Kerley B lines** (i.e., increased marking of lung interlobular septa caused by pulmonary edema), **cephalization of pulmonary vessels** (i.e., increased marking of superior pulmonary vessels caused by congestion and stasis); echocardiogram can assess chamber size and function

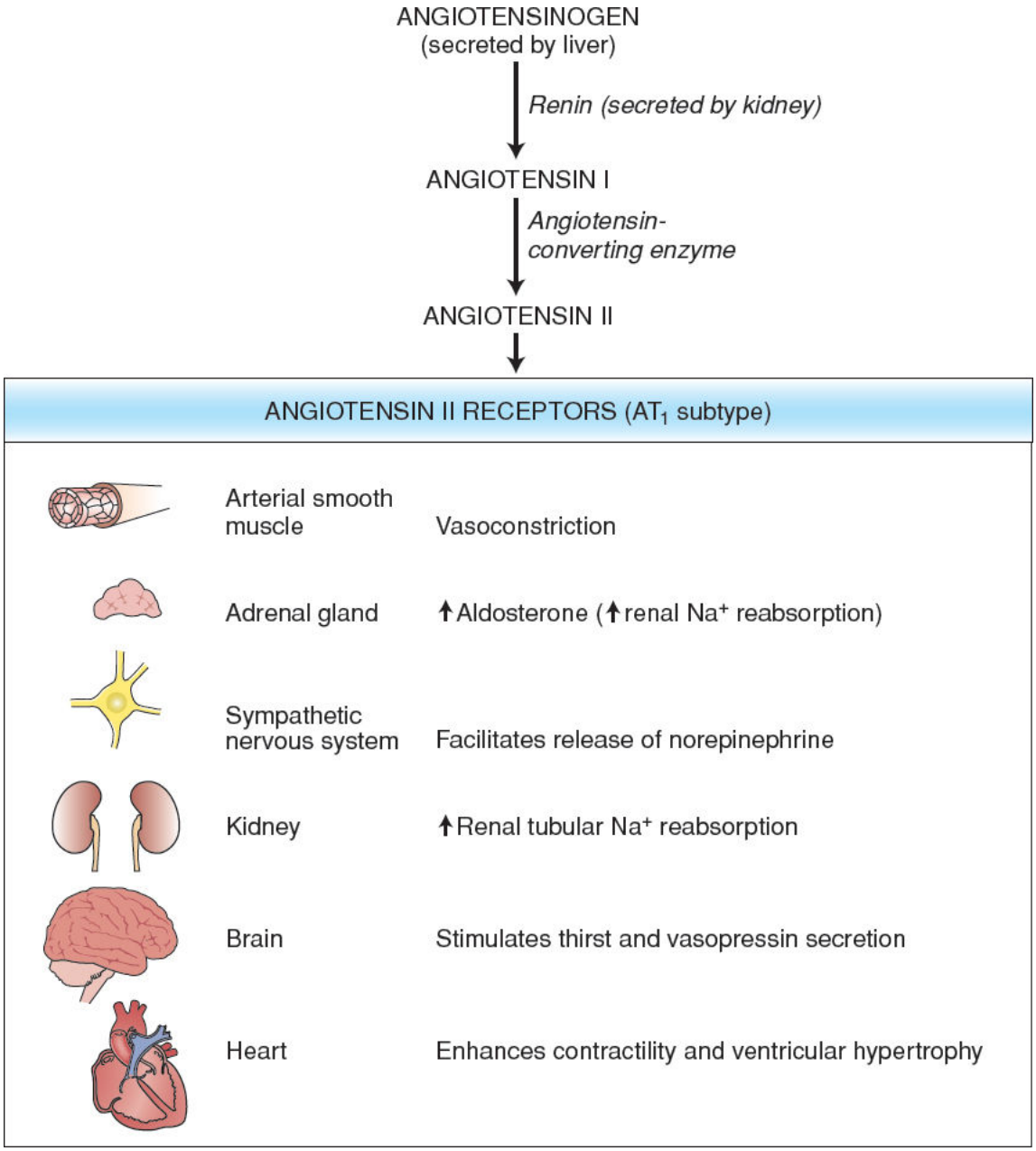


FIGURE **1-16**
Renin–angiotensin–aldosterone system and its end effects, which contribute to hypertension.
ACE-I acts to inhibit the conversion of angiotensin I to angiotensin II, and ARB block angiotensin II activity at the receptor level. ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blockers.
(Modified from Lilly, L. S. [2011]. *Pathophysiology of Heart Disease* [5th ed.]. Baltimore, MD: Lippincott Williams & Wilkins, with permission.)

7. **ECG** = possible findings consistent with ischemic disease, possible LVH
8. **Treatment**
   a. Systolic dysfunction—start pharmacologic therapy with vasodilators (nitrate), **loop diuretics** (decrease preload), and ACE-I or angiotensin receptor blockers (ARB) (decrease preload and afterload and increase CO); add β-blocker once patient is stable (not on acute phase) on **ACE-I;** add aldosterone antagonist (spironolactone or eplerenone) in select patients; digoxin (increases contractility) can be added to improve symptoms (see Figure 1-16)
   b. Diastolic dysfunction—use calcium channel blocker, ARB, or ACE-I to control blood pressure; β-blockers are useful for controlling HR and decreasing cardiac workload
   c. Treat underlying conditions that cause dysfunction (e.g., HTN, valvular pathology); salt-restricted diet helps avoid excessive intravascular fluid volume; assistive devices or cardiac transplant may be required in progressive cases

NEXT
STEP

ACE-I, a-blockers (bisoprolol, carvedilol, or extended-release metoprolol), and **aldosterone antagonists** have been shown to decrease mortality in CHF; consider incorporating these drugs in the treatment plans, when appropriate, because other medications have not been proved to reduce mortality.

VII. Cardiomyopathies (See Figure 1-17; Table 1-8)

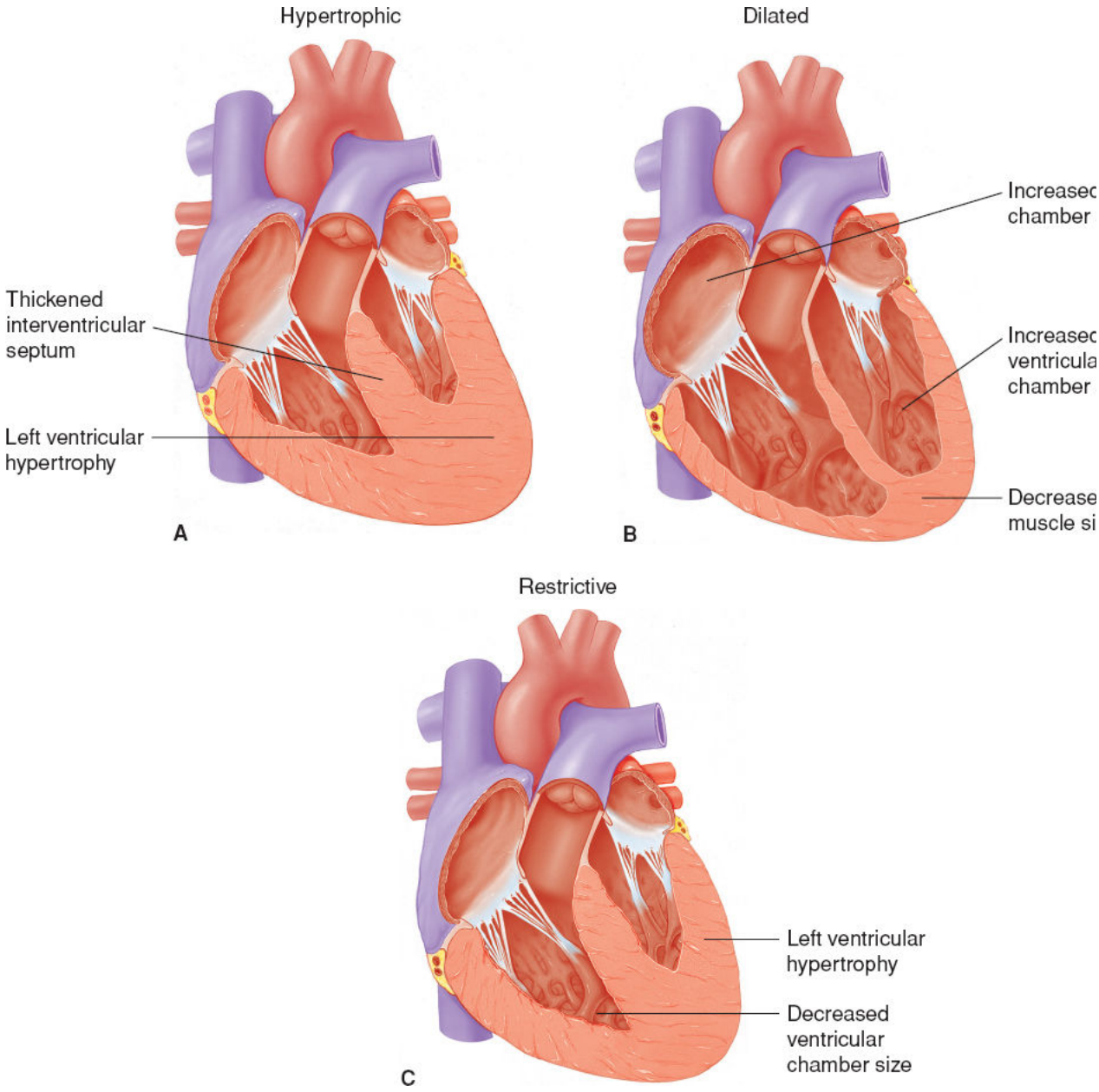


FIGURE 1-17
Diagrams of most common variations of cardiomyopathy.
A: Hypertrophic: note ventricular wall and septal thickening leading to outlet obstruction. **B:** Dilated: note decreased wall thickness and increased ventricular size. **C:** Restrictive: note increased ventricular wall thickness and decreased chamber size.
(From Anatomical Chart Company. [2010]. *Atlas of Pathophysiology* [3rd ed., p. 45]. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins.)

Table 1-8 Cardiomyopathies

Cardiomyopathy (Description)	Causes	Symptoms	Examination
Hypertrophic (ventricular hypertrophy; thickened septum causes decreased filling; LV outflow obstruction; both systolic and diastolic dysfunction)	• Congenital (**autosomal dominant**)	• Syncope • Dyspnea • Palpitations • Chest pain • **Symptoms worse with exertion**	• S_4 • Systolic murmu Valsalva, softer • Diffuse, forcefu impulse • ECG may show LVH, abnormal
Dilated (ventricular dilation causes systolic dysfunction)	• **Idiopathic** • Alcohol use • Beriberi • Coxsackievirus B myocarditis • Cocaine use • Doxorubicin • HIV • Pregnancy • Hemochromatosis • Ischemic heart disease • Chagas disease	• Similar to CHF and bivalvular regurgitation	• S_3 • **Systolic and d murmurs** • ECG may show T-wave changes tachycardia, LB
Restrictive (decreased heart compliance causes impaired diastolic filling)	• Sarcoidosis • Amyloidosis	• Similar to CHF with right-sided symptoms worse	• Ascites • JVD • Biopsy is diagn

ACE-I, angiotensin-converting enzyme inhibitors; CHF, congestive heart failure; CXR, chest x-ray; ECG, electrocardiogram; Echo, echocardiogram; JV
ventricular hypertrophy.

NEXT
STEP

Differentiate restrictive cardiomyopathy from constrictive pericarditis with CT or MRI.

***Quick* HIT**

Squatting relieves symptoms in hypertrophic cardiomyopathy.

***Quick* HIT**

Hypertrophic cardiomyopathy is the most common cause of sudden death in **young athletes.**

***Quick* HIT**

Dilated cardiomyopathy accounts for 90% of all cardiomyopathies.

VIII. Valvular Diseases

A. Murmurs (See Figure 1-18; Table 1-9)

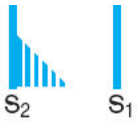
Diagram				
Murmur Type	Systolic ejection	Holosystolic	Late systolic	Early diastolic
Examples (Location/ Radiation)	Aortic stenosis (2nd right interspace → neck but may radiate widely) Pulmonic stenosis (2nd–3rd left interspace)	Mitral regurgitation (Apex → axilla) Tricuspid regurgitation (LLSB → RLSB)	Mitral valve prolapse (Apex → axilla)	Aortic regurgitati (Along left side c sternum) Pulmonic regurg (Upper left side c sternum)

FIGURE **1-18**

Common murmurs associated with valvular diseases.
LLSB, left lower sternal border; RLSB, right lower sternal border.
(Modified from Lilly, L. S. [2011]. *Pathophysiology of Heart Disease* [5th ed.]. Baltimore, MD: Lippincott Williams & Wilkins, with permission.)

Table 1-9 Valvular Diseases

Valvular Disease (Description)	Causes	Symptoms	Examination	Radiology
Aortic stenosis (narrowing of aortic valve causes obstructed blood flow from LV)	• **Congenital defect** • RHD • Calcification in elderly patients • Tertiary syphilis	• Chest pain • Dyspnea on exertion • **Syncope**	• Weak, prolonged pulse • **Crescendo–decrescendo systolic murmur** radiating from right upper sternal border to carotids • Weak S_2 • Valsalva decreases murmur	• Calcified aortic valve, dilated aorta on CXR • Echo and cardiac catheterization helpful for diagnosis
Mitral regurgitation (mitral valve incompetency causes blood backflow to LA)	• Mitral valve prolapse (floppy valve) • **RHD** • Papillary muscle dysfunction • Endocarditis • LV dilation	• Asymptomatic in early/mild cases • Palpitations • Dyspnea on exertion • Orthopnea • Paroxysmal nocturnal dyspnea	• Harsh blowing **holosystolic murmur** radiating from apex to axilla • S_3 • Widely split S_2 • Midsystolic click	• LVH; LA enlargement on CXR • Echo helpful for diagnosis
Aortic regurgitation (aortic valve incompetency causes blood backflow to LV)	• Congenital defect • Endocarditis • RHD • Tertiary syphilis • Aortic root dilatation (possibly from aortic dissection)	• Initially asymptomatic • Dyspnea on exertion • Chest pain • Orthopnea	• Bounding pulses • Widened pulse pressure • **Diastolic decrescendo murmur** at right second intercostal space • Late diastolic rumble (**Austin Flint murmur**) • Capillary pulsations in nail bed, more visible when pressure is applied (**Quincke sign**)	• Dilated aorta; LV enlargement on CXR • Echo helpful for diagnosis
Mitral stenosis (obstructed blood flow to LV causes increased LA volume)	• **RHD**	• Initially asymptomatic (~10 yr) • Dyspnea on exertion • Orthopnea • Paroxysmal nocturnal dyspnea • Peripheral edema • Hepatomegaly	• Opening snap after S_2 • Diastolic rumble • Loud S_1	• RVH; LA enlargement; mitral valve calcification on CXR • Echo helpful for diagnosis
Mitral valve prolapse (MVP) (redundant leaflet[s] prolapses toward the left atrium during systole)	• Connective tissue disorders	• Usually asymptomatic • Palpitations • Atypical chest pain • Some anxiety reactions have been linked • Fatigue	• Mid-to-late systolic click or murmur • Crescendo into S_2 • Standing or preload decreases will increase murmur • Squatting or increasing preload decreases murmur	• Echo helpful for diagnosis as most will be asymptomatic

Tricuspid regurgitation (TR)	• May be present in up to 70% of normal adults • Secondary to RV dilation • LV failure • RV infarction • Inferior wall MI • Pulmonary HTN leading to cor pulmonale • **Tricuspid endocarditis**	• Asymptomatic unless patient develops pulmonary HTN or right HF	• Blowing holosystolic murmur heard in left lower sternal border • Intensified with inspiration • Reduced with expiration	• Echo can help quantify the amount of regurgitation and measure pulmonary pressures

ACE-I, angiotensin-converting enzyme inhibitors; Afib, atrial fibrillation; CXR, chest x-ray; Echo, echocardiogram; LA, left atrium; LV, left ventricle; LV trophy; RHD, rheumatic heart disease; RVH, right ventricular hypertrophy.

B. Acute Rheumatic Fever

1. Uncommon sequela of **untreated group A streptococcus** infection
2. Streptococcus infection can provoke autoantibodies that attack joints and heart valves (mitral > aortic > tricuspid).
3. Incidence is low in the United States because of antibiotic treatment
4. The term "**rheumatic heart disease**" describes both the acute carditis (pericarditis, myocarditis, valvulitis) and chronic valvular damage
5. **H/P** = migratory arthritis, hot and swollen joints, fever, subcutaneous nodules on extensor surfaces, Sydenham chorea (i.e., purposeless involuntary movement), erythema marginatum (i.e., painless rash)
6. Diagnosis made using Jones criteria (see Figure 1-19).
7. **Workup** = increased ESR, C-reactive protein (CRP), and white blood cell (WBC) count; 90% of patients have antistreptococcal antibodies
8. **ECG** = increased PR interval
9. **Treatment** = NSAIDs for joint inflammation; use corticosteroids, if carditis is severe; β-lactam (penicillin family) antibiotic for infection
10. **Complications** = progressive valve damage if untreated

Quick HIT

RHD only occurs in 3% of untreated streptococcal infections.

JONES CRITERIA for Acute Rheumatic Fever — Think J♥NES PEACE

Major Criteria	Minor Criteria
J: Joints (polyarthritis, hot/swollen joints)	P: Previous rheumatic fever
♥: Heart (carditis, valve damage)	E: ECG with PR prolongation
N: Nodules (subcutaneous, extensor surfaces)	A: Arthralgias
E: Erythema marginatum (painless rash)	C: CRP and ESR elevated
S: Sydenham chorea (flinching movement disorder)	E: Elevated temperature

Diagnosis of RHD is made with a history of recent streptococcal infection and either the presence of 2 major criteria or 1 major with 2 minor criteria.

FIGURE 1-19
JONES criteria mnemonic for diagnosis of rheumatic heart disease (RHD).
CRP, C-reactive protein; ECG, electrocardiogram; ESR, erythrocyte sedimentation rate; RHD, rheumatic heart disease.

Quick HIT

ST elevation is seen in acute pericarditis as well as in MI, but acute pericarditis also demonstrates **PR depression** and ST elevation in **most leads** (MI frequently does not show PR depression, and ST elevation is focal).

NEXT
STEP

If ST elevation is seen on ECG, full workup is required to rule out MI.

NEXT
STEP

Pericardial effusions are usually **transudates** (low in proteins, specific gravity <1.012); if **exudates** (rich in proteins, specific gravity >1.020) are collected during pericardiocentesis, perform workup for neoplasm, fibrotic disease, or tuberculous pericarditis.

NEXT
STEP

With a finding of **Beck triad** (hypotension, distant heart sounds, and distended neck veins), think of cardiac tamponade and perform an urgent pericardiocentesis!

IX. Pericardial Diseases

A. Acute Pericarditis

1. Acute inflammation of the pericardial sac accompanied by pericardial effusion
2. Caused by **viral infection,** tuberculosis, systemic lupus erythematosus (SLE), uremia, neoplasm, drug toxicity (e.g., isoniazid, hydralazine), post-MI inflammation **(Dressler syndrome), radiation, recent heart surgery**
3. **H/P** = anterior chest pain with inspiration (i.e., **pleuritic chest pain**), dyspnea, cough; **pain lessens with leaning forward;** fever, **friction rub** (best heard when leaning forward); pulsus paradoxus (i.e., fall in systolic blood pressure >10 mm Hg with inspiration) occurs because increased physiologic right ventricle (RV) filling during inspiration combined with pathologic LV compression by pericardial effusion causes impaired LV filling, decreased stroke volume, and decreased inspiratory systolic blood pressure
4. **ECG** = global **ST elevation,** PR depression
5. **Workup** = CXR is helpful in ruling out other systemic causes; effusion frequently seen on echocardiogram
6. **Treatment** = treat underlying cause; pericardiocentesis for large effusions; nonsteroidal anti-inflammatory drugs (NSAIDs) for pain and inflammation; colchicine may be useful for preventing recurrence owing to viral or idiopathic causes
7. **Complications** = chronic constrictive pericarditis if untreated

B. Chronic Constrictive Pericarditis

1. Sequela of chronic untreated pericardial irritation
2. Diffuse thickening of pericardium with possible calcifications leads to decreased diastolic filling and decreased CO
3. Most commonly caused by **radiation** or **heart surgery**
4. **H/P** = symptoms consistent with HF (JVD, dyspnea on exertion, orthopnea, peripheral edema), increasing JVD with inspiration (**Kussmaul sign**); Afib common
5. **Workup** = cardiac catheterization shows **equal pressure in all chambers,** possible pericardial calcifications on CXR; echocardiogram, computed tomography (CT), and magnetic resonance imaging (MRI) show pericardial thickening
6. **Treatment** = NSAIDs, colchicine, corticosteroids; surgical excision of pericardium (high mortality)

C. Cardiac Tamponade

1. Large pericardial effusion causes compression of heart and **greatly decreased CO;** can result from progressive, **acute pericarditis, chest trauma,** LV rupture following MI, or dissecting aortic aneurysm
2. High mortality
3. **H/P** = dyspnea, tachycardia, tachypnea; JVD, pulsus paradoxus
4. **Workup** = enlarged cardiac silhouette on CXR; large effusion seen on echocardiogram
5. **ECG** = low-voltage, sinus tachycardia; electrical alternans is relatively specific but not sensitive
6. **Treatment** = **immediate pericardiocentesis**

X. Myocardial Infections

A. Myocarditis

1. Inflammatory reaction in heart limited to cardiac muscle involvement

2. Most commonly caused by infection (e.g., viruses [**Coxsackie virus,** parvovirus B19, HHV-6, adenovirus, echovirus, Epstein–Barr virus (EBV), cytomegalovirus (CMV), influenza virus], bacteria, rickettsiae, fungi, parasites)
3. Occasionally caused by **drug toxicity** (e.g., doxorubicin, chloroquine, penicillins, sulfonamides, cocaine, radiation), toxins, or endocrine abnormalities
4. **H/P** = patient may report history of recent upper respiratory infection; pleuritic chest pain, dyspnea, S_3 or S_4 heart sound, possible diastolic murmur, possible friction rub
5. **ECG** = ST- and T-wave changes, conduction abnormalities
6. **Workup** = possible cardiomegaly on CXR; echocardiogram useful in assessing heart function; difficult to diagnose because of variations in laboratory findings; viral titers and serology may help suggest a particular infectious agent; myocardial biopsy frequently shows myocyte inflammation with primarily monocytes and macrophages and focal areas of necrosis
7. **Treatment** = treat infection; stop offending medications; avoid exertional activity; treat HF symptoms as for acute exacerbation of HF

Quick HIT

Myocarditis in South and Central America is commonly caused by *Trypanosoma cruzi* (**Chagas disease**) and, in these cases, may be associated with **achalasia.**

Quick HIT

Several of the drugs that cause myocarditis are used in **cancer** therapy (cyclophosphamide, doxorubicin, daunorubicin).

Quick HIT

Prosthetic valves are particularly susceptible to *Staphylococcus epidermidis* and *Staphylococcus aureus* infections.

B. Endocarditis

1. Bacterial infection of endocardium (i.e., inner lining of heart), with or without valve involvement
2. More common in patients with **congenital heart defects, IV drug abuse,** or prosthetic valves

Table 1-10 Duke Criteria for Diagnosis of Infective Endocarditis

Definitive diagnosis of infective endocarditis requires:	• Direct histologic evidence of infective endocarditis **OR** • Positive Gram stain or culture from surgical debridement of cardiac abscess or autopsy specimen **OR** • 2 major criteria **OR** • 1 major and 3 minor criteria **OR** • 5 minor criteria
Major Criteria	**Minor Criteria**
• Serial blood cultures positive for organisms associated with infective endocarditis • Presence of vegetations or cardiac abscess seen on echocardiogram • Evidence of new-onset valvular regurgitation • Blood culture positive for *Coxiella burnetii*	• Predisposing heart condition or intravenous drug use • Fever ≥38°C • Vascular phenomenon (e.g., arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial hemorrhage, conjunctival hemorrhage, Janeway lesions) • Immunologic phenomenon (e.g., glomerulonephritis, Osler nodes, Roth spots, positive rheumatoid factor) • Positive cultures not meeting requirements for major criteria **OR** • Serologic evidence of infection without positive culture

3. Patients with SLE may present in a similar manner with noninfective endocarditis (**Libman–Sacks endocarditis**)
4. Both acute (sudden presentation) and subacute (insidious progression) forms
   a. **Acute endocarditis** is caused by *Staphylococcus aureus, Streptococcus pneumoniae, Streptococcus pyogenes, Neisseria gonorrhoeae*
   b. **Subacute endocarditis** is caused by viridans streptococci, *Enterococcus,* fungi, and *Staphylococcus epidermidis*
5. **Duke criteria** are used as guide for making diagnosis (see Table 1-10)
6. **H/P** = fever (very high in acute form), chills, night sweats, fatigue, arthralgias; possible new murmur; small, tender nodules on finger and toe pads (i.e., **Osler nodes**); peripheral petechiae (i.e., **Janeway lesions**), subungual petechiae (i.e., **splinter hemorrhages**), retinal hemorrhages (i.e., **Roth spots**)
7. **Workup** = serial blood cultures will grow same pathogen; increased ESR; increased CRP; echocardiogram (preferably TEE) may show vegetations on valves; CXR may reveal congestion consistent with septic emboli and right-sided HF
8. **Treatment** = **long-term (4 to 6 weeks) IV antibiotics** (initially broad spectrum, then bug specific); β-lactam plus an aminoglycoside is the most commonly used regimen (adjusted for resistance and particular pathogen); antibiotic

prophylaxis before surgery or dental work if valves are damaged; valve replacement may be necessary for severely damaged valves

9. **Complications** = severe damage to endocardium and valves, **septic embolization,** or abscess formation, if untreated

XI. Shock

A. Circulatory collapse in which blood delivery is inadequate for tissue demands (see Table 1-11)
B. High mortality without timely treatment
C. **H/P** = history should consider allergies, changes in medications, recent medication use, infection history, or recent cardiac/neurologic events; hypotension, cool/clammy skin, changes in mental status, decreased urine output
D. **Workup** = complete blood count (CBC), electrolyte panel, arterial blood gases (ABG), cardiac enzymes, liver function tests, lactic acid, prothrombin time or partial thromboplastin time (PT/PTT), toxicology screen; urinalysis should be included in workup

Table 1-11 Common Types of Shock

Type of Shock	Mechanism	Cause	Treatment
Cardiogenic	Failure of myocardial pump	MI, arrhythmias, cardiac contusion/tamponade, pulmonary embolism	Inotropes (dobutamine), intra-ao PTCA (for MI)
Septic	Decreased total peripheral resistance	Gram-negative bacteria, DIC, possibly endotoxin mediated	Treat underlying infection, press nephrine), IV fluids
Hypovolemic	Inadequate blood or plasma volume	Hemorrhage, severe burns, trauma	IV fluids, transfusions, surgery m stop volume loss; specialized dre may be required with severe bur ing fluid loss
Anaphylactic	Generalized type I hypersensitivity reaction	Massive degranulation of mast cells and basophils in response to allergic reaction	Maintain airway, epinephrine, di fluids
Neurogenic	Widespread peripheral vasodila- tion and bradycardia	Brain or spinal cord injury	IV fluids, pressor agents, atropin

DIC, disseminated intravascular coagulation; IV, intravenous; MI, myocardial infarction; PTCA, percutaneous transluminal coronary angioplasty.

XII. Vascular Diseases

A. Aortic Conditions

1. **Abdominal aortic aneurysm (AAA)**
   a. Localized dilation of aorta, most commonly inferior to the renal arteries
   b. **Risk factors** = tobacco use, age >55 years, atherosclerosis, HTN, family history, fluoroquinolone use
   c. **H/P** = **frequently asymptomatic** until later progression; possible lower back pain; **pulsating abdominal mass, abdominal bruits;** hypotension and severe pain occur with any rupture
   d. **Radiology** = ultrasound (US) can detect location and size quickly; CT or MRI is used for more accurate localization and size determination
   e. **Screening** = United States Preventive Services Task Force (USPSTF) recommends a one-time screening US for men aged 65 to 75 years with a history of smoking
   f. **Treatment** = monitor with periodic US if <5.5 cm diameter in men or <5.0 cm in women; surgical repair (open or using endovascular stenting) if symptomatic or ≥5.5 cm diameter in men or ≥5.0 cm in women
   g. **Complications** = untreated aortic aneurysms can rupture with >90% mortality
2. **Aortic dissection**
   a. Intimal tear leads to blood entering media, causing formation of false lumen
   b. Classification (two types)
      (1) **Stanford A** aortic dissection involves ascending aorta
      (2) **Stanford B** is distal to left subclavian artery
      or
      (3) DeBakey I ascending to descending aorta
      (4) DeBakey II ascending aorta
      (5) DeBakey III descending aorta

c. **Risk factors** = HTN, smoking, coarctation of the aorta, syphilis, Ehlers–Danlos syndrome, Marfan syndrome, trauma (rare)
d. **H/P** = acute, "**ripping**" chest pain, syncope; decreased peripheral pulses, normal or increased blood pressure
e. **ECG** = normal or LVH
f. **Workup** = widening of aorta and superior mediastinum on CXR; CT with contrast, echocardiogram, MRI, magnetic resonance angiography (MRA), or angiography good for definite diagnosis
g. **Treatment** = stabilize blood pressure if unstable; Stanford A dissections need emergency surgery; Stanford B dissections can be treated medically unless rupture or occlusion develops
   (1) β-Blockers: decrease shearing forces; improve HR and BP
   (2) Nicardipine: vasodilation to decrease BP; use after β-blocker initiation
   (3) Nitroprusside: vasodilation to decrease BP; use after β-blocker initiation; fallen out of fashion due to complicated storage
h. **Complications** = possible MI, renal insufficiency, ischemic colitis, stroke, or paraplegia

Quick HIT

Normal aortic diameter is 1.5 to 2.5 cm; an increase to twice this size or more is considered aneurysmal.

Quick HIT

Rupture of an aortic aneurysm is usually fatal.

NEXT
STEP

If a patient presents with new severe chest pain, an immediate ECG may help to differentiate an aortic dissection from an acute MI (ECG will be normal or will show mild LV hypertrophy in aortic dissection and will be abnormal in MI, except during early evolution).

MNEMONIC

Remember the six Ps to grade PVD severity: **P**ain, **P**allor, **P**oikilothermia, **P**ulselessness, **P**aresthesia, and **P**aralysis.

Quick HIT

Removal or sclerotherapy of the saphenous vein is discouraged because of its potential use in bypass grafting.

B. Peripheral Vascular Disease (PVD)

1. Occlusion of peripheral blood supply secondary to atherosclerosis
2. **Risk factors** = HTN, DM, CAD, smoking
3. **H/P** = leg pain with activity that improves with rest (i.e., **intermittent claudication**), resting leg pain in severe disease; dry skin, skin ulcers, decreased hair growth in affected area; male erectile dysfunction with aortoiliac disease
4. **Workup** = ankle–brachial index (ABI) is ratio of systolic blood pressure at ankle to that at brachial artery; ABI ≤0.9 indicates vascular insufficiency at ankle; ABI <0.4 indicates severe disease (frequently seen with resting pain)
5. **Radiology** = US is useful for locating stenosis and variations in blood pressure; CT or MR angiography or traditional angiography will map narrowing in the arterial distribution of interest
6. **Treatment** = exercise (increases collateral circulation); instruction in foot examination (early detection of ulcers from vascular insufficiency); treatment of underlying diseases; ASA, **pentoxifylline,** or **cilostazol** to help to slow occlusion; percutaneous transluminal angioplasty (PTA) indicated for failed nonoperative treatment, significant disability caused by claudication, or predictable benefit and improvement in prognosis; bypass grafting if incapacitating claudication, resting pain, or necrotic foot lesions develop; prolonged ischemia may require limb amputation

Quick HIT

Virchow triad = blood stasis, hypercoagulability, and vascular damage increase patients' risk of DVT.

Quick HIT

Homan sign (calf pain with passive foot dorsiflexion) is unreliable for DVT detection.

NEXT

STEP

Patients with recent surgery or who are at increased risk for hemorrhage should receive an **IVC filter** instead of anticoagulation to reduce the risk of pulmonary embolism.

C. Venous Conditions

1. **Varicosities**
   a. Incompetent venous valves that cause elongation, dilation, and tortuosity of veins
   b. **H/P** = usually asymptomatic; pain and fatigue that lessen with leg elevation; possible visible or palpable veins, increased local pigmentation, edema, or ulceration
   c. **Treatment** = exercise, compression hosiery, leg elevation; surgical removal or injection sclerotherapy for cosmetic improvement or symptomatic varicosities
2. **Arteriovenous malformations** (**AVM**)
   a. Abnormal communications between arteries and veins
   b. Congenital or acquired
   c. **H/P** = palpable, warm, pulsating masses, if superficial; painful if mass compresses adjacent structures
   d. Large AVM can cause local ischemia and increase the risk of thrombus formation
   e. **Treatment** = surgical removal or sclerosis, if symptomatic, or if located in brain or bowel
3. **Deep vein thrombosis (DVT)**
   a. Development of thrombosis in large vein; most common in lower extremity
   b. Location, in order of decreasing frequency: **calf,** femoral, popliteal, and iliac veins
   c. Can cause inflammation of affected vein (i.e., **thrombophlebitis**)
   d. **Risk factors** = **prolonged inactivity** (travel, immobilization), HF, hypercoagulable states, neoplasm, **pregnancy,** OCP use, **tobacco use,** vascular trauma
   e. **H/P** = possibly asymptomatic; deep leg pain, swelling, warmth
   f. **Workup** = D-dimer will be elevated with DVT formation, but test is more useful in using a normal result to rule out DVT
   g. **Radiology** = compressive venous US is used for detection
   h. **Treatment** = leg elevation; low–molecular-weight heparin or unfractionated heparin initially, warfarin for long-term management; inferior vena cava (IVC) filter should be placed in a patient with contraindications to anticoagulation
   i. **Complications** = clot can embolize to lungs (i.e., **pulmonary embolus**) with 40% mortality; chronic DVT can cause chronic venous insufficiency
4. **Lymphedema**
   a. Disruption of lymphatic circulation
   b. Primary (or congenital) is rare, most likely caused by surgeries involving lymph node dissection, or parasitic infections (in developing countries)
   c. **H/P** = peripheral edema and chronic infections of the extremities may happen; in mastectomy patients it is seen more in upper extremity; may be seen in patients with Turner syndrome
   d. **Workup** = clinical, labs, and imaging may be used to rule out other causes of edema (i.e., cardiac, metabolic)
   e. **Treatment** = manage symptoms, pressure garments, awareness of concomitant risk for infection and treatment for usual (gram+) bacteria. Diuretics are generally contraindicated

D. Vasculitis

1. **Temporal (giant cell) arteritis**
   a. Commonly caused by subacute granulomatous inflammation of the external carotid and vertebral arteries
   b. **Risk factors** = **women** > **men, 50 years of age and older**
   c. Half of patients also have **polymyalgia rheumatica**
   d. **H/P** = **new onset of headache** (unilateral or bilateral) with scalp pain, **temporal region tenderness,** jaw claudication, **transient or permanent monocular blindness,** weight loss, myalgias, arthralgias, fever; funduscopic examination should be performed to address vision loss (may show thrombosis of ophthalmic or ciliary arteries)
   e. **Workup** = increased ESR; temporal artery biopsy shows inflammation in vessel media and lymphocytes, plasma cells, or giant cells in vessel adventitia; US may show stenosis or occlusion of temporal or occipital arteries
   f. **Treatment** = prednisone for 1 to 2 months followed by tapering; low-dose ASA to reduce risk of vision loss or stroke from vessel occlusion; vitamin D and calcium supplementation to reduce risk of osteoporosis from prolonged high-dose corticosteroid use; ophthalmology follow-up
2. **Takayasu arteritis**
   a. Inflammation of aortic arch and its branches
   b. Can cause cerebrovascular and myocardial ischemia
   c. **Risk factors** = Asian heritage, women 10 to 40 years of age
   d. **H/P** = malaise, vertigo, syncope; fever, decreased carotid and limb pulses
   e. **Workup** = biopsy of affected vessel shows plasma cells and lymphocytes in media and adventitia, giant cells, and vascular fibrosis
   f. **Radiology** = arteriography may detect abnormal vessels and stenoses; **CT** or **MRI** is useful for detecting vessel wall abnormalities
   g. **Treatment** = corticosteroids, immunosuppressive agents; bypass grafting of obstructed vessels

3. **Kawasaki disease**
   a. Necrotizing inflammation of large, medium, and small vessels
   b. Most commonly seen in **young children**
   c. Coronary vasculitis develops in 25% of patients, leading to possible aneurysm, MI, or sudden death.
   d. **H/P** = fever, lymphadenopathy, conjunctival lesions, maculopapular rash, edema, eventual desquamation of hands and feet
   e. **Workup** = possible autoantibodies to endothelial cells; echocardiogram can detect coronary artery aneurysms (particularly useful when performed with dobutamine stress test); angiography can detect coronary vessel irregularities
   f. **Treatment** = ASA, IV gamma globulin; frequently self-limited
4. **Polyarteritis nodosa**
   a. Inflammation of small or medium arteries leads to ischemia
   b. Affects kidneys, heart, gastrointestinal (GI) tract, muscles, nerves, joints; **spares the lungs**
   c. **Risk factors** = **hepatitis B or C;** young > elderly; men > women
   d. **H/P** = fever, HTN, hematuria, anemia, neuropathy, weight loss, joint pain, palpable purpura, or ulcers on skin
   e. **Workup** = increased WBC, decreased hemoglobin (Hgb) and hematocrit, increased ESR, proteinuria, hematuria; negative perinuclear antineutrophil cytoplasmic antibodies (**p-ANCA**); arterial biopsy may help in diagnosis; **angiography** may show numerous aneurysms
   f. **Treatment** = corticosteroids, immunosuppressive agents
5. **Eosinophilic granulomatosis with polyangiitis (Churg–Strauss syndrome)**
   a. Inflammation of small or medium arteries
   b. **H/P** = **asthmatic symptoms,** fatigue, malaise, mononeuropathy (pain, paresthesia, or weakness); erythematous or papular rash
   c. **Workup** = increased serum eosinophils, increased ESR, p-ANCA; lung biopsy may show eosinophilic granulomas
   d. **Treatment** = corticosteroids, immunosuppressive agents
6. **Henoch–Schönlein purpura**
   a. IgA immune complex–mediated vasculitis affecting arterioles, capillaries, and venules
   b. More frequently in **children** than adults
   c. **H/P** = **recent upper respiratory infection; palpable purpura** on the buttocks and lower extremities, abdominal pain and GI bleeding, polyarticular arthritis/arthralgias, hematuria
   d. **Workup** = biopsy of purpura demonstrates **IgA deposition;** similar findings in renal biopsy
   e. **Treatment** = frequently self-limited; use corticosteroids for severe GI symptoms

NEXT
STEP

If temporal arteritis is suggested from the H/P, do not wait for temporal artery biopsy to start prednisone.

QUESTIONS

1. A 38-year-old male is evaluated at this PCP for a routine evaluation. Today his examination is remarkable for a BP of 147/78 mm Hg on both extremities while the patient is calm and seated. The patient has no other complaints and remainder of examination is unremarkable. Initial laboratory tests are normal. What is the next best step?

   A. Start patient on an antihypertensive medication
   B. Recommend lifestyle modifications and recheck in 2 months
   C. Refer to emergency department for admission for hypertensive urgency
   D. Send to cardiologist emergently for recommendations

2. A 52-year-old male is on a routine evaluation and is found to have persistent elevated BPs despite prior intervention. He currently only takes medications for his DM. His blood glucose today is within expected range. If the decision is to start an antihypertensive medication, which one should be strongly considered as first line for this patient?

   A. Hydralazine
   B. Atenolol
   C. Amlodipine
   D. Lisinopril

3. A 60-year-old male is evaluated by his PCP after starting a recent lipid-lowering agent. The patient feels well despite some mild muscle aches in the early days after therapy initiation. The labs today show moderate elevation of AST and ALT, with normal tests otherwise. What is the most likely medication causing the patient's findings?

   A. Cholestyramine
   B. Ezetimibe
   C. Niacin
   D. Simvastatin

4. True or False? Nitroglycerin can be used to rule in or rule out myocardial ischemia as the cause of chest pain.

   A. True
   B. False

5. True or False? A negative stress test rules out coronary artery disease.

   A. True
   B. False

6. A 65-year-old male with PMHx of DM, HTN, hyperlipidemia presents with an acute myocardial infarction of several hours in evolution. He has cardiac intervention performed without complications. Which of the following poses the earliest risk of sudden cardiac death post-myocardial infarction?

   A. Ventricular wall rupture
   B. Pulmonary embolism
   C. An arrhythmia (Vfib/Vtach)
   D. Ventricular wall aneurysm

7. A 56-year-old male with history of COPD presents complaining of worsening cough and increased sputum to the primary care doctor. On evaluation, the patient is calm and in no severe distress with scattered wheezing heard on auscultation. The rest of the examination is normal and the patient has no other complaints. An ECG is performed. This ECG is an example of?

   A. Atrial fibrillation
   B. Atrial flutter
   C. Multifocal atrial tachycardia
   D. Ventricular tachycardia

8. A 67-year-old female with Hx of HTN, DM, CAD, CHF presents to the emergency department after 3 days of worsening palpitations. The patient denies any chest pain or shortness of breath. Physical examination is remarkable for tachycardia upon palpation. What is the diagnosis?

   A. Atrial fibrillation
   B. Atrial flutter
   C. Multifocal atrial tachycardia
   D. Ventricular tachycardia

9. A 62-year-old man presents to the primary care complaining of worsening shortness of breath, orthopnea, and fatigue. A week ago the patient was admitted to the hospital after having a "heart attack." On physical examination the patient seems mildly uncomfortable, has an audible S_3 on auscultation, and bilateral leg edema. What laboratory test do you expect to see elevated on this patient?

   A. White blood cell count
   B. Lactic acid
   C. BUN and creatinine
   D. Brain natriuretic peptide

10. True or False. A patient presents with an acute exacerbation of congestive heart failure. The patient is in tripod position, tachypneic, diaphoretic, and hypertensive. Initial management includes a β-blocker like metoprolol.

    A. True
    B. False

11. A 70-year-old male with Hx of HTN, CAD, and an “irregular rhythm” is evaluated in the emergency department for fatigue and syncope. On evaluation, the patient shows atrial fibrillation and a crescendo–decrescendo systolic murmur in the carotids. This patient’s reason for syncope is due to what valvular disorder?

    A. Aortic stenosis
    B. Mitral valve prolapse
    C. Mitral stenosis
    D. Tricuspid regurgitation

12. The management of the above valvular disorder is…

    A. Antiarrhythmics
    B. Diuresis
    C. Valve replacement
    D. Antibiotics

13. A 40-year-old male complains of fever and multiple swollen joints with pain. Physical examination reveals subcutaneous nodules, and a difficult-to-distinguish new heart murmur. This patient should be evaluated for what condition?

    A. IV drug abuse
    B. Human immunodeficiency virus
    C. Rheumatic fever
    D. Aortic regurgitation

14. A 16-year-old male comes to the emergency room after having a syncopal event while in physical education class. An ECG shows LVH and abnormal “dagger-like” Q waves. Physical examination is remarkable for a systolic murmur that increases with Valsalva maneuvers. Family explains how his father died suddenly at an early age for some heart condition. This is concerning for?

    A. Dehydration
    B. Rheumatic heart disease
    C. Hypertrophic cardiomyopathy
    D. Valvular insufficiency

15. A patient with Hx of Lupus presents to the primary care doctor after several days of worsening fever, shortness of breath, and cough. Physical examination reveals a friction rub. What do you expect to see on this patient’s ECG?

    A. Sinus bradycardia
    B. Diffuse ST-segment elevations
    C. PR interval depression
    D. Both B and C

16. A 55-year-old female is evaluated by her primary care physician after a flu-like illness with chest discomfort and shortness of breath. Her studies including ECG, CT of the chest, and cardiac enzymes have been reported as negative. Her influenza test was positive at onset. Physical examination reveals audible S_4, not present before. Echocardiogram shows abnormal heart function. This patient may be showing symptoms of:

    A. Post-viral myocarditis
    B. Acute myocardial infarction
    C. Pulmonary embolism
    D. Post-viral pneumonia

17. A 67-year-old male presents with shortness of breath, chest pain, and feeling faint. He has PMHx of CAD, MI, CHF, HTN, DM, and renal insufficiency. His vital signs show being afebrile, hypotension, tachypnea, and tachycardia. His physical examination shows peripheral edema and moist mucous membranes. This type of shock is most likely:

    A. Septic shock
    B. Hypovolemic shock
    C. Cardiogenic shock
    D. Neurogenic shock

18. A 55-year-old female presents via ambulance to the emergency department with abdominal pain after a motor vehicle accident. On evaluation, vital signs show hypotension, tachycardia, and tachypnea. Physical examination reveals abdominal tenderness to palpation and some seatbelt abrasions in the abdomen. This patient’s shock presentation is most likely:

    A. Septic shock
    B. Hypovolemic shock
    C. Cardiogenic shock
    D. Neurogenic shock

19. A 60-year-old male comes in for evaluation of abdominal pain and a pulsating mass in the mid-abdominal area. He has PMHx of HTN and currently is a smoker. On evaluation, the patient is moderately hypertensive and shows no abdominal tenderness to palpation of epigastrium. An acceptable initial approach to this patient is:

    A. Chest x-ray
    B. Abdominal x-ray
    C. Abdominal vascular MRI
    D. Abdominal vascular ultrasound

20. A 37-year-old female with no past medical history presents with localized swelling of her right lower extremity. The patient was recently admitted for a gallbladder surgery. She is diagnosed with a DVT. Which of the following is a risk factor for DVT?

    A. Oral contraceptive use
    B. Prolonged immobility
    C. Prior history of DVTs
    D. All of the above

2
Gastrointestinal Disorders

I. Oral and Esophageal Conditions

A. Salivary Gland Disorders

1. Dysfunction in sublingual, submandibular, or parotid glands resulting from ductal obstruction or inflammation
2. May be caused by sialolithiasis (ductal stone) in any salivary gland; parotid disease can also be caused by sarcoidosis, infection, or neoplasm
3. **H/P** = enlarged and painful glands; pain worsens during eating; parotid glands may have painless swelling
4. **Treatment** = warm compresses, massage, or lemon drops may help remove ductal stones; antibiotics and hydration for infection; surgery may be required for relief in refractory cases

B. Dysphagia

1. Difficulty swallowing because of oropharyngeal or esophageal transport dysfunction or pain with swallowing (i.e., odynophagia)
2. May be caused by neuromuscular disorders (e.g., achalasia, motility disorders, scleroderma) or obstruction (e.g., peptic strictures, esophageal webs or rings, cancer, radiation fibrosis)
3. **Obstructive** pathology tends to limit swallowing of **solids; neuromuscular** pathology tends to limit swallowing of **solids and liquids**
4. **H/P** = feeling of "**food stuck in throat**" when swallowing, cough, solids (mechanical pathology) or solids and liquids (dysmotility) may be difficult to swallow
5. **Workup** = manometry measures esophageal pressure and may detect neuromuscular abnormality
6. **Radiology** = barium swallow and esophagogastroduodenoscopy (EGD) may be helpful for diagnosis
7. **Treatment** = varies with etiology

NEXT
STEP

If a patient presents with dysphagia, perform a **barium swallow** before an EGD because of the lower associated risks of the former.

C. Achalasia

1. Acquired neuromuscular disorder of esophagus with **impaired peristalsis and decreased lower esophageal sphincter (LES) relaxation** because of intramural neuron dysfunction
2. Idiopathic; most commonly affects persons 25 to 60 years of age. Adenocarcinoma of proximal stomach is second most common cause
3. **H/P** = gradually progressive dysphagia of **solids and liquids**, regurgitation, cough, aspiration (pulmonary complications), heartburn, weight loss from poor intake, chest pain
4. **Workup** = manometry shows increased LES pressure, incomplete LES relaxation, and decreased peristalsis
5. **Radiology** = barium swallow shows "**bird's beak**" sign with tapering at the LES (see Figure 2-1); EGD needed to rule out malignancy
6. **Treatment** = nitrates and calcium channel blockers relax LES but are rarely used because of simultaneous cardiac effects; pneumatic dilation (most effective, 5% risk of perforation), botulinum injections (needs repeat injections every 2 years), or myotomy relieves obstruction. Patients should be instructed to chew food to pea soup consistency prior to swallowing

Quick **HIT**

Secondary causes of achalasia include **Chagas disease**, neoplasm, and scleroderma.

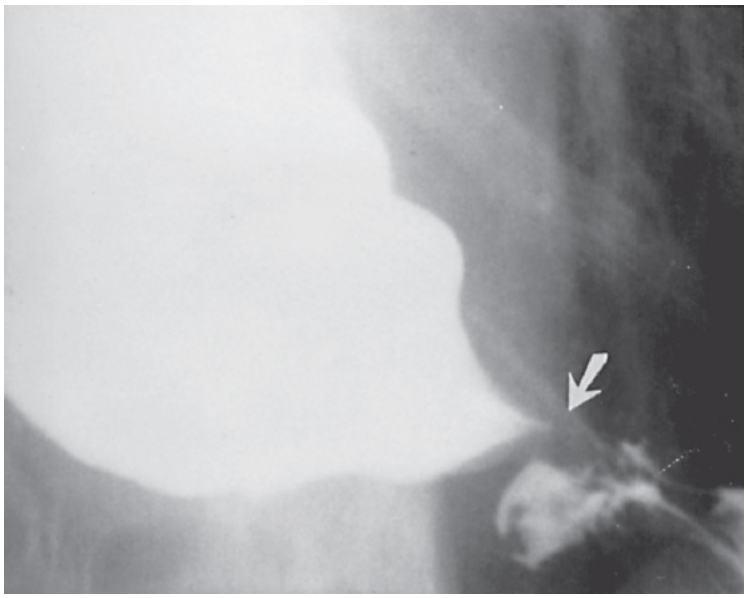


FIGURE 2-1
Achalasia.
Barium swallow in a patient with achalasia; note the distended proximal esophagus with distal tapering and "bird's beak" sign (*white arrow*).
(From Eisenberg, R. L. [2003]. *An Atlas of Differential Diagnosis* [4th ed., p. 397]. Philadelphia, PA: Lippincott Williams & Wilkins; with permission.)

7. **Complications** = myotomy can cause gastroesophageal reflux disease (GERD)

Quick HIT

Nitrates relieve pain from diffuse esophageal spasm but worsen symptoms of GERD.

D. Diffuse Esophageal Spasm

1. Neuromuscular disorder in which nonperistaltic contractions of the esophagus occur; sphincter function is normal in contrast to achalasia
2. **H/P** = noncardiac chest pain that may radiate to jaw, dysphagia
3. **Workup** = manometry shows nonperistaltic, uncoordinated esophageal contractions
4. **Radiology** = barium swallow shows "**corkscrew**" pattern in 50% of patients (see Figure 2-2)
5. **Treatment** = calcium channel blockers, nitrates, or tricyclic antidepressants help reduce chest pain and dysphagia

E. Esophageal Hiatal Hernias

1. There are two types: sliding and paraesophageal
   a. Sliding hiatal hernias account for >90% of cases. In this type, both the gastroesophageal junction and a portion of the stomach herniate into the thorax through the esophageal hiatus
   b. Paraesophageal hiatal hernias account for <5% of cases. In this type, the stomach herniates into the thorax through the esophageal hiatus, but the gastroesophageal junction does not. This hernia can become strangulated and requires surgical correction

F. Mallory–Weiss Syndrome

1. Mucosal tear at gastroesophageal junction as a result of forceful vomiting or retching; usually after several episodes, but may happen with just one episode
2. **Risk factors** = binge drinking, alcoholism, any disorder with prolonged vomiting
3. **H/P** = most cases present with hematemesis (or streaks); 90% stop bleeding without any treatment
4. **Treatment** = if bleeding continues, may need surgical repair of tear or angiographic embolization; acid-suppressive medications to improve healing

G. Zenker Diverticulum

1. Outpouching in upper posterior esophagus caused by smooth muscle weakness; usually from chronic motility disorders of esophagus; found in upper third of esophagus
2. **H/P** = bad breath, difficulty initiating swallowing, **regurgitation of food several days after eating**, occasional dysphagia, feeling of aspiration, neck mass that increases in size while drinking liquids
3. **Radiology** = barium swallow shows outpouching (see Figure 2-3)
4. **Treatment** = cricopharyngeal myotomy or diverticulectomy
5. **Complications** = EGD can perforate weakness in esophageal wall; vocal cord paralysis, mediastinitis possible with surgery

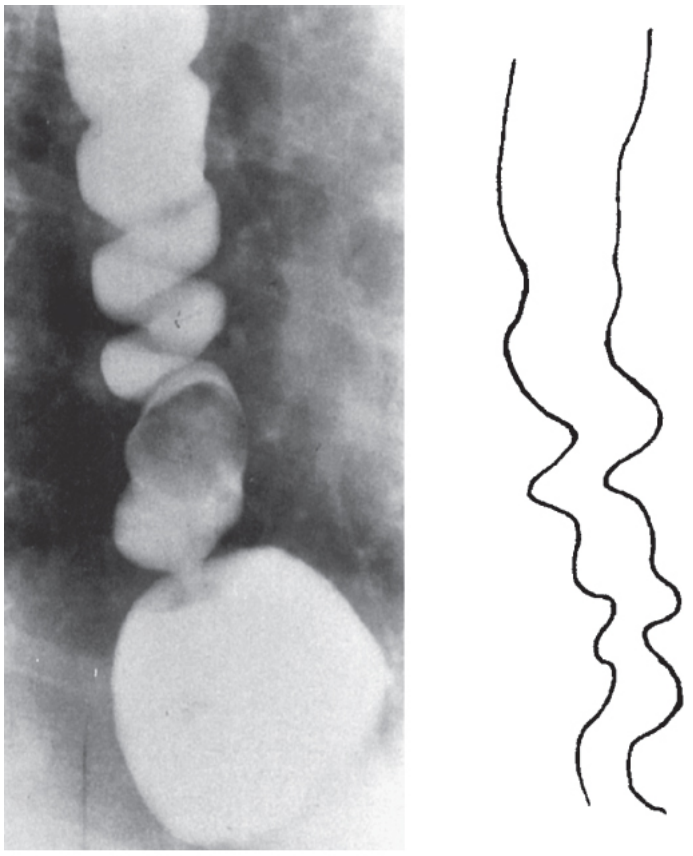


FIGURE 2-2
Diffuse esophageal spasm.
A: Barium swallow in a patient with diffuse esophageal spasm; notice the "corkscrew" pattern throughout the visible esophagus. **B:** Illustration of diffuse esophageal spasm demonstrating twisting "corkscrew" pattern.
(From Eisenberg, R. L. [2010]. *Clinical Imaging: An Atlas of Differential Diagnosis* [5th ed.]. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; with permission.)

H. Gastroesophageal Reflux Disease

1. Low pressure in LES leads to abnormal reflux of gastric contents into esophagus
2. **Risk factors** = obesity, hiatal hernia, pregnancy, scleroderma
3. Symptoms can worsen with consumption of alcohol and fatty foods or with tobacco use
4. **H/P** = **burning chest pain** ("heartburn") 30 to 90 minutes after eating, sour taste in mouth, regurgitation, dysphagia, odynophagia, nausea, cough; pain may worsen when lying down and lessen with standing
5. **Workup** = esophageal pH monitoring can detect increased acidity from reflux
6. **Radiology** = usually unneeded for diagnosis; EGD, chest radiograph, or barium swallow can help rule out neoplasm, Barrett esophagus, and hiatal hernia
7. **Treatment**
   a. Elevation of head of bed, weight loss, dietary modification
   b. Initial medications are antacids followed by H_2 antagonists or proton pump inhibitors (PPI) (see Table 2-1)
   c. Refractory disease may be treated with Nissen fundoplication or hiatal hernia repair
8. **Complications** = esophageal ulceration, esophageal stricture, Barrett esophagus, adenocarcinoma

Quick HIT

Symptoms of GERD can resemble those of asthma or myocardial infarction.

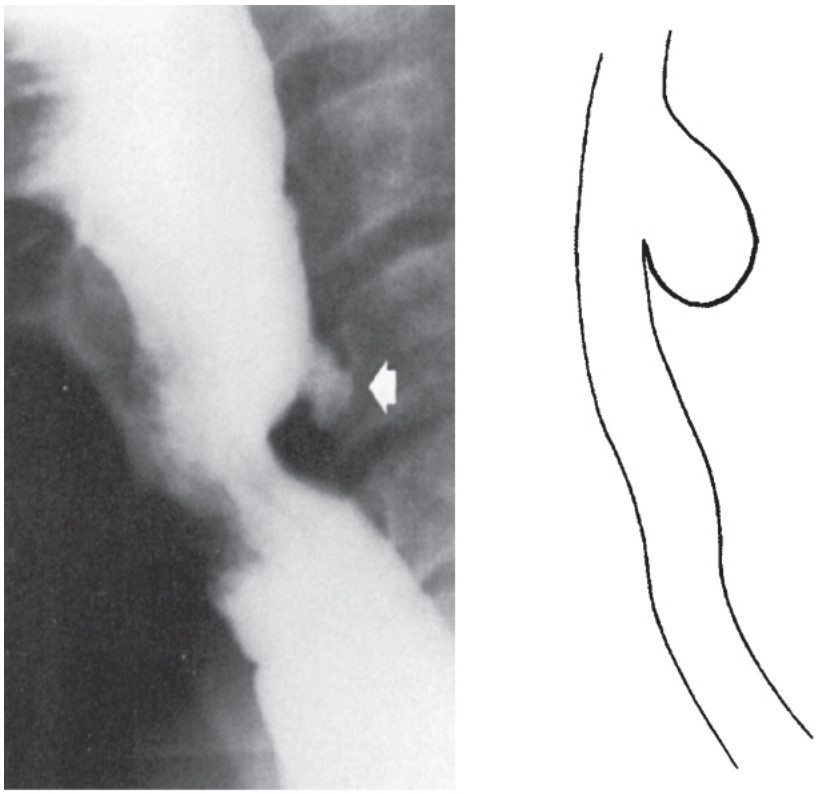


FIGURE 2-3
Zenker diverticulum.
A: Barium swallow in a patient with a small Zenker diverticulum (*white arrow*). **B:** Illustration of Zenker diverticulum demonstrating outpouching of esophagus.
(From Eisenberg, R. L. [2010]. *Clinical Imaging: An Atlas of Differential Diagnosis* [5th ed.]. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; with permission.)

I. Esophageal Cancer

1. **Squamous cell carcinoma** (more common worldwide) or adenocarcinoma (more common in the United States) of esophagus
2. **Barrett esophagus** (intestinal metaplasia of distal esophagus secondary to chronic GERD) commonly precedes adenocarcinoma
3. **Risk factors** = alcohol, tobacco, chronic GERD, obesity (only for adenocarcinoma)
4. **H/P** = progressive dysphagia (initially solids, later solids and liquids), weight loss, odynophagia, reflux, gastrointestinal (GI) bleeding, vomiting, weakness, cough, hoarseness
5. **Workup** = biopsy used to make diagnosis
6. **Radiology** = barium swallow shows narrowing of esophagus and abnormal mass (see Figure 2-4); magnetic resonance imaging (MRI), computed tomography (CT) with contrast, or positron emission tomography (PET) scan can determine extension and metastases; EGD used to identify mass and perform biopsy
7. **Treatment** = surgical resection (including total esophagectomy) for early-stage disease; radiation and chemotherapy used in nonoperative (advanced) cases or as neoadjuvant therapy to surgery
8. **Complications** = poor prognosis; local extension and metastases are frequently present by time of diagnosis

Table 2-1 Medications Used in Treatment of GERD

Medication	Mechanism	Adverse Effects	Presc
Antacids (calcium carbonate, aluminum hydroxide, etc.)	Neutralize gastric acid	Constipation (aluminum), nausea, diarrhea (magnesium)	Initial t
H_2 antagonists (cimetidine, ranitidine, etc.)	Reversibly block histamine H_2 receptors to inhibit gastric acid secretion	Headache, diarrhea, rare thrombocytopenia; cimetidine may cause gynecomastia and impotence	Patient antacid
PPI (omeprazole, lansoprazole, etc.)	Irreversibly inhibit parietal cell proton pump (H^+/K^+ ATPase) to block gastric acid secretion	Well tolerated; may increase effects of warfarin, benzodiazepines, or phenytoin in some patients	Patient antacid

GERD, gastroesophageal reflux disease; H^+, hydrogen ion; K^+, potassium ion; PPI, proton pump inhibitors.

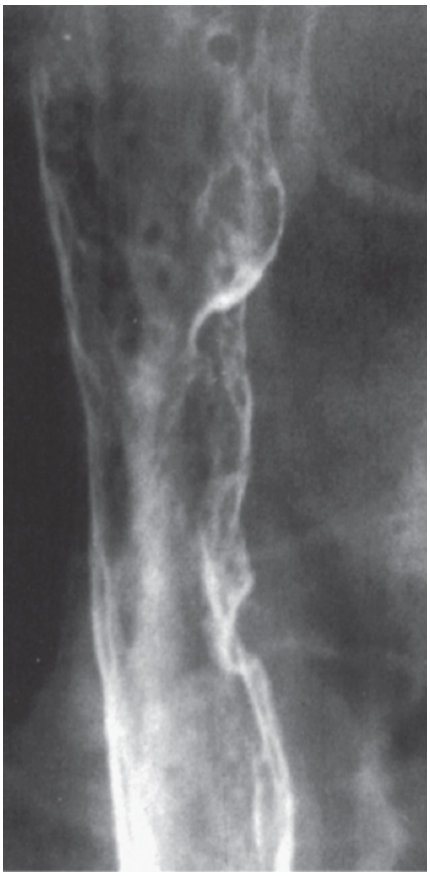


FIGURE 2-4
Barium swallow in a patient with squamous cell carcinoma of the esophagus; note the irregularity of the left esophageal wall due to neoplastic mass.
(From Eisenberg, R. L. [1996]. *Gastrointestinal Radiology: A Pattern Approach* [3rd ed.]. Philadelphia, PA: Lippincott-Raven; with permission.)

II. Gastrointestinal Infections

A. Viral Gastroenteritis

1. Self-limited viral infection of GI tract
2. Common agents include **Norwalk virus**, Coxsackievirus, echovirus, and adenovirus; rotavirus is common in children
3. **H/P** = nausea, vomiting, diarrhea, abdominal pain, myalgias; low-grade fever
4. **Labs** = no fecal white blood cells; viral culture indicates pathogen (usually unnecessary)
5. **Treatment** = self-limited (48 to 72 hours); maintain hydration status

B. Bacterial Gastroenteritis (See Table 2-2)

C. Parasitic and Protozoan GI Infections (See Table 2-3; Figure 2-5)

D. Hepatitis

1. Inflammatory disease of the liver is most commonly caused by **viral infection**; it can also result from alcohol or toxins
2. Acute hepatitis is initial disease; chronic form is disease lasting >6 months
3. **Risk factors** = intravenous drug abuse (IVDA), alcoholism, travel to developing nations, poor sanitation
4. Patterns of transmission vary with virus type (see Table 2-4)

Table 2-2 Common Pathogens in Bacterial Gastroenteritis

Pathogen	Source	Signs and Symptoms	Treatment
Bacillus cereus	Fried rice	**Vomiting** within several hours of eating, diarrhea later	Self-limited; hyd
Campylobacter jejuni	Poultry (second most common foodborne bacterial GI infection)	**Bloody** diarrhea, abdominal pain, fever; rare Guillain–Barré syndrome	Hydration, eryth self-limited
Clostridium botulinum	Honey, home-canned foods	Nausea, vomiting, diarrhea, **flaccid paralysis**	Botulism antitox self-limited
Clostridium difficile	**Antibiotic-induced suppression** of normal colonic flora	**Watery or bloody** diarrhea; gray pseudomembranes seen on colonic mucosa	Metronidazole,
Escherichia coli (enterotoxigenic)	Food/water (**travelers'** diarrhea)	**Watery** diarrhea, vomiting, fever	Hydration; self-l with FQ)
E. coli type **O157:H7** (enterohemorrhagic)	Ground beef, indirect fecal contamination	**Bloody** diarrhea, vomiting, fever, abdominal pain (risk of HUS)	Hydration; self-l actually worsen toxin release
Staphylococcus aureus	Room-temperature food (caused by preformed toxin)	**Vomiting** within several hours of eating; diarrhea later	Self-limited; hyd
Salmonella species	Eggs, poultry, milk, fresh produce **(most common foodborne bacterial GI infection)**	Nausea, abdominal pain, **bloody** diarrhea, fever, vomiting	Hydration; self-l compromised pa
Shigella species	Food/water; associated with overcrowding	Fever, nausea, vomiting, **severe bloody** diarrhea, abdominal pain (risk of HUS)	Hydration; self-l TMP-SMX in se
Vibrio cholerae	Water, seafood	**Copious watery** diarrhea, signs of dehydration	**Hydration**; tetr decreases disea
Vibrio parahaemolyticus	Seafood (oysters)	Abdominal pain, **watery** diarrhea within 24 hrs of eating	Hydration; self-l
Yersinia enterocolitica	Pork, fresh produce	Abdominal pain, **bloody** diarrhea, right lower quadrant pain, fever	Hydration; self-l

FQ, fluoroquinolone; GI, gastrointestinal; HUS, hemolytic uremic syndrome; TMP-SMX, trimethoprim-sulfamethoxazole.

Table 2-3 Common Pathogens in Parasitic and Protozoan Gastrointestinal Infections

Pathogen	Source	Signs and Symptoms	Treatm
Giardia lamblia (Figure 2-1)	Surface water (usually limited to wilderness or other countries)	**Greasy**, foul-smelling diarrhea; abdominal pain, malaise; cysts and trophozoites seen in stool sample	Metron
Entamoeba histolytica	Water, areas of poor sanitation	Mild to severe **bloody** diarrhea, abdominal pain; cysts and trophozoites seen in stool sample	Metron
Cryptosporidium parvum	Food/water; immunocompromised patients	**Watery** diarrhea, abdominal pain, malaise; acid-fast stain of stool shows parasites	Control nitazox
Trichinella spiralis	Undercooked pork	Fever, **myalgias**, periorbital edema; eosinophilia	Albend CNS or
Taenia solium (intestinal taeniasis)	Ingestion of cysts in undercooked pork	Nausea, abdominal pain	Praziqu
Taenia solium (cysticercosis)	Fecal/oral transmission of eggs from feces of human with intestinal taeniasis	Cysts in muscles, subcutaneous tissues, eyes and extraocular muscles, brain (**neurocysticercosis**); may cause seizures	Albend oids for

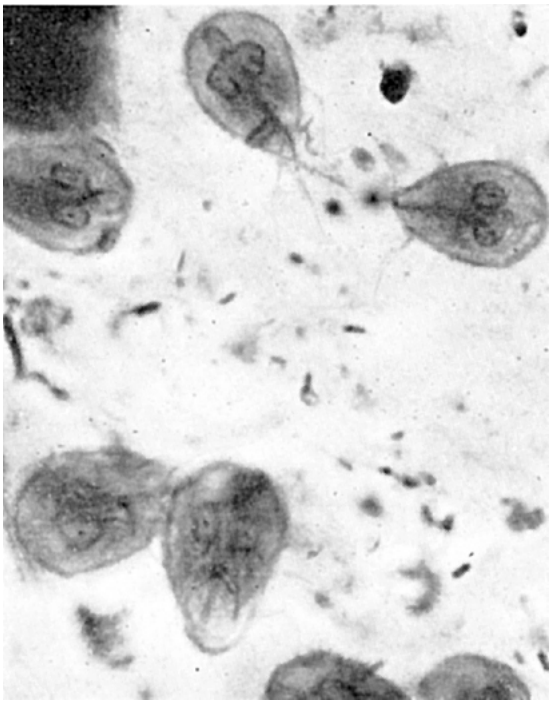


FIGURE 2-5
Giardiasis; several trophozoites are seen with characteristic pear-shaped and paired nuclei resembling owls' eyes.
(From Diallo, A. O., & Chandrasekha, V. [2005]. *Microbiology Recall*. Philadelphia, PA: Lippincott Williams & Wilkins; with permission.)

Table 2-4 Characteristics of Viral Hepatitis

Hepatitis Virus	Virus Type	Spread	Treatment	Prevention	Comp
A (HAV)	Picornavirus (single-stranded RNA)	Food (**shellfish**), fecal–oral	Self-limited; supportive care	Vaccine before travel	Can oc
B (HBV)	Hepadnavirus (double-stranded DNA)	Blood, other body fluids (including **sexual contact**)	HBV immediately after exposure in unvaccinated patients; IFN-α or antivirals (lamivudine, adefovir, entecavir)	**Vaccine**	5% of develo cirrhos **hepat** persist develo failure
C (HCV)	Flavivirus (single-stranded RNA)	**Blood**, possibly sexual contact	IFN-α; consider ribavirin	No vaccine	80% o **chron** chroni slightl hepato persist
D	Delta agent (incomplete single-stranded RNA)	Blood; **requires coexistent hepatitis B infection**	IFN-α	Hepatitis B vaccine	Severe persist
E	Calicivirus (single-stranded RNA)	Water, fecal–oral	Self-limited; supportive care	No vaccine	High m occurri

HAV, hepatitis A virus; HBV, hepatitis B virus; HCV, hepatitis C virus; IFN, interferon.

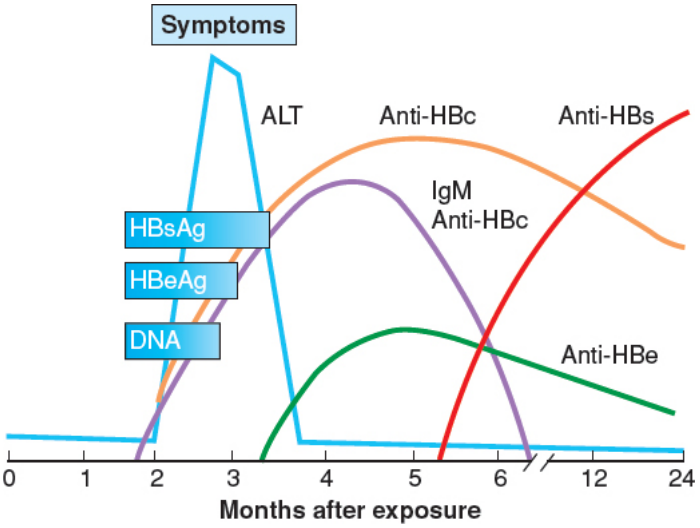


FIGURE 2-6
Trends in serology and symptoms seen in various courses in acute hepatitis B virus (HBV) infection with resolution of disease.
HBV surface antigen (HBsAg) and HBV e antigen (HBeAg) are detectable from approximately 1 to 4 months and coincide with appearance of symptoms. Antibodies are indicative of previous infection or vaccination. ALT, alanine aminotransferase.
(From Nettina, S. M. [2015]. *The Lippincott Manual of Nursing Practice* [10th ed., p. 715]. Philadelphia, PA: Wolters Kluwer; with permission.)

5. **H/P** = possibly asymptomatic; malaise, arthralgias, fatigue, nausea, vomiting, right upper quadrant (RUQ) pain; jaundice, scleral icterus, tender hepatomegaly, splenomegaly, lymphadenopathy
6. **Workup** = bilirubinuria, **increased aspartate aminotransferase (AST), increased alanine aminotransferase (ALT)**, increased bilirubin (total), increased alkaline phosphatase
   a. Hepatitis A virus (HAV): anti-HAV IgM antibodies present during illness; anti-HAV IgG antibodies present after resolution
   b. Hepatitis B virus (HBV): antigens and antibodies detected vary with disease state (see Figure 2-6; Table 2-5)

c. Hepatitis C virus (HCV): anti-HCV antibodies and positive HCV polymerase chain reaction indicate infection (see Figure 2-7)

7. **Treatment** = rest, frequently self-limited (**except HCV**); interferon-α (IFN-α) or antivirals for HBV; IFN-α ± ribavirin for HCV; hospitalization for hepatic failure; immunoglobulin given to close contacts of patients with HAV; HAV vaccine given to travelers to developing nations; HBV vaccine routinely given to children and health care workers

Quick HIT

Bacterial GI infections are most frequently related to contaminated food consumption.

Quick HIT

Hemolytic uremic syndrome (HUS) is a complication of *Escherichia coli* O157:H7 infection and is characterized by thrombocytopenia, hemolytic anemia, and acute renal failure; it is usually self-limited.

Table 2-5 Serologies Seen in Various Disease States of HBV Infection

Course of Disease	HBV Surface Antigen (HBsAg)	HBV e Antigen (HBeAg)	HBV Surface Antibody (Anti-HBs)	HE (A
Acute infection (4–12-wk postexposure)	Positive	Positive	Negative	Pos
Acute infection window period (12–20-wk postexposure)	Negative	Negative	Negative	Pos
Chronic infection, active viral replication	Positive	Positive	Negative	Pos
Chronic infection, lesser viral replication (good prognosis)	Positive	Negative	Negative	Pos
Past infection (recovered)	Negative	Negative	Positive	Pos
Vaccination	Negative	Negative	Positive	Ne

HBV, hepatitis B virus.

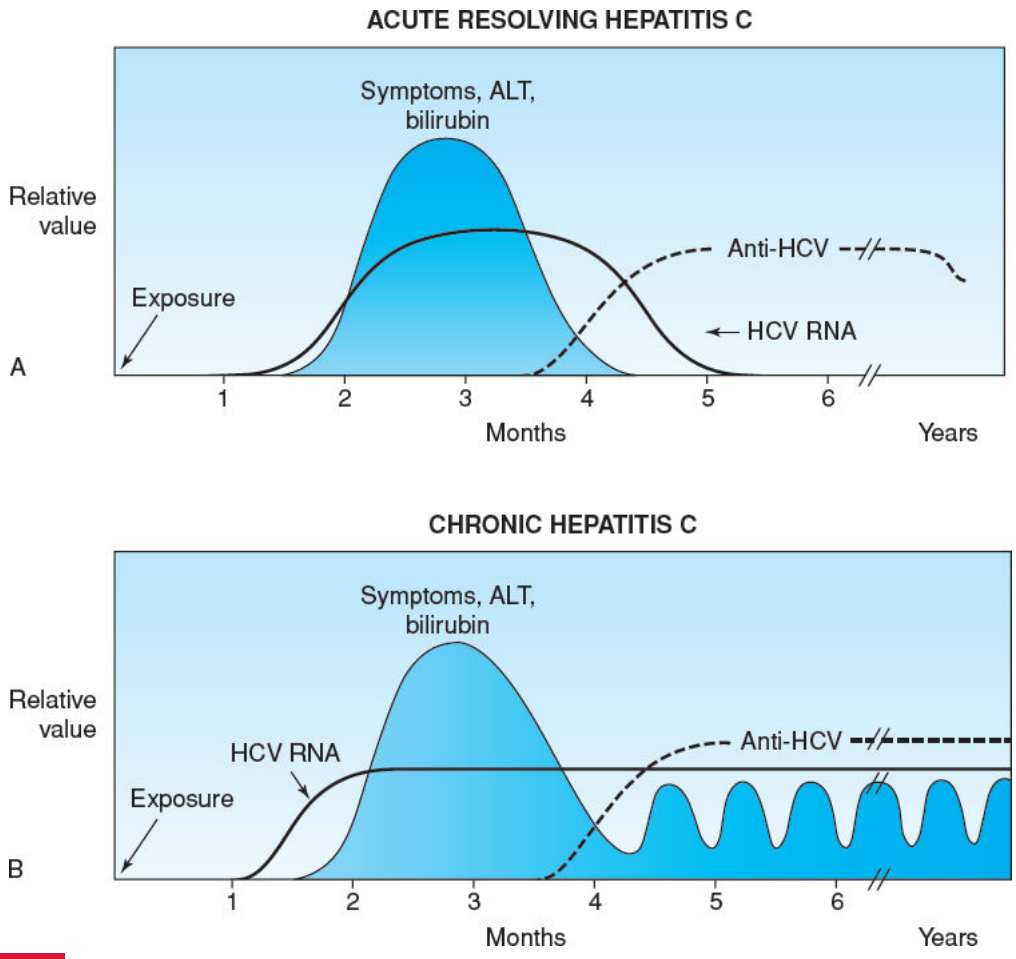


FIGURE **2-7**

Trends in serology and symptoms seen in hepatitis C virus (HCV) infection.
A: Acute resolving infection. **B:** Chronic HCV infection with intermittent exacerbations of symptoms. ALT, alanine aminotransferase.
(From Rubin, R., & Strayer, D. S. [2012]. *Rubin's Pathology Image Collection* [6th ed., p. 702]. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; with permission.)

III. Gastric Conditions

A. Hiatal Hernia

1. Herniation of part of stomach above diaphragm
2. Types
   a. **Sliding:** gastroesophageal junction and stomach displaced through diaphragm (95% of cases)
   b. **Paraesophageal:** stomach protrudes through diaphragm, but gastroesophageal junction remains in normal location
3. **H/P** = possibly asymptomatic; symptoms associated with GERD
4. **Radiology** = barium swallow shows portion of stomach above diaphragm; chest radiograph may detect hernia without barium swallow if air in stomach is visible above diaphragm
5. **Treatment** = sliding hernias can be treated with reflux control; paraesophageal hernias may need surgical repair (e.g., gastropexy, Nissen fundoplication)
6. **Complications** = incarceration of stomach in herniation (seen in paraesophageal type)

B. Gastritis

1. Inflammation of gastric mucosa
2. Can be **acute (erosive)** or **chronic (nonerosive)**
3. Acute gastritis is characterized by rapidly developing, superficial lesions secondary to nonsteroidal anti-inflammatory drug (**NSAID**) use, alcohol, ingestion of corrosive materials, or **stress from severe illness**; it can involve any region of the stomach

Quick HIT

In pernicious anemia, autoantibodies destroy parietal cells, leading to low levels of intrinsic factor, vitamin B_{12} malabsorption, and megaloblastic anemia.

Table 2-6 Characteristics of Type A and B Chronic Gastritis

Characteristic	Type A	Type B
Frequency	10% of cases	90% of cases
Site	Fundus	Antrum
Pathology	Autoantibodies for parietal cells	Associated with *Helicobacter pylori* infection
Labs	Decreased gastric acid level, decreased gastrin	Increased gastric acid level
Associated conditions	Pernicious anemia, achlorhydria, thyroiditis	Peptic ulcer disease, gastric cancer

4. Chronic gastritis can occur in either the antrum or fundus of the stomach (see Table 2-6)
5. **H/P** = possibly asymptomatic; epigastric pain, indigestion, nausea, vomiting, hematemesis, melena; symptoms more common for acute form
6. **Workup** = positive urea breath test (detects increase in pH from ammonia-producing bacteria) and positive IgG antibody to *Helicobacter pylori* with existing infection; ratio of pepsinogen isoenzymes useful to detect autoimmune cause; **antral biopsy** can detect *H. pylori* infection
7. **Radiology** = EGD allows visualization of gastric mucosa to detect lesions and perform biopsy
8. **Treatment**
   a. Treat acute form as peptic ulcer disease (PUD) and stop alcohol and offending medications; give H_2 antagonists or PPI to patients with severe illnesses
   b. Type A chronic gastritis requires vitamin B_{12} replacement
   c. Type B chronic gastritis requires eradication of *H. pylori* through multidrug treatment (typically, PPI, clarithromycin, and either amoxicillin or metronidazole for 7 to 14 days)

Quick HIT

Ulcers can also develop secondary to stress from severe burns (**Curling ulcers**) or intracranial injuries (**Cushing ulcers**).

NEXT
STEP

In refractory cases of PUD, gastrin level should be determined to detect Zollinger–Ellison syndrome (increased gastrin).

C. Peptic Ulcer Disease

1. Erosion of gastric and duodenal mucosa secondary to impaired endothelial defenses and increased gastric acidity (see Table 2-7)
2. ***H. pylori*** is involved in pathology in **most gastric ulcers** and **almost all duodenal ulcers**
3. **Risk factors** = ***H. pylori* infection, NSAID** use, tobacco, alcohol, corticosteroids; males > females

Table 2-7 Distinguishing Between Gastric and Duodenal Ulcers

Characteristic	Gastric Ulcer	Duodenal Ulcer
Patients	Age >50 yrs old, *Helicobacter pylori* infection, NSAID users	Younger, *H. pylori* infection
Frequency	25% of cases	75% of cases
Timing of pain	**Soon after** eating	**2–4 hrs after** eating
Gastric acid level	Normal/low	High
Gastrin level	High	Normal
Effect of eating	May **worsen** symptoms and cause nausea and vomiting	**Initial improvement** in symptoms, with later **worsening**

NSAID, nonsteroidal anti-inflammatory drug.

4. **H/P** = periodic **burning epigastric pain** that can change (better or worse) with eating, nausea, hematemesis, melena, hematochezia; epigastric tenderness; abdominal rigidity, rebound tenderness, and rigidity seen following acute perforation of ulcer
5. **Workup** = positive urea breath test, IgG antibodies, or biopsy detect *H. pylori*; complete blood count (CBC) can assess degree of GI bleeding
6. **Radiology** = abdominal x-ray (AXR) to detect perforation (free air under diaphragm seen following perforation); barium swallow AXR can demonstrate collections of barium in ulcerations; EGD used to perform biopsy and detect active bleeding
7. Treatment

a. **Active bleeding** must be ruled out with CBC and EGD in patients with concerning symptoms; symptoms lasting >2 months need EGD to rule out gastric adenocarcinoma
b. Decrease gastric acid levels with **PPI** and **H_2 antagonist**; protect mucosa with sucralfate, bismuth subsalicylate, or misoprostol; **eliminate *H. pylori* infection** (as described previously for treatment of gastritis)
c. Surgery is required to repair acute perforations; persistent, nonneoplastic refractory cases may require parietal cell vagotomy or antrectomy

8. **Complications** = hemorrhage (posterior ulcers may erode into **gastroduodenal artery**), perforation (most commonly anterior ulcers), lymphoproliferative disease

D. Zollinger–Ellison Syndrome

1. Syndrome secondary to gastrin-producing tumor most frequently located in duodenum (70% cases) or pancreas
2. Associated with malabsorption disorders
3. **H/P** = **refractory PUD**, abdominal pain, nausea, vomiting, indigestion, diarrhea, steatorrhea, possible history of other endocrine abnormalities
4. **Workup** = **increased fasting gastrin**; positive secretin stimulation test (i.e., administration of secretin causes higher than expected serum gastrin levels); specific gastrin sampling in several pancreatic or abdominal veins can help localize tumor
5. **Radiology** = somatostatin receptor imaging using single-photon emission computed tomography (SPECT) can localize tumors; angiography may detect tumor if hypervascular
6. **Treatment** = surgical resection can be performed for nonmetastatic disease in which a tumor can be localized (best chance in extrapancreatic tumors); PPI and H_2 antagonists may ease symptoms; octreotide may help reduce symptoms in metastatic disease
7. **Complications** = occasionally associated with other endocrine tumors (e.g., multiple endocrine neoplasia I [MEN I]); 60% of lesions are malignant

E. Gastric Cancer

1. **Adenocarcinoma** (common) or squamous cell carcinoma (rare; caused by invasion from esophagus) affecting stomach
2. Types
   a. **Ulcerating:** resembles ulcers seen in PUD
   b. **Polypoid:** large, intraluminal neoplasms
   c. **Superficial spreading:** mucosal and submucosal involvement only; best prognosis
   d. **Linitis plastica:** all layers of stomach involved; decreased stomach elasticity; poor prognosis
3. **Risk factors** = *H. pylori*, **family history**, Japanese person living in Japan, tobacco, alcohol, vitamin C deficiency, high consumption of preserved foods; males > females
4. **H/P** = weight loss, anorexia, early satiety, vomiting, dysphagia, epigastric pain; enlarged left supraclavicular lymph node (i.e., **Virchow node**) or periumbilical node (i.e., **Sister Mary Joseph node**)
5. **Workup** = increased carcinoembryonic antigen (CEA), increased 2-glucuronidase in gastric secretions, anemia if active bleeding; biopsy used for diagnosis
6. **Radiology** = barium swallow may show mass or thickened “leather bottle” stomach (linitis plastica); **EGD** used to perform biopsy and visualize ulcers
7. **Treatment** = subtotal gastrectomy for lesions in distal third of stomach, total gastrectomy for lesions in middle or upper stomach or invasive lesions; adjuvant chemotherapy and radiation therapy
8. **Complications** = early detection has high cure rate (>70%) but poor prognosis in later detection (<15% 5-year survival)

Quick HIT

Barium swallow radiographic findings that suggest the presence of a malignant lesion associated with an ulcer include **abnormal-appearing mucosal folds** in the region of the ulcer, presence of a **mass** near the ulcer, and irregular **filling defects** in the base of the ulcer.

NEXT
STEP

Workup for patients <40 years of age in whom concern exists for PUD can frequently be done with **noninvasive** testing; older patients or those with a previous ulcer should have an **EGD** performed.

NEXT
STEP

Give cyclooxygenase-2 (COX-2) selective NSAID to patients with PUD who require NSAID therapy.

Quick HIT

PPI must be stopped before gastrin level testing to collect an accurate measurement.

Quick HIT

Celiac and tropical sprue exhibit the same symptoms, but only celiac sprue responds to removal of gluten from the diet, and tropical sprue occurs in patients who have spent time in the tropics.

Quick HIT

The general presentation of malabsorption includes weight loss, **bloating**, **diarrhea**, possible **steatorrhea**, glossitis, dermatitis, and edema.

IV. Intestinal Conditions

A. Malabsorption Disorders (See Figures 2-8 and 2-9)

1. **Celiac disease**
   a. Genetic disorder characterized by gluten intolerance (e.g., wheat, barley, rye)
   b. Immune-mediated process with IgA anti-tissue transglutaminase (anti-TTG) and antiendomysial antibodies that cause jejunal mucosal damage
   c. **H/P** = failure to thrive, bloating, and abnormal stools in infants; diarrhea, steatorrhea, weight loss, and bloating in adults; some patients will exhibit depression, anxiety, or arthralgias; associated with Down syndrome; associated with dermatitis herpetiformis
   d. **Workup** = positive antiendomysial and antigliadin antibodies in serum; biopsy shows blunting of duodenal and jejunal villi
   e. **Treatment** = removal of gluten from diet (can still eat corn, rice); refractory disease may require corticosteroids
2. **Tropical sprue**
   a. Malabsorption syndrome similar to celiac sprue, with possible infectious or toxic etiology
   b. Acquired disorder in patients living in **tropical areas**; can present years after leaving tropics
   c. **H/P** = similar presentation to celiac sprue
   d. **Workup** = no antiendomysial and anti-TTG antibodies; acute GI infection, celiac sprue, and autoimmune diseases should be ruled out with cultures and appropriate serology
   e. **Treatment** = folic acid replacement, tetracycline; removal of gluten from diet has no effect

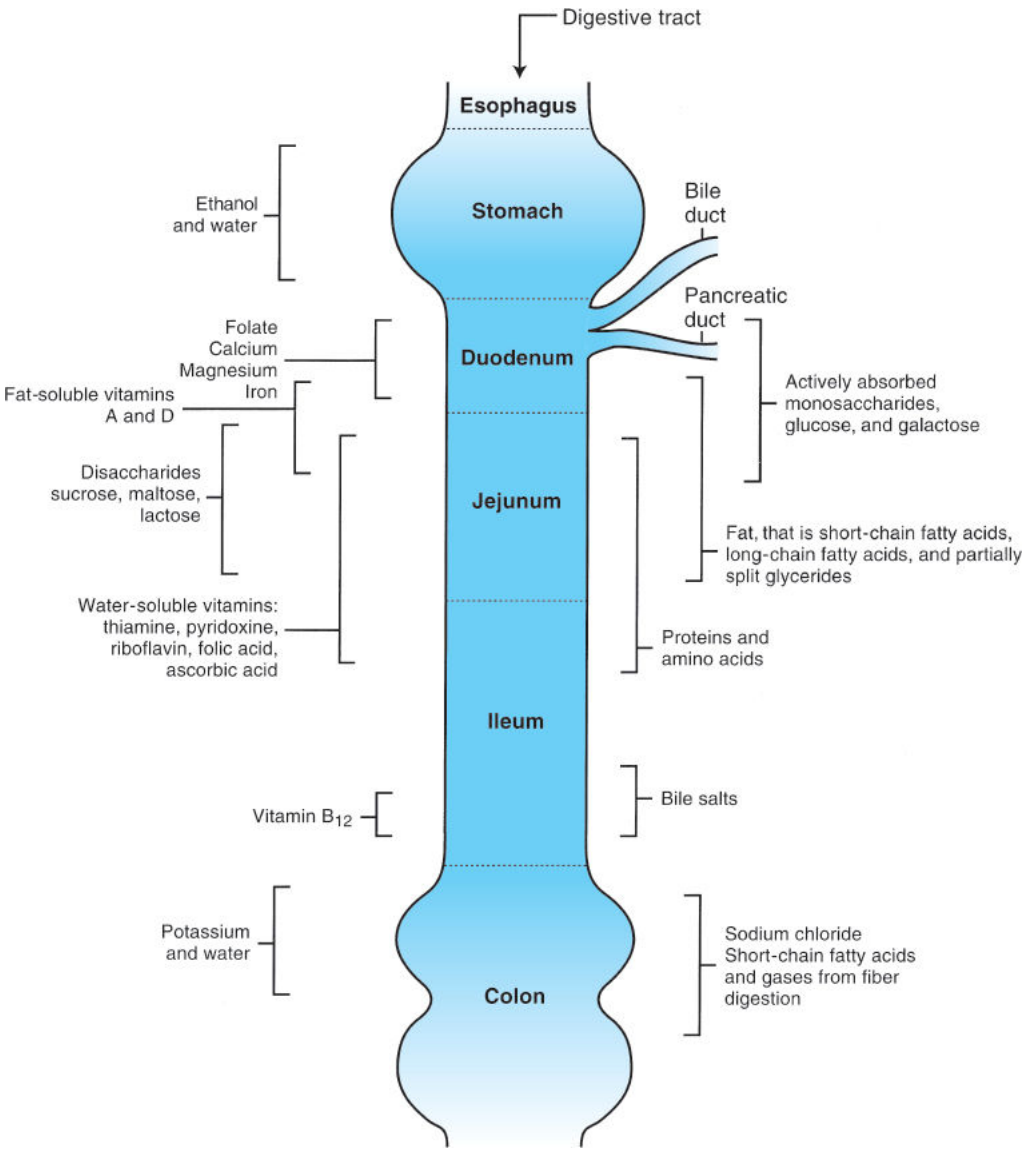


FIGURE **2-8**

Location of absorption of vitamins, minerals, and nutrients throughout the gastrointestinal (GI) tract.
(Modified from Ryan, J. P. [1997]. *Physiology*. New York: McGraw Hill; Mehta, S., Milder, E. A., Mirachi, A. J., et al. [2007]. *Step-Up: A High-Yield, Systems-Based Review for the USMLE Step 1* [3rd ed.]. Philadelphia, PA: Lippincott Williams & Wilkins.)

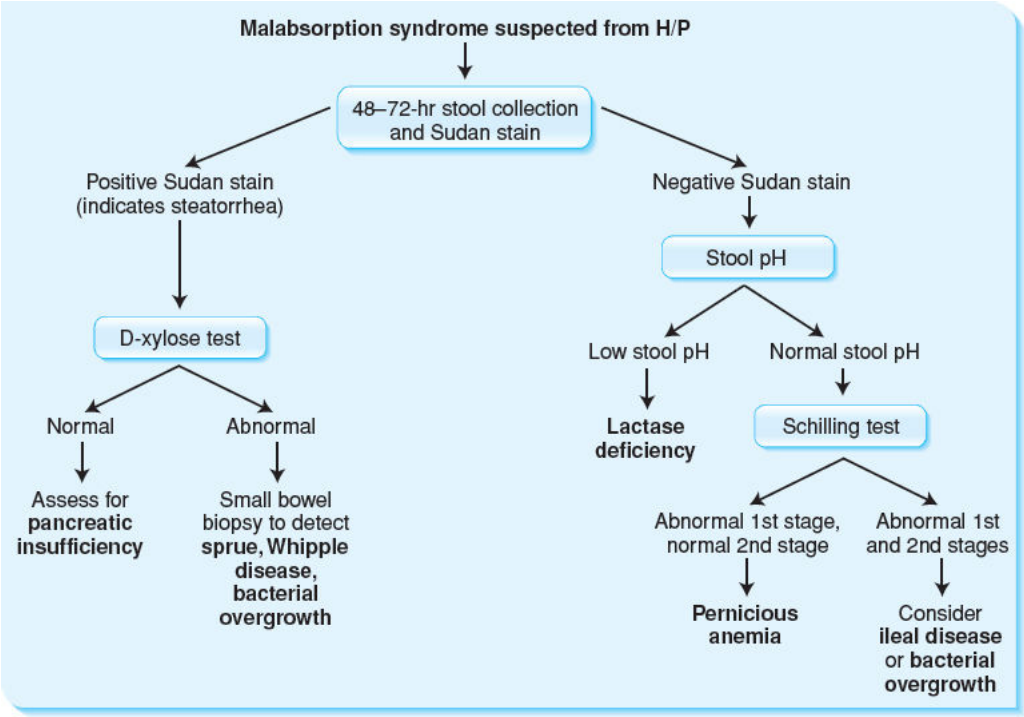


FIGURE **2-9**
Diagnostic pathway for suspected malabsorption syndrome.

3. **Lactose intolerance**
   a. Malabsorption syndrome resulting from deficiency of lactase; can also be secondary to Crohn disease or bacterial overgrowth
   b. Lactose not metabolized in jejunum, leading to osmotic diarrhea
   c. **H/P** = diarrhea, abdominal pain, flatulence, and bloating after dairy consumption
   d. **Workup** = positive lactose tolerance test (i.e., minimal increase in serum glucose following ingestion of lactose), positive lactose breath hydrogen test after lactose meal
   e. **Treatment** = lactose-restricted or lactose-free diet; adequate dietary protein, fat, calcium, and vitamins; lactase replacement may benefit some patients
4. **Whipple disease**
   a. Malabsorption disorder secondary to ***Tropheryma whippelii*** infection and likely immune deficiency (unknown if innate to host or caused by infection); multiple organs involved
   b. **Risk factors** = white males with European ancestry
   c. **H/P** = weight loss, joint pain, abdominal pain, diarrhea, dementia, cough, bloating, steatorrhea; fever, vision abnormalities, lymphadenopathy, new heart murmur; severe wasting late in disease course
   d. **Workup** = jejunal biopsy shows foamy macrophages on periodic acid–Schiff (PAS) stain and villous atrophy
   e. **Treatment** = trimethoprim-sulfamethoxazole (TMP-SMX) or ceftriaxone for 12 months
   f. **Complications** = high mortality if untreated

B. Diarrhea

1. Increased frequency of bowel movements and increased stool liquidity; **>200 g/day stool production**
2. **Risk factors** = infection, recent travel
3. Acute diarrhea (<2-week duration) is usually caused by infection (see Figure 2-10)

Quick HIT

Lactase deficiency is the most common cause of **adult chronic diarrhea**.

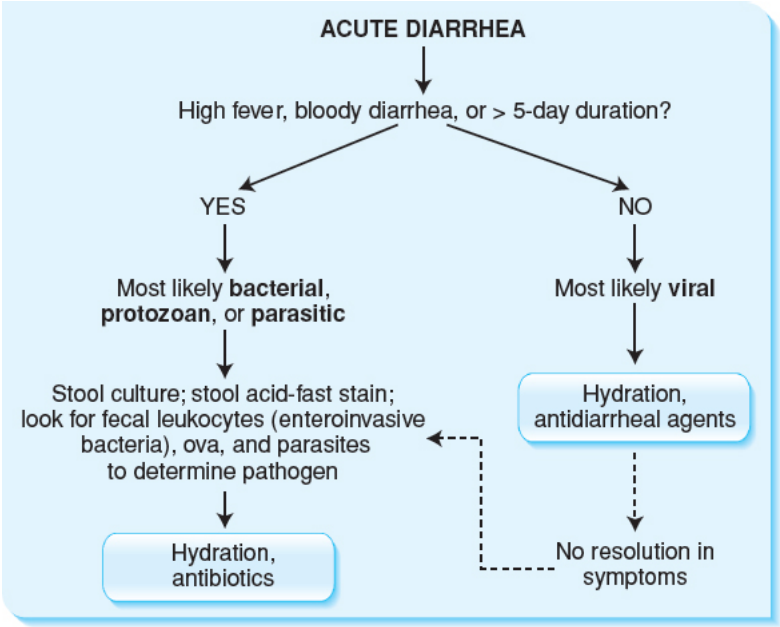


FIGURE **2-10**
Diagnostic and treatment pathways for acute diarrhea.

Quick HIT

Rotavirus is the most common cause of acute diarrhea in children.

4. Chronic diarrhea has longer duration of symptoms and may result from malabsorption or motility disorders (see Figure 2-11)
   a. **Secretory** diarrheas are usually **hormone mediated** or caused by enterotoxic bacteria
   b. **Osmotic** diarrheas are caused by **solute collecting in bowel lumen**, leading to increased water in bowel; occur after eating, lessen with fasting
   c. **Inflammatory** diarrhea results from an autoimmune inflammatory process or chronic infection
5. Pediatric diarrhea is most commonly caused by infection, antibiotic use, or related to immunosuppression
6. **Treatment** = hydration, treat underlying cause

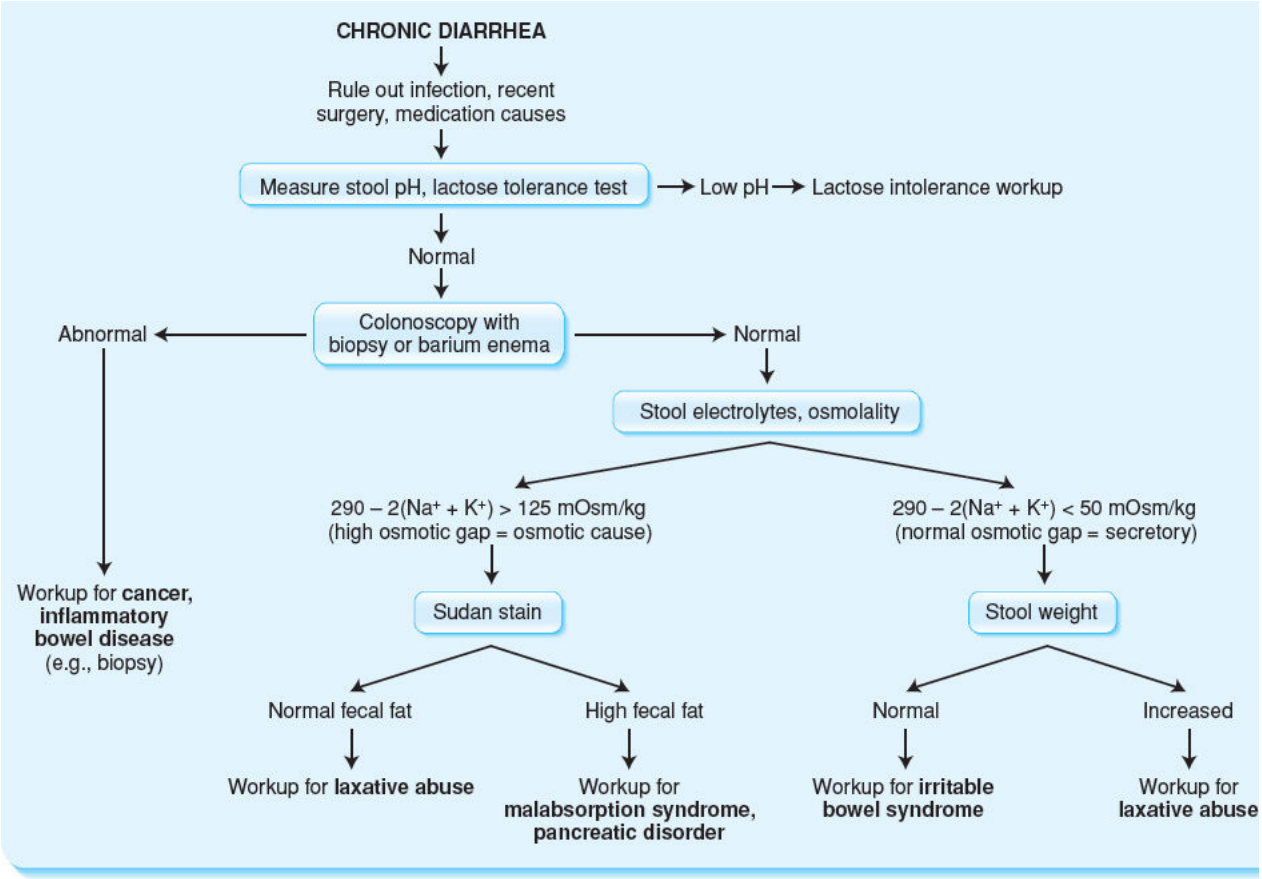


FIGURE **2-11**
Diagnostic pathway for chronic diarrhea.

Table 2-8 Rome III Criteria for Diagnosis of Irritable Bowel Disease

Recurrent abdominal pain or discomfort at least 3 days per month in the last 3 months, associated with two or more of the following:

- Improvement of pain with defecation
- Change in frequency of stool
- Change in form/appearance of stool

C. Irritable Bowel Syndrome (IBS)

1. Idiopathic disorder with chronic abdominal pain and irregular **bowel habits** (see Table 2-8)
2. Most commonly begins during **teens** or **young adulthood**; females > males (2:1)
3. **H/P** = abdominal pain, diarrhea, constipation, bloating, nausea, possible vomiting; mild abdominal tenderness
4. **Workup** = rule out other GI diseases with CBC, electrolytes, stool culture
5. **Radiology** = consider AXR, abdominal CT, or barium studies to rule out other GI causes; colonoscopy may be performed in older patients to rule out neoplasm
6. **Treatment** = assurance from physician, high-fiber diet, possible psychosocial therapy; antispasmodic, antidepressants, serotonin receptor antagonists have shown use in lessening symptoms

Quick HIT

Half of patients with IBS have comorbid psychiatric disorders.

D. Inflammatory Bowel Disease (IBD) (See Table 2-9)

1. Disease of small and large bowel, with a constellation of symptoms associated with inflammatory bowel processes, autoimmune reactions, extraintestinal manifestations, and multiple complications

Table 2-9 Comparison of Crohn Disease and Ulcerative Colitis

	Crohn Disease	Ulcerative Colitis
Site of involvement	**Entire GI tract may be involved** with multiple **"skipped"** areas; distal ileum most commonly involved; **entire bowel wall affected**	**Continuous disease beginning at rectum** and **extending possibly as far as distal ileum**; only mucosa and submucosa affected
Symptoms	Abdominal pain, weight loss, **watery** diarrhea	Abdominal pain, urgency, **bloody** diarrhea, tenesmus, nausea, vomiting, weight loss
Physical examination	Fever, right lower quadrant **abdominal mass**, abdominal tenderness, **perianal fissures and fistulas**, oral ulcers	Fever, abdominal tenderness, orthostatic hypotension, tachycardia, gross blood on rectal examination
Extraintestinal manifestations	Arthritis, ankylosing spondylitis, uveitis, nephrolithiasis	Arthritis, uveitis, ankylosing spondylitis, primary sclerosing cholangitis, erythema nodosum, pyoderma gangrenosum
Labs	ASCA frequently positive, pANCA rarely positive; hemoccult positive stool; biopsy diagnostic	ASCA rarely positive, pANCA frequently positive; biopsy diagnostic
Radiology	Colonoscopy shows colonic ulcers, strictures, **"cobblestoning,"** fissures, and **"skipped"** areas of bowel; barium enema shows fissures, ulcers, and bowel edema	Colonoscopy shows **continuous involvement**, pseudopolyps, friable mucosa; barium enema shows **"lead pipe"** colon without haustra and colon shortening
Treatment	Mesalamine, broad-spectrum antibiotics, corticosteroids, immunosuppressives; surgical resections of severely affected areas, fistulas, or strictures	Mesalamine, supplemental iron, corticosteroids, immunosuppressives; total **colectomy is curative**
Complications	Abscess formation, fistulas, fissures, malabsorption	**Significantly increased risk of colon cancer**, hemorrhage, toxic megacolon, bowel obstruction

ASCA, anti-yeast *Saccharomyces cerevisiae* antibodies; GI, gastrointestinal; pANCA, perinuclear antineutrophil cytoplasmic antibodies.

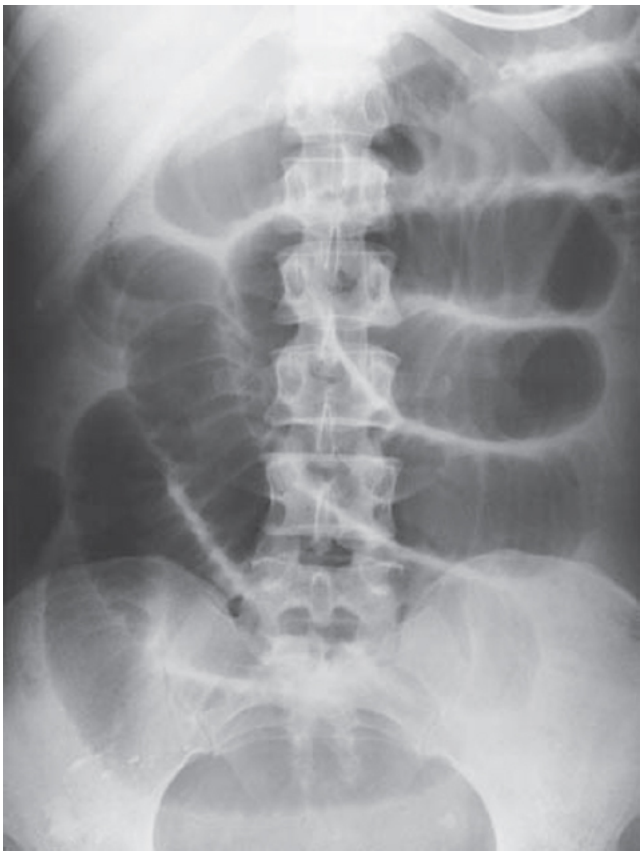


FIGURE 2-12
Abdominal radiograph in a patient with small bowel obstruction.
Note the multiple loops of dilated bowel with a ladderlike appearance.
(From Yamada, T., Alpers, D. H., Laine, L., Kaplowitz, N., Owyang, C., & Powel, D. W. [2003]. *Textbook of Gastroenterology* [4th ed.]. Philadelphia, PA: Lippincott Williams & Wilkins; with permission.)

2. Types = Crohn disease, ulcerative colitis
3. **Risk factors** = Ashkenazi Jews; whites > blacks; presents in teens or early 20s

Quick HIT

E. Bowel Obstruction (See Figures 2-12 and 2-13; Table 2-10)

1. Mechanical obstruction of small or large bowel that can lead to vascular compromise
2. The most common causes of obstruction are **adhesions**, **hernias**, and **neoplasms**

Small bowel obstruction most commonly results from **adhesion** formation, whereas **large** bowel obstruction is most commonly caused by **neoplasm**.

F. Ischemic Colitis

1. Ischemia and necrosis of bowel secondary to vascular compromise
2. Caused by embolus, bowel obstruction, inadequate systemic perfusion, medication, or surgery-induced vascular compromise
3. **Risk factors** = diabetes mellitus (DM), atherosclerosis, congestive heart failure, peripheral vascular disease, lupus
4. **H/P** = acute abdominal pain, bloody diarrhea, vomiting; mild abdominal tenderness
5. **Workup** = increased white blood cell count (WBC), increased serum lactate
6. **Radiology** = barium enema shows diffuse submucosal changes from localized bleeding (i.e., "thumb printing"); sigmoidoscopy may show bloody and edematous mucosa; CT may show air within bowel wall and bowel wall thickening
7. **Treatment** = intravenous (IV) fluids, bowel rest, antibiotics for GI bacteria; surgical resection of necrotic bowel
8. **Complications** = high mortality in cases of irreversible damage

Quick **HIT**

The left side of the colon is most commonly involved in ischemic colitis; the rectum is frequently spared because of collateral circulation.

Quick **HIT**

Abdominal pain for ischemic colitis is less severe than **small bowel ischemic**, which is significant and **out of proportion to examination**.

G. Appendicitis

1. Inflammation of appendix with possible infection or perforation
2. Caused by lymphoid hyperplasia (children), fibroid bands (adults), or fecaliths (adults)
3. **H/P** = dull periumbilical pain followed by nausea, vomiting, and anorexia; pain gradually moves to right lower quadrant and increases; **tenderness at McBurney point** (1/3 distance from right anterior-superior iliac spine to umbilicus), rebound tenderness, **psoas sign** (psoas pain on passive hip extension), fever, **Rovsing sign** (right lower quadrant pain with left lower quadrant palpation); perforation produces severe pain and distention with rebound tenderness, rigidity, and guarding

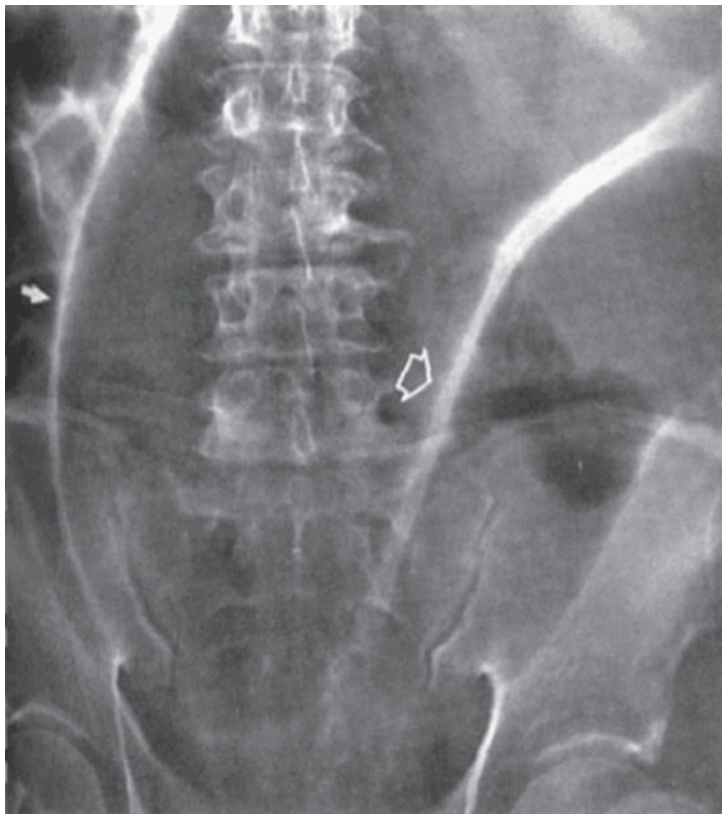


FIGURE **2-13**

Abdominal radiograph in a patient with large bowel obstruction due to sigmoid volvulus; note significantly dilated bowel lumen. Of note are the dense line markings where the walls of two dilated loops of bowel are pressed against each other (*open arrow*) and the dense markings where a dilated loop of bowel is compressed against the cecum (*solid arrow*).
(From Eisenberg, R. L. [2003]. *Gastrointestinal Radiology: A Pattern Approach* [4th ed.]. Philadelphia, PA: Lippincott-Raven; with permission.)

4. **Workup** = increased WBC with left shift
5. **Radiology** = AXR or chest x-ray may show fecalith or free air under the diaphragm (due to perforation); **CT most sensitive test** and may show bowel wall thickening, appendicolith, abscess, phlegmon, free fluid, or right lower quadrant fat stranding
6. **Treatment** = **appendectomy**; antibiotics added (covering gram-negatives and anaerobes) for ruptured appendix
7. **Complications** = abscess formation, perforation

NEXT
STEP

Always get a β-human chorionic gonadotropin (β-hCG) test in a woman of child-bearing age with abdominal pain to **rule out pregnancy**.

Table 2-10 Comparison of Small and Large Bowel Obstruction

	Small Bowel Obstruction	Large Bowel Obstruction
Causes	**Adhesions, incarcerated hernias**, neoplasm, intussusception, volvulus, Crohn disease, congenital stricture	**Neoplasm**, diverticulitis, volvulus, congenital stricture
Symptoms	Abdominal pain, **vomiting**, distention, obstipation	Abdominal pain, obstipation, distention, nausea, **late feculent vomiting**
Physical examination	Abdominal tenderness, visible peristaltic waves, high-pitched bowel sounds, absence of bowel sounds, fever	Abdominal tenderness, palpable mass, high-pitched bowel sounds, absence of bowel sounds
Radiology	AXR shows **ladderlike dilated loops of bowel**, air–fluid levels	AXR shows **bowel distention proximal to obstruction**; barium enema may detect obstruction near rectum
Treatment	Make patient NPO, maintain hydration; nasogastric decompression may relieve obstruction, but if unsuccessful, surgery is required	Make patient NPO, maintain hydration; colonoscopy may relieve obstruction, but if unsuccessful, surgery is required

AXR, abdominal x-ray; NPO, nothing by mouth.

H. Ileus

1. **Paralytic obstruction** of bowel secondary to decreased peristalsis
2. Caused by infection, ischemia, **recent surgery**, DM, opioid use
3. **H/P** = vague abdominal pain, nausea, vomiting, bloating, no bowel movements, inability to tolerate meals; decreased bowel sounds, no rebound tenderness
4. **Radiology** = AXR shows distention of affected bowel, air–fluid levels; barium enema can help rule out obstruction
5. **Treatment** = stop opioids, make patient NPO (i.e., nothing by mouth); colonoscopic decompression if no resolution

NEXT
STEP

With a high clinical suspicion of appendicitis, go right to surgery and do not wait for radiologic examinations.

I. Volvulus

1. **Rotation of bowel** creates obstruction and possible ischemia; most commonly occurs at cecum and sigmoid colon
2. Tends to occur in **elderly** and **infants**
3. **H/P** = distention, abdominal pain, vomiting, obstipation; possible palpable abdominal mass
4. **Radiology** = AXR may show **"double bubble"** proximal and distal to volvulus; barium enema shows **"bird's beak"** for distal volvulus
5. **Treatment** = possibly self-limited; colonoscopic decompression of sigmoid volvulus; surgical repair or resection may be required in cecal volvulus or failed colonoscopic detorsion

Quick **HIT**

Postoperative ileus typically lasts <**5 days**. Small bowel recovers in 24 hours, stomach in 48 to 72 hours, and large bowel in 3 to 5 days.

J. Diverticulosis

1. Outpouchings of colonic **mucosa** and **submucosa** that herniate through muscular layer (i.e., **diverticulosis**); may erode into colonic blood vessel to cause bleeding
2. **Risk factors** = low-fiber diet, high-fat diet, >60 years of age
3. **H/P** = frequently **asymptomatic** during uncomplicated diverticulosis; occasional cramping, bloating, flatulence, irregular defecation, vague left lower quadrant abdominal pain relieved with defecation; possible painless rectal bleeding if erosion into vessel occurs
4. **Workup** = positive stool guaiac test during bleeding
5. **Radiology** = **diverticula seen on barium enema** and colonoscopy (see Figure 2-14)
6. **Treatment** = high-fiber diet may help prevent development of additional diverticula or diverticular bleeding; no evidence to support avoidance of seeds, nuts, corn, etc.
7. **Complications** = **diverticulitis**, diverticular colitis (i.e., inflammation of section of colon)

Quick **HIT**

Diverticular disease most frequently occurs in the sigmoid colon and is the most common cause of **acute lower GI bleeding** in patients **over 40 years of age**.

K. Diverticulitis

1. Obstruction of a diverticulum leading to significant inflammation, focal bowel wall necrosis, and **perforation**; poor containment of colonic rupture leads to peritonitis
2. **H/P** = **left lower quadrant pain**, nausea, vomiting, melena, hematochezia; abdominal tenderness, possible palpable abdominal mass, fever, abdominal distention
3. **Workup** = increased WBC
4. **Radiology** = CXR or AXR may demonstrate free air under the diaphragm; CT shows increased soft tissue density caused by inflammation, colonic diverticula, bowel wall thickening, and possible abscess formation
5. **Treatment**
   a. Mild early cases without perforation can be treated by bowel rest (liquids only for at least 3 days) and PO antibiotics (e.g., fluoroquinolone and metronidazole, TMP-SMX and metronidazole, or amoxicillin-clavulanate)
   b. **Surgery** required in most severe cases to resect involved segment of colon and remove any obstruction or fistula; diverting colostomy performed in cases of peritonitis (reanastomosis in 3 months)
   c. Broad-spectrum antibiotics required for any case of bowel rupture
6. **Complications** = colonic abscess, fistula formation, sepsis

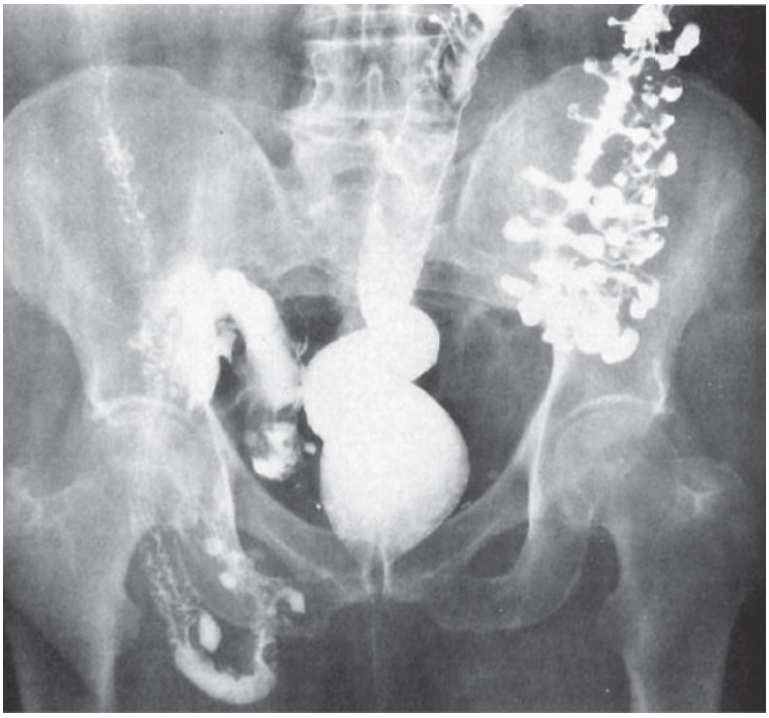


FIGURE **2-14**

Barium enema in a patient with diverticular disease; numerous diverticula can be seen in the left colon.
(Modified from Daffner, R. H., & Hartman, M. [2013]. *Clinical Radiology: The Essentials* [4th ed., p. 273]. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; with permission.)

L. Rectal Conditions

1. **Hemorrhoids**
   a. Internal and external engorged rectal veins causing bleeding (**bright red blood**)
   b. **Internal** hemorrhoids arise from superior rectal veins above the pectinate line (columnar rectal epithelium); characteristically **painless**
   c. **External** hemorrhoids arise from **inferior** rectal veins below the pectinate line (squamous rectal epithelium); frequently **painful** (especially if thrombosed)
   d. **Radiology** = sigmoidoscopy used to rule out other causes of bleeding
   e. **Treatment** = warm baths, increase fiber in diet, avoid prolonged straining; sclerotherapy, ligation, or excision can be performed for worsening symptoms
2. **Anal fissures**
   a. Painful, bleeding tears in posterior wall of anus secondary to trauma during defecation or anal intercourse
   b. **Treatment** = stool softeners, sitz baths, topical nitroglycerin (second line); partial sphincterotomy may be performed for recurrent fissures
3. **Anorectal abscesses**
   a. Infection of anal crypts, internal hemorrhoids, or hair follicle leading to abscess formation
   b. **H/P** = throbbing rectal pain; fever, tenderness on digital examination
   c. **Treatment** = antibiotics, surgical incision and drainage
4. **Rectal fistula**
   a. Formation of tract between rectum and adjacent structures from unknown cause or secondary to **IBD** or abscess formation
   b. **H/P** = mild pain during defecation; possible visible site draining pus
   c. **Treatment** = fistulotomy; treat patients with Crohn disease with antibiotics and immunosuppressants unless refractory disease
5. **Pilonidal disease**
   a. Presence of one or more cutaneous sinus tracts in the superior midline gluteal cleft
   b. Obstruction of sinus tract by hair or debris can lead to cyst and abscess formation
   c. **H/P** = usually asymptomatic; obstruction of sinus leads to mildly painful cyst with drainage (possibly purulent); small cysts can progress to larger abscesses
   d. **Treatment** = incision and drainage of abscesses; surgical closure of sinus tracts may prevent recurrence

NEXT
STEP

If a patient has significant rectal pain and the only finding on colonoscopy is internal hemorrhoids, a workup must be performed to locate another cause of symptoms (e.g., abscess or fissure).

M. Carcinoid Tumor

1. Tumors arising from neuroectodermal cells that function as amine precursor uptake and decarboxylation (APUD) cells
2. Most commonly in bronchopulmonary tree, ileum, rectum, appendix
3. **H/P** = possibly asymptomatic; abdominal pain; possible **carcinoid syndrome** (i.e., flushing, diarrhea, bronchoconstriction, tricuspid/pulmonary valvular disease) caused by serotonin secretion by tumor (only seen with liver metastases or extra-GI involvement)
4. **Workup** = increased 5-hydroxyindoleacetic acid (5-HIAA) in urine, increased serum serotonin level
5. **Radiology** = CT or indium-labeled octreotide scintigraphy can localize tumor
6. **Treatment** = tumors <2 cm have very low incidence of metastases and should be resected; tumors >2 cm have high risk of metastases and require extensive resection; metastatic disease treated with IFN-α, octreotide, and embolization

Quick HIT

Iron deficiency anemia in elderly men and postmenopausal women is considered colon cancer until proven otherwise.

Quick HIT

Hematochezia can result from a heavy upper GI bleed.

Quick HIT

Familial adenomatous polyposis (FAP), Gardner syndrome, and Turcot syndrome are caused by a mutation in the adenomatous polyposis coli (***APC***) gene.

N. Colorectal Cancer

1. Neoplasm of large bowel or rectum; most commonly adenocarcinoma
2. **Risk factors** = family history, ulcerative colitis, **colonic polyps**, hereditary polyposis syndromes, low-fiber/high-fat diet, previous colon cancer, alcohol, smoking, DM
3. Spreads to regional lymph nodes; **metastasizes** most commonly to **lung** and **liver**
4. **H/P** = change in bowel habits (more common in left-sided disease), weakness, right-sided abdominal pain (in right-sided disease), constipation, hematochezia, melena, anemia due to blood loss, malaise, weight loss; abdominal or rectal mass may be palpated
5. **Workup** = **positive stool guaiac test**, decreased hemoglobin, decreased hematocrit; biopsy is diagnostic; CEA, which is increased in 70% of patients, is useful for monitoring treatment success and cancer recurrence
6. **Radiology** = barium enema may detect lesion; colonoscopy may detect lesion and obtain biopsy specimens; CT or PET used to determine local extent of disease and spread of metastases
7. **Treatment**
   a. **Surgical resection** plus regional lymph node dissection; adjuvant chemotherapy in cases of positive lymph nodes; palliative resections are helpful in metastatic disease to reduce symptoms and remove obstruction
   b. Preventative colectomy may be indicated for hereditary syndromes (see Table 2-11)
   c. Duke classification can be used for prognosis (see Table 2-12); CEA and serial colonoscopy may be followed after treatment to monitor for recurrence

Table 2-11 Familial Colon Tumor Syndromes

Hereditary Disease	Characteristics
Familial adenomatous polyposis (FAP)	Hundreds of polyps in colon; near-certain development of malignant neoplasm; prophylactic subtotal colectomy recommended
Gardner syndrome	Similar to FAP with addition of common bone and soft tissue tumors
Turcot syndrome	Many colonic adenomas with high malignant potential; comorbid malignant CNS tumors
Juvenile polyposis	Hamartomatous polyps of colon, small bowel, and stomach that frequently are source of GI bleeding; slightly increased risk of malignancy later in life
Peutz–Jeghers syndrome	Polyps are hamartomas with low risk of malignancy; mucocutaneous pigmentation of mouth, hands, and genitals
Hereditary nonpolyposis colorectal cancer (HNPCC)	Multiple genetic mutations; cancer arises from normal-appearing mucosa; neoplasms tend to form in proximal colon

CNS, central nervous system; GI, gastrointestinal.

Table 2-12 Duke Classification System for Staging and Corresponding Prognosis of Colorectal Cancer

Class	Equivalent TNM Stage	Description	Cure Rate
A	I	Tumor confined to bowel wall	90%
B	II	Penetration of tumor into colonic serosa or perirectal fat	80%
C	III	Lymph node involvement	<60%
D	IV	Distant metastases	<5%

TNM, tumor, node, metastasis.

8. **Prevention**
   a. Regular screening for colon cancer recommended in patients >50 years of age
   b. Annual fecal occult blood test (FOBT)
   c. Flexible sigmoidoscopy every 5 years (in addition to FOBT)
   d. **Colonoscopy** is more sensitive than sigmoidoscopy but carries a 0.1% risk of perforation; it is now considered preferable over sigmoidoscopy by several expert groups and is recommended to be performed every 10 years; it should definitely be chosen over sigmoidoscopy for patients with a hereditary high risk of colon cancer

O. GI Bleeding

1. Caused by either upper (i.e., proximal to ligament of Treitz) or lower (i.e., distal to ligament of Treitz) sources
2. Bright red blood (e.g., hematochezia) suggests a rapid or heavy bleed; dark blood (e.g., melena, coffee-grounds emesis) suggests either blood that has passed through much of the GI tract or has been sitting in the stomach for some time (see Figure 2-15)

Quick HIT

Hematocrit is **not** a good indicator of acute volume status.

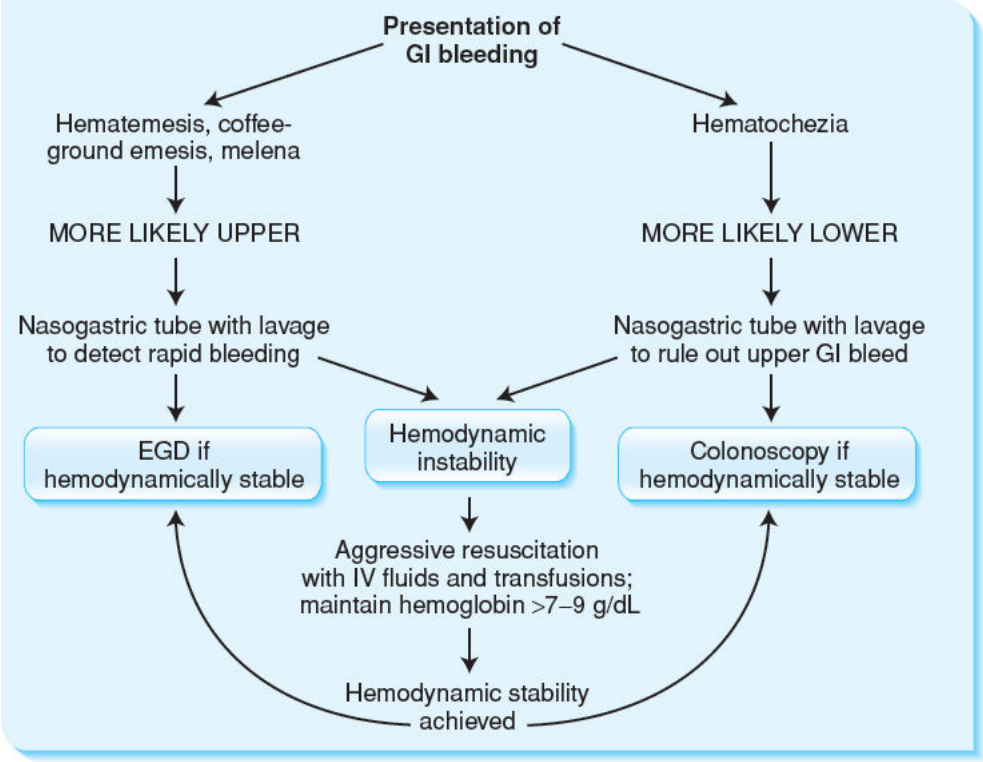


FIGURE 2-15
Diagnostic pathway for gastrointestinal (GI) bleeding.
EGD, esophagogastroduodenoscopy; IV, intravenous.

3. Common causes of upper GI bleeds are **PUD**, Mallory–Weiss tears (longitudinal esophageal tears secondary to violent retching), esophagitis, **esophageal varices**, and gastritis

4. Common causes of lower GI bleeds are **diverticulosis**, **neoplasm**, ulcerative colitis, mesenteric ischemia, arteriovenous malformations (AVMs), hemorrhoids, and Meckel diverticulum
5. **Diagnostics** = EGD or colonoscopy shows most sources of bleeding; barium studies may detect defects; capsule endoscopy may show sources of bleeding in the small intestine; technetium-tagged red blood cell (RBC) scan may help localize intermittent bleeding; angiography can help locate AVMs
6. **Treatment** = **fluid replacement** is vital; transfusion for increased blood loss; some small bleeds stop automatically; **treat underlying cause**; PPI for upper GI bleeds until gastric cause ruled out; prophylactic antibiotics and β-blockers in patients with a known history of cirrhosis; sclerotherapy may help stop bleeding from varices; vasopressin may stop bleeding from AVMs and diverticula; surgical resection of tumors and diverticula may be needed

MNEMONIC

Remember the causes of acute pancreatitis by the mnemonic **PANCREATITIS**:

- hyper**P**arathyroid (hypercalcemia)
- **A**lcohol
- **N**eoplasm
- **C**holelithiasis
- **R**x (drugs)
- **E**RCP
- **A**bdominal surgery
- Hyper**T**riglyceridemia
- **I**nfection (mumps)
- **T**rauma
- **I**diopathic
- **S**corpion bite

V. Pancreatic Disorders

A. Pancreatitis (See Tables 2-13 and 2-14)

1. **Acute** or **chronic** inflammation of pancreas associated with anatomic defects, chronic **alcohol use**, acute ductal obstruction, drugs, **gallstones**
2. Initially, results from leak of pancreatic enzymes into pancreatic and surrounding tissues; later caused by pancreatic tissue necrosis; prognosis determined by Ranson criteria

B. Pancreatic Pseudocyst

1. Fluid collection arising from pancreas consisting of enzyme-rich fluids contained in sac of inflamed membranous tissue

Table 2-13 Comparison of Acute and Chronic Pancreatitis

	Acute Pancreatitis	Chronic Pancreatitis
Onset	**Sudden**, severe	**Recurrent**
Risk factors	**Gallstones**, **chronic alcohol abuse**, trauma, hypercalcemia, hyperlipidemia, drugs	**Chronic alcohol abuse**, congenital defect
History/physical	Acute epigastric pain radiating to back, nausea, vomiting, **Grey Turner sign** (ecchymosis of flank), **Cullen sign** (periumbilical ecchymosis), fever, tachycardia; hypotension, shock if severe	Recurrent epigastric pain, steatorrhea, weight loss, nausea, constipation
Labs	Increased amylase and lipase	Mildly increased amylase and lipase, glycosuria; **low fecal elastase**
Radiology	AXR may show dilated loop of bowel near pancreas (**sentinel loop**) or right colon distended until near pancreas (colon **cutoff sign**); CXR may show pleural effusion, hemidiaphragm elevation; CT may show **pseudocyst** or enlarged pancreas; US may detect gallstones	Abdominal radiograph may show **pancreatic calcifications**; CT may show calcifications, pancreatic enlargement, or pseudocyst; MRCP or ERCP may be helpful for diagnosis
Treatment	Hydration, pain control with opioids, nasogastric suction, make patient NPO, stop offending agent; debridement of necrotic tissue	Stop alcohol use, opioid analgesia, enzyme supplementation, dietary modification (small, low-fat meals); surgery may be required to repair ductal damage
Complications	Pancreatic abscess, **pseudocyst**, necrosis, fistula formation, renal failure, chronic pancreatitis, hemorrhage, **shock**, DIC, sepsis, respiratory failure	Ductal obstruction, pseudocyst, **malnutrition**, glucose intolerance, pancreatic cancer

CT, computed tomography; CXR, chest x-ray; DIC, disseminated intravascular coagulation; ERCP, endoscopic retrograde cholangiopancreatography; MRCP, magnetic resonance cholangiopancreatography; US, ultrasound.

Table 2-14 Ranson Criteria for Determining Prognosis During Acute Pancreatitis

Increased Mortality Associated With Three or More of the Following:

On Admission	During Initial 48 hrs After Admission
Serum glucose >200 mg/dL	Serum calcium <8 mg/dL
Serum AST >250 IU/L	Hematocrit decreases >10%
Serum LDH >350 IU/L	Pao_2 <60 mm Hg
>55 yrs of age	BUN increases >5 mg/dL
WBC >16,000/mL	Base deficit >4 mEq/L
	Fluid sequestration >6 L

BUN, blood urea nitrogen; LDH, lactate dehydrogenase; Pao_2, partial pressure of arterial oxygen; WBC, white blood cell count.

2. **H/P** = usually asymptomatic; **recent acute pancreatitis**, epigastric pain; fever
3. **Workup** = increased WBC, increased amylase; aspiration of pseudocyst demonstrates very high amylase content
4. **Radiology** = pseudocyst visible on ultrasound (US) or CT
5. **Treatment** = possibly self-resolving; drainage (surgical, endoscopic, or percutaneous) indicated if lasting >6 weeks, painful, or rapidly growing; debride necrotic pancreatic tissue
6. **Complications** = rupture, hemorrhage, abscess or pseudoaneurysm formation

MNEMONIC

Remember Ranson criteria for increased mortality from acute pancreatitis on **admission** by the mnemonic **GA LAW:**

- **G**lucose >200 mg/dL
- **A**ST >250 IU/L
- **L**DH >350 IU/L
- **A**ge >55 years
- **W**BC >16,000/mL

C. Exocrine Pancreatic Cancer

1. Adenocarcinoma of pancreas most commonly in head of pancreas
2. **Risk factors** = chronic pancreatitis, DM, family history, tobacco, high-fat diet; male > female, obesity, sedentary lifestyle

3. **H/P** = **abdominal pain radiating to back**, anorexia, nausea, vomiting, weight loss, fatigue, steatorrhea; jaundice if bile duct obstructed (painless jaundice is possible); palpable, nontender gallbladder (i.e., **Courvoisier sign**); splenomegaly (if in tail), palpable deep abdominal mass, ascites
4. **Workup** = possible hyperglycemia; increased **CEA** and **CA 19–9** tumor markers; increased bilirubin (total and direct) and increased alkaline phosphatase with bile duct obstruction; biopsy used to make diagnosis
5. **Radiology** = CT shows mass, dilated pancreas, local spread, and dilated bile ducts; US also useful for imaging mass, but not as sensitive as CT; endoscopic retrograde cholangiopancreatography (ERCP) locates tumors not seen with CT; endoscopic US often helpful for staging and to guide fine-needle aspiration biopsy
6. **Treatment**
   a. Nonmetastatic disease limited to head of pancreas may be resected with **Whipple procedure** (i.e., removal of pancreatic head, distal stomach, duodenum, proximal jejunum, common bile duct, and gallbladder)
   b. Lesions in body or tail rarely amenable to surgery but can be resected via subtotal pancreatectomy if found early
   c. Adjuvant chemotherapy may be beneficial in resectable disease
   d. Enzyme deficiency treated with replacement therapy
   e. Stenting of pancreatic ducts, biliary ducts, or duodenum can be performed as palliative therapy in advanced disease
7. **Complications** = usually not detected until progressed; **5-year survival <2%**; 20% to 30% 5-year survival following successful Whipple procedure; migratory thrombophlebitis (i.e., **Trousseau syndrome**)

MNEMONIC

Ranson criteria for increased mortality from acute pancreatitis **during initial 48 hrs after admission** may be remembered by the mnemonic **Calvin & HOBBeS:**

- **C**alcium <8 mg/dL
- **H**ct decrease >10%
- **O$_2$** (Pao$_2$) <60 mm Hg
- **B**UN increase >5 mg/dL
- **B**ase deficit >4 mEq/L
- **S**equestration of fluid >6 L

NEXT
STEP

If Whipple triad is seen (**symptoms of hypoglycemia while fasting, hypoglycemia, and improvement in symptoms with carbohydrate load**), perform a workup for insulinoma.

Quick **HIT**

Insulinomas are almost always **solitary**; multiple insulinomas may be seen in **MEN 1**.

D. Endocrine Pancreatic Cancers

1. Neoplasms involving glandular pancreatic tissue
2. Frequently difficult to locate; may be seen with CT or MRI
3. **Zollinger–Ellison syndrome** (see earlier discussion under “Gastric Conditions” section)
4. **Insulinoma**
   a. Insulin-secreting β-islet cell tumor causing **hypoglycemia**
   b. **H/P** = headache, visual changes, confusion, weakness, mood instability, palpitations, diaphoresis
   c. **Workup** = **increased fasting insulin**, spontaneous hypoglycemia, high C-peptide
   d. **Radiology** = CT, US, or indium-labeled octreotide scintigraphy may be useful for localizing tumor
   e. **Treatment** = surgical resection; diazoxide or octreotide may relieve symptoms in unresectable disease
5. **Glucagonoma**
   a. Glucagon-secreting α-cell tumor causing hyperglycemia
   b. May present as refractory DM
   c. **H/P** = abdominal pain, diarrhea, weight loss, mental status changes; exfoliating rash (**necrolytic migratory erythema**); **symptoms of DM**
   d. **Workup** = hyperglycemia, **increased glucagon**; biopsy confirms diagnosis
   e. **Radiology** = CT or endoscopic US may localize tumor
   f. **Treatment** = surgical resection if localized lesion; octreotide, IFN-α, chemotherapy, and embolization may be used in metastatic disease
   g. **Complications** = frequently malignant; poor prognosis
6. **VIPoma**
   a. Vasoactive intestinal peptide (VIP)–producing tumor of non–β-islet cells
   b. **H/P** = **watery diarrhea**, weakness, nausea, vomiting, abdominal pain
   c. **Workup** = increased serum VIP, stool osmolality suggests secretory cause
   d. **Radiology** = CT may detect tumor

e. **Treatment** = surgical resection for localized tumors; corticosteroids, chemotherapy, octreotide, and embolization used in metastatic disease

MNEMONIC

Remember the 5 **F**s for patients susceptible to gallstone formation: **F**emale, **F**ertile, **F**at, **F**orty (years of age), and **F**amily history.

NEXT
STEP

If a positive Murphy sign (**palpation of RUQ during inspiration stops inspiration secondary to pain**) is detected, suspect acute cholecystitis and perform a US.

VI. Biliary Disorders

A. Cholelithiasis

1. Gallstone formation in the gallbladder that can cause cystic duct obstruction
2. **Risk factors** = age >40 years, obesity, female, multiparity, oral contraceptive use, total parenteral nutrition (TPN), recent rapid weight loss, family history, DM
3. Most stones are composed of **cholesterol**; others are calcium bilirubinate (i.e., **pigmented stones**) secondary to chronic hemolysis
4. **H/P** = possibly asymptomatic; postprandial abdominal pain (**worst in RUQ**), nausea, vomiting, indigestion, flatulence; RUQ tenderness, palpable gallbladder
5. **Radiology** = US may show gallstones (see Figure 2-16); AXR will only show some pigmented stones (because of calcium content and high iron content from bilirubin)
6. **Treatment** = dietary modification (decrease fatty food intake), bile salts (dissolve stones), shock wave lithotripsy (uses sound waves to break up stones); **cholecystectomy** is typically performed in symptomatic patients
7. **Complications** = recurrent stones, **acute cholecystitis, pancreatitis**

B. Acute Cholecystitis

1. Inflammation of gallbladder commonly caused by **gallstone obstruction of cystic duct**; acalculous cholecystitis can occur in patients on TPN or in those who are critically ill
2. **H/P** = RUQ pain radiating to back, nausea, vomiting, anorexia; fever, palpable gallbladder, RUQ tenderness; symptoms more severe and longer in duration than typical cholelithiasis
3. **Workup** = increased WBC; increased bilirubin (total and direct) and increased alkaline phosphatase seen when condition is related to impacted stone or cholangitis

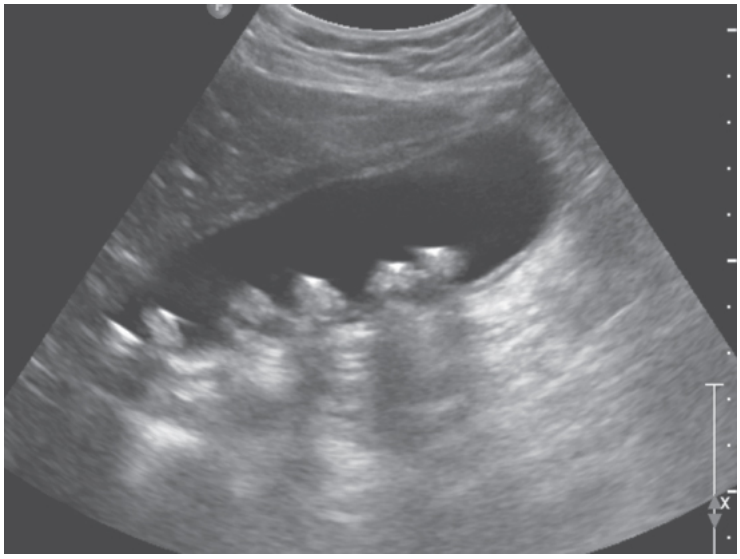


FIGURE 2-16
Ultrasound demonstrating multiple gallstones in the gallbladder.
Note the shadow caused by gallstones, which may be more apparent than the gallstones themselves in several cases.
(From Kawamura, D. M., & Lunsford, B. M. [2012]. *Diagnostic Medical Sonography, Abdomen and Superficial Structures* [3rd ed., p. 180]. Philadelphia, PA: Lippincott Williams & Wilkins; with permission.)

4. **Radiology** = US may show gallstones, sludge, thickened gallbladder wall, or sonographic Murphy sign; hepatic iminodiacetic acid (**HIDA**) scan will detect cystic duct obstruction (gallbladder fails to fill normally during scan)
5. **Treatment** = hydration, antibiotics, **cholecystectomy** (frequently delayed after 24 to 48 hours of supportive care); patients with more mild symptoms can be treated with lithotripsy and bile salts; patients who are not stable for surgery can be treated with ERCP delivery of stone solvents
6. **Complications** = perforation, gallstone ileus, abscess formation

C. Cholangitis

1. Infection of bile ducts secondary to ductal obstruction
2. **Risk factors** = cholelithiasis, anatomic duct defect, biliary cancer
3. **H/P** = RUQ pain, chills; **jaundice, fever, RUQ tenderness**; change in mental status or signs of shock seen in severe cases (see Figure 2-17)
4. **Workup** = increased WBC, increased bilirubin (total and direct), increased alkaline phosphatase, increased AST and ALT, increased amylase and/or lipase with associated pancreatic inflammation, **positive blood cultures**
5. **Radiology** = magnetic resonance cholangiopancreatography (MRCP), US may detect obstruction; HIDA scan is more sensitive and also an option
6. **Treatment** = hydration, IV antibiotics, endoscopic biliary drainage followed by delayed cholecystectomy; severe symptoms demand **emergency bile duct decompression** and relief of obstruction

NEXT
STEP

If Charcot triad (**RUQ pain, jaundice, and fever**) is seen, suspect cholangitis and perform a US or HIDA scan.

Quick **HIT**

The addition of shock and altered mentation to the Charcot triad is also known as Reynolds pentad of ascending cholangitis.

D. Gallbladder Cancer

1. Adenocarcinoma of gallbladder associated with cholelithiasis, chronic infection, and biliary tract disease; generally poor prognosis
2. **H/P** = similar symptoms to acute cholecystitis; anorexia, weight loss, abdominal pain radiating to back; palpable gallbladder, jaundice
3. **Workup** = increased bilirubin (total and direct), increased alkaline phosphatase, increased cholesterol; biopsy provides diagnosis
4. **Radiology** = abdominal radiograph may show **calcified gallbladder** (i.e., porcelain gallbladder); US or endoscopic US may detect invasive mass; ERCP can localize lesion and perform biopsy
5. **Treatment** = cholecystectomy, lymph node dissection, partial removal of adjacent hepatic tissue; adjuvant radiation therapy and chemotherapy may reduce recurrence rates and are used as primary therapies in unresectable disease

NEXT
STEP

A **calcified gallbladder** is highly suggestive of chronic cholecystitis but may represent cancer in 10% to 30%, and cholecystectomy should be performed promptly to confirm diagnosis.

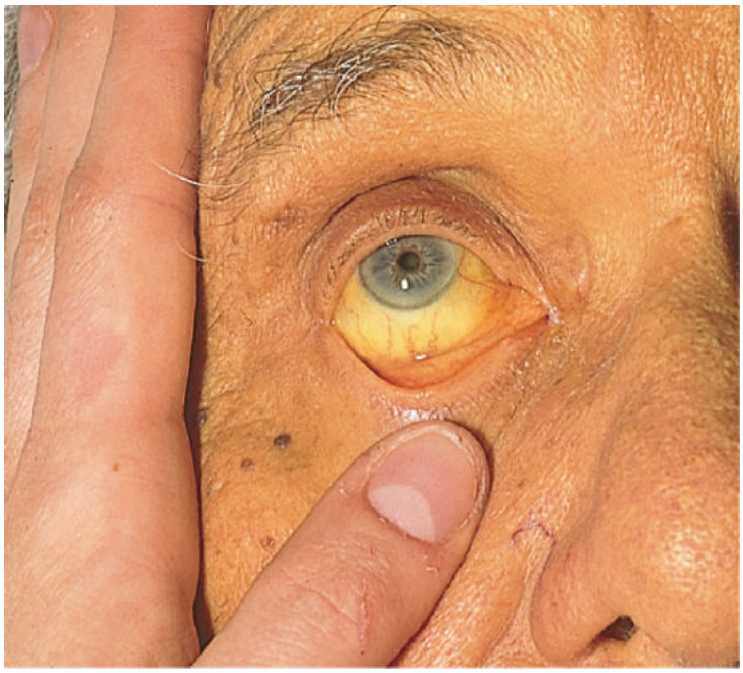


FIGURE 2-17
Jaundice in a patient with hyperbilirubinemia.
Note the yellow sclera and skin compared with the normal hue of the examiner's hand.
(From Bickley, L. S., & Szilagyi, P. [2012]. *Bates' Guide to Physical Examination and History Taking* [11th ed., p. 184]. Philadelphia, PA: Lippincott Williams & Wilkins; with permission.)

E. Primary Biliary Cirrhosis (PBC)

1. Autoimmune disease with intrahepatic bile duct destruction leading to accumulation of cholesterol, bile acids, and bilirubin
2. **Risk factors** = rheumatoid arthritis, Sjögren syndrome, scleroderma; **female** > **male**
3. **H/P** = possibly asymptomatic; fatigue, pruritus, arthralgias; jaundice, xanthomas, skin hyperpigmentation, hepatosplenomegaly
4. **Workup** = increased alkaline phosphatase, increased γ-glutamyl transferase (GGT), normal AST and ALT, increased cholesterol, increased bilirubin (total and direct) later in disease course; positive antinuclear antibody (ANA), **positive antimitochondrial antibodies**; workup may indicate comorbid autoimmune diseases; biopsy shows inflammation and necrosis in bile ducts
5. **Treatment** = ursodeoxycholic acid improves liver function and reduces symptoms; colchicine or methotrexate can be added in more severe cases; liver transplant needed in progressive disease

Quick HIT

Gender, presence or absence of antimitochondrial antibodies, and ERCP distinguish PBC from PSC.

F. Primary Sclerosing Cholangitis (PSC)

1. Progressive destruction of intra- and extrahepatic bile ducts leading to fibrosis and cirrhosis
2. **Risk factors** = ulcerative colitis; **male** > **female**
3. **H/P** = possibly asymptomatic; fatigue, pruritus, RUQ pain; fever, night sweats, jaundice, xanthomas
4. **Workup** = increased alkaline phosphatase, increased GGT, normal AST and ALT, increased cholesterol, increased bilirubin (total and direct), possible positive perinuclear antineutrophil cytoplasmic antibodies (pANCA); biopsy appears similar to that for PBC
5. **Radiology** = ERCP shows stricturing and irregularity of extra- and intrahepatic bile ducts (i.e., **"beads on string"**)
6. **Treatment** = endoscopic stenting of strictures; surgical resection of affected ducts and liver transplant may be required in progressive cases

Quick HIT

Prehepatic conditions cause an increase in **indirect bilirubin**; **posthepatic** conditions cause an increase in **direct bilirubin**; **intrahepatic** conditions can cause an increase of **either** or **both** types of bilirubin.

G. Disorders of Hepatic Bilirubin Transport

1. **Normal bilirubin transport**
   a. Unconjugated bilirubin from RBC hemolysis exists in venous circulation

b. Unconjugated bilirubin enters hepatocytes and is conjugated by glucuronosyltransferase
c. Conjugated bilirubin reenters venous circulation
d. Abnormal levels of unconjugated bilirubin versus conjugated bilirubin versus both types can help indicate location of pathology and narrow differential diagnosis (see Table 2-15)

Table 2-15 Causes of Conjugated and Unconjugated Bilirubinemia

Increased Total Bilirubin		
Hyperbilirubinemia	**Cause**	**Examples**
Unconjugated (indirect)	Excess bilirubin production	Hemolytic anemia Disorders of erythropoiesis Internal hemorrhage resorption
	Impaired conjugation	Physiologic jaundice of newborn Deficiency of glucuronosyltransferase (Gilbert disease, Crigler–Najjar syndrome) Hepatocellular disease (cirrhosis, hepatitis)
Conjugated (direct)	Decreased hepatic bilirubin excretion	Impaired bilirubin transport (Dubin–Johnson syndrome, Rotor syndrome) Hepatocellular disease (cirrhosis, hepatitis) Drug impairment
	Extrahepatic biliary obstruction	Intrahepatic bile duct disease (PBC, PSC) Gallstone obstruction of bile ducts (choledocholithiasis) Pancreatic or biliary cancer Biliary atresia

PBC, primary biliary cirrhosis; PSC, primary sclerosing cholangitis.

2. **Gilbert disease**
   a. Autosomal recessive or dominant disease with **mild deficiency** of glucuronosyltransferase
   b. **H/P** = mild jaundice following fasting, exercise, or stress
   c. **Workup** = increased indirect bilirubin >5 mg/dL
   d. **Treatment** = none necessary
3. **Crigler–Najjar syndrome type I**
   a. Autosomal recessive disease with **severe deficiency** in glucuronosyltransferase
   b. **H/P** = persistent jaundice and central nervous system (CNS) symptoms (due to kernicterus) in **infants**
   c. **Workup** = increased indirect bilirubin <5 mg/dL
   d. **Treatment** = phototherapy, plasmapheresis, calcium phosphate combined with orlistat; liver transplantation is an option
   e. **Complications** = early kernicterus can cause permanent CNS damage
4. **Crigler–Najjar syndrome type II**
   a. Mild deficiency of glucuronosyltransferase; phenotypically similar to Gilbert syndrome
   b. Can be treated with phenobarbital, which induces hepatic synthesis of glucuronyltransferase, and reduces jaundice

***Quick* HIT**

In viral hepatitis, AST and ALT are equally high; in alcohol-related liver disease, AST > ALT by >2:1 ratio.

VII. Hepatic Disorders

A. Alcohol-related Liver Disease

1. Progressive liver damage secondary to **chronic alcohol abuse**
2. Initially characterized by fatty deposits in liver; reversible with alcohol cessation
3. Continued alcoholism causes hepatic inflammation and early necrosis
4. Progressive damage results in cirrhosis
5. **H/P** = asymptomatic for many years of alcoholism; anorexia, nausea, vomiting late in disease course; abdominal tenderness, ascites, splenomegaly, hepatomegaly, fever, jaundice, testicular atrophy, gynecomastia, digital clubbing
6. **Workup** = increased ALT, increased AST, increased GGT, increased alkaline phosphatase, increased bilirubin (total and direct), prolonged prothrombin time (PT), decreased lipids, increased WBC; biopsy provides diagnosis (**fatty liver**, many polymorphonuclear leukocytes [PMNs], areas of necrosis)
7. **Treatment** = **cessation of alcohol use**, thiamine, folate, high caloric intake (2,500 to 3,000 kcal/day); liver transplant is a consideration in patients who are able to maintain abstinence from alcohol
8. **Complications** = cirrhosis, hepatic encephalopathy, coagulation disorders

B. Cirrhosis

1. **Persistent liver damage** leading to **necrosis** and **fibrosis** of hepatic parenchyma
2. Caused by **alcoholism**, chronic **HBV** or **HCV** infection, chronic bile duct obstruction and chronic cholestasis (PBC/PSC), and hepatic parenchymal diseases (hemochromatosis, Wilson disease, α_1-antitrypsin deficiency, nonalcoholic steatohepatitis, autoimmune hepatitis)
3. **H/P** = general signs and symptoms may include weakness, weight loss, digital clubbing, Dupuytren contractures in hands; **portal hypertension** leads to esophageal varices and possibly variceal bleeding, abdominal wall varicosities (**caput medusae**), hepatosplenomegaly, **ascites**; **liver failure** leads to jaundice, coagulopathy, peripheral edema, mental status changes (from encephalopathy), asterixis (asynchronous flapping of hands), testicular atrophy and gynecomastia (in men), spider telangiectasias, palmar erythema
4. **Workup** = increased ALT, increased AST, increased GGT, increased alkaline phosphatase, decreased albumin, anemia, decreased platelets, prolonged PT; paracentesis of ascites shows fluid with <2.5 g/dL protein, WBC <300/μL, normal glucose level, and decreased amylase; biopsy shows fibrosis and hepatic necrosis
5. **Radiology** = US detects small, nodular liver
6. **Treatment** = **nonreversible**, but progression may be halted; stop offending agent (e.g., alcohol); treat varices with β-blockers or sclerotherapy to reduce bleeding risk; lactulose and rifaximin may improve encephalopathy; liver transplant may be needed in progressive cases
7. **Complications** = **portal hypertension**, varices (caused by venous hypertension), ascites, **hepatic encephalopathy** (because of poor filtering of blood), renal failure, spontaneous bacterial peritonitis

C. Portal Hypertension

1. Increase in portal vein pressure giving it a **higher pressure than the inferior vena cava**; may result from prehepatic, intrahepatic, or posthepatic causes
2. Prehepatic causes include portal vein thrombosis
3. Intrahepatic causes include **cirrhosis**, schistosomiasis, parenchymal disease, and granulomatous disease
4. Posthepatic causes include **right-sided heart failure**, hepatic vein thrombosis, and Budd–Chiari syndrome (i.e., hepatic vein thrombosis secondary to hypercoagulability)
5. Shunting of blood into systemic veins causes varices in several locations (see Figure 2-18)
6. **H/P** = **ascites**, abdominal pain, change in mental status (from hepatic encephalopathy), hematemesis (caused by esophageal varices), symptoms of cirrhosis; **hepatomegaly**, splenomegaly, fever, abdominal wall varices, testicular atrophy, gynecomastia
7. **Workup** = paracentesis shows ascites with serum-ascites albumin gradient (SAAG) ≥1.1
8. **Radiology** = CT may show ascites and obstructing mass; EGD may show esophageal varices
9. **Treatment**
   a. Salt restriction and diuretics (furosemide and spironolactone) for ascites
   b. IV antibiotics for bacterial peritonitis (or with variceal hemorrhage)
   c. Dialysis for renal failure
   d. Vasopressin or sclerotherapy for bleeding varices
   e. **Hepatic shunting** via laparotomy or transjugular intrahepatic portosystemic shunting (TIPS) is short-term solution for severe disease; **liver transplant** often required as eventual treatment in progressive cases

NEXT
STEP

If paracentesis detects very high albumin and LDH equal to 60% serum LDH, worry about a neoplastic etiology and do a full workup for cancer.

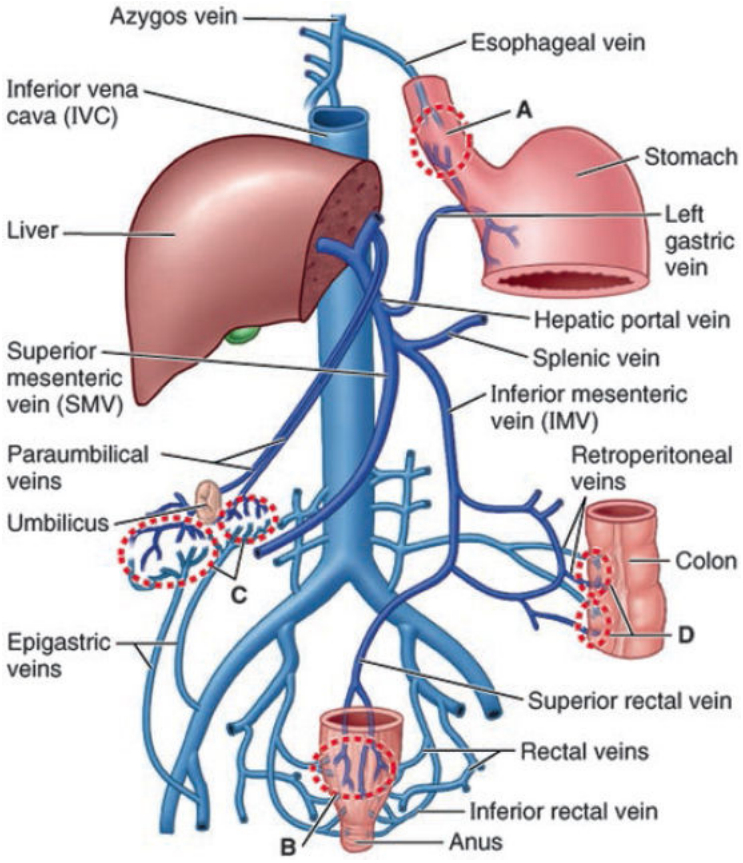


FIGURE **2-18**

Portal-systemic anastomoses and common sites of varices in portal hypertension.
These anastomoses provide collateral circulation in cases of obstruction in the liver or hepatic portal vein. *Darker blue*, portal tributaries; *lighter blue*, systemic tributaries; *A*, anastomoses between esophageal veins; *B*, anastomoses between rectal veins; *C*, anastomoses between paraumbilical veins (portal) and small epigastric veins of the anterior abdominal wall; *D*, anastomoses between the twigs of colic veins (portal) and the retroperitoneal veins.
(From Moore, K. L., Agur, A. M. R., & Dalley, A. F. [2013]. *Clinically Oriented Anatomy* [5th ed., p. 167]. Philadelphia, PA: Lippincott Williams & Wilkins; with permission.)

Quick HIT

Spontaneous bacterial peritonitis can result from systemic infection and comorbid portal hypertension; paracentesis will show >250 PMN/μL, total protein >1 g/dL, glucose <50 mg/dL, and lactate dehydrogenase (LDH) > normal serum LDH.

D. Hemochromatosis

1. Autosomal recessive disease of iron absorption
2. **Excess iron absorption** causes iron deposition in liver, pancreas, heart, and pituitary, leading to eventual fibrosis
3. Rarely is result of chronic blood transfusions or alcoholism
4. **H/P** = abdominal pain, polydipsia, polyuria, arthralgias, impotence, lethargy; **pigmented rash** (bronze hue), hepatomegaly, testicular atrophy; may see symptoms and signs that resemble DM and CHF
5. **Workup** = increased iron, increased ferritin, increased transferrin saturation, slightly increased AST and ALT; biopsy shows increased iron content in liver, but diagnosis is usually made by genetic testing
6. **Treatment** = **weekly or biweekly phlebotomy** until normal iron, then monthly phlebotomy; avoid excess alcohol consumption; deferoxamine for iron chelation
7. **Complications** = cirrhosis, hepatoma, CHF, DM, hypopituitarism

E. Wilson Disease

1. Autosomal recessive disorder of impaired copper secretion, primarily in young adults
2. **Excess copper deposits** in liver, brain, cornea
3. **H/P** = psychiatric disturbances (e.g., depression, neuroses, **personality changes**), **loss of coordination**, dysphagia; jaundice, tremor, possible green-brown rings in cornea (i.e., **Kayser–Fleischer rings**), hepatomegaly; signs may precede symptoms
4. **Workup** = decreased serum ceruloplasmin, increased urinary copper, slightly increased AST and ALT; biopsy shows increased copper deposits in liver
5. **Treatment** = **trientine** or penicillamine for copper chelation; lifelong zinc for maintenance therapy; dietary copper restriction (no organ meats, shellfish, chocolate, nuts, or mushrooms), supplementary vitamin B_6; liver transplantation may be needed in cases of liver failure
6. **Complications** = fulminant hepatic failure, cirrhosis

F. α_1-Antitrypsin Deficiency

1. Codominant disorder with decreased α_1-antitrypsin production leading to cirrhosis and panlobular **emphysema**
2. Most symptoms arise from emphysemic component of disease
3. **Workup** = increased AST, increased ALT; **pulmonary function tests (PFTs) demonstrate obstructive disease**
4. **Treatment** = liver transplant or lung transplant may be needed in severe cases; enzyme replacement may be helpful in stopping disease progression

G. Hepatic Neoplasms

1. **Benign tumors** (e.g., hepatic adenoma, focal nodular hyperplasia, hemangiomas, hepatic cysts)
   a. Benign hepatic tumors found more commonly in **women with history of oral contraceptive use**
   b. **H/P** = frequently asymptomatic; possible RUQ fullness
   c. **Radiology** = CT, MRI, or angiography detects hypervascular liver mass
   d. **Treatment** = frequently untreated; larger tumors may be resected or embolized to prevent rupture
2. **Hepatocellular carcinoma (hepatoma)**
   a. Malignant tumor of hepatic parenchyma
   b. **Risk factors** = **HBV or HCV infection**, cirrhosis, hemochromatosis, excessive consumption of aflatoxin from *Aspergillus*-infected food, schistosomiasis
   c. **H/P** = RUQ pain, weight loss, malaise, anorexia, diarrhea, dyspnea; jaundice, hepatomegaly, bruit over liver, ascites
   d. **Workup** = slightly increased AST and ALT, increased alkaline phosphatase, increased bilirubin (total and direct), **increased α-fetoprotein**; biopsy provides diagnosis but risks causing substantial hemorrhage
   e. **Radiology** = CT, MRI, or US shows liver mass; angiography may show increased vascularity; PET can be used to determine extent of spread
   f. **Treatment** = surgical resection of small tumors (lobectomy or partial hepatectomy) and chemotherapy; transplant may be an option for limited disease; radiofrequency ablation and chemoembolization are options for unresectable tumors
   g. **Complications** = poor prognosis; portal vein obstruction, Budd–Chiari syndrome, liver failure

Quick HIT

Liver metastases from breast, lung, or colon cancers are much more common than primary liver cancers.

Quick HIT

Biopsy of hepatic masses is usually contraindicated because of hypervascularity and risk of hemorrhage.

Quick HIT

Paraneoplastic syndromes associated with hepatoma include hypoglycemia, excessive RBC production, refractory watery diarrhea, hypercalcemia, and variable skin lesions.

QUESTIONS

1. A 60-year-old woman with PMHx of DM walks into her primary care doctor complaining of progressive trouble swallowing solids and now liquids occasionally. The patient explains that sometimes she feels like recently chewed food “comes back up undigested.” She denied any recent weight loss, travel, or recent illness. What is the most common cause of this patient’s symptoms?

   A. Adenocarcinoma of proximal stomach
   B. Achalasia
   C. Scleroderma
   D. Esophageal cancer

2. A 45-year-old obese male with no PMHx presents to his primary care doctor’s office due to constant burning of chest that happens every 40 minutes after eating with a sour taste in mouth. The discomfort improves when he stands but worsens when he lies down. His workup includes a normal ECG and chest x-ray. The most common reason for this patient’s symptoms?

   A. Esophageal spasm
   B. Myocardial infarction
   C. Gastroesophageal reflux disease
   D. Esophageal cancer

3. A previously healthy 28-year-old male comes in today with worsening abdominal discomfort in RUQ and jaundice for about 5 days. The patient denies IV drug abuse, alcohol intake, or unprotected sex. He recently returned from travel in a cruise. Physical examination shows jaundice and scleral icterus. Labs show elevated bilirubin and similarly elevated ALT and AST enzymes. What is the most likely cause of his signs and symptoms?

   A. Acute gastroenteritis
   B. Hepatitis C
   C. Hepatitis A
   D. Hepatitis D

4. A 58-year-old woman with history of chronic urinary tract infections comes in to the emergency department with 1 week of non-resolving watery diarrhea that has occasional bloody streaks. The patient recently finished a course of antibiotics. On physical examination, she appears mildly dehydrated, and is tachycardic. Her abdominal exam is benign. She denies any recent travel or dietary changes. What is the most likely organism responsible for her symptoms?

   A. *E. coli*
   B. *V. cholerae*
   C. *Salmonella*
   D. *C. difficile*

5. A young male presents to the doctor’s office due to worsening abdominal epigastric pain and discomfort after foods with occasional nausea. He has been taking over the counter pain medication for severe dental pain for about 1 week. He is a social alcohol drinker, but recently is not able to tolerate most drinks due to symptoms. His initial workup is within normal limits and physical examination is unremarkable, except for mild epigastric pain. What is the most common cause of patient’s symptoms?

   A. Acute gastritis
   B. GERD
   C. Hiatal hernia
   D. Viral gastroenteritis

6. A 50-year-old male comes in with abdominal burning pain soon after eating. He denies chronic medications used, alcohol use, or change in diet. Physical examination is unremarkable. The patient tests positive on a urea breath test. What is the most likely diagnosis and cause of symptoms?

   A. Duodenal ulcer, NSAID use
   B. Gastric ulcer, *H. pylori*
   C. Chronic gastritis
   D. Zollinger–Ellison syndrome

7. A 22-year-old male presents with 4 months of abdominal cramps, weight loss, generalized joint aches, and watery diarrhea. Physical examination includes mild dehydration, oral ulcers, and a perianal fissure. Initial workup shows a positive hemoccult test. Colonoscopy reveals cobblestoning, colonic ulcers, and skipped lesions. What is the most likely diagnosis?

   A. Crohn disease
   B. Ulcerative colitis
   C. Irritable bowel syndrome
   D. Ischemic colitis

8. A 78-year-old female with history of constipation presents with abdominal pain and fever to the emergency department. Physical examination reveals LLQ tenderness to palpation with abdominal distention. An abdominal plain film shows constipation, hemoccult is negative, blood work shows leukocytosis, and urine is unremarkable. The most likely cause of fever, distention, and pain is due to:

   A. Ulcerative colitis
   B. Ischemic colitis
   C. Diverticulitis

D. Lower GI bleed

9. A patient comes in with recurrent headaches, confusion, weakness, and diaphoresis. He has been found with persistent and recurrent hypoglycemia while fasting without any hypoglycemic medications given. This is most likely due to:

   A. Glucagonoma
   B. Zollinger–Ellison syndrome
   C. Pancreatic pseudocyst
   D. Insulinoma

10. A 35-year-old man with chronic alcoholism presents with severe sudden-onset epigastric abdominal pain with radiation to his back. He is actively vomiting in the emergency room. Physical examination reveals a dehydrated male with signs of alcohol intoxication. Workup shows a normal ECG and chest x-ray. What is the most likely cause of this patient's symptoms?

    A. Pancreatitis
    B. Gastric ulcer
    C. Alcohol withdrawal
    D. Viral gastritis

11. A 43-year-old female comes in to the emergency department to get evaluated for nausea, vomiting, epigastric pain for 8 hours, and fever. On physical examination she has a positive Murphy sign. She has had similar pains before, but never lasted this long. The next step is:

    A. Abdominal x-ray
    B. Abdominal and pelvic CT scan
    C. Endoscopic evaluation
    D. Abdominal ultrasound

12. A 67-year-old female with PMHx of HTN, high cholesterol, and gallstones is brought in by her son being to be evaluated for onset of RUQ abdominal pain, jaundice, fever, and changes in mental status since today. Physical examination reveals scleral icterus, dehydration/hypotension, and RUQ tenderness. Blood work shows elevated liver enzymes (AST, ALT, alkaline phosphatase), bilirubin, and leukocytosis. This is a classic presentation of:

    A. Cholecystitis
    B. Porcelain gallbladder
    C. Ascending cholangitis
    D. Biliary cirrhosis

13. A patient with chronic alcoholism is being evaluated by his PCP due to skin color changes. The patient's blood work shows anemia, low platelets, and prolonged PT/INR. Physical examination shows jaundice and abdominal distention with a fluid wave on palpation. He denies any IV drug abuse, recent illness, or travel. The patient takes no medications currently. This patient is most likely showing signs and symptoms of:

    A. Cirrhosis
    B. Wilson disease
    C. Cholangitis
    D. Hepatic adenoma

14. A young male comes in his doctor's office to get evaluated for discoloration around his eyes, difficulties concentrating, and tremors. Upon evaluation, this patient shows a green-brown ring in his corneas, jaundice, and hepatomegaly. What is the most likely diagnosis?

    A. Portal hypertension
    B. Cirrhosis
    C. Hepatitis C
    D. Wilson disease

15. A 9-day-old boy is brought in to a pediatric emergency room due to projectile vomiting after every feed. On evaluation, the child appears dehydrated and hungry; an olive-sized mass is found around the RUQ. The blood work shows hypochloremia and metabolic alkalosis. What diagnostic test would you perform?

    A. Abdominal x-ray
    B. Abdominal ultrasound
    C. CT scan of abdomen
    D. Barium swallow

16. A premature baby is brought back to the hospital due to poor feeding, abdominal distention, bloody stools, and bilious description of vomit. Blood work shows metabolic acidosis. The child appears ill and dehydrated. X-ray shows bowel distention with air within bowel loops. This child is suffering from:

    A. Pyloric stenosis
    B. Intussusception
    C. Necrotizing enterocolitis
    D. Lactose intolerance

3
Hematology and Oncology

I. Anemias

A. Red Blood Cell (RBC) Physiology

1. RBCs serve to transport O_2 from the alveoli to tissues via the bloodstream and CO_2 from tissue to lungs.
2. Normal hemoglobin (Hgb) A serves as a binding protein for O_2 and CO_2, and its affinity for O_2 follows the Hgb–O_2 dissociation curve (see Figure 3-1).
   a. **Alkalosis,** decreased body temperature, and increased Hgb F (fetal) shift curve to the left.
   b. **Acidosis,** increased body temperature, **high altitude,** and exercise shift curve to the right.
3. Circulating RBCs, myeloid cells, and lymphoid cells all originate from the same pluripotent stem cells in bone marrow (see Figure 3-2).
4. RBCs become enucleated during maturation in bone marrow and depend on glycolysis for survival.

NEXT
STEP

If a patient presents with carbon monoxide poisoning (carbon monoxide displaces O_2 on Hgb, leading to insufficient delivery of O_2 to tissues), administer **100% O_2** via face mask to increase the alveolar concentration of O_2 and decrease the opportunities for carbon monoxide to bind to Hgb.

Quick **HIT**

Carbon monoxide poisoning includes signs of mental status changes, cherry red lips, and hypoxia despite normal pulse oximetry readings.

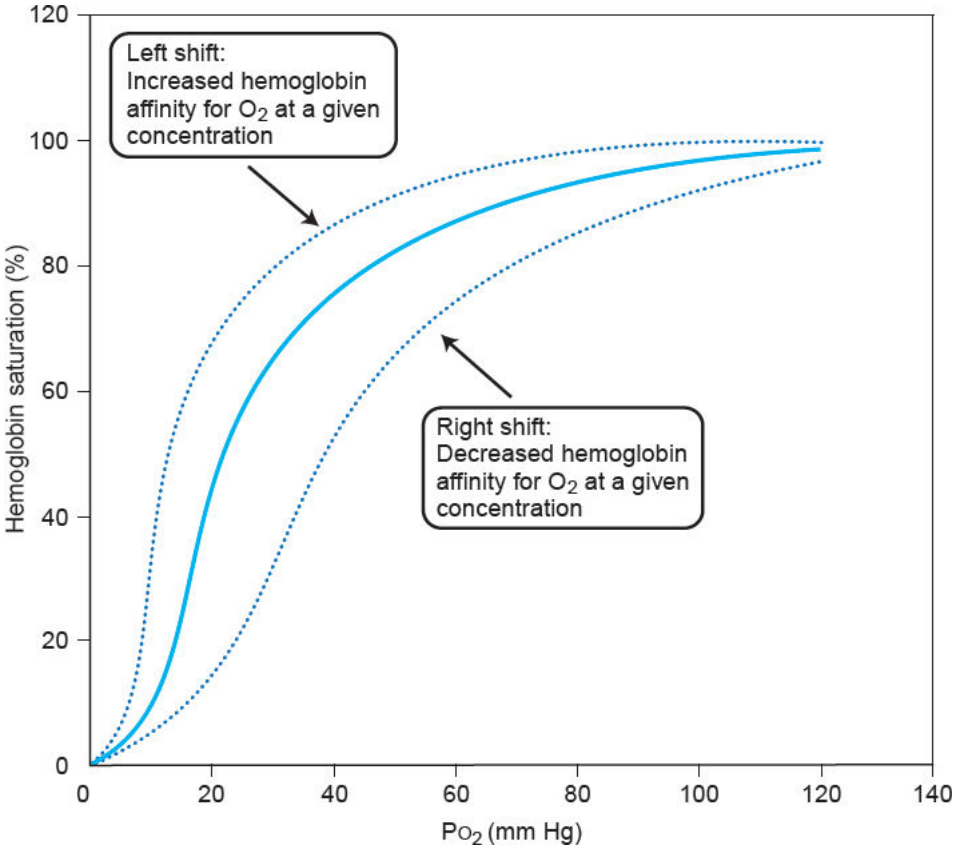


FIGURE 3-1
Hemoglobin–oxygen dissociation curve.

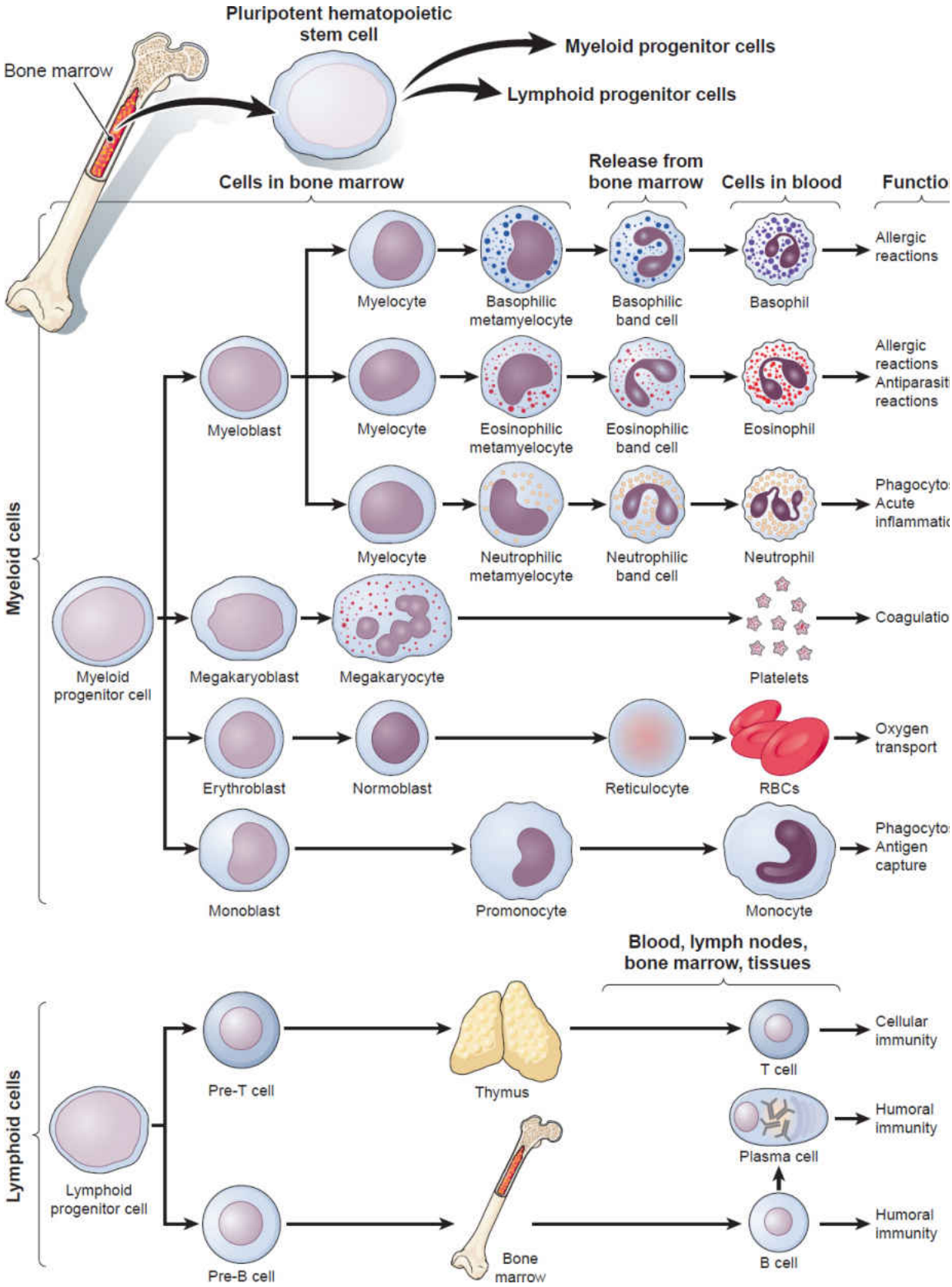


FIGURE 3-2
Development of myeloid and lymphoid cell lines from pluripotent stem cells in bone marrow.
(From McConnell, T. H. [2014]. *The Nature of Disease: Pathology for the Health Professions* [2nd ed., p. 181]. Philadelphia, PA: Lippincott Williams & Wilkins; with permission.)

5. Normal Hgb concentration and hematocrit (Hct):
   a. 14 to 18 g/dL and 42% to 52% in men
   b. 12 to 16 g/dL and 37% to 47% in women
   c. Low Hgb and Hct (i.e., anemia) result in insufficient supply of O_2 to tissues and cause ischemia. As a general rule, blood transfusions are not recommended unless Hgb is <7 g/dL or the patient requires increased oxygen-carrying capacity

6. Types of anemia are characterized by mechanism of pathology and mean corpuscular volume (MCV) (see Table 3-1).

MNEMONIC

Remember the list of common microcytic anemias by the mnemonic **L**ook **F**or **T**hose **S**mall **C**ells: **L**ead poisoning, **Fe** (iron) deficiency, **T**halassemia, **S**ideroblastic, **C**hronic disease.

Table 3-1 Classification of Anemias by Mean Corpuscular Volume (MCV) and Common

Microcytic (MCV <80 fL)	Normocytic (MCV 80–100 fL)	Macrocytic (MCV >100 fL)
Iron deficiency	Hemolytic	Folate deficiency
Lead poisoning	Chronic disease	Vitamin B_{12} deficiency
Chronic disease	Hypovolemia	Liver disease
Sideroblastic		Alcohol abuse
Thalassemias		

B. Hemolytic Anemia

1. Anemia that results when RBC lifespan is shortened and marrow production of RBCs is not capable of meeting demand for new cells (see Table 3-2)
2. Can be caused by defects in RBC membrane, RBC enzyme defects, hemoglobinopathies, or extracellular effects
3. **H/P** = possibly asymptomatic (when loss is slow); weakness, fatigue, dyspnea on exertion; **pallor,** tachycardia, tachypnea, increased pulse pressure, possible systolic murmur, **jaundice;** severe cases may have palpitations, syncope, mental status changes, angina, chills, abdominal pain, **hepatosplenomegaly,** and **brownish discoloration of urine**
4. **Workup** = decreased Hgb, decreased Hct, **increased reticulocyte count, increased bilirubin (indirect)**, increased lactate dehydrogenase (LDH), **normal MCV,** decreased serum haptoglobin; Coombs test is helpful for making diagnosis
5. Coombs test
   a. Coombs reagent (rabbit immunoglobulin M [IgM] directed against human immunoglobulin G [IgG] and complement) is mixed with RBCs to aid in diagnosis of hemolytic anemia
   b. Direct test: Coombs reagent mixed with RBCs; agglutination indicates presence of IgG and complement on RBC membranes (e.g., warm and cold agglutinin disease)
   c. Indirect test: patient serum mixed with type O RBCs which, in turn, are mixed with Coombs reagent; agglutination indicates presence of anti-RBC antibodies in serum (e.g., Rh alloimmunization)
6. **Blood smear** = **schistocytes** (RBC fragments), spherocytes, and/or burr cells (see Figures 3-3 and 3-4)

***Quick* HIT**

Mean RBC lifespan is 120 days.

***Quick* HIT**

Iron deficiency anemia is the **most common** form of anemia.

***Quick* HIT**

Consider iron deficiency anemia in **elderly** patients **caused by colon cancer** until such is ruled out.

C. Iron Deficiency Anemia

1. Anemia resulting from insufficient heme production secondary to **insufficient iron supplies**
2. Iron deficiency results from **blood loss,** poor dietary intake or absorption from the gastrointestinal (GI) tract, pregnancy, or menstruation
3. **H/P** = fatigue, weakness, dyspnea on exertion, **pica** (i.e., craving to eat ice, dirt, etc.), restless legs; pallor, tachycardia, tachypnea, increased pulse pressure, possible systolic murmur; **angular cheilitis** (i.e., irritation of lips and corners of mouth), **spooning of nails** in severe cases

Table 3-2 Types of Hemolytic Anemias

Type	Pathology	Blood Smear	Coombs Test	Other Diagnostic Aids	Treatme
Drug induced	Binds to RBC membrane and causes oxidative destruction, induces production of **antidrug antibodies**, forms **immune complexes** that fix complement, or induce **anti-Rh antibodies**	Burr cells, schistocytes	**Direct Coombs+** (unless due to oxidative destruction)	Recent penicillin, methyldopa, quinidine, other drug use	Stop offer
Immune	**Anti-RBC antibodies**, autoimmune disease, possibly drug induced	Spherocytes (warm agglutinins), RBC agglutination (cold agglutinins)	**Direct Coombs+**	**Warm-reacting antibodies** (IgG) or **cold-reacting antibodies** (IgM)	Corticoste **cold exp** cold-react ies), stop agent; spl be needed cases
Mechanical	RBCs broken by force or **turbulent flow**	**Schistocytes**	Negative	**Prosthetic heart valve**, HTN, coagulation disorder	Treat unde
Hereditary spherocytosis (see Figure 3-3)	Genetic **defect of RBC membranes** resulting in spherical RBCs	**Spherocytes**	Negative	**Hepatosplenomegaly**	Splenecto
G6PD deficiency	Deficiency of G6PD (enzyme required to repair oxidative damage to RBCs); ingestion of oxidant (fava beans, high-dose ASA, sulfa drugs, dapsone, quinine, quinidine, primaquine, nitrofurantoin) causes excessive hemolysis	RBCs with **"bites"** taken out of them, **Heinz bodies** (small densities of Hgb in RBC)	Negative	**Low G6PD** (by indirect measurement); dizziness, fatigue begins within days of ingesting oxidant; mild form in blacks, more severe form in people of Mediterranean decent	Avoid oxic sion may severe cas

ASA, aspirin; G6PD, glucose-6-phosphate dehydrogenase; HTN, hypertension; RBC, red blood cell.

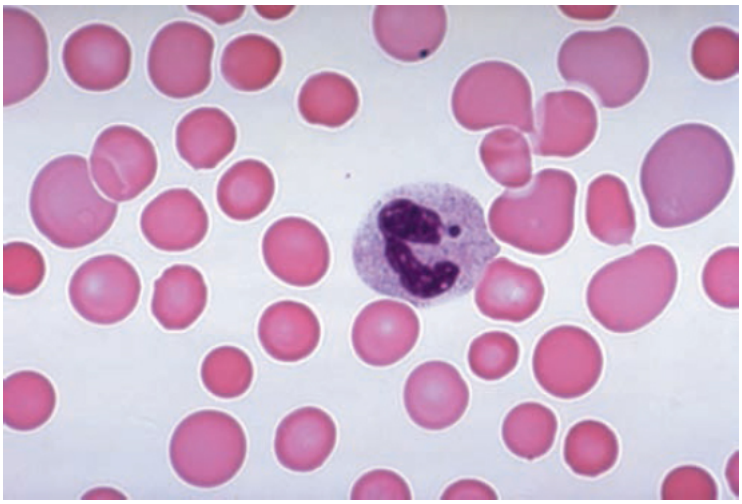


FIGURE 3-3
Hereditary spherocytosis.
Blood smear shows numerous spherocytes with decreased diameter, increased staining, and absence of central pallor.
(From Rubin, R., & Strayer, D. S. [2013]. *Rubin's Pathology* [6th ed., p. 964]. Philadelphia, PA: Lippincott Williams & Wilkins; with permission.)

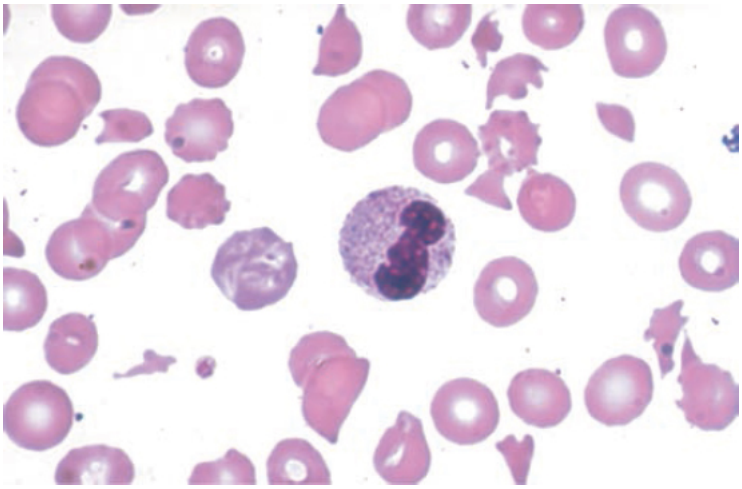


FIGURE 3-4
Microangiopathic hemolytic anemia demonstrating multiple schistocytes (fragmented red blood cells [RBCs]).
(From Rubin, R., & Strayer, D. S. [2013]. *Rubin's Pathology* [6th ed., p. 971]. Philadelphia, PA: Lippincott Williams & Wilkins; with permission.)

4. **Workup** = decreased Hgb, decreased Hct, decreased MCV, decreased or normal reticulocyte count, decreased **ferritin,** decreased iron, increased transferrin (i.e., total iron-binding capacity), positive stool guaiac possible if secondary to GI losses (see Table 3-3)
5. **Blood smear** = microcytic hypochromic RBCs (see Figure 3-5)
6. **Treatment** = iron supplementation (several months of treatment required to replete stores), determine cause of iron loss

Table 3-3 Laboratory Distinction of Microcytic Anemias

Type	Serum Iron	Ferritin	TIBC (transferrin)	Iron: TIBC Ratio	Blood Smear
Iron deficiency	↓	↓	↑	Low (<12)	Hypochromic, microcytic
Chronic disease	↓	Normal or ↑	↓	Normal (>18)	Hypochromic, normocyti
Lead poisoning	Normal or ↑	Normal or ↑	Normal or ↓	Normal	Stippled, microcytic RBC
Sideroblastic	↑	↑	↓	Normal	Ringed sideroblasts (in b
Thalassemia	Normal or ↑	Normal or ↑	Normal	↑ in β-thalassemia	Microcytic RBCs, target stippling (β)

RBC, red blood cell; TIBC, total iron-binding capacity; ↑, increased; ↓, decreased.

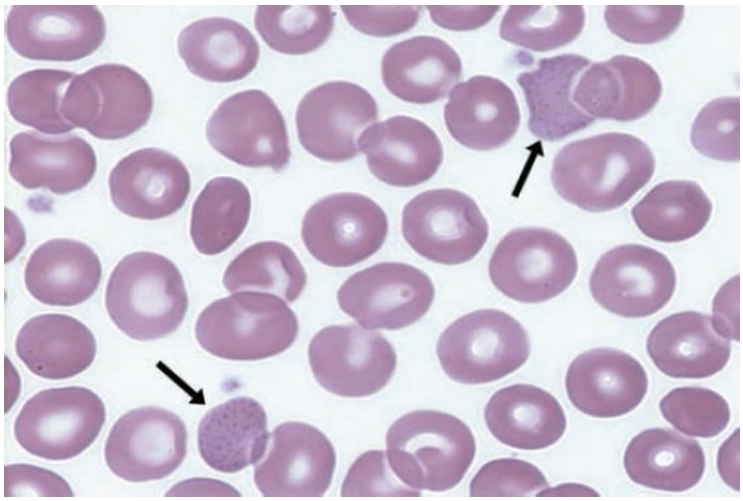


FIGURE 3-5
Lead poisoning anemia.
Note the hypochromic red blood cells (RBCs) and basophilic stippling seen in some cells (*arrows*).
(From Anderson, S. C., & Poulsen, K. B. [2014]. *Anderson's Atlas of Hematology* [2nd ed., p. 224]. Philadelphia, PA: Lippincott Williams & Wilkins; with permission.)

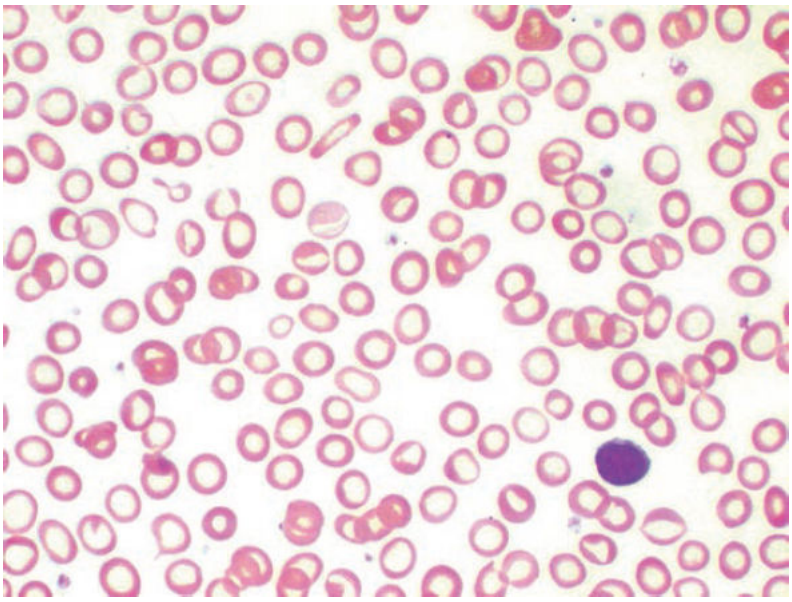


FIGURE 3-6
Microcytic hypochromic red blood cells (RBCs) characteristic of iron deficiency anemia.
(From Rubin, R., & Strayer, D. S. [2008]. *Rubin's Pathology: Clinicopathologic Foundations of Medicine* [5th ed., p. 865]. Philadelphia, PA: Lippincott Williams & Wilkins; with permission.)

D. Lead Poisoning Anemia

1. Anemia resulting from heme synthesis inhibition by lead ingestion (more common in children, especially those in urban environments)
2. Similar presentation may be seen in anemia caused by alcoholism or isoniazid use
3. **H/P** = fatigue, weakness, abdominal pain, arthralgias, headache, impaired short-term memory; pallor, mental developmental delays, **gingival lead lines, peripheral neuropathy** (e.g., decreased motor control of extremities)
4. **Workup** = decreased Hgb, decreased Hct, decreased MCV, increased serum lead (see Table 3-3)
5. **Blood smear** = microcytic RBCs, **basophilic stippling of RBCs** (see Figure 3-6)
6. Treatment = remove source of lead; EDTA or dimercaptosuccinic acid (DMSA) if needed for lead chelation (add dimercaprol in children with severe lead intoxication)

Quick HIT

Folate deficiency is the most common cause of **megaloblastic** anemia.

E. Folate Deficiency Anemia

1. Anemia resulting from inadequate folate intake, increased folate need (e.g., poor nutrition, chemotherapy), or drug-induced folate metabolism defects (e.g., methotrexate, trimethoprim, phenytoin)
2. **H/P** = **poor nutrition,** fatigue, weakness, dyspnea on exertion, diarrhea, **sore tongue;** pallor, tachycardia, tachypnea, increased pulse pressure, possible systolic murmur; **no neurologic symptoms**
3. **Workup** = decreased Hgb, decreased Hct, **increased MCV,** decreased serum folate, decreased red cell folate level, decreased reticulocyte count
4. **Blood smear** = **macrocytic RBCs, hypersegmented neutrophils**
5. **Treatment** = oral folate supplementation

Quick HIT

Inadequate folate intake is seen with **alcoholism** and in the elderly because of poor nutrition.

F. Vitamin B_{12} Deficiency Anemia

1. **Pernicious anemia** (i.e., autoimmune anemia owing to lack of intrinsic factor) or anemia resulting from inadequate vitamin B_{12} intake, ileal resection, bacterial overgrowth in GI tract, or *Diphyllobothrium latum* infection (a worm)
2. **H/P** = fatigue, weakness, dyspnea on exertion, memory loss; pallor, tachycardia, tachypnea, increased pulse pressure, possible systolic murmur, **symmetric paresthesias,** loss of vibration sense, **ataxia,** possible dementia
3. **Workup** = decreased Hgb, decreased Hct, **increased MCV,** decreased vitamin B_{12}
4. **Blood smear** = **macrocytic RBCs, hypersegmented neutrophils** (see Figure 3-7)
5. **Treatment** = monthly intramuscular vitamin B_{12} injections, dietary supplementation of vitamin B_{12}, intranasal vitamin B_{12}

Quick HIT

Inadequate vitamin B_{12} intake is usually only seen in **strict vegetarians** (vegans).

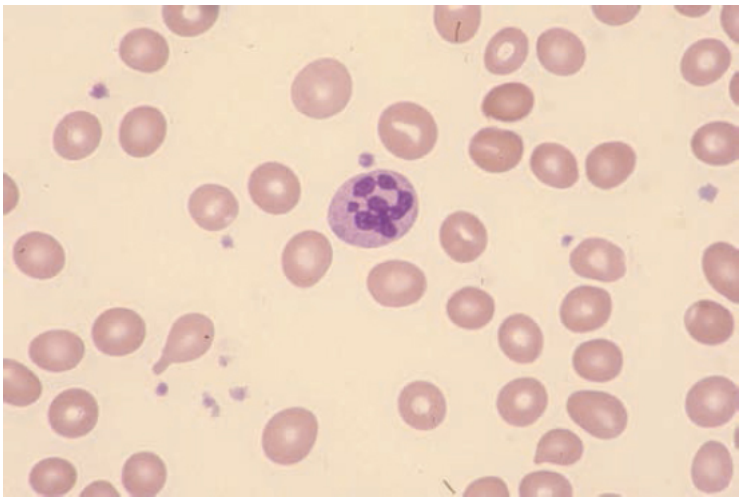


FIGURE 3-7
Anemia caused by vitamin B_{12} deficiency.
Note the macrocytic red blood cells (RBCs) and presence of a hypersegmented neutrophil.
(From Anderson, S. C., & Poulsen, K. B. [2003]. *Anderson's Atlas of Hematology*. Philadelphia, PA: Lippincott Williams & Wilkins, Figure IIA3.3; with permission.)

G. Anemia of Chronic Disease

1. Anemia occurring in patients with neoplasia, diabetes mellitus, autoimmune disorders, or long-standing infections
2. Frequently associated with trapping of iron in macrophages, decreased erythropoietin production, and increased hepcidin levels (inhibitor of iron absorption and mobilization)
3. **H/P** = history of appropriate disease state, fatigue, weakness, dyspnea on exertion; tachycardia, pallor
4. **Workup** = **mildly decreased Hgb and Hct,** normal or decreased MCV, decreased iron, decreased transferrin, normal or increased ferritin (see Table 3-3)
5. **Blood smear** = normocytic RBCs
6. **Treatment** = **treat underlying disorder;** supplemental erythropoietin

Quick HIT

Folate deficiency caused by inadequate dietary intake develops significantly more quickly than vitamin B_{12} deficiency from inadequate intake.

H. Aplastic Anemia

1. **Pancytopenia** resulting from bone marrow failure
2. Due to **radiation,** drugs (e.g., chloramphenicol, sulfonamides, phenytoin, chemotherapeutics), toxins, viral infections, or idiopathic and congenital causes
3. **H/P** = fatigue, weakness, **persistent infections, poor clotting** with possible uncontrolled bleeding, easy bruising, persistent menstruation; pallor, petechiae, tachycardia, tachypnea, systolic murmur, increased pulse pressure
4. **Workup** = decreased Hgb, decreased Hct, decreased white blood cells (WBCs), decreased platelets; bone marrow biopsy shows **hypocellularity** and fatty infiltrate
5. **Treatment** = stop offending agent; transfusions for acute anemia and thrombocytopenia; immunosuppressive agents and bone marrow transplant

Quick HIT

Aplastic anemia in a sickle cell patient is classically caused by **parvovirus B19**.

II. Genetic Disorders of Hemoglobin

A. Sideroblastic Anemia

1. Anemia caused by **defective heme synthesis** resulting in decreased Hgb levels in cells
2. Can be a genetic disorder or caused by alcohol, isoniazid, or lead poisoning (patient history is useful for differentiating cause)

3. **H/P** = fatigue, weakness, dyspnea on exertion, angina; pallor, tachycardia, tachypnea, increased pulse pressure, hepatosplenomegaly, possible systolic murmur
4. **Workup** = decreased Hgb, decreased Hct, increased ferritin, increased iron, decreased transferrin, possible decreased MCV (see Table 3-3)

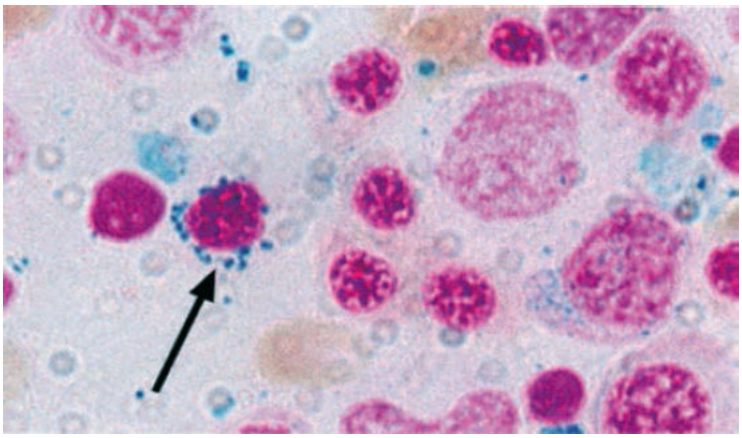


FIGURE 3-8
Bone marrow in a patient with sideroblastic anemia.
Note several red blood cells (RBCs) surrounded by rings of iron granules (ring sideroblasts) (*arrow*).
(From Handin, R. I., Lux, S. E., & Stossel, T. P. [2003]. *Blood: Principles and Practice of Hematology* [2nd ed., Color Figure 3-6D]. Philadelphia, PA: Lippincott Williams & Wilkins; with permission of Robert I. Handin, MD.)

5. **Blood smear** = **multiple sizes of RBCs** with normocytic, **microcytic,** and macrocytic cells possible; **ringed sideroblasts** (RBC precursors) in the bone marrow (see Figure 3-8)
6. **Treatment**
   a. Hereditary cases: vitamin B_6 may normalize Hgb concentrations
   b. Acquired cases: supplemental erythropoietin
   c. Both types: significant iron overload requires therapeutic phlebotomy (mild cases) or chelation with deferoxamine (more severe cases); transfusion may be required in severe cases
7. **Complications** = 10% patients progress to acute leukemia

Quick HIT

Patients with α-thalassemia minima usually have a normal MCV.

B. Thalassemia

1. Hgb defects resulting from abnormal production of heme α-globin or β-globin subunits
2. Disease state arises from unbalanced production ratio of α- and β-chains (see Table 3-4)
3. **Normal Hgb**
   a. Composed of two α-chains and two β-chains
   b. Four genes determine α-chain synthesis; two genes determine β-chain synthesis

Table 3-4 Variants of α- and β-Thalassemias

Thalassemia Type	Variant	Number of Abnormal Alleles	Characteristics
α	α-Thalassemia minima	1	Generally **asymptomatic**; children of carriers thalassemia, pending genotype of other paren
	α-Thalassemia minor	2	Reduced α-globin production; **mild anemia**; target cells on blood smear
	Hemoglobin H disease	3	Minimal α-globin production; **chronic hemol** splenomegaly; microcytic RBCs on blood smea blood; decreased lifespan
	Hydrops fetalis	4	Hemoglobin Bart's (no α-globin production); **fe**
β	β-Thalassemia minor	1	Reduced β-globin production; mild anemia; in A2; patients can lead normal lives; transfusion during periods of stress
	β-Thalassemia major	2	No β-globin production; asymptomatic until d bin; growth retardation, developmental delays hepatosplenomegaly, anemia; increase in hem microcytic RBCs on blood smear; patients die transfusions

RBCs, red blood cells.

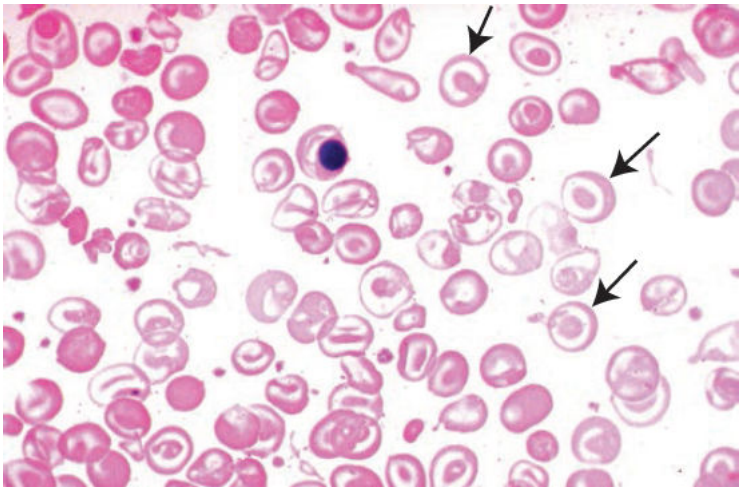


FIGURE 3-9
Thalassemia.
The peripheral blood erythrocytes are hypochromic and microcytic and show anisocytosis, poikilocytosis, and target cells (*arrows*).
(From Rubin, R., & Strayer, D. S. [2008]. *Rubin's Pathology: Clinicopathologic Foundations of Medicine* [5th ed., p. 871]. Philadelphia, PA: Lippincott Williams & Wilkins; with permission.)

4. **α-Thalassemia**
   a. More prevalent in people of Asian or African descent
   b. Variants have between one and four defective alleles
5. **β-Thalassemia**
   a. More prevalent in patients of Mediterranean descent
   b. Variants have either one or two defective alleles.
6. **Workup** = **decreased MCV,** increased reticulocyte count, increased Hgb Bart's (i.e., Hgb that binds O_2 but is unable to release it to tissues in hydrops fetalis), increased Hgb A_2 or F in β-thalassemia; Hgb electrophoresis can detect genetic abnormalities and severity of defects (see Table 3-3)
7. **Blood smear**
   a. α-Thalassemia: abnormally shaped microcytic RBCs, target cells (see Figure 3-9)
   b. β-Thalassemia: RBCs in variable size and shape (including microcytic cells) with target cells
8. **Treatment**
   a. α-Thalassemia minor or minima and β-thalassemia minor frequently are asymptomatic and only require symptomatic treatment during periods of stress.
   b. Folate supplementation may be helpful in all symptomatic forms and mild forms during stress.
   c. **Transfusions** are required for more severe variants and may be needed for mild forms during periods of stress.

d. **Iron chelation** may be required in patients receiving chronic transfusions.
e. Bone marrow transplant may be helpful in children with minimal hepatomegaly, no portal fibrosis, and adequate iron chelation therapy.

9. **Complications** = **chronic iron overload** from repeat transfusions causes damage to heart and liver; patients with Hgb H disease and β-thalassemia major have high childhood mortality without transfusion therapy; children of asymptomatic parents with defective genes are still at risk for developing disease, depending on inherited alleles

NEXT
STEP

If microcytic anemia is found on blood smear, rule out thalassemia before administering supplemental iron to prevent iron overload.

Quick **HIT**

β-Globin defects:

- In sickle cell disease, causes production of **defective β-chains.**
- In β-thalassemia, causes **decreased production of normal β-chains.**

Quick **HIT**

Heterozygous **carriers** of sickle cell defect (sickle cell trait) are **asymptomatic** and carry **improved resistance to malaria**.

Quick **HIT**

Presence of fetal Hgb in newborns delays presentation of sickle cell symptoms until after 6 months of age, when fetal Hgb levels have decreased.

C. Sickle Cell Disease

1. Autosomal recessive defect in β-globin chain of Hgb, leading to production of **abnormal Hgb S** that is poorly soluble when deoxygenated
2. Acidosis, hypoxia, and dehydration cause Hgb S molecules to polymerize and distort RBCs into a **sickle shape** that is **more susceptible to hemolysis** and **vascular clumping** than normal cells
3. More common in people of African heritage. About 1 in 12 people of African descent carries sickle cell trait. People with sickle cell trait do not have anemia and have a normal expectancy
4. **H/P** = frequently asymptomatic between crises; stressful events (e.g., infection, illness, trauma, hypoxia) induce **sickle cell crisis** characterized by **deep bone pain**, chest pain, new stroke onset, painful swelling of hands and feet, dyspnea, priapism (i.e., painful, prolonged erection); growth retardation, splenomegaly, jaundice, fever, tachypnea, leg ulcers seen on examination
5. **Workup**
   a. Decreased Hct, increased reticulocyte count, increased polymorphonuclear (PMN) cells, decreased serum haptoglobin, increased bilirubin (indirect).
   b. Hgb electrophoresis detects Hgb S without normal Hgb A; Hgb F may be increased.
   c. SICKLEDEX solubility test can detect Hgb abnormalities but cannot differentiate between carrier trait and homozygous disease state.
6. **Radiology** = "codfish" vertebrae; lung infiltrates in acute chest syndrome (radiologic findings in setting of chest pain and dyspnea)
7. **Blood smear** = target cells, nucleated RBCs; **deoxygenation of blood produces sickle cells** (see Figure 3-10)
8. **Treatment**
   a. **Hydration**, **supplemental O_2**, and **analgesics** (frequently narcotics required) during **sickle cell crises**.
   b. Hydroxyurea (increases Hgb F production) and avoidance of crisis stimuli decrease frequency of crises.
   c. Pneumococcal vaccine reduces risk of infection in asplenic patients; prophylactic penicillin should be given until 5 years of age to help prevent pneumococcal infection in asplenic children.
   d. Chronic transfusions may help keep the level of Hgb S as low as possible.
   e. Hematopoietic stem cell transplantation and gene therapy show future promise as potential cures.
9. **Complications**
   a. Chronic anemia, pulmonary hypertension, heart failure, **aplastic crisis** (usually secondary to parvovirus B19 infection), **acute chest syndrome** (i.e., acute pneumonia, pulmonary infarction, and embolus)
   b. Autosplenectomy, stroke, osteonecrosis, and multiple organ ischemia (particularly kidney, heart, retina) can result secondary to **vascular occlusion**
   c. Increased risk of infection by **encapsulated organisms**

d. Life expectancy is decreased to about 35 years if more than three crises per year. If less than three crises per year, life expectancy is about 50 years

Quick HIT

Patients with sickle cell disease are particularly susceptible to *Salmonella* **osteomyelitis** and **sepsis** by **encapsulated organisms** (*Streptococcus pneumoniae*, *Haemophilus influenzae*, *Neisseria meningitidis*, *Klebsiella*).

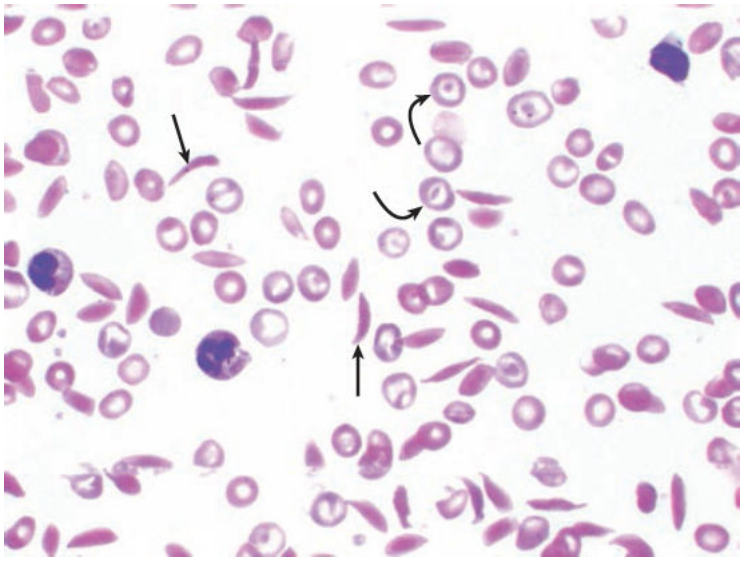


FIGURE 3-10
Sickle cell anemia.
Sickled cells (*straight arrows*) and target cells (*curved arrows*) are evident.
(From Rubin, R., & Strayer, D. S. [2008]. *Rubin's Pathology: Clinicopathologic Foundations of Medicine* [5th ed., p. 874]. Philadelphia, PA: Lippincott Williams & Wilkins; with permission.)

III. Leukocyte Disorders and Hypersensitivity

A. Lymphopenia Without Immune Deficiency

1. Decreased lymphocyte count seen in diseases with **increased cortisol** levels or after chemotherapy, radiation, or lymphoma; antibody production not affected
2. **H/P** = repeated infections with possible recent history of chemotherapy or radiation
3. **Workup** = decreased WBCs, especially B and T lymphocytes
4. **Treatment** = if possible, stop offending agents; bone marrow transplant may be needed

B. Eosinophilia

1. Abnormally high levels of eosinophils seen in Addison disease, neoplasm, asthma, allergic drug reactions, collagen vascular diseases, transplant rejection, and parasitic infections
2. **H/P** = **asymptomatic;** history of predisposing condition
3. **Workup** = increased eosinophil count
4. **Treatment** = treat underlying disorder; stop offending agent

C. Neutropenia

1. Decreased neutrophil count seen with some viral infections (e.g., hepatitis, human immunodeficiency virus [HIV], Epstein–Barr virus [EBV]), drugs (e.g., clozapine, antithyroid medications, sulfasalazine, methimazole, trimethoprim-sulfamethoxazole [TMP-SMX]), chemotherapy, and aplastic anemia
2. **H/P** = weakness, chills, fatigue, **recurrent infections;** fever
3. **Workup** = decreased neutrophil count
4. **Treatment** = treat underlying disorder, stop offending agents, granulocyte colony- stimulating factor, corticosteroids; antibiotics whenever infection suspected

MNEMONIC

Remember the types of hypersensitivity reactions by the mnemonic **ACID: A**naphylactic, **C**omplement mediated, **I**mmune complex mediated, and **D**elayed.

D. Hypersensitivity Reactions

1. Allergen-induced immunologic response by body involving cellular or humoral mechanisms (see Table 3-5)
2. **Workup** = skin allergen testing or radioallergosorbent test (RAST) may be useful in determining specific allergies
3. **Treatment**
   a. **Contact prevention** and **avoidance** of offending agents is important
   b. Type I: antihistamines, leukotriene inhibitors, bronchodilators, and corticosteroids may improve symptoms after reaction; desensitization may be considered to avoid recurrent reactions; if anaphylaxis is a concern, epinephrine injections should be kept readily available
   c. Type II: anti-inflammatories or immunosuppressive agents, possibly plasmapheresis
   d. Type III: anti-inflammatories
   e. Type IV: corticosteroids or immunosuppressive agents

Table 3-5 Types of Hypersensitivity Reactions

Type	Mediated By	Mechanism	Examples
I	IgE antibodies attached to mast cells	Antigens react with antibody to cause **mast cell degranulation** and histamine release	Allergic rhinitis, asthma, **a**
II	IgM and IgG antibodies	Cellular antigens react with antibodies to initiate **complement cascade** and cell death	**Drug-induced or immun anemia**, hemolytic disease
III	IgM and IgG immune complexes	Antibodies bind to soluble antigens to form **immune complexes**, which are then deposited in tissue and initiate complement cascade	Arthus reaction, serum sick phritis
IV	T cells and macrophages	**T cells** present antigens to macrophages and secrete lymphokines that induce macrophages to destroy surrounding tissue	Transplant rejection, **allerg titis**, PPD testing

PPD, purified protein derivative.

E. Anaphylaxis

1. Severe type I hypersensitivity reaction after reexposure to allergen (penicillins, insect stings, latex, eggs, nuts, and seafood are common causes)
2. **H/P** = symptoms and signs typically occur 5 to 60 minutes after exposure; tingling in skin, itching, cough, chest tightness, **difficulty swallowing and breathing** (secondary to angioedema), syncope; tachycardia, wheezing, urticaria, **hypotension,** arrhythmias
3. **Workup** = skin testing or RAST can confirm allergic response; increased histamine and tryptase
4. **Treatment** = **subcutaneous epinephrine, intubation** (if closed airway), antihistamines, bronchodilators, recumbent positioning, intravenous (IV) hydration; vasopressors may be needed for severe hypotension; avoidance of stimuli is key to prevention; elective desensitization therapy may be appropriate following an episode, depending on allergen, to avoid future incidents

NEXT
STEP

Epinephrine should be given **immediately** to a person having an anaphylactic reaction without waiting for additional tests.

IV. Clotting Disorders

A. Normal Clotting Function

1. **Platelets**
   a. Circulate in plasma
   b. Important in **primary control** of bleeding
   c. Cause local vasoconstriction and form platelet plug at site of vascular injury in response to adenosine diphosphate (ADP) secreted by injured cells
   d. Bleeding time can be used to assess platelet function but is poorly reproducible and time consuming

NEXT
STEP

Monitor **heparin** anticoagulation with **PTT.**

Quick HIT

Low–molecular-weight heparins (LMWH) do **not** require monitoring by PTT.

2. **Coagulation cascade**
   a. Responsible for formation of **fibrin clot** at the site of injury (see Figure 3-11)
   b. **Intrinsic pathway** induced by exposure to negatively charged foreign substances; measured by partial thromboplastin time (**PTT**)
   c. **Extrinsic pathway** induced by tissue factor exposed at the site of injury; measured by prothrombin time (**PT**)

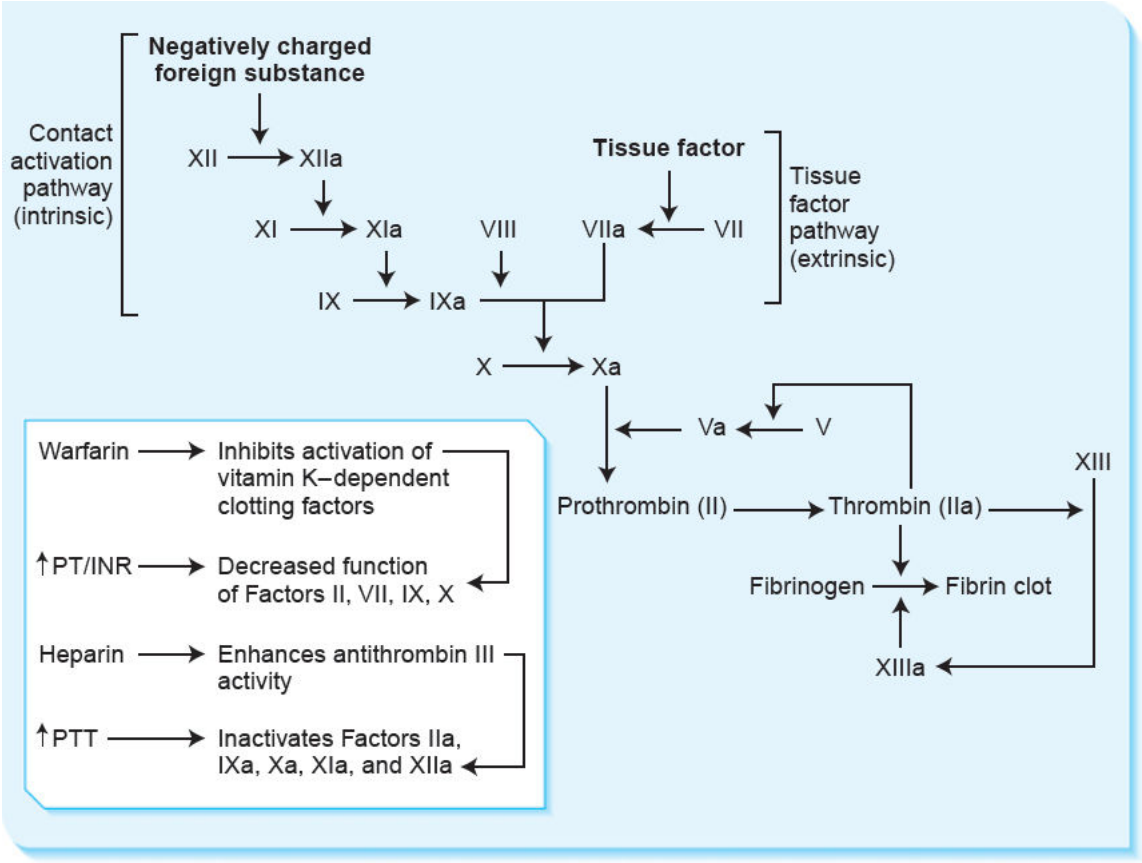


FIGURE 3-11
Coagulation cascade.
INR, international normalized ratio; PT, prothrombin time; PTT, partial thromboplastin time.

Table 3-6 Common Anticoagulant Drugs

Drug	Mechanism	Role	Adverse Effects
ASA	Inhibits platelet aggregation by inhibiting cyclooxygenase activity to suppress thromboxane A_2 synthesis	Decreases thrombus risk in CAD and post-MI; decreases postoperative thrombus risk	Increased risk of hemorrhagic stroke, **GI bleeding**
Thienopyridines (e.g., clopidogrel, ticlopidine)	Blocks ADP receptors to suppress fibrinogen binding to injury and platelet adhesion	Decreases risk of repeat MI or stroke in patients with prior MI, stroke, or PVD; decreases thrombus risk in post vascular intervention patients	Increased risk of hemorrhage, **GI bleeding**
GP IIb/IIIa inhibitors (e.g., abciximab, tirofiban, eptifibatide)	Inhibits platelet aggregation by binding to platelet GP IIb/IIIa receptors	Reduces risk of thrombus in unstable angina or following coronary vessel intervention	Increased risk of hemorrhage, nausea, back pain, hypotension
Adenosine reuptake inhibitors (e.g., dipyridamole)	Inhibits activity of adenosine deaminase and phosphodiesterase to inhibit platelet aggregation	Used in combination with ASA in patients with recent stroke or with warfarin following artificial heart valve replacement	Dizziness, headache, nausea
Heparin	Binds to **antithrombin** to increase activity and prevent clot formation	Postoperative prophylaxis for DVT and PE, dialysis, decreases post-MI thrombus risk, safer than warfarin during pregnancy	Hemorrhage, hypersensitivity, **thrombocytopenia**, narrow therapeutic window
Low–molecular-weight heparin (e.g., enoxaparin, dalteparin)	Binds to **factor Xa** to prevent clot formation	Postoperative prophylaxis for DVT and PE, safest option during pregnancy	Hemorrhage, fever, rare thrombocytopenia
Direct thrombin inhibitors (e.g., lepirudin, argatroban)	Highly selective inhibitors of thrombin to suppress activity of factors V, IX, and XIII and platelet aggregation	Alternative anticoagulation in patients with history of heparin-induced thrombocytopenia (HIT)	Hemorrhage, hypotension
Direct factor Xa inhibitors (e.g., apixaban, rivaroxaban)	Highly selective inhibition of factor Xa without activity against thrombin	DVT prophylaxis, anticoagulation following acute DVT or PE	Hemorrhage, fever, anemia, edema, rash, constipation
Warfarin	Antagonizes vitamin K-dependent carboxylation of factors II, VII, IX, and X	**Long-term** anticoagulation post-thrombotic event or in cases of increased thrombus risk (postsurgery, Afib, artificial valves)	Hemorrhage, numerous **drug interactions, teratogenicity**

ADP, adenosine diphosphate; ASA, aspirin; Afib, atrial fibrillation; CAD, coronary artery disease; DVT, deep vein thrombosis; GI, gastrointestinal; GP, glycoprotein; MI, myocardial infarction; PE, pulmonary embolism; PVD, peripheral vascular disease.

3. **Antithrombotic drugs**
   a. Used to prevent or treat pathologic clot (thrombus) formation (e.g., deep vein thrombosis [DVT], thromboembolic stroke, mural thrombus, pulmonary embolism [PE], postsurgical or traumatic thrombus, etc.)
   b. Can affect platelet function, intrinsic pathway, or extrinsic pathway (see Table 3-6)

NEXT
STEP

Monitor **warfarin** anticoagulation with a normalized PT (i.e., **international normalized ratio [INR]**) to track relative effect on the extrinsic pathway.

Quick **HIT**

Do not start warfarin therapy for a thrombus until after starting LMWH or until PTT is therapeutic on unfractionated heparin because warfarin inhibits proteins C and S to cause a short period of **hypercoagulability** immediately after therapy is initiated.

B. Thrombocytopenia

1. Decreased number of platelets (<150,000) leading to increased risk of hemorrhage
2. May be idiopathic, autoimmune, or result from external causes (e.g., drugs, infection, nutrition) (see Table 3-7)
3. **H/P** = possibly asymptomatic; mucosal bleeding, petechiae, purpura, multiple ecchymoses
4. **Workup** = platelets <150,000/μL, increased bleeding time
5. **Blood smear** = may show low platelet numbers, small platelets, abnormal platelet granules, or neutrophil granules depending on etiology

Table 3-7 Causes of Thrombocytopenia

Cause	Pathology	Diagnosis	Treatment
Impaired production (drugs, infection, aplastic anemia, folate/vitamin B_{12} deficiency, alcohol, cirrhosis)	**Absent** or **reduced** megakaryocytes caused by offending agent or **abnormal megakaryocytes** because of metabolic deficiency	Findings consistent with precipitating condition; bone marrow biopsy helpful for diagnosis	Stop offending agent, treat underlying disorder, bone marro transplantation
Abnormal pooling	**Splenic platelet sequestration**	Splenomegaly, normal bone marrow biopsy, 90% platelets may be sequestered	May not be required; splenecto if symptomatic
Heparin-induced thrombocytopenia (HIT)	Development of antiplatelet antibodies that cause widespread platelet destruction in response to heparin therapy	Diffuse thrombus formation, sudden decrease (>50%) in platelet level, positive serotonin release assay, positive heparin-induced platelet aggregation assay	Stop all heparin use; direct thro bin inhibitors for thrombi
Immune thrombocytopenia (ITP)	**Autoimmune** B-cell directed production of antiplatelet antibodies	Other explanations for thrombocytopenia ruled out, **platelets commonly <50,000**	Self-limited in children; adults require corticosteroids, delayed splenectomy, intravenous (IV) immunoglobulin, plasmapheresi or recombinant factor VIIa
Thrombotic thrombocytopenic purpura-hemolytic uremic syndrome (TTP-HUS)	Diffuses platelet aggregation due to autoantibodies against a preventative enzyme; associated with endothelial injury and *Escherichia coli* O157:H7 infection	**Hemolytic anemia, acute renal failure, thrombocytopenia** without severe bleeding, neurologic sequelae, ± fever	Corticosteroids, plasmapheresis FFP
Antiphospholipid syndrome	Development of antiphospholipid antibodies during pregnancy leading to arterial and venous thrombosis	During pregnancy, presence of antiphospholipid or lupus anticoagulant antibodies	Anticoagulation with heparin ar warfarin, hydroxychloroquine
HELLP syndrome	Sequela of eclampsia associated with elevated liver enzymes and hemolytic anemia	During pregnancy, HTN, increased LFTs, decreased Hgb, schistocytes on blood smear	Induce delivery if fetus >34 wee of gestation; anti-HTN drugs an corticosteroids to speed fetal lu maturity if preterm

FFP, fresh frozen plasma; HELLP, hemolysis, elevated liver enzymes, and low platelet counts; HTN, hypertension; LFTs, liver function tests.

C. von Willebrand Disease

1. Autosomal dominant disease with deficiencies of **von Willebrand factor** (vWF) and sometimes **factor VIII,** leading to abnormal clotting and platelet function. Most common inherited bleeding disorder
2. **H/P** = easy bruising, mucosal bleeding (nose, gums), menorrhagia; multiple sites of bruising and mucosal bleeding on examination; antiplatelet drug administration can induce bleeding
3. **Workup** = **increased PTT, increased bleeding time,** decreased factor VIII antigen, decreased vWF antigen, decreased ristocetin cofactor activity
4. **Treatment** = desmopressin during minor bleeding, vWF concentrate and factor VIII concentrate before surgery or during major bleeding, avoidance of aspirin (ASA)

Quick HIT

Administration of FFP is indicated in patients with severe bleeding from warfarin or heparin. Other indications include reversal agents such as vitamin K and protamine.

Quick HIT

vWF and factor VIII are the only clotting factors not synthesized exclusively by the liver and remain at normal levels, whereas other factor levels decrease in liver failure.

Quick HIT

Patients using **warfarin** can present with a clinical picture similar to that of vitamin K deficiency.

D. Vitamin K Deficiency

1. Inadequate vitamin K supply because of poor intake, malabsorption, or eradication of vitamin K-producing GI flora (secondary to prolonged antibiotic use)
2. Vitamin K is required in synthesis of factors II, VII, IX, and X
3. **H/P** = easy bruising, mucosal bleeding, melena, hematuria, delayed clot formation
4. **Workup** = increased PT, increased INR
5. **Treatment** = oral or intramuscular vitamin K, fresh frozen plasma (FFP)

E. Hemophilia

1. X-linked recessive disease with deficiency of either factor VIII (hemophilia A) or factor IX (hemophilia B)
2. **H/P** = **uncontrolled bleeding** occurring spontaneously or after minimal trauma, excessive bleeding following surgical or dental procedures; **hemarthroses** (i.e., bleeding in joints), intramuscular bleeding, and GI or genitourinary bleeding may be evident on examination
3. **Workup** = **increased PTT, normal PT, normal bleeding time,** decreased factor VIII or IX antigen
4. **Treatment** = **factor VIII or IX replacement,** desmopressin (may increase factor VIII production in hemophilia A), transfusions frequently needed in cases of large blood loss; hemarthroses and intracranial bleeds require aggressive factor replacement
5. **Complications** = death from severe, uncontrolled bleeding; arthropathy from recurrent hemarthroses frequently requires eventual joint replacement

Quick **HIT**

Hemophiliacs tend not to develop significant bleeds unless they have **<5%** clotting activity.

MNEMONIC

Remember the signs of thrombotic thrombocytopenic purpura-hemolytic uremic syndrome (TTP-HUS) by the mnemonic **N**asty **F**ever **T**orched **H**is **K**idneys: **N**eurologic deficits, **F**ever, **T**hrombocytopenia, **H**emolytic anemia, **K**idney failure.

F. Disseminated Intravascular Coagulation (DIC)

1. Widespread abnormal coagulation caused by sepsis, severe trauma, neoplasm, or obstetric complications.
   a. Initial coagulopathy with widespread clot formation occurs because of extensive activation of the clotting cascade by endothelial tissue factor released during bacteremia.
   b. Deficiency in clotting factors results from extensive clotting.
   c. Abnormal bleeding results from clotting factor deficiencies.
2. **H/P** = appropriate history of precipitating condition; uncontrolled bleeding from wounds and surgical sites, hematemesis, dyspnea; jaundice, digital cyanosis, hypotension, tachycardia, possible neurologic or renal insufficiency signs, possible shock
3. **Workup** = decreased platelets, increased PT, increased PTT, decreased fibrinogen, **increased fibrin split products, increased D-dimer,** decreased Hct
4. **Blood smear** = schistocytes, few platelets
5. **Treatment** = **treat underlying disorder;** platelets, FFP, cryoprecipitate; heparin may be needed for chronic thrombi
6. **Complications** = poor prognosis without early treatment; thrombi cause numerous infarcts

Quick **HIT**

Bleeding in **DIC** occurs because **pathologic clotting uses up supplies** of platelets and coagulation factors; bleeding in other clotting disorders occurs because of insufficient production, abnormal production, or early destruction of platelets or coagulation factors.

V. Hematologic Infections

Quick **HIT**

Encapsulated organisms are a more common cause of sepsis in **asplenic** patients (e.g., sickle cell disease) than in other patients.

A. Sepsis

1. Bacteremia with an associated **excessive systemic inflammatory response** leading to global tissue hypoxia and possibly organ dysfunction

2. Diagnostic criteria for systemic inflammatory response syndrome (SIRS) are two of the following:
   a. Temperature >38.3°C or <36°C
   b. Heart rate >90 beats/min
   c. Respiratory rate >20 breaths/min or $PaCO_2$ <32 mm Hg
   d. WBC >12,000 cells/mm^3 or <4,000 cells/mm^3, or >10% immature (band) forms
3. Common community-acquired pathogens include *Streptococcus*, *Staphylococcus*, *Escherichia coli*, *Klebsiella*, *Pseudomonas*, and *Neisseria meningitidis*
4. Common nosocomial pathogens include *Staphylococcus*, gram-negative bacilli, anaerobes, *Pseudomonas*, and *Candida* species
5. **H/P** = malaise, chills, nausea, vomiting; fever or hypothermia, mental status changes, tachycardia, tachypnea; may progress to **septic shock** with hypotension, cool extremities (initially warm), and petechiae
6. **Workup** = aims to identify possible source; increased (>12,000/mL) or decreased (<4,000/mL) WBCs; positive urine, blood, or sputum cultures to diagnose infection; labs may detect signs of DIC
7. **Radiology** = chest x-ray may show infiltrates and pneumonia

Quick HIT

Staphylococcus aureus is a common cause of sepsis in intravenous drug abusers.

8. **Treatment**
   a. Secure airway, supply adequate oxygenation (may require intubation and ventilation)
   b. Hydration, vasopressors, inotropes, and transfusions to maintain tissue perfusion
   c. Glucocorticoids may be beneficial in select patients
   d. Broad-spectrum antibiotics **initially,** then pathogen-specific antibiotics when agent identified by culture; remove (or change) possible routes of infection (Foley catheter, IV, etc.)
   e. Maintain glycemic control (glucose 140 to 180 mg/dL)
9. **Complications** = septic shock, DIC

NEXT
STEP

Do not start antibiotics until **after** first blood culture has been collected to avoid false-negative cultures.

B. Malaria

1. Parasitic infection by ***Plasmodium*** spp. (*P. vivax*, *P. falciparum*, *P. ovale*, *P. malariae*) transmitted by *Anopheles* mosquito
2. **H/P** = **chills,** diaphoresis, headache, myalgias, fatigue, nausea, abdominal pain, vomiting, diarrhea; **periodic fever** at approximately 1- to 3-day intervals, splenomegaly; *P. falciparum* infection can include decreased consciousness, pulmonary edema, and renal insufficiency
3. **Workup** = polymerase chain reaction (PCR) for *Plasmodium* is highly sensitive
4. **Blood smear** = Giemsa stain shows *Plasmodium* spp. (see Figure 3-12)
5. **Treatment** = **antimalarials** (e.g., chloroquine, primaquine, quinine); atovaquone, proguanil, or mefloquine used in chloroquine-resistant *P. falciparum*

Quick HIT

Although rare in the United States, malaria is extremely common in other countries, especially in sub-Saharan Africa, tropical South America, India, and Southeast Asia. Travelers to these areas should take antimalarial prophylaxis.

C. Infectious Mononucleosis

1. Infection by **EBV** affecting B cells and oropharyngeal epithelium
2. Transmitted by **intimate contact** (e.g., kissing, intercourse)
3. **H/P** = fatigue, sore throat, malaise; lymphadenopathy, splenomegaly, fever, tonsillar exudates
4. **Workup** = positive heterophile antibodies (i.e., Monospot test), positive EBV serology, elevated liver function tests (LFTs), increased WBCs, hemolytic anemia, thrombocytopenia
5. **Blood smear** = increased number of lymphocytes (some with abnormal appearance)
6. **Treatment** = self-limited; supportive care
7. **Complications** = splenic rupture is rare, but patients should refrain from contact sports for 1 month after symptom onset; rare aplastic anemia; DIC; thrombotic thrombocytopenic purpura; fulminant liver failure

Quick HIT

Symptoms of mononucleosis do not appear until 2 to 5 weeks after infection with EBV.

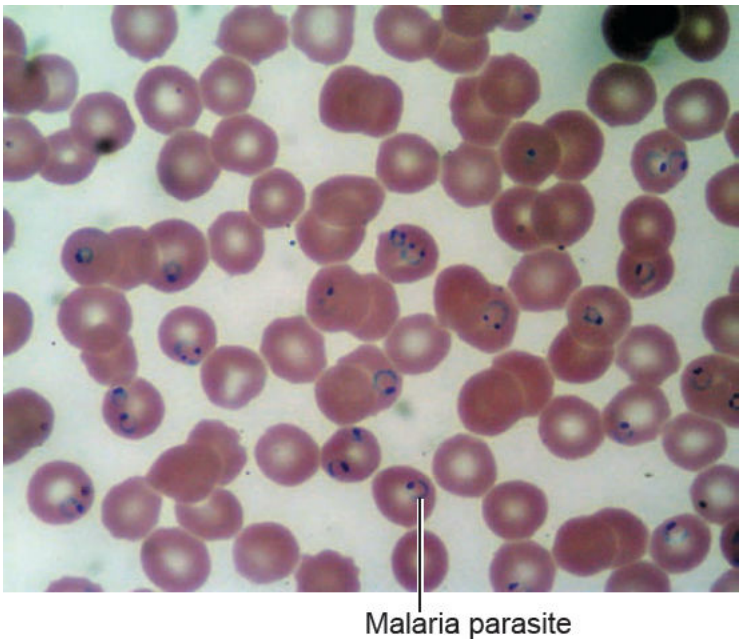


FIGURE 3-12
Peripheral blood demonstrating *Plasmodium* infection (malaria).
(From McConnell, T. H. [2007]. *The Nature of Disease: Pathology for the Health Professions* [p. 245]. Philadelphia, PA: Lippincott Williams & Wilkins; with permission.)

Quick HIT

HIV infection has greatest prevalence in sub-Saharan Africa, where transmission is typically through heterosexual contact.

D. Human Immunodeficiency Virus (HIV)

1. RNA retrovirus (HIV-1 and HIV-2 are most common strains) that infects CD4 lymphocytes (**helper T cells**) and destroys them, eventually leading to **acquired immunodeficiency syndrome** (**AIDS**)
   a. Both strains transmitted in same manner; they share same risks for opportunistic infections and are treated in same manner.
   b. Compared with HIV-1, HIV-2 progresses more slowly, is less infectious in early disease, is more infectious in late disease, and is less common in the United States.
   c. Serologic tests for the two strains are slightly different and do not cross-react consistently.
2. Virus uses reverse transcriptase to incorporate genetic material into host cell genome and produce copies of DNA
3. Transmitted via **bodily fluids** (e.g., blood, semen, vaginal secretions, breast milk)
4. **Risk factors** (United States) = homosexual or bisexual males, intravenous drug abuse (IVDA), blood transfusions before the mid-1980s (e.g., hemophiliacs), multiple sexual partners, heterosexual partners of other high-risk individuals, infants born to infected mothers, accidental exposure to bodily fluids (e.g., needle sticks, fluid splashes) among health care workers (low probability but possible); higher prevalence among black and Latino populations
5. **Acute H/P** = **flu-like symptoms** (e.g., myalgias, nausea, vomiting, diarrhea, fatigue), sore throat, weight loss; **mucosal ulcers,** fever, lymphadenopathy, viral rash; symptoms typically develop 2 to 4 weeks after exposure and last 2 weeks
6. Following acute infection, patient enters **latent phase** with few or no symptoms and low viral load that lasts months to years (time increases with treatment)
7. **Late H/P** (i.e., AIDS) = **opportunistic infections** and **AIDS-defining illnesses** begin to present; weight loss, night sweats, dementia (see Table 3-8)

NEXT
STEP

Although the rate of HIV transmission through needle sticks (i.e., health care workers) is very low (0.3%), prophylactic tenofovir, emtricitabine, and raltegravir should be started immediately if there is an appreciable risk of transmission; HIV antibody tests should be performed immediately, 6 weeks, 3 months, and 6 months after exposure to determine if transmission occurred; treatment should be continued for 4 weeks.

Table 3-8 Common Opportunistic Infections, Neoplasms, and Complications Seen in Acquired Immunodeficiency Syndrome (AIDS)

Condition/Infection	When Seen	History/Physical	Diagnosis	Treatr
Herpes zoster/simplex	CD4 <500	Shingles, oral or genital lesions	Tzanck smear, viral culture	Acyclov
Kaposi sarcoma	CD4 <250	**Purple subcutaneous nodules** on face, chest, or extremities	Biopsy of lesions	Topical apy, las
Parasitic diarrhea (*Isospora, Strongyloides, Cryptosporidium*)	CD4 <500	Prolonged diarrhea, malaise, weight loss, abdominal pain	Stool culture, parasite evaluation	Antiret metron paromo
Wasting syndrome	CD4 <100	Weight loss >10% baseline weight, chronic diarrhea, chronic weakness, fever	Clinical diagnosis, EMG suggests peripheral nerve dysfunction	Exercis
Coccidioidomycosis	CD4 <250	Cough, fever, dyspnea	Bilateral reticulonodular infiltrates on CXR, positive antibody screen	Fluconaz ampho
AIDS dementia	CD4 <200	Confusion, mental status changes, **generalized neurologic symptoms**, including tremor	History of declining mental function, generalized neurologic symptoms, elevated β_2-microglobulin in CSF, cerebral atrophy on CT or MRI	May im ral ther
Bacterial pneumonia (*Streptococcus pneumoniae, Haemophilus influenzae, Nocardia*)	CD4 <200	**Rapid onset**, productive cough, high fevers	Gram stain, lobar consolidation on CXR	Cephal macrol

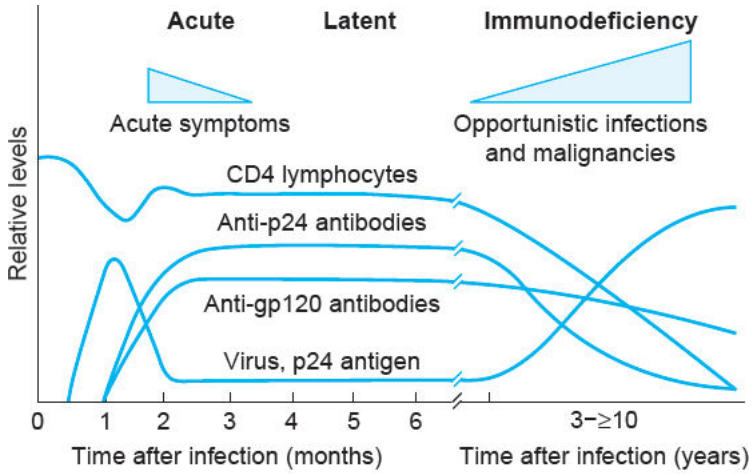
Candida esophagitis	CD4 <200	Dysphagia, **odynophagia**	Endoscopy with biopsy, Gram stain on lesion scrapings	Topical or oral fluconazole or ketoconazole
Cervical cancer	CD4 <200	History of human papilloma virus	Detected by screening Papanicolaou (Pap) smear, biopsy confirms diagnosis	Resection, topical 5-fluorouracil, radiation therapy, chemotherapy
Pneumocystis jiroveci pneumonia (PCP)	CD4 <200	**Gradual onset, nonproductive cough**, dyspnea on exertion, fever	Bilateral infiltrates on CXR, increased LDH, sputum Gram stain	TMP-SMX, corticosteroids
Tuberculosis	CD4 <200, high-risk groups/prisons	Cough, night sweats, weight loss, fever	**Acid-fast bacilli**, cavitary defects and hilar adenopathy on CXR, positive PPD (must be checked with anergy test)	Isoniazid, rifampin, pyrazinamide, ethambutol
Histoplasmosis	CD4 <150	Abdominal pain, GI bleeding, skin lesions, dyspnea, meningitis	Bilateral infiltrates on CXR, positive antigen test	Long-term amphotericin B or itraconazole
Cerebral toxoplasmosis	CD4 <100	Headache, confusion, possible **focal neurologic symptoms**	**Positive *Toxoplasma* IgG antibody**, ring-enhancing lesions on CT or MRI	Pyrimethamine, sulfadiazine, clindamycin (**chronic treatment may be needed**)
Lymphoma (CNS or non-Hodgkin)	CD4 <100	Headache, confusion, possible **focal neurologic symptoms**	CT or MRI shows lesion, biopsy confirms diagnosis	Chemotherapy, radiation
Progressive multifocal leukoencephalopathy (JC virus)	CD4 <100	Ataxia, motor deficits, mental status changes	Positive PCR for JC virus DNA	May improve with antiretroviral therapy
Cryptococcal meningitis	CD4 <50	Headache, neck stiffness, fever, mental status changes	Elevated pressure on lumbar puncture, **yeast seen with India ink** stain of CSF, **positive cryptococcal antigen** in CSF or serum	Amphotericin B, fluconazole
Cytomegalovirus (CMV)	**CD4 <50**	**Vision loss**, esophagitis, diarrhea	Viral titer, yellow infiltrates with hemorrhage on funduscopic examination	Ganciclovir, foscarnet, valganciclovir
Mycobacterium avium complex (MAC)	**CD4 <50**	Fatigue, weight loss, fever, diarrhea, abdominal pain, lymphadenopathy, hepatosplenomegaly	Blood cultures	Clarithromycin, azithromycin, ethambutol, rifabutin, rifampin

AIDS, acquired immune deficiency syndrome; CNS, central nervous system; CSF, cerebrospinal fluid; CT, computed tomography; CXR, chest x-ray; DNA, deoxyribonucleic acid; EMG, electromyogram; GI, gastrointestinal; LDH, lactate dehydrogenase; MRI, magnetic resonance imaging; PCR, polymerase chain reaction; PPD, purified protein derivative; TMP-SMX, trimethoprim-sulfamethoxazole.

8. **Workup**
   a. Enzyme-linked immunosorbent assay (ELISA) detects HIV antibodies and is 99% sensitive; if positive, repeat ELISA performed (see Figure 3-13).
   b. Following two positive ELISAs, **Western blot** (lower sensitivity but high specificity) is performed to rule out false-positive findings.
   c. Rapid serologic tests are being used as initial screening test with increasing frequency, but positive results require standard serologic testing for confirmation.
   d. **CD4 count** is used to track extent of disease progression (AIDS is defined by CD4 <200).
   e. **Viral load** indicates the rate of disease progression (low during latent phase and high once AIDS is diagnosed) and may be useful in detection of acute infection during presentation with symptoms of seroconversion.
   f. Other nonspecific lab findings include decreased WBCs (during acute infection and again after development of AIDS), increased LFT findings, and mildly decreased Hgb and platelets.

Quick HIT

It may take up to **6 months** for HIV antibodies to appear in the serum.



Note: p24 and gp120 are viral proteins that serve as markers for HIV infection.

FIGURE 3-13

Serologic profile of human immunodeficiency virus (HIV) infection.
Note: p24 and gp120 are viral proteins that serve as markers for HIV infection.
(From Mehta, S., Milder, E. A., Mirachi, A. J., & Milder, E. [2006]. *Step-Up: A High-Yield, Systems-Based Review for the USMLE Step 1* [3rd ed., p. 210]. Philadelphia, PA: Lippincott Williams & Wilkins.)

9. **Treatment**
   a. **Antiretroviral therapy** should be initiated for all HIV-infected patients, regardless of CD4 count or viral load.
   b. Utility of starting antiretroviral therapy in acute infection is controversial and currently not universally recommended (performed in health care workers).
   c. Common initial **highly active antiretroviral treatment** (**HAART**) regimens
      (1) Start with two nucleoside reverse transcriptase inhibitors and either a protease inhibitor or non-nucleoside reverse transcriptase inhibitor (three antiretroviral drug minimum) (see Table 3-9).
      (2) Low-dose ritonavir can be added to the initial regimen to increase protease inhibitor activity.
      (3) Combination therapy (i.e., multiple drugs combined in one pill) will decrease number of pills taken at one time and help avoid dosing schedule mishaps.
   d. Compliance with therapy is vital to delaying disease progression; significant side effects associated with antiretroviral drugs are a major deterrent to good compliance.
   e. Indications for changing antiretroviral regimen include failure to keep viral load <50/mL, drug toxicity, poor compliance, and suboptimal regimen.
      (1) Patients with virologic failure should be tested for viral drug resistance, reviewed for drug interactions, and considered for drug substitution or addition of another drug.
      (2) Drug toxicity may be amenable to changing drugs.
      (3) Poor compliance can be approached by decreasing complexity of regimen (i.e., using combination pills) or enlisting family or friends to assist patient.
      (4) Suboptimal regimens can be improved with drug substitution.
   f. Antibiotic prophylaxis for opportunistic infections is started as below:
      (1) TMP-SMX for *Pneumocystis jiroveci* pneumonia (PCP) when CD4 count <200
      (2) Azithromycin for *Mycobacterium avium* complex (MAC) when CD4 count <100
   g. Close following of serology is important for dictating the direction of care.
   h. Pregnant mothers with HIV should be treated to keep viral load low and should be given zidovudine during labor; newborns to HIV-positive mothers should be given zidovudine for 6 weeks after birth and should be tested for presence of virus (anti-HIV antibodies will always be present in these children) in the initial 6 months of life.
10. **Complications** = opportunistic infections, neoplasms, cardiomyopathy, neuropathy, AIDS dementia complex, arthritis, polymyositis, anemia; although several advancements in treatment have been made, no cure or effective vaccine has been developed

Quick HIT

Mother-to-infant transmission of HIV is **rare** when viral load is <1,000.

Table 3-9 Antiviral Medications Used in Treatment of Human Immunodeficiency Virus (HIV)

Drug Class	Examples of Drug	Mechanism	Adverse Effects
Nucleoside reverse transcriptase inhibitors	**Abacavir** Emtricitabine Lamivudine **Zidovudine** Tenofovir (nucleotide RTI)	Inhibit production of viral genome, prevent incorporation of viral DNA into host genome through reverse transcriptase inhibition	**Lactic acidosis, li** pancreatitis, hypers tions (abacavir), bor (zidovudine)
Non-nucleoside reverse transcriptase inhibitors	Efavirenz Etravirine Rilpivirine	Inhibit reverse transcriptase activity to prevent viral replication	**Rash**; efavirenz cau effects and is terat
Protease inhibitors	Atazanavir Darunavir Fosamprenavir Lopinavir Ritonavir	Interfere with viral replication to cause production of nonfunctional viruses	**Hyperglycemia, h** **demia**, GI toxicity, l (atazanavir)
Integrase inhibitor	Elvitegravir Raltegravir	Inhibit the final step in integration of viral DNA into host DNA	Neutropenia, pancr ity, hyperglycemia
Fusion inhibitor	Enfuvirtide	Bind to gp41, inhibit viral ability to fuse with CD4 membrane and enter cell	Hypersensitivity rea injection site, bacte
CCR5 antagonist	Maraviroc	Inhibit viral CCR5 coreceptor → block viral entry to host cell	Fever, cough, upper tions, peripheral ne

VI. Hematologic Neoplastic Conditions

Quick HIT

HIV-positive mothers should **not** breastfeed their infants to reduce risk of transmission.

A. Polycythemia Vera

1. Myeloproliferative disorder of bone marrow stem cells leading to **increased production** of RBCS, WBCs, and platelets
2. Tends to occur after age 60 years; many progress to leukemia
3. **H/P** = fatigue, headache, **burning pain in hands or feet, pruritus** (especially after contact with warm water), tinnitus, blurred vision, epistaxis, abdominal pain; **splenomegaly,** hepatomegaly, large retinal veins on funduscopic examination
4. **Workup** = **increased Hgb, increased Hct,** increased RBC mass, increased or normal WBCs and platelets, decreased erythropoietin; biopsy shows hypercellular marrow
5. **Treatment** = serial phlebotomy, antihistamines (for pruritus), ASA (thrombus prophylaxis), hydroxyurea (bone marrow suppression)
6. **Complications** = thrombus formation, **leukemia** (acute and chronic myelogenous), stroke

Quick HIT

The most common cause of increased RBC production is **chronic hypoxia**.

B. Multiple Myeloma

1. Malignant proliferation of **plasma cells;** increased incidence with prior monoclonal gammopathy of undetermined significance (MGUS)
2. Abnormal monoclonal protein (**M protein**) produced from IgG and IgA heavy chains and κ and λ light chains (these light chains are known as **Bence Jones proteins**)
3. **H/P** = **back pain,** radicular pain, weakness, fatigue, weight loss, constipation, **pathologic fractures,** frequent infections; pallor, bone tenderness
4. **Workup** = decreased Hgb, decreased Hct, decreased WBCs, increased blood urea nitrogen (BUN) and creatinine (secondary to renal insufficiency), increased Ca^{2+}; serum protein electrophoresis (SPEP) and urine protein

electrophoresis (UPEP) detect high M protein and Bence Jones proteins; bone marrow biopsy shows increased plasma cells
5. **Radiology** = "**punched-out**" lesions in long bones and skull
6. **Treatment** = radiation, chemotherapy, bone marrow transplant, repair of fractures, treat infections
7. **Complications** = renal failure, recurrent infections, hypercalcemia, spinal cord compression; poor prognosis with survival for 2 to 3 years after diagnosis

C. Lymphoma

1. Malignant transformation of lymphocytes primarily in **lymph nodes** that can also involve bloodstream or nonlymphatic organs
2. Categorized as Hodgkin and non-Hodgkin variants (see Table 3-10, Figure 3-14)

Quick HIT

ALL is the **most common cancer** in **children**.

Quick HIT

Most ALL originates in **B-cell precursors.**

D. Leukemia

1. Malignant transformation of myeloid or lymphoid cells involving bloodstream and bone marrow
2. **Acute** leukemia tends to involve immature cells, whereas **chronic** leukemia involves more mature cells
3. Bone marrow involvement can cause pancytopenia
4. **Acute lymphocytic leukemia** (ALL)
   a. **Most common in children** (2 to 5 years of age); whites > blacks
   b. Proliferation of cells of **lymphoid** origin (lymphocytes)
   c. **H/P** = **bone pain,** frequent infections, fatigue, dyspnea on exertion, easy bruising; fever, pallor, purpura, hepatosplenomegaly, lymphadenopathy
   d. **Workup** = decreased Hgb, decreased Hct, decreased platelets, decreased WBCs, increased uric acid, increased LDH; bone marrow biopsy shows **abundant blasts;** Philadelphia chromosome (i.e., translocation of chromosomes 9 and 22 in *BCR-ABL* genes) found in 15% **adult** cases

Table 3-10 Characteristics of Hodgkin and Non-Hodgkin Lymphomas

Characteristic	Hodgkin Lymphoma	Non-Hodgkin Lymphoma
Cells of origin	B cells	Lymphocytes (**most commonly B cells**) or natural killer cells
Classification (low to higher grade)	Nodular sclerosis (**most common**, women = men, fibrosis of lymph nodes), mixed cellularity, lymphocyte-rich (rare, best prognosis), lymphocyte-depleted (very rare, worst prognosis)	Many types, common variants include diffuse large B cell (**most common**), follicular small cell (B cells, t[14;18]), small lymphocytic (same disease as CLL), Burkitt (**EBV related**, t[8;14], **"starry sky" pattern**), peripheral (**T cells**)
Risk factors, patient population	Bimodal age distribution (peaks at 20 and 65 years of age), men > women (except for nodular sclerosis subtype)	EBV, HIV, congenital immunodeficiencies, rheumatic disease
History and physical	Painless lymphadenopathy (**neck**), weight loss, pruritus, night sweats, fever, hepatosplenomegaly	Painless lymphadenopathy (**generalized**), weight loss, fever, night sweats
Labs	Lymph node biopsy shows **Reed–Sternberg cells** (see Figure 3-14)	Lymph node or bone marrow biopsy shows lymphocyte proliferation (**cleaved cells seen in follicular small cell variant**)
Treatment	Radiation, chemotherapy	Palliative radiation, chemotherapy
Prognosis	**Good**, 80% cure rate unless far progressed	**Poor** (months for aggressive types, years for less aggressive variants), worsens with increasing age

CLL, chronic lymphocytic leukemia; EBV, Epstein–Barr virus; HIV, human immunodeficiency virus.

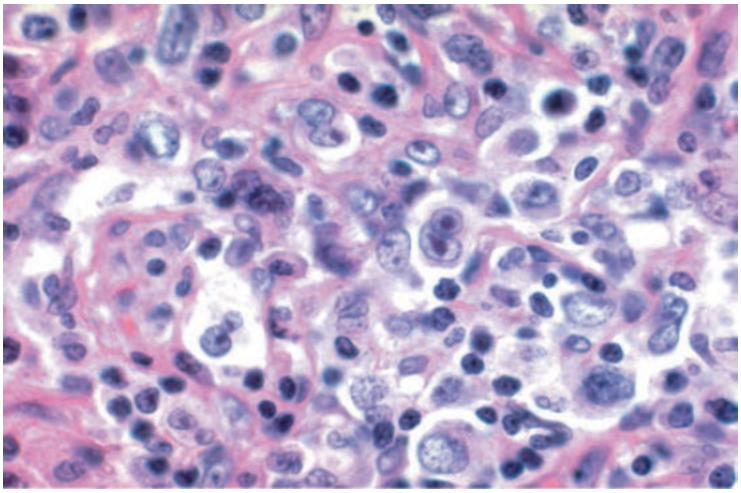


FIGURE 3-14
Hodgkin disease; histologic section of lymph node demonstrates pathognomonic binucleated Reed–Sternberg cells that resemble owls' eyes.
(From Rubin, R., & Strayer, D. S. [2012]. *Rubin's Pathology* [6th ed., p. 1026]. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; with permission.)

e. **Blood smear** = numerous blasts (see Figure 3-15)
f. **Treatment** = chemotherapy (induction followed by maintenance dosing), bone marrow transplant
g. **Complications** = although 5-year survival rates are good (85%) in children, adults have worse prognosis; presence of Philadelphia chromosome carries poor prognosis

5. **Acute myelogenous leukemia** (AML)
a. Proliferation of **myeloid** cells; both children and adults affected
b. **H/P** = fatigue, easy bruising, dyspnea on exertion, frequent infections, arthralgias; fever, pallor, hepatosplenomegaly, mucosal bleeding, ocular hemorrhages
c. **Workup** = decreased Hgb, decreased Hct, decreased platelets, decreased WBCs; bone marrow biopsy shows **blasts** of myeloid origin and staining with **myeloperoxidase**
d. **Blood smear** = large myeloblasts with **notched nuclei** and **Auer rods** (see Figure 3-16)
e. **Treatment** = chemotherapy (regimen guided by cytogenetic analysis), bone marrow transplant
f. **Complications** = relapse common, DIC; long-term survival is poor despite frequently successful remissions

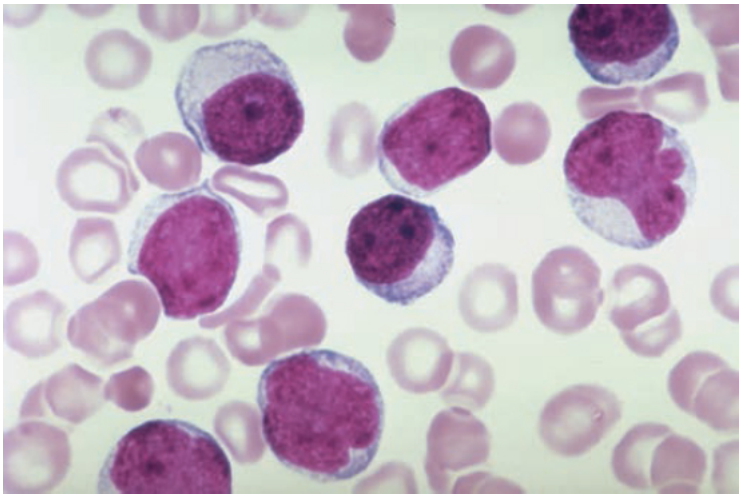


FIGURE 3-15
Acute lymphocytic leukemia.
Note lymphoblasts with irregular nuclei and prominent nucleoli.
(From Rubin, R., Strayer, D. S., & Bubin, E. [2012]. *Rubin's Pathology* [6th ed., p. 1026]. Philadelphia, PA: Lippincott Williams & Wilkins; with permission.)

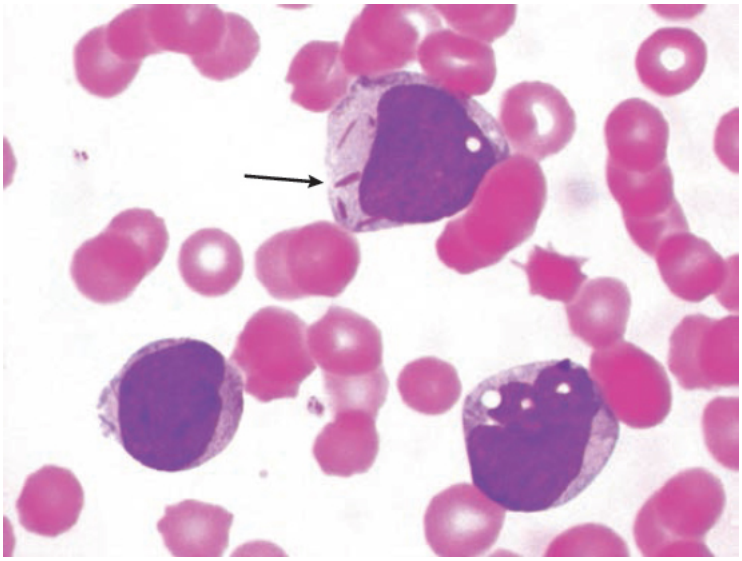


FIGURE 3-16
Acute promyelocytic leukemia (a subtype of AML).
Prominent Auer rods are seen (*arrow*).
(From Rubin, R., & Strayer, D. S. [2008]. *Rubin's Pathology: Clinicopathologic Foundations of Medicine* [5th ed., p. 903]. Philadelphia, PA: Lippincott Williams & Wilkins; with permission.)

6. **Chronic lymphocytic leukemia** (CLL)
   a. Proliferation of **mature B cells** in patients >65 years of age
   b. **H/P** = fatigue, frequent infection (secondary to no plasma cells), night sweats; fevers, lymphadenopathy, hepatosplenomegaly
   c. **Workup** = **increased WBCs** (may be >100,000/μL); bone marrow shows lymphocyte infiltration
   d. **Blood smear** = numerous small lymphocytes, **smudge cells** (see Figure 3-17)
   e. **Treatment** = supportive therapy, chemotherapy, radiation for bulky lymphoid masses, splenectomy for splenomegaly
   f. **Complications** = malignant B cells may form autoantibodies, leading to severe hemolytic anemia; course of disease tends to be either indolent (>10-year survival) or aggressive with high mortality within 4 years

Quick HIT

CLL and small lymphocytic lymphoma are considered to be the same disease process in different stages of evolution.

Quick HIT

Patients with CLL are asymptomatic 25% of the time and may be diagnosed following a workup for an abnormal CBC performed for an unrelated reason.

7. **Chronic myelogenous leukemia** (CML)
   a. Proliferation of **mature myeloid** cells seen in middle-aged adults; can be associated with **radiation exposure**
   b. Follows stable course for several years before progressing into **blast crisis** (i.e., rapid worsening of neoplasm) that is usually fatal

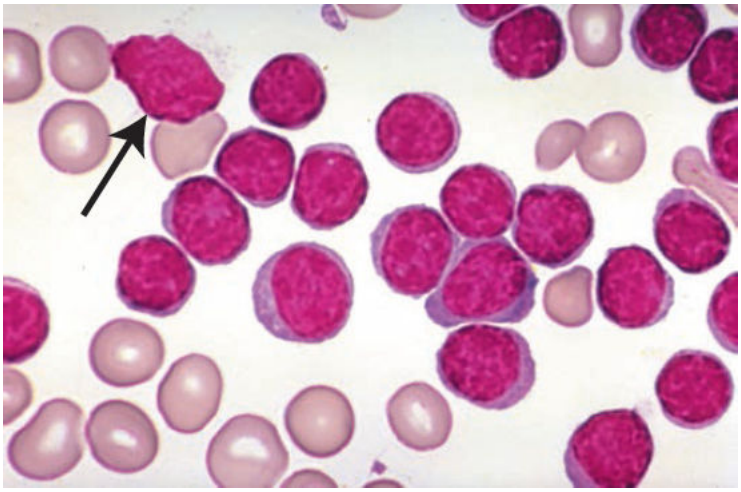


FIGURE 3-17
Chronic lymphocytic leukemia.
Note small lymphocytes of comparable size to nearby red blood cells (RBCs) and presence of smudge cells (fragile lymphocytes disrupted during smear preparation) in upper portion of image.
(From Rubin, R., & Strayer, D. S. [2008]. *Rubin's Pathology: Clinicopathologic Foundations of Medicine* [5th ed., p. 916]. Philadelphia, PA: Lippincott Williams & Wilkins; with permission.)

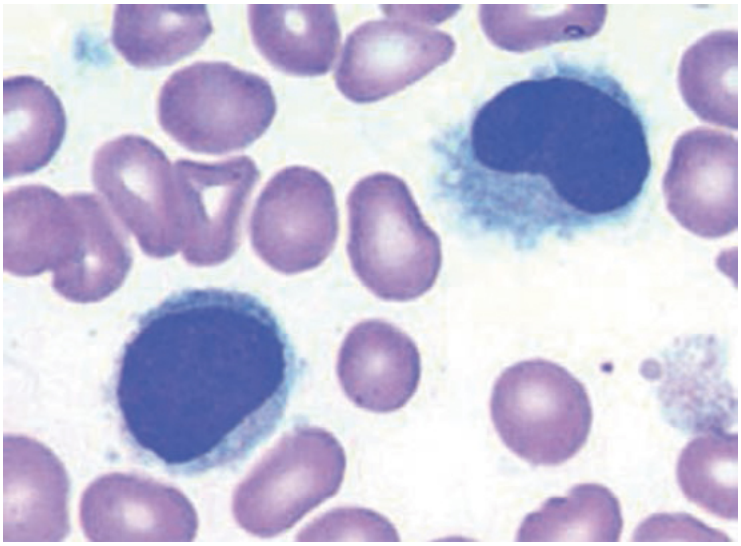


FIGURE 3-18
Hairy cells typical of hairy cell leukemia.
Note the numerous cytoplasmic projections giving the cell its name.
(From Rubin, R., & Strayer, D. [2012]. *Rubin's Pathology: Clinicopathologic Foundations of Medicine* [6th ed., p. 1017]. Philadelphia, PA: Lippincott Williams & Wilkins.)

c. **H/P** = possibly asymptomatic before progression; fatigue, weight loss, night sweats; fever, splenomegaly; blast crisis presents with worsening symptoms and bone pain
d. **Workup** = **increased WBCs** (>100,000/μL) with high proportion of neutrophils, decreased leukocyte alkaline phosphatase; bone marrow shows granulocyte hyperplasia; cytogenetic analysis demonstrates **Philadelphia chromosome** (t[9;22]) or *BCR-ABL* fusion gene
e. **Treatment** = chemotherapy (imatinib is promising agent), bone marrow transplant in younger patients
f. **Complications** = blast crisis signals rapid progression and is usually fatal

8. **Hairy cell leukemia**
a. Proliferation of B cells most frequently in middle-aged men
b. Similar in appearance to CLL (but better prognosis); now considered an indolent type of non-Hodgkin lymphoma
c. **H/P** = fatigue, frequent infections, abdominal fullness, no night sweats; no fever, **massive splenomegaly, no lymphadenopathy**
d. **Workup** = decreased Hgb, Hct, platelets, and WBCs (rarely, WBCs increased); bone marrow biopsy shows lymphocyte infiltration
e. **Blood smear** = numerous lymphocytes with "**hairy**" projections (irregular cytoplasmic projections) (see Figure 3-18)
f. **Treatment** = chemotherapy once patients develop symptomatic cytopenia

Quick HIT

The Philadelphia chromosome (t[9;22]) or *BCR-ABL* gene is almost always seen in CML but may also be seen in about 5% of ALL cases and rarely in AML.

VII. Oncologic Therapy

A. Treatment Strategy

1. **Eradication** of neoplastic cells is the ultimate goal.
2. If eradication is not possible, therapy seeks to delay disease progression or serve a **palliative** role.
3. Mass effect of tumors and paraneoplastic syndromes can cause effects that are treated with surgery, radiation, or chemotherapy to relieve symptoms even when overall prognosis is bleak.

B. Cancer Surgery

1. Performed to **reduce mass** of solid tumors or **remove** well-contained tumors
2. Resection of surrounding tissue frequently performed to increase chances of removing microscopic extensions of tumor
3. Many procedures carry significant morbidities and prolonged recoveries because of size of surgery or organ removal (e.g., Whipple procedure for pancreatic cancer, gastrectomy for gastric cancer)

C. Radiation Therapy

1. Performed to **necrose** tumor cells and **decrease tumor size**
2. May be curative in some cancers (some head and neck tumors); serves palliative role in several cases (e.g., Pancoast tumor)
3. Adverse effects include impaired surgical wound healing, fibrosis of tissue, skin irritation, esophagitis, gastritis, pneumonitis, neurologic deficits, bone marrow suppression, and **radiation-induced malignancies** (e.g., thyroid, CML, sarcomas)

D. Chemotherapy

1. Aims to eradicate smaller populations of neoplastic cells and destroy cells not removed through surgery or radiation (see Table 3-11)
2. Can sensitize neoplastic cells to radiation therapy (i.e., radiosensitizers)
3. Can be primary treatment modality in certain cancers particularly receptive to pharmacologic therapy
4. **Multiple drugs** with different cell cycle–specific targets are frequently combined to increase neoplastic cell death while minimizing toxicity to normal tissues, to have an effect against a broader range of cells, and to slow development of resistance
5. Adverse effects include bone marrow suppression, alopecia, GI upset, infertility, neurotoxicity, hepatotoxicity, skin changes, pulmonary fibrosis, cardiomyopathy, and renal toxicity

Table 3-11 Mechanisms and Classes of Chemotherapeutic Drugs

Mechanism	Drug Class	Examples
Free radical production causing cytotoxic alkylation of DNA and RNA	Nitrogen mustard alkylating agents Nitrosourea alkylating agents Alkyl sulfonate alkylating agents Ethyleneimine or methylmelamine alkylating agents Triazene alkylating agents	Cyclophosphamide, chlorambucil, ifosfamide, mechlorethamine Carmustine, streptozocin Busulfan Thiotepa, hexamethylmelamine Dacarbazine
Inhibition of spindle proteins to stop mitosis or cause cytotoxic polymerization	Vinca alkaloids Taxanes	Etoposide, vinblastine, vincristine Paclitaxel, docetaxel
Inhibition of DNA and RNA synthesis	Antibiotics Monoamine oxidase inhibitors	Bleomycin, dactinomycin, daunorubicin, doxorubicin, mitomycin Procarbazine
Interference with enzyme regulation or DNA and RNA activity	Antimetabolites Platinum analogs	Cytarabine, 5-fluorouracil, methotrexate, mercaptopurine Carboplatin, cisplatin
Modulation of hormones to cause tumor remission	Steroid hormones and antagonists	Prednisone, tamoxifen, estrogens, leuprolide

QUESTIONS

1. A 68-year-old male with history of hypertension and atrial fibrillation is being evaluated for acute fatigue, generalized weakness, and dyspnea on exertion. Evaluation reveals skin pallor and mild irregular tachycardia. There is no leg edema. Blood work shows normal renal function, and microcytic anemia with an Hgb of 6.3 g/dL and an INR of 2. What is the next step in the evaluation?

   A. Obtain a chest x-ray
   B. Obtain hemoccult test
   C. Repeat blood work
   D. Consult hematologist

2. A previously healthy female strict vegetarian is being evaluated for generalized weakness. She is an occasional drinker. His blood work shows macrocytic anemia with an Hgb of 7.5 g/dL. What is the likely cause of this anemia?

   A. Iron deficiency
   B. Alcohol abuse
   C. Pregnancy
   D. Vitamin deficiency

3. A 17-year-old male with history of sickle cell arrives to urgent care for evaluation of fever, and cough with sputum. He is not compliant with treatment or follow-up appointments. He does not have any pain at this time. Chest x-ray reveals a single lobe pulmonary infiltrate. This patient is at risk from severe infection by:

   A. Influenza
   B. *Streptococcus pneumoniae*
   C. Mycoplasma
   D. *Staphylococcus* sp.

4. Patients with sickle cell are at risk of aplastic crises by infection from which organism?

   A. Influenza
   B. Coxsackie
   C. *Salmonella* sp.
   D. Parvovirus

5. A 26-year-old male arrives to the Emergency Room after a bee sting. The patient admits to a severe allergic reaction from a prior bee sting. On evaluation patient has an urticarial rash, appears uncomfortable, is wheezing and diffusely swollen. What is the best first treatment option for this patient?

   A. Antihistamines
   B. Steroids
   C. Epinephrine
   D. Leukotriene inhibitor

6. A patient presents with a burning sensation in the anterior thigh. Upon evaluation of the patient undressed a raised erythematous lesion is seen in the proximal left anterior thigh, it resembles the appearance of a 5c coin. What type of hypersensitivity reaction is this?

   A. Type I
   B. Type II
   C. Type III
   D. Type IV

7. A 3-year-old child is being evaluated for acute diarrhea and weakness. On evaluation the child appears pale and dehydrated with punctate petechiae and mild swelling in lower extremities. Blood work reveals hemolytic anemia, renal failure, and thrombocytopenia. What is the likely cause of the patient's presentation?

   A. *Escherichia coli*
   B. Salmonella
   C. Splenic sequestration
   D. Drug induced

8. An 18-year-old female comes in for evaluation of heavy menses and recent onset of bleeding gums. Her mother is concerned because a similar disease runs in the family. What is the most likely bleeding disorder?

   A. Thrombotic thrombocytopenic purpura
   B. Hemophilia A
   C. von Willebrand disease
   D. Vitamin K deficiency

9. A 15-year-old male arrives to his primary care doctor to be evaluated for severe sore throat. He is complaining of generalized body aches, fatigue, fever, and pain with swallowing. Evaluation reveals enlarged purulent tonsils. Strep test is negative. This patient should avoid:

   A. Travel within the next 2 weeks
   B. NSAIDs for 3 months
   C. Antibiotics
   D. Contact sports

10. A 33-year-old female with history of HIV/AIDS comes for evaluation of a worsening cough, fever, and chills. The patient is noncompliant with recommended treatment. Evaluation reveals oral candidiasis. Her last known CD4 count was 175

one month ago. Her chest x-ray shows bilateral “batwing” infiltrates and blood work shows elevated LDH. This is likely a presentation of which disease?

A. Tuberculosis
B. *Pneumocystis jiroveci*
C. *Histoplasmosis*
D. *Staphylococcus*

11. A 60-year-old man presents with complaint of fatigue, headache, and a sensation of burning after every shower. Evaluation reveals enlarged spleen. Blood work shows markedly elevated Hgb and platelets. What is the likely diagnosis?

A. Disseminated intravascular coagulation
B. Allergic reaction
C. Fish poisoning
D. Polycythemia vera

12. A 65-year-old man presents with worsening back pain for several months. He had an x-ray of the spine performed that showed “punched out lesions.” This is concerning for:

A. Multiple myeloma
B. Lymphoma
C. Tuberculosis
D. Avascular necrosis

4

Selected Topics in Emergency Medicine, Critical Care, and Surgery

EMERGENCY MEDICINE

I. Accidents and Injury

A. Burns (See Figure 4-1)

1. Injury to epithelial surface and deeper tissues caused by exposure to significant heat, radiation, caustic chemicals, or electrical shock
2. Classified by depth of involvement
   a. **First degree:** epidermis only involved
   b. **Second degree:** partial-thickness dermal involvement (blisters)
   c. **Third degree:** full-thickness dermal and possibly deeper tissue involvement
   d. **Fourth degree:** additional involvement of muscle and bone
3. Extent of burns is estimated by "rule of 9s" (see Figure 4-2)
4. **History and physical (H/P)** = dependent on degree:
   a. First- and second-degree burns are erythematous and painful; blisters are also seen in second-degree burns.
   b. Third-degree burns are painless, and skin appears charred, leathery, or gray.
   c. Electrical burns may appear similar to fourth-degree burns, show severe damage at entrance and exit sites of electrical current, and have cardiac and neurologic symptoms (e.g., ventricular fibrillation [Vfib], seizures, loss of vision).

Quick **HIT**

Burns secondary to **electrical shock** are sometimes called fourth-degree burns because they may involve muscles, bones, and other internal structures.

NEXT

STEP

Determine IV fluid resuscitation need in second-degree (and higher) burns with the **Parkland formula:** lactated Ringer solution given in total volume of (**[4 mL] ë [kg body mass] ë [% body surface area burned]).** Half of volume is given during the initial 8 hours, and the remaining half is given over the following 16 hours.

5. **Treatment**
   a. Remove any burning agents to prevent further injury (e.g., burning or soaked clothing); caustic chemicals should be diluted or neutralized.
   b. **Outpatient** treatment is sufficient for **first-degree** and minor second-degree burns (e.g., cooling and cleansing, bandaging, topical antimicrobials). Blisters should not be broken for cleansing.

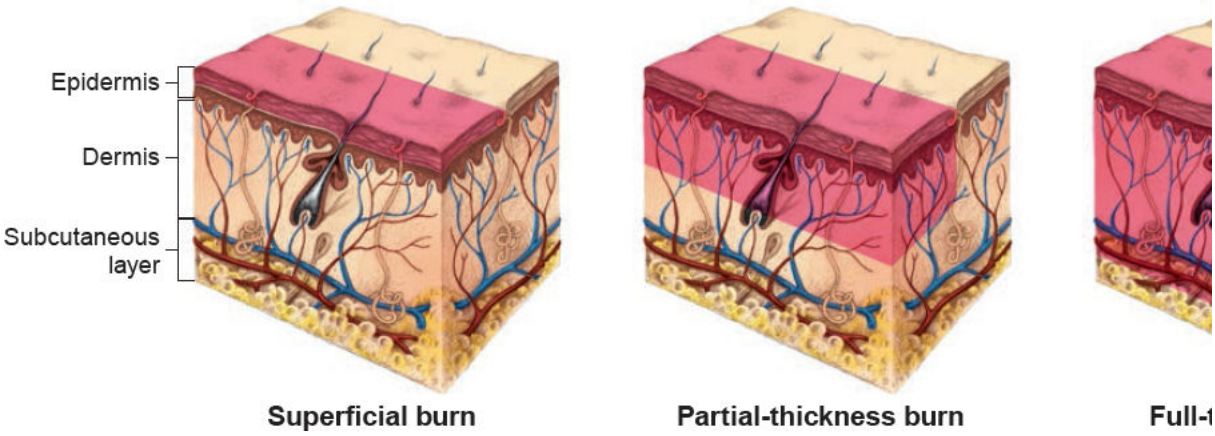


FIGURE 4-1

Evaluating burn severity.

A: Superficial partial-thickness burn. **B:** Deep partial-thickness burn. **C:** Full-thickness burn. (From *Lippincott's Nursing Procedures* [6th ed.]. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; 2013.)

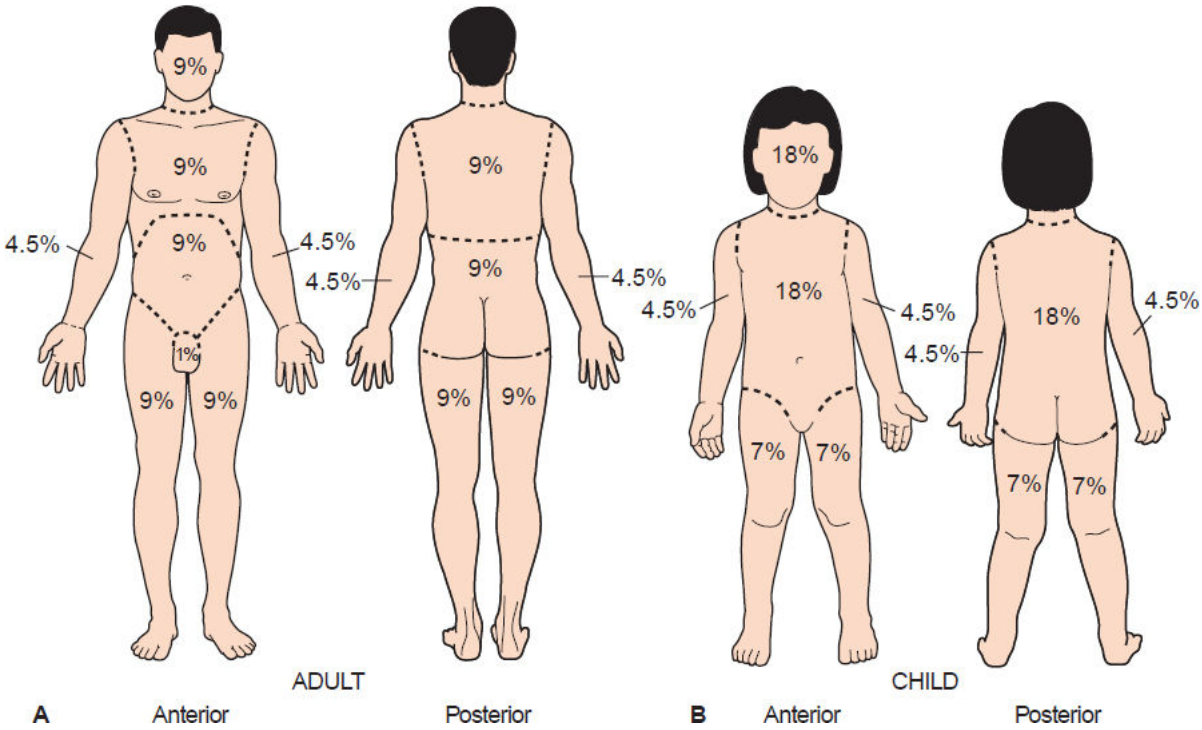


FIGURE 4-2

"Rule of 9s" for calculating extent of burns.

A: The surface anatomy of the adult is divided into sections of 9% body surface area (genitals are considered 1% surface area). Note that the distribution considers both the front and back of the head and arms as one contribution. **B:** Because of its greater relative size, the contribution of the head is increased in the child. Note that the front and back for the head, arms, and legs are considered as one contribution.

c. **Inpatient or transfer to burn center** treatment (e.g., intravenous [IV] hydration, wound care, possible escharotomy) is required for **second-degree** burns >10% body surface area, **third-degree** burns >2% body surface area, or second- and third-degree burns affecting face, hands, genitalia, or major skin flexion creases.
d. Second- and third-degree burns >25% body surface area or involving the face require **airway management** (frequently intubation), IV fluids, and careful control of body temperature (increased risk of hypothermia). Also require **inpatient or transfer to burn center**.
e. Patients with significant **smoke inhalation** (diagnosed by increased carboxyhemoglobin levels) should receive high-flow O_2 and close monitoring for respiratory compromise requiring intubation.
f. Cardiac and neurologic issues in **electrical** burns should be managed to decrease mortality.
g. Nasogastric tube should be placed when there is gastrointestinal (GI) involvement (ileus will frequently develop).
h. Generous use of analgesics and/or regional anesthesia for **pain control.**
i. **Antimicrobial agents** (e.g., topical silver sulfadiazine or bacitracin) should be used in dressings to decrease risk of infection, and tetanus toxoid should be administered if immunization status is unknown or not up to date.
j. Nonadherent bandaging or biologic dressings should be applied directly to severe burns; dressings should not be wrapped around affected areas because of potential swelling and constriction.
k. Surgical debridement and exploration should be performed to remove necrotic tissue and to determine extent of deeper tissue involvement; plastic reconstructive surgery with skin grafting may be needed.

6. **Complications**

a. **Infection** (especially *Pseudomonas*, sepsis), stress ulcers (Curling type), aspiration, dehydration, ileus, renal insufficiency (caused by rhabdomyolysis), compartment syndrome, epithelial contractions (may limit range of motion).
b. Electrical burns are associated with arrhythmias, seizures, bony injury, compartment syndrome, rhabdomyolysis, acute kidney injury.
c. Risk factors for **mortality** include age >60 years, >40% body surface area involvement, and inhalation injury; patients carry a 0.3%, 3%, 33%, or 90% chance of death if they have zero, one, two, or three of these risk factors, respectively.

B. Drowning

1. Hypoxemia resulting from **submersion** in some type of fluid, usually water.
2. Aspiration of **any type** of water causes **pulmonary damage** (e.g., decreased lung compliance, ventilation–perfusion mismatch, shunting) and **cerebral hypoxia**, but pathophysiology of late-stage drowning varies by fluid type.
   a. **Fresh water:** hypotonic fluid is absorbed from alveoli into vasculature, resulting in decreased electrolyte concentrations and red blood cell (RBC) lysis.
   b. **Salt water:** hypertonic fluid creates an osmotic gradient that draws fluid from pulmonary capillaries into alveoli and causes **pulmonary edema** and increased serum electrolyte concentrations.
3. **H/P** = prolonged submersion in liquid (pools, bathtubs, and buckets are frequent sites); cyanosis, decreased consciousness; patient may not be breathing or may have cardiac arrest.
4. **Treatment** = secure airway and perform resuscitation; **supplemental O_2**, nasogastric tube placement, maintenance of adequate body temperature; any symptoms of hypoxia following aspiration require inpatient admission for neurovascular monitoring and possible diuresis and bronchodilator therapy.
5. **Complications** = correlate with degree and length of hypoxemia and include brain damage and hypothermia.

Quick HIT

Drowning is most common in **children <5 years of age** and in **males** between 15 and 25 years of age.

C. Choking

1. **Aspiration of foreign body** into trachea or bronchi preventing normal gas exchange
2. Food is a common cause in all ages; toys, coins, and other small objects are common in children
3. **H/P** = patient eating or child playing with small objects; gagging, coughing, or wheezing that progresses to stridor with increased severity of obstruction
4. **Radiology** = chest x-ray (CXR) may be useful in identifying item and determining location; bronchoscopy may visualize item
5. **Treatment**
   a. Actively coughing patients should be encouraged to remain calm and to keep coughing to dislodge object.
   b. Patients unable to breathe should be given the **Heimlich maneuver**.
   c. Direct laryngoscopy with the use of “Magill” forceps may be an alternative.
   d. Emergent tracheotomy may be required in a patient with continued obstruction.
   e. Rigid bronchoscopy may be required to remove objects.
   f. Administration of IV corticosteroids before extraction attempt may ease removal by decreasing bronchial inflammation.
6. **Complications** = atelectasis, pneumonia, lung abscess; hypoxemia can cause complications similar to those seen with drowning

Quick HIT

The right mainstem bronchus is the most common location of aspirated items that pass beyond the trachea because of its greater vertical orientation compared with the left main bronchus.

D. Heat Emergencies

1. **Hyperthermia** (can be associated with **physical exertion** or comorbid medical condition) that occurs because of failure of thermoregulation
2. Categorized as heat stroke or heat exhaustion (see Table 4-1)

E. Hypothermia

1. Body temperature <**95°F**/35°C from cold exposure
2. **Risk factors** = alcohol intoxication, elderly
3. **H/P** = lethargy, weakness, severe shivering (rhabdomyolysis), confusion; decreased body temperature, possible arrhythmias, hypotension
4. **Electrocardiogram (ECG)** = **J waves (Osborn waves)**, can present with bradycardia, but more commonly possible ventricular tachycardia (Vtach) or Vfib (see Figure 4-3)
5. **Treatment** = warm patient externally (e.g., warm bed, bath, blankets) or internally (e.g., warm IV fluids, bladder irrigation, peritoneal lavage, or warm gastric fluids); treat arrhythmias and hypotension as appropriate (see Chapter 1,

Cardiovascular Disorders). Some dysrhythmias may not improve or resolve until temperature is corrected

Quick HIT

In the final stage of hypothermia, the patient will stop shivering, be unable to maintain body temperature, and will undergo a fatal increase of blood viscosity.

Table 4-1 Heat Emergencies

Disorder	Heat Exhaustion	Heat Stroke
Symptoms	Weakness, headache, substantial sweating	Confusion, blurred vision, nausea, no or little sweating
Body temperature	Slightly increased	Substantially elevated
Labs	Usually normal	Increased WBC, increased BUN, increased creatinine
Treatment	Hydration (oral unless progressive symptoms), electrolyte replacement	Evaporative cooling (spray naked patient with lukewarm water and then fan); benzodiazepines if seizures are present; antipyretics are **not** effective
Complications	Progression to heat stroke	Rhabdomyolysis, seizures, brain damage, death

BUN, blood urea nitrogen; WBC, white blood cell count.

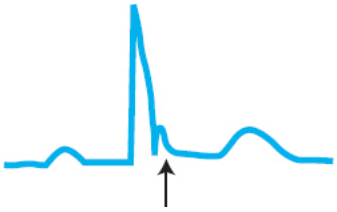


FIGURE 4-3
Diagram of electrocardiogram demonstrating a J wave (*arrow*), a characteristic finding in hypothermia.

Table 4-2 Common Types of Bites and Stings

Type of Bite	Symptoms	Treatment	Complicatio
Snake (rattlesnake, copperhead, water moccasin, coral snake)	Pain and swelling at bite, progressive dyspnea, toxin-induced DIC	Immobilize extremity and cleanse wound; **antivenin** likely required	Effects more se increased mort treatment
Scorpion	Severe pain and swelling at site of sting; increased sweating, vomiting, diarrhea	Antivenin, atropine, phenobarbital	Acute pancreat toxicity, respira
Spider			
Black widow	Muscle pain and spasms, localized diaphoresis, abdominal pain, autonomic stimulation	Local wound care, benzodiazepines, antivenin	Ileus, cardiovas
Brown recluse	Increasing pain at site, possible ulceration and necrosis	Local wound care, dapsone to prevent tissue necrosis	Hemolytic aner olysis
Mammals	Pain and swelling at bite, penetrating trauma, depending on size of bite	Saline irrigation, debridement, tetanus and rabies prophylaxis, antibiotics for infection	Infection (staph *multocida,* rabi
Human	Pain and swelling at bite, tender local lymphadenopathy	Saline irrigation, broad coverage antibiotics, debridement, thorough documentation	High incidence primary closure entation

DIC, disseminated intravascular coagulation.

F. Bites and Stings (See Table 4-2)

1. Injection of venom from bite or sting of snakes (e.g., in the United States: rattlesnake, copperhead, water moccasin, coral snake), spiders (e.g., black widow, brown recluse), or other animals (e.g., scorpion)
2. Venom contains neurotoxins, cardiotoxins, or proteolytic enzymes that can potentially be fatal

II. Toxicology

A. General Principles

1. Initial evaluation must focus on **determining type of poison ingested**; patient history, witness input, and clues found near patient (e.g., empty bottles of medications, other medications, etc.) help in making diagnosis.
2. The sooner treatment is begun after toxic exposure, the better the outcome.
3. Types of poisoning therapy (see Table 4-3):
   a. Induced vomiting is **rarely** performed and **rarely** useful. If given the option ipecac is almost always the *wrong* answer.
   b. **Charcoal**: blocks absorption of poisons; repeat doses every few hours; not useful for alcohols or metals.
   c. Gastric lavage: usually reserved for intubated patients within initial hour after ingestion. This modality has fallen out of practice in the majority of intoxications (increased risk of aspiration).
   d. **Antidotes**: reverse or inhibit poison activity; use depends on identification of agent.
   e. Dialysis or exchange transfusion: used in cases of severe symptoms or when other treatments are unsuccessful.

NEXT
STEP

Beware of alcohol abusers who come into the emergency department **fictitiously** saying that they have ingested ethylene glycol and need ethanol for treatment; check for sweet breath and a toxin screen before giving ethanol.

Table 4-3 Common Poisons and Antidotes (bold show highlights)

Substance	Symptoms	Treatment
Drugs		
Acetaminophen	Nausea, **hepatic insufficiency/failure**	*N*-acetylcysteine
Anticholinergics	Dry mouth, urinary retention, QRS widening on ECG	Physostigmine
Benzodiazepines	Sedation, **respiratory depression**	Flumazenil (reserve only, not chronic ab
β-Blockers	Bradycardia, hypotension, **hypoglycemia**, pulmonary edema	Glucagon, calcium,
Calcium channel blockers	Bradycardia, hypotension, **euglycemic**	Glucagon, calcium,
Cocaine	Tachycardia, agitation, **coronary vasospasm (MI)**	Supportive care
Cyanide	Headache, nausea, vomiting, altered mental status	Nitrates, hydroxoc
Digoxin	Nausea, vomiting, visual changes, arrhythmias	Digoxin antibodies
Heparin	Excessive bleeding, easy bruising	Protamine sulfate
Isoniazid	Neuropathy, hepatotoxicity	Vitamin B_6
Isopropyl alcohol	Decreased consciousness, nausea, abdominal pain	Supportive care
Methanol	Headache, visual changes, dizziness	Ethanol, fomepizol
Opioids	Pinpoint pupils, **respiratory depression**	Naloxone
Salicylates	Nausea, vomiting, tinnitus, hyperventilation, anion gap, **metabolic acidosis**	Charcoal, dialysis,
Sulfonylureas	Hypoglycemia	Octreotide and dex
Tricyclic antidepressants	Dry mouth, urinary retention, **QRS widening** on ECG leading to **Torsades de pointes** (a form of Vtach)	Sodium bicarbonat
Warfarin	Excessive bleeding, easy bruising	Vitamin K, FFP
Industrial Chemicals		
Caustics (acids, alkali)	Severe oropharyngeal and gastric irritation or burns, drooling, odynophagia, abdominal pain, gastric perforation symptoms	Copious irrigation (attempt neutralizat
Ethylene glycol	Ataxia, hallucinations, seizures, sweet breath	Ethanol, dialysis
Organophosphates (insecticides, fertilizers)	**Diarrhea, urination**, miosis, bronchospasm, **bradycardia,** excitation of skeletal muscle, lacrimation, sweating, and **salivation**	Atropine, pralidoxi
Metals		
Iron	Nausea, constipation, hepatotoxicity	Deferoxamine
Lead	Peripheral neuropathy, anemia	Succimer, dimercap
Mercury	Renal insufficiency, tremor, mental status changes	Dimercaprol

ECG, electrocardiogram; EDTA, ethylenediaminetetraacetic acid; FFP, fresh frozen plasma.

4. Supportive care includes airway protection, IV hydration, cardiac support (e.g., treatment for hypertension, hypotension, arrhythmias); control of seizures is an important adjunct to management of the poison itself.

NEXT
STEP

Organophosphates can also be absorbed through the **skin**, so all contaminated clothing must be removed from patients with this type of poisoning.

B. Ingested Poisons

1. Poisoning through oral ingestion of a particular toxin
2. Can occur in children from accidental ingestion of cleaning products, medications, or personal care products
3. Can occur in elderly patients from accidental repeat dosing of usual medications
4. Can be intentional (i.e., suicide attempt)

NEXT
STEP

Any patient with significant **thermal burns**, burns of the **face**, or exposure to large quantities of **smoke** (e.g., house fires) requires a workup for **carbon monoxide poisoning** and **thermal airway injury**.

C. Carbon Monoxide Poisoning

1. Hypoxemia that results from inhalation of carbon monoxide from car fumes, smoke, or paint thinner
2. Carbon monoxide displaces O_2 on hemoglobin (Hgb) and prevents O_2 delivery to tissues
3. **H/P** = sufficient exposure, headache, dizziness, nausea, myalgias; cherry red lips, mental status changes, possible hypotension
4. **Labs** = increased carboxyhemoglobin on blood gas analysis; **normal pulse oximetry**
5. **Treatment** = **100% O_2** (displaces carbon monoxide from Hgb) or **hyperbaric O_2** therapy; patients with smoke inhalation may require intubation secondary to upper airway edema

Quick HIT

Pulse oximetry may appear **normal** in carbon monoxide poisoning.

Quick HIT

Indications for hyperbaric O_2: CO >25%, pregnant with CO >15%, **any** neurologic symptoms, syncope, cardiac ischemia.

III. Cardiovascular Emergencies

This section discusses only emergent cardiovascular conditions that require resuscitation and immediate treatment—refer to Chapters 1 and 11 on Cardiovascular and Neurologic Disorders for additional information regarding MI, arrhythmias, and stroke.

Quick HIT

Cardiac arrest lasting >10 minutes without cardiac output is generally considered consistent with severe brain injury or brain death.

A. Cardiac Arrest

1. Cessation of cardiac function resulting in acutely insufficient cardiac output.
2. Requires immediate treatment to prevent systemic ischemic morbidity and death (see Figure 4-4).
3. Treatment of **Vfib** and **Vtach** requires alternating attempts at electrical and pharmacologic cardioversion (see Figure 4-5).
4. **Pulseless electrical activity** (PEA) consists of detectable cardiac electrical conduction with the absence of cardiac output (see Figure 4-6).
5. **Asystole** is the absence of cardiac activity (see Figure 4-6).

Quick HIT

Do not resuscitate (DNR) status should be documented for any inpatient; documentation can be provided by a close relative or primary care provider to guide potential resuscitation attempts.

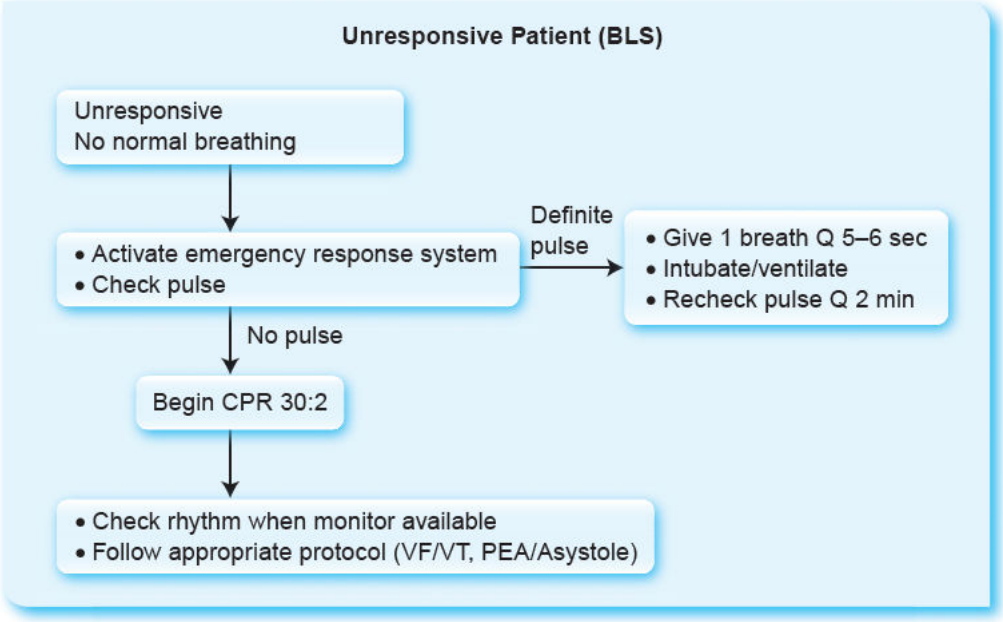


FIGURE 4-4
Initial treatment protocol for the unresponsive patient.
CPR, cardiopulmonary resuscitation; PEA, pulseless electrical activity; VF, ventricular fibrillation; VT, ventricular tachycardia.

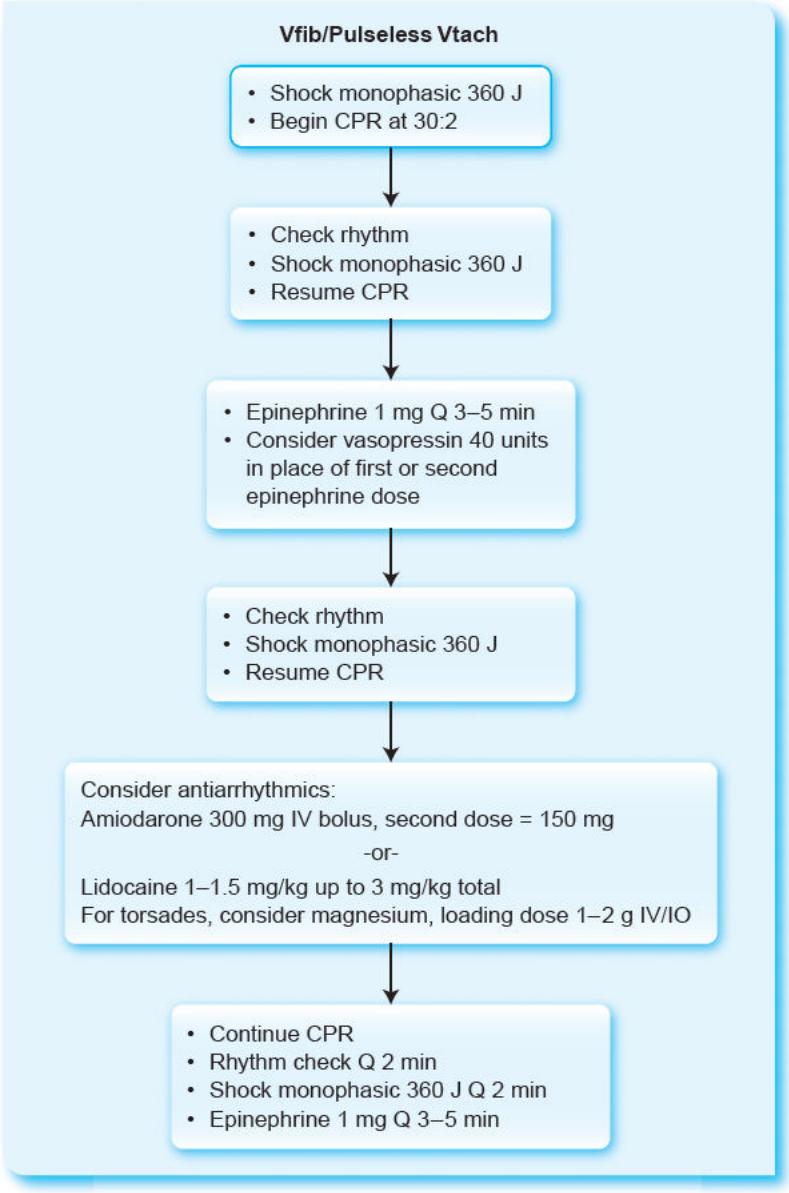


FIGURE **4-5**

Treatment protocol for ventricular fibrillation or pulseless ventricular tachycardia.
CPR, cardiopulmonary resuscitation; IO, intraoral; IV, intravenous.

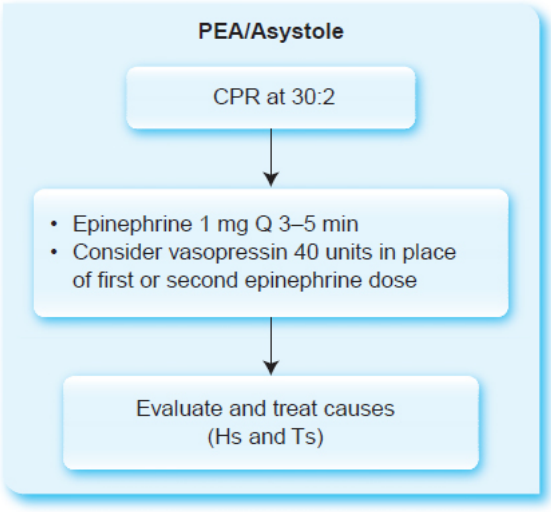


FIGURE **4-6**

Treatment protocol for pulseless electrical activity and asystole.
CPR, cardiopulmonary resuscitation.

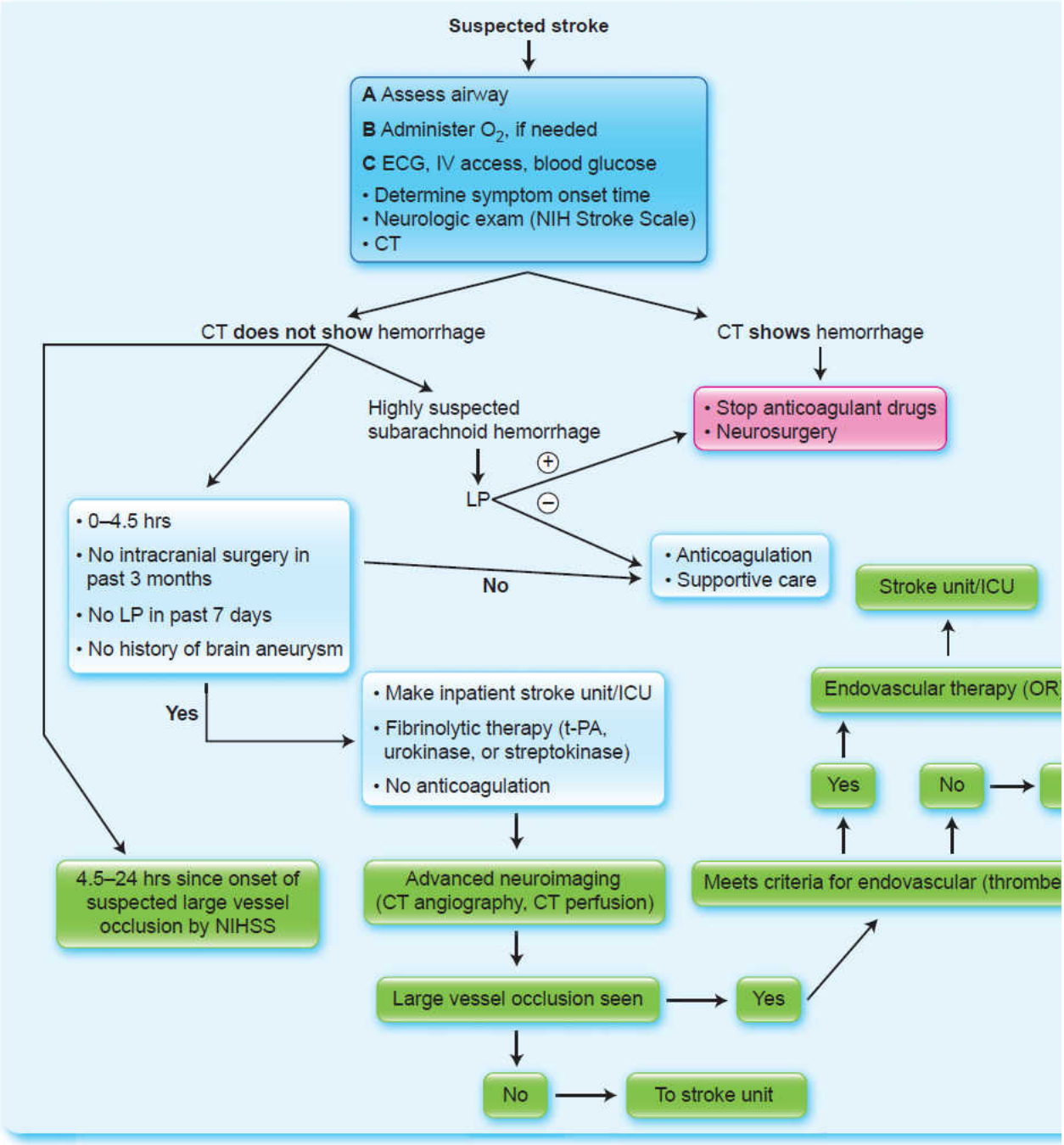


FIGURE **4-7**

Treatment algorithm for suspected acute stroke.

CT, computed tomography; ECG, electrocardiogram; IV, intravenous; LP, lumbar puncture; t-PA, tissue plasminogen activator.

MNEMONIC

Remember the common causes of PEA by the **Hs** and **Ts: H**ypovolemia, **H**ypoxia, **H**yperkalemia, **H**ypokalemia, **H**ypothermia, **H**ydrogen ions (acidosis), **T**amponade, **T**ension pneumothorax, **T**hrombosis (myocardial infarction or pulmonary embolism), **T**ablets/**t**oxins (drugs).

B. Acute Stroke (See Figure 4-7; Chapter 11, Neurologic Disorders)

1. Initial workup differentiates between ischemic and hemorrhagic types.
2. Appropriateness for thrombolysis, mechanical thrombectomy, or reversal of bleeding should be considered.

IV. Traumatology

A. Mechanisms of Injury

1. **Acceleration–deceleration injuries**
   a. Seen in falls, blunt trauma, and **motor vehicle accidents**
   b. Injury secondary to shearing forces in tissues and organs caused by sudden changes in momentum and sudden forces applied to tethered portions of organs (e.g., aortic arch, mesentery)
2. **Penetrating injuries**
   a. Include **gunshot wounds, stab wounds**
   b. Missile damages tissue in path of trajectory and causes indirect damage from fragmented bone and external objects
   c. Shock wave from projectile impact and thermal effects can cause additional tissue damage (particularly high-velocity projectiles)

NEXT
STEP

Count and pair all entrance and exit gunshot wounds to suggest a number of insulting bullets and to deduce a path for each bullet.

B. Trauma Assessment

1. Patient assessment is performed in an organized manner to detect all injuries and judge their severity.
2. Initial assessment focuses on patient **ABCs**.
3. Secure **a**irway is established (may require intubation), oxygenation is stabilized (**b**reathing), adequate **c**irculation is confirmed, venous access is secured, and bleeding is controlled.
4. Secondary assessment consists of a highly detailed examination to detect all wounds, fractures, signs of internal injury, and neurologic insult.
5. The Glasgow Coma Scale (GCS) is used to objectify injury severity (see Table 4-4).

NEXT
STEP

Address the ABCs and secondary survey **in order**. Do not proceed to the next step of the examination until the current segment has been addressed.

Quick **HIT**

The use of **ultrasound** in the assessment of trauma is reserved for the secondary survey and evaluated abdominal compartments and thoracic cavity for free fluid or pneumothorax.

Quick **HIT**

Loss of consciousness is considered to be caused by **head trauma** until ruled out.

Table 4-4 Glasgow Coma Scale[a]

Category	Condition	Points
Eye opening	Spontaneous	4
	To voice	3
	To pain	2
	None	1
Verbal response	Oriented	5
	Confused	4
	Inappropriate words	3
	Incomprehensible	2
	None	1
Motor response	Obeys commands	6
	Localizes pain	5
	Withdraws from pain	4
	Flexion with pain	3
	Extension with pain	2
	None	1

[a]Total score is calculated by adding component score for each category.
12+: minor brain injury with probable recovery.
9–11: moderate severity requiring close observation for changes.
8 or less: coma; ≤8 after 6 hrs associated with 50% mortality.

C. Head Trauma

1. Head trauma can result in cerebral or subarachnoid hemorrhage (see Chapter 11, **Neurologic Disorders**)
2. Cerebral damage can be at the point of insult (i.e., **coup**) or on the opposite side of the head (i.e., **contrecoup**)
3. **H/P** = evaluation should assess **level of consciousness**, sensation, motor activity, bowel and bladder continence, **pupil responsiveness to light** (nonresponsiveness or unequal response suggests cerebral injury), presence of skull fracture (e.g., discoloration over mastoid, blood draining from ears or nose), and intracranial pressure
4. **Radiology** = **head** computed tomography (CT) should be performed for any unconscious patient to detect intracranial hemorrhage; cervical CT or x-rays (anteroposterior, lateral, open-mouth odontoid) should be performed to detect skull or cervical fractures
5. **Treatment** = maintain cerebral perfusion; decrease high intracranial pressure by elevating head of bed, IV mannitol, or hyperventilation; refer any intracranial injury to neurosurgery for possible decompression

Quick **HIT**

Hypertension with bradycardia is suggestive of increased intracranial pressure (Cushing phenomenon).

NEXT
STEP

Rule out **cervical fracture** and **spinal cord injury** before performing any examination requiring head movement.

D. Spinal Cord Trauma (See Chapter 11, Neurologic Disorders)

1. Neurologic injury in any segment of the spinal cord from trauma resulting from direct injury, compression, or inflammation
2. **H/P** = thorough **neurologic examination must** be performed to detect any deficits in sensation, motor activity, or autonomic function
3. **Radiology** = imaging should examine all cervical vertebrae and other vertebral sections of spine considered at risk for injury; **CT** is replacing x-ray as the standard tool for assessing bony injury of the spine; magnetic resonance imaging (MRI) should be performed in any patient with a normal CT scan and abnormal neurologic examination or central spine pain to rule out ligamentous injury or cord edema
4. **Treatment** = spine must be stabilized until injury ruled out; give IV corticosteroids for 24 hours if presenting within initial 8 hours following injury (unless pregnant, isolated cauda equina injury, or child); injuries should be referred to orthopedic surgery or neurosurgery for definitive treatment

Quick HIT

The spine is considered **unstable** in any **unconscious** patient and should not be moved until neurologic injury has been ruled out with examination and radiology.

E. Neck Trauma

1. Neck is divided into **zones** based on anatomic site of injury; injury can involve trachea, esophagus, vascular structures, cervical spine, or spinal cord. Penetrating injuries violating the platysma should be further evaluated by contrast imaging or in the operating room (see Figure 4-8)
2. **H/P** = examination should focus on cervical neurologic deficits and signs of vascular damage in neck (e.g., hematoma, worsening mental status)

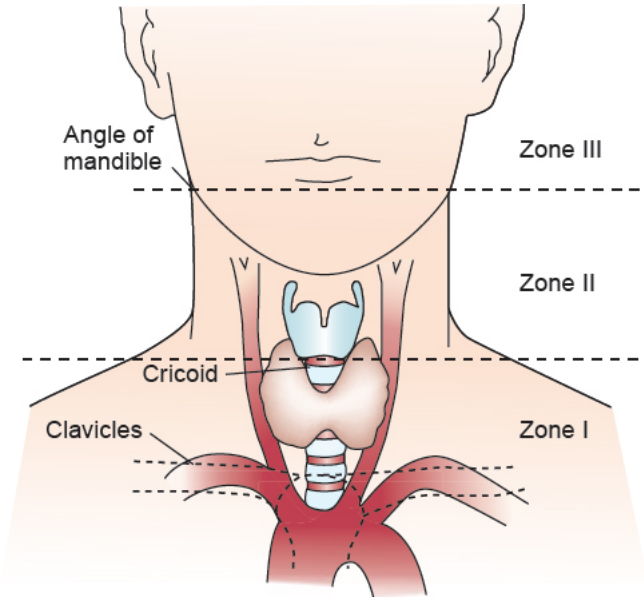


FIGURE 4-8
Zones of the neck used to determine treatment for traumatic injury.

3. **Radiology** = potential studies include cervical x-ray, CT of cervical spine, carotid Doppler ultrasound (US), esophagogastroduodenoscopy (EGD), angiography, or bronchoscopy (particularly zones I and III)
4. **Treatment**
   a. Penetrating trauma with stable vital signs may be treated **conservatively**.
   b. Exploration of zones I and III is difficult and should be carried out only if vascular injury is suspected.
   c. Intubation is frequently required because of airway occlusion.
   d. Prophylactic antibiotics may be indicated because of increased risk of contamination by oropharyngeal flora.

F. Chest Trauma

1. Can result in injury to lungs, heart, or GI system
2. Aortic rupture (caused by sudden acceleration and deceleration), tension pneumothorax, hemothorax, and cardiac tamponade are potentially fatal injuries
3. **H/P** = examination should look for signs of pneumothorax (e.g., hyperresonance, decreased breath sounds), flail chest (e.g., multiple rib fractures), **tamponade** (e.g., decreased breath sounds, jugular venous distention, and pulsus paradoxus), and aortic rupture (e.g., unstable vital signs); ECG and central venous pressure are useful in assessing cardiac function

4. **Radiology**
   a. CXR and neck x-rays may show pneumothorax, hemothorax, cardiac hemorrhage, aortic injury, or rib fractures.
   b. **Chest CT** is important to assess for air leaks, hematoma formation, and pulmonary collapse.
   c. EGD and bronchoscopy are used to assess injury to esophagus and bronchi.
   d. Angiography can detect vascular injury.
5. **Treatment** = urgent **thoracotomy** for certain types of thoracic cavity **hemorrhages; pericardiocentesis** for suspected cardiac **tamponade**; chest tube for pneumothorax or hemothorax; ventilatory support may be required for multiple rib fractures (flail chest)

G. Abdominal Trauma

1. Can cause injury to any abdominal organ or severe bleeding from the aorta, aortic branches, mesentery, spleen, or liver.
2. Penetrating trauma requires exploratory laparotomy; blunt trauma may be treated conservatively in the absence of signs of an acute abdomen.
3. **H/P**
   a. In cases where exploratory laparotomy is not automatically performed, examination must look for signs of **abdominal bleeding** (e.g., decreased blood pressure, cyanosis, anxiety, flank discoloration, severe abdominal tenderness, abdominal rigidity, shock).
   b. **Peritoneal lavage** (i.e., saline infused by catheter into abdominal cavity and then removed and examined) is useful for detecting presence of blood or fecal matter in uncertain cases.

Quick HIT

Sites of significant (>**1,500 mL**) blood loss frequently not found by physical examination include blood left at the **injury scene**, **pleural cavity** bleeding (seen with CXR), **intra-abdominal** bleeding (seen with CT or ultrasound [US]), **pelvic** bleeding (seen with CT), and bleeding into the **thighs** (seen on x-ray).

4. **Radiology**
   a. CT is sensitive for detecting abdominal fluid.
   b. Extended focused assessment with sonography in trauma (**e-FAST**) is a quick and sensitive means of determining the presence of free abdominal fluid, solid organ injury, and pneumothorax and has become the primary test performed for evaluation of blunt abdominal trauma at most trauma centers.
   c. Abdominal x-ray may detect free air or large collections of blood but is of less utility than CT or FAST.

NEXT
STEP

The **hemodynamically unstable** patient with blunt trauma should be taken to the **operating room** and not to radiology, if FAST sonogram is not available in the emergency department.

5. **Treatment**
   a. All **penetrating abdominal trauma** needs **exploratory laparotomy**.
   b. Diagnosed **intra-abdominal bleeding** or visceral damage from blunt trauma requires **laparotomy** for repair if the patient is hemodynamically unstable.
   c. **Retroperitoneal hematomas** in the **upper** abdomen (pancreas, kidneys) require laparotomy for repair.
   d. **Low retroperitoneal bleeding** should be treated with **angiography** and **embolization** if caused by blunt trauma and **laparotomy** if from penetrating trauma.

H. Genitourinary and Pelvic Trauma

1. Injury can result from initial insult or indirectly from fracture of the pelvis.
2. **H/P**
   a. Examination should look for blood at the **urethral meatus** or hematuria (indicative of urologic injury), or scrotal or penile hematoma.
   b. Pelvic examination should be performed in women.
   c. Patients with a **pelvis fracture** should be given a thorough **neurovascular examination**.

Quick HIT

A Foley catheter should **never** be placed in a patient with a **suspected urethral rupture** (e.g., blood seen at the urethral meatus) to avoid further urologic injury unless performed under cystoscopic guidance.

3. **Radiology**
   a. Intravenous pyelogram (IVP) can detect renal pelvis injury.
   b. **Retrograde urethrogram** or cystogram can detect urethral or bladder injury.
   c. X-ray can detect pelvis fracture.

d. **CT** can detect renal damage and pelvic blood collections.

4. **Treatment**
   a. **Penetrating** injuries need **surgical exploration**.
   b. Urethral, intraperitoneal bladder, and renal pelvis injuries require cystoscopy and surgical repair; **extraperitoneal bladder** and **renal parenchymal** injuries may be treated **nonoperatively**.
   c. Pelvic fractures may be treated nonoperatively if stable and with open reduction and internal fixation when unstable.

NEXT
STEP

Perform a **fasciotomy** in any patient with a combined bone and neurovascular extremity injury because of the high risk of **compartment syndrome**.

I. Extremity Trauma

1. Injury can involve **bones**, **vasculature**, **soft tissues**, or **nerves** in extremities.
2. **H/P** = a thorough **neurovascular examination** must be performed; gross deformities are indicative of fracture.
3. **Radiology** = x-ray or CT detects fractures; angiography can detect vascular injury; MRI may be required to detect soft tissue injuries.
4. **Treatment**
   a. Superficial or soft tissue wounds require irrigation and approximation (e.g., sutures, Steri-Strips, dermatologic adhesive).
   b. Bone injury alone is treated with immobilization, if stable and internal, or external fixation, if unstable.
   c. Combined bone, vessel, and nerve injuries are treated by fracture repair **followed** by vascular and neurologic repair.
   d. Large wounds frequently require debridement or amputation.

NEXT
STEP

Serial neurovascular examinations should be performed following any type of treatment for an extremity to detect an evolving or iatrogenic neurologic injury.

J. Trauma During Pregnancy

1. Leading cause of **nonobstetric** maternal death
2. Anatomic differences
   a. Inferior vena cava (IVC) compression by the uterus makes pregnant women more susceptible to **poor cardiac output** following injury
   b. Decreased risk of GI injury from lower abdominal trauma because of **superior displacement of bowel** by the uterus (but greater risk of GI injury from upper abdominal or chest trauma)
3. Low risk of fetal death with minor injuries (high risk in life-threatening injuries)
4. Trauma increases the risk of **placental abruption**
5. **H/P** = immediate assessment of cardiovascular stability, mother should be evaluated for injury **before** the fetus, examination should be performed with mother in **left lateral decubitus position** to minimize IVC compression, obstetric assessment performed following maternal stabilization

Quick **HIT**

Criteria that should be met in posttraumatic pregnant women before discharge are **contractions no more frequent than every 10 minutes, no vaginal bleeding, no abdominal pain**, and a **normal fetal heart tracing**.

6. **Treatment** = needs of **mother** are **prioritized**; caesarian section should be performed for fetuses >24 weeks of gestation that are in **distress** or in any mother with **cardiovascular compromise** not responsive to early cardiopulmonary resuscitation (CPR); mother should be monitored for 4 to 48 hours (based on severity of trauma) to detect fetal distress; **RhoGAM** should be given to any Rh^- mother with bleeding

V. Abuse and Sexual Assault

A. Abuse

1. Most frequently seen in children, spouses or partners (especially women), and the elderly
2. Abuse can be physical, emotional, sexual, or exploitative; neglect
3. **Child** abuse
   a. Neglect, the most prevalent form of child abuse, constitutes the **failure to provide** the physical, emotional, educational, and medical needs of a child

b. **H/P** = several red flags should raise suspicion in **history** (e.g., inconsistent with injury, vague details, changes in story, blame placed on others, implausibility), **parental actions** (e.g., aggressive nature, delay in seeking treatment, lack of emotional attachment or concern), and **physical examination** (e.g., injuries inconsistent with history, multiple injuries at various stages of healing, pathognomonic injuries, signs of neglect, abnormal behavioral responses to being examined)
c. **Treatment** = physician has **obligation** to report any suspected cases of abuse to child protective services
d. Suspected cases should be **well documented**

4. **Spousal or partner abuse**
   a. **H/P** = similar red flags as for child abuse; presentation to physician frequently for a vague symptom (e.g., chronic abdominal pain, headaches, depression, recurrent sexually transmitted diseases); **history** may be **inconsistent** with **injury**; partner may be very attentive or vigilant during visit
   b. Patient should be interviewed **without** partner present
   c. **Treatment** = initial approach should focus on safety of patient; provide victim with information on safety plans, escape strategies, legal rights, and shelters; care should be taken not to force victim into any action; reporting of abuse is typically nonmandatory (unless it involves child abuse)
5. **Elder abuse**
   a. Abuse in a patient >60 years of age occurring at the hands of a caregiver (e.g., family, friends, institution)
   b. **H/P** = red flags as seen with child and domestic abuse; multiple bruises or fractures, malnutrition, depression, or **signs of neglect**
   c. **Treatment** = placement in a safe facility; facilitate contact with social services that can help facilitate safe care; physician has **obligation** to report suspected cases to an official state agency

Quick **HIT**

Injuries suggestive of child abuse include multiple simultaneous facial injuries, bruises in patterns of objects, bruises over trunk and abdomen, multiple burns (especially in shape of object), rib or skull fractures, long bone fractures in nonambulatory children.

Quick **HIT**

A physician who has reason to suspect child abuse but does not report it or act to protect the child **may be held liable** for subsequent injury or mortality.

Quick **HIT**

Most women in an abusive relationship who are killed by their abuser are killed **when trying to leave their abuser**.

B. Sexual Assault

1. **Nonconsensual** sexual activity with physical contact; forced intercourse is **rape**.
2. Victims can be children or adults.
3. **H/P**
   a. **Detailed history** must be collected and thoroughly documented in cases where patient reports assault.
   b. Examination should focus on the entire body, with particular attention to genitals, anus, and mouth to look for signs of assault.
   c. Patients who have not admitted to being assaulted may appear depressed or very uncomfortable with examination.
4. **Labs**
   a. Collect oral, vaginal, and penile cultures to test for sexually transmitted diseases.
   b. In cases of rape, all injuries must be well documented and vaginal fluid and pubic hair should be collected for evidence (i.e., rape kit).
   c. Pregnancy testing should be performed to look for incidental conception occurring during assault.
5. **Treatment** = careful and well-documented collection of all details and evidence important to future follow-up and legal action; referral to **social support systems** and **counseling** is very important; appropriate treatment should be given for infections.

Quick **HIT**

Another health care worker (chaperone) must be present when a sexual examination is performed, and the patient should be made to feel as comfortable as possible with the history and physical examination.

BASIC CRITICAL CARE

I. Issues in the Intensive Care Unit

A. Role of the Intensive Care Unit (ICU)

1. Provides intensive nursing care for **critically ill patients**
2. Patients may require intubation, ventilation, **invasive monitoring, vasoactive** and antiarrhythmic medications, and close nursing supervision

B. Pulmonary Concerns

1. **Intubation** and **ventilation** required when a patient is at risk for airway obstruction or needs support in breathing.
2. Ventilator support is required in patients to maintain respiratory effort or in poor-oxygenation states (see Chapter 6, **Pulmonary Disorders**).

Quick HIT

The **left subclavian** and **right internal jugular** veins provide the easiest access for Swan–Ganz catheter insertion.

C. Invasive Monitoring

1. **Arterial line** (A-line)
   a. Placed in either radial, femoral, axillary, brachial, or dorsalis pedis artery
   b. Used to record more accurate blood pressure than blood pressure cuff
2. **Pulmonary artery catheter** (Swan–Ganz catheter)
   a. Catheter inserted through subclavian or jugular vein; runs through heart to pulmonary artery
   b. Measures pressures in **right atrium** and **pulmonary** artery; balloon can be inflated at catheter tip to fill pulmonary artery lumen and measure wedge pressure (equivalent to **left atrium pressure**)
   c. Also, may measure **cardiac output**, mixed venous O_2 saturation, systemic vascular resistance

II. Hemodynamic Stability

Quick HIT

AB^+ patients are **"universal recipients";** they can **receive any** donor blood type because they have no antibodies to blood antigens in their plasma, but they can **donate only** to other **AB^+** patients.

A. Transfusions

1. Infusion of blood products to treat insufficient supply of a given blood component (see Table 4-5)
2. ABO blood groups
   a. Blood is defined by **A** and **B** antigens and antibodies to absent antigens.
   b. Blood with **both** antigens **will not have antibodies** to either antigen in plasma (i.e., AB blood type).
   c. Blood with **neither** antigen will have **antibodies to both** antigens in plasma (i.e., O blood type).
   d. Transfusions must be matched for each patient's particular ABO blood type.

Quick HIT

O^- patients are **"universal donors."** RBCs from these patients will not induce antibody reactions in other patients, but they can **receive only** blood from other O^- donors.

3. **Rh blood groups**
   a. Patients are either Rh antigen positive (Rh^+) or negative (Rh^-).
   b. **Rh^-** patients have **antibodies to Rh factor** in plasma.
   c. Transfusions must be matched for each patient's Rh factor.

Quick HIT

Clerical errors are the most common cause of transfusion reactions.

4. **Transfusion reactions**
   a. Reaction that occurs when incompatible blood is infused into a patient
   b. Types

(1) **Nonhemolytic febrile:** most common reaction (3% of transfusions); caused by cytokines generated by cells in the blood component to be transfused while in storage; onset 1 to 6 hours after transfusion; fevers, chills, rigors, malaise; treated with acetaminophen; recurrence is uncommon
(2) **Acute hemolytic:** one in 250,000 transfusions; caused by **ABO incompatibility**; onset during transfusion; fever, chills, nausea, flushing, tachycardia, tachypnea, hypotension; severe destruction of donor RBCs; requires aggressive supportive care
(3) **Delayed hemolytic:** caused by antibodies to Kidd or D (Rh) antigens; onset 2 to 10 days after transfusion; slight fever, falling H/H, mild increase in **unconjugated bilirubin**; no acute therapy needed but determine responsible antibody type to help prevent future reactions
(4) **Anaphylactic:** one in 50,000 transfusions; rapid onset of shock and hypotension; some cases may be caused by anti-IgA IgG antibodies (in patient with IgA deficiency) that bind IgA on the surface of donor RBCs and trigger mast cell degranulation; requires epinephrine, volume maintenance, and airway maintenance
(5) **Minor allergic reactions:** three percent of transfusions; caused by plasma present in donor blood; urticaria; treated with diphenhydramine
(6) **Posttransfusion purpura:** thrombocytopenia developing 5 to 10 days after transfusion; occurs primarily in women sensitized by pregnancy; treated with IVIg or plasmapheresis

c. **H/P** = occurs in patient receiving transfusion; pain in vein receiving transfusion, chills; flushing, pruritus; fever, jaundice
d. **Labs** = both patient's and donor's blood should be rechecked and retyped
e. **Treatment** = **acetaminophen, diphenhydramine**, stop transfusion; mannitol or bicarbonate may be required in severe reactions to prevent hemolytic debris from clogging vessels; vasopressors may be required if significant hypotension develops

Table 4-5 Types of Blood Products Used in Transfusions

Blood Product	Definition	Indications
Whole blood	Donor blood not separated into components (full-volume blood)	Rarely used except for massive transfusions for severe blood loss
Packed RBCs	RBCs separated from other donor blood components (2/3 volume of transfusion unit is RBCs)	Product of choice for treatment of low Hct due to blood loss or anemia
Autologous blood	Blood donated by patient before elective surgery or other treatment Blood is frozen until needed by patient	Elective surgery or chemotherapy
FFP	Plasma from which cellular components have been separated	Warfarin overdose, clotting factor deficiency, DIC, TTP
Cryoprecipitate	Clotting factor and vWF-rich precipitate collected during thawing of FFP Same indications as FFP	Smaller volume than FFP Preferable to FFP in cases where large transfusion volume is unwanted
Platelets	Platelets separated from other plasma components	Thrombocytopenia not due to rapid platelet destruction
Clotting factors	Concentrations of a specific clotting factor pooled from multiple donors	Specific clotting factor deficiencies (e.g., hemophiliac)

DIC, disseminated intravascular coagulation; FFP, fresh frozen plasma; Hct, hematocrit; RBCs, red blood cells; TTP, thrombotic thrombocytopenic purpura; vWF, von Willebrand factor.

B. Vasoactive Medications

1. Drugs used to **maintain hemodynamic stability** by increasing blood pressure (i.e., vasopressors) and cardiac output (i.e., inotropes) or decreasing blood pressure and cardiac output (i.e., vasodilators and negative inotropic agents)
2. Vasopressors frequently used in cases of shock and insufficient cardiac output (see Table 4-6)
3. Vasodilators reduce vascular tone; negative inotropic drugs decrease cardiac contractility (see Chapter 1, **Cardiovascular Disorders**)

Table 4-6 Vasopressors and Inotropes Commonly Used in the Intensive Care Unit

Drug	Mechanism	Effects	Indication
Phenylephrine	Agonist for α-adrenergic receptors ($\alpha_1 > \alpha_2$)	Vasoconstriction, reflex bradycardia	Sepsis, shock
Norepinephrine	Agonist for α_1- and β_1-adrenergic receptors	Vasoconstriction, mildly increased contractility	Shock
Epinephrine	Agonist for primarily β_1 and, to a lesser extent, α_1- and β_2-adrenergic receptors; α-effects (vasoconstriction) predominate at high doses	Increased contractility (increased CO), vasodilation at low doses; increased contractility and vasoconstriction at higher doses	**Anaphylacti** postbypass hy
Dopamine	Agonist for β_1-adrenergic receptors (low dose) and α-adrenergic receptors (high dose)	Increased heart rate and contractility (increased CO), vasoconstriction (high dose only)	**Shock**
Dobutamine	Agonist for β_1-adrenergic receptors	Increased heart rate and contractility (increased CO), mild reflex vasodilation	**CHF**, cardioge
Isoproterenol	Agonist for β_1- and β_2-adrenergic receptors	Increased heart rate and contractility (increased CO), vasodilation	Contractility s arrest
Vasopressin	ADH analog with weak pressor effect	Vasoconstriction	Resistant sept vasopressor

ADH, antidiuretic hormone; CHF, congestive heart failure; CO, cardiac output.

BASIC SURGICAL CONCERNS

Most surgical issues are discussed in the chapters concerning the appropriate systems. The following sections reflect concerns not addressed elsewhere.

I. Pre- and Postoperative Issues

A. Preoperative Risk Assessment

1. In elective surgery, a patient must be assessed before operation to determine if he or she will tolerate a procedure and what the likelihood is of an adverse cardiopulmonary event.

Quick HIT

The greatest risk for postoperative MI is **within the initial 48 hours** after surgery.

2. **Cardiac risk**
   a. Cardiac function (i.e., ejection fraction, rate, rhythm), exercise capacity, cardiac disease (e.g., congestive heart failure, CAD, recent MI), and age assessed before surgery.
   b. Young, healthy patients may be cleared with a normal ECG by a primary care physician.
   c. Other patients should be cleared by a cardiologist and/or following appropriate cardiac functional testing.
   d. Findings consistent with high surgical risk for a cardiac event
      (1) **Age:** >70 years
      (2) **Pulmonary:** forced expiratory volume in 1 second (FEV_1)/forced vital capacity (FVC) <70% expected, Pco_2 >45 mm Hg, pulmonary edema
      (3) **Cardiac:** MI within past 30 days, poorly controlled nonsinus arrhythmia, pathologic Q waves on preoperative ECG, severe valvular disease, decompensated congestive heart failure with poor ejection fraction
      (4) **Renal:** creatinine (Cr) >2 or 50% increase from baseline
      (5) **Surgery type:** vascular, anticipated high blood loss
   e. Patients determined to be at **high risk** for cardiac complications should **not be operated on** until cardiac function is stabilized unless surgical need is emergent.
   f. Minimally invasive techniques may be appropriate in high-risk patients.
   g. Postoperative noninvasive cardiac monitoring is frequently recommended for patients determined to have increased cardiac risk.

3. **Pulmonary concerns**
   a. **Smoking** increases risk of infection and postoperative ventilation.
   b. Smoking should be stopped before surgery; nicotine replacement may help patients stop smoking 8 weeks before surgery.
   c. Patients with chronic obstructive pulmonary disease (COPD) should be given preoperative antibiotics if showing signs of infection.
   d. A preoperative **CXR** is an important screening tool in any patient age >50 years, a history of pulmonary disease, or anticipated surgical time >3 hours.
   e. Patients with respiratory concerns (e.g., smokers, COPD, myasthenia gravis) should have pulmonary function tests performed to assess their respiratory capacity and to anticipate the need for lengthy ventilation and tracheostomy placement.
   f. **Incentive spirometry**, deep breathing exercises, pain control, and **physical therapy** are all very important postoperatively to help prevent **atelectasis, pneumonia**, and **pulmonary embolism**.
   g. Bronchodilators and inhaled steroids may be beneficial in postoperative patients with pre-existing disease.
4. **Renal concerns**
   a. Patients with renal insufficiency may have electrolyte abnormalities, anemia, or poor immune function.
   b. **Dialysis** may be required before surgery in some patients with renal insufficiency.
   c. ***N*-acetylcysteine** may be used as a renal protectant in patients with renal insufficiency who are expected to receive intraoperative contrast.
5. **Hepatic concerns**
   a. Mortality increases with increased bilirubin, decreased albumin, prolonged prothrombin time (PT), and encephalopathy.
   b. Electrolyte disorders, coagulopathy, and encephalopathy should be corrected before operation.
   c. Surgery should be avoided (unless emergent) in patients with significant hepatitis, cirrhosis, or extrahepatic manifestations of liver disease.
6. **Diabetes mellitus (DM)**
   a. **Diabetic** patients have increased infection risk, worse wound healing, increased cardiac complication risk, and increased postoperative mortality.
   b. Blood sugar levels should be well controlled via subcutaneous insulin sliding scale and frequent glucose checks; glycemic fluctuations can increase postoperatively and may require greater insulin administration than at baseline.
7. **Coagulation concerns**
   a. A history of **abnormal bleeding** or **easy bruising** should raise concerns for a coagulopathy (increased risk of bleeding complications intraoperatively and postoperatively).
   b. Patients taking **warfarin** before surgery should **stop** their warfarin use **3 to 4 days** before surgery; international normalized ratio (INR) should be kept <1.5 for any surgery with significant bleeding risk.
   c. Fresh frozen plasma (FFP) and vitamin K may be used for rapid reversal of warfarin therapy.
   d. Patients with **recent thromboembolism** should be anticoagulated with **heparin** or **low–molecular-weight heparin** (LMWH) after stopping warfarin use until surgery and then restarted on warfarin postoperatively; heparin or LMWH should be restarted 12-hour postoperatively and continued until a therapeutic INR (>2.0) is reached.
   e. Patients not on prior warfarin therapy may be anticoagulated with **aspirin, antiplatelet drugs**, or **LMWH** per surgeon's preference.
   f. In general, warfarin, heparin, and LMWH are associated with a **lower risk** of postoperative **thromboembolism** than aspirin or antiplatelet medications but carry a **greater risk** of **postoperative bleeding complications**.

Quick **HIT**

LMWH should not be restarted for at least 2 hours after removal of an epidural catheter to avoid formation of an epidural hematoma.

Table 4-7 Causes of Postoperative Fever

Cause	When Seen	Diagnosis	Treatment
Pneumonia	**After** third postoperative day	**Productive** cough, positive sputum Gram stain or culture, infiltrates or consolidation on CXR	Antibiotics, b
Urinary tract infection	**3–5** days postoperatively	Urine Gram stain or culture, urine nitrates, presence of **Foley catheter**	Antibiotics re
Wound/IV catheter infection	**5–8** days postoperatively	Red, warm surgical wound; drainage from wound (possibly purulent)	Antibiotics, ir age, surgical
Deep vein thrombosis	Any time postoperatively	Lower extremity warmth and tenderness; US demonstrates noncompressible vein	Anticoagulati
Pulmonary embolism	Any time postoperatively	Dyspnea, tachycardia, pleuritic chest pain, **increased A-a gradient, V/Q mismatch**	Anticoagulati
Medications	Any time postoperatively	Onset linked to new medication; antibiotics are frequent cause	Stop offendir
Transfusion reaction	Any time postoperatively	Begins after initiation of transfusion; confirmed by donor/recipient blood compatibility workup	Acetaminoph hydramine, st symptoms pe

A-a, alveolar-arterial; CXR, chest x-ray; IVC, inferior vena cava; US, ultrasound; V/Q, ventilation–perfusion.

B. Postoperative Fever

1. Fever develops postoperatively from pulmonary, infectious, vascular, or pharmacologic causes (see Table 4-7; Figure 4-9).
2. Any postoperative fever should be evaluated with a **CXR**, complete blood count (CBC), and urinalysis; **urine** and **blood cultures** should also be performed for any fever beyond the first postoperative day.

Quick HIT

Postoperative fevers are caused by the 5 Ws:

- **Wind** (pneumonia)
- **Water** (urinary tract infection)
- **Wound** (wound infection)
- **Walking** (deep vein thrombosis, pulmonary embolism)
- **Wonder drugs** (medications)

C. Wounds and Healing

1. **Types of wounds**
   a. **Clean:** surgical incisions through disinfected skin; no GI or respiratory entry; 1% to 3% infection risk
   b. **Clean-contaminated:** similar to clean wounds but with GI or respiratory entry; 2% to 8% infection risk
   c. **Contaminated:** gross contact of wound with GI or genitourinary contents; traumatic wounds; 6% to 15% infection risk
   d. **Dirty:** established infection in tissue before incision; continued infection following procedure, including debridement; ranges from 7% to 40% infection risk

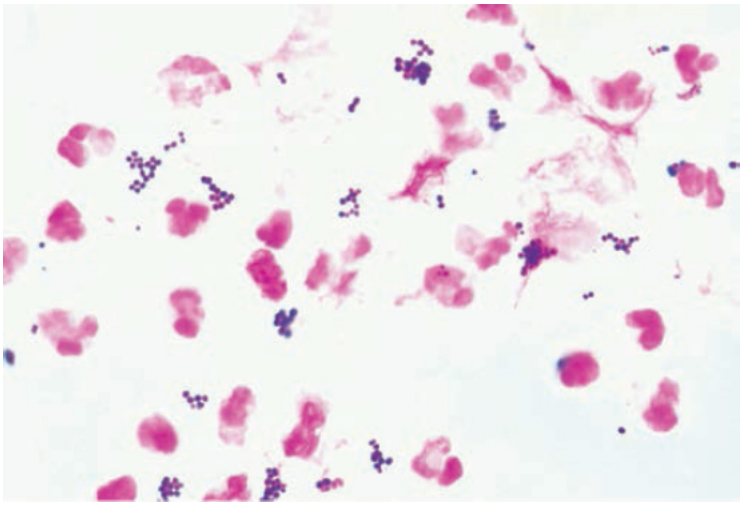


FIGURE 4-9
Gram stain for a patient with staphylococcal bacteremia. Note organization of bacteria in grapelike clusters.
(From McClatchey, K. D. [2002]. *Clinical Laboratory Medicine* [2nd ed., Figure 51-1]. Philadelphia, PA: Lippincott Williams & Wilkins; with permission.)

2. **Wound approximation and healing**
   a. **Primary intention:** low risk of infection (clean and clean-contaminated wounds or contaminated wounds with good clean-up in healthy patient); full closure of tissue and skin performed
   b. **Secondary intention:** higher risk for infection; wound left open and allowed to heal through epithelialization
   c. **Delayed primary closure:** heavily contaminated wounds; left open for a few days and cleaned before wound closure
   d. **Skin grafts:** portion of epidermis and dermis from other body site transferred to wounds that are too large to close by themselves; large deeper grafts with revascularization are called flaps
3. Closed wounds require dressings for **initial 48 hours** after closure
4. Open wounds require debridement and specialized dressings
5. Wound healing can be inhibited by malnutrition, corticosteroids, smoking, hepatic or renal failure, or DM

Quick HIT

Atelectasis is no longer considered to be a cause of postoperative fever.

II. Surgical Emergencies

A. Acute Abdomen

1. **Severe abdominal pain** and rigidity lasting up to several hours that require **prompt** treatment (see Table 4-8)

Table 4-8 Causes of Acute Abdomen

Condition	History and Physical	Diagnosis	Treatment
Obstruction/strangulation (from adhesions, hernias, tumors)	**Previous surgery**, abdominal distention, crampy pain, nausea, vomiting, high-pitched bowel sounds	CT or AXR shows distended loops of bowel and air–fluid levels; barium studies may locate site of obstruction	**Surgical lysis of** hernia repair, surgi of tumors
Diverticulitis	**Left lower quadrant** pain (may progress over several days), blood in stool	CT or AXR may show free air from perforation; increased WBC	Surgical repair
Massive GI hemorrhage (perforation)	Sudden severe pain, **hematemesis**, **hematochezia**, hypotension	Colonoscopy or EGD visualizes lesion; technetium scan may detect smaller bleeding sources	Octreotide, **angiog embolization**, sur of detectable site o
Appendicitis	**Right lower quadrant** and **periumbilical** pain, psoas sign, rectal examination tenderness	Increased WBC; thickened appendix or fecalith on CT if unruptured; free air on CT or AXR if perforated	**Appendectomy**
Mesenteric ischemia	Severe abdominal pain **out of proportion to examination**, bloody diarrhea	Bowel wall thickening and air within bowel wall on CT; increased WBC and serum lactate	NPO, antibiotics, re necrotic bowel
Pancreatitis	**Upper abdominal** and **back** pain, nausea, vomiting, history of gallstones or alcoholism	CT shows inflamed pancreas; increased amylase and lipase	Nasogastric tube, N analgesics
Ruptured ectopic pregnancy	**Amenorrhea**, lower abdominal pain, possible vaginal bleeding, or palpable pelvic mass	US **unable** to locate intrauterine pregnancy in presence of **positive urine pregnancy test**	Surgical excision
Pelvic inflammatory disease	Lower abdominal pain, vaginal discharge, cervical motion pain	Increased WBC; positive serology for *Chlamydia* or *Neisseria gonorrhoeae*	Antibiotics, treat se partners

AXR, abdominal x-ray; CT, computed tomography; EGD, esophagogastroduodenoscopy; GI, gastrointestinal; NPO, nothing by mouth; US, ultrasound; WBC, white

2. **H/P** = **abdominal pain** (severe or crampy, rapidly or gradually progressive), nausea, vomiting, possible history of recent surgery; fever, abdominal tenderness (with possible **rebound tenderness**, rigidity, **guarding**, spasm, or mass), possible hypotension; pelvic or testicular examination should be performed to rule out gynecologic or testicular condition
3. **Labs** = increased white blood cell count (WBC) in cases of infection or bowel perforation; increased amylase in pancreatitis; increased liver function tests with hepatobiliary dysfunction
4. **Radiology** = abdominal or pelvic CT or abdominal radiograph helpful to recognize bowel gas patterns, air collections, and calcifications; IVP, barium studies, or US may also be helpful
5. **Treatment** = adequate pain control; **emergent laparotomy** or **laparoscopy** may be needed depending on pathology

B. Malignant Hyperthermia

1. Rare genetic disorder in which certain anesthetics (e.g., halothane, succinylcholine) induce hyperthermia (104°F/40°C)
2. **H/P** = symptoms begin after anesthesia use; rigidity, cyanosis, tachycardia, continually rising **body temperature**
3. Uncontrolled hyperthermia can lead to arrhythmias, disseminated intravascular coagulation (DIC), acidosis, cerebral dysfunction, and electrolyte abnormalities
4. **Labs** = mixed acidosis acutely; abnormal increase in muscle contraction following in vitro treatment with halothane or caffeine (testing performed as outpatient)
5. **Treatment** = evaporative cooling (i.e., patient sprayed with water and placed in front of fans), cold inhaled O_2, cold GI lavage, cool IV fluids, **dantrolene**, **stop offending agent**

III. Transplantation

Quick HIT

Individuals with a specific infection (e.g., **hepatitis**) may be used as donors for patients with the same infection if no significant donor organ injury is detected.

A. Indications and Selection

1. Organ transplantation is considered in cases of **end-stage organ failure** that are untreatable by other means or are incompatible with survival without treatment by extraordinary means (e.g., frequent dialysis).

2. **Transplant frequency** (see Table 4-9)
   a. Renal transplants are the most common type.
   b. Liver, bone marrow, pancreas, heart, lung, skin, and corneal transplants also performed.
   c. Small bowel transplant has been performed on a very limited basis with limited success.
3. **Donor selection**
   a. Donors are most frequently brain dead or living voluntary donors without cancer, sepsis, or organ insufficiency.
   b. Donors are selected based on **ABO blood group compatibility**, **cross-match compatibility** (i.e., presence of antidonor antibodies on recipient T cells), and **HLA antigen matching**.
   c. HLA antigen matching is **more** important for **kidney** and **pancreas** transplants and **less** important for **heart** and **liver**.
4. Transplant rejection can be hyperacute, acute, or chronic (see Table 4-10).
5. Patients must be given **immunosuppressive** agents to reduce risk of rejection (see Table 4-11).
6. Transplant recipients have greater risks of infection (secondary to immunosuppression), **cancer** (e.g., skin, B-cell lymphoma, oral squamous cell, cervical, vaginal), and infertility.

B. Graft versus Host Disease

1. Reaction of **donor** immune cells in transplanted bone marrow to host cells
2. Host is immunocompromised to avoid transplant rejection and is unable to prevent attack by donor cells

Table 4-9 Common Types of Organ Transplantation

Type	Indications	Contraindications	Results
Bone marrow	**Aplastic anemia, induction chemotherapy**, leukemia, lymphoma, hematopoietic disorders	Donor–recipient mismatch, recipient with high risk for developing posttransplant infection	Improved quality o term survival if su posttransplant
Heart (may be performed with lung transplant)	Severe heart disease (CAD, congenital defects, cardiomyopathy) with estimated death within 2 yrs without transplant	**Pulmonary hypertension, smoking** (prior 6 mo), renal insufficiency, COPD, >70 yrs of age, terminal illness	Acute rejection co mortality risk in in **5-yr** survival
Lung	**COPD** (particularly α_1-antitrypsin deficiency), primary pulmonary hypertension, **cystic fibrosis**; estimated death within 2 yrs	**Smoking** (prior 6 mo), poor cardiac function, renal or hepatic insufficiency, terminal illness, >65 yrs of age, HIV	Most have at leas acute rejection, pr **56% 3-yr** survival, **tion** common
Liver	Chronic hepatitis B or **C**, alcoholic cirrhosis, primary biliary cirrhosis, primary sclerosing cholangitis, biliary atresia, progressive Wilson disease	**Active alcoholism**, multiple **suicide** attempts (e.g., acetaminophen poisoning), liver cancer, cirrhosis from chronic hepatitis (may receive transplants from donors with hepatitis)	40% acute rejecti relates with patie of surgery (genera survival)
Renal	**End-stage renal disease** requiring dialysis (glomerulonephritis, DM, polycystic kidney disease, interstitial nephritis, renal hypertension)	Stable health (dialysis is always an option for unstable patients)	Living-donor kidne rejection and 91% cadaver kidneys h rejection and 85%
Pancreas (frequently performed with renal transplant)	**DM type I** with renal failure	Age >60 yrs, CAD, PVD, obesity, **DM type II**	80% 3-yr survival, common

CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; HIV, human immunodeficiency virus; PVD, periph

3. **Risk factors** = HLA antigen mismatch, old age, donor–host gender disparity, **immunosuppression**
4. **H/P** = **maculopapular rash**, abdominal pain, nausea, vomiting, diarrhea, recurrent infections, easy bleeding
5. **Labs** = increased liver function tests, decreased immunoglobulin levels, decreased platelets; biopsy of skin or liver detects an inflammatory reaction with significant cell death
6. **Treatment** = corticosteroids, tacrolimus, and mycophenolate are useful for decreasing graft response; thalidomide and hydroxychloroquine are used in chronic disease
7. **Complications** = patients without an early response to therapy frequently develop **chronic** disease with skin sclerosis, hepatic insufficiency, GI ulceration, and pulmonary fibrosis

Table 4-10 Forms of Transplant Rejection

Type	When Seen	Cause	Treatment
Hyperacute	**Initial 24 hrs** after transplantation	Antidonor antibodies in recipient	**Untreatable**; should be cross-matching
Acute	**6 days–1 yr** after transplantation	Antidonor T-cell proliferation in recipient	**Frequently reversible** pressive agents
Chronic	>**1 yr** after transplantation	Development of multiple cellular and humoral immune reactions to donor tissue	Usually untreatable; imm serve some role

Table 4-11 Immunosuppressive Drugs to Prevent Transplant Rejection

Drug	Indication	Mechanism	Adverse Effects
Cyclosporine	Rejection prevention	**Helper** T-cell inhibition	**Nephrotoxicity**, androgeni
Azathioprine	Rejection prevention	Inhibits T-cell proliferation	**Leukopenia**
Tacrolimus	Rejection prevention and reversal	Inhibitor of T-cell function	**Nephrotoxicity**, neurotoxic
Corticosteroids	Rejection prevention and reversal	Inhibits **all leukocyte** activity	Cushing syndrome, weight g
Muromonab-CD3 (OKT3)	Rejection reversal and **early** rejection maintenance	Inhibitor of T-cell function and depletes T-cell population	Induces **one-time cytokine** bronchospasm), leukopenia; **term therapy**
Rapamycin	Rejection prevention	Helper T-cell inhibition	Thrombocytopenia, hyperlipi
Mycophenolic acid	Rejection prevention	Inhibits T-cell proliferation	**Leukopenia**, GI toxicity
Antithymocyte globulin	Rejection reversal and **early** rejection maintenance	Depletes T-cell population	Limited to **short-term thera**
Hydroxychloroquine	Chronic graft vs. host disease	Inhibits antigen processing	Visual disturbances
Thalidomide	Chronic graft vs. host disease	Inhibits T-cell function and migration	Sedation, constipation, terat

AVN, avascular necrosis; GI, gastrointestinal; HTN, hypertension.

QUESTIONS

1. A 33-year-old male comes to a community emergency department by ambulance after being pulled out of a neighborhood warehouse that caught fire. The patient was trapped in a room and was initially found unconscious. Patient arrives awake with complaint of shortness of breath. Vitals are T: 36.1 C, HR: 125, RR: 26, BP: 100/58, O_2 Sat: 95%. On physical examination, there is evidence of burns with blisters involving the left arm and leg circumferentially and the trunk anteriorly. The face appears to have burns as well. The hairs of the face are burnt. In addition to IV fluids, what is the best next step?

   A. Topical antibiotics and admission
   B. Discharge with oral antibiotics
   C. Intubation and transfer
   D. Break blisters and bandages

2. A 65-year-old male is brought in via ambulance after being found down in his yard following a syncopal event. The patient is awake on arrival. Paramedics documented a temperature of 105.2 F. The patient appears confused but can give information. The vitals in ED still show an elevated temperature at 104 F, an HR of 115, BP 140/85, RR 18, O_2 Sat 95%. The patient woke up with no complaints today and was not feeling ill. He, currently, only complaints of feeling thirsty. The wife adds that he was out in the sun for several hours doing yard work. His physical and neurologic examination is unremarkable except for his mild confusion, hyperthermia, and tachycardia. There is no sweating noted. Blood work shows elevated creatinine kinase, BUN, and creatinine. What is the likely reason for this patient's syncopal event and confusion?

   A. Aortic dissection
   B. Myocardial infarction
   C. Heat stroke
   D. Heat exhaustion

3. A 23-year-old female comes in to the emergency department brought in by her mother. Her mother arrived home after her daughter called her claiming she was going to attempt suicide. On arrival, the mother found an empty bottle of her hypertension medication next to her daughter. The patient has been struggling with depression for several months. The patient is awake and tearful. She reports this is her first suicide attempt and admits to drinking an unknown number of pills. Ingestion occurred 3 hours ago. The patient's vital signs are HR 40, BP 91/50, RR 18, O_2 Sat 95%. The patient feels drowsy. Blood work reveals hypoglycemia at 45 mg/dL and no evidence of acetaminophen, salicylate, or benzodiazepine ingestion. Which is the best antidote for this toxic ingestion?

   A. Activated charcoal
   B. Naloxone
   C. Glucagon
   D. Gastric lavage
   E. Flumazenil

4. A 28-year-old male comes in after accidentally being exposed to a chemical at a work-related accident. The patient was standing next to a plastic container where many chemicals are held when a rise in pressure made the container explode and spill contents over him. He also reports possible accidental ingestion as well as local skin irritation from chemical. During the evaluation, the patient has started to present with crampy abdominal pain, diarrhea, urinary incontinence, profuse sweating, and increased sputum from hypersalivation. His vital signs are HR 44, BP 100/60, RR 23, O_2 Sat 95%. In addition to full body decontamination, what treatments should be started?

   A. Charcoal, dialysis, sodium bicarbonate
   B. Glucagon, calcium, insulin, dextrose
   C. Supportive care
   D. Atropine, pralidoxime

5. A 73-year-old man is brought in by ambulance due to onset of sudden left-sided weakness while he was having breakfast. The onset of symptoms has been less than 1 hour. The patient has never had a prior stroke and has history of high blood pressure, and high cholesterol. There is no history of smoking or drugs. The patient does not take any blood thinners. The patient works from home and wants anything possible done to regain function. Initial assessment reveals an NIH Stroke Scale of 8. Vital signs show HR 83, BP 160/90, RR 18, O_2 Sat 95%, Temp 98.7 C. A CT scan of the head reveals no acute hemorrhage, no acute lesions or masses. The best next step is?

   A. Admit, consult neurology
   B. Consider aspirin, admit
   C. Consider aspirin, neurology consultation, admit
   D. Consider fibrinolytic therapy, thrombectomy, admit

6. A patient is brought in by ambulance after suffering multiple injuries in a multiple vehicle collision. The patient was a restrained driver requiring prolonged extrication. There was severe damage to the vehicle. Since paramedic arrival on scene patient has remained awake but confused. The patient was placed on a backboard with a C-collar in place. In the emergency department the patient remains confused, not following commands, and lethargic. There are multiple lacerations and contusions to the face with active profuse oropharyngeal bleeding. What is the best next step in the assessment and management?

   A. Bag-valve mask oxygenation
   B. Remove C-collar
   C. Endotracheal intubation
   D. Perform FAST ultrasound

7. A 45-year-old male comes in with flank pain to the doctor’s office. He has noted decreased urination with dark-colored urine. He has history of a renal transplant received 1 month ago. After the surgery, he was feeling well with no complications. He reports medication compliance. The patient denied any recent illness, trauma, or new medications. His vital signs are normal. The physical examination shows bilateral mild pitting edema. Blood work reveals elevated kidney function tests from baseline. What type of rejection is this patient suffering?

   A. Hyperacute
   B. Acute
   C. Intermediate
   D. Chronic

5
Musculoskeletal Disorders

I. Common Adult Orthopedic Conditions

A. Osteoarthritis (OA)/Degenerative Joint Disease

1. Chronic, noninflammatory joint degeneration involving **articular cartilage deterioration**
2. Most commonly affects **hips, knees,** ankles, hands, wrists, and shoulders; can cause spinal stenosis in vertebral bodies
3. **Risk factors** = advanced age, family history, obesity, previous joint trauma, repetitive joint stress (heavy labor occupations)
4. **History and Physical (H/P)** = joint crepitus, insidious onset of joint stiffness and pain that **worsens with activity and weight bearing** and is relieved by rest, no systemic symptoms; patients have decreased range of motion, bony protuberances in the distal interphalangeal (DIP) (i.e., **Heberden nodes**) and proximal interphalangeal (PIP) (i.e., **Bouchard nodes**) joints
5. **Labs** = normal erythrocyte sedimentation rate (ESR); <2,000 leukocytes on joint aspiration
6. **Radiology** = x-ray demonstrates osteophyte formation, joint space narrowing, subchondral bone sclerosis, and subchondral bone cyst formation (see Figure 5-1)
7. **Treatment** = activity modification, heat, analgesics (e.g., nonsteroidal anti-inflammatory drugs [NSAIDs]), weight loss, physical therapy, corticosteroid or hyaluronic acid injections, joint replacement in advanced cases

Quick HIT

- **Osteoarthritis:** typically **asymmetric** and may only affect one joint; DIP joints are frequently involved in hands.
- **RA:** affects joints on both sides of the body in a **symmetric** distribution; DIP joints are spared in hands.

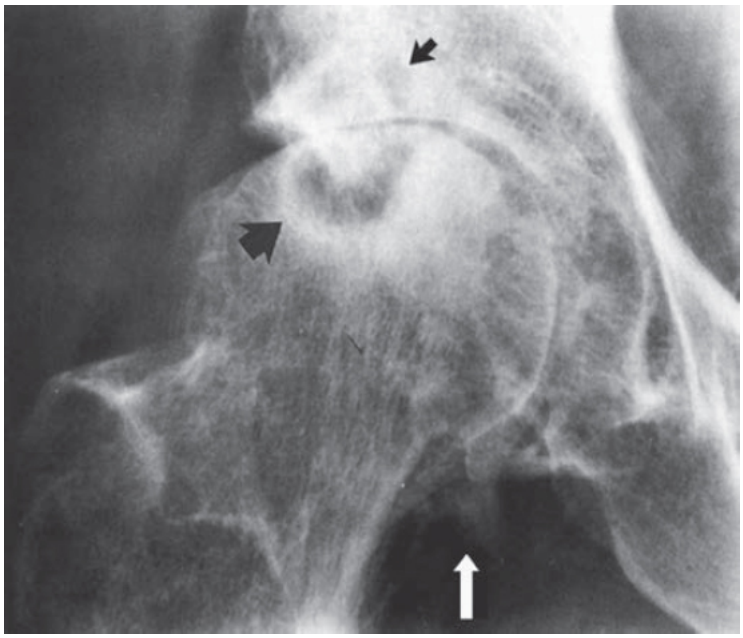


FIGURE 5-1
Osteoarthritis in a right hip joint; synovial cysts (*black arrows*) and osteophytes (*white arrow*) are evident.
(Modified from Daffner, R. H. & Hartman, M. [2013]. *Clinical radiology: The essentials* [4th ed., p. 383]. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins.)

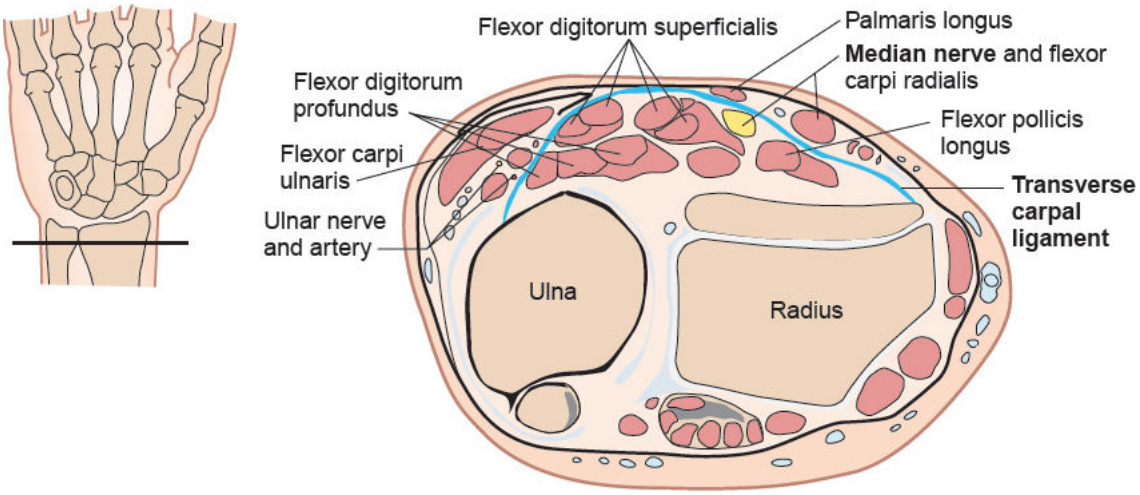


FIGURE **5-2**
Tendinous and neurovascular structures superficial and deep to the transverse carpal ligament in the wrist.
(Modified from Moore, K. L., Agur, A. M. R., & Dalley, A. F. [2013]. *Clinically oriented anatomy* [7th ed.]. Baltimore, MD: Lippincott Williams & Wilkins.)

B. Carpal Tunnel Syndrome

1. Syndrome resulting from **median** compression at the wrist (see Figure 5-2)
2. **Risk factors**
   a. Pregnancy, rheumatoid arthritis (RA), diabetes mellitus (DM), acromegaly, hypothyroidism, obesity, **overuse** (activities requiring significant wrist motion, including typing, piano playing, writing, etc.)
      a. Most common in persons 30 to 55 years of age; female > male
3. **H/P**
   a. Wrist pain that radiates up arm and worsens with hand flexion and grasping, decreased hand strength, numbness in thumb and in index and middle fingers; decreased palmar two-point discrimination, except on the radial side of the palm
   b. Positive **Tinel** sign (i.e., tapping over carpal tunnel elicits wrist tingling and pain) and **Phalen** sign (i.e., placing dorsal side of hands together and flexing wrists 90 degrees cause the onset of symptoms within a minute)
   c. Thenar muscle atrophy is seen in long-term cases
4. **Electromyogram (EMG)** = can be used in addition to nerve conduction studies to evaluate nerve compromise (will show impaired conduction)
5. **Treatment** = wrist splints, **activity modification**, NSAIDs, corticosteroid injections, surgical release of the transverse carpal ligament

NEXT
STEP

Suspect axillary nerve injury in cases of **deltoid** malfunction (inability to extend arm) or shoulder numbness following shoulder dislocation.

NEXT
STEP

An **open** fracture (fracture penetrates skin **and** is exposed to outside environment) requires thorough **irrigation** in the operating room and antibiotics to reduce the risk of **infection**.

C. Dislocations

1. **Shoulder**
   a. Most commonly **anterior** (posteriorly directed force on distal humerus or forearm during abduction causes cantilever effect that drives humeral head forward and tears anterior shoulder capsule)
   b. **Posterior** dislocations most frequently occur following **seizures** and **electrical shock** (strong contraction in internally rotated, adducted arm causes humeral head dislocation)
   c. **Treatment** = urgent closed reduction, sling; chronic dislocations may require surgery to improve joint stability
   d. **Complications** = axillary artery and nerve injury, increased risk of future dislocations
2. **Hip**
   a. Most commonly **posterior** via a posteriorly directed force on an internally rotated, flexed, and adducted hip (e.g., dashboard injury)
   b. **Treatment** = closed reduction, bracing, abduction pillow
3. **Knee**
   a. Most commonly **anterior** (40%) by a hyperextension mechanism

b. **Posterior** dislocations (33%) often involve an injury to the popliteal artery (25%) and often happen from dashboard injury
c. **Treatment** = spontaneous reduction happens in up to 50%. Otherwise, immediate closed reduction and splint extremity in 15 degrees of flexion
d. **Complications** = common peroneal nerve injury (25%), popliteal artery injury, compartment syndrome

4. **Patella**
a. Most commonly dislocated **laterally**, knee held in slight flexion. Diagnosis is clinical, and x-ray is rarely required
b. X-rays should be obtained post reduction to evaluate for other injuries
c. **Treatment** = closed reduction, knee is extended while the free hand slides patella into place. Sedation rarely needed for this procedure. Knee sling versus immobilizer
d. **Complications** = comminuted fractures can happen, patella alta or baja, chronic dislocations, joint or bursa effusions

D. Fractures

1. Fractures are associated with a particular mechanism of injury and carry different options, depending on location (see Table 5-1)

Quick HIT

Computed tomography (CT) is generally more useful in the diagnosis of **bone** pathology, whereas **MRI** is more useful for **soft tissue** injuries.

E. Sprains

1. Injuries to **ligaments** and surrounding soft tissues in a joint; structures are partially or completely torn at ligament–bone interface or within ligament; most common in the ankle and knee
2. **H/P** = pain in involved joint with weight bearing or movement
3. **Treatment** = **RICE: R**est, **I**cing, **C**ompression of swelling, **E**levation of joint; analgesics

F. Ligament Tears

1. Occur from excessive stress across joints
2. **H/P** = pain and swelling that worsens with joint stress, decreased joint range of motion; ligamentous **instability** on joint stress testing
3. **Radiology** = magnetic resonance imaging (MRI) may confirm tear
4. **Treatment** = initially, as for sprains; may require surgical repair

Quick HIT

A medially directed blow to the lateral side of the knee (i.e., a valgus stress) can cause the **unhappy triad: lateral meniscus** tear, **medial collateral ligament** (MCL) tear, and **ACL** tear.

G. Meniscus Tears (Knee)

1. Result from repetitive microtrauma and degeneration or forceful twisting of a planted knee
2. Frequently associated with anterior cruciate ligament (**ACL**) injury (especially from blunt trauma or sports injuries)
3. **H/P** = vague pain inside knee joint, clicking or locking of joint; pain along joint line near tear
4. **Radiology** = MRI may detect tear
5. **Treatment** = NSAIDs, physical therapy, arthroscopic repair or debridement
6. **Complications** = meniscal debridement predisposes knee to developing OA at an earlier age

Quick HIT

Young athletes may get an **exertional** compartment syndrome during athletic activity with mild elevation of compartment pressures that **resolves following activity cessation** and carries a **minimal risk** of significant tissue ischemia.

H. Rotator Cuff (Shoulder)

1. Majority occur due to chronic impingement in patients over 40 years old. Acute tears tend to be related to acute trauma (shoulder dislocations, or FOOSH); **supraspinatus** most commonly affected
2. **H/P** = gradual progressive pain and weakness for several weeks, worse at night, inability to abduct or externally rotate arm against resistance, positive drop arm test; tearing pain (in acute injuries); tenderness of lateral and upper arm or subacromial region
3. **Radiology** = MRI may confirm tear; ultrasound (US) can aid in diagnosis
4. **Treatment** = NSAIDs, ice, arm sling in acute pain, physical therapy, surgery in full thickness tears
5. **Complications** = chronic pain, decreased ROM and function of affected shoulder

MNEMONIC

SItS (S = Supraspinatus, I = Infraspinatus, t (not in caps) = teres minor (differentiates from teres major), S = Subscapularis)

I. AC Joint Separation (Shoulder)

1. Results from excessive force on adducted arm, usually a fall onto tip of shoulder
2. **H/P** = Pain on palpation of AC joint and adduction of arm, difficulty elevating shoulder; severe forms can show shoulder drop

Table 5-1 Common Fractures, Their Mechanism of Injury, and Appropriate Treatment

Type	Bones Involved	History and Physical	Treatment	Clinical Pearls
Colles	Distal radius ± distal ulna	**Fall on outstretched hand**, distal radius is posteriorly displaced and angulated (forearm profile looks like a **dinner fork**)	Closed reduction Long arm cast Possible surgery	Most common wrist fracture, particularly common in osteoporotic bone
Smith	Distal radius	Fall on flexed wrists, distal radius is anteriorly displaced	Cast Closed reduction Possible surgery	Much less common than Colles fracture
Scaphoid	Scaphoid	"Snuffbox" tenderness, fall on radially deviated outstretched hand	Thumb spica cast Possible surgery	Increased risk of AVN; **not seen on x-ray for 1–2 wks after injury**; most common carpal fracture
Boxer	Fifth-metacarpal neck	Punching hard object or surface with a strong force applied to fifth metacarpal	Closed reduction Ulnar gutter splint Surgical pinning	Beware the **"fight bite"**—open wounds from teeth will need surgical exploration to rule out tendon involvement; antibiotics
Humerus	Humerus	Trauma (motor vehicle accident, blunt trauma, etc.)	Closed reduction Splint Possible surgery	With wrist drop or weakened thumb abduction, think **radial nerve injury**
Monteggia	Fracture of proximal one-third of ulna with dislocation of radial head	Fall on outstretched arm with arm hyperpronated	Closed reduction of radial head Surgical repair of ulna	
Galeazzi	Fracture of distal shaft of radius and dislocation of DRUJ	Trauma (direct blow or fall)	Surgical repair Cast forearm in supination to maintain reduction of DRUJ	
Hip	Femoral head or neck	Fall, motor vehicle accident, trauma Injured leg is shortened and externally rotated Frequently occurs from strong axial force (e.g., fall or knee hitting a car dashboard)	Surgical repair May require joint replacement	Increased risk for **AVN** and DVT (should **anticoagulate** patient); particularly common in osteoporotic bone
Femur	Femoral diaphysis	Trauma	Surgical repair	Increased risk of fat embolization
Tibial	Tibia	Trauma	Cast Surgical repair	Increased risk for **compartment syndrome**
Ankle	Medial, lateral, and/or posterior malleoli	Trauma, excessive twist of ankle (most commonly supination and external rotation)	Cast Possible surgical repair	
Rib	Nonfloating ribs	Trauma, pain worse during deep breathing	Pain control Possible splinting	
Pelvic	Pelvis	Major trauma	Pain control surgical repair, if in weight-bearing portion	**High risk of major blood loss**

AVN, avascular necrosis; DRUJ, distal radial ulnar joint; DVT, deep vein thrombosis.

3. **Treatment** = conservative with sling and NSAIDs for minor tears with no clavicular displacement; severe forms may require ORIF

J. Compartment Syndrome

1. Trauma (surgical or accidental) in extremities leads to reperfusion injury and swelling of fascial compartments; **intracompartmental swelling** can cause compression of neurovascular structures leading to **ischemia** of soft tissues within compartment and distal to site of compression.
2. Most common in **lower leg** (e.g., tibial fracture) and forearm
3. **H/P** = **6 Ps** are signs of progression (**Pain, Pallor, Poikilothermia, Pulselessness, Paresthesia, Paralysis**); compartment pain with passive stretching is best screening test
4. **Labs** = elevated compartment pressures (needle inserted into compartment and attached to manometer to determine pressures)
5. **Treatment** = **emergent fasciotomy** for pressures >30 mm Hg or for pressures within 20 mm Hg of diastolic blood pressure

Quick HIT

A painful leg that has a pulse **never** rules out compartment syndrome.

K. Foot Injuries

1. **Plantar fasciitis** = presents as heel or plantar pain, worse in the morning with gradual improvement during the day; inflammation of plantar aponeurosis, usually from overuse.
   a. Clinical diagnosis: The vast majority improve within 1 year.
   b. **H/P** = tenderness to palpation of plantar surface that worsens with dorsiflexion of toes; tenderness on medial calcaneus
   c. **Treatment** = rest, ice, NSAIDs, heel or arch supports; stretching exercises or steroid injections in refractory cases
2. **Morton neuroma** = interdigital neuroma likely due to mechanical injury; causes burning pain and numbness of foot.
   a. Clinical diagnosis: Can be caused by running or high heels.
   b. **H/P** = pressing around the 3rd and 4th metatarsal joints causes pain and clicking sound (Mulder sign); a small mass sometimes can be palpated
   c. **Radiology** = US and MRI can sometimes help confirm diagnosis
   d. **Treatment** = hard-sole footwear; injections/surgery for refractory cases
3. **Stress fracture** = midfoot pain from repetitive tension, usually associated with a dramatic increase in physical activity; the 2nd metatarsal area is most commonly affected, but can also happen in 5th metatarsal
   a. **H/P** = tenderness over midfoot on palpation, pain with use or flexion/extension, subsides with rest
   b. **Radiology** = x-rays usually normal initially; positive after 2 to 3 weeks; frequently missed. MRI or CT more sensitive in early stages
   c. **Treatment** = conservative, hard-sole footwear; walking boot for 5th toe involvement
4. **Jones fracture** = fracture at the junction of the metaphysis and diaphysis of the 5th toe; commonly happens with ankle sprains in dancers when forefoot is planted and heel is elevated
   a. **H/P** = tenderness to palpation of lateral base of 5th metatarsal, pain with use
   b. **Radiology** = x-ray is diagnostic
   c. **Treatment** = if nondisplaced 6 to 8 weeks in cast with nonweight bearing; if displacement is seen surgery is required
   d. **Complications** = risk of nonunion and avascular necrosis (watershed zone)

II. Spine

A. Back Pain

1. Back pain can be caused by musculoskeletal, neurologic, neoplastic, infectious, or rheumatic causes (see Figure 5-3)
2. **Treatment** = NSAIDs, physical therapy, or rest for muscular injuries

Quick HIT

90% of back pain caused by muscular injury resolves within 6 weeks, regardless of treatment.

B. Degenerative Disc Disease

1. Vertebral disc is composed of a dense annulus fibrosus and a gelatinous nucleus pulposus

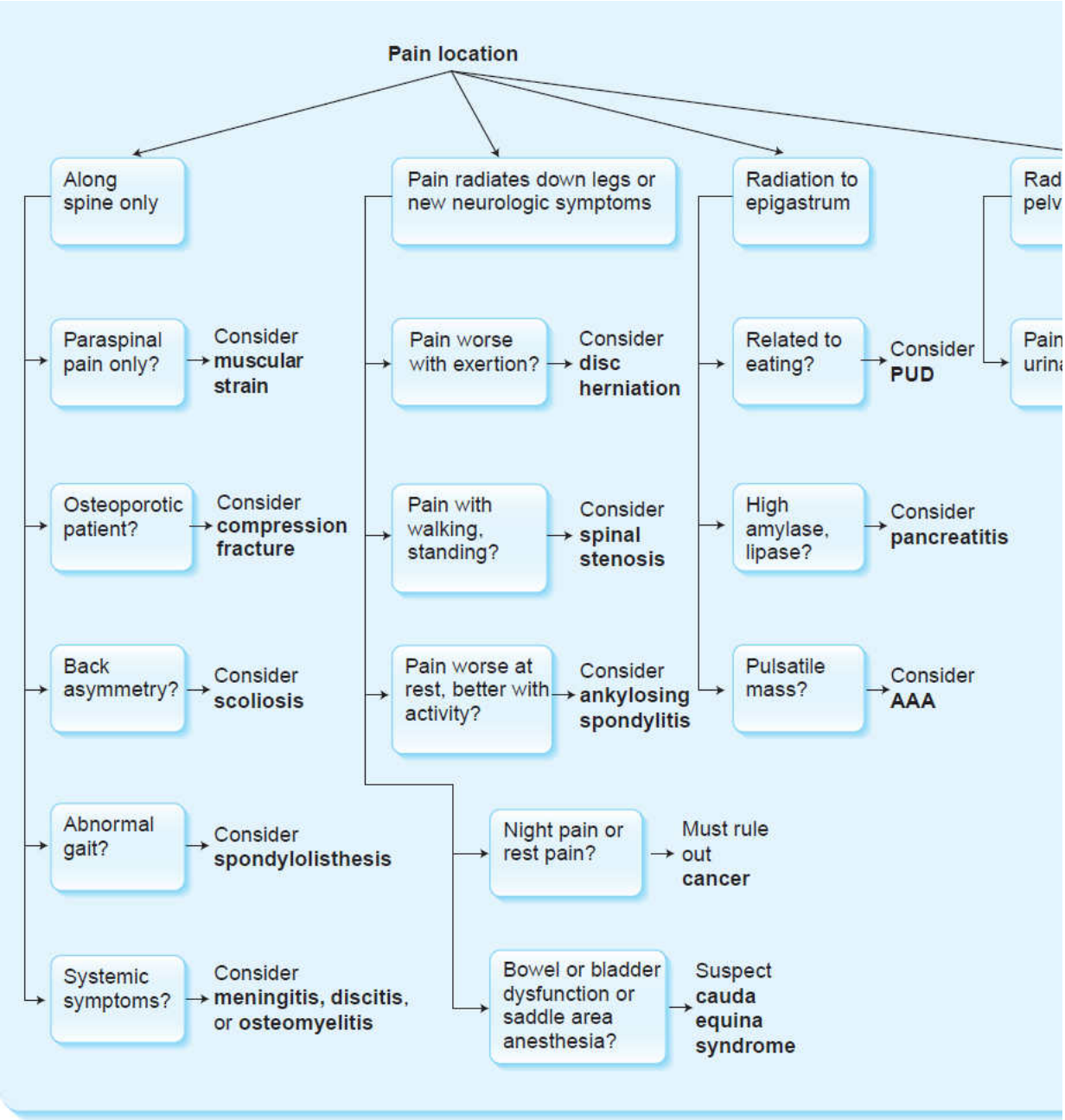


FIGURE **5-3**
Differential diagnosis for back pain.

2. Degenerative changes in disc lead to **herniation** (most frequently, posterior or posterior lateral) of nucleus pulposus and subsequent **nerve impingement**
3. Herniation is most common in the lumbosacral region (L4–L5, L5–S1 discs) but can also be cervical (see Figure 5-4)
4. **H/P** = pain extending from the nerve root **along path of compressed nerve;** characteristic sensory and motor deficits, depending on nerve root involved; pain worsens with straight leg raises or Valsalva maneuver (see Table 5-2)
5. **Radiology** = MRI confirms diagnosis; CT is helpful for analysis of bone structure
6. **Treatment** = disease may be self-limited; NSAIDs, activity modification, epidural injection of anti-inflammatory agents, or surgical decompression can be used, depending on symptom duration and severity

C. Spinal Stenosis

1. Generalized narrowing of bony spaces in the spine secondary to arthritic changes, causing nerve compression
2. Most common in middle-aged and **older** adults
3. **H/P** = radiating pain that is worse with standing and walking (“pseudoclaudication”), pain relieved when leaning forward while walking or walking uphill
4. **Radiology** = CT or x-ray confirms diagnosis; MRI may also be helpful to rule out herniation
5. **Treatment** = analgesics (e.g., NSAIDs), physical therapy, epidural injections, surgical decompression

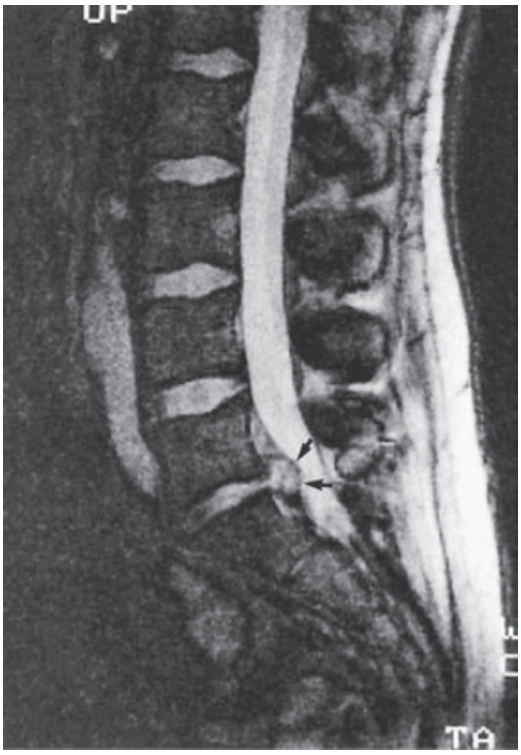


FIGURE 5-4
Magnetic resonance imaging (MRI) of lumbar spine demonstrating herniation of L5–S1 disc (*arrows*) and compression of spinal cord.
(From Daffner, R. H. & Hartman, M. [2013]. *Clinical radiology: The essentials* [4th ed., p. 487]. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins.)

NEXT
STEP

Treat **cauda equina syndrome** with **immediate** surgical decompression because it can quickly result in permanent neurologic injury.

MNEMONIC

Remember the organization of the brachial plexus by the mnemonic **R**eal **T**exans **D**rink **C**old **B**eer: **R**oots, **T**runks, **D**ivisions, **C**ords, **B**ranches (proximal to distal).

D. Cauda Equina Syndrome

1. Cauda equina is the extension of the dural–arachnoid sac beyond the inferior tip of the spinal cord and the complex of terminal nerve roots contained within it
2. Trauma can damage nerves running in the sac; neoplasms can cause nerve compression
3. **H/P** = **urinary retention** with overflow incontinence, change in bowel habits; anesthesia in perineal region (i.e., **saddle anesthesia**), decreased rectal tone or bulbocavernosus reflex
4. **Treatment** = **emergency** surgical decompression of cauda equina; intravenous (IV) corticosteroids commonly given to decrease spinal cord inflammation; radiation used in cases of neoplasm

Table 5-2 H/P for Compression of Specific Cervical and Lumbosacral Nerve Roots

Nerve Root	Reflex	Motor Deficit	Sensory Deficit
C5	Biceps	Deltoid, biceps	Anterior shoulder
C6	Brachioradialis	Biceps, wrist extensors	Lateral forearm
C7	Triceps	Triceps, wrist flexors, finger extensors	Posterior forearm
C8	None	Finger flexors	Fourth and fifth fingers
T1	None	Finger interossei	Axilla
L4	Patellar	Tibialis anterior (foot dorsiflexion)	Medial leg
L5	None	Extensor hallucis longus (first-toe dorsiflexion)	Lateral lower leg, first
S1	Achilles	Peroneus longus and brevis (foot eversion), gastrocnemius (foot plantar flexion)	Lateral foot

H/P, history and physical.

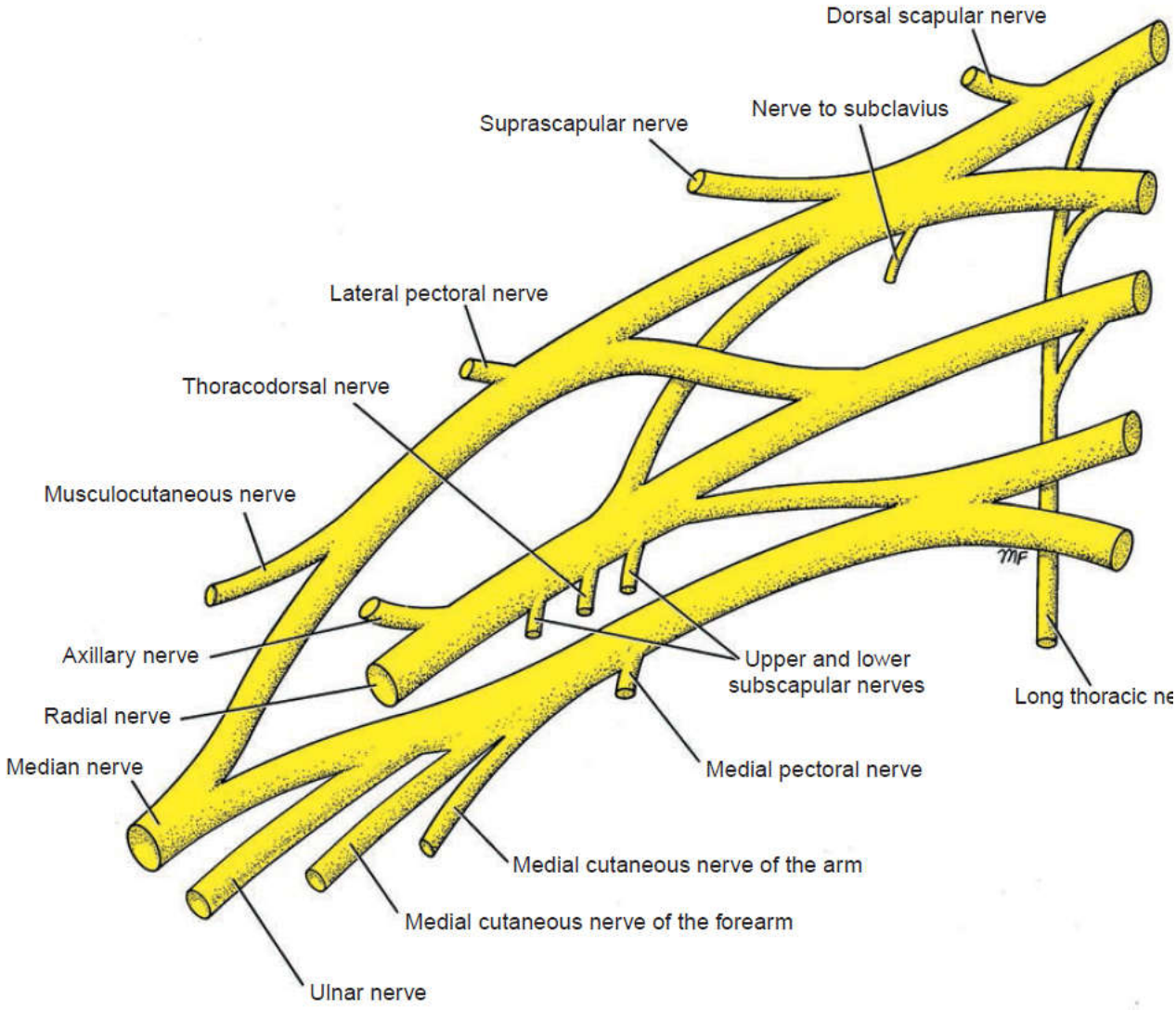


FIGURE 5-5
Diagram of major neural branches of the brachial plexus.
(From Snell, R. S. [2008]. *Clinical anatomy by regions* [8th ed., p. 772]. Philadelphia, PA: Lippincott Williams & Wilkins.)

E. Brachial Plexus

1. The brachial plexus is composed of nerve roots C5–T1 and innervates the upper extremity (see Figure 5-5).

2. Brachial plexus disorders are related to specific mechanisms of injury (see Table 5-3).

Table 5-3 Common Brachial Plexus Disorders

Condition	Site of Injury	Cause of Injury	Clinical Features
Erb–Duchenne palsy	Superior trunk	Hyperadduction of arm causing widening of the humeral-glenoid gap (e.g., **birth, shoulder dystocia**)	**Waiter's tip** (arm extend with pronated forearm)
Claw hand	Ulnar nerve	Epiphyseal separation of medial epicondyle of humerus	Weak finger adduction, p fifth-finger flexion, clawe fingers from **lumbrical v**
Wrist drop	Posterior cord or radial nerve	Mid-humerus fracture causes nerve impingement or tear	Inability to extend wrist o sensation from dorsal har
Deltoid paralysis	Axillary nerve	**Anterior shoulder dislocation** causes axillary nerve impingement or stretching	Impaired shoulder abduct
Klumpke palsy	Posterior or medial cords	Hyperabduction of arm places excess tension on lower cords and nearby sympathetic chain	**Claw hand**, poor wrist a association with Horner s

III. Metabolic Bone Diseases

A. Osteoporosis

1. Substantial osteopenia (i.e., decreased bone density) but normal mineralization in existing bone stock
2. Results from decreased bone formation or increased resorption of bone
3. Peak bone mass occurs at 20 to 25 years of age
4. **Risk factors** = inadequate dietary calcium during young adulthood, smoking, excessive alcohol consumption, sedentary lifestyle, decreased estrogen or testosterone (e.g., postmenopausal), long-term steroid use, hyperparathyroidism, hyperthyroidism; typical patients are thin (low body weight), White, postmenopausal women (advanced age), Asian ethnicity, chronic liver or renal disease
5. **H/P** = usually asymptomatic until fractures (e.g., Colles, femoral neck, and vertebral) and neurovascular impingement occur
6. **Radiology** = decreased bone density evident on dual-energy x-ray absorptiometry (DEXA), x-ray, and CT
7. **Treatment**
   a. Prevention is key, with exercise and sufficient calcium and vitamin D in diet (especially before the peak bone density age of 35 years) important for maintaining bone stock.
   b. **Bisphosphonates** decrease osteoclast activity (less bone resorption), increase bone density, and decrease fracture risk.
   c. Selective estrogen receptor modulators (e.g., raloxifene) help increase bone density with fewer adverse effects than classic hormone replacement therapy.
   d. Pulsatile teriparatide (recombinant human parathyroid hormone) stimulates osteoblasts and bone remodeling; it may be used for up to 2 years.

Quick HIT

Osteoporosis is **less** likely to occur in **obese** people, because the increased load placed on bones helps to prevent osteopenia.

Quick HIT

Hormone and electrolyte levels will be normal for age in osteoporosis unless an underlying **endocrine** disorder exists.

Quick HIT

X-rays will only show changes in osteoporotic bone after significant bone loss.

Quick HIT

Hormone replacement therapy is no longer considered acceptable for osteoporosis prevention because it carries increased risks for breast cancer, deep vein thrombosis (DVT), coronary artery disease (CAD), and stroke.

B. Osteopetrosis

1. Increased bone density caused by impaired osteoclast activity
2. **H/P** = increased incidence of fractures, possible blindness or deafness, variable neurologic symptoms (from bony compression of nerves), impaired fracture healing
3. **Labs** = decreased hemoglobin (Hgb), decreased hematocrit (Hct) (via narrowing of marrow cavities), increased acid phosphatase, increased creatine kinase (CK)
4. **Radiology** = general increased bone density seen on x-ray, including thickening of cranium and vertebrae
5. **Treatment** = transfusion of marrow components necessary for osteoclast production, activity restriction

C. Paget Disease of Bone

1. Overactive osteoclasts and osteoblasts leading to excessive bone turnover and disorganized bony architecture
2. **H/P** = possibly, asymptomatic or deep bone pain, increased incidence of fractures; **tibial bowing,** kyphosis, **increased cranial diameter,** deafness (from changes in auditory ossicles)
3. **Labs** = increased alkaline phosphatase; increased urine hydroxyproline; normal calcium and phosphorus
4. **Radiology** = x-rays may demonstrate osteolytic lesions and expanded hyperdense bone; bone scan will detect diffuse "hot spots" in areas of active disease
5. **Treatment** = bisphosphonates, calcitonin

NEXT
STEP

If a patient complains, "my hats no longer fit," consider a workup for Paget disease or osteopetrosis.

D. Osteogenesis Imperfecta

1. Defective production of collagen from a genetic disorder
2. Diagnosis primarily made during childhood
3. **H/P** = frequent **fractures** from **minimal** trauma, **blue sclerae,** skin and teeth deformities, possible deafness, joint hypermobility (may resemble child abuse)
4. **Treatment** = activity restriction, surgical correction of bony misalignment, bisphosphonates decrease fracture risk

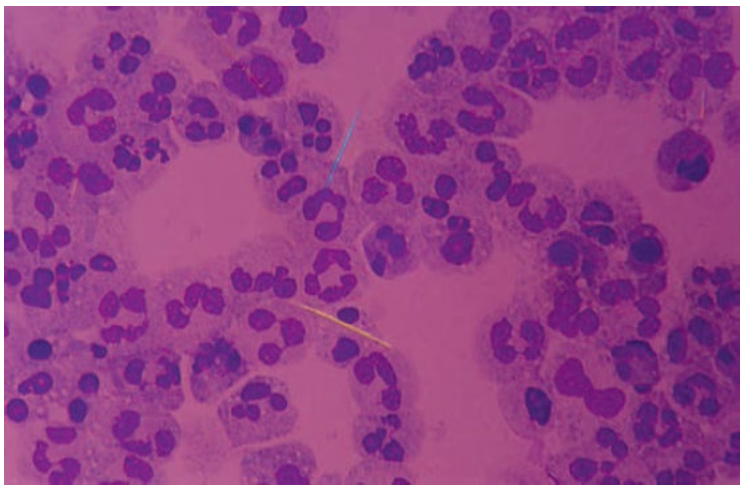


FIGURE **5-6**
Synovial aspirate from patient with gout.
Note needle-shaped, negatively birefringent sodium urate crystals that are visible under polarized light microscopy.
(From McClatchey, K. D. [2002]. *Clinical laboratory medicine* [2nd ed., Figure 27-17]. Philadelphia, PA: Lippincott Williams & Wilkins; with permission.)

NEXT
STEP

Allopurinol should **not** be administered in acute attacks of gout.

E. Gout

1. Peripheral monoarthritis caused by deposition of **sodium urate crystals** in joints

2. **Risk factors** = renal disease, male gender, obesity, excessive consumption of purine-rich foods, urate underexcretion, diuretic use, cyclosporine use, cancer, hemoglobinopathies
3. **H/P**
   a. **Sudden severe pain** and **swelling** in one joint that frequently starts at night
   b. First metatarsophalangeal joint most commonly affected (i.e., **podagra**); ankle, knee, and foot joints also common sites
   c. Possible concurrent fever, chills, or malaise
4. **Labs** = serum uric acid can be normal or increased; joint aspiration shows **needle- shaped**, **negatively birefringent crystals** and several white blood cells (WBCs) (see Figure 5-6)
5. **Radiology** = x-ray may rarely show bony erosions in chronic cases, and possibly tophi
6. **Treatment**
   a. NSAIDs (especially indomethacin), colchicine, corticosteroids
   b. Decreasing alcohol and diuretic use and avoiding foods high in purines (e.g., red meats, fish) may help prevent exacerbations
   c. Allopurinol (inhibits uric acid formation) or probenecid (inhibits kidney uric acid resorption) used in cases of chronic gout to prevent flare-ups
7. **Complications** = long-standing disease leads to chronic tophaceous gout with formation of nodular tophi (large deposits of crystals in soft tissues), leading to permanent deformity

Quick HIT

Podagra rules out CPPD and suggests a diagnosis of **gout**.

F. Pseudogout (Calcium Pyrophosphate Dihydrate Deposition Disease or CPPD)

1. Calcium pyrophosphate dihydrate crystal deposition in joints
2. Familial condition associated with other endocrine diseases (e.g., DM, hyperparathyroidism)
3. **H/P** = similar presentation to gout but **less severe symptoms; knee** and **wrist** most commonly initially affected joints
4. **Labs** = joint aspiration shows **positively birefringent, rhomboid crystals** (see Figure 5-7)
5. **Radiology** = x-ray may show chondrocalcinosis (i.e., calcification of articular cartilage in joints)
6. **Treatment** = NSAIDs, colchicine

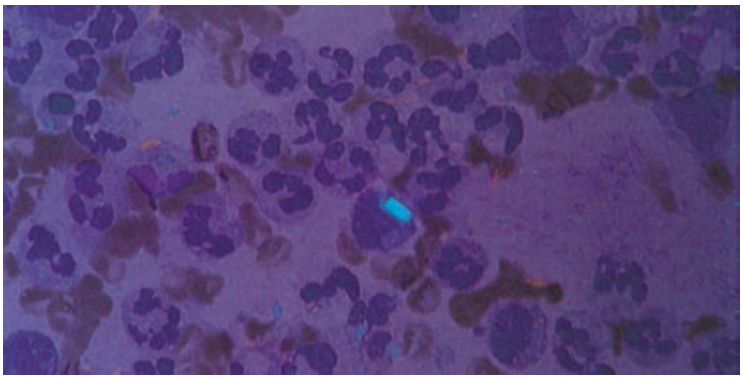


FIGURE 5-7
Synovial aspirate from a patient with calcium pyrophosphate dihydrate deposition disease; under polarized light microscopy, rhomboid-shaped calcium pyrophosphate dihydrate crystals appear positively birefringent.
(From McClatchey, K. D. [2002]. *Clinical laboratory medicine* [2nd ed., Figure 27-22]. Philadelphia, PA: Lippincott Williams & Wilkins; with permission.)

IV. Infection

A. Septic Joint and Septic Arthritis

1. Most commonly occurs through **hematogenous spread** of bacteria, extension of local infection, or direct inoculation (e.g., open fracture)
2. Most commonly caused by ***Staphylococcus aureus;*** consider ***Neisseria gonorrhoeae*** in young, sexually active patients
3. Consider gram-negative rods in patients with DM, cancer, or other underlying illnesses
4. Pre-existing arthritis increases risk of progressive damage to cartilage
5. **H/P** = sudden onset of joint pain (usually monoarticular); warm, red, tender, swollen joint, pain with any motion (i.e., micromotion tenderness), possible overlying skin lesions; children may show vague signs of pain and refusal to walk
6. **Labs** = increased WBCs, ESR, and C-reactive protein (CRP); joint aspiration shows **numerous WBCs** (lower for *N. gonorrhoeae* than *S. aureus*) with a high percentage of neutrophils and decreased glucose; positive cultures (frequent false-negative findings for *N. gonorrhoeae*) (see Table 5-4)
7. **Treatment** = **surgical irrigation and drainage** (I&D) required for any infection other than *N. gonorrhoeae;* for *N. gonorrhoeae*, use IV ceftriaxone and doxycycline for possible *Chlamydia* coinfection; for *S. aureus*, use penicillinase-resistant penicillin; for gram-negative bacteria, use aminoglycosides

Quick HIT

The body's inflammatory response to bacteria in the joint is the cause of cartilage destruction in joint sepsis.

Quick HIT

Because the inflammatory response to ***N. gonorrhoeae*** is not as severe as that for other bacteria, I&D is not required for treatment.

Quick HIT

Although ***S. aureus*** is the ***most*** common cause of osteomyelitis in general, ***Salmonella*** is the most common cause in patients with sickle cell disease.

Pseudomonas osteomyelitis is more common in IV drug users than in other populations.

B. Osteomyelitis

1. **Bone infection** via hematogenous spread or local extension
2. ***S. aureus*** and *Pseudomonas* most common causes; consider *Salmonella* in patients with **sickle cell disease**
3. **H/P** = bone pain, tenderness, fever, chills; possible skin involvement with a draining sinus
4. **Labs** = increased WBC, ESR, and CRP; cultures needed to define appropriate antibiotic therapy

Table 5-4 Findings in Aspirated Joint Fluid for Common Inflammatory Joint Conditions

Conditions	Joint Aspiration Leukocytes	Histology
Osteoarthritis, trauma	<2,000/mm	May see signs of hemarthrosis (bleeding into joint) for trauma; otherwise negative
Inflammatory arthropathies (e.g., rheumatoid arthritis, gout, pseudogout)	5,000–50,000/mm	Needle-shaped, negatively birefringent crystals for **gout** Positively birefringent rhomboid crystals for **pseudogout**
Septic joint	>50,000/mm	Many **WBCs**; infrequently, bacteria seen

WBCs, white blood cells.

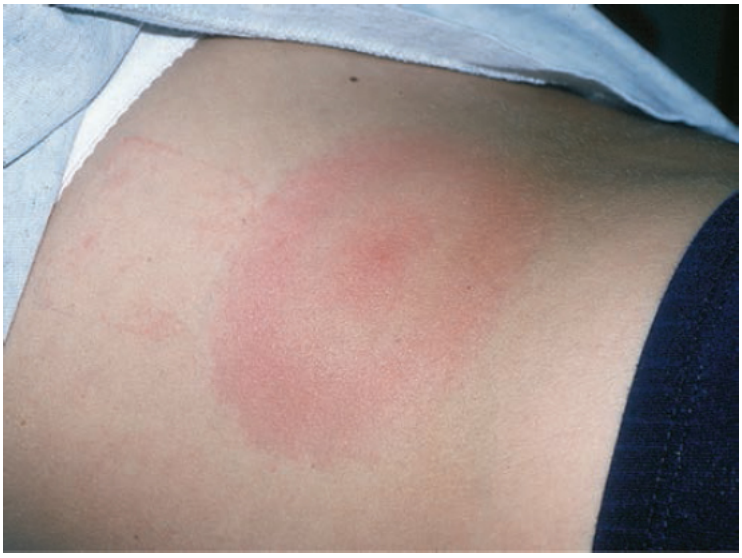


FIGURE 5-8
A patient with Lyme disease exhibiting erythema chronicum migrans (bull's eye rash).
(From Goodheart, H. P. [2003]. *Goodheart's photoguide of common skin disorders* [2nd ed., Figure 7-19]. Philadelphia, PA: Lippincott Williams & Wilkins; with permission.)

5. **Radiology** = x-rays are not helpful initially and only show signs of infection after 10 days; MRI demonstrates bone edema early in disease; bone scan will show increased uptake after 72 hours; tagged-WBC scan is more sensitive than standard bone scan
6. **Treatment** = IV antibiotics for 4 to 6 weeks (empiric initially, pathogen specific following culture); I&D must be performed for an abscess inside the bone (i.e., sequestrum) or in surrounding tissue
7. **Complications** = inadequately treated infection can lead to chronic osteomyelitis that is difficult to cure or may require amputation

C. Lyme Disease

1. Caused by *Borrelia burgdorferi*; the organism is delivered through the bite of the *Ixodes* tick
2. **H/P**
   a. Early localized stage: chills, fatigue, arthralgias, headache; **erythema chronicum migrans** (i.e., bull's eye rash), fever (see Figure 5-8)
   b. Early disseminated stage: **myocarditis weeks to months** after infection, cardiac arrhythmias, heart block, **Bell palsy,** sensory-motor neuropathies, aseptic meningitis, or meningoencephalitis
   c. Late disseminated stage: a **few months to years** later, chronic synovitis, **monoarthritis or oligoarthritis,** subacute encephalopathy, or polyneuropathy may develop
3. **Labs** = positive enzyme-linked immunosorbent assay (ELISA) and western blot tests for antibodies; joint aspiration is not helpful
4. **Treatment** = **doxycycline**, amoxicillin, or cefuroxime (oral form can be used in early disease, but IV forms are required in disseminated disease)

V. Rheumatologic Diseases

A. RA

1. Chronic inflammatory disorder with infiltration of synovial joints by inflammatory cells and progressive erosion of cartilage and bone
2. **Synovial hypertrophy** with granulation tissue formation on articular cartilage (i.e., **pannus formation**) caused by joint inflammation
3. Most commonly seen in middle-aged women; increased frequency in people with HLA-DR4 serotype
4. **PIP** and metacarpophalangeal (**MCP**) joints are usually first involved; **symmetric polyarthropathy** develops, involving ankles, knees, shoulders, hips, elbows, and spine
5. **H/P**
   a. Malaise, weight loss, insidious onset of **morning stiffness with pain,** decreased mobility
   b. Warm joints, joint swelling, fevers, ulnar deviation of fingers; MCP hypertrophy, **swan-neck deformities** (i.e., flexed DIP plus hyperextended PIP), **boutonniere deformities** (i.e., flexed PIP), subcutaneous nodules, pleuritis, pericarditis, scleritis

Table 5-5 Immunologic Markers Found in Rheumatic Diseases

Disease	Immunologic Markers
Systemic lupus erythematosus (SLE)	ANA (95% of patients) Anti-dsDNA antibodies (60% of patients) Anti-Sm antibodies False-positive RPR or VDRL (syphilis test)
Drug-induced lupus	Antihistone antibodies ANA
Rheumatoid arthritis (RA)	RF (75% of patients) ACPA ANA (<50% of patients) HLA-DR4 common
Polymyositis or dermatomyositis	ANA Anti-Jo-1 antibodies
Ankylosing spondylitis	HLA-B27 (90% of patients)
Psoriatic arthritis	Possible HLA-B27
Scleroderma	Anti-scl-70 ANA
CREST syndrome	Anticentromere antibodies
Mixed connective tissue disease (MCTD)	Anti-RNP ANA
Sjögren syndrome	Anti-Ro (anti-SSA) ANA Anti-La (anti-SSB) ANA

ANA, antinuclear antibodies; CREST, calcinosis, Raynaud, esophageal dysmotility, sclerodactyly, and telangiectasias; dsDNA, double-stranded DNA; RF, rheumatoid factor; RPR, rapid plasma reagin; VDRL, venereal disease research laboratory test.

6. **Labs**
   a. Rheumatoid factor (RF) positive in 75% of patients but not specific for the disease
   b. Positive anti-citrullinated peptide antibodies (ACPA) is >90% specific for RA
   c. Positive antinuclear antibodies (ANA) in 40% of patients (see Table 5-5)
   d. Joint aspiration shows 5,000 to 50,000 leukocytes

7. **Radiology** = x-rays may demonstrate soft tissue swellings, joint space narrowing, marginal bony erosions, or subluxation; MRI is more sensitive than x-ray for detecting similar findings
8. **Treatment** = **disease-modifying antirheumatic drugs (DMARDs)**
   a. Hydroxychloroquine or sulfasalazine for mild disease
   b. Methotrexate or TNF-α inhibitors (e.g., etanercept, adalimumab) for moderate disease
   c. Leflunomide, anakinra, or combination therapy for severe or refractory disease
   d. Glucocorticoids and NSAIDs may be used for acute flares of arthritis

NEXT
STEP

Check purified protein derivative (PPD) to screen for latent tuberculosis before starting a TNF-α inhibitor.

B. Systemic Lupus Erythematosus (SLE)

1. Multisystem autoimmune disorder involving a variety of autoantibodies affecting several body systems.
2. Antibody-mediated cellular attack occurs with deposition of antigen–antibody complexes in affected tissues.
3. **Risk factors** = young women, Blacks, Asians, Hispanics.
4. Sulfonamides, hydralazine, isoniazid, phenytoin, and procainamide can cause similar symptoms that **resolve** when the **drug is discontinued**.

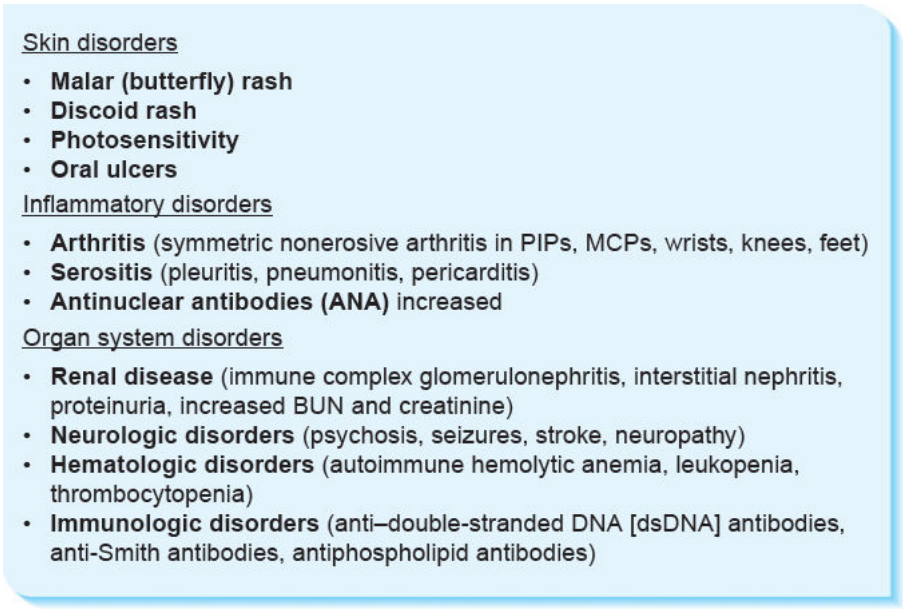


FIGURE 5-9
Diagnostic criteria for systemic lupus erythematosus.
BUN, blood urea nitrogen; MCPs, metacarpophalangeal joints; PIPs, proximal interphalangeal joints.

5. **H/P**
   a. Common findings include malar and discoid rashes, serositis, oral ulcers, arthritis, photosensitivity, CNS symptoms, cardiac symptoms, and renal symptoms (see Figure 5-9).
   b. Can also experience fevers, malaise, weight loss, abdominal pain, vomiting, conjunctivitis, blindness.
   c. Any combination of symptoms is possible and can change during the course of the disease.
6. **Labs**
   a. Positive ANA in 95% of patients (see Table 5-5)
   b. Anti–double-stranded DNA (dsDNA) antibodies found in 60% of patients but not found in other rheumatologic disorders
   c. Presence of anti-Sm antibodies is very specific for disease
   d. Antihistone antibodies may be seen with drug-induced lupus-like symptoms
   e. Patients frequently have a **false-positive test** for **syphilis**
   f. Antiphospholipid (anticardiolipin) antibodies
   g. Decreased complement (C3 and C4)
7. **Treatment** = avoidance of sun, NSAIDs given for pain, hydroxychloroquine improves skin and renal symptoms, corticosteroids given for immunosuppression and to decrease exacerbations, other immunosuppressant drugs given in cases resistant to corticosteroids, anticoagulation required if patient considered hypercoagulable
8. **Complications** = lupus anticoagulant and anticardiolipin antibodies increase the risks of miscarriage and fetal death; disease follows variable course, with some cases remaining benign and others progressing rapidly; patient death results from progressive impairment of lung, heart, brain, and kidney function

Quick HIT

Weakness is a symptom of **polymyositis** but not of polymyalgia rheumatica.

C. Polymyositis and Dermatomyositis

1. Progressive systemic diseases with skeletal muscle inflammation; one-third of patients with polymyositis also have dermatomyositis (i.e., polymyositis with skin manifestations)
2. **Risk factors** = more common in women, Blacks, elderly
3. **H/P**
   a. Symmetric progressive **proximal** muscle weakness (occurs in **legs first**) and myalgias, muscle atrophy in later stages of disease
   b. Cutaneous manifestations of dermatomyositis are a **red heliotropic rash** on the face, upper extremities, chest, or back; violet discoloration of eyelids or scaly patches over hand joints
   c. Patients with lung involvement have dyspnea and poor oxygenation saturation
4. **Labs**
   a. Increased creatinine, aldolase, CK, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and lactate dehydrogenase (LDH)
   b. ANA frequently positive
   c. Anti-Jo-1 antibodies in patients with interstitial lung disease (see Table 9-5)
   d. Muscle biopsy shows inflammatory cells and muscle degeneration, inflammatory cells **within** muscle fascicles in **polymyositis**, and **surrounding** muscle fascicles in **dermatomyositis**
5. **EMG** = spontaneous fibrillations
6. **Treatment** = high-dose glucocorticoids for 4 to 6 weeks followed by a 6- to 12-month taper; azathioprine or methotrexate if unresponsive to glucocorticoids; IV immune globulin or rituximab can be added to regimen in resistant cases
7. **Complications** = possible interstitial lung disease, increased risk of several malignancies

Quick HIT

Patients with PMR will frequently experience significant symptomatic improvement after just 1 day of corticosteroid administration.

D. Polymyalgia Rheumatica (PMR)

1. Rheumatic disease with multiple sites of joint pain and frequently associated with **temporal arteritis;** most common in elderly women (see Chapter 1, **Cardiovascular Disorders**)
2. **H/P** = pain and stiffness in shoulder and pelvic girdle, difficulty raising arms and getting out of bed because of pain, malaise, unexplained weight loss; fever, minimal joint swelling, muscle strength maintained, although movement limited by pain
3. **Labs** = decreased Hct, **markedly increased ESR**, negative RF
4. **Radiology** = MRI demonstrates increased signal at tendon sheaths and synovial tissue outside of joints; positron emission tomographic (PET) scan shows increased uptake in large vessels
5. **Treatment** = low-dose corticosteroids, followed by tapered dosing

NEXT
STEP

Once polymyalgia rheumatica has been diagnosed, the patient should automatically have a workup for **temporal arteritis**.

E. Fibromyalgia

1. Disease causing **chronic pain** in muscles and tendons in absence of apparent inflammation
2. Unknown etiology, but frequently associated with **depression**, anxiety, and irritable bowel disease
3. Possible predisposition with hypothyroidism, RA, sleep apnea; more common in women 20 to 50 years of age
4. **H/P** = myalgias and weakness without inflammation; “trigger points” on examination (i.e., specific locations that when stimulated reproduce pain symptoms), fatigue; possible depression, sleep disturbances, dizziness, headaches, and mood disturbances
5. **Treatment** = stretching, antidepressants (e.g., tricyclic antidepressants [TCAs], selective serotonin reuptake inhibitors [SSRIs]), patient education, physical therapy modalities

F. Ankylosing Spondylitis

1. Chronic inflammatory disease of the **spine** and pelvis that results in eventual bone fusion
2. **Risk factors** = 20 to 40 years of age, male > female, White > Black
3. **H/P**

a. Hip and low back pain that is **worse in the morning** and **following inactivity; pain improves over course of day**
b. Possible limited range of motion in spine, hip, or chest
c. Painful kyphosis that is relieved by bending forward
d. Possible self-limited anterior uveitis

4. **Labs** = positive HLA-B27 in 90% of patients, increased or normal ESR, negative RF, negative ANA (see Table 5-5)
5. **Radiology** = x-ray shows **bamboo spine** (multiple vertebral fusions); MRI shows increased signal in sacroiliac joints and vertebrae
6. **Treatment** = physical therapy, NSAIDs; exercise helps to prevent or delay permanent deformities; sulfasalazine, methotrexate, or anti-TNF drugs may be beneficial in more significant disease; joint replacement may be needed in extremities

G. Psoriatic Arthritis

1. Arthritis that develops in 10% to 20% of patients with **psoriasis**; DIP joints and spine most commonly affected
2. **H/P** = asymmetric joint pain and stiffness, symptoms worse in morning and improve with activity, symptoms usually less severe than RA, possible anterior uveitis; joint line pain, pain with stress on joints, pitting of nails
3. **Labs** = negative RF and ANA, possible positive HLA-B27 (see Table 5-5)
4. **Radiology** = x-rays show findings similar to RA and highly destructive lesions of DIP and PIP joints (i.e., “pencil-in-cup” deformities); MRI is more sensitive in finding marrow edema
5. **Treatment** = NSAIDs, methotrexate, sulfasalazine, or anti-TNF drugs, depending on severity

MNEMONIC

Remember the seronegative spondyloarthropathies (arthritic conditions involving the spine that are negative for rheumatoid factor) by the mnemonic **PAIR**:

Psoriatic arthritis
Ankylosing spondylitis
Inflammatory bowel disease–associated arthritis
Reactive arthritis

H. Scleroderma

1. Chronic multisystem sclerosis with accumulation of connective tissue, skin thickening, and visceral involvement
2. **H/P** = arthralgias, myalgias, hand swelling, **Raynaud phenomenon** (i.e., blue distal extremities caused by arteriolar spasm), **skin thickening, esophageal dysmotility,** intestinal hypomotility, dyspnea, possible arrhythmias or heart failure
3. **Labs** = positive anti-scl-70 ANA (see Table 5-5)
4. **CREST syndrome** is a variant with **C**alcinosis, **R**aynaud phenomenon, **E**sophageal dysmotility, **S**clerodactyly, and **T**elangiectasias
   a. Skin thickening limited to distal extremities and face
   b. Labs show anticentromere antibodies (see Table 5-5)
   c. Better prognosis than scleroderma
5. **Treatment** = supportive care; angiotensin-converting enzyme inhibitors (ACE-I) for malignant renal hypertension; calcium channel blockers and avoidance of caffeine, nicotine, and decongestants to relieve Raynaud symptoms; methotrexate or corticosteroids may improve skin thickening and pulmonary symptoms
6. **Complications** = pulmonary fibrosis, heart failure, acute renal failure caused by malignant renal hypertension

Quick **HIT**

Raynaud phenomenon may prohibit accurate measuring of pulse oximetry via a fingertip probe.

I. Mixed Connective Tissue Disease (MCTD)

1. Overlapping features of SLE, scleroderma, and polymyositis
2. Can progress to a single diagnosis
3. **H/P** = **Raynaud phenomenon,** polyarthralgias, arthritis, swollen hands, proximal muscle weakness, esophageal hypomotility, pulmonary symptoms; absence of renal and neurologic symptoms
4. **Labs** = positive anti-ribonucleoprotein (RNP) ANA (see Table 5-5)
5. **Treatment** = NSAIDs, corticosteroids, ACE-I, supportive measures

J. Sjögren Syndrome

1. Autoimmune disorder with lymphocytic infiltration of exocrine glands
2. Can be seen in association with RA, SLE, or primary biliary cirrhosis
3. **H/P** = **dry eyes, dry mouth,** enlarged parotid glands, purpura on legs, peripheral neuropathy, possible symmetric arthritis associated with other autoimmune conditions
4. **Labs** = positive anti-Ro (anti-SSA) and anti-La (anti-SSB) antibodies (see Table 5-5)

5. **Treatment** = supportive care, corticosteroids for significant symptoms

Quick HIT

Sicca syndrome is Sjögren syndrome **without** a secondary autoimmune association.

NEXT
STEP

Because most bone tumors are metastases and not primary tumors, any patient with a new bone tumor should have a full workup to look for a tumor source.

VI. Neoplasms

A. Bone Metastases

1. **Most common** bone tumors in adults
2. Can result from nearly any primary tumor (most commonly breast, renal cell, prostate, lung, thyroid, lymphoma)
3. **H/P** = presence of primary form of cancer; deep bone pain, possible palpable bone mass, **fractures following minor trauma**
4. **Labs** = biopsy is important to identifying source of metastasis
5. **Radiology** = x-ray identifies lesion in a bone; bone scan suggests extent of metastases in body; MRI useful to determine extent of a lesion
6. **Treatment** = chemotherapy as for primary tumor; bisphosphonates help slow bone loss; radiation therapy helps to decrease metastasis size; fixation of fractures required; prophylactic fixation may be performed for impending fractures

MNEMONIC

Remember the tumors that metastasize to bone by the mnemonic **P**ermanently **R**elocated **T**umors **L**ike **L**ong **B**ones: **P**rostate, **R**enal cell, **T**hyroid, **L**ung, **L**ymphoma, **B**reast.

B. Osteosarcoma

1. Most common **primary** malignant bone tumor; more common in adolescents, male > female
2. Most frequently involves distal femur, proximal tibia, or proximal humerus
3. **Risk factors** = Paget disease of bone, p53 genetic mutations, familial retinoblastoma, radiation exposure, bone infarcts
4. **H/P** = deep bony pain, later development of palpable bony mass
5. **Labs** = increased alkaline phosphatase, increased ESR, increased LDH; biopsy provides definitive diagnosis
6. **Radiology** = x-ray shows bone lesion with a **sunburst** pattern and **Codman triangle** (i.e., periosteal new bone formation at the diaphyseal end of the lesion) (see Figure 5-10); MRI or PET scan useful for determining extent of lesion; chest CT routinely performed to look for metastases
7. **Treatment** = radical surgical excision, chemotherapy
8. **Complications** = 90% 5-year survival rate for low-grade disease, 50% 5-year survival for higher-grade lesions

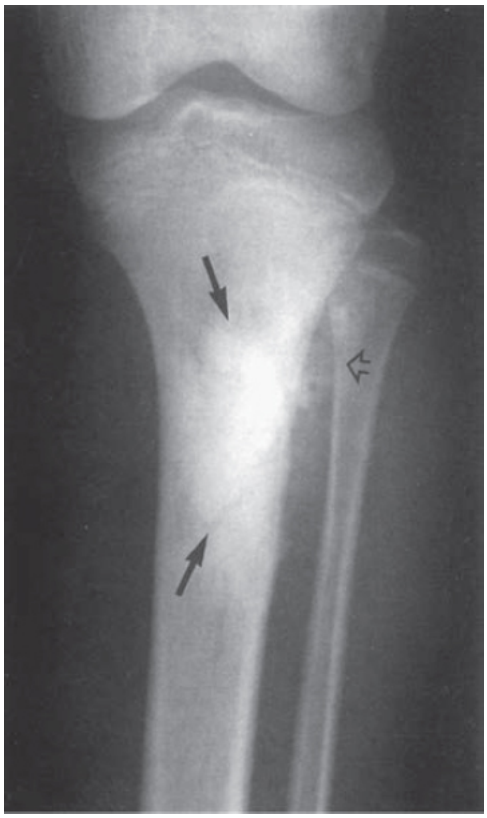


FIGURE **5-10**
Osteosarcoma in left proximal tibia.
Note the dense sunburst pattern of the lesion (*solid black arrows*) and presence of Codman triangle (*open arrow*).
(From Daffner, R. H. & Hartman, M. [2013]. *Clinical radiology: The essentials* [4th ed., p. 357]. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins.)

C. Ewing Sarcoma

1. Highly malignant cartilage tumor occurring in diaphysis of long bones; most common in **children**, 5 to 15 years of age
2. **H/P** = bony pain, tissue swelling, fever, fatigue, weight loss, fractures with minor trauma; possible palpable mass
3. **Labs** = increased WBCs, decreased Hgb, increased ESR; biopsy important for making diagnosis
4. **Radiology** = x-ray may detect large destructive lesions with significant periosteal reaction (Codman triangle, or "onion-skin" bone lesion); MRI determines extent of lesion
5. **Treatment** = radiation, adjuvant chemotherapy, radical excision
6. **Complications** = 60% 5-year survival rate when both radiation and chemotherapy are used in nonmetastatic disease, 20% 5-year survival with metastases

Quick HIT

A bony growth on a long bone that sits on top of cortical bone and is **not continuous** with the normal cancellous bone is concerning for a malignant lesion.

D. Osteochondroma

1. Most common **benign** bone tumor in metaphysis of long bones; more common in patients <25 years of age, male > female
2. Typically occurs in lower femur or upper tibia
3. **H/P** = irritated soft tissues overlying mass, mass itself frequently nontender; palpable hard mass
4. **Radiology** = x-ray shows bony growth off metaphysis of long bone; CT or MRI shows cancellous portion of long bone to be continuous with interior of lesion
5. **Treatment** = none necessary unless causing soft tissue irritation or neurovascular compromise or if continued growth occurs (surgical excision indicated)
6. **Complications** = rare (1%) transformation into chondrosarcoma

QUESTIONS

1. A 30-year-old woman comes to emergency room to be evaluated for 2 months of worsening sharp pain in her left hand. The pain intensifies in afternoons and usually includes the first, second, and third digits of the left hand. These symptoms mildly improve when the hands are shaken. No other areas are hurting or affected. She has tried over-the-counter remedies with little to no benefit. Vitals are normal and physical examination shows tenderness over percussion over volar aspect of writs. The rest of the examination is normal. She denied smoking, drugs, or alcohol. There is also no history of trauma. Which is the best first step for this patient's condition?

   A. Local steroid injection
   B. Surgery for decompression
   C. Oral steroids
   D. Wrist splinting
   E. Nonsteroidal anti-inflammatory drugs (NSAIDs)

2. A 45-year-old fisherman comes via ambulance to the hospital after suffering an accident on his way home. The patient was restrained in a vehicle with no airbag deployment. He remembers the accident vividly and remembers being unable to ambulate in scene. Paramedics noted a left lower-extremity deformity on their transport. In the ED no deformity is noted. However, there is a decreased dorsalis pedis pulse in the left foot. The patient's only complaint is leg pain. The patient can flex the hips with pain. What is the likely cause of this patient's pain and findings?

   A. Knee effusion
   B. Hip dislocation
   C. Knee dislocation
   D. Pelvic trauma

3. A 48-year-old female arrives in the emergency department (ED) with worsening back pain. She has had multiple visits to the ED with similar complaints. Today she claims the pain is different and associated with numbness in her thighs. She denies any recent illness, trauma, or fever. There is no history of surgeries or IV drug abuse. She had a single episode of urinary incontinence when the pain started, which she associated with pain onset. Vital signs are normal. Physical examination reveals a distended bladder. Plain films of the back are unremarkable. What is the most likely cause of back pain?

   A. Epidural abscess
   B. Disk herniation
   C. Cauda equina syndrome
   D. Ankylosing spondylitis

4. A 69-year-old man arrives to a regular oncologic checkup. The patient is currently on his last dose of chemotherapy for prostate cancer. Upon questioning, the patient complained of a mild to moderate onset back pain that is not resolving despite NSAIDs and ice. The patient has had no fever, falls, or mechanical trauma. He initially thought it was a "pulled muscle." Vital signs are normal. The physical examination reveals point tenderness in the lower thoracic spine, loss of sensation below umbilicus, and hyperreflexia at knees. What is the appropriate next step in management for this condition?

   A. Antibiotics and steroids
   B. Radiation therapy
   C. Surgical repair
   D. Biopsy

5. A 58-year-old woman comes to a routine health checkup. She feels well today. She was briefly admitted to a hospital last year for an episode of a rib fracture arising from a strong case of acute bronchitis. She takes no medications and has received no surgical interventions. The patient smoked for 5 years until she was 23 years old and drinks a glass of wine every night. Her vitals in the office are in normal range and her BMI is 35. Physical examination is unremarkable. Which of these is this patient's strongest risk factor for future bone fractures?

   A. Current alcohol use
   B. Smoking history
   C. Obesity
   D. Estrogen deficiency

6. A 58-year-old man comes to the office for a follow-up from a complaint of headaches for the last 3 months. He rides a motorcycle to work and feels the helmet being too tight lately and assumed this was causing his pain. He denies any vision changes, difficulty walking, or any other complaints. Upon laboratory evaluation his alkaline phosphatase is elevated, other tests are normal. A CT scan of the head showed no masses or lesions but showed thickened skull with some lytic lesions. This patient would likely benefit from?

   A. Calcium and vitamin D
   B. Testosterone
   C. Prednisone taper
   D. Radiation therapy

7. A 54-year-old man comes to the emergency department with 3 days of worsening left knee pain. There is associated redness and swelling of the knee. There is no reported trauma or fever, but he has felt some chills today. The pain worsens with weight bearing. Currently he cannot ambulate without assistance. He has past medical history of gout, diabetes, and hypertension. He denies any use of alcohol, drugs, or smoking. In the ED his temperature is 38.5°C and his pulse is 108 bpm. Other vitals are normal. On physical examination the left knee is tender to palpation with localized swelling and no redness. The rest of the examination is normal. Which of the following is the best step in management?

A. Synovial fluid analysis
B. X-ray of the knee
C. Indomethacin and outpatient follow-up
D. Serum uric acid

8. A 28-year-old man comes to the primary care office complaining of lower-extremity pain for 8 days. He suffered a minor fall 10 days ago injuring his left knee anteriorly. Initially he saw a mild abrasion, but was able to ambulate. He has past medical history of sickle cell disease. During the past week, there has been description of fever, and bone pain. X-ray shows no abnormality. Which of the following is the likely organism causing the patient's symptoms?

   A. Pseudomonas sp.
   B. Streptococcus sp.
   C. Borrelia burgdorferi
   D. Salmonella sp.

9. A 40-year-old female comes in to the emergency department brought in by EMS after an motor vehicle collision (MVC) today. The patient was a restrained driver. She was ambulatory on scene. The patient denied loss of consciousness. She recalls the accident happened when the car in front of her suddenly stopped. The car was moving at 10 mph when the accident happened. She has a chronic history of neck and back pain usually worse in the morning. She has midline tenderness of cervical spine and appears to be stiff and angulated forward. She denies this being an acute problem. You decide to perform cervical spine x-rays. What do you expect to see in x-rays?

   A. Pencil in cup deformity
   B. Soft tissue swelling
   C. Bamboo spine
   D. Bilateral facet dislocation

10. A 43-year-old female is being evaluated at the office for chronic pain and swelling of her hands worse in the mornings. The patient feels her fingers have started deforming. She has had subjective fevers and warmth of the hands. There is no report of trauma. There has been no recent trauma, or insect bites. The vital signs are all normal. The x-ray shows soft tissue swelling and joint space narrowing. Physical examination shows a swan-neck deformity of the distal fingers and subcutaneous nodules. Which of the following is the most specific for diagnosing this patient's condition?

    A. Rheumatoid factor (RF)
    B. Anti-citrullinated peptide antibodies (ACPA)
    C. Antinuclear antibodies (ANA)
    D. Anti-Jo antibodies

11. An 18-year-old male comes to the office due to onset of bony pain for 2 months. The pain is localized to the left proximal humerus. He has now noticed a "bump" in his area of pain. He reports no weight loss, fever, trauma, injections at site, insect bites, or swelling. His vital signs are normal. He denied use of alcohol, smoking, or drugs. Physical examination reveals a hard palpable bony mass in the proximal humerus of the left side. LDH, ESR, and alkaline phosphatase are elevated. The rest of the blood work is otherwise normal. An x-ray reveals a lesion at the palpable mass site described as a sunburst pattern by radiologist. What is the most likely diagnosis?

    A. Ewing sarcoma
    B. Osteosarcoma
    C. Bone metastases
    D. Osteomyelitis

12. A 20-year-old man is seen today for a follow-up visit regarding a bony growth happening in his proximal anterior tibia. There is no report of fever, weight loss, night sweats, recent injury, or redness. There is no pain at site. X-ray shows bony growth off metaphysis that is continuous with cortex of long bone with no lesions seen. Blood work is normal. Physical examination is unremarkable and neurovascular status is intact. What is the best treatment for this condition?

    A. Chemotherapy
    B. Radiation
    C. Radical excision
    D. Follow-up outpatient

6
Pulmonary Disorders

I. Measures of Pulmonary Function

A. Pulmonary Function Tests (PFTs)

1. Uses for PFTs
   a. Categorizing various types of lung processes and changes in lung air volumes
   b. Assessing severity of pulmonary disease
   c. Evaluating success of treatment
2. Specific measurements
   a. **Lung volumes** (see Figure 6-1; Tables 6-1 and 6-2)
   b. **Airflow** (see Figure 6-2)
      (1) FEV_1/FVC is ratio of air volume expired in 1 second to functional vital capacity (FEV = forced expiratory volume).
      (2) $FEF_{25–75\%}$ is forced expiratory flow rate between 25% and 75% of FVC.
   c. **Alveolar membrane permeability**
      (1) **Diffusing capacity of lungs,** or D_{Lco}, is a relative measurement of the lungs' ability to transfer gases from alveoli to pulmonary capillaries.
      (2) PFTs usually list D_{Lco} as a percentage of the normal expected value.

Quick HIT

Normal FEV_1/FVC is 80%; <80% suggests obstructive pathology; >110% suggests a restrictive pattern.

Quick HIT

Upper respiratory infections are those that occur in the **sinuses** or **pharynx; lower** respiratory infections are those that occur in the **lungs** or **bronchi.**

Quick HIT

Prescribing antibiotics for viral rhinitis is a contributing factor to the development of resistant strains of bacteria.

B. Alveolar-arterial (A-a) Gradient (See Table 6-3)

1. This measurement compares the oxygenation status of alveoli (PAo_2) to arterial blood (Pao_2).
2. **Normal A-a gradient = 5 to 15 mm Hg.**
3. Increased A-a gradient is seen in pulmonary embolism (PE), pulmonary edema, and right-to-left vascular shunts.
4. False-normal A-a gradient may be seen in cases of hypoventilation or at high altitudes.

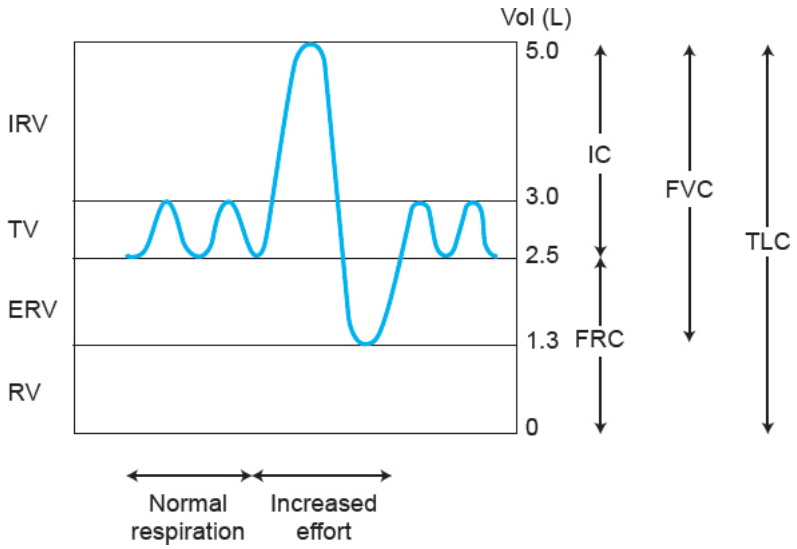


FIGURE 6-1

Healthy lung volumes and variation with effort of breathing.
ERV, expiratory reserve volume; FRC, functional reserve capacity; FVC, functional vital capacity; IC, inspiratory capacity; IRV, inspiratory reserve volume; RV, residual volume; TLC, total lung capacity; TV, tidal volume.

Table 6-1 Definitions of Lung Volume Terms and Formulas

Lung Volume	Definition
Tidal volume (TV)	Inspiratory volume during normal respiration
Inspiratory reserve volume (IRV)	Air volume beyond normal tidal volume that is filled during maximal inspiration
Inspiratory capacity (IC)	Total inspiratory air volume considering both tidal volume and inspiratory reserve volume **(IC = TV + IRV)**
Expiratory reserve volume (ERV)	Air volume beyond tidal volume that can be expired during normal respiration
Residual volume (RV)	Remaining air volume left in lungs following maximal expiration
Functional reserve capacity (FRC)	Air volume remaining in lungs after expiration of tidal volume **(FRC = RV + ERV)**
Functional vital capacity (FVC)	Maximal air volume that can be inspired and expired **(FVC = IC + ERV)**
Total lung capacity (TLC)	Total air volume of lungs **(TLC = FVC + RV)**

Table 6-2 Changes in Pulmonary Function Tests From Normal Lung to Obstructive and Restrictive Disease States

Measurement	Obstructive	Restrictive
TLC	↑	↓
FVC	↓	↓
RV	↑	↓
FRC	↑	↓
FEV_1	↓	↓
FEV_1/FVC	↓ (70%)	Normal or ↑

FEV_1, 1-second forced expiratory volume; FRC, functional reserve capacity; FVC, functional vital capacity; RV, residual volume; TLC, total lung capacity; ↑, increase; ↓, decrease.

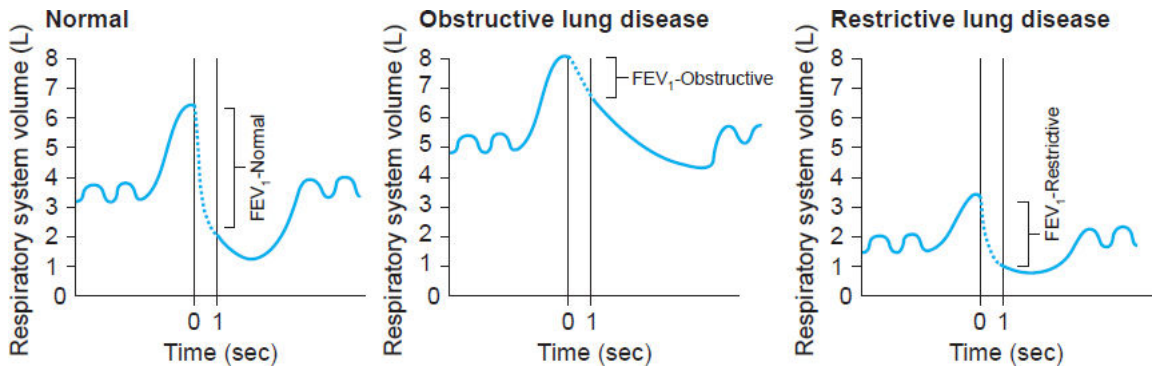


FIGURE **6-2**

Spirometry tracings for normal respiration compared with obstructive and restrictive pulmonary diseases.
FEV_1, 1-second forced expiratory volume.
(Modified from Mehta, S., Milder, E. A., Mirachi, A. J., & Milder, E. [2006]. *Step-Up: A high-yield, systems-based review for the USMLE Step 1* [3rd ed., p. 96]. Philadelphia, PA: Lippincott Williams & Wilkins; with permission.)

Table 6-3 Calculation of the Alveolar-arterial (A-a) Gradient

Variable	Definition	Value
Pao_2	Arterial O_2 content	Measured directly from arterial blood gas sample; normal value is roughly **90–100 mm Hg**
PAo_2	Alveolar O_2 content	Calculated as: $= (\text{Atmospheric air pressure}) \times (FiO_2) - \frac{PaCO_2}{0.8}$ for **room air**, this becomes: $= 713 \text{ mm Hg} \times 0.21 - \frac{PaCO_2}{0.8}$ $= 150 \text{ mm Hg} - \frac{PaCO_2}{0.8}$
$PaCO_2$	Arterial CO_2 content	Measured directly from arterial blood gas sample; normal value is roughly **40 mm Hg**
Fio_2	Fraction of O_2 in inspired air	For room air, this fraction is typically **0.21**
A-a gradient	Difference between alveolar and arterial oxygenation status	$\mathbf{PAO_2 - PaO_2} = 713 \text{ mm Hg} \times 0.21 - \frac{PaCO_2}{0.8} - PaO_2$; **5–15 mm Hg is considered a normal**

Quick HIT

Lemierre syndrome is a suppurative thrombophlebitis of the internal jugular vein thought to spread from pharyngitis caused by *Fusobacterium necrophorum*.

II. Respiratory Infections

A. Upper Respiratory Infections (URIs) (See Figure 6-3)

1. **Common cold (viral rhinitis)**
   a. Inflammation of the upper airways most commonly caused by rhinovirus, coronavirus, influenza, or respiratory syncytial virus
   b. **History and physical (H/P)** = nasal congestion, sore throat, **rhinorrhea, nonproductive cough;** possible fever

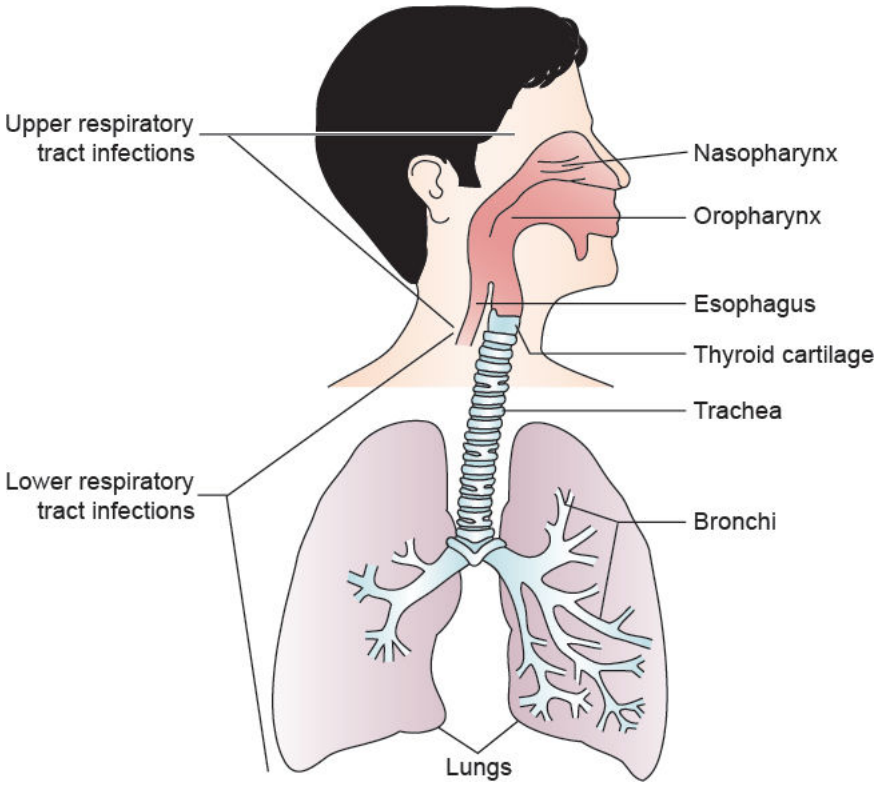


FIGURE 6-3
Diagram of the upper and lower respiratory regions and appropriate sites of infection.

c. **Diagnosis** = diagnosed clinically in the absence of other features suggesting streptococcal pharyngitis, sinusitis, bronchitis, or pneumonia
d. **Treatment** = rest, analgesia, treat symptoms; antibiotics are **not** helpful

2. **Pharyngitis and tonsillitis**
a. Pharyngeal infection caused by group A β-**hemolytic streptococci ("strep throat")** or by viral causes
b. **H/P** = **sore throat,** lymphadenopathy, possible nasal congestion; fever, red and swollen pharynx, **tonsillar exudates** (more common with bacterial infection)
c. **Diagnosis** = **Centor criteria:** used for prediction of streptococcal pharyngitis with one point for each of the following:
(1) **Absence of cough**
(2) **Tonsillar exudates**
(3) **History of fever**
(4) **Swollen tender anterior cervical nodes**
i. 0 or 1 point: no antibiotic or culture needed
ii. 2 to 4 points: rapid streptococcal antigen test should be obtained with antibiotic treatment if positive
d. **Treatment** = self-limited; β-lactam antibiotics (e.g., penicillin, amoxicillin, etc.), steroids such as dexamethasone can decrease illness duration
e. **Complications**
(1) Untreated infection can cause acute rheumatic fever and **rheumatic heart disease;** treatment does not affect the development of poststreptococcal glomerulonephritis (characterized by a high antistreptolysin O titer).
(2) Peritonsillar abscess: collection of purulent material between the palatine tonsil requiring surgical incision and drainage or aspiration.

3. **Viral influenza**
a. Generalized infection with URI symptoms caused by one of several influenza viruses
b. **H/P** = arthralgias, **myalgias,** sore throat, nasal congestion, nonproductive cough, nausea, **vomiting, diarrhea; high fevers** (typically >100°F/37.8°C and can reach up to 106°F/41°C), lymphadenopathy
c. **Labs** = rapid antigen immunoassay of respiratory secretions (nasal swab); polymerase chain reaction (PCR) has better sensitivity but takes several hours
d. **Treatment** = treat symptoms; self-limited (several days), but **oseltamivir** or **zanamivir** may shorten course of disease; annual vaccination is recommended for all persons >6 months old

4. **Sinusitis**
a. Sinus infection is inflammation of the paranasal sinus and nasal cavity, associated with allergic rhinitis, barotrauma, viral infection, prolonged nasogastric tube placement, or asthma
b. **Acute sinusitis** is usually caused by a viral infection. Bacterial causes include *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Moraxella catarrhalis*
c. **Chronic sinusitis** (lasting >3 months) is usually caused by sinus obstruction, nasal polyps, associated with allergic and fungal causes
d. **H/P** = **pain over infected sinuses,** nasal congestion, fever, purulent nasal discharge, maxillary toothache, pain on palpation of affected sinuses; transillumination test (i.e., light held close to sinuses) may detect congestion in frontal of

maxillary sinuses but is **unreliable**

e. **Diagnosis** = clinical diagnosis based on H/P; labs and imaging are not recommended for uncomplicated acute sinusitis. For chronic sinusitis ENT referral for nasal endoscopy is recommended

f. **Treatment**

(1) Acute sinusitis: treat symptoms with analgesics, antipyretics, intranasal corticosteroids; antibiotics such as amoxicillin or amoxicillin/clavulanate for 1 to 2 weeks in acute cases are indicated if suspected bacterial cause; symptoms >10 days, fever >39°C, purulent nasal discharge

(2) Chronic sinusitis: smoking cessation, intranasal corticosteroids, nasal saline irrigation

Quick HIT

Approximately **3%** of untreated streptococcal infections will result in rheumatic heart disease.

Quick HIT

Signs of a peritonsillar abscess include difficulty opening the mouth, asymmetric tonsils, and displacement of the uvula away from the abscess.

Quick HIT

Acute sinusitis can spread cavernous sinus, leading to cavernous sinus thrombosis affecting cranial nerves III, IV, V, VI with patients exhibiting headache and diplopia.

Quick HIT

Sinusitis most commonly affects the maxillary sinuses.

B. Lower Respiratory Infections (See Figure 6-3)

1. **Acute bronchitis**
   a. Inflammation of trachea and bronchi
   b. **H/P** = **cough,** wheezing, rhonchi
   c. **Diagnosis** = clinical diagnosis; chest x-ray (CXR) not indicated unless concerned for pneumonia
   d. **Treatment** = antibiotics not indicated as etiology is viral
2. **Pneumonia**
   a. Infection of the bronchoalveolar tree can be caused by common nasopharyngeal bacteria or bacteria, viruses, or fungi from the surrounding environment; common causes vary by age group (see Tables 6-4 and 6-5)

Table 6-4 Overview of Etiologies of Pneumonia

Pathogen	Patients Affected	Characteristic Symptoms	Treatment
Viral pneumonia			
Viral (influenza, parainfluenza, adenovirus, cytomegalovirus, respiratory syncytial virus)	**Most common pneumonia in children;** common in adults	Classic symptoms[a]; **nonproductive cough**	**Self-limited**
Typical bacterial pneumonia			
Streptococcus pneumoniae	**Most common pneumonia in adults;** higher risk of infection in patients with sickle cell disease	Classic symptoms; high fevers, pleuritic pain, **productive cough**	β-Lactams, macrolides
Haemophilus influenzae	Patients with COPD; higher risk of infection in patients with sickle cell disease	Classic symptoms; **slower onset**	β-Lactams, TMP-SMX
Staphylococcus aureus	Nosocomial pneumonia, immunocompromised patients	Classic symptoms; abscess formation	β-Lactams
Klebsiella pneumoniae	Alcoholics, patients with high risk of aspiration, patients staying in the hospital for extended amounts of time, patients with sickle cell disease	Classic symptoms; **"currant-jelly"** sputum	Both cephalosporins and aminoglycosides (gentamicin, tobramycin)
Pseudomonas aeruginosa	Chronically ill and immunocompromised patients, **patients with cystic fibrosis**, nosocomial pneumonia	Classic symptoms; rapid onset	Fluoroquinolones (ciprofloxacin), aminoglycosides, third-generation cephalosporins
Group B *streptococcus*	Neonates and infants	Respiratory distress, lethargy	β-Lactams
Enterobacter sp.	Nosocomial pneumonia, elderly patients	Classic symptoms	TMP-SMX
Atypical bacterial pneumonia			
Mycoplasma pneumoniae	**Young adults**	Less severe symptoms; possible rash; **positive cold agglutinin test**	Macrolides (azithromycin, clarithromycin, erythromycin)
Legionella pneumophila	Associated with **aerosolized water** (air conditioners)	Slow onset of classic symptoms; nausea, diarrhea, confusion, or ataxia	Macrolides, fluoroquinolones
Chlamydophila pneumoniae	More common in very young and elderly	Slow onset of classic symptoms; frequent sinusitis	Doxycycline, macrolides
Fungal pneumonia			
Fungi	Travelers to **Southwest United States** (coccidioidomycosis), **caves** (histoplasmosis), or Central America (blastomycosis)	Less severe symptoms; subacute disease for initial history	Antifungal agents (amphotericin B, fluconazole [*Coccidioides*], itraconazole [*Histoplasma, Blastomyces*])
Pneumocystis jirovecii	Immunocompromised patients (HIV) (CD4 count <200)	Slow onset of classic symptoms; GI symptoms	TMP-SMX

[a]Classic symptoms = productive or nonproductive cough, dyspnea, chills, night sweats, pleuritic chest pain.

COPD, chronic obstructive pulmonary disease; GI, gastrointestinal; HIV, human immunodeficiency virus; TMP-SMX, trimethoprim-sulfamethoxazole.

Table 6-5 Most Common Etiologies of Pneumonia by Age Group

Age Group	Community Acquired	Nosocomial
Neonatal	Group B streptococcus *Escherichia coli* *Klebsiella pneumoniae* *S. aureus* *Streptococcus pneumoniae*	*Staphylococcus aureus* Group B streptococcus *K. pneumoniae* Respiratory syncytial virus
Infant–5 yrs of age	Respiratory syncytial virus *S. pneumoniae* *S. aureus* *Mycoplasma pneumoniae* *Chlamydophila pneumoniae*	*S. aureus* *K. pneumoniae* Respiratory syncytial virus
5–20 yrs of age	*S. pneumoniae* *M. pneumoniae* *C. pneumoniae* Respiratory syncytial virus	*S. aureus* *K. pneumoniae* Respiratory syncytial virus
20–40 yrs of age	*M. pneumoniae* *S. pneumoniae* Viruses (various) *C. pneumoniae*	*S. pneumoniae* Viruses (various) *S. aureus*
40–60 yrs of age	*S. pneumoniae* *M. pneumoniae*	*S. pneumoniae* *Haemophilus influenzae* *S. aureus* *Enterobacter* spp.
60+ yrs of age	*S. pneumoniae* *H. influenzae* *C. pneumoniae* *S. aureus* *E. coli* Respiratory syncytial virus	*S. pneumoniae* *H. influenzae* *S. aureus* *Enterobacter* spp.

Modified from Mehta, S., Milder, E. A., Mirachi, A. J., & Milder, E. (2006). *Step-Up: A high-yield, systems-based review for the USMLE step 1* (3rd ed., p. 109). Philadelphia, PA: Lippincott Williams & Wilkins; with permission.

b. **H/P** = productive or nonproductive cough, dyspnea, chills, **pleuritic chest pain; decreased breath sounds**, rales, wheezing, **dullness to percussion,** egophony (i.e., change in voice quality heard during auscultation over a consolidated region of lung), tactile fremitus, **tachypnea**
c. **Diagnosis** = CXR may show lobar consolidation, infiltrations, pleural effusion, or general increased density of lung fields. Leukocytosis is common but not specific. Positive sputum culture and possible positive blood culture with bacterial or fungal cause (see Figure 6-4). Atypical bacteria will not be visible on Gram stain and blood culture
d. **Treatment** = viral pneumonia is self-limited and only requires supportive care; bacterial and fungal pneumonias require antibiotics. Initial approach is to determine inpatient versus outpatient treatment. CURB-65 is a clinical decision tool that can be utilized to decide this: 1 to 2 consider inpatient treatment, 3 to 4 = admission
   (1) **C**onfusion
   (2) **U**remia (BUN >19)
   (3) **R**espiratory rate >30/min
   (4) **B**lood pressure (SBP <90 mm Hg or < DBP <60 mm Hg)
   (5) Age >**65**

Organisms are not initially identified, therefore pneumonia is treated empirically with the following:

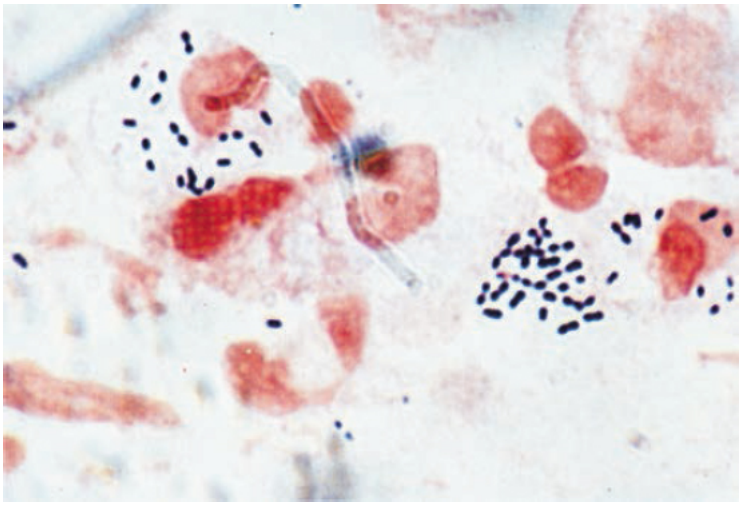


FIGURE 6-4
Paired gram-positive cocci seen in sputum consistent with *Streptococcus pneumoniae* pneumonia.
(From Washington, W., Allen, S., & Janda, W., et al. [2006]. *Koneman's color atlas and textbook of diagnostic microbiology* [6th ed., p. 304]. Philadelphia, PA: Lippincott Williams & Wilkins; with permission.)

3. **Community-acquired pneumonia**
   a. Outpatient:
      (1) Healthy: oral azithromycin or doxycycline
      (2) Comorbidities (CHF, COPD, CKD, diabetes, ETOH, immunosuppression or use of antibiotics within the previous 3 months)
         i. Levofloxacin or moxifloxacin OR
         ii. Amoxicillin/clavulanate PLUS azithromycin or doxycycline
   b. Inpatient:
      (1) Ceftriaxone PLUS
      (2) Azithromycin or doxycycline OR
      (3) Levofloxacin or moxifloxacin
4. **Health care–associated pneumonia (HCAP)** is identified by risk factors as follows:
   a. Hospitalization >2 days within 90 days
   b. IV antibiotic therapy or chemotherapy within 30 days
   c. Nursing home within 90 days
   d. Wound care, tracheostomy care, or ventilator care within 30 days
   e. Chronic dialysis within 30 days
5. All patients with HCAP require inpatient treatment with:
   a. Cefepime or ceftazidime or piperacillin/tazobactam PLUS
   b. Azithromycin or levofloxacin PLUS
   c. Vancomycin or linezolid
6. **Aspiration pneumonia**
   a. Infection of the lung secondary to inhalation of colonized oropharyngeal secretions.
   b. Risk factors include altered consciousness, neurologic disease–causing dysphagia, anatomic abnormalities, and mechanical causes that impair cough reflex, swallowing, and protection of the airway.
   c. **H/P** = indolent presentation of fever, cough, altered mental status, tachypnea, decreased breath sounds, rales.
   d. **Diagnosis** = clinical diagnosis; leukocytosis may be present, but nonspecific. CXR may reveal an infiltrate in gravity-dependent regions of the lung. The posterior segments of the upper lobes and superior segments of the lower lobes are often involved in supine patients. In upright patients, the posterior segments of the lower lobes are involved.
   e. **Treatment** = **b**road spectrum antibiotics covering streptococci and anaerobes such as clindamycin IV or ampicillin/sulbactam IV.

Quick HIT

Symptoms and signs of tuberculosis are more common in **reactivated** disease, and primary disease may be asymptomatic.

7. **Tuberculosis (TB)**
   a. Pulmonary infection caused by *Mycobacterium tuberculosis*

Table 6-6 Criteria Used to Determine Positive PPD for Tuberculosis

Size of Induration[a]	When Considered Positive
5 mm	HIV positive, close contact with TB-infected patient, signs of TB seen on CXR
10 mm	Homeless patients, immigrants from developing nations, IVDA patients, chronically ill patients, health care workers, patients with recent incarceration
15 mm	Always considered positive

[a] Induration is considered the firm cutaneous region and not the region of erythema.
CXR, chest x-ray; HIV, human immunodeficiency virus; IVDA, intravenous drug abuse; PPD, purified protein derivative; TB, tuberculosis.

b. Following primary infection, disease enters inactive state; untreated infections can become reactivated (most active cases) and extend to extrapulmonary sites (i.e., miliary TB)
c. **Risk factors** = immunosuppression (HIV/AIDS), alcoholism, lung disease, DM, advanced age, homelessness, malnourishment, crowded living conditions, and close proximity to infected patients (e.g., **health care workers**); TB is significantly more common in **developing nations** than in the United States
d. **H/P** = cough, hemoptysis, dyspnea, weight loss, night sweats; fever, rales
e. **Diagnosis** = positive purified protein derivative (PPD) tuberculin skin test is screening test for exposure (see Table 6-6); positive sputum acid-fast stain, positive mycobacterial culture (may take weeks, so not useful in planning therapy); one bronchoscopy is considered equal to three sputum samples for specimen collection (see Figure 6-5)
f. **Radiology** = CXR may show apical fibronodular infiltrates (reactivated disease), lower lobe infiltrates (primary lesion), and calcified granulomas/lymph nodes (Ghon complexes)
g. **Treatment** = **respiratory isolation** for any inpatient; report all diagnosed cases to local and state health agencies; **multidrug treatment** initially with isoniazid (INH), rifampin, pyrazinamide, and ethambutol for 2 months, followed by INH and rifampin only for 4 months; give vitamin B_6 with INH to prevent peripheral neuritis; monthly sputum acid-fast tests should be performed during therapy to confirm adequate treatment; treat all patients with an asymptomatic positive PPD with INH for 9 months (or various alternate regimens)
h. **Complications** = meningitis, bone involvement (i.e., Pott disease), widespread dissemination to multiple organs (i.e., miliary TB)

NEXT
STEP

A positive PPD should be followed by a CXR to look for signs of TB.

Quick **HIT**

Recipients of the Bacillus Calmette– Guérin (BCG) vaccine (commonly used in other countries) will show a false-positive PPD.

MNEMONIC

Remember the multidrug regimen for TB as **RIPE** (**R**ifampin, **I**soniazid, **P**yrazinamide, **E**thambutol).

Quick **HIT**

Gram-positive bacteria typically cause community-acquired pneumonia; gram-negative bacteria typically cause nosocomial pneumonia.

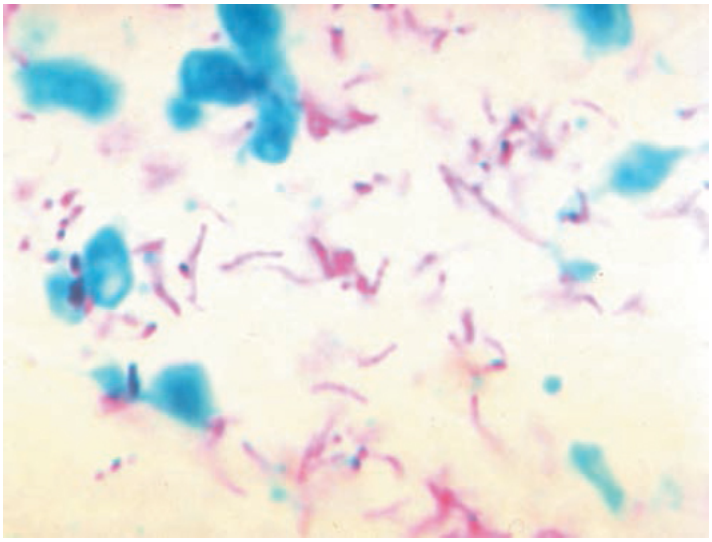


FIGURE 6-5
Numerous acid-fast bacilli seen in pulmonary histologic section consistent with *Mycobacterium tuberculosis* infection.
(From Rubin, R., & Strayer, D. S. [2012]. *Pathology* [6th ed., p. 386]. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; with permission.)

III. Acute Respiratory Distress Syndrome

A. Clinical syndrome of lung injury characterized by **refractory hypoxemia** caused by sepsis, trauma, aspiration, near drowning, drug overdose, shock, or lung infection that exhibits, decreased lung compliance, and bilateral pulmonary edema, and carries a **high mortality**
B. **H/P** = acute dyspnea, tachypnea, hypoxemia with often rapid progression into respiratory failure; wheezing, rales, rhonchi
C. **Diagnosis** = CXR or CT will show bilateral diffuse opacities often with no cardiomegaly. **Pao_2: Fio_2 ratio will be <300**. Brain natriuretic peptide (BNP) will often be low or normal
D. **Treatment** = treatment in **intensive care unit** with mechanical ventilation frequently required; mechanical ventilation should include positive end-expiratory pressure (PEEP), increased inspiratory times, and Fio_2 adjusted to maintain O_2 saturation (Sao_2) >90%; **underlying cause must be treated;** keep fluid volumes low to prevent pulmonary edema; use of extracorporeal membrane oxygenation (ECMO) may improve outcome in severe cases

MNEMONIC

Remember the common causes of ARDS by the acronym ARDS: **A**spiration/**A**cute pancreatitis/**A**ir or **A**mniotic embolism, **R**adiation, **D**rug overdose/**D**iffuse lung disease/**D**IC/**D**rowning, **S**hock/**S**epsis/**S**moke inhalation.

IV. Obstructive Airway Diseases

A. Asthma

1. Chronic inflammatory disorder characterized by reversible airway obstruction with bronchial hyperactivity, mucus plugging, and smooth muscle hypertrophy
2. **Exacerbations** (i.e., sudden bronchoconstriction and airway inflammation) can be triggered by allergens (e.g., dust, smoke, pollen, fumes, pet dander), URI, exercise, stress, β-blockers, and aspirin (rare)
3. **Risk factors** = family history of asthma, allergies, atopic dermatitis, low socioeconomic status
4. Disease can be worse in childhood and improve with age
5. **H/P** = cough, dyspnea, wheezing, chest tightness; tachypnea, tachycardia, **prolonged expiratory duration,** decreased breath sounds, wheezing, **accessory muscle use,** possible pulsus paradoxus (abnormal decrease in systolic blood pressure during inspiration); cyanosis, decreased arterial O_2 saturation (Sao_2) on pulse oximetry, or difficulty talking in severe attacks
6. **Diagnosis**
   a. **Spirometry:** peak expiratory flow rate (PEFR) decreased and used along with clinical symptoms and frequency of medication use to classify disease as mild intermittent, mild persistent, moderate persistent, or severe (see Table 6-8); PFT shows decreased FEV_1, normal/elevated D_{Lco}.
   b. **ABG** not routinely needed for exacerbations; however may show mild hypoxia and respiratory alkalosis. An ABG indicating a normalizing Pco_2 suggests impending respiratory failure.
   c. **CXR** is usually normal, but can show hyperinflation. Routine imaging is not necessary unless there are suspicions of other pathologies.
7. **Treatment** = algorithm of medications depends on classification of disease severity (see Tables 6-7 and 6-8); patient education for avoidance of exacerbating factors and recognition of impending respiratory collapse is important for long-

term control

NEXT
STEP

Status asthmaticus is a prolonged, nonresponsive asthma attack that can be fatal and should be treated with **aggressive** bronchodilator therapy, corticosteroids, epinephrine, magnesium, O_2, and, possibly, intubation.

NEXT
STEP

A normal CO_2 during an exacerbation signals impending respiratory failure and requires additional β_2-agonists, supplemental O_2, and, possibly, ventilation.

MNEMONIC

Patients with **chronic bronchitis** are **"blue bloaters"** because secondary development of cor pulmonale causes cyanosis and peripheral edema; patients with **emphysema** are **"pink puffers"** because of their pursed-lip breathing, dyspnea, and barrel chests.

B. Chronic Bronchitis

1. Chronic bronchial inflammation **associated with tobacco use** (common) or chronic asthma (uncommon); occurs in continuum with emphysema as **chronic obstructive pulmonary disease (COPD)**
2. **H/P** = productive cough, recurrent respiratory infections, dyspnea; wheezing, rhonchi
3. Diagnosis made with history of **productive cough for 3 months of the year for >2 years**

Table 6-7 Commonly Used Medications for Treatment of Asthma

Medication	Mechanism of Action	Role
Rapid-acting β_2-agonists (albuterol, pirbuterol, bitolterol)	Bronchodilators that relax airway smooth muscle; have rapid onset of action	First-line therapy in mild intermittent cases and during exacerbations
Long-acting β_2-agonists (salmeterol, formoterol, sustained-release albuterol)	Bronchodilators that relax airway smooth muscle; have gradual onset and sustained activity	Regular use in patients with moderate persistent or severe asthma
Inhaled corticosteroids (beclomethasone, flunisolide)	Decrease number and activity of cells involved with airway inflammation	Mild persistent or worse cases; frequently combined with β_2-agonist use
Leukotriene inhibitors (montelukast, zafirlukast, zileuton)	Block activity or production of leukotrienes that are involved in inflammation and bronchospasm	Oral agents; adjunctive therapy in mild persistent or worse cases
Theophylline	Bronchodilator	Former first-line therapy, but now replaced by β_2-agonists because of side effects (tachycardia, seizures) and interactions with other drugs; may be useful as adjunct in mild persistent or worse cases
Anticholinergic agents (ipratropium)	Blocks vagal-mediated smooth muscle contraction	Adjunctive therapy in moderate to severe cases
Systemic steroids (methylprednisolone, prednisone)	Similar action to inhaled steroids; stronger effect than inhaled preparation	Adjunctive therapy in severe, refractory cases

4. **Labs** = PFTs show gradually worsening signs of obstructive disease as condition progresses
5. **Treatment** = **tobacco cessation**, antibiotics given for URI because of the greater incidence of a bacterial etiology; bronchodilators and corticosteroids during exacerbations
6. **Complications** = emphysema frequently results without smoking cessation

NEXT
STEP

To differentiate between emphysema and chronic bronchitis, check the $\mathbf{D_{Lco}}$; it is normal in chronic bronchitis but decreased in emphysema.

Table 6-8 Classification of Asthma Severity and Treatment Algorithms

Type	Symptoms	PEFR	Treatment of Exacerbations	Long-Term
Mild intermittent	• ≤2 times/wk • Nocturnal awakening ≤2 times/mo • May only occur during exercise	• When asymptomatic, >80% predicted value	• Inhaled short-acting β_2-agonist as needed • IV corticosteroids if persistent symptoms	• No daily m • May use m known trig
Mild persistent	• Bronchodilator use >2 times/wk • Nocturnal awakening >every 2 wks	• >20% fluctuations over time	• Inhaled short-acting β_2-agonist as needed • IV corticosteroids if persistent symptoms	• Inhaled lo • Consider m leukotrien ylline
Moderate persistent	• Daily symptoms • Daily bronchodilator use • Symptoms interfere with activity • Nocturnal awakening >1 time/wk	• 60–80% predicted value	• Inhaled short-acting β_2-agonist as needed • IV corticosteroids if persistent symptoms	• Inhaled lo corticoste β_2-agonist • Consider l or theophy
Severe	• Symptoms with minimal activity • Awake multiple times/night • Require multiple medications on daily basis	• Wide variations • Rarely >70% predicted value • Associated FEV_1 <60% predicted value	• Inhaled short-acting β_2-agonist as needed • IV corticosteroids if persistent symptoms	• Inhaled hi steroids a β_2-agonist • Consider s roids

FEV_1, 1-second forced expiratory volume; IV, intravenous; PEFR, peak expiratory flow rate.

Quick HIT

The common form of emphysema has a centrilobular distribution, whereas the form associated with α_1-antitrypsin deficiency has a panlobular distribution.

C. Emphysema (Later Stage—COPD)

1. Long-term tobacco use leads to chronic bronchoalveolar inflammation associated with release of proteolytic enzymes by neutrophils and macrophages; **destruction of alveoli and bronchioles** results with panacinar airspace enlargement and a decreased capillary bed
2. Less common form (appears at younger age) caused by α_1-antitrypsin deficiency
3. **H/P** = **dyspnea,** possible productive cough, morning headache; barrel chested, pursed-lip breathing, prolonged expiratory duration, decreased heart sounds, decreased breath sounds, wheezing, rhonchi, accessory muscle use, jugular venous distension (JVD); exacerbations present with worsening symptoms
4. **Diagnosis**
   a. **PFT** shows decreased FEV_1, **decreased FEV_1/FVC,** increased total lung capacity (TLC), decreased PEFR
   b. **ABG** during acute exacerbations shows decreased O_2 and increased CO_2 (beyond a baseline increase already seen in these patients)
   c. **CXR** shows **flat diaphragm, hyperinflated lungs,** subpleural blebs and bullae (i.e., small fluid-filled sacs), and decreased vascular markings
5. **Treatment** = **smoking cessation; supplemental O_2**; inhaled, short-acting β_2-agonists; inhaled anticholinergics; inhaled corticosteroids and long-acting β_2-agonists may be useful in severe cases; antibiotics given for respiratory infections; pneumococcal and influenza vaccines important to reduce infection risk; enzyme replacement may have a role in α_1-antitrypsin deficiency therapy; lung transplant may be an option in late severe disease
6. **Complications** = chronic respiratory decompensation, cor pulmonale, frequent respiratory infections, frequent comorbid lung cancer

NEXT STEP

If a patient with COPD has a resting Sao_2 ≤88%, a home O_2 program should be initiated.

D. Bronchiectasis

1. **Permanent dilation** of small and medium bronchi because of destruction of bronchial elastic components
2. Occurs secondary to **chronic airway obstruction,** chronic tobacco use, TB, fungal infections, severe pneumonia, or cystic fibrosis
3. **H/P** = persistent, productive cough; hemoptysis, frequent respiratory infections, dyspnea; **copious sputum,** wheezing, rales, and hypoxemia
4. **Radiology** = multiple cysts and bronchial crowding seen on CXR; CT shows dilation of bronchi, bronchial wall thickening, and bronchial wall cysts
5. **Treatment** = pulmonary hygiene (e.g., hydration, sputum removal), chest physical therapy; antibiotics when sputum production increases; inhaled β_2-agonists and corticosteroids may reduce symptoms; resection of severely diseased regions of lung indicated for hemorrhage, substantial sputum production, or inviability
6. **Complications** = cor pulmonale, massive hemoptysis, abscess formation

V. Respiratory Neoplasms

A. Solitary Pulmonary Nodule

1. A lung nodule <5 cm diameter may be discovered incidentally on CXR or CT (see Figures 6-6 and 6-7).
2. Can be granuloma, hamartoma, cancer (primary or metastasis), carcinoid tumor, or pneumonia

Quick HIT

Solitary pulmonary nodules are cancerous in 40% of cases.

Quick HIT

Smoking cessation is the only action shown to prevent lung cancer in active smokers (**never smoking** also prevents lung cancer).

B. Lung Cancer

1. Most frequently associated with tobacco use (roughly 90% of cases); can also be caused by occupational exposures (e.g., smoke, asbestos, radon)
2. Classified according to cell lineage and histologic appearance (see Table 6-9)
3. **H/P** = possibly asymptomatic; hemoptysis, cough, dyspnea, chest pain, fatigue, weight loss, frequent pulmonary infections; additional symptoms may accompany **paraneoplastic syndromes** (see Table 6-10); local extension of tumors may result in the following:

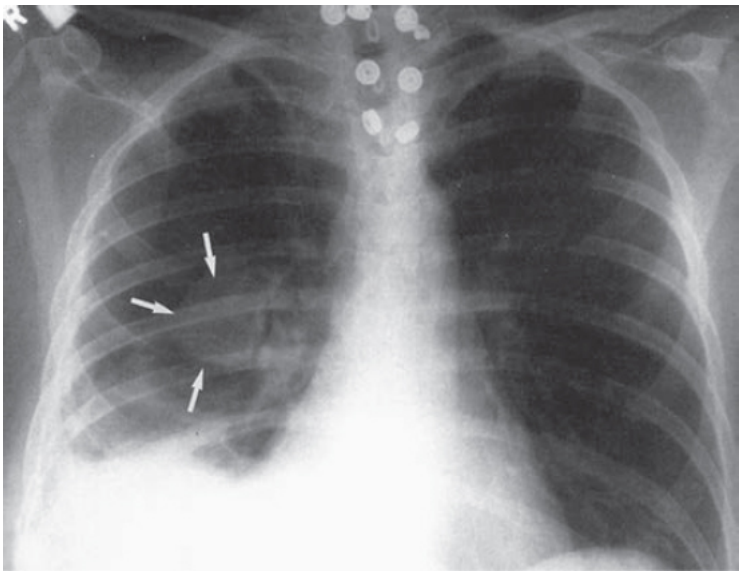


FIGURE 6-6

Chest x-ray demonstrating a solitary pulmonary nodule (*arrows*); in this patient, the finding was determined to be a loculated pleural effusion.

(From Daffner, R. H., & Hartman, M. [2013]. *Clinical radiology: The essentials* [4th ed., p. 116]. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; with permission.)

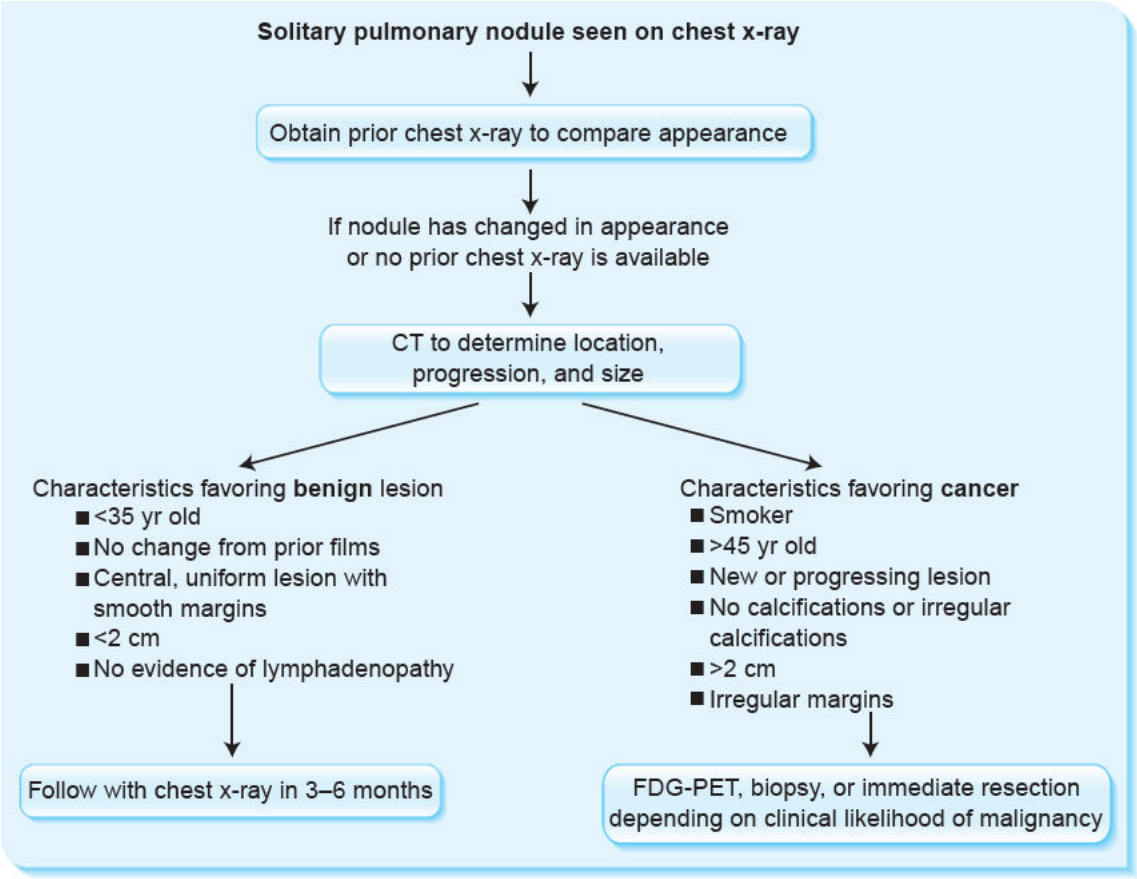


FIGURE 6-7
Workup of the solitary pulmonary nodule.
CT, computed tomography; FDG-PET, fluorodeoxyglucose-positron emission tomography

Quick HIT

Metastases make up 10% of solitary cancerous lesions and are most commonly associated with breast, colon, prostate, endometrial, and cervical cancers.

Quick HIT

Adenocarcinoma is the most common type of lung cancer seen in **nonsmokers**.

a. **Horner syndrome:** miosis, ptosis, and anhidrosis caused by invasion of cervical ganglia
b. **Pancoast syndrome:** Horner syndrome plus brachial plexus involvement
c. **Superior vena cava syndrome:** obstruction of venous drainage through superior vena cava and associated facial swelling and CNS symptoms

4. **Diagnosis** = initially seen on CXR or CT as pulmonary nodule; bronchoscopy with biopsy and brushings or fine needle aspiration of lesion are diagnostic

Table 6-9 Common Types of Primary Lung Cancer

Primary Lung Cancer Type	Primary Malignancies (%)	Location	Characteristics
Squamous cell carcinoma	25–35	Central	Cavitary lesions; direct extension to hilar lymph nodes
Adenocarcinoma	25–35	Peripheral	Wide metastases; can be caused by asbestos; pleural effusions show increased hyaluronidase levels; bronchioloalveolar cancer is a subtype that is low grade and occurs in single nodules
Small-cell carcinoma	20–25	Central	Rapidly growing; early distant metastases; several paraneoplastic syndromes
Large-cell carcinoma	5–15	Peripheral	Late distant metastases, early cavitation

Table 6-10 Common Paraneoplastic Syndromes Associated With Primary Lung Cancers

Primary Lung Cancer Type	Associated Paraneoplastic Syndromes
Squamous cell	Hypercalcemia Dermatomyositis
Adenocarcinoma	Disseminated intravascular coagulation (DIC) Thrombophlebitis Microangiopathic hemolytic anemia Dermatomyositis
Small cell	Cushing syndrome Syndrome of inappropriate ADH secretion (SIADH) Ectopic growth hormone and ACTH secretion Peripheral neuropathy Subacute cerebellar degeneration Lambert–Eaton syndrome (similar presentation to myasthenia gravis) Subacute sensory neuropathy Limbic encephalitis Dermatomyositis
Large cell	Gynecomastia Dermatomyositis

ACTH, adrenocorticotropic hormone; ADH, antidiuretic hormone.

5. **Treatment** = use of **surgical resection, chemotherapy,** and/or **radiation therapy** based on **type** of lung cancer (large cell, squamous cell, or adenocarcinoma vs. small cell) and **staging** disease (based on local extension, lymph node involvement, and presence of metastases) (see Table 6-11)
6. **Complications** = **poor prognosis** (approximately 10% 5-year survival); recurrence for primary tumors

C. Laryngeal Cancer

1. Squamous cell cancer of the larynx **associated with tobacco and alcohol use**
2. **H/P** = **hoarseness that worsens with time** (over several weeks), dysphagia, ear pain, hemoptysis; laryngoscopy may visualize mass and airway obstruction

Table 6-11 Treatment for Lung Cancer Based on Staging Algorithm

Neoplasm Type	Staging	Surgery	Chemotherapy	Ra
Non–small cell (squamous cell, adenocarcinoma, large cell)	No mediastinal invasion, **no lymph node involvement beyond ipsilateral hilar nodes**, no metastases	**Surgical resection** (lobectomy, video-assisted thoracoscopic surgery)	Adjuvant therapy to surgery	Pri ina or the
	No mediastinal invasion or metastases, **has extension to ipsilateral mediastinal nodes**	Consider if significant decrease in tumor size following radiation	Induction therapy if considering surgery or adjuvant to radiation	Pri po pe
	Mediastinal invasion, distant nodes, and/or metastases	None	Palliative	Pal
Small cell	Small lesion, no nodal spread, no metastases	Consider for very small lesions	**Primary therapy**	Ad che
	All other lesions	None	**Primary therapy**	Ad che

3. **Diagnosis**
   a. **Biopsy** is diagnostic
   b. Magnetic resonance imaging (MRI) or CT with contrast detects soft tissue mass; positron emission tomography (PET) may be useful for detecting lesions earlier in disease course
4. **Treatment** = partial or total laryngectomy used to remove lesions confined to larynx; radiation therapy can be used in conjunction with surgery or as sole therapy in extensive lesions; advanced cases may require combination of surgery, radiation, and chemotherapy to resect lesion while preserving surrounding structures

VI. Interstitial Lung Diseases and Other Lung Diseases

A. Idiopathic Pulmonary Fibrosis (IPF)

1. Inflammatory lung disease causing lung fibrosis; it is of unknown cause and generally affects patients >50 years of age
2. **H/P** = progressive exercise intolerance, cough, dyspnea; dry crackles, JVD, tachypnea, and possible digital clubbing
3. **Diagnosis**
   a. PFT = **restrictive lung disease** characteristics (e.g., FEV_1/FVC normal, decreased FVC, decreased TLC, decreased compliance)
   b. Bronchioalveolar lavage = increased polymorphonuclear (PMN) cells
   c. Lung biopsy = extensive fibrosis and loss of parenchymal architecture
   d. CXR = reticulonodular pattern and **"honeycomb"** lung in advanced cases
   e. CT = lung fields with **"ground glass"** appearance
4. **Treatment** = smoking cessation, oxygen, lung transplant is frequently indicated
5. **Complications** = progressive lung fibrosis with frequent mortality within 5 years; most patients do not survive sufficiently long to receive a lung transplant

B. Sarcoidosis

1. Systemic disease characterized by **noncaseating granulomas,** hilar adenopathy, pulmonary infiltrates, and skin lesions; unknown etiology
2. **Risk factors** = blacks > whites; females > males; most frequently occurs between 25 and 45 years of age
3. **H/P** = cough, dyspnea, fatigue, weight loss, arthritis (knees, ankles), chest pain; fever, erythema nodosum (i.e., tender red nodules on shins and arms), lymphadenopathy, vision loss, cranial nerve palsies
4. **Diagnosis**
   a. **Biopsy** = definitive test, should be performed on most accessible organ involved
   b. **CXR/CT** = bilateral hilar lymphadenopathy is **classic**
   c. **PFT** = decreased FVC and decreased D_{Lco}
   d. **Labs** = increased serum angiotensin-converting enzyme (ACE), increased calcium, hypercalciuria, increased alkaline phosphatase, decreased WBC, increased erythrocyte sedimentation rate (ESR)
5. **Treatment** = occasionally self-resolving; corticosteroids in chronic cases; lung transplantation is rarely required (only in severe cases)

C. Pneumoconioses

1. Interstitial lung diseases that result from long-term occupational exposure to substances that cause pulmonary inflammation (see Table 6-12)

2. **H/P** = symptoms begin when significant pulmonary fibrosis has occurred (several years between exposure and onset of symptoms is common); cough, dyspnea on exertion, heavy sputum production; rales and wheezing are heard on auscultation, digital clubbing
3. **Labs** = PFT shows a restrictive pattern
4. **Radiology** = CXR shows multinodular opacities; CT shows signs of pulmonary fibrosis
5. **Treatment** = usually, no successful treatments are available for these conditions; **prevention** (e.g., proper air filters, following safe-handling recommendations) **is vital to avoiding disease**

Table 6-12 Common Pneumoconioses and How to Diagnose Them

Disease	Exposure	Labs	Radiology	Complicati
Asbestosis	Working with insulation, construction, demolition, building maintenance, automobiles	PFT shows restrictive pattern; asbestos fibers seen in **pleural biopsy**[a]	Multinodular opacities, pleural effusions, blurring of heart/diaphragm; chest CT shows linear pleural/parenchymal fibrosis	Increased risk **mesotheliom** synergistic eff
Silicosis	Mining, pottery making, sandblasting, cutting granite	PFT shows restrictive pattern	Small apical nodular opacities; hilar adenopathy	**Increased ris** progressive fib
Coal worker disease	**Coal mining**	PFT shows restrictive pattern	Small apical nodular opacities	Progressive fib
Berylliosis	**Electronics**, ceramics, tool, die manufacturing	Pulmonary edema, diffuse granuloma formation	Diffuse infiltrates; hilar adenopathy	Increased risk need chronic c to maintain res

[a]Not needed for diagnosis with known exposure to asbestos and suggestive radiographic workup.
CT, computed tomography; PFT, pulmonary function test; TB, tuberculosis.

D. Goodpasture Syndrome

1. Progressive autoimmune disease of lungs and kidneys caused by **antiglomerular basement membrane (anti-GBM) antibodies** and characterized by intra-alveolar hemorrhage and glomerulonephritis
2. **H/P** = **hemoptysis,** dyspnea, fatigue, recent respiratory infection
3. **Labs** = positive **anti-GBM antibodies;** urinalysis shows proteinuria, hematuria, and granular casts; renal biopsy shows crescentic glomerulonephritis and IgG deposition along glomerular capillaries
4. **Radiology** = CXR shows bilateral alveolar infiltration
5. **Treatment** = plasmapheresis to remove autoantibodies; corticosteroids, and immunosuppressive agents

E. Granulomatosis With Polyangiitis (Wegener)

1. Rare disease caused by systemic vasculitis that mainly affects lungs and kidneys, causing formation of noncaseating granulomas and destruction of lung parenchyma; previously called Wegener granulomatosis
2. **H/P** = hemoptysis, dyspnea, myalgias, chronic sinusitis; **ulcerations of nasopharynx,** fever; additional symptoms from renal (e.g., mild hematuria), CNS (e.g., hearing loss, sensory neuropathy, cranial nerve dysfunction), ophthalmologic (e.g., conjunctivitis, proptosis, corneal ulceration, diplopia), and cardiac (e.g., arrhythmia) involvement
3. **Diagnosis** = **positive cytoplasmic antineutrophil cytoplasmic antibody (c-ANCA);** biopsy shows **noncaseating granulomas;** renal biopsy detects vasculitic process; hematuria
4. **Treatment** = cytotoxic therapy (e.g., cyclophosphamide), corticosteroids
5. **Complications** = rapidly fatal if untreated

Quick HIT

Patients with sarcoidosis frequently show anergy (no reaction) to a skin test or PPD.

VII. Vascular and Thromboembolic Pulmonary Conditions

A. Pulmonary Embolism

1. Occlusion of pulmonary vasculature by a dislodged thrombus
2. Increasing pulmonary artery pressure caused by occlusion leads to right-sided heart failure, hypoxia, and pulmonary infarction
3. **Risk factors** = **immobilization, cancer,** prolonged travel, recent surgery, pregnancy, oral contraceptive use, hypercoagulability, obesity, fractures, prior DVT, or severe burns
4. **H/P** = **sudden dyspnea,** pleuritic chest pain, cough, hemoptysis, syncope, fever, tachypnea, tachycardia, cyanosis

5. **Diagnosis**
   a. **Labs** = increased D-dimer (indicated in patients with low probability of PE); ABG is nonspecific but may show hypoxia
   b. **Electrocardiogram (ECG)** = sinus tachycardia most common finding, may show S wave in lead I and T-wave inversion in lead III
   c. **Radiology**
      (1) **CXR** = is nonspecific, most common findings are atelectasis, pleural effusions, or an elevated hemidiaphragm. Classic findings include Hampton hump (wedge-shaped opacity) and Westermark sign (focal oligemia).
      (2) **CT angiography** = imaging of choice with a high sensitivity and specificity.
      (3) **Ventilation/perfusion (V/Q) scan** = detects areas of V/Q mismatch, reported in probability. If high probability, then treatment is recommended; if normal, then PE is ruled out. Low and moderate probability PEs do not exclude diagnosis of PE.
      (4) **Pulmonary angiography** = reference standard, but use limited due to invasiveness.
   d. **Treatment** = anticoagulation, multiple options
      (1) **Low–molecular-weight heparin (LMWH)** or **unfractionated heparin** (titrated for PTT 1.5 to 2.5 times normal); patients treated with unfractionated heparin need to be converted to either LMWH or **warfarin** (given to achieve goal international normalized ratio [INR] 2 to 3)
      (2) **Direct oral anticoagulants (DOAC)** = **rivaroxaban, apixaban, dabigatran, and edoxaban**; do not require INR monitoring
      (3) **Inferior vena cava (IVC) filters** can be considered if anticoagulant therapy is contraindicated, if there is recurrence of PE despite anticoagulation, or if patient has poor cardiopulmonary reserve
      (4) **Systemic thrombolytics** = in patients with massive PE (shock/persistent hypotension)

Quick **HIT**

95% of PEs arise from a deep venous thrombosis (DVT) in the leg.

MNEMONIC

Risk factors for PE may be remembered as the 7 **H**s: **H**eredity (genetic hypocoagulability), **H**istory (prior DVT or PE), **H**ypomobility (fracture, prolonged travel, surgery, obesity), **H**ypovolemia (dehydration), **H**ypercoagulability (cancer, smoking), **H**ormones (pregnancy, oral contraceptive pill [OCP] use), and **H**yperhomocysteinemia.

NEXT
STEP

A positive or negative V/Q scan is diagnostic or rules out PE, but an equivocal scan indicates need for further testing.

B. Pulmonary Hypertension

1. Increased mean pulmonary artery pressure (>25 mm Hg at rest) caused by **PE, valvular disease,** left-to-right shunts, COPD, or idiopathic causes
2. **H/P** = dyspnea, fatigue, deep chest pain, cough, syncope, cyanosis; digital clubbing, **loud** S_2, JVD, hepatomegaly
3. **Diagnosis**
   a. **Labs** = increased RBC (polycythemia)
   b. **ECG** = Right ventricular hypertrophy, right-axis deviation
   c. **CXR** = large pulmonary artery and right ventricle
   d. **Echocardiogram** = estimates pulmonary pressures; right ventricular/atrial hypertrophy can be present
   e. **Cardiac catheterization** = gold standard, confirms diagnostic by directly measuring pressures
4. **Treatment** = treat underlying condition; supplemental O_2 helps maintain blood oxygenation; vasodilators indicated for idiopathic and pulmonary causes to decrease pulmonary vascular resistance; anticoagulants indicated in patients with idiopathic, embolic, or cardiac causes to decrease risk of pulmonary thrombus formation

Quick **HIT**

LMWH is an acceptable alternative to heparin and does not require partial thromboplastin time (PTT) monitoring.

C. Pulmonary Edema

1. Increased fluid in lungs caused by increased pulmonary venous pressure and hydrostatic leak of fluid from vessels
2. Caused by **left-sided heart failure**, myocardial infarction (MI), **valvular disease,** arrhythmias, ARDS
3. **H/P** = dyspnea, **orthopnea, paroxysmal nocturnal dyspnea;** tachycardia, frothy sputum, wheezing, rhonchi, rales, dullness to percussion, peripheral edema, S_3 or S_4 heart sound, hypertension
4. **Diagnosis**
   a. **Labs** = increased BNP or abnormal cardiac enzymes help elucidate a cardiac cause

b. **ECG** = T-wave abnormalities or QT prolongation are common changes and can occur suddenly with acute onset
c. **Radiology** = CXR shows fluid throughout lungs, cephalization of vessels (i.e., vascular markings in upper lung fields), and Kerley B lines (i.e., prominent horizontal interstitial markings in lower lung fields)

5. **Treatment** = treat underlying condition; diuretics, salt restriction, O_2, vasodilators; nitrates promote redistribution of fluid in peripheral (rather than pulmonary) vasculature

Quick HIT

A pulmonary wedge pressure measured with a Swan– Ganz catheter is suggestive of a cardiac cause for pulmonary edema if >18 mm Hg and is suggestive of ARDS if <18 mm Hg.

Quick HIT

25% of pleural effusions are associated with neoplasm.

VIII. Pleural Diseases

A. Pleural Effusion

1. Accumulation of fluid in pleural space.
2. **H/P** = dyspnea, cough, pleuritic chest pain, weakness; decreased breath sounds, dullness to percussion, decreased tactile fremitus
3. **Diagnosis**
   a. **CXR** = shows blunting of costophrenic angles; lateral decubitus view can demonstrate if fluid is loculated
   b. **Thoracentesis** = pleural fluid analysis used for protein and LDH levels (i.e., transudate vs. exudates), glucose (low in TB, malignancy, autoimmune diseases), pH (acidic in malignancy, TB, empyema), amylase (high in pancreatitis, esophageal rupture, some malignancies), triglycerides (high in thoracic duct rupture), Gram stain, and cytology (see Table 6-13)
4. **Treatment** = **treat underlying condition;** relieve pressure on lung with thoracocentesis and chest tube placement; for cases with empyema (i.e., effusion of pus due to infection), a chest tube is required; if recurrent malignant effusion occurs, use pleurodesis (talc or other irritant) to scar the pleural layers together

Table 6-13 Distinctive Characteristics and Causes of Types of Pleural Effusions

Effusion	Pleural: Serum Protein Ratio	Pleural: Serum LDH Ratio	Total Pleural LDH	Causes
Transudate	<0.5	<0.6	<2/3 the upper limit of normal serum LDH	CHF, cirrhosis, kidne (nephrotic syndrom
Exudate	>0.5	>0.6	>2/3 the upper limit of normal serum LDH	Infection, cancer, va

CHF, congestive heart failure; LDH, lactate dehydrogenase.

Table 6-14 Types of Pneumothorax and Their Causes

Type of Pneumothorax	Mechanism	Causes
Closed	Internal rupture of respiratory system; chest wall intact	Spontaneous, COPD, TB, blunt trauma
Open	Passage of air through opening in chest wall	Penetrating trauma, iatrogenic (central line placement, thoracocentesis, biopsy)
Tension	Open pneumothorax; "ball-valve" condition allows air to enter but not leave pleural space	Trauma

COPD, chronic obstructive pulmonary disease; TB, tuberculosis.

B. Pneumothorax (PTX)

1. Collection of air in pleural space that predisposes patient to pulmonary collapse
2. Can occur spontaneously (less common) or secondary to trauma or a pulmonary medical condition (more common) (see Table 6-14)
3. **H/P** = **unilateral chest pain,** dyspnea; **decreased chest wall movement,** unilateral decreased breath sounds, increased resonance to percussion, decreased tactile fremitus; respiratory distress, decreased Sao_2, hypotension, JVD, or tracheal deviation suggests tension PTX
4. **Diagnosis**

a. **CXR** = shows lung retraction and mediastinal shift away from affected side; tension PTX will demonstrate tracheal deviation (see Figure 6-8)
b. **Ultrasound** = at bedside, highly sensitive
c. Tension PTX is a clinical diagnosis that should not be delayed by imaging

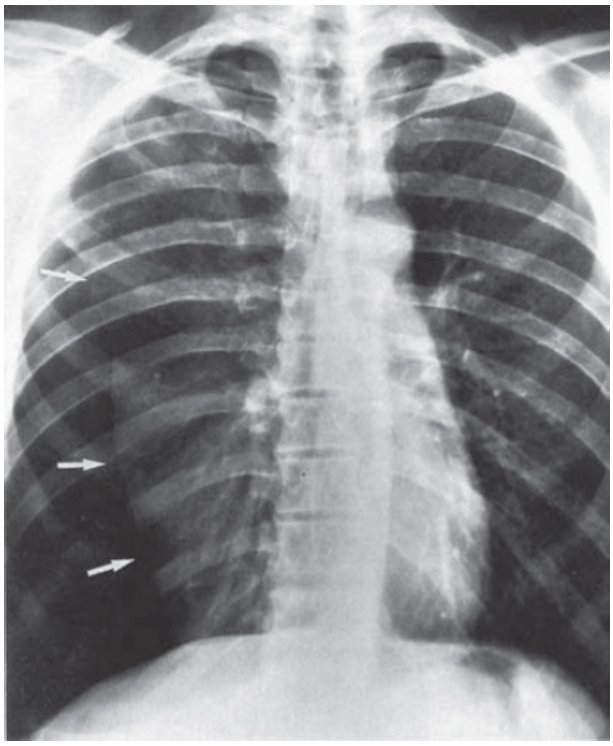


FIGURE 6-8
Chest x-ray demonstrating tension pneumothorax.
Note compressed visceral pleural edge (*arrows*) caused by intrapleural air and tracheal deviation and mediastinal shift toward the left.
(From Daffner, R. H., & Hartman, M. [2013]. *Clinical radiology: The essentials* [4th ed., p. 138]. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; with permission.)

MNEMONIC

Remember the common causes of PTX by the acronym **A CHEST IN: A**sthma, **C**ystic fibrosis, **H**IV (acquired immunodeficiency syndrome [AIDS]), **E**mphysema, **S**pontaneous **T**rauma, **I**atrogenic, **N**eoplasm.

5. **Treatment**
   a. Small (<15% lung field) PTX may resolve with supplemental O_2 only.
   b. Larger (>15%) PTX requires **chest tube placement**.
   c. Open PTX with small wound is treated with chest tube and occlusive dressing.
   d. Tension PTX requires **immediate needle decompression** (4th or 5th intercostal space at the midaxillary line, or the 2nd or 3rd intercostal space at the midclavicular line) and chest tube placement.

***Quick* HIT**

The classic patient for a spontaneous closed pneumothorax is a young, thin, and tall male.

NEXT
STEP

With clinical suspicion for tension pneumothorax, do not wait for a CXR—perform **immediate needle decompression**.

C. Hemothorax

1. Collection of blood in pleural space caused by trauma, malignancy, TB, or pulmonary
2. **H/P** = dyspnea, pleuritic chest pain, weakness; decreased breath sounds, dullness to percussion, decreased tactile fremitus
3. **Diagnosis** = **CXR** resembles that for pleural effusion (i.e., blunting of costophrenic angles); upright preferred over supine

4. **Treatment** = supplemental O_2, chest tube placement; thoracotomy is recommended if there is drainage of >1,500 mL after initial chest tube insertion or continuous drainage of 200 mL/hr over 4 hours
5. **Complications** = exsanguination, empyema; fibrosis can occur if blood is not drained from pleural space

D. Malignant Mesothelioma

1. Uncommon tumor occurring on visceral pleura or pericardium with very poor prognosis
2. **Increased incidence with asbestos exposure** (occurs 20 years after exposure), especially in smokers. Affects mostly men
3. **H/P** = nonpleuritic chest pain, dyspnea; dullness to percussion over lung bases, palpable chest wall mass, scoliosis toward lesion
4. **Diagnosis**
   a. **Pleural biopsy** is usually diagnostic
   b. **CXR** = shows pleural thickening, pleural effusion
   c. **Chest CT** = can display extent of local disease
   d. **PET scan** = can be used to detect extrathoracic disease
5. **Treatment** = extrapleural pneumonectomy with adjuvant chemotherapy and radiation therapy; chemotherapy alone used for unresectable disease

Quick HIT

Malignant mesothelioma is usually secondary to asbestos exposure, but **non–small-cell lung cancer** (such as adenocarcinoma) is far more common than mesothelioma in individuals exposed to asbestos.

IX. Sleep Apnea

A. **Episodic cessation of airflow during sleep leading to desaturations and frequent arousals**
B. **Types**

1. **Obstructive:** obstruction of upper airway during sleep with continued respiratory effort; most often associated with obesity or abnormal pharyngeal anatomy
2. **Central:** loss of central respiratory drive leads to cessation of airflow **and** respiratory effort
3. **Mixed:** combines both obstructive and central characteristics

C. **Risk factors** = obesity, sedative use; males more than females
D. Etiology is unknown but may be linked to abnormal feedback control during sleep or decreased sensitivity of upper airway muscles to stimulation
E. **H/P** = fatigue, excessive daytime sleepiness, snoring, gasping, or choking during sleep, morning headaches or confusion, obesity common, anatomic abnormalities of palate or pharynx may be visible
F. **Diagnosis** = based on clinical signs and symptoms; **polysomnography** = definitive test that measures apnea index (AI; average apneic episodes per hour), Sao_2, and number of arousals
G. **Treatment**

1. **Obstructive** = consider weight loss (possibly bariatric surgery) and stop sedative use; **continuous positive airway pressure (CPAP)** is helpful in chronic cases to maintain airway patency; surgical correction of tonsillar hypertrophy, polyp removal, correction of congenital upper airway deformities, or tracheostomy may be necessary in severe or refractory cases
2. **Central** = respiratory stimulants; phrenic nerve pacemaking may be needed in severe cases

Quick HIT

Bariatric surgery is associated with resolution of sleep apnea in 86% of cases.

X. Pulmonary Surgical Concerns

A. Atelectasis

1. Localized alveolar collapse; **common after surgery and anesthesia** (generally not clinically serious); can also occur in asthmatics, after foreign body aspiration, or from mass effect (e.g., tumors, pulmonary lesions, or lymphadenopathy)
2. **H/P** = asymptomatic if mild or slow development; pleuritic chest pain, dyspnea; fever, decreased breath sounds, dullness to percussion over affected area
3. **Diagnosis** = **CXR** will show fluffy infiltrates in mild cases and lobar collapse in cases of airway obstruction
4. **Treatment** = **incentive spirometry,** ambulation, and inpatient physical therapy are important for prevention in the hospital and postoperatively; severe cases require upper airway suctioning or bronchoscopy with deeper suctioning

Quick HIT

Atelectasis is frequently blamed for postoperative fever, but the relationship is more likely coincidental than causal.

Quick HIT

If atelectasis lasts >72 hours, pneumonia is likely to develop.

B. Intubation

1. Placement of tube into trachea to maintain airway patency and allow mechanical ventilation during anesthesia and times of respiratory distress
2. Almost all intubations are performed **orally** (nasal intubation performed for oral surgery, jaw surgery, and in cases when a laryngoscope cannot help to visualize the vocal cords)
3. **Placement**
   a. Appropriate sedatives ± paralytics administered
   b. Patient positioned with moderate cervical flexion
   c. Laryngoscope inserted into mouth and used to lift jaw and visualize lower pharynx (pressure applied to **cricoid** may aid in visualization)
   d. Endotracheal tube inserted past vocal cords (**direct visualization is important**)
   e. Proper placement is checked by measuring **end tidal CO_2** (rise should follow expiration) and confirming bilateral lung expansion with **auscultation**
   f. Endotracheal tube cuff is inflated, and tube is secured
4. **Complications** = dental injury during placement, placement of tube in esophagus, increased risk of infection
5. If intubation is required for >3 weeks, convert to a **tracheostomy** (i.e., surgical insertion of breathing tube through anterior neck into trachea)

NEXT
STEP

It is important to **visualize** insertion of the endotracheal tube between the vocal cords to reduce the risk of **esophageal** placement.

C. Ventilation

1. Ventilation is assisted respiration that is required during surgery under anesthesia; it may also be required to maintain patent airway or in cases where the patient is not able to breathe without assistance (e.g., neurologic injury, respiratory decompensation, oxygenation failure, decreased respiratory drive).
2. Inspiration is ventilator driven; expiration occurs through natural recoil of the lungs.
3. Tidal volume (TV), respiratory rate, Fio_2, and inspiratory pressure (i.e., pressure forcing each inspiration) may be adjusted depending on patient's respiratory drive, pulmonary compliance, and oxygenation status.
4. Patients are weaned from the ventilator by changing from more patient-independent modes to more patient-dependent modes.
5. **Extubation** (removal of the tube) can be performed when the patient is capable of breathing independently.

QUESTIONS

1. A 70-year-old woman with a history of end-stage renal disease on dialysis presents to the emergency department with a complaint of cough and fever. Her temperature is 38.4°C, heart rate is 115/min, respiratory rate is 32/min, blood pressure is 130/80 mm Hg, and oxygen saturation is 94% on room air. Chest x-ray reveals a left lower lobe infiltrate. What is the correct treatment and disposition for the patient?

   A. IV ciprofloxacin and admit
   B. IV ceftriaxone, IV azithromycin, and admit
   C. Oral doxycycline and discharge
   D. IV cefepime, IV azithromycin, IV vancomycin, and admit
   E. IV cefepime, IV vancomycin, and admit

2. A 32-year-old man with a history of chronic kidney disease presents to his primary care physician with a complaint of cough and congestion for 2 weeks and now with hemoptysis since yesterday. Denies headache, chest pain, and vomiting. Physical examination is remarkable for multiple ulcers in the posterior pharynx and coarse breath sounds bilaterally. What is the most likely diagnosis?

   A. Cystic fibrosis
   B. Lung cancer
   C. Goodpasture syndrome
   D. Granulomatosis with polyangiitis (Wegener)
   E. Pulmonary fibrosis

3. A 30-year-old-male with a history of asthma presents to the emergency department with dyspnea. The patient has had similar episodes in the past. His temperature is 99°F, blood pressure is 120/70 mm Hg, heart rate is 102/min, respiratory rate is 28/min, and oxygen saturation is 93% on 15-L nonrebreather mask. On examination, there is diffuse bilateral expiratory wheezing with intercostal retractions and accessory muscle use. The patient receives nebulized albuterol and ipratropium, IV methylprednisolone, and IV magnesium with minimal relief. What is the next best step?

   A. Intubation
   B. Oral theophylline
   C. Bilateral chest tubes
   D. Nebulized hypertonic saline
   E. IM epinephrine

4. A 22-year-old male presents with acute chest pain and dyspnea following a motor vehicle accident. His heart rate is 130/min, respiratory rate is 30/min, blood pressure is 80/60 mm Hg, and oxygen saturation is 84% on room air. On examination, there are diminished breath sounds along the right lung fields with tracheal deviation to the left. What is the next best step?

   A. Prepare for chest tube
   B. Needle decompression
   C. Chest x-ray
   D. CT scan of chest
   E. Cardiothoracic surgery consultation

5. A 24-year-old male with no medical problems presents to the urgent care center with cough for 5 days. He describes the cough as productive with green sputum. He denies any recent travel, weight loss, fever, night sweats, chest pain, shortness of breath, and leg pain/swelling. Also denies any prison time or recreational drug use. Vital signs are within normal limits. On examination, his breath sounds are clear to auscultation. What is the next step?

   A. Reassurance
   B. Oral azithromycin
   C. Prednisone
   D. CT scan of the chest
   E. Oral doxycycline

6. A 24-year-old woman presents to the pulmonologist for an evaluation of her asthma. She denies fever, night sweats, and weight loss. She is only on an albuterol inhaler as needed. She does admit to lately using albuterol more frequently around 3 to 4 times a week and waking up due to the asthma 2 to 3 times a month. Her vital signs and examination are unremarkable. She has no other concerns. What is the next step?

   A. Reassurance
   B. Start inhaled beclomethasone
   C. Start oral corticosteroids
   D. Start inhaled salmeterol
   E. Start oral montelukast

7. A 55-year-old male presents to the emergency department with a complaint of dyspnea. The dyspnea worsens with exertion and is associated with sharp pleuritic right-sided chest pain. The patient is currently on chemotherapy for colorectal cancer. His heart rate is 120/min, respiratory rate is 26/min, blood pressure is 120/80 mm Hg, oxygen saturation is 93% on room air, and temperature is 99.2°F. Physical examination is unremarkable. What is the next step?

   A. CT angiogram of the chest
   B. Broad spectrum antibiotics
   C. Troponin level
   D. Tube thoracostomy
   E. Bronchoscopy

8. A 78-year-old woman is sent to the emergency department due to dyspnea. A chest x-ray is performed which reveals a pleural effusion to the left chest. A thoracentesis is performed and reveals the following.
   Pleural fluid to serum protein ratio: 0.8
   Pleural fluid to serum LDH ratio: 0.9
   What is the most likely diagnosis?

   A. Congestive heart failure
   B. Pneumonia
   C. Cirrhosis
   D. Fluid overload secondary to kidney disease
   E. Acute respiratory distress syndrome (ARDS)

9. A 38-year-old man with a history of sickle cell disease presents to the clinic with a productive cough and fever. On examination, decreased breath sounds and rales are heard of the right lower lung fields. A chest x-ray is performed which reveals a right lower lobe infiltrate. What is the most likely bacterial cause of this patient's condition?

   A. *Klebsiella pneumoniae*
   B. *Pseudomonas aeruginosa*
   C. *Mycoplasma pneumoniae*
   D. *Streptococcus pneumoniae*
   E. Group B streptococcus

10. A 45-year-old male ICU nurse with no medical problems presents to the employee clinic for a follow-up of his tuberculosis PPD screening. It is interpreted as a positive PPD. The patient denies fever and cough. He does report a 20-lb weight loss over the year and intermittent night sweats. What is the best next step?

    A. Chest x-ray
    B. CT angiogram of the chest
    C. Bronchoscopy
    D. Multidrug treatment with isoniazid, rifampin, pyrazinamide, and ethambutol
    E. Repeat PPD testing

7
Genitourinary Disorders

I. Disorders of the Kidney

A. Pyelonephritis

1. Infection of renal parenchyma most commonly caused by *Escherichia coli; Staphylococcus saprophyticus, Klebsiella*, and *Proteus* are less common pathogens; *Candida* is a potential cause in immunocompromised patients
2. Most commonly occurs as **sequelae of ascending urinary tract infection (UTI)**
3. **Risk factors** = urinary obstruction, immunocompromised, history of previous pyelonephritis, diabetes mellitus (DM), sexual intercourse >three times/week, new sexual partner, spermicide use
4. **H/P** = **fever, vomiting**, flank pain, urinary frequency, dysuria, urgency; **costovertebral tenderness**
5. **Diagnosis** = elevated WBC, **white blood cell casts in urine**; positive urine cultures with $>10^5$ CFU/mL urine
6. **Treatment** = IV cephalosporins (third generation), fluoroquinolones, aminoglycosides as inpatient for severe cases; oral fluoroquinolones, cephalosporins, or cotrimoxazole for 10 to 14 days

Quick HIT

Fluoroquinolones have comparable bioavailability for the oral and IV formulations.

Quick HIT

The **uretero–vesical junction** is the most common site of renal stone impaction.

B. Nephrolithiasis (See Table 7-1)

1. Kidney stones are often only symptomatic when a stone causes an obstruction in the urinary tract.
2. **Risk factors** = family history, prior nephrolithiasis, low fluid intake, frequent UTIs, **hypercalcemia**, **hyperparathyroidism**, certain drugs (e.g., acetazolamide, loop diuretics); males > females.

Table 7-1 Types of Nephrolithiasis (Renal Stones)

Type	Frequency	Cause	Radiology	Notes
Calcium oxalate	72%	**Idiopathic hypercalciuria**, small bowel diseases	Radiopaque	Most patients have no identifiable cause
Struvite ($Mg\text{-}NH_4\text{-}PO_4$)	12%	**Urinary tract infection** (with urease-positive bacteria: *Proteus, Klebsiella*)	Radiopaque	More common in **women**; may form staghorn calculi
Calcium phosphate	8%	**Hyperparathyroidism**, renal tubular acidosis	Radiopaque	
Uric acid	7%	Chronic acidic/concentrated urine, chemotherapeutic drugs, gout	**Radiolucent**	Treat by alkalinizing urine
Cystine	1%	Cystinuria, amino acid transport defects	Radiopaque	May form staghorn calculi

Table 7-2 Common Causes of Hematuria

Age	Temporary Hematuria	Persistent Hematuria
<20 yrs	Idiopathic UTI Exercise Trauma Endometriosis (women)	Glomerular disease
20–50 yrs	Idiopathic UTI Nephrolithiasis Exercise Trauma Endometriosis (women)	Adult polycystic kidney disease Neoplasm (bladder, kidney, prostate) Glomerular disease
>50 yrs	Idiopathic UTI Nephrolithiasis Trauma	Adult polycystic kidney disease BPH (men) Neoplasm (bladder, kidney, prostate) Glomerular disease

BPH, benign prostatic hyperplasia; UTI, urinary tract infection.

3. **H/P** = **acute severe colicky flank pain** that radiates to lower abdomen or groin, vomiting, dysuria; possible gross hematuria.
4. **Diagnosis** = noncontrast CT scan is the test of choice in adults. In children or during pregnancy US is preferred. Urinalysis (U/A) shows hematuria (see Table 7-2). U/A should also be evaluated for infection. BUN and creatinine levels should be obtained.
5. **Treatment** = nonsteroidal anti-inflammatory drugs (NSAIDs) are drug of choice for pain control. Stones <5 mm usually pass spontaneously. Stones 5 to 10 mm may pass spontaneously; if unable to or if patient has intractable pain, extracorporeal shock wave lithotripsy (ESWL) is recommended for ureteral stones <10 mm. Ureteral stones >10 mm may require surgery.
6. **Complications** = infected kidney stones require antibiotics; urgent urology consultation for decompression necessary for patients presenting with signs of sepsis and infected kidney stones.

***Quick* HIT**

Patients with kidney stones should be hospitalized if they have intractable pain and/or vomiting, infected stones, a solitary kidney, or renal failure/insufficiency.

C. Hydronephrosis

1. **Dilation of renal calyces** as a result of increased pressure in the distal urinary tract
2. Caused by increased intrarenal pressure from urinary tract obstruction (e.g., stones, anatomic defects, extraurinary/intraurinary mass)
3. Can lead to permanent damage of renal parenchyma
4. **H/P** = possibly asymptomatic; dull or intermittent flank pain with history of UTI; anuria suggests significant bilateral ureteral obstruction
5. **Diagnosis** = US, CT, or intravenous pyelogram (IVP) detects dilation (see Figure 7-1)
6. **Treatment** = Foley catheter if obstruction is lower tract, drainage via nephrostomy tube; treat underlying obstruction (balloon dilation of ureter and placement of double-J stent in ureter may allow urine flow)
7. **Complications** = renal failure

NEXT
STEP

Rule out bladder or urethral obstruction in an anuric patient by attempting bladder catheterization.

***Quick* HIT**

10% to 15% of patients with polycystic kidney disease develop a **subarachnoid hemorrhage**.

D. Polycystic Kidney Disease

1. Hereditary syndrome characterized by the formation of multiple cysts in one or both kidneys leading to eventual chronic kidney disease (CKD) with progression to end-stage renal disease (see Figure 7-2)

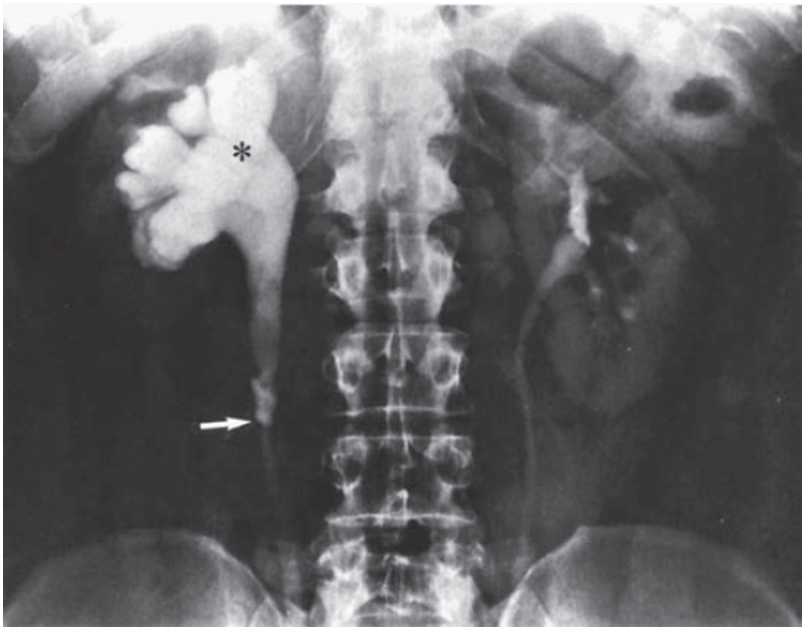


FIGURE 7-1
Intravenous pyelogram demonstrating hydronephrosis in the right kidney (*asterisk*); renal pelvis dilation is evident as is a radiopaque stone in the right ureter (*arrow*); the left kidney appears normal.
(From Daffner, R. H., & Hartman M. [2013]. *Clinical Radiology: The Essentials* [4th ed., p. 315]. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins.)

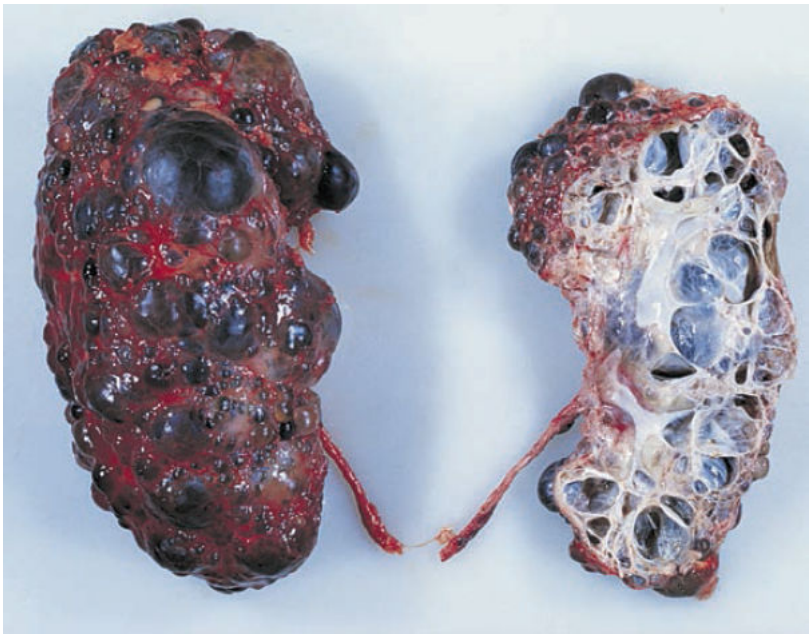


FIGURE 7-2
Autosomal dominant polycystic kidney disease.
Note enlargement of the kidney with many cysts of various sizes.
(From Rubin R., & Strayer, D. S. [2012]. *Rubin's Pathology* [6th ed., p. 759]. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; with permission.)

2. Types
   a. **Autosomal dominant: most common form**; affects **adults**; large multicystic kidneys that function poorly
   b. **Autosomal recessive**: rare form; presents in **children**; fatal in initial years of life (without transplant)
3. **H/P** = asymptomatic until adulthood (dominant form); flank pain, abdominal pain, chronic UTI, gross hematuria; large, palpable kidneys; hypertension; symptoms exacerbated by cyst rupture
4. **Diagnosis** = US is preferred; CT and MRI can be considered. All modalities will reveal **large multicystic kidneys**; genetic testing can also be done
5. **Treatment** = no treatment exists to reverse disease progression; blood pressure control and treatment of UTIs can slow progression. Ultimately patients who progress to end-stage renal disease will require either transplantation or dialysis
6. **Complications** = end-stage renal disease, hepatic cysts, intestinal diverticula, intracranial berry aneurysms, subarachnoid hemorrhage

Quick HIT

Malignancies that cause increased erythropoietin: hepatocellular carcinoma, pheochromocytoma, and hemangioblastoma

E. Renal Cell Carcinoma

1. Most common primary malignant neoplasm of renal parenchyma
2. **Risk factors** = **tobacco smoking**, obesity, hypertension
3. **H/P** = often detected incidentally on abdominal imaging; flank pain, weight loss; abdominal mass, HTN, hematuria
4. **Diagnosis** = CT is test of choice. MRI and US are alternatives. Biopsy can be considered, if surgical resection is not performed. Labs can show a polycythemia (secondary to increased erythropoietin activity); U/A shows hematuria
5. **Treatment** = nephrectomy or renal-sparing resection with lymph-node dissection (typically performed without biopsy for solid mass with adequate radiographic imaging); immunotherapy, radiation therapy, and chemotherapy used for metastatic or unresectable disease but infrequently improve survival
6. **Complications** = poor prognosis if not caught in early stages; early recognition significantly improves prognosis

F. Interstitial Nephropathy (Acute Interstitial Nephritis)

1. Immune-mediated tubulointerstitial injury caused by **drugs, toxins**, infection, or autoimmune processes
2. Most common causes are medications that include antibiotics, NSAIDs, allopurinol, proton pump inhibitors (PPIs), and diuretics (in addition to several other drugs)
3. **H/P** = symptoms of acute kidney injury (AKI), nausea, vomiting, malaise, arthralgia, rash; fever
4. **Labs** = increased Cr and BUN, eosinophilia; U/A may show eosinophils, pyuria, hematuria, and WBC casts; renal biopsy shows infiltration of inflammatory cells and renal tubular necrosis
5. **Treatment** = stop offending agent; supportive care until renal recovery; corticosteroids may be beneficial in refractory cases
6. **Complications** = **acute tubular necrosis (ATN)**, renal failure

II. Glomerular Diseases

A. Nephritic Syndromes (See Table 7-3)

1. Acute **hematuria** and proteinuria that result secondary to **glomerular inflammation**
2. **H/P** = varies with pathology; oliguria and gross hematuria (evidenced by brown urine) are common
3. **Labs** = vary with pathology; increased BUN, increased Cr; hematuria and proteinuria seen on U/A; 24-hour urine collection measures protein as <3.5 g/day
4. **Treatment** = varies with pathology; dialysis or renal transplantation may be required in cases of renal failure

Quick HIT

Both nephritic and nephrotic syndromes involve diseases of the glomeruli; they are differentiated by the absence (nephritic) or presence (nephrotic) of proteinuria >3.5 g/day.

B. Nephrotic Syndromes (See Table 7-4)

1. Significant proteinuria **(>3.5 g/day**) associated with hypoalbuminemia and hyperlipidemia
2. Frequently subsequent to glomerulonephritis
3. **H/P** = varies with pathology; generally **edema**, foamy urine, dyspnea, hypertension, ascites
4. **Labs** = vary with pathology; generally decreased albumin and hyperlipidemia; proteinuria >3.5 g/day seen on 24-hour urine collection
5. **Treatment** = varies with pathology; frequently includes diuretics and dietary salt and protein restriction

Table 7-3 Nephritic Syndromes

Type	Pathology	H/P	Labs	Treatment
Postinfectious glomerulonephritis	Sequelae of systemic infection (most commonly **group A streptococcus**)	Recent infection, oliguria, edema, brown urine, hypertension; more common in **children**	Hematuria and proteinuria in urinalysis, high antistreptolysin O titer, **subepithelial "humps"** of IgG and C3 on renal basement membrane on electron microscopy	Self-limited, supportive treatment (decrease edema and hypertension)
IgA nephropathy (Berger disease)	Uncertain but may be related to infection; deposition of IgA immune complexes in mesangial cells	Hematuria, flank pain, low-grade fever	**Increased serum IgA**, mesangial cell proliferation on electron microscopy	Occasionally self-limited; give ACE-I and statins for persistent proteinuria; give corticosteroids if nephrotic syndrome develops
Goodpasture syndrome	Deposition of antiglomerular and antialveolar basement membrane antibodies (renal disease is a subtype of rapidly progressive (crescentic) glomerulonephritis [RPGN])	Dyspnea, hemoptysis, myalgias, hematuria	**Serum IgG antiglomerular basement membrane antibodies**, anemia, pulmonary infiltrates on CXR, **linear pattern of IgG antibody deposition** on fluorescence microscopy of glomeruli	Plasmapheresis, corticosteroids, immunosuppressive agents; can progress to renal failure
Alport syndrome	Hereditary defect in collagen IV in basement membrane	Hematuria, symptoms of renal failure, **high-frequency hearing loss**, **eye disease** (cataracts, lenticonus)	Red cell casts, hematuria, proteinuria, and pyuria on urinalysis; **"split basement membrane"** on electron microscopy	Variable prognosis with no therapy identified to halt cases of renal failure; ACE-I may reduce proteinuria; renal transplant may be complicated by Alport-related development of Goodpasture syndrome
RPGN	**Rapidly progressive renal failure** from idiopathic causes or associated with other glomerular diseases or systemic infection	Sudden renal failure, weakness, nausea, weight loss, dyspnea, hemoptysis, myalgias, fever, oliguria	Deposition of inflammatory cells and eventually fibrous material in Bowman capsule, and crescent formation (basement membrane wrinkling) on electron microscopy; pauci-immune RPGN is ANCA1	Poor prognosis with rapid progression to renal failure; corticosteroids, plasmapheresis, and immunosuppressive agents may be helpful; renal transplant frequently required
Lupus nephritis (mesangial, membranous, focal proliferative, and diffuse proliferative types)	Complication of systemic lupus erythematosus involving proliferation of endothelial and mesangial cells	Possibly asymptomatic, possible hypertension or renal failure; may develop nephrotic syndrome	**ANA, anti-DNA antibodies**; hematuria and possible proteinuria on urinalysis	Corticosteroids or immunosuppressive agents can delay renal failure; ACE-I and statins help reduce proteinuria
Granulomatosis with polyangiitis (Wegener)—also see Chapter 6, Pulmonary Disorders	Similar to crescentic disease with addition of **pulmonary involvement** granulomatous inflammation of airways and renal vasculature	Weight loss, respiratory symptoms, hematuria, fever	**c-ANCA**; deposition of immune complexes in renal vessels seen on electron microscopy; pulmonary biopsy helpful in diagnosis	Corticosteroids, cytotoxic agents (cyclophosphamide); variable prognosis

ACE-I, angiotensin-converting enzyme inhibitor; ANA, antinuclear antibody; ANCA, antineutrophil cytoplasmic antibody; c-ANCA, cytoplasmic antineutrophil cytoplasmic antibody; CXR, chest x-ray; H/P, history and physical.

Table 7-4 Nephrotic Syndromes

Type	Pathology	H/P	Labs	Treatment
Minimal change disease	Idiopathic; may involve effacement (flattening) of foot processes on basement membrane	Possible hypertension, increased frequency of infections; most common cause of nephrotic syndrome in **children**	Hyperlipidemia, hypoalbuminemia; proteinuria on urinalysis; flattening of basement membrane foot processes seen on electron microscopy	Corticosteroids, cytotoxic agents
Focal segmental glomerular sclerosis	Frequently idiopathic or associated with drug use or **HIV**; segmental sclerosis of glomeruli	Possible hypertension; most common cause of nephrotic syndrome in **adults** in the United States (especially in Blacks and Latinos)	Hyperlipidemia, hypoalbuminemia; hematuria and high proteinuria on urinalysis; sclerotic changes seen in some glomeruli on electron microscopy	Corticosteroids, cytotoxic agents, ACE-I, statins; progressive cases that require renal transplant (uncommon) frequently have recurrence
Membranous nephropathy	Idiopathic or associated with infection, systemic lupus erythematosus, neoplasm, or drugs; thickening of basement membrane	Edema, dyspnea; history of infection or medication use may lead to diagnosis; associated with hepatitis B and C	Hyperlipidemia, hypoalbuminemia; proteinuria on urinalysis; **"spike and dome" basement membrane thickening** on electron microscopy	Corticosteroids, cytotoxic agents, ACE-I, statins; variable rates of renal failure and renal vein thrombosis (requires anticoagulation)
Membranoproliferative glomerulonephritis	Idiopathic or associated with infection or autoimmune disease; thickening of basement membrane; associated hepatitis B and C, SLE, and subacute bacterial endocarditis	Edema, HTN; history of systemic infection or autoimmune condition; gradual progression to renal failure	Hyperlipidemia, hypoalbuminemia, possible hypocomplementemia; proteinuria and possible hematuria on urinalysis; IgG deposits may be seen on basement membrane on fluorescence microscopy; **basement membrane thickening with double-layer "train track" appearance** on electron microscopy	Corticosteroids combined with either aspirin or dipyridamole may delay progression to renal failure
Diabetic nephropathy (diffuse, nodular)	Basement membrane and mesangial thickening related to diabetic vascular changes	History of DM, hypertension, progressive renal failure	Hyperlipidemia, hypoalbuminemia; proteinuria on urinalysis; basement membrane thickening on electron microscopy seen in both types; round nodules (**Kimmelstiel–Wilson nodules**) seen within glomeruli in nodular type	Treat underlying DM; dietary protein restriction; ACE-I; tight blood pressure control
Amyloidosis	Deposition of amyloid protein fibrils in glomeruli and/or renal vasculature; may also involve many other tissues (heart, GI tract nerve tissue, etc.)	Edema, may progress to renal failure; other findings depend on extrarenal tissues involved	Hyperlipidemia, hypoalbuminemia, may have elevated creatinine; proteinuria on urinalysis; Congo red stain of biopsy shows **apple-green birefringence** on polarized light	Melphalan, hematopoietic stem cell transplant, renal transplant

ACE-I, angiotensin-converting enzyme inhibitor; DM, diabetes mellitus; GI, gastrointestinal; H/P, history and physical; HTN, hypertension; SLE, systemic lupus erythematosus.

III. Renal Failure

A. Acute Kidney Injury (AKI)

1. Sudden decrease in renal function resulting from prerenal, intrarenal, or postrenal causes
   a. Prerenal
      (1) Decreased renal perfusion
      (2) Shock: cardiogenic, septic, anaphylactic, hemorrhagic
      (3) Hypovolemia: dehydration, diuretics
      (4) Structural: renal artery stenosis, abdominal aortic aneurysm

Table 7-5 Differentiating by Laboratory Values Between Prerenal, Renal, and Postrenal Failure

Lab	Prerenal	Renal	Postrenal
FENa	<1%	>1%	>1%
Urine Na (mEq/L)	<20	>40	>40
BUN:Creatinine	>20	<20	<20

Table 7-6 Urinalysis Abnormalities Matched With Renal Pathology and Location

Urinalysis	Location	Cause
RBC casts	Glomerular	Nephritic syndrome
WBC casts	Interstitium	Interstitial nephritis Pyelonephritis
Eosinophils	Interstitium	Interstitial nephritis
Granular casts	Tubule	ATN
Hyaline casts	Prerenal or postrenal	Prerenal or postrenal failure

ATN, acute tubular necrosis; RBC, red blood cells; WBC, white blood cells.

b. Intrinsic renal
   (1) Tubular: ATN is the most common cause of intrinsic renal failure. Causes include prolonged ischemia (prerenal causes), toxins (medications, contrast media), rhabdomyolysis
   (2) Glomerular: acute glomerulonephritis (see above)
   (3) Interstitial: acute interstitial nephritis (see above)
c. Postrenal = obstruction of urethra (BPH), bladder, bilateral ureters, bilateral kidneys from stones, tumors, and adhesions (see Tables 7-5 and 7-6)

2. **H/P** = may initially be asymptomatic; fatigue, anorexia, nausea, oliguria, gross hematuria, flank pain, or mental status changes; hypertension, fever, edema
3. **Labs** (see Table 7-5)
4. **Radiology** = US, CT, IVP, or renal angiography may be useful to detect masses, hydronephrosis, abnormal blood flow, obstruction, or vasculitis
5. **Treatment** = prevent fluid overload, stop drugs causing ATN; dietary protein restriction, corticosteroids, dialysis

NEXT
STEP

The BUN:creatinine ratio is a quick way to help determine the cause of AKI (**ratio >20 if prerenal cause**).

***Quick* HIT**

CKD does not occur until >90% of the renal parenchyma is sclerosed or necrotic.

B. Chronic Kidney Disease (CKD)

1. Progressive damage of renal parenchyma that is present for more than 3 months
2. Causes include diabetes, hypertension, and glomerulonephritis
3. **H/P** = gradual development of uremic syndrome (i.e., changes in mental status, decreased consciousness, HTN, pericarditis, anorexia, nausea, vomiting, gastrointestinal [GI] bleeding)
4. **Labs** = Increased Cr and BUN. Increased K^+, decreased Na^+, increased phosphate, decreased Ca^{2+}, anemia, metabolic acidosis, proteinuria
5. **Radiology** = US may show hydronephrosis or shrunken kidneys
6. **Treatment** = control blood pressure and diabetes, restrict dietary salt and protein, correct electrolyte abnormalities, treat underlying condition; dialysis or renal transplant may be needed in progressive cases
7. **Complications** = end-stage renal disease, renal osteodystrophy (i.e., bone degeneration secondary to low serum Ca^{2+}), severe anemia (caused by decreased erythropoietin)

C. Dialysis

1. Induced filtering of blood required when kidney function is inadequate or serum composition increases risk of mortality
2. Types
   a. **Hemodialysis:** machine filters blood and returns filtered plasma to vasculature; synthetic grafts or surgical arteriovenous fistulas in the forearm are utilized for access
   b. **Peritoneal dialysis**
      (1) Dialysate fluid pumped into peritoneum via a permanent catheter
      (2) Substances in the blood diffuse across the peritoneum from the surrounding vasculature to the dialysate fluid according to osmotic drive (peritoneum serves as a filter)
      (3) Dialysate fluid containing solutes is pumped out of peritoneal cavity
3. **Indications** = refractory hyperkalemia, severe metabolic acidosis, refractory fluid overload, symptomatic uremia
4. **Complications** = infection at access sites, fluid overload with dyspnea

IV. Acid–Base Disorders

A. Renal Tubular Acidosis (See Table 7-7)

1. Abnormalities in renal tubular H^+ secretion or HCO_3^- reabsorption
2. Leads to nonanion gap metabolic acidosis

Table 7-7 Characteristics of Types of Renal Tubular Acidosis

	Distal (Type 1)	Proximal (Type 2)	Low Renin/Aldo
Defect	Impaired H1 secretion leading to secondary hyperaldosteronism	HCO_3^- reabsorption	Primary or secondar
Cause	Idiopathic, autoimmune diseases, drugs, chronic infection, nephrocalcinosis, cirrhosis, SLE, obstructive nephropathy	Idiopathic, multiple myeloma, Fanconi syndrome, Wilson disease, amyloidosis, vitamin D deficiency, autoimmune diseases	Primary renin or ald **DM**, Addison diseas interstitial disease
Urine pH	>**5.3**	<5.3	<5.3
Serum electrolytes	Low K^+, variable HCO_3^-	Low K^+, low HCO_3^-	**High** K^+, high Cl^-
Radiology	Possible **stones**	**Bone lesions**	
Treatment	Oral HCO_3^-, K^+, thiazide diuretic	Oral HCO_3^-, K^+; thiazide or loop diuretic	Fludrocortisone, K^+

DM, diabetes mellitus; SLE, systemic lupus erythematosus.

B. Acid–Base Physiology

1. In a healthy person, serum pH is regulated by **HCO_3^-** reabsorption (proximal tubule of kidneys) and blood **Pco_2** (respiratory activity)
2. In a healthy person:
   a. pH = 7.40
   b. Pco_2 = 40 mm Hg
   c. Po_2 = 100 mm Hg
   d. HCO_3^- = 24 mEq/L
3. Pco_2 and pH can be measured with arterial blood gas; HCO_3^- is calculated by the Henderson–Hasselbach equation:

$$pH = pKa + \log\left(\frac{HCO_3^-}{0.03 \times PCO_2}\right)$$

4. pH >7.42 → alkalosis; pH <7.3 → acidosis
5. Disturbances because of **HCO_3^-** abnormalities are metabolic; disturbances caused by **Pco_2** levels are **respiratory**
6. For any disturbance, the body tries to compensate and normalize serum pH

MNEMONIC

Remember the causes of high anion gap metabolic acidosis by the mnemonic **MUD PILES**:

Methanol
Uremia
Diabetic ketoacidosis
Propylene glycol
Isoniazid/**I**ron
Lactic acidosis
Ethylene glycol
Salicylates

C. Acid–Base Disturbances (See Figure 7-3, Table 7-8)

1. **Anion gap**
   a. Difference between serum Na^+ and Cl^- and HCO_3^- ion concentrations
   b. **Anion gap = $[Na^+]$ - $[Cl^-]$ - $[HCO_3^-]$** (normal = 8 to 12)

c. Normal anion gap acidosis suggests HCO_3^- loss
d. Increased anion gap acidosis suggests H^+ excess

2. **Mixed disorder**
a. Combination of multiple acid–base disturbances
b. Detected when corrected, HCO_3^- is different from measured value

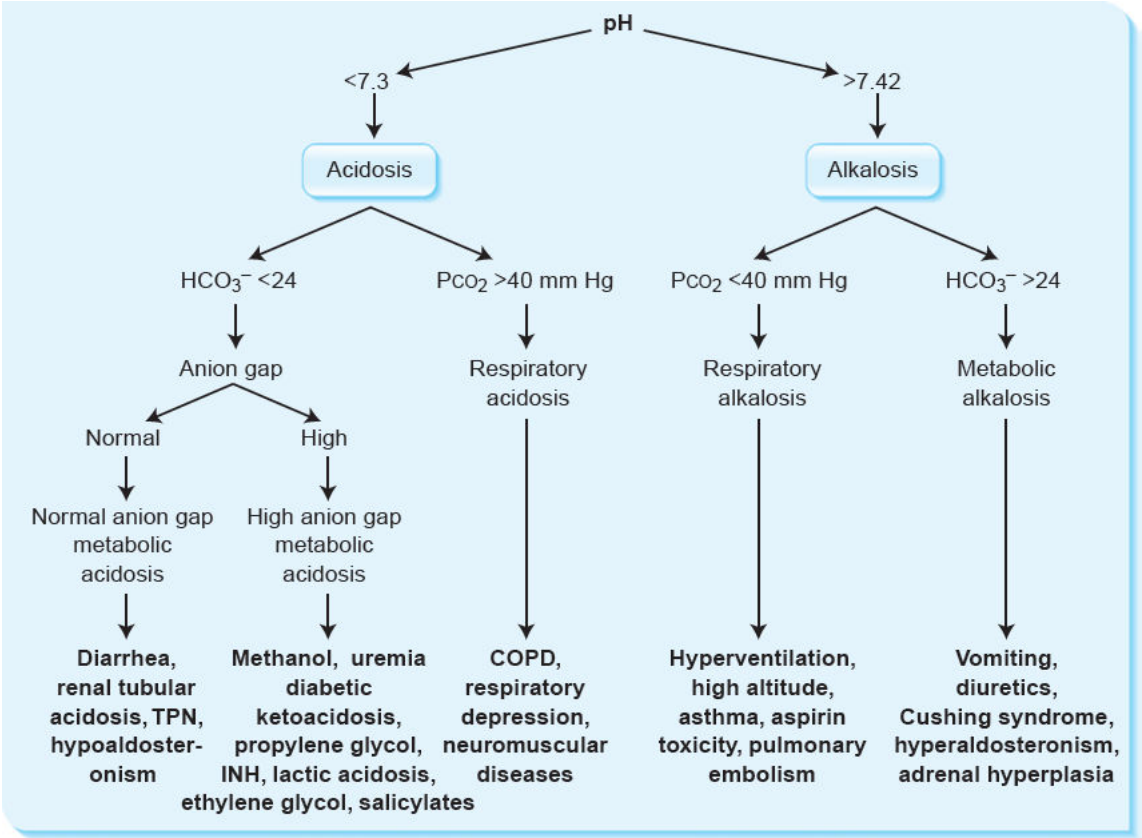


FIGURE 7-3
Differentiation of acid–base disturbances and related causes.
Note: Compensatory mechanisms should be checked to differentiate solitary from mixed disturbances. COPD, chronic obstructive pulmonary disease; TPN, total parenteral nutrition.

Table 7-8 Acid–Base Disturbances and Compensatory Mechanisms

Disorder	pH	(H^+)	(HCO_3^-)	Pco_2	Compensation	Common Causes
Metabolic acidosis	↓	↑	↓↓	↓	Hyperventilation	Diarrhea, diabetic ket renal tubular acidosis
Metabolic alkalosis	↑	↓	↑↑	↑	Hypoventilation	Vomiting, diuretics, C dosteronism, adrenal
Respiratory acidosis	↓	↑	↑	↑↑	Increased HCO_3^- reabsorption	COPD, respiratory dep diseases
Respiratory alkalosis	↑	↓	↓	↓↓	Decreased HCO_3^- reabsorption	Hyperventilation, high toxicity, pulmonary er

COPD, chronic obstructive pulmonary disease; ↑, high; ↓, low; ↑↑, very high; ↓↓, very low.

c. Corrected HCO_3^- = measured anion gap − normal anion gap + measured HCO_3^- (for which 12 = value of normal anion gap)
d. If corrected, HCO_3^- is:
(1) Normal, disturbance is solitary high anion gap acidosis
(2) Increased, disturbance is metabolic alkalosis with high anion gap acidosis
(3) Decreased, disturbance is nonanion gap acidosis with high anion gap acidosis

V. Electrolyte Disorders

A. Hypernatremia

1. Serum Na^+ >145 mEq/L
2. Classified by volume status of patient
   a. Hypovolemic: volume depletion, commonly from diarrhea and diuretics
   b. Euvolemic: associated with diabetes insipidus
   c. Hypervolemic: iatrogenic, due to intake of administration of hypertonic saline or salt poisoning
3. **H/P** = thirst, weakness, muscle cramps, lethargy, decreased consciousness, mental status changes, seizures
4. **Treatment**
   a. Gradual hydration with normal saline for inadequate fluid intake or excess fluid loss (maximal Na^+ reduction = 8 to 10 mEq/day), overcorrection can lead to cerebral edema
   b. Approximate required correction in a patient with purely fluid losses as a cause of hypernatremia can be determined through calculation of the **water deficit**:

$$\text{Water Deficit} = \text{Total body water} \times \left(\frac{[\text{Na}]}{140} - 1\right)$$

$$\text{Water Deficit} = (0.60 \times [\text{mass in kg}]) \times \left(\frac{[\text{Na}]}{140} - 1\right)$$

   c. Half of deficit is given in 24 hours in addition to maintenance fluids, remainder is given over following 24 to 48 hours; close monitoring of Na^+ is required to avoid excessive correction
   d. For patients with euvolemic hypernatremia desmopressin can be given for central diabetes insipidus and salt restriction and increased free water intake is recommended for nephrogenic diabetes insipidus, while also treating the underlying cause
   e. For patients with hypervolemic hypernatremia, discontinue offending agent. Consider diuretics
5. **Complications** = seizures, CNS damage; too rapid hydration can cause **cerebral edema**

Quick **HIT**

Pseudohyponatremia is an artifact of hyperlipidemia in which serum Na^+ falsely appears to be low.

NEXT
STEP

To calculate (Na^+) that will result from correction of hyperglycemia, add 1.6 mEq/L Na^+ for every 100 mg/dL glucose >100 mg/dL.

B. Hyponatremia

1. Serum Na^+ <135 mEq/L (see Figure 7-4)
2. **H/P** = nausea, weakness, altered mental status, seizures
3. **Treatment** = for isotonic and hypertonic, treat underlying condition (stop offending agent, correct hyperglycemia or hyperlipidemia, etc.); for hypotonic hyponatremia, treat with normal saline and closely monitor (increase serum Na^+ no more than 6 to 12 mEq/L in first 24 hours); however, if severe with seizure or altered mental status (Na <120 mEq/L) then administer hypertonic (3%) saline
4. **Complications** = CNS damage; overly rapid correction with hypertonic saline can cause **central pontine myelinolysis**

NEXT
STEP

Pseudohyperkalemia occurs from red blood cell hemolysis following blood collection, so K^+ should be measured **immediately** in drawn blood and increased serum K^+ should be confirmed with a **repeat blood sample** using a large-gauge needle.

C. Hyperkalemia

1. Serum K^+ >5.0 mEq/L
2. Caused by metabolic acidosis, aldosterone deficiency, adrenal insufficiency, renal failure, rhabdomyolysis, tumor lysis syndrome, K^+-sparing diuretics, ACEi/ARBs
3. **H/P** = weakness, nausea, vomiting; **arrhythmias**; paralysis or paresthesia in severe cases

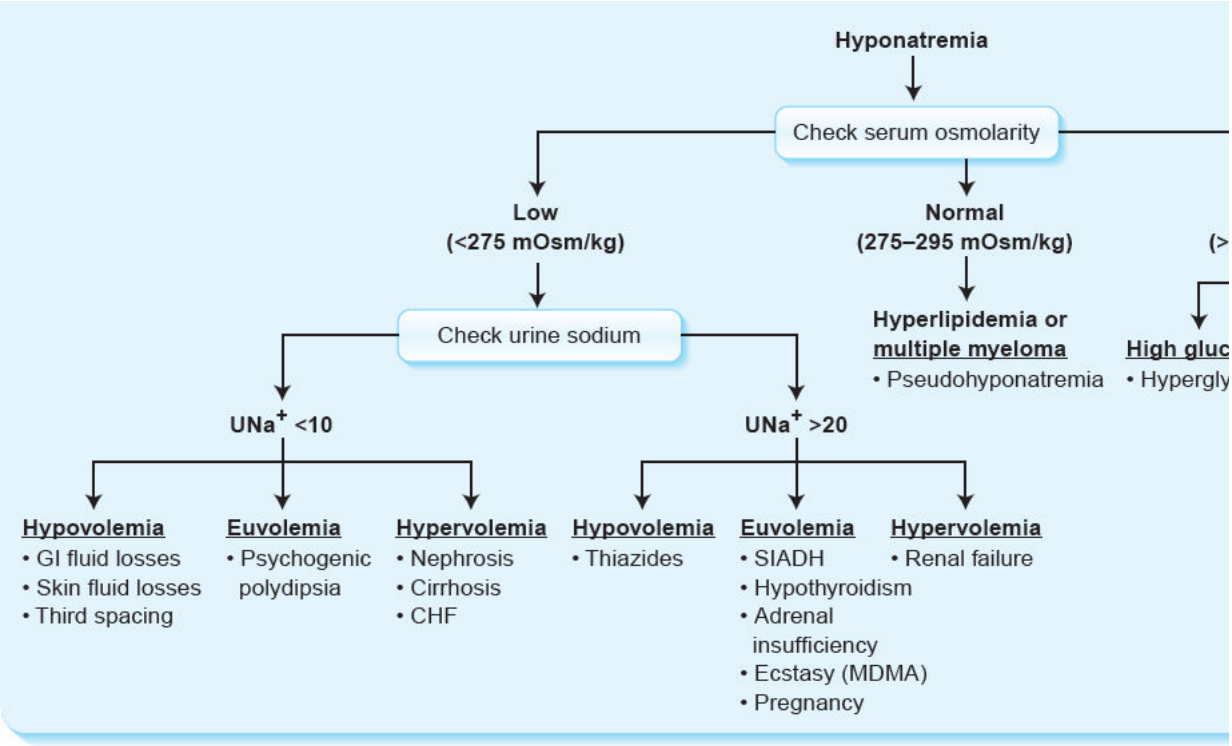


FIGURE **7-4**

Evaluation of hyponatremia.

ACE-I, angiotensin-converting enzyme inhibitor; CHF, congestive heart failure; FENa, fractional excretion of Na—(Urine [Na^+] × serum Cr) / (serum [Na^+] × Urine Cr); SIADH, syndrome of inappropriate ADH secretion.

4. **Electrocardiogram (ECG)** = **tall, peaked T waves,** widening of QRS complex, bradycardia; sine wave pattern, ventricular fibrillation in severe cases
5. **Treatment** = If K^+ >6.5 mEq/L and/or ECG changes then treat with the following:
   a. Calcium gluconate = stabilizes cardiac membrane
   b. $NaHCO_3$, insulin and dextrose = shifts K^+ into the cells
   c. Albuterol = encourages K^+ uptake by cells
   d. Sodium polystyrene sulfonate = binds K^+ and removes it through the GI tract
   e. Dialysis = required in refractory cases

D. Hypokalemia

1. Serum K^+ <3.5 mEq/L
2. Caused by poor dietary intake, metabolic/respiratory alkalosis, hypothermia, vomiting, diarrhea, hyperaldosteronism, insulin excess (e.g., treatment of diabetic ketoacidosis), K^+-wasting diuretics (loop, thiazide), or renal tubular acidosis types I and II (see Figure 7-5)
3. **H/P** = Fatigue, weakness, paresthesias and/or paralysis; hyporeflexia, arrhythmias
4. **ECG** = **T-wave flattening**, ST depression, **U waves**
5. **Treatment** = treat underlying disorder; give oral or IV KCl (10 to 20 mEq/hr). Consider simultaneously giving IV magnesium, as hypomagnesaemia can cause refractory hypokalemia
6. **Complications** = overly rapid replacement can lead to **arrhythmias**

Quick HIT

Hypercalcemia is characterized by **"bones"** (fractures), **"stones"** (nephrolithiasis), **"groans"** (GI symptoms), and **"psychiatric overtones"** (changes in mental status).

E. Hypercalcemia

1. Serum Ca^{2+} >10.5 mg/dL
2. Caused by **hyperparathyroidism, neoplasm**, immobilization, thiazide diuretics, high ingestion of calcium carbonate and milk (milk-alkali syndrome; more often seen in children), sarcoidosis, or hypervitaminosis A or D
3. **H/P** = bone pain, easy fractures, nausea, vomiting, constipation, weakness, mental status changes
4. **Labs** = elevated total calcium (albumin corrected) and ionized calcium; increased parathyroid hormone in hyperparathyroidism; normal or low parathyroid hormone as well as increased parathyroid hormone-related peptide (PTHrP) frequently seen with neoplasm; increased vitamins A or D seen in hypervitaminosis

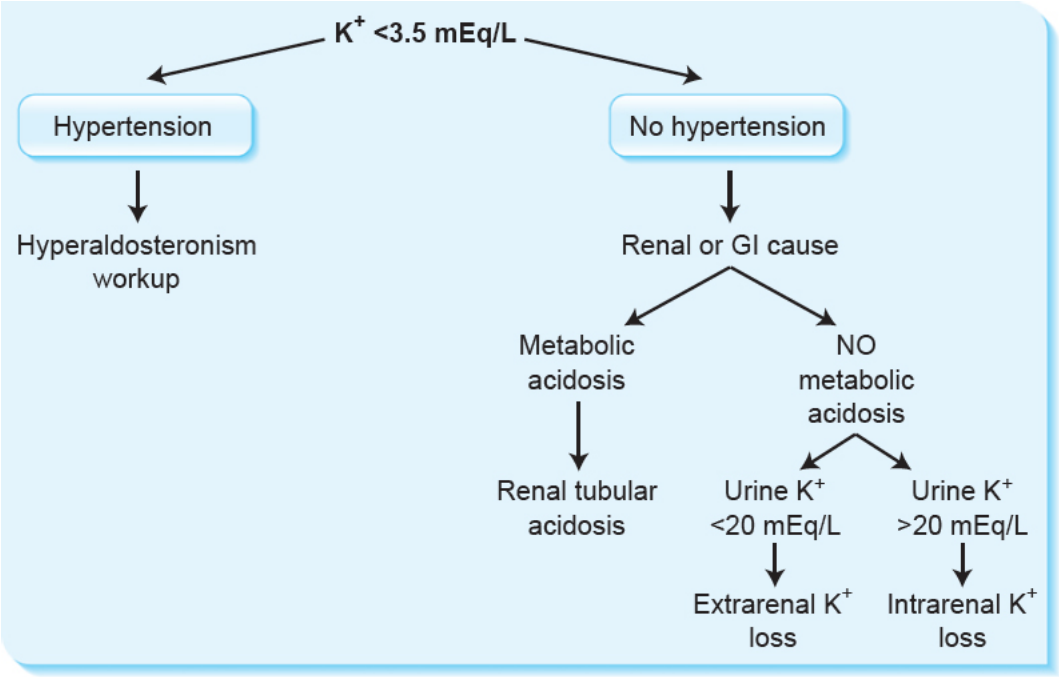


FIGURE 7-5
Evaluation of hypokalemia.
GI, gastrointestinal.

5. **ECG** = shortened QT interval
6. **Treatment** = treat underlying disorder; IV hydration; calcitonin and **bisphosphonates** in cases of excess bone reabsorption; glucocorticoids in malignancy or granulomatous disease; surgery indicated for hyperparathyroidism and resectable neoplasms

NEXT
STEP

Differentiate between **familial hypocalciuric hypercalcemia** (genetic disorder of Ca^{2+}-sensing receptors) and other causes of hypercalcemia by noting a family history of hypercalcemia, low urine Ca^{2+}, and absence of osteopenia, nephrolithiasis, and mental status changes in the former.

F. Hypocalcemia

1. Serum Ca^{2+} <8.5 mg/dL
2. Caused by hypoparathyroidism, hyperphosphatemia, chronic renal failure, vitamin D deficiency, **loop diuretics**, pancreatitis, or alcoholism
3. **H/P** = abdominal cramps, dyspnea; tetany, **Chvostek sign** (i.e., tapping facial nerve causes spasm), carpopedal spasm when blood pressure cuff inflated (i.e., **Trousseau sign**)
4. **Labs** = decreased serum Ca^{2+} (total serum Ca^{2+} should be adjusted for hypoalbuminemia, lower limit of normal Ca^{2+} decreases 0.8 mg/dL for each 1 g/dL albumin <4; ionized calcium will not be affected by albumin levels); increased phosphate seen with hypoparathyroidism and renal failure
5. **ECG** = prolonged QT interval
6. **Treatment** = treat underlying disorder; oral Ca^{2+} or IV Ca^{2+} for severe symptoms; vitamin D supplementation, if necessary

Quick HIT

Thiazide diuretics are **"Ca^{2+}-sparing"** and can **cause** hypercalcemia.

Quick HIT

Cultured urine should be from a midstream sample (**clean catch**) to avoid contamination from skin flora.

VI. Bladder and Ureteral Disorders

A. Urinary Tract Infection (UTI)

1. Ascending infection of urethra, bladder, and ureters resulting from inoculation of lower urinary tract (rarely hematogenous spread)
2. Most commonly due to *E. coli, S. saprophyticus, Proteus, Klebsiella, Enterobacter*, *Pseudomonas*, and *Enterococcus*
3. **Risk factors** = Foley catheter, vesicoureteral reflux, pregnancy, DM, sexual intercourse, immunocompromised; female > male
4. **H/P** = **urinary frequency**, dysuria, suprapubic pain, urgency, flank pain
5. **Labs** = U/A shows nitrates (specific, but not sensitive), increased leukocyte esterase (sensitive, but not specific), and white blood cells in urine; urine culture will show **>10^5 pathogen colonies/mL**
6. **Treatment**
   a. **Uncomplicated** = healthy, nonpregnant, premenopausal females: nitrofurantoin for 5 days is first line (avoid in pyelonephritis); trimethoprim-sulfamethoxazole (TMP-SMX), or fluoroquinolones for 3 days
   b. **Complicated** = elderly, male, anatomical abnormalities, diabetes, kidney disease, immunocompromised, relapses: fluoroquinolones for 7 to 14 days
   c. **Asymptomatic bacteriuria** = defined as >10^5 CFU/mL of bacteria with no symptoms do not require treatment unless patient is pregnant, as they are at increased risks for ascending infection and preterm labor if untreated
   d. **Pregnancy** = nitrofurantoin or cephalexin for 7 days
7. **Complications** = abscess formation, pyelonephritis, renal failure, prostatitis

NEXT
STEP

Perform a workup for sexually transmitted urethritis in any **man** with a suspected UTI because the symptoms may appear similar.

B. Urinary Incontinence

1. Involuntary leakage of urine; more common in the elderly
2. First step in evaluation is to evaluate for causes of secondary incontinence (UTI, impaired mobility, fecal impaction, atrophic vaginitis, or delirium)
3. **Urge incontinence** (detrusor overactivity)
   a. Leakage of urine due to uninhibited bladder contractions
   b. **H/P** = diagnosis usually made by history of urgency, frequent voiding of small amounts of urine, and possibly incontinence
   c. **Treatment** = bladder training, antimuscarinics (oxybutynin, tolterodine)
4. **Stress incontinence**
   a. Leakage of urine during physical exertion, coughing, sneezing, or any maneuver that increases abdominal pressure due to decreased anatomic support of and function of the urinary sphincter
   b. **Risk factors** = female sex, multiparity, obesity
   c. **H/P** = incontinence accompanies coughing, sneezing, laughing, exercise, lifting heavy objects; diagnosis usually made by history and bladder diary; urodynamic testing by a urologist may be helpful but is usually not necessary
   d. **Treatment** = pelvic floor muscle training, surgical therapy (midurethral sling)
5. **Overflow incontinence**
   a. Continuous leakage of urine due to incomplete bladder emptying
   b. More common in men
   c. **Causes** = bladder outlet obstruction (benign prostatic hyperplasia [BPH], urethral strictures), impaired detrusor contractility, neurogenic bladder
   d. **H/P** = weak urinary stream, dribbling, frequency, hesitancy, and nocturia; bladder diary is very helpful; palpable distended bladder
   e. **Testing** = automated bladder scanner or catheterized postvoid residual detects full bladder after voiding
   f. **Treatment** = treat underlying obstruction with surgery as needed; treat detrusor underactivity with sacral nerve stimulation; intermittent self-catheterization is sometimes required

C. Bladder Cancer

1. **Transitional cell (urothelial) carcinoma** (common), squamous cell cancer (uncommon), or adenocarcinoma of the bladder (uncommon)
2. **Risk factors** = **tobacco**, schistosomiasis, cyclophosphamide, aniline dyes, aromatic amines
3. **H/P** = **painless gross hematuria**; suprapubic pain, frequency, dysuria, urgency; palpable suprapubic mass
4. **Labs** = U/A shows hematuria; urine cytology shows malignant cells; biopsy confirms diagnosis
5. **Radiology** = cystoscopy; CT, MRI, or IV urography may detect mass
6. **Treatment** = transurethral resection for superficial tumors; partial or total cystectomy for more invasive tumors; adjuvant intravesical chemotherapy and radiation therapy commonly utilized; regional radiation therapy and systemic chemotherapy for large tumors and metastatic disease
7. **Complications** = urinary tract obstruction

VII. Male Reproduction

A. Urethritis

1. Infection of urethra caused by sexually transmitted ***Neisseria gonorrhoeae*** or ***Chlamydia trachomatis***
2. **H/P** = dysuria, frequency, urgency, burning urination**; purulent urethral discharge** seen with *N. gonorrhoeae*
3. **Labs** = both confirmed with nucleic acid–amplification testing
4. **Treatment** = single-dose IM ceftriaxone with PO doxycycline or azithromycin used to treat both possible infections simultaneously; **treat sexual partners**
5. **Complications** = urethral strictures, disseminated gonococcal infection

B. Prostatitis

1. Inflammation of prostate from infectious or noninfectious causes
2. **H/P** = perineal pain, dysuria, frequency, urgency; fever, tender prostate on digital rectal examination
3. **Labs** = may be suggestive of UTI; possible hematuria; white blood cells seen in prostatic secretions
4. **Treatment** = TMP-SMX or fluoroquinolone (frequently for 4 to 6 weeks); treat for sexually transmitted diseases (STDs) in sexually active males

Quick HIT

BPH develops in the **central zone** of the prostate adjacent to the urethra and does not predispose patients to prostate cancer.

C. Benign Prostatic Hyperplasia (BPH)

1. **Benign enlargement of prostate** seen with increasing frequency as men age beyond 45 years
2. **H/P** = urinary **hesitancy**, straining, **weak or intermittent stream**, dribbling; frequency, urgency, **nocturia**; digital examination detects uniformly enlarged, rubbery prostate
3. **Labs** = possible mild increase in prostate-specific antigen (PSA); rule out infection (U/A), cancer (biopsy), and renal failure (serum electrolytes, BUN, Cr)
4. **Radiology** = transrectal US shows enlarged prostate
5. **Treatment** = behavioral changes (limit fluid intake at night, avoid alcohol, etc.), α_1 **blockers** (e.g., tamsulosin, etc.), and **5α-reductase inhibitors** (e.g., finasteride, etc.) improve symptoms; surgery needed for refractory cases (i.e., transurethral resection of prostate [TURP]); transurethral needle ablation may be performed in men who are poor surgical candidates

Quick HIT

Prostate cancer is the most **common nondermatologic cancer** in men; however, lung cancer is the greatest cause of **cancer-related death** in males, whereas **prostate** cancer is the **second** highest.

D. Prostate Cancer

1. Adenocarcinoma occurring in peripheral zone of prostate
2. **Risk factors** = increased age, family history, high-fat diet, prostatitis
3. **H/P** = frequently asymptomatic; weakened urinary stream, urinary retention, weight loss, back pain in later disease; **nodular or irregular prostate on digital examination**, lymphedema
4. **Labs** = U/A may show hematuria and pyuria; **increased PSA**, increased alkaline phosphatase; biopsy provides diagnosis
5. **Radiology** = transrectal US shows irregular prostate; bone scan, chest x-ray (CXR), and CT may detect metastases
6. **Treatment**
   a. Good prognosis with early treatment
   b. Watchful waiting in low-risk population with <10 years life expectancy
   c. Radical prostatectomy
   d. Radiation therapy
   e. Follow up with PSA posttreatment to monitor for metastases and recurrence
   f. Antiandrogen therapy (i.e., hormone therapy or orchiectomy) with chemotherapy can be used to improve symptoms in high-grade or metastatic disease
7. **Complications** = **incontinence** and **impotence** are common with radical prostatectomy

Quick HIT

Supporting the scrotum does **not** relieve pain in testicular torsion but does relieve pain in epididymitis (Prehn sign).

E. Epididymitis

1. Inflammation of epididymis associated with testicular inflammation
2. Caused by retrograde ascent of STDs or urinary tract bacteria
3. **H/P** = epididymal **pain relieved by supporting scrotum (Prehn sign)**, dysuria; scrotal tenderness, swollen/indurated epididymis
4. **Labs** = U/A may show white blood cells; test for *N. gonorrhoeae* and *C. trachomatis* with nucleic acid amplification testing of urine sample
5. **Treatment** = ceftriaxone and azithromycin or doxycycline if suspicious for sexually transmitted etiology. Otherwise treat as UTI; NSAIDs and scrotal support for noninfectious causes

F. Testicular Torsion

1. **Twisting of spermatic cord** leading to **vascular insufficiency** of testes
2. **H/P** = very painful and swollen testes, nausea, vomiting, fever, **testes displaced superiorly**, transverse testicular orientation, absent cremasteric reflex
3. **Radiology** = US shows decreased blood flow to torsed testis
4. **Treatment** = emergent **surgical reduction**; testes attached to scrotal wall (i.e., orchiopexy) to prevent recurrence. Manual detorsion (rotating testicle medial to lateral, like opening a book) can be attempted while waiting for definitive care
5. **Complications** = testicular ischemia or infarction without prompt treatment, leading to infertility

G. Testicular Cancer

1. Germ cell (seminomatous, nonseminomatous) or stromal cell (Leydig, Sertoli, or granulosa cell) tumors of testicles
2. **Risk factors** = prior history of testicular cancer, undescended testes, family history, Klinefelter syndrome
3. **H/P** = **painless testicular mass**, possible gynecomastia or lower abdominal pain; GI or pulmonary symptoms can result from metastases
4. **Labs** = increased β-human chorionic gonadotropin (β-hCG) and increased α-fetoprotein in germ cell tumors; increased estrogen in stromal cell tumors
5. **Radiology** = US may detect dense testicular mass; CXR or CT can detect extent of tumor and metastases
6. **Treatment** = radical orchiectomy with/without chemotherapy and radiation therapy for early-stage seminomas; radical orchiectomy with/without retroperitoneal lymph node dissection or chemotherapy for early stage nonseminomas
7. **Complications** = **prognosis is very good**, but nonseminomas have lower cure rates and increased risk of recurrence

Quick HIT

95% of testicular malignancies are of a germ cell origin.

Quick HIT

Testicular cancer is the most common cancer in men between 15 and 35 years of age.

H. Erectile Dysfunction

1. Inability to obtain or maintain erection during sexual activity
2. Caused by denervation, **vascular insufficiency**, endocrine abnormalities, psychological concerns, drugs, or alcoholism
3. **H/P** = history of trauma, surgery, or infection can be contributory; examination should consider vascular (decreased pulses and perfusion), hormonal (testicular atrophy or gynecomastia), and neurologic (decrease anal wink reflex and paresthesias) etiologies
4. **Labs** = possible decreased testosterone, decreased luteinizing hormone (LH), or increased prolactin
5. **Treatment** = treat underlying condition; stop offending agents; psychological counseling and sexual education; oral phosphodiesterase-5 inhibitors may help maintain penile vascular engorgement

QUESTIONS

1. A 20-year-old healthy, nonpregnant female presents to the emergency department with dysuria for 5 days. She vomited two times today and is now experiencing right flank pain. Vital signs are within normal limits. Examination is remarkable for suprapubic tenderness. She is able to tolerate drinking water in the emergency department. What is the most appropriate plan for the patient? Urine dip is with positive nitrites and leukocyte esterase.

   A. IV ceftriaxone and hospital admission
   B. IV gentamicin and hospital admission
   C. Oral trimethoprim-sulfamethoxazole and discharge home
   D. Oral penicillin and discharge home
   E. Oral nitrofurantoin and discharge home

2. An 18-year-old male with no medical problems presents to the emergency department with severe right flank pain. A CT scan of the abdomen and pelvis is performed and reveals a 5-mm stone in the ureterovesicular junction with some moderate hydronephrosis. A urinalysis is ordered and is positive for nitrite and displays >100 white blood cells/HPF and 50 to 100 red blood cells/HPF. What is the best next step?

   A. Pain control and discharge home
   B. Pain control, IV antibiotics, and urology consultation
   C. Pain control and hospital admission
   D. Pain control, oral antibiotics, and discharge home
   E. Pain control, tamsulosin, and discharge home

3. A 31-year-old previously healthy male presents with generalized weakness and episodes of gross hematuria. He does note a recent sore throat around 3 weeks ago. He denies any other complaints. Vital signs are within normal limits except for a blood pressure of 180/90 mm Hg. Physical examination is remarkable for bilateral pedal edema. Urinalysis is positive for proteinuria and RBC casts. What is the most likely diagnosis?

   A. Nephrotic syndrome
   B. Postinfectious glomerulonephritis
   C. Interstitial nephritis
   D. Acute tubular necrosis
   E. Pyelonephritis

4. A 74-year-old woman presents to the emergency department from a skilled nursing facility with altered mental status. She has a history of hypertension, diabetes type 2, and dementia. Vital signs are within normal limits. Examination is remarkable for dry mucous membranes. Laboratory results reveal the following: blood urea nitrogen 64 mg/dL, serum creatinine 1.2 mg/dL. What is the best next treatment option for this patient?

   A. IV normal saline bolus
   B. Fluid restriction
   C. Hemodialysis
   D. IV hypertonic saline
   E. IV antibiotics

5. A 50-year-old male with a history of chronic kidney disease presents with nausea and generalized weakness. Laboratory studies reveal a potassium of 6.5 mEq/L. An ECG is performed which shows peaked T waves with a wide QRS interval. Which is the following should be given immediately?

   A. IV calcium gluconate
   B. Albuterol nebulizer
   C. IV insulin and IV dextrose
   D. Oral furosemide
   E. Oral sodium polystyrene sulfonate

6. Which of the following is an indication for emergent dialysis in a patient with kidney failure?

   A. Hyperkalemia
   B. Asymptomatic uremia
   C. Refractory fluid overload
   D. Hypernatremia
   E. A pH of 7.20

7. A 12-year-old boy presents to the emergency department with several right testicular pain. On examination, his right testicle appears elevated and in a horizontal lie. What is the next best step?

   A. Scrotal ultrasound
   B. Emergency urology consult
   C. Abdominal x-Ray
   D. Urinalysis
   E. Attempt manual detorsion in a lateral to medial direction

8. A 36-year-old man presents to the emergency department with an acute, sudden-onset headache that started 12 hours ago. He has never experienced a headache like this before. He has a history of polycystic kidney disease. A CT of the brain is performed and shows no acute pathology. What is the next best step?

   A. MRI of the brain
   B. Lumbar puncture
   C. Cerebral angiogram
   D. Pain control and discharge home

E. Oxygen via nasal cannula

9. A 30-year-old male presents with left testicular pain for 3 days. He denies any fever or dysuria. He admits to being sexually active. Vital signs are within normal limits. On examination, the testicle is in normal position with an intact cremasteric reflex. There is tenderness and swelling of the left epididymis. Which of the following is the best treatment approach?

   A. Oral ibuprofen
   B. IM ceftriaxone and oral doxycycline
   C. Manual detorsion
   D. Oral ciprofloxacin
   E. Oral levofloxacin

10. A 68-year-old man presents to the clinic with a complaint of lower back and perineal pain. He also complaints of chills and dysuria. On rectal examination, the prostate is tender. Which of the following is the best treatment option?

   A. Oral nitrofurantoin for 7 days
   B. Oral penicillin for 4 weeks
   C. Oral trimethoprim-sulfamethoxazole for 1 week
   D. Oral ciprofloxacin for 4 weeks
   E. One dose of IM fosfomycin

8
Endocrine Disorders

I. Disorders of Glucose Metabolism

A. Normal Glucose Metabolism

1. Regulated by pancreatic enzymes insulin and glucagon
2. **Insulin**
   a. Secreted by pancreatic β-**islet cells** in response to glucose intake and feeding (strongest stimuli, but also influenced by other protein and neural inputs)
   b. Secretion decreases with fasting and exercise (i.e., feedback relationship with nutrient supply)
   c. Induces glucose and amino acid uptake by muscle, adipose cells, and liver
   d. Drives conversion of glucose to glycogen, fatty acids, and pyruvate
   e. Induces storage of glucose metabolites in tissue (e.g., glycogen in liver, fatty acids in adipose cells, protein anabolism)
   f. Inhibits lipolysis in adipose tissue
   g. **C-peptide** is a byproduct of endogenous insulin production and can be measured to guide appropriate diagnosis and treatment
3. **Glucagon**
   a. Secreted by α-**islet cells** primarily in response to decreased glucose and protein intake
   b. Promotes mobilization of glycogen and fatty acids
4. **Insulin:** glucagon ratio determines state of glucose metabolism

Quick HIT

C-peptide is elevated in insulinomas. Recurrent hypoglycemia from exogenous administration of insulin can be identified by low levels of C-peptide despite elevated insulin levels.

Quick HIT

Rubella, Coxsackie virus, and mumps have been associated with onset of β-islet cell destruction leading to DM type I.

Quick HIT

Hemoglobin A_{1c} is a good measure for how well therapy has controlled serum glucose over a 3-month period or for how compliant a patient has been with prescribed therapy.

Quick HIT

Dawn phenomenon is early morning hyperglycemia due to natural release of cortisol, growth hormone glucagon, and epinephrine during the night.

Somogyi effect is rebound hyperglycemia after the overabundance of exogenous insulin (and subsequent hypoglycemia) stimulates the release of counter- regulatory hormones.

B. Diabetes Mellitus (DM) Type I (Juvenile Onset Diabetes, Insulin-Dependent Diabetes)

1. **Loss of ability to produce insulin** most likely caused by autoimmune destruction of β-islet cells
2. Association with human leukocyte antigens HLA-DR3, HLA-DR4, and HLA-DQ genotypes
3. Age of presentation has a bimodal age distribution (first peak at 4 to 6 years, second peak at 10 to 14 years)
4. **H/P** = **polyuria, polydipsia, polyphagia,** weight loss; more rapid onset than type II DM
5. **Labs** = hyperglycemia, glycosuria (i.e., glucose in urine), serum and urine ketones, increased hemoglobin A_{1c} (indicates hyperglycemia over prior 3 months and used to monitor adequacy of control) (see Table 8-1); may have elevated levels of **anti-glutamic acid decarboxylate** (anti-GAD) and **anti-islet cells**
6. **Treatment** = scheduled insulin injections (see Figure 8-1, Table 8-2) or continuous insulin infusion via insulin pump; monitoring of serum glucose at home to guide insulin and dietary adjustments; close multidiscipline follow-up to monitor development of complications

7. **Complications** = **diabetic ketoacidosis** (DKA), hypoglycemia (secondary to excess insulin administration), Dawn phenomenon, **Somogyi effect,** retinopathy, neuropathy, nephropathy, atherosclerosis

C. DM Type II (Adult Onset Diabetes, Non–Insulin-Dependent Diabetes)

1. Development of **tissue resistance to insulin,** leading to hyperglycemia and gradual decrease in the ability of β-islet cells to produce insulin (see Table 8-3)

Table 8-1 Plasma Glucose Diagnostic Criteria for Diabetes Mellitus[a]

Plasma Glucose Test	Level (mg/dL)	And …
Random plasma glucose	≥200	With symptoms of DM
Fasting plasma glucose	≥126	On two separate occasions
Plasma glucose	≥200	2 hours after 75 g oral glucose load[b]
Hemoglobin A_{1c}	≥6.5%	

[a]Diagnosis is based on the occurrence of at least one of the above findings.
[b]This is a positive oral glucose tolerance test.
DM, diabetes mellitus.

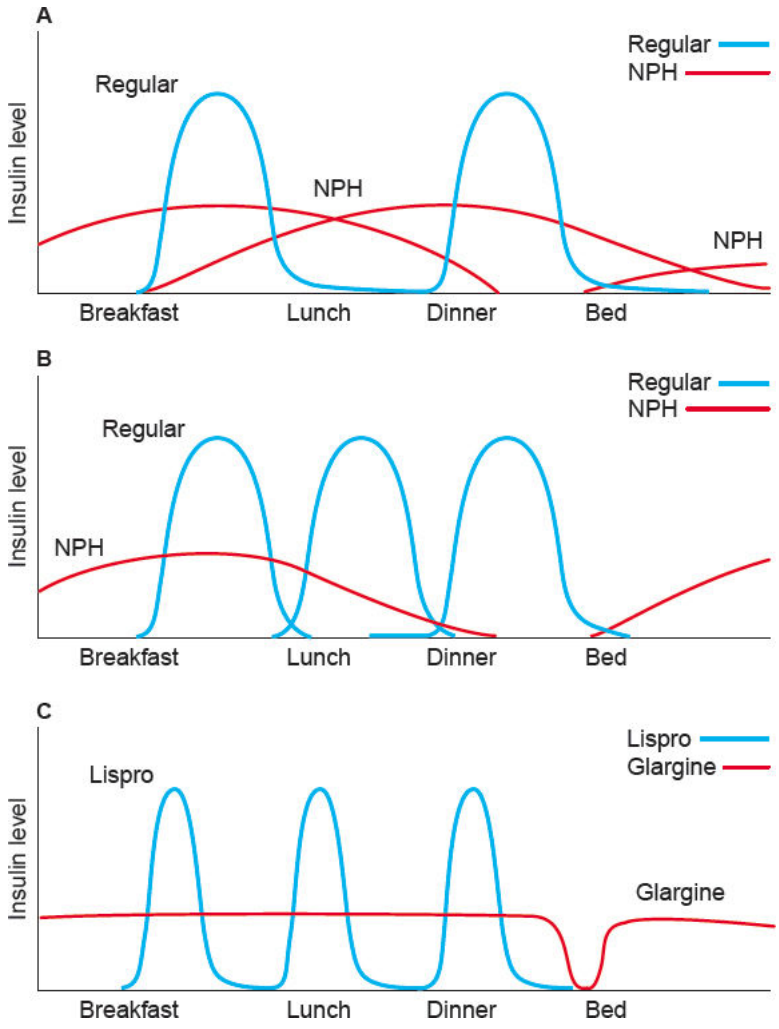


FIGURE 8-1
Examples of insulin regimens in diabetes mellitus.
A: Injection of regular and NPH insulin (in 2:1 ratio) together at breakfast followed by a second regular insulin dose at dinner and a second NPH dose at bedtime. In some cases, the second dose of NPH can be given concomitantly with the second regular insulin dose at dinner. **B:** Adjustment in regimen A to achieve tighter, shorter time control by adding an additional dose of regular insulin at lunch and only administering NPH at bedtime. In patients with overnight hypoglycemia, insulin detemir can be substituted for NPH. **C:** Tight control regimen using very rapid acting insulin at meals and a bedtime dose of insulin glargine. NPH, neutral protamine Hagedorn insulin.

2. **Risk factors** = family history, obesity, metabolic syndrome, lack of exercise, gestational diabetes
3. Historically diagnosed **after age 40 years,** but mean age of diagnosis is decreasing. Some guidelines recommend screening for patients with blood pressure greater than 135/80 mm Hg and overweight patients
4. **H/P** = asymptomatic in early stages with **gradual onset** of symptoms; polyuria, polydipsia, polyphagia, acanthosis nigricans; symptoms related to complications can present before actual diagnosis

Quick HIT

An increasing number of obese patients with DM type II are being diagnosed at ages **<40** years because of the increasing prevalence of **obesity**.

Table 8-2 Formulations of Injected Insulin

Type of Insulin	Time of Onset of Action	Peak Effect (hour[s])	Duration of Action (hours)
Very rapid acting[a] (e.g., lispro, aspart, glulisine)	10 minutes	1	2–4
Regular[a]	30 minutes	2–4	5–8
NPH	2 hours	6–10	18–24
Insulin glargine	2 hours	No peak	24+
Insulin detemir	2 hours	No peak	6–24

[a]Appropriate for use in continuous infusion pump.
NPH, neutral protamine Hagedorn insulin.

Table 8-3 Comparisons of Diabetes Mellitus Types I and II

	DM Type I	DM Type II
Cause	Likely autoimmune destruction of β-islet cells	Development of insulin resistance in tissues
Inheritance/genetics	HLA linked	Strong family history
Age of onset	Usually <15 years	Frequently >40 years
Onset of symptoms	Rapid	Gradual
Pancreatic effects	β-Islet cell depletion	Gradual decrease in β-islet cells
Serum insulin	Low	Increased or normal; low in later disease
Body type	Thin	Obese
Acute complications	DKA	HHS
Treatment	Insulin	Oral hypoglycemic agents, possibly insulin

DKA, diabetic ketoacidosis; DM, diabetes mellitus; HHS, hyperosmolar hyperglycemic state; HLA, human leukocyte antigen.

5. **Labs** = similar to those for DM type I, except **negative** for antibodies (anti-GAD and anti-islet cells)
6. **Treatment**
   a. Initial therapy focuses on nutrition (reduced calorie intake, carbohydrate control, and consistency), exercise, and weight loss.
   b. Metformin is frequently the first oral agent prescribed (see Table 8-4).
   c. If hemoglobin A_{1c} remains >7 after 2 to 3 months of monotherapy, add sulfonylurea, thiazolidinedione, or insulin.
   d. If patient begins to exhibit signs of decreased insulin production or if hemoglobin A_{lc} is consistently >8.5, add insulin regimen.
   e. Close monitoring of blood glucose levels is important to directing therapy.
7. **Complications** = **hyperosmolar hyperglycemic nonketotic syndrome** (HHNS), retinopathy, nephropathy, neuropathy, atherosclerosis

Quick HIT

DKA occurs most frequently in patients with **DM type I** and is **uncommonly seen** in **DM type II.**

Quick HIT

HHS is seen in patients with **DM type II** and is **not seen** in patients with **DM type I** because sufficient insulin production is required to prevent DKA from occurring first.

D. Complications of Diabetes

1. **Diabetic ketoacidosis**
   a. Extremely low insulin and glucagon excess cause degradation of triglycerides into fatty acids and eventual conversion into **ketoacids**

Table 8-4 Noninsulin Drugs Used in Treatment of Diabetes Mellitus Type II

Drug	Mechanism	Role	Adverse Effects
Biguanides (metformin)	**Decrease hepatic gluconeogenesis, increase insulin sensitivity**, reduce LDL, raise HDL	Frequently first-line drug	GI disturbance, rare lactic acidosis, decreased vitamin B_{12} absorption; contraindicated in patients with hepatic or renal insufficiency
Sulfonylureas (glyburide, glimepiride, glipizide)	**Stimulate insulin release** from β-islet cells, reduce serum glucagon, increase binding of insulin to tissue receptors	Frequently used after metformin	**Hypoglycemia;** contraindicated in patients with hepatic or renal insufficiency (greater risk of hypoglycemia)
Thiazolidinediones (pioglitazone, rosiglitazone)	Decrease hepatic gluconeogenesis, **increase insulin sensitivity**	Adjunct to other drugs or monotherapy	Weight gain and fluid retention (contraindicated in CHF), increased serum LDL
DPP-IV inhibitors (sitagliptin, saxagliptin, linagliptin, alogliptin)	**Inhibit degradation of incretin** hormones → decrease glucagon, increase insulin, delay gastric emptying	Adjunct to other drugs	Diarrhea, constipation, edema
Incretin mimetics (exenatide, liraglutide)	Agonize GLP-1 receptors → decrease glucagon, increase insulin, delay gastric emptying	SC injection; adjunct to other drugs	Mild weight loss, **nausea**, hypoglycemia, slight risk of pancreatitis
SGLT-2 inhibitors (dapagliflozin, canagliflozin)	**Inhibit renal reabsorption of glucose, lowering blood glucose**	**Adjunct therapy for patients inadequately controlled on two drugs; only useful in patients with normal renal function**	Mild hypoglycemia, recurrent UTI, **genital fungal infections**
α-Glucosidase inhibitors (acarbose)	**Decrease GI absorption** of starch and disaccharides	Adjunct to other drugs; may be used in patients with DM type I	Diarrhea, flatulence, GI disturbance
Meglitinides (repaglinide, nateglinide)	**Stimulate insulin release** from β-islet cells	Used as secondary drug with metformin or rarely as initial drug	**Hypoglycemia**; significantly more expensive than sulfonylureas with no therapeutic advantage
Pramlintide	Amyline analog; delay gastric emptying, promote satiety	Injectable drug used only in conjunction with insulin (type I or type II DM)	Nausea, hypoglycemia

DM, diabetes mellitus; DPP-IV, dipeptidyl peptidase-IV; GI, gastrointestinal; GLP-1, glucagon-like peptide-1; LDL, low-density lipoprotein; MI, myocardial infarction; SGLT, sodium-glucose linked transporter; UTI, urinary tract infection.

   b. Occurs in patients with DM type I who do not take prescribed insulin or those who have infections, high stress, myocardial infarction (MI), or high alcohol use
   c. **H/P** = weakness, polyuria, polydipsia, **abdominal pain, vomiting;** dry mucous membranes, decreased skin turgor, fruity odor on breath, hyperventilation (**Kussmaul respirations** = deep, labored, regular breathing); mental status changes develop with worsening dehydration; children are at higher risk of developing **cerebral edema**
   d. **Labs** = **glucose >250 to 800 mg/dL** (rarely >1,000), decreased Na^+, normal or increased serum K^+ (total body K^+ is decreased), decreased phosphate, high anion gap metabolic acidosis, **serum and urine ketones**
   e. **Treatment** = intravenous (IV) fluids, insulin, KCl; treat underlying disorder (success of treatment may be confirmed by **closure of anion gap**)
2. **Hyperosmolar hyperglycemic state (HHS)**
   a. Extremely high glucose with profound dehydration
   b. Occurs in patients with DM type II with lengthy infections, stress, or illness; insulin production is sufficient to prevent DKA by suppressing lipolysis and ketogenesis
   c. **H/P** = polyuria, polydipsia, dehydration, mental status changes; seizures and stroke can occur in severe cases
   d. **Labs** = **glucose 600 mg/dL** (frequently >1,000), no acidosis, serum osmolality >320 mmol/kg
   e. **Treatment** = IV fluids, insulin, correction of electrolyte abnormalities; treat underlying disorder

NEXT
STEP

Differentiate DKA from HHS using serum glucose, presence of acidosis, and history of type of DM.

3. **Diabetic retinopathy**
   a. Vascular occlusion and ischemia, with or without neovascularization in retina, leading to visual changes
   b. Associated with microaneurysms, hemorrhages, infarcts, and macular edema
   c. **Background retinopathy (no neovascularization)** makes up most cases; proliferative retinopathy (with neovascularization) has increased risk of hemorrhages
   d. **H/P** = **progressive vision loss;** retinal changes seen on funduscopic examination (e.g., arteriovenous nicking, hemorrhages, edema, infarcts)
   e. **Treatment** = **control diabetes,** antihypertension (anti-HTN) therapy, annual follow-up with ophthalmology, laser photocoagulation for neovascularization, injection of intravitreal corticosteroids to reduce macular edema
   f. **Complications** = vision loss, early cataracts and glaucoma, retinal detachment
4. **Diabetic nephropathy**
   a. Intercapillary glomerulosclerosis, mesangial expansion, and basement membrane degeneration that develops after long-term DM
   b. Slightly greater risk in DM type I than in DM type II
   c. Initially presents with proteinuria; renal insufficiency later develops with nephrotic syndrome
   d. **H/P** = develops after several years with DM (20+); lab abnormalities may appear well before symptoms; symptoms and signs of renal insufficiency (e.g., HTN, uremia) develop as renal function deteriorates
   e. **Labs** = hypoalbuminemia, increased creatinine (Cr), increased blood urea nitrogen (BUN); urinalysis shows proteinuria and microalbuminuria; electron microscopy shows basement membrane thickening and Kimmelstiel–Wilson nodules in glomeruli
   f. **Treatment** = **strict glucose and blood pressure control;** angiotensin-converting enzyme inhibitor (ACE-I) or angiotensin receptor blocker (ARB) to decrease blood pressure, low protein diet, infection prevention; dialysis may eventually be required
   g. **Complications** = end-stage renal disease

Quick HIT

Patients with sensory neuropathy are at **increased risk** for developing **foot infections** and need to be taught to check their feet regularly to avoid ulcer formation.

5. **Diabetic neuropathy**
   a. Neural damage and conduction defects leading to sensory, motor, and autonomic nerve dysfunction
   b. Caused by multiple factors including oxidative stress, advanced glycated end products, and microvascular injury
   c. **Sensorimotor polyneuropathy** is the most common and longer nerves are affected first
   d. **Sensory** neuropathy begins in feet and progresses in stocking–glove pattern; symptoms include **paresthesia and neural pain** due to damage to small nerve fibers, and **decreased vibratory and pain** sensation due to damage to large nerve fibers
   e. **Motor** neuropathy may be distally or proximally distributed and may be characterized by weakness or loss of coordination
   f. **Autonomic** neuropathy can cause postural hypotension, impotence, incontinence, and diabetic gastroparesis (i.e., delayed gastric emptying)
   g. **Treatment** = **control diabetes;** neural pain can be treated with tricyclic antidepressants, carbamazepine, or gabapentin; narcotics or tramadol can be considered for persistent neural pain; patients should be taught how to perform regular foot examinations
   h. **Complications** = **Charcot joints, diabetic foot ulcers;** amputation may be needed to treat progressive infections and deformity

Quick HIT

Repetitive foot trauma in cases of impaired pain sensation can lead to severe foot deformity and joint destruction **(Charcot joints)**.

6. **Atherosclerosis**
   a. Incidence greatly increased in diabetic patients secondary to macrovascular disease
   b. Increased risk of coronary artery disease and peripheral vascular disease (PVD), leading to increased risk of MI, distal ischemia, and ulcer formation secondary to poor healing and infection
   c. **Treatment** = control HTN and hyperlipidemia; daily aspirin (ASA) therapy
   d. **Complications** = MI (frequently silent), PVD, poor healing of trauma and infections

Quick HIT

Diabetic patients are at an increased risk of **silent MI** because of impaired pain sensation.

Quick HIT

Cardiac complications are the **greatest cause of death** in diabetic patients.

E. Hypoglycemia (See Table 8-5)

1. Inadequate blood glucose that can result in an inadequate supply of glucose to tissues and brain damage
2. **H/P** = faintness, weakness, diaphoresis, and palpitations because of responsive excess secretion of epinephrine (attempt to mobilize glycogen); headache, confusion, mental status changes, and decreased consciousness because of inadequate supply of glucose to the brain

Table 8-5 Causes of Hypoglycemia

Cause	Pathology	Diagnosis	Treatment
Reactive	Decrease in serum glucose **after eating** (postsurgical or idiopathic)	Hypoglycemia and symptoms improve with carbohydrate meal	Frequent sma
Iatrogenic (excess insulin)	**Excess insulin** administration or adverse effect of **sulfonylurea** or meglitinide use	**Increased insulin in presence of hypoglycemia**, adjustment of drug regimen reduces symptoms	Adjust insulin different oral
Insulinoma[a]	**β-Islet cell tumor** producing excess insulin	Increased insulin in presence of hypoglycemia, may be detected on CT or MRI	Surgical rese
Fasting	**Underproduction of glucose** because of hormone deficiencies, malnutrition, or liver disease	Lab abnormalities and history associated with particular etiology	Proper nutriti ment
Alcohol induced	Glycogen depletion and **gluconeogenesis inhibition** by high concentrations of alcohol	History of alcohol use, serum ethanol >45 mg/dL	Proper nutriti quantity alcol
Pituitary/adrenal insufficiency	Decreased cortisol production leads to insufficient hepatic gluconeogenesis in response to hypoglycemia	Low serum cortisol; site of defect determined by ACTH activity tests; possible other comorbid endocrine abnormalities	Cortisol repla

[a]A similar presentation would be expected for tumors with paraneoplastic production of insulin or insulin-like substance.
ACTH, adrenocorticotropic hormone; CT, computed tomography; MRI, magnetic resonance imaging.

Quick HIT

T_4 is converted to T_3 in serum; T_3 is more potent than T_4 but has a shorter half-life.

Quick HIT

If TBG levels increase (e.g., pregnancy, oral contraceptive use), total T_4 increases but free T_4 remains normal.

II. Thyroid Disorders

A. Thyroid Function

1. Thyroid hormones induce central nervous system (CNS) maturation during growth, increase basal metabolic rate, increase cardiac output, and promote bone growth.
2. Thyrotropin-releasing hormone (TRH) secretion from hypothalamus is stimulated by cold and inhibited by stress (see Figure 8-2).
3. TRH induces secretion of thyroid-stimulating hormone (TSH) in the anterior pituitary.
4. TSH secretion is also controlled by feedback inhibition from thyroxine (T_4) thyroid hormone.
5. Metabolic effects are determined by free T_4 and triiodothyronine (T_3); remaining thyroid hormones bound to thyroid-binding globulin (TBG).

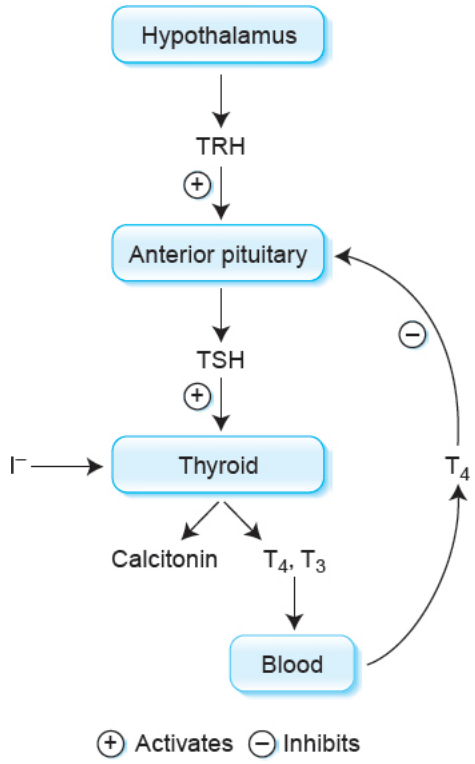


FIGURE **8-2**

Hypothalamopituitary regulation of thyroid hormone production.

I^-, iodine; T_3, triiodothyronine; T_4, thyroxine; TRH, thyroid-releasing hormone; TSH, thyroid-stimulating hormone.

***Quick* HIT**

Nephrotic syndrome and androgen use decrease TBG levels, leading to decreased total T_4 but normal free T_4.

B. Hyperthyroidism

1. Excess production of thyroid hormones
2. Multiple causes, but **Graves' disease** is most common (see Table 8-6)
3. **H/P** = weight loss, increased appetite, **heat intolerance, anxiety,** diaphoresis, palpitations, increased bowel frequency, **muscle weakness;** staring or lid lag, tremor, tachycardia, increased cardiac contractility, increased pulse pressure, warm skin, hyperreflexia, possible atrial fibrillation, goiter

Table 8-6 Causes of Hyperthyroidism

Etiology	Pathology	Aids in Diagnosis	Treatment
Graves' disease	Autoimmune **TSI antibodies** bind to TSH receptors in thyroid and stimulate thyroid hormone production	**Exophthalmos, pretibial myxedema**, painless goiter; TSI found in serum; **high uptake on thyroid scan**	Thionamides (methi euthyroidism in mar **tion** with radioactiv **thyroidectomy** for can be used for sym
Toxic adenoma (Plummer disease)/toxic multinodular goiter	**Single or multiple hyperactive nodules** produce excess thyroid hormones	Thyroid scan shows **increased uptake** at site(s) of nodule(s)	Thionamides, radioa resection
Subacute thyroiditis (de Quervain thyroiditis)	Enlarged thyroid due to possible viral stimulus	**Painful goiter**, mild symptoms of hyperthyroidism, neck pain, **fever;** increased ESR; **decreased uptake on thyroid scan**	Self-limited; NSAID treat symptoms; thy be needed if hypoth gland recovery
Silent thyroiditis	Temporary thyroiditis that **may follow pregnancy**	Painless goiter; **low uptake on thyroid scan; biopsy shows inflammation**	Self-limited; β-bloc
Factitious hyperthyroidism	Excess thyroid hormone ingestion	**No goiter** in cases of hyperthyroidism; **normal** thyroid scan	Stop excess ingesti

ESA, erythrocyte sedimentation rate; NSAIDs, nonsteroidal anti-inflammatory drugs; PTU, propylthiouracil; TSH, thyroid-stimulating hormone; T immunoglobulin.

4. **Labs** = **decreased TSH,** increased total T_4, free T_4, total T_3, and T_3 resin uptake
5. **Complications** = HTN, arrhythmias, **thyroid storm,** osteoporosis; **neonatal Graves' disease** (thyroid-stimulating immunoglobulin [TSI] antibodies can cross the placenta and cause newborns to develop thyrotoxicosis)

C. Thyroid Storm

1. Severe hyperthyroidism induced by infection, surgery, or stress in patients with pre-existing hyperthyroidism
2. **H/P** = existing symptoms of hyperthyroidism, severe diaphoresis, vomiting, diarrhea; tachycardia, fever, **mental status changes**
3. **Labs** = increased T_4 and T_3, decreased TSH
4. **Treatment** = similar to treatment of hyperthyroidism but higher doses of medications given in greater frequency and **given in the following order:** β-blockers (**propranolol,** controls adrenergic effects), thionamides (**methimazole or propylthiouracil [PTU]** block hormone synthesis), IV sodium **iodine** (blocks thyroid hormone release), **hydrocortisone** (inhibits conversion of T_4 to T_3); surgery or radioablation when patient is stable
5. **Complications** = 25% to 50% mortality; treatment options can also have complications: thionamides can cause agranulocytosis, surgery has risk of hypoparathyroidism and vocal cord paralysis (injury to recurrent laryngeal nerve)

D. Hypothyroidism

1. Insufficient production of thyroid hormones
2. Most cases are of primary hypothyroidism; **autoimmune** (Hashimoto thyroiditis); post viral (subacute thyroiditis); drug induced (**lithium, amiodarone**); iatrogenic (ablation)
3. **H/P** = **fatigue,** weight gain, constipation, **periorbital edema,** loss of eyebrows, **cold intolerance,** myalgia, menorrhagia, **depression,** HTN, hyperlipidemia, bradycardia, hyporeflexia
4. **Labs** = **increased TSH,** decreased total T_4, free T_4, total T_3
5. **Complications** = HTN, **myxedema coma**, encephalopathy, carpal tunnel syndrome

E. Hashimoto Thyroiditis

1. Most common cause of hypothyroidism
2. Autoimmune condition characterized by chronic thyroiditis; most commonly in middle-aged women
3. **H/P** = symptoms of hypothyroidism, usually with **painless goiter**
4. **Labs** = **increased TSH,** decreased total T_4, decreased free T_4, **antithyroid peroxidase (anti-TPO),** and **antithyroglobulin antibodies;** lymphocytic infiltrates and fibrosis seen on biopsy
5. **Radiology** = **decreased uptake** on thyroid scan (i.e., "cold scan")
6. **Treatment** = lifelong levothyroxine replacement

NEXT
STEP

To determine if an enlarged thyroid or thyroid mass is caused by excess thyroid activity or a malignancy, perform a thyroid scan (measures uptake of radioactive iodine to indicate normal, excessive, or absent thyroid function).

F. Myxedema Coma

1. Severe presentation hypothyroidism
2. Medical emergency due to a high mortality rate
3. **H/P** = **decreased mental status**, **hypothermia,** bradycardia, hypotension; despite its name, patients do not necessarily present in a coma state
4. **Labs** = **increased TSH**, decreased total T_4, free T_4, total T_3, hyponatremia, hypoglycemia
5. **Treatment** = supportive care, airway protection, **levothyroxine IV,** fluids, dextrose, hydrocortisone (until adrenal insufficiency is excluded)

G. Euthyroid Sick Syndrome

1. Low levels of serum thyroid hormone due to a systemic illness
2. Also known as "low T_3 syndrome" or "nonthyroidal illness syndrome"
3. **H/P** = patients with critical illness, typically on intensive care units, trauma, DKA, starvation
4. **Labs** = decreased total and free T_3, normal T_4 and TSH
5. **Treatment** = usually no treatment required other than treating underlying illness

Table 8-7 Types of Thyroid Carcinoma

Type	Cells Affected	Frequency	Characteristics	Prognosis
Papillary	Columnar cells of gland	**Most common form** (78% cases); most common in younger patients	Begins as slow-growing nodule; eventually metastasizes to local cervical lymph nodes	**Good;** few re type has sligh (50% 10-yr su
Follicular	Follicular or thyroid epithelial cells	Second most common form (15% cases)	Firm, "cold" thyroid nodule, invades the tumor capsule and vessels (hematogenous spread)	Directly relate and metastas prognosis
Medullary	Parafollicular C cells	4% of thyroid cancers	**Produces calcitonin;** may present with other endocrine tumors (MEN IIa and IIb)	Worse in olde ses common a
Anaplastic	Poorly differentiated neoplasm	1% of thyroid cancers	**Very aggressive;** local extension causes hoarseness, dysphagia	Poor

MEN IIa, multiple endocrine neoplasia type IIa.

H. Thyroid Carcinoma

1. Workup of thyroid nodules
   a. Thyroid nodules are usually benign and increase in frequency with age.
   b. Nodules should be evaluated with TSH levels, thyroid function tests, ultrasound (US), and fine needle aspiration (FNA) with biopsy.
   c. "Cold" nodules exhibit decreased radioactive iodide (I^-) uptake (from decreased metabolic activity); "hot" nodules exhibit increased iodide uptake (from increased metabolic activity).
   d. Increased risk of malignancy = male, children, adults over the age of 60 years and under the age of 30 years, history of neck irradiation, poor iodide uptake on thyroid scan (cold nodule), solid nodule on US.
   e. Malignant nodules can arise from a variety of thyroid cell types (see Table 8-7).
2. **H/P** = nontender nodule in anterior neck, dysphagia, hoarseness; possible cervical lymphadenopathy
3. **Labs** = biopsy provides diagnosis; thyroid hormones normal or decreased
4. **Radiology** = US used to determine size and local extension; thyroid scan may differentiate hot from cold nodule (malignant nodules more likely to be cold)
5. **Treatment**
   a. Benign small cystic nodules may be observed.
   b. Benign solid nodules are treated with surgery, radioablation, and postoperative levothyroxine to stop thyroid hormone overproduction and decrease risk of malignant conversion.
   c. Malignant tumors require surgical resection (lobectomy for nonanaplastic tumors <1 cm diameter, total thyroidectomy for larger tumors) and radioiodine ablation.
   d. Radiation therapy for tumors with local extension; chemotherapy for metastatic tumors.

e. Thyroid replacement (levothyroxine) needed after surgery.

Quick HIT

Hypothyroidism can result from autoimmune processes, **thyroid surgery**, thyroid radioablation, pituitary dysfunction, chronic lithium use, and chronic iodide use.

NEXT
STEP

If decreased TSH and hypothyroidism are seen, suspect a pituitary or hypothalamic etiology.

Quick HIT

Two frequent complications of thyroid surgery are **hoarseness** (secondary to damage of the recurrent laryngeal nerve) and **hypocalcemia** (secondary to surgical hypoparathyroidism).

III. Parathyroid Disorders

A. Parathyroid Function

1. Plasma calcium (Ca^{2+}) regulation (see Figure 8-3)
   a. **Parathyroid hormone** (PTH): **secreted in response to low serum Ca^{2+}**; induces osteoclasts to reabsorb bone and increases plasma Ca^{2+}; induces kidneys to increase conversion of 25-(OH) vitamin D to 1,25-$(OH)_2$ vitamin D, decreases phosphate reabsorption, and increases distal tubule Ca^{2+} reabsorption for net increase in plasma Ca^{2+}

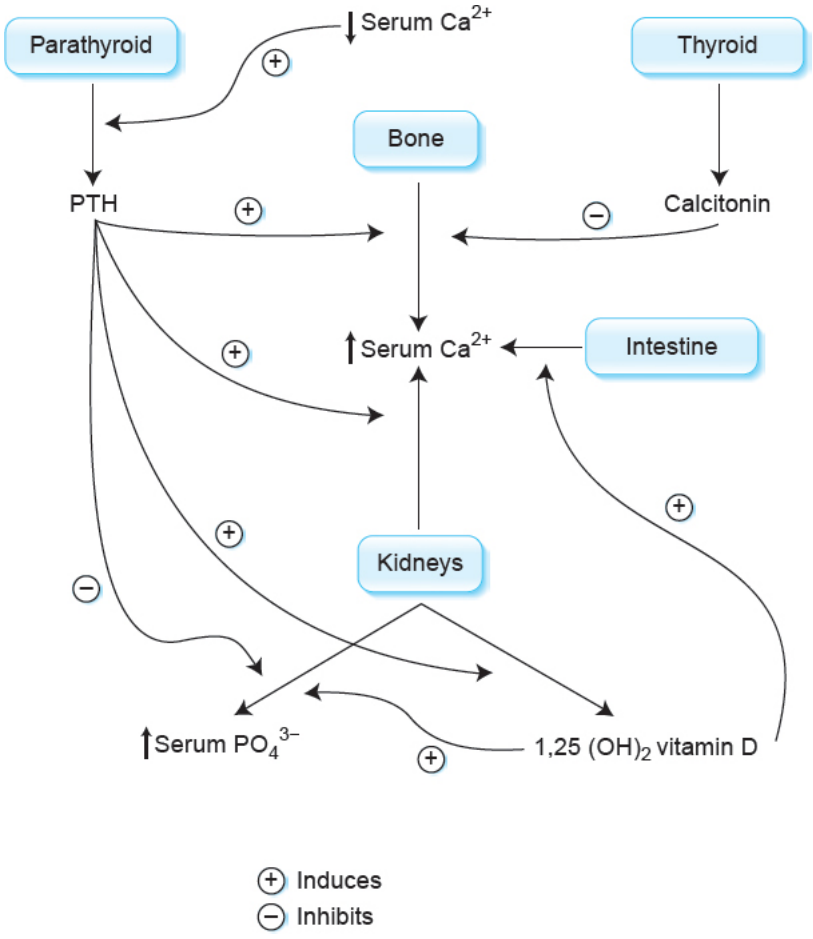


FIGURE 8-3
Serum Ca^{2+} regulation.
PTH, parathyroid hormone.

b. **1,25-$(OH)_2$ vitamin D:** metabolite of dietary vitamin D; production in kidneys increases with PTH secretion; increases intestinal Ca^{2+} absorption; increases renal proximal tubule phosphate reabsorption (in opposition to PTH-induced phosphate wasting)
c. **Calcitonin:** secreted by thyroid parafollicular cells; inhibits bone reabsorption

MNEMONIC

Remember the **"bones," "stones," "groans,"** and **"psychiatric overtones"** of hypercalcemia in cases of hyperparathyroidism.

Quick HIT

Decreased Ca^{2+} with increased PTH suggests a hyperparathyroidism secondary to **malnutrition**, malabsorption, **renal disease**, or calcium-wasting drugs.

B. Primary Hyperparathyroidism

1. **Excess PTH secretion**, leading to **hypercalcemia** and osteopenia
2. Most cases result from **single adenoma;** remaining cases mostly occur with hyperplasia of all four glands; parathyroid cancer is rare
3. **H/P** = frequently asymptomatic; symptoms of hypercalcemia may be present (e.g., bone pain, nausea and vomiting, mental status changes, renal stones, constipation, weakness, increased risk of fracture) (see Chapter 7, **Genitourinary Disorders**, for further discussion of hypercalcemia)
4. **Labs** = increased Ca^{2+}, decreased phosphate, increased urine Ca^{2+}, increased PTH
5. **Radiology** = decreased bone density on dual x-ray absorptiometry (DXA) scan
6. **Treatment** = surgical resection (i.e., parathyroidectomy) of single adenoma; for four-gland hyperplasia, all glands are removed, and a portion of one gland is implanted in the muscle of forearm to maintain some PTH production; treat hypercalcemia with IV fluids and bisphosphonates
7. **Complications** = osteoporosis, kidney stones, renal disease

C. Hypoparathyroidism

1. PTH deficiency caused by **surgical removal** of parathyroids (most common) or autoimmune degeneration of glands (uncommon), leading to hypocalcemia
2. **H/P** = tingling in lips and fingers, dry skin, weakness, abdominal pain, tetany, dyspnea; possible tachycardia, **prolonged QT,** seizures, movement disorders, cataracts, dental hypoplasia, positive **Trousseau** (i.e., carpal spasm when blood pressure cuff inflated) and **Chvostek signs** (i.e., tapping of facial nerve causes spasm) (see Chapter 7, **Genitourinary Disorders**)
3. **Labs** = decreased Ca^{2+}, increased phosphate, decreased PTH
4. **Radiology** = x-rays may demonstrate osteosclerosis or increased bone density
5. **Treatment** = Ca^{2+} and vitamin D supplementation

D. Pseudohypoparathyroidism

1. Hypocalcemia resulting from tissue **nonresponsiveness to PTH**
2. Associated with developmental and skeletal abnormalities (e.g., **Albright hereditary osteodystrophy**)
3. Hypomagnesemia (seen in chronic alcoholics and burn victims) can also lead to pseudohypoparathyroidism
4. **H/P** = symptoms of hypocalcemia, short stature, seizures, poor mental development in children
5. **Labs** = decreased Ca^{2+}, increased phosphate, **increased PTH;** administration of PTH causes no change in serum or urine Ca^{2+}
6. **Treatment** = Ca^{2+} and vitamin D supplementation; magnesium in cases of hypomagnesemia

IV. Pituitary and Hypothalamic Disorders

A. Hypothalamic–Pituitary Function

1. Hypothalamus responds to stimuli by modulating pituitary activity (see Figure 8-4).
   a. Hormones are released into the hypophyseal portal system to regulate subsequent hormone release from the anterior pituitary.
   b. Anterior pituitary hormone secretion is regulated by feedback mechanisms in addition to the hypothalamus.
   c. Impulses sent through the hypothalamo-hypophyseal tract regulate hormone release from the posterior pituitary.
2. Anterior pituitary lacks nerve terminals and is responsible for secretion of prolactin, adrenocorticotropic hormone (ACTH), TSH, growth hormone (GH), follicle-stimulating hormone (FSH), and luteinizing hormone (LH).
3. Posterior pituitary is a neural extension of the hypothalamus and is responsible for antidiuretic hormone (ADH) and oxytocin secretion.

Quick HIT

Prolactinoma is the most common pituitary tumor.

B. Hyperprolactinemia

1. Excess **prolactin** secretion by anterior pituitary
   a. Causes decreased LH and FSH secretion, galactorrhea (i.e., milk secretion), and amenorrhea in women
   b. Causes gynecomastia in men
2. Can result from **pregnancy, prolactinoma,** drugs that block dopamine synthesis (e.g., phenothiazines, risperidone, haloperidol, methyldopa, verapamil), dopamine depleting drugs, or hypothalamic damage
3. **H/P** = **amenorrhea and galactorrhea (women);** decreased libido, erectile dysfunction, and **gynecomastia (men);** bitemporal hemianopsia can result from mass effect of tumor in sella turcica
4. **Labs** = increased prolactin; if adenoma, prolactin >300 ng/mL and TRH administration causes no additional prolactin secretion
5. **Radiology** = magnetic resonance imaging (MRI) may detect pituitary tumor
6. **Treatment** = dopamine agonists (e.g., cabergoline, bromocriptine, pergolide), stopping offending agents; transsphenoidal surgery and radiation therapy should be performed in refractory cases

NEXT
STEP

Compare current appearance of adult patients to multiple pictures at younger ages to aid in the detection of a gradual enlargement in features seen in acromegaly.

C. Acromegaly

1. Excess secretion of **GH** by anterior pituitary caused by adenoma
2. **H/P** = **enlargement** of hands and feet, coarsening of facial features (e.g., enlargement of nose, jaw, and skin folds), thickened skin, increased body hair growth, joint pain (caused by osteoarthritis), neural pain (because of nerve entrapment); changes may be gradual

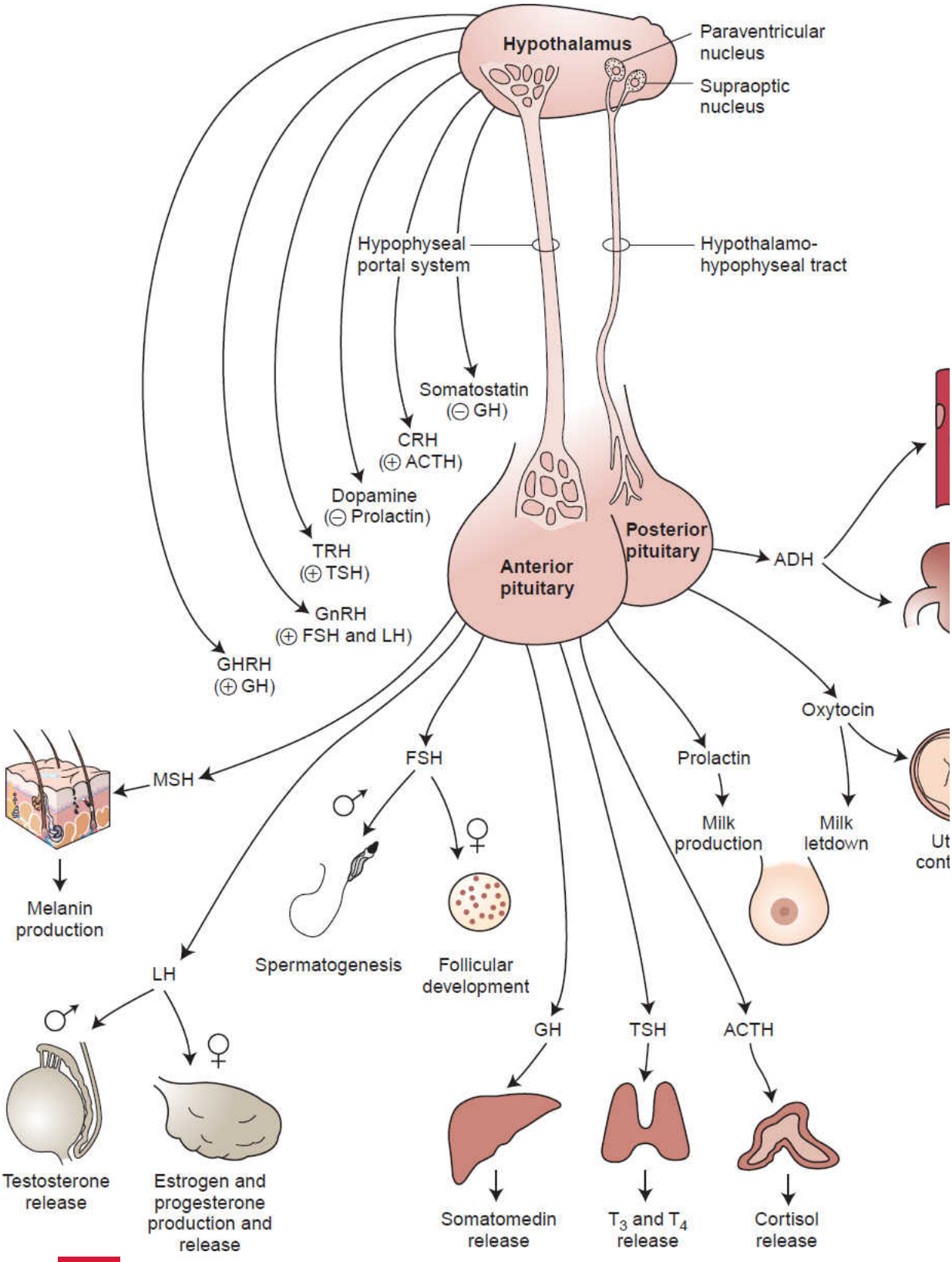


FIGURE **8-4**

Hypothalamopituitary axis.

ACTH, adrenocorticotropic hormone; ADH, antidiuretic hormone; CRH, corticotrophin-releasing hormone; GH, growth hormone; GHRH, growth hormone– releasing hormone; GnRH, gonadotropin-releasing hormone; FSH, follicle-stimulating hormone; LH, luteinizing hormone; PRH, prolactin-releasing hormone; T_3, triiodothyronine; T_4, thyroxine; TRH, thyrotropin-releasing hormone; TSH, thyroid-stimulating hormone.

(From Mehta, S., Milder, E. A., Mirachi, A. J., & Milder, E. [2006]. *Step-Up: A high-yield, systems-based review for the USMLE Step 1* [3rd ed., p. 165]. Philadelphia, PA: Lippincott Williams & Wilkins.)

3. Heart, lungs, spleen, liver, and kidneys become enlarged and can cause symptoms secondary to dysfunction
4. **Labs** = elevated hepatic insulin-like growth factor (**IGF-1**) is the most sensitive test, increased GH 1 to 2 hours following 100 g glucose load (GH decreases in normal cases) is a more specific test
5. **Radiology** = computed tomography (CT) or MRI may detect tumor; x-rays may demonstrate increased bone density

6. **Treatment** = surgical resection of adenoma; dopamine agonists or octreotide to lessen effects of GH; radiation therapy may be useful in cases unresponsive to surgical or medical treatment
7. **Complications** = **cardiac failure**, DM, spinal cord compression, vision loss secondary to pressure of tumor on optic nerve

NEXT
STEP

For a child with extremely **advanced growth for the given age** (gigantism), perform a workup for increased GH.

Quick HIT

Patients with acromegaly have **insulin resistance** (similar to DM type II) and develop diabetes in 10% of cases.

D. Hypopituitarism

1. **Deficiency of all anterior pituitary hormones** caused by tumor, hemorrhagic infarction (i.e., pituitary apoplexy), surgical resection, trauma, sarcoidosis, tuberculosis, postpartum necrosis (i.e., **Sheehan syndrome**), or dysfunction of the hypothalamus
2. Some pituitary hormones are kept in storage, and target organs may maintain some autonomous function, so symptoms specific to deficiency of each type of hormone appear at various times (see Table 8-8)
3. **Labs**
   a. LH/FSH: decreased LH, FSH, estrogen (women), and testosterone (men); menstruation does not occur following administration of medroxyprogesterone
   b. GH: decreased GH; no increase in GH after administration of insulin
   c. TSH: decreased TSH, T_4, and T_3 uptake
   d. Prolactin: decreased prolactin (most noticeable postpartum)
   e. ACTH: decreased ACTH; cortisol does not increase following administration of insulin (normally should increase at least 10 µg/dL); ACTH and 11-deoxycortisol do not increase following administration of metyrapone
4. **Treatment** = treat underlying cause, if possible; treatment depends on which hormones are deficient
   a. GH: **recombinant hormone replacement therapy**
   b. LH/FSH: testosterone replacement in men; estrogen–progesterone pill for women; gonadotropin-releasing hormone (GnRH) can be used in men or women desiring fertility
   c. TSH: levothyroxine
   d. Prolactin: no need to treat (women will be unable to lactate)
   e. ACTH: hydrocortisone, dexamethasone, or prednisone

Table 8-8 Progression of Hormone Deficiency in Hypopituitarism

Order of Loss	Hormone(s)	Symptoms
1	GH	Growth failure and short stature in children
2	LH, FSH	Infertility, decreased libido, and decreased pubic hair; amenorrhea and genital atrophy in women; impotence and testicular atrophy in men
3	TSH	Hypothyroidism leading to fatigue and cold intolerance; no goiter
4	Prolactin	No postpartum lactation
5	ACTH, MSH	Adrenal insufficiency leading to fatigue, weight loss, decreased appetite, and poor response to stress; decreased skin pigment because of low MSH

ACTH, adrenocorticotropic hormone; FSH, follicle-stimulating hormone; GH, growth hormone; LH, luteinizing hormone; MSH, melanocyte-stimulating hormone; TSH, thyroid-stimulating hormone.

Quick HIT

ACTH and melanocyte-stimulating hormone (**MSH**) arise from the same precursors and follow the same trend in their serum concentrations.

E. Disorders of Posterior Pituitary

1. Syndrome of inappropriate ADH secretion (SAIDH) (see Chapter 7, **Genitourinary Disorders**)
2. Diabetes insipidus (see Chapter 7, **Genitourinary Disorders**)

V. Adrenal Disorders

A. Adrenal Function (See Table 8-9)

Table 8-9 Function of Zones in Adrenal Cortex and Medulla

Region	Stimulation	Secretory Products	Action of Secretory Products
Zona glomerulosa (cortex)	Renin–angiotensin system	Aldosterone	Conserve body sodium, maintains body fluid volume
Zona fasciculata (cortex)	ACTH	Cortisol	Maintains glucose production from proteins, aids in fat metabolism, aids in vascular regulation, influences immune response, aids in nervous regulation
Zona reticularis (cortex)	ACTH	Androgens	Development of secondary sexual characteristics, increased bone and muscle mass, promotes male sexual differentiation and sperm production
Medulla	Preganglionic sympathetic neurons	Epinephrine, norepinephrine	Postsynaptic neurotransmitter in sympathetic autonomic system, induces sympathetic effects (glucose mobilization, increase heart contractility and rate, etc.)

ACTH, adrenocorticotropic hormone.

***Quick* HIT**

Excess corticosteroid administration is the **most common** cause of Cushing syndrome.

NEXT
STEP

To determine the cause of cortisol excess, screen patients with symptoms of Cushing syndrome with the following:

- **Low dexamethasone suppression test:** 1–2 mg dexamethasone given at night; low cortisol normally found next morning; no decrease in cortisol seen in Cushing syndrome;
- **High-dose dexamethasone suppression test:** 8 mg/day for 2 days; used to determine cause of cortisol excess.

B. Cushing Syndrome

1. Syndrome of **excess cortisol** is caused by **excess corticosteroid administration, pituitary adenoma** (i.e., Cushing disease), paraneoplastic ACTH production, or adrenal tumor
2. **H/P** = weakness, depression, menstrual irregularities, polydipsia, polyuria, increased libido, impotence; HTN, **acne**, **increased hair growth,** central obesity, **proximal muscle weakness**, **"buffalo hump"** (i.e., hunchback-like hump on back), **"moon facies"** (i.e., rounded face caused by increased fat deposition), **purple striae** on abdomen, cataracts
3. **Labs** = (in addition to those depicted in Figure 8-5) hyperglycemia, glycosuria, decreased K^+
4. **Treatment** = adjust corticosteroid dosing in cases of excess administration; surgical resection or pituitary irradiation for pituitary tumors; surgical resection for some nonpituitary tumors; octreotide may improve symptoms in paraneoplastic syndromes; cortisol replacement may be needed after surgery
5. **Complications** = increased risk of mortality from cardiovascular or thromboembolic complications; increased infection risk, **avascular necrosis of hip,** hypopituitarism, or adrenal insufficiency after surgery

C. Hyperaldosteronism

1. Primary hyperaldosteronism is due to an adrenal adenoma (i.e., Conn syndrome); secondary hyperaldosteronism is due to activation of the renin–angiotensin aldosterone system secondary to perceived low blood pressure in the kidneys (e.g., renal artery stenosis, heart failure, cirrhosis, nephrotic syndrome)
2. **H/P** = headache, weakness, paresthesia; recalcitrant **HTN,** tetany
3. **Labs** = **decreased K+, metabolic alkalosis,** mildly increased Na^+, decreased renin (Conn syndrome only), **increased 24-hour urine aldosterone; high ratio of plasma aldosterone concentration (PAC) to plasma renin activity (PRA)** indicates primary hyperaldosteronism
4. **Radiology** = CT or MRI may detect adrenal mass
5. **Treatment** = surgical resection of tumor (primary hyperaldosteronism); treat underlying disorder causing renin–angiotensin system hyperactivity (in secondary hyperaldosteronism); aldosterone antagonists (e.g., spironolactone) improve hypokalemia until definitive therapy administered

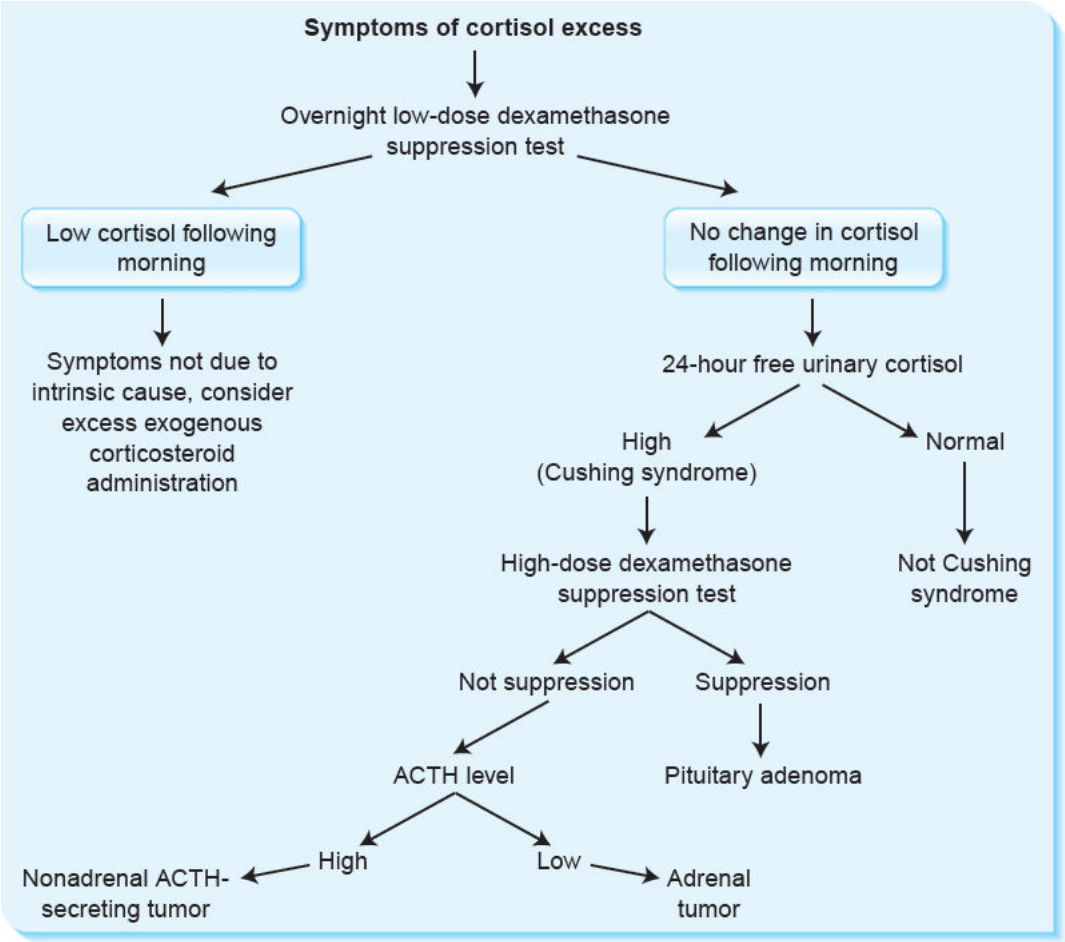


FIGURE 8-5
Example of diagnostic algorithm for a patient with suspected Cushing syndrome caused by cortisol excess.
ACTH, adrenocorticotropic hormone.

D. Adrenal Insufficiency

1. **Mineralocorticoid** (i.e., aldosterone) or **glucocorticoid** (i.e., cortisol) **deficiency** caused by adrenal disease or ACTH insufficiency
2. Type
   a. **Addison disease** (primary insufficiency): autoimmune destruction of adrenal cortices caused by autoimmune disease (most common cause in developed countries), infection, or hemorrhage; can occur with other endocrine autoimmune processes
   b. **Secondary corticoadrenal insufficiency:** due to insufficient ACTH production by pituitary
   c. **Tertiary corticoadrenal insufficiency:** because of insufficient corticotropin-releasing hormone (CRH) secretion by hypothalamus, most commonly due to chronic corticosteroid use

NEXT
STEP

Examine patients with adrenal insufficiency for **increased skin pigmentation**; this finding is **seen in Addison disease** (secondary to increased MSH production accompanying increased ACTH production) but **not in secondary or tertiary insufficiency**.

3. **H/P** = weakness, **fatigue,** anorexia, weight loss, nausea and vomiting (more common in primary disease), myalgias, arthralgias, decreased libido (women), memory impairment, depression, mild psychosis; **hypotension,** possible **increased skin pigmentation** (because of feedback influence of melanocyte-stimulating hormone [MSH])
4. **Labs**
   a. Decreased Na^+ and increased K^+ secondary to low aldosterone, eosinophilia, decreased cortisol
   b. Increased ACTH with Addison disease; decreased ACTH with secondary or tertiary insufficiency
   c. Decreased cortisol that increases following ACTH analog (cosyntropin) administration in secondary or tertiary insufficiency but not in Addison disease
5. **Treatment** = treat underlying disease; **glucocorticoid replacement** (e.g., hydrocortisone, dexamethasone, prednisone), **mineralocorticoid replacement** (may not be needed in secondary or tertiary disease), dehydroepiandrosterone (DHEA), and hydration to achieve adequate volume status; titrate cortisol levels for periods of stress (increased need) and to avoid exacerbating secondary adrenal insufficiency

6. **Complications** = **addisonian crisis** (i.e., severe weakness, fever, mental status changes, and vascular collapse caused by stress and increased cortisol need; treat with IV glucose and hydrocortisone or vasopressors), secondary insufficiency caused by excess cortisol replacement

Quick HIT

Symptoms of Cushing syndrome can take up to a year to resolve following therapy.

Quick HIT

Cortisol deficiency is usually not symptomatic in CAH because hyperplasia can maintain cortisol in the low-normal range despite enzyme deficiency.

Quick HIT

21-α-Hydroxylase deficiency is the **most common** form of CAH.

Quick HIT

Pheochromocytoma rule of 10s: 10% malignant, 10% multiple, 10% bilateral, 10% extra-adrenal, 10% children, 10% familial, 10% calcify.

NEXT
STEP

Patients with **intermittent tachycardia** and **HTN** with sympathetic symptoms should have a pheochromocytoma workup included in their evaluation.

E. Congenital Adrenal Hyperplasia (CAH)

1. Enzymatic defect in synthesis of cortisol, resulting in decreased cortisol, reactive increase in ACTH production, adrenal hyperplasia, and androgen excess (see Figure 8-6)
2. **17-α-Hydroxylase deficiency**
   a. Deoxycorticosterone overproduction; cortisol, androgen, and estrogen deficiencies
   b. **H/P** = **amenorrhea (women), ambiguous genitalia (men);** HTN
   c. **Labs** = **decreased K^+, increased Na^+, decreased androgens,** decreased 17-α-hydroxyprogesterone
3. **21-α-Hydroxylase deficiency**
   a. (Usually) partial deficiency of enzyme resulting in excess androstenedione and insufficient cortisol and aldosterone
   b. **H/P** = ambiguous genitalia (female infants), virilization (women), macrogenitosomia and precocious puberty (men); dehydration and **hypotension** in more severe cases
   c. **Labs** = **decreased Na+, increased K+**, increased androgens
4. **11-β-Hydroxylase deficiency**
   a. Enzyme deficiency resulting in **excess deoxycorticosterone,** deoxycortisol, and androgens and insufficient cortisol and aldosterone
   b. **H/P** = ambiguous genitalia (female infants), virilization (women), macrogenitosomia and precocious puberty (men); **HTN** (secondary to deoxycorticosterone)
   c. **Labs** = increased deoxycorticosterone, increased deoxycortisol, increased androgens
5. **Treatment**
   a. 17-α-Hydroxylase deficiency: cortisol replacement to achieve ACTH suppression; most children raised as females; estrogen–progesterone replacement given to genotypic females at puberty; genotypic males may have reconstructive surgery of genitals

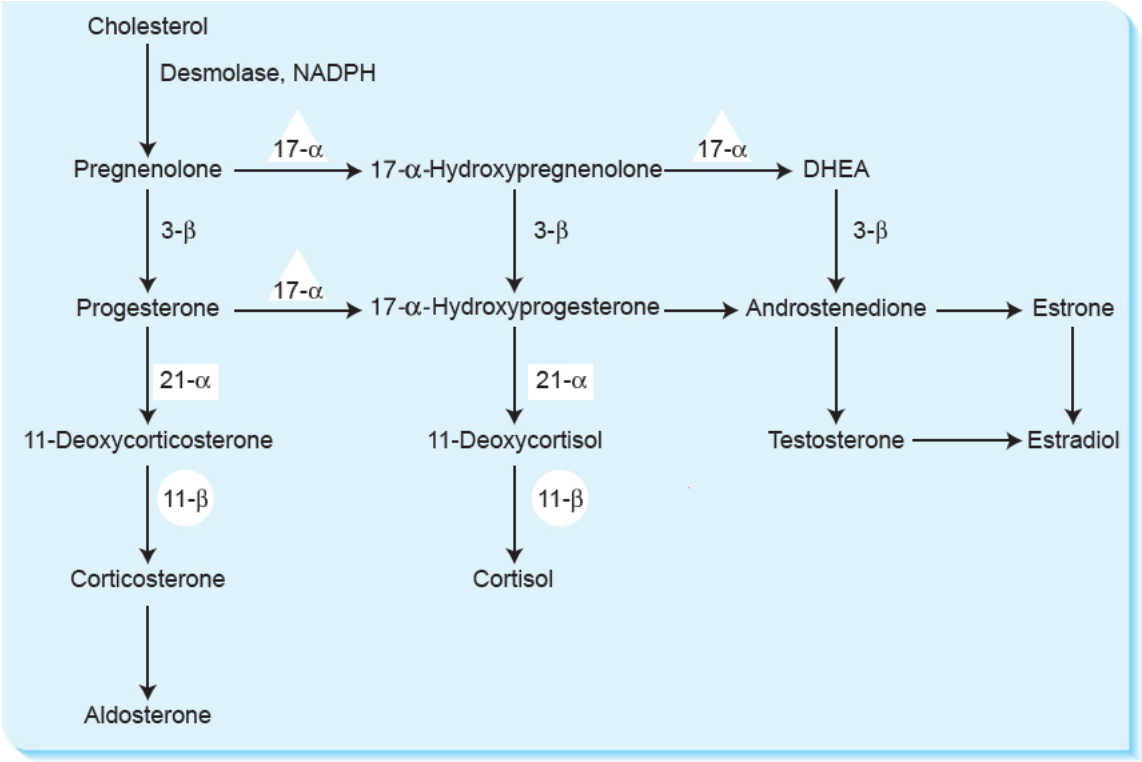


FIGURE **8-6**

Steroid hormone synthesis and causes of congenital adrenal hyperplasia.
Note the blocks in the pathway from 17-α-hydroxylase deficiency (*triangles*), 21-α-hydroxylase deficiency (*rectangles*), and 11-β-hydroxylase deficiency (*circles*). 3β, 3β-hydroxysteroid dehydrogenase; 11β, 11β-hydroxylase; 17α, 17α-hydroxylase; 21α, 21α-hydroxylase; DHEA, dehydroepiandrosterone; NADPH, nicotinamide adenine dinucleotide phosphate (reduced form).

b. 21-α-Hydroxylase deficiency: cortisol replacement therapy for ACTH suppression; fludrocortisone for mineralocorticoid replacement; reconstructive genital surgery
c. 11-β-Hydroxylase deficiency: cortisol replacement (hydrocortisone or dexamethasone) for ACTH suppression; anti-HTN may be required for persistent HTN

***Quick* HIT**

Mutation of the **RET proto-oncogene** is found in most cases of multiple endocrine neoplasia (MEN) type IIa and IIb.

MNEMONIC

Remember MEN type I as **3 Ps: P**arathyroid hyperplasia, **P**ituitary, **P**ancreas. MEN type IIa can be remembered as **1 M and 2 Ps: M**edullary thyroid carcinoma, **P**arathyroid hyperplasia, and **P**heochromocytoma. MEN type IIb can be remembered by the **2 Ms and 1 P: M**ucosal neuromas, **M**edullary thyroid carcinoma, and **P**heochromocytoma.

F. Pheochromocytoma

1. Adrenal medulla tumor that secretes epinephrine and norepinephrine, leading to stimulation of sympathetic nervous system; rarely extra-adrenal in location
2. **H/P** = sudden palpitations, chest pain, **diaphoresis, headache,** anxiety; intermittent **tachycardia, HTN**
3. **Labs** = increased 24-hour urinary catecholamines and metanephrines; increased plasma-free metanephrines; increased 24-hour urinary vanillylmandelic acid (VMA) (test performed infrequently because of limited sensitivity/specificity)
4. **Imaging** = CT or MRI of abdomen (**95% are intra-abdominal**); fluorodeoxyglucose (FDG)-positron emission tomography (PET) or metaiodobenzylguanidine (MIBG) scan for localizing metastatic disease
5. **Treatment** = surgical resection; α- and β-blockers used before and during surgery to control blood pressure; α-blocker must be given **before** β-blocker to avoid hypertensive crisis from unopposed α stimulation

VI. Multiple Endocrine Neoplasia (MEN)

A. Autosomal dominant syndromes involving dysfunction of multiple endocrine glands (see Table 8-10)

B. Gland dysfunction may be secondary to hyperplasia or neoplasm

Table 8-10 Types of Multiple Endocrine Neoplasia (MEN)

Type	Endocrine Involvement	Characteristics	Treatment
I	Parathyroid adenoma Pancreas (islet cell) or GI endocrine tumors Pituitary adenoma	Hyperparathyroidism, hypercalcemia, **possible Zollinger–Ellison syndrome**, various **pituitary disorders** (e.g., acromegaly, Cushing syndrome, galactorrhea)	Subtotal parathyroidect resection of pancreatic surgical resection of pit
IIa	Medullary thyroid cancer Parathyroid hyperplasia Pheochromocytoma	**Medullary carcinoma**, increased calcitonin, **hyperparathyroidism**, hypercalcemia, increased serum and urine catecholamines	Total thyroidectomy, su pheochromocytoma, sul ectomy
IIb	Mucosal neuromas Medullary thyroid cancer Pheochromocytoma	**Medullary carcinoma**, increased calcitonin, hypercalcemia, **Marfanoid body habitus**, mucosal nodules	Total thyroidectomy, su pheochromocytoma

QUESTIONS

1. A 40-year-old female presents with AMS. She has a history of type I DM and vitiligo. Her vital signs are as follows: heart rate 140/min, blood pressure 144/85 mm Hg, respiratory rate is 22/min, saturation 98%, temp 37.8°C. On physical examination, she is awake and alert but anxious and confused; there is a diffusely enlarged thyroid; diaphoresis; and increased reflexes. Sodium is 139, chloride 103, bicarbonate 22, glucose is 180 mg/dL, TSH levels 0.08 mU/L (normal 0.4 to 5.0 mU/L), free T4 3.8 ng/dL (normal 0.8 to 1.8 ng/dL). Of the following, which is the best next step in management?

   A. Radioablation
   B. Propranolol
   C. PTU
   D. Insulin
   E. Hydrocortisone

2. A 50-year-old female with history of hypertension is admitted to the hospital for persistent hypoglycemia. She initially arrived with weakness and diaphoresis to the emergency department. Her glucose level at the time was 48 mg/dL. She denies any recent illness, drug use or recent alcohol intake. Upon reviewing chart, you notice she has been hospitalized multiple times for similar symptoms. Electrolytes are within normal levels. TSH levels 0.9 mU/L (normal 0.4 to 5.0 mU/L), free T4 0.9 ng/dL(normal 0.8 to 1.8 ng/dL). Despite treatment with glucose, patient continues to have hypoglycemia episodes during hospital admission. Which of the following may help in the diagnosis of this patient?

   A. Free T3
   B. Urine metanephrines
   C. C-peptide
   D. Prolactin

3. A 14-day-old boy is brought to the ED because of vomiting and decreased feeding for 2 days. He was born at term, vaginal delivery without complications. His vital signs are as follows: heart rate 176/min, blood pressure 58/36 mm Hg, respiratory rate is 46/min, saturation 98%, temp 37°C. On physical examination, you notice he is crying, fontanelle is depressed, no cardiac murmurs, lungs are clear to auscultation, capillary refill is 3 to 4 seconds. Genital examination is unremarkable. Na 128, K 6.1, glucose 30, BUN 24, creatinine 0.8. Despite treatment with fluids, glucose, and antibiotics, the child continues to have episodes of hypoglycemia and electrolyte abnormalities. Which of the following is most likely to be decreased in this patient?

   A. Aldosterone
   B. 17-Hydroxyprogesterone
   C. Dehydroepiandrosterone
   D. Testosterone

4. A 46-year-old female arrives at the office with a complaint of general weakness. She denies any fever, vomiting, diarrhea, abdominal pain, weight loss, or recent illness. Upon further questioning she mentions that lately she has been feeling constipated. She denies having any history of prior systemic illness, surgeries, taking any medication, smoking, or drug intake. Recently she had a small fall and suffered a wrist fracture. Physical examination shows no abnormalities. Laboratory results are as follows: Na 138, K 4, bicarbonate 24, chloride 100, BUN 13, creatinine 0.6, calcium 12.0, phosphorus 2.1.
   Which of the following is a likely finding in this patient?

   A. Increased urine calcium
   B. Decreased urine calcium
   C. Decreased PTH
   D. Decrease in vitamin D

5. A 38-year-old female presents to the office with complaint of menstrual abnormalities. Her last period was about 3 months before and she used to have a regular menstrual cycle. Upon further questioning, she also mentions a milky nipple discharge. She has a history of schizophrenia and takes haloperidol. She denies using alcohol, tobacco, or illicit drugs. Physical examination is normal. Which of the following would be the most important next step?

   A. β-hCG test
   B. Prolactin levels
   C. Brain MRI
   D. FSH levels

6. A 40-year-old female presents with complaint of left hip pain. The pain started 1 day prior. Initially it was mild but has worsened since. She denies any trauma, fever, chills, recent illness, or prior similar episodes. She has a history of rheumatoid arthritis. Her vital signs are as follows: heart rate 96/min, blood pressure 151/86 mm Hg, respiratory rate is 18/min, saturation 98%, temp 37°C. On physical examination you noticed facial hair and abdominal striae. The left hip has decreased range of motion due to pain but otherwise normal. This patient is at risk of what complication?

   A. Cardiovascular disease
   B. Hypoglycemia episodes
   C. Weight loss
   D. Increased muscle mass

9
Dermatology

I. Infections

A. Cellulitis

1. Acute bacterial infection of the dermis and subcutaneous tissue most frequently caused by **group A streptococci**
2. **Risk factors** = **intravenous (IV) drug use, diabetes mellitus (DM)**, immunocompromise, penetration of skin (e.g., skin ulcer, surgery, trauma), previous cellulitis, venous or lymphatic dysfunction
3. **History and physical (H/P)** = **erythema**, swollen and painful skin, myalgias, chills; warmth in involved area, fever; skin findings may be near wound (see Figure 9-1)
4. **Labs** = increased white blood cell count (WBC), erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP)
5. **Treatment** = oral cephalosporins or penicillinase-resistant β-lactams for 10 to 14 days; IV antibiotics for severe cases or bacteremia; patients with purulence present and/or at risk for MRSA should receive co-trimoxazole or linezolid or IV vancomycin if severe
6. **Complications** = abscess, sepsis, necrotizing fasciitis; 20% to 50% recurrence rate

Quick HIT

Skin and wound cultures are rarely useful in cellulitis because they frequently contain other normal skin flora or findings are false negative.

B. Skin Abscess

1. **Subcutaneous** collection of pus most commonly caused by staphylococcal bacteria, usually MRSA
2. Can occur as collection of multiple infected hair follicles (i.e., carbuncle)
3. **Hidradenitis suppurativa**
   a. Chronic follicular occlusion and **apocrine gland** inflammation resulting in recurrent abscesses in the axilla, groin, and perineum
   b. Chronic infection leads to scarring
   c. May require both antibiotics and surgical excision for treatment

Quick HIT

Anaerobic bacteria are more commonly a cause of abscesses in the lower back and perineal regions than in other parts of the body.

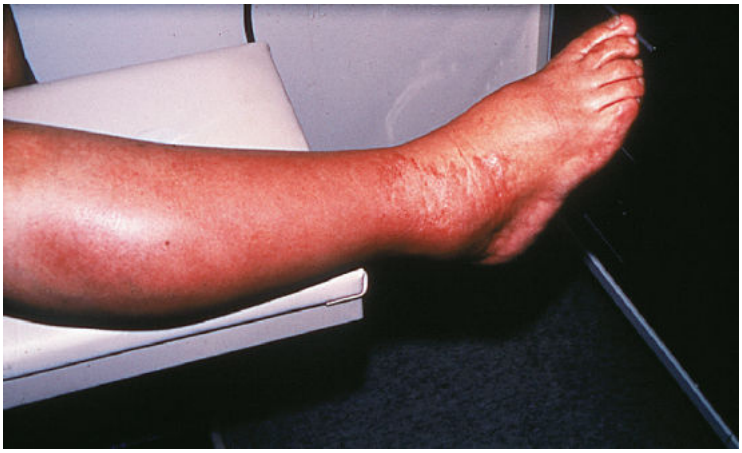


FIGURE 9-1
Cellulitis of the right pretibial region.
Note the erythematous, swollen skin with mild desquamation.
(From Goodheart, H. P. [2003]. *Photoguide of Common Disorders* [2nd ed.]. Philadelphia, PA: Lippincott Williams & Wilkins; with permission; Figure 2-69.)

4. **H/P** = erythematous, fluctuant, and localized swelling in skin; tender on palpation; pain frequently relieved by rupture of abscess
5. **Labs** = gram stain and culture of abscess recommended for complicated or recurrent cases
6. **Treatment** = **incision and drainage**; antibiotics (such as co-trimoxazole, that cover MRSA)
7. **Complications** = sepsis, facial abscess can lead to cavernous sinus thrombosis

C. Necrotizing Fasciitis

1. Quickly spreading group polymicrobial infection of **fascial planes** leading to extensive soft tissue destruction and systemic infection
2. **H/P** = pain out of proportion of examination, erythematous, warm, and swollen skin; **loss of sensation** in involved tissue, fever, crepitus in infected skin, purple discoloration, bullae, rapid progression
3. **Labs** = increased WBC, ESR, and CRP; hyponatremia, operative culture useful for determining pathogen
4. **Radiology** = x-ray or computed tomography (CT) may detect subcutaneous collections of air
5. **Treatment** = prompt surgical debridement, incision, and drainage; broad-spectrum IV antibiotics
6. **Complications** = sepsis, compartment syndrome, high mortality (25% patients)

D. Gangrene

1. Tissue necrosis because of **poor vascular supply** or severe infection (occasionally, *Clostridium perfringens*); described as wet or dry, depending on appearance
2. **H/P** = prior skin infection or penetrating wound, severe pain in skin; fever, hypotension, skin crepitus, **rotten-smelling skin**
3. **Labs** = wound culture
4. **Radiology** = subcutaneous air seen on x-ray or CT for wet gangrene; angiography or magnetic resonance angiography (MRA) may demonstrate vascular insufficiency
5. **Treatment** = incision and drainage, debridement, antibiotics; amputation frequently required

Quick HIT

Dry gangrene, gradual necrosis of skin from vascular insufficiency, features hard and dry skin. **Wet gangrene**, necrosis caused by acute vascular obstruction or infection, features blistering and swelling of the involved area.

E. Impetigo

1. **Contagious** skin infection most commonly found in **children**; most commonly caused by ***Staphylococcus aureus***
2. **H/P** = facial pruritus; **yellow crusted lesions** around mucocutaneous surfaces; erythematous vesicles (blisters) (see Figure 9-2)
3. **Treatment** = topical antibiotics (mupirocin), oral antibiotics if severe or in outbreaks: dicloxacillin or cephalexin

Quick HIT

No proven association exists between acne vulgaris and certain types of food.

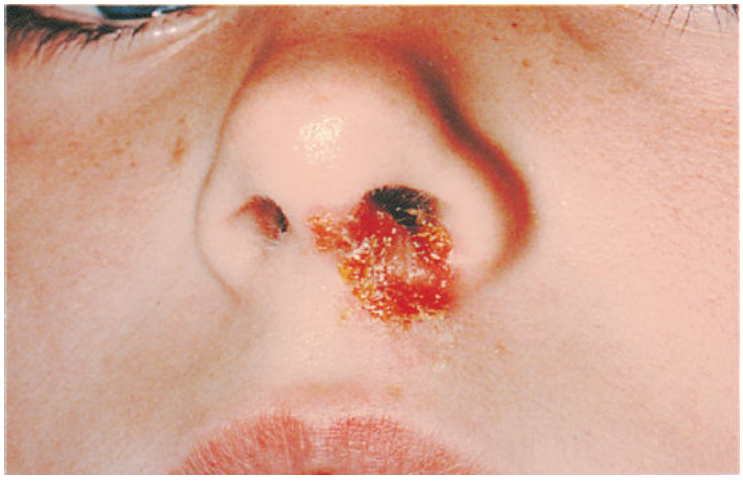


FIGURE 9-2
Impetigo involving left nostril caused by *Staphylococcus aureus* infection.
Note presence of greasy yellow scales within lesion.
(From Smeltzer, S. C., Bare, B., Hinkle, J. L., & Cheever, K. H. [2010]. *Brunner and Suddarth's Textbook of Medical-Surgical Nursing* [12th ed., p. 1687]. Philadelphia, PA: Lippincott Williams & Wilkins; with permission.)

Quick HIT

Acne usually decreases in severity as adolescence ends. **Corticosteroid use** and **androgen** production disorders are common causes of outbreaks in adulthood.

F. Acne Vulgaris

1. Inflammation of hair follicles and sebaceous glands associated with ***Propionibacterium acnes***, adolescence, androgens, and obstruction of pores by exfoliated skin or personal care products
2. **H/P**
   a. Erythematous pustules, papules, or nodules predominantly on face, neck, chest, and back
3. **Treatment**
   a. Topical **retinoids** are the recommended first-line treatment.
   b. Antibiotics (oral or topical) may inhibit bacterial growth (second-line therapy, used in conjunction with a topical retinoid).
   c. Topical benzoyl peroxide has antimicrobial properties (second-line therapy, often used in conjunction with a topical retinoid and an antibiotic).
   d. Oral contraceptives may be useful in women who are unresponsive to above therapy.
   e. Oral isotretinoin (vitamin A analog) given for severe cases but requires close monitoring of liver enzymes (hepatotoxicity risk) and for women contraception and monthly hCG testing (birth defects risk).
   f. Soaps have little effect on the condition.
4. **Complications** = acne can result in permanent scarring

NEXT
STEP

Women should have at least two **negative urine pregnancy tests** before an oral isotretinoin is prescribed.

G. Herpes Simplex Virus (HSV)

1. Recurrent viral infection of mucocutaneous surfaces caused by HSV-1 or HSV-2.
2. HSV transmitted through contact with **oral** or **genital fluids.**
3. **HSV-1** causes primarily **oral** disease; **HSV-2** causes primarily **genital** disease.
4. After primary infection, viral genetic material remains in sensory ganglia; stress will cause reactivation of disease in distribution of involved nerves.
5. **H/P** = small painful vesicles around mouth (HSV-1) or genitals (HSV-2) lasting several days (see Figure 9-3); primary infection usually presents with more severe symptoms and a flu-like illness.
6. **Labs** = viral culture, HSV antigen testing, PCR of HSV DNA.
7. **Treatment** = incurable, so treatment should be directed at minimizing symptoms and exacerbations; acyclovir, famciclovir, or valacyclovir shortens duration of recurrences and may decrease number of recurrences in patients with frequent eruptions; therapy can either be intermittent (episodic) or continuous (suppressive).
8. **Complications**
   a. Transmission from **infected mother to newborn** can cause disseminated disease with severe neurologic involvement.
   b. In immunosuppressed patients can lead to encephalitis, pneumonitis, and hepatitis.

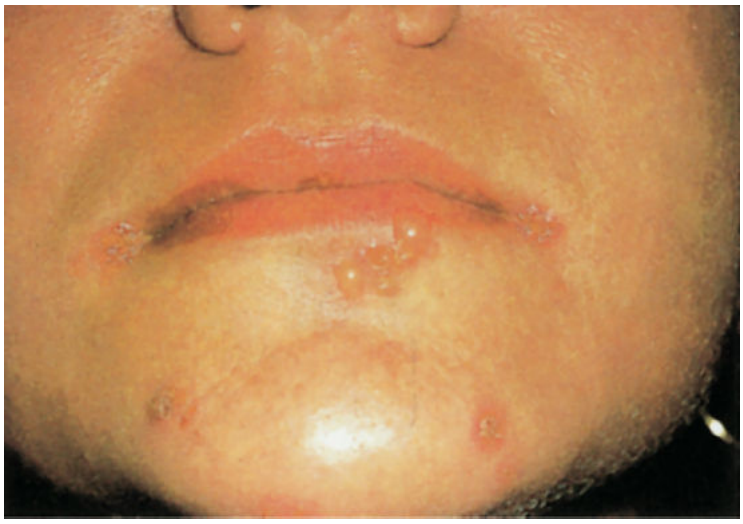


FIGURE 9-3
Herpes simplex.
These perioral vesicles are more indicative of infection with herpes simplex virus type 1 than type 2.
(From Weber, J., & Kelley, J. [2010]. *Health Assessment in Nursing* [4th ed., p. 294]. Philadelphia, PA: Lippincott Williams & Wilkins; with permission.)

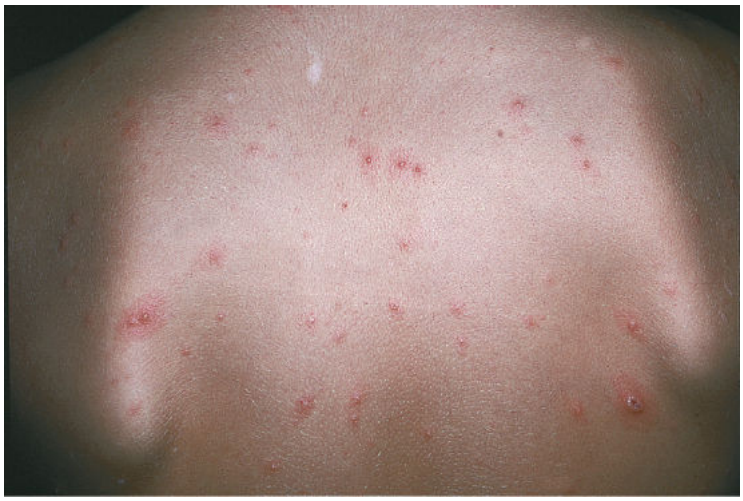


FIGURE 9-4
Chicken pox in a child caused by varicella-zoster infection.
While the small crusted vesicles are distributed across the body in the childhood form, reactivated infection in adults (shingles) occurs in a single dermatome.
(From Goodheart, H. P. [2003]. *Goodheart's Photoguide of Common Skin Disorders* [2nd ed.]. Philadelphia, PA: Lippincott Williams & Wilkins; with permission; Figure 8-2.)

H. Varicella

1. Infection by varicella-zoster virus can present as primary disease (i.e., chickenpox) or recurrent disease (i.e., shingles) (see Figure 9-4)
2. Chickenpox and shingles have different presentations, despite being caused by the same viral infection (see Table 9-1)

NEXT
STEP

Check varicella immunity status (received vaccine or had chickenpox as child) in all **pregnant** women; **varicella immune globulin** should be given to all nonimmune pregnant women who contract the disease.

I. Verruca Vulgaris (Warts)

1. Benign epithelial tumors caused by local infection by one of many types of **human papillomavirus** (HPV)
2. **H/P** = well-defined lesions of thickened epithelium, may appear flat (plantar warts) or raised; occasional tenderness to palpation
3. **Treatment** = occasionally self-limited; salicylic acid or cryotherapy may be required for removal
4. **Complications** = some forms of HPV (types 6 and 11) that cause genital warts are associated with cervical cancer (see Chapter 12, **Gynecologic and Breast Disorders**)

Quick **HIT**

Immunocompromised patients are at an increased risk for developing **encephalopathy** or **retinitis** as complications from varicella infection.

Table 9-1 Characteristics of Primary (Chickenpox) and Recurrent (Shingles) Varicella

Varicella Condition	Chickenpox (Primary)	Shingles (Recurrent)
Patients affected	More common in **children**	Patient with prior history of varicella-zoster infection
Timing of presentation	Symptoms 2+ wks after infection occurs; symptoms of headache, malaise, myalgias, and fever precede development of lesions by <3 days	Myalgias, fever, malaise preceding lesions by approximately 3 days
Type of lesion	Small, red macules that evolve into papules and then vesicles that eventually become crusted	Small, red macules that evolve into papules and then vesicles that eventually become crusted
Distribution of lesions	**Wide** distribution	Limited to single or few distinct **dermatomes**; involvement of multiple dermatomes indicates **disseminated** disease
Course of disease	Lesions may develop up to 1 wk and resolve a few days after appearing; infective until lesions crust over	Lesions exist for a week and may be **painful**; infective until lesions crust over
Treatment	Antipruritics aid symptoms; acyclovir used in severe cases or in immunocompromised patients; **vaccination** has reduced disease incidence significantly	Acyclovir, analgesics, possible corticosteroids
Complications	More severe course in older and pregnant patients (increased risk of varicella pneumonia); can have severe consequences if passed from **infected mother to unborn fetus**	Postherpetic neuralgia (long-lasting pain at site of eruption), trigeminal neuropathy

J. Molluscum Contagiosum

1. Viral skin infection (poxvirus) most frequently seen in children and in immunocompromised patients
2. **H/P** = painless, **shiny papules** with **central umbilication**
3. **Labs** = Giemsa and Wright stains on histology show large inclusion bodies, however diagnosis often made clinically
4. **Treatment** = frequently self-limited; chemical, laser, or cryotherapy for removal

K. Scabies

1. Cutaneous infestation by *Sarcoptes scabiei* mite
2. **Risk factors** = **crowded living conditions**, poor hygiene
3. **H/P** = severe pruritus at site of involvement (most commonly webs of fingers and toes) that worsens after a hot bath; **mite burrows** with nearby papules may be seen on close examination of skin
4. **Labs** = mites and eggs may be seen in skin scrapings under microscope
5. **Treatment**
   a. Permethrin cream or oral ivermectin; diphenhydramine to relieve pruritus
   b. All clothing, towels, and linens must be washed in hot water
   c. **Complications** = **infection of close contacts** common

L. Fungal Infections

1. Cutaneous fungal infections typically characteristic for a specific body region (see Table 9-2; Figure 9-5)
2. Frequently associated with **warm or moist environments**, obesity, DM, or recent antibiotic use

Table 9-2 Common Cutaneous Fungal Infections

Condition	Fungus	Lesions	Diagnosis	Treat
Tinea versicolor (pityriasis versicolor)	*Malassezia furfur*	Salmon-colored, light brown, or hypopigmented macules, most frequently on chest and back; lesions do not tan and may scale when scraped	KOH preparation shows short hyphae and spores ("spaghetti and meatballs")	Topica for se ketoc
Tinea not caused by *M. furfur*. Described by location: corporis (body), cruris (groin), pedis (feet), unguium (nail beds), capitis (scalp)	• *Microsporum* • *Trichophyton* • *Epidermophyton*	Pruritic, erythematous, scaly plaques with central clearing	KOH preparation shows hyphae	• Top for • Ora for
Intertrigo	*Candida albicans*	Pruritic, painful, erythematous plaques with pustules most commonly in skin creases	KOH preparation shows pseudohyphae	• Top • Top

KOH, potassium hydroxide.

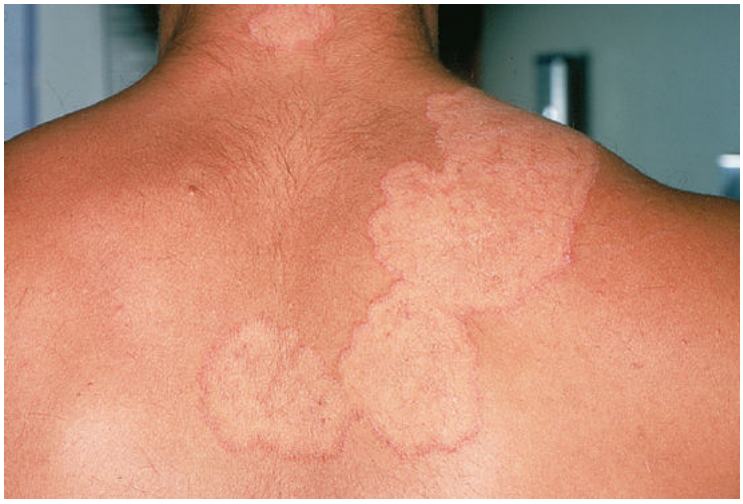


FIGURE 9-5
Tinea corporis; fungal infection of skin characterized by scaly rash on the body, with central clearing and a popular border.
(From Goodheart, H. P. [2009]. *Goodheart's Photoguide of Common Skin Disorders* [3rd ed., p. 121]. Philadelphia, PA: Lippincott Williams & Wilkins; with permission.)

II. Inflammatory Skin Conditions

A. Hypersensitivity Reactions in Skin

1. Allergic reaction seen in skin because of cutaneous **contact** or **ingestion** of a given allergen (e.g., drugs)
2. Mechanism of reaction
   a. **Type I:** caused by mast cell degranulation; light, diffuse rash (i.e., urticaria) appears soon after exposure and lasts only several hours
   b. **Type IV:** caused by lymphocyte activity; measles-like (i.e., morbilliform, maculopapular) rash appears several days after second exposure to allergen (mechanism for most allergic contact dermatitis)

Quick HIT

Common causes of allergic contact dermatitis include plants (poison ivy, poison oak, etc.), nickel, soaps, and **latex**.

3. **H/P**
   a. Pruritus, erythematous rash in distinct patterns (lines, shapes) in contact dermatitis.
   b. Ingestion of an allergen (e.g., food, drug reaction) can cause rash in a characteristic location or in a poorly defined area.

c. History of drug ingestion, contact with allergen, or previous reaction is helpful for diagnosis (see Figure 9-6).

NEXT
STEP

Use the pattern of a rash to distinguish an **external** cause (**defined** shape) from an **internal** cause (**nondefined** distribution) of rash.

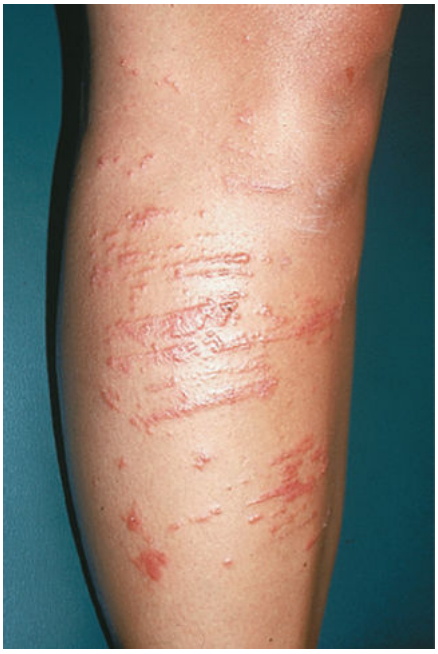


FIGURE **9-6**
Contact dermatitis.
Contact dermatitis caused by exposure to poison ivy. Note the linearity of the rash consistent with an external cause.
(From Goodheart, H. P. [2003]. *Goodheart's Photoguide of Common Skin Disorders* [2nd ed.]. Philadelphia, PA: Lippincott Williams & Wilkins; with permission; Figure 2-48.)

4. **Treatment**
   a. Stop offending agent or remove contact with allergen.
   b. Mild cases can be treated with topical corticosteroids and antihistamines.
   c. Oral corticosteroids may be required in worse cases.
   d. Epinephrine indicated in severe cases causing angioedema of the airway and/or anaphylaxis.

B. Erythema Multiforme

1. More serious cutaneous hypersensitivity reaction caused by **drugs, infection**, or vaccination
2. **H/P** = malaise, myalgias, pruritus; macules (i.e., small, nonpalpable lesions); plaques (i.e., large nonpalpable lesions) or vesicles on extremities (especially palms, soles); **target lesions** (i.e., erythematous center surrounded by pale inner ring and erythematous outer ring) may be evident
3. **Labs** = increased eosinophils; skin biopsy shows increased lymphocytes and necrotic keratinocytes
4. **Treatment** = may be self-limited; stop offending agent; corticosteroids, analgesics

Quick **HIT**

Penicillins, sulfonamides, nonsteroidal anti-inflammatory drugs (NSAIDs), oral contraceptives, and anticonvulsant medications are agents most frequently associated with erythema multiforme.

C. Stevens–Johnson Syndrome

1. Severe form of erythema multiforme involving mucous membranes and severe plaque formation involving <10% body surface area (BSA)
2. **Skin sloughing** may be evident; high risk of dehydration
3. **H/P** = prodromal symptoms of malaise, body aches, fever; rash is polymorphous with macules, target lesions, erythema, bullae, and exfoliation. Positive Nikolsky sign (epidermis shed in large sheets with light friction)
4. **Treatment** = **stop offending agent**; IV fluids; frequently treated in burn unit

D. Toxic Epidermal Necrolysis (TEN)

1. Most severe form of hypersensitivity reaction with **significant skin sloughing** and **full-thickness epidermal necrosis** involving >30% BSA (see Figure 9-7)
2. **Labs** = decreased WBC, decreased hemoglobin, decreased hematocrit, increased alanine aminotransferase (ALT), increased aspartate aminotransferase (AST)
3. **Treatment**
   a. **Stop offending agent.**
   b. Treat patient in **burn center**, IV hydration, IV immune globulin.
   c. Acyclovir may be useful in cases caused by HSV.

Quick HIT

HSV and *Mycoplasma pneumoniae* are common infectious causes of erythema multiforme.

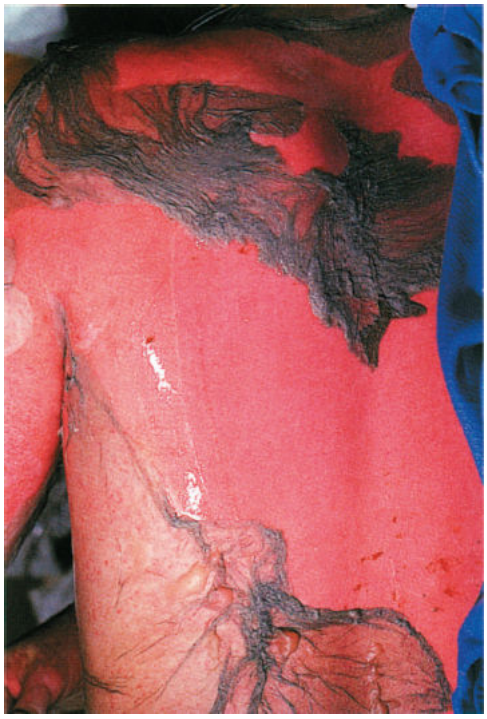


FIGURE 9-7
Toxic epidermal necrolysis (TEN).
This severe dermatologic condition begins as a generalized erythematous rash that progresses into widespread desquamation and erosion formation. (From Elder, D. E., Elenitsas, R., Rubin, A. I., Ioffreda, M., Miller, J., & Miller, F. O. [2013]. *Atlas and Synopsis of Lever's Histopathology of the Skin* [3rd ed., p. 179]. Philadelphia, PA: Lippincott Williams & Wilkins; with permission.)

E. Seborrheic Dermatitis

1. Chronic hyperproliferation of epidermis most commonly on **scalp** or face
2. Most common in adolescents and infants, associated with Malassezia
3. **H/P** = pruritus; erythematous **plaques with yellow, greasy scales**
4. **Treatment** = emollients in infants, shampoo containing selenium or ketoconazole when scalp involved; topical corticosteroids and antifungals used for other regions
5. **Complications** = frequent recurrence

Quick HIT

"Cradle cap" is seborrheic dermatitis of the scalp in infants.

F. Atopic Dermatitis (i.e., Eczema)

1. Chronic inflammatory skin rash characterized by **dry skin patches** with papules
2. Both **infantile** (resolves with initial years of life) and **adult** (recurrent) forms exist
3. **Risk factors** = **asthma**, allergic rhinitis, family history
4. **H/P** = pruritus; erythematous patches of dry skin with possible vesicles on flexor surfaces, dorsum of hands and feet, chest, back, or face; lesions more commonly on face and scalp in infants (see Figure 9-8)
5. **Treatment** = avoidance of precipitating factors, moisturizing creams, topical corticosteroids; severe cases can be treated with oral corticosteroids and antihistamines
6. **Complications** = **eczema herpeticum, superimposed HSV**

Quick HIT

Of patients with psoriasis, 10% to 20% also have **psoriatic arthritis** (see Chapter 5, **Musculoskeletal Disorders**).

G. Psoriasis

1. Inflammatory skin disorder characterized by epidermal hyperproliferation
2. **H/P** = possible pruritus; sharply demarcated **erythematous plaques** with **silvery scales** on **extensor surfaces** that bleed easily with scale removal (i.e., Auspitz sign), possible small pustules, pitted nails, lifting of nails (see Figure 9-9)
3. **Labs** = unnecessary for diagnosis; skin biopsy shows thickened epidermis, absent granular cell layer, and nucleated cells in stratum corneum
4. **Treatment** = emollients, topical corticosteroids; phototherapy, methotrexate, cyclosporine can be used in severe disease

Quick HIT

Rash distribution in pityriasis rosea occurs in a **"Christmas tree"** pattern.

H. Pityriasis Rosea

1. Mild inflammatory skin disorder in children and young adults with possible viral association characterized by papular lesions on the trunk and extremities
2. **H/P**
   a. Pruritus; oval erythematous papules covered with white scale located primarily on chest, back, and extremities
   b. Rash begins with appearance of **"herald patch"** (i.e., single round lesion up to 5 cm in diameter) a few days before generalized eruption (see Figure 9-10)
3. **Treatment** = self-limited; topical steroids, antihistamines

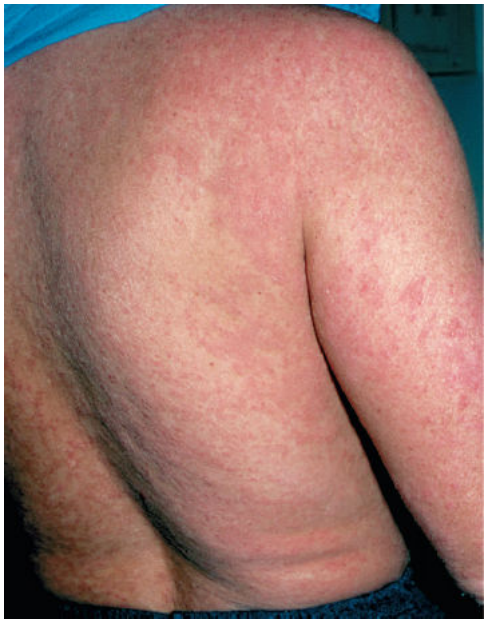


FIGURE 9-8
Adult atopic dermatitis (eczema) characterized by erythematous patches of dry skin.
(From Goodheart, H. P. [2003]. *Goodheart's Photoguide of Common Skin Disorders* [2nd ed.]. Philadelphia, PA: Lippincott Williams & Wilkins; with permission; Figure 2-8.)

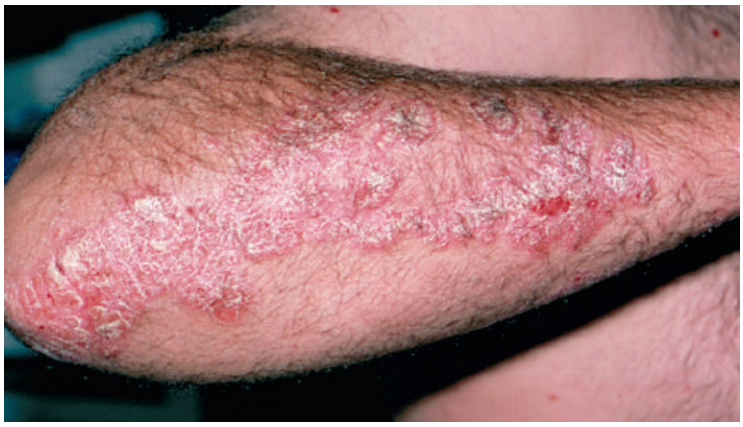


FIGURE 9-9
Psoriasis.
Red plaques with silver scales on extensor forearm surface of a patient with psoriasis; similar lesions are also seen on the extensor surfaces of the knee.
(From Goodheart, H. P. [2003]. *Goodheart's Photoguide of Common Skin Disorders* [2nd ed.]. Philadelphia, PA: Lippincott Williams & Wilkins; with permission; Figure 2-23.)

I. Erythema Nodosum

1. Inflammation of **dermis and adipose tissue** resulting in painful erythematous nodules; most commonly on anterior tibias but can also affect trunk and other extremities
2. Caused by delayed immunologic reaction to infection, collagen vascular diseases, inflammatory bowel disease, or drugs
3. **H/P** = malaise, arthralgias; tender **erythematous nodules** (usually pretibial), fever
4. **Labs** = possible positive antistreptolysin O titer (when associated with streptococcal infection), increased ESR; skin biopsy may show fatty inflammation
5. **Treatment** = self-limited; NSAIDs, potassium iodide

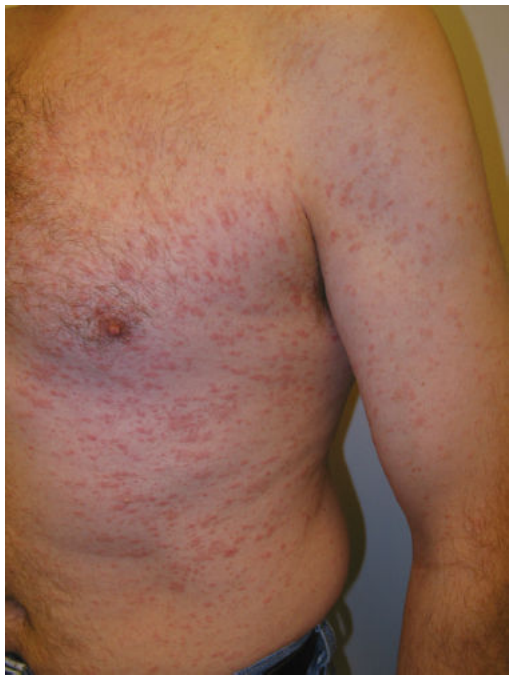


FIGURE 9-10
Pityriasis rosea.
These scaled papules fan out across the chest or back to give the overall appearance of a Christmas tree pattern. (Image provided by Stedman's.)

III. Bullous Diseases

A. Pemphigus Vulgaris

1. Autoimmune disorder characterized by autoantibodies to adhesion molecules in epidermis
2. Patients usually middle aged or elderly
3. **H/P** = **painful**, **fragile blisters** in oropharynx and on chest, face, and perineal region; blisters rupture easily and erosions are common, positive Nikolsky sign (see Figure 9-11)
4. **Labs** = skin biopsy shows separating of epidermal cells (i.e., **acantholysis**) with intact basement membrane; immunofluorescence demonstrates antiepidermal antibodies

5. **Treatment** = corticosteroids, azathioprine, or cyclophosphamide
6. **Complications** = sepsis, high mortality without treatment

B. Bullous Pemphigoid

1. Autoimmune disorder characterized by autoantibodies to epidermal basement membrane
2. Most patients >65 years of age
3. **H/P** = **widespread blistering/bullae** (especially on flexor surfaces and perineal region), pruritus; erosions can form with blister rupture, negative Nikolsky sign (see Figure 9-12)
4. **Labs** = immunofluorescence shows antibasement membrane antibodies
5. **Treatment** = oral or topical corticosteroids or azathioprine

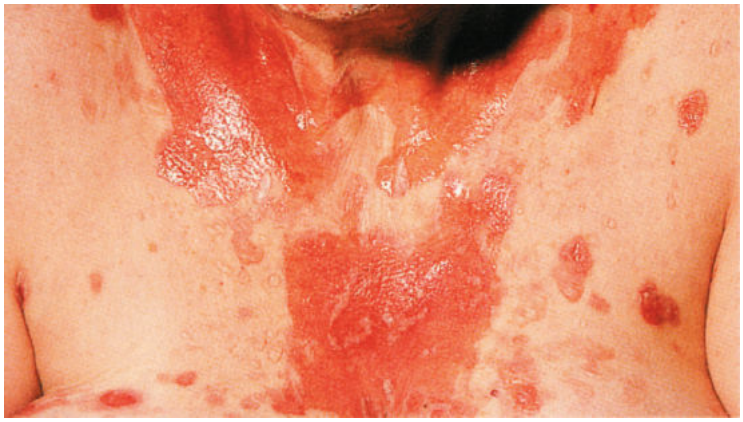


FIGURE **9-11**
Pemphigus vulgaris.
Fragile bullae develop, which rupture, easily leading to widespread erosions and desquamation.
(From Elder, D. E., Elenitsas, R., Rubin, A. I., Ioffreda, M., Miller, J., & Miller, F. O. [2013]. *Atlas and Synopsis of Lever's Histopathology of the Skin* [3rd ed., p. 188]. Philadelphia, PA: Lippincott Williams & Wilkins; with permission.)

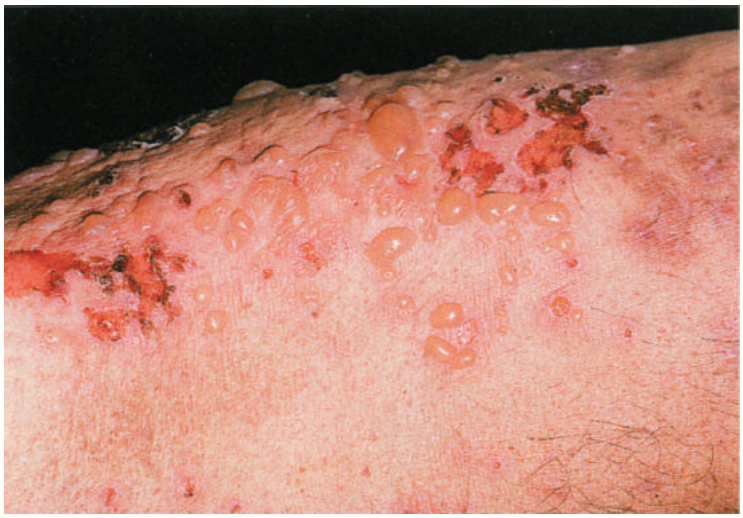


FIGURE **9-12**
Bullous pemphigoid.
Multiple large bullae form on an erythematous base leading to severe erosions.
(From Elder, D. E., Elenitsas, R., Rubin, A. I., Ioffreda, M., Miller, J., & Miller, F. O. [2013]. *Atlas and Synopsis of Lever's Histopathology of the Skin* [3rd ed., p. 197]. Philadelphia, PA: Lippincott Williams & Wilkins; with permission.)

C. Porphyria Cutanea Tarda

1. Disease resulting from deficiency of hepatic uroporphyrinogen decarboxylase, an enzyme involved in heme metabolism
2. **Risk factors** = alcoholism, **hepatitis C**, iron overload, estrogen use, smoking
3. **H/P** = **chronic painless blistering lesions** on sun-exposed skin (especially the dorsa of hands, forearms, neck, face, ears, feet), **hyperpigmented skin, hypertrichosis**; ruptured blisters heal poorly and result in scarring
4. **Labs** = **elevated AST and ALT, increased total plasma porphyrin**, increased urine porphyrins, decreased uroporphyrinogen decarboxylase
5. **Treatment** = periodic phlebotomy; low-dose chloroquine or hydroxychloroquine; sunscreen use; avoidance of triggers such as sun exposure, alcohol, estrogens, tobacco, iron supplements

IV. Neoplasms

A. Actinic Keratosis

1. **Precancerous** skin lesion that can progress to squamous cell cancer
2. **Risk factors** = **sun exposure**
3. **H/P** = erythematous **papule** with rough, **scaly, small lesions** found in **sun-exposed** areas (see Figure 9-13)
4. **Labs** = biopsy shows dysplasia of epithelium (deeper epithelial cells show variations in shape and nuclei with increased staining)
5. **Treatment** = topical 5-fluorouracil or imiquimod, cryotherapy
6. **Complications** = 0.1%/year risk of progression to **squamous cell carcinoma** (60% of squamous cell carcinomas arise from **actinic keratosis**)

Quick HIT

Seborrheic keratosis is a common, benign tumor of immature keratinocytes with a hyperpigmented, warty, "stuck on" appearance.

NEXT
STEP

Even when actinic keratosis is the suggested diagnosis, biopsy a lesion to rule out squamous cell cancer.

B. Squamous Cell Carcinoma

1. Skin cancer involving **squamous** cells of epithelium
2. **Risk factors** = **sun exposure** (particularly **UVB** radiation), **actinic keratosis**, fair complexion, chronic wounds, scarring
3. **H/P** = painless, erythematous plaque with scaling in sun-exposed area; progressive lesions may bleed, ulcerate, or be painful (see Figure 9-14)
4. **Labs** = biopsy shows anaplastic epidermal cells extending to dermis
5. **Treatment** = surgical excision; **Mohs excision** (i.e., serial shallow excisions with histologic analysis to minimize cosmetic damage) may be performed for lesions on face; radiation may be helpful in large lesions
6. **Complications** = progresses slowly but can be a large lesion by the time of diagnosis if located in poorly visualized region (back, scalp); 5% to 10% of cases metastasize

Quick HIT

Use of a good **sunscreen** (≥SPF 15) is important in the prevention of skin cancer associated with sun exposure.

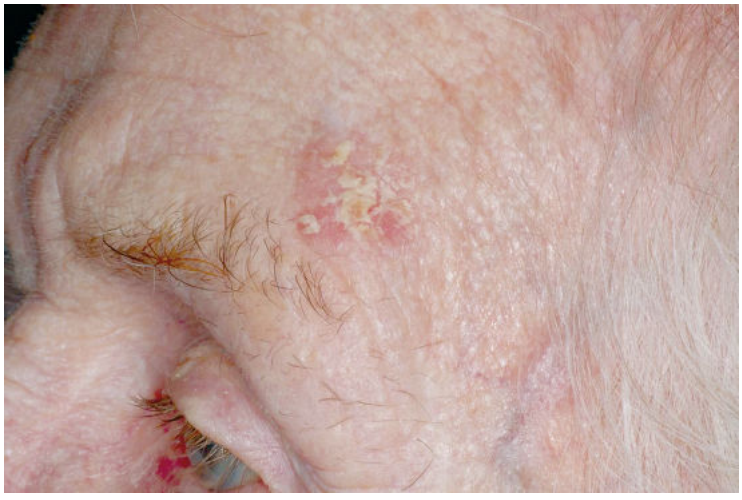


FIGURE 9-13
Actinic keratosis.
These lesions are superficial papules covered by dry scales and are a result of sun exposure.
(From Elder, D. E. [2015]. *Lever's Histopathology of the Skin* [11th ed., p. 987]. Philadelphia, PA: Lippincott Williams & Wilkins; with permission.)

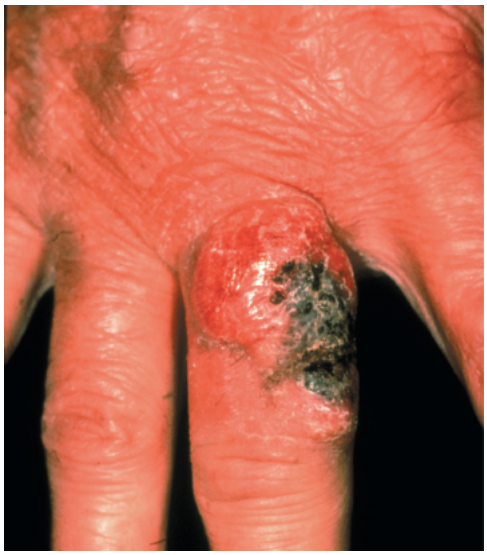


FIGURE 9-14
Squamous cell carcinoma with erythematous base and ulceration.
(From Rubin, R., & Strayer, D. S. [2012]. *Rubin's. Pathology* [6th ed., p. 1163]. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; with permission.)

C. Basal Cell Carcinoma

1. Skin cancer arising in **basal** epidermal cells
2. **Risk factors** = **sun exposure**
3. **H/P** = **pearly papule** with fine vascular markings (i.e., **telangiectasias**) and central ulceration (see Figure 9-15)
4. **Labs** = biopsy shows basophilic-staining basal epidermal cells arranged in palisades
5. **Treatment** = surgical excision, Mohs excision, radiation, or cryotherapy
6. **Complications** = lesions rarely metastasize

Quick HIT

Basal cell carcinoma is the **most common** type of skin cancer.

D. Melanoma

1. Malignant melanocyte tumor that spreads rapidly
2. **Risk factors** = **sun exposure**, fair complexion, family history, numerous nevi (i.e., moles)
3. Types

Quick HIT

Shave biopsy should **never** be used to study a suspicious melanotic lesion because it does not provide sufficient tissue for clear diagnosis and cannot be used to measure lesion depth.

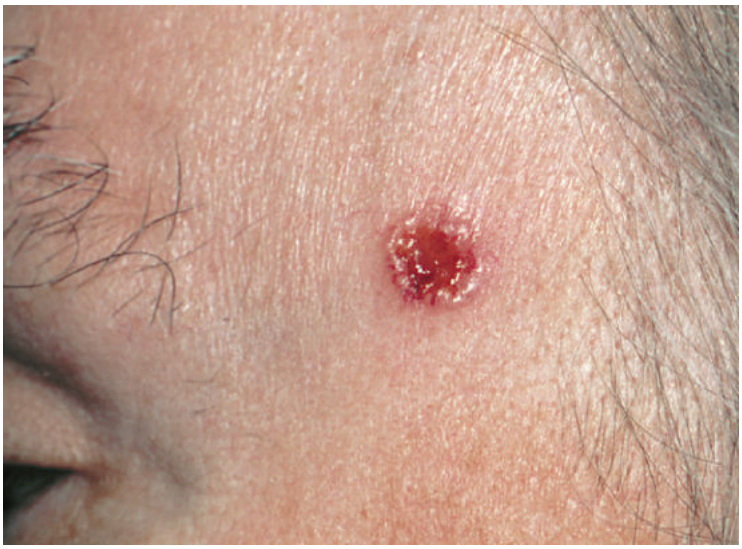


FIGURE **9-15**
Basal cell carcinoma.
Note the pearly appearance of a papule with central ulceration.
(From Goodheart, H. P. [2003]. *Goodheart's Photoguide of Common Skin Disorders* [2nd ed.]. Philadelphia, PA: Lippincott Williams & Wilkins; with permission; Figure 22-17.)

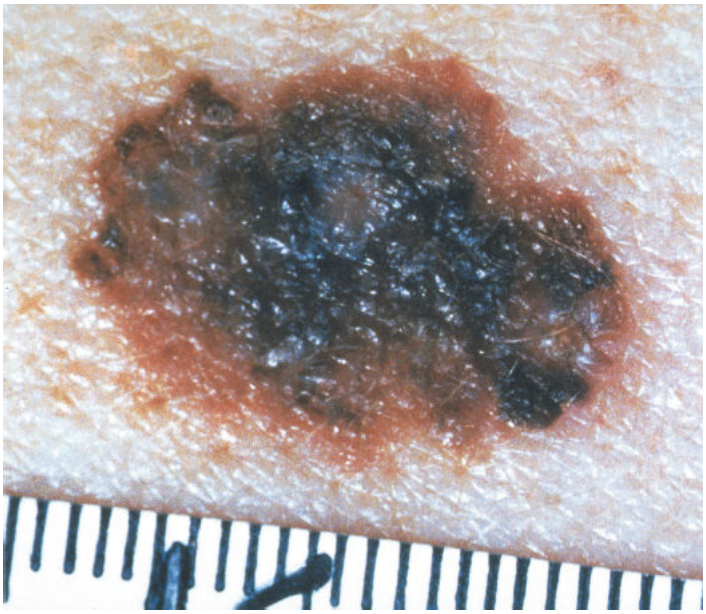


FIGURE **9-16**
Melanoma, superficial spreading type.
Note the ABCDs of the lesion: asymmetry, irregular border, inconsistent color, and large diameter (>20 mm).
(From Rubin, R., & Strayer, D. S. [2012]. *Rubin's Pathology* [6th ed., p. 1151]. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; with permission.)

a. **Superficial spreading:** most common type; grows laterally before invasive growth occurs
b. **Nodular:** grows only vertically and becomes invasive rapidly; difficult to detect, ulcerates
c. **Acral lentiginous:** involves palms, soles, and nail beds
d. **Lentigo maligna:** long-lasting in situ stage before vertical growth

4. **H/P**

Quick HIT

Nevi should be followed to look for the ABCDEs of melanoma: **A**symmetry, **B**order (irregular), **C**olor (variable), **D**iameter (>6 mm), and **E**nlargement.

a. **Painless**, pigmented lesion with recent changes in appearance
b. Lesions have irregular borders, multiple colors, and can be large or rapidly growing (see Figure 9-16)
c. In contrast, melanocytic nevi are more symmetric, have more regular borders, are homogeneously colored, and remain relatively the same size over time (see Figure 9-17)

5. **Labs** = excisional biopsy shows atypical melanocytes and possible invasion into dermis

6. **Treatment** = surgical excision (0.5-cm margin if in situ, 1-cm margin if <2-mm thick, 2-cm margin if >2-mm thick) with possible lymph node dissection; chemotherapy and radiation therapy if metastatic
7. **Complications** = aggressive cancer; lesions may have metastasized by time of discovery (most commonly, lung, brain, and gastrointestinal tract)

Quick HIT

The most important prognostic factor for melanoma is **thickness of lesion** (>0.76 mm associated with increased risk of metastasis).

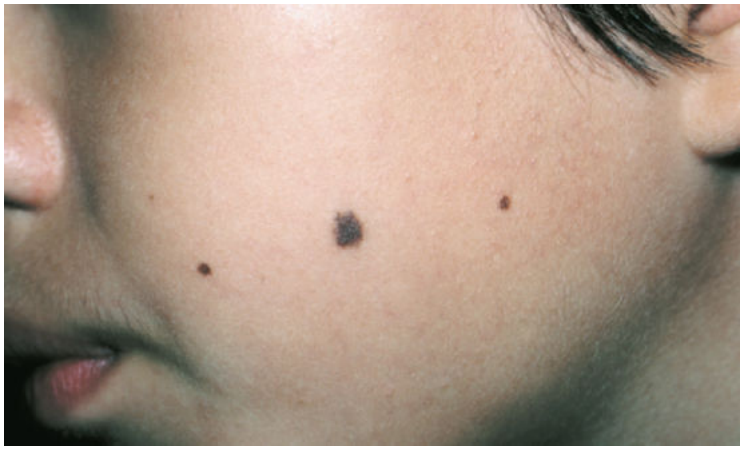


FIGURE 9-17
Melanocytic nevus.
Unlike melanoma, this lesion is nearly symmetric, has better border regularity, is of more consistent color, and is smaller in diameter.
(From Goodheart, H. P. [2008]. *Goodheart's Photoguide of Common Skin Disorders* [3rd ed., p. 364]. Philadelphia, PA: Lippincott Williams & Wilkins; with permission.)

V. Plastic Surgery

A. Grafts and Flaps (See Table 9-3)

1. Transfer of skin and soft tissues from one location of body to another for use in wound repair
2. Skin grafts can be autografts (i.e., from healthy tissue on same patient), allografts (i.e., donor tissue from another individual), or xenografts (i.e., donor tissue from another species)
3. Flaps can be rotational or transpositional (i.e., left partially attached to donor site and rotated or stretched to cover wound) or free flaps (i.e., flap completely removed from donor site and transferred in whole to wound)

Quick HIT

Periodic skin checks should be performed in anyone with a history of significant sun exposure and a positive family history for melanoma.

B. Reconstructive Surgery

1. Repair of soft tissue defects caused by surgery, congenital anomalies, or wounds
2. Multiple types of tissue are used to recreate normal anatomy (e.g., skin, muscle, bone, cartilage, vessels, nerves)
3. Examples
   a. Maxillofacial: cleft lip repair, cleft palate repair, facial trauma
   b. Breast: reconstruction with muscle flaps or implants following mastectomy
   c. Genitourinary: repair of epispadias, hypospadias, or genital agenesis
   d. Soft tissues: following sarcoma excision or for filling defects

C. Cosmetic Surgery

1. Surgical alteration of appearance
2. Can be performed to remove anatomic anomalies or results of massive weight loss, surgery, or injury (e.g., gynecomastia, postmastectomy, excessive skin, difficulty breathing)
3. More often used to combat effects of **aging** or to **modify** physical appearance
4. Examples
   a. Facial: facelift, brow lift, blepharoplasty (i.e., repair of baggy eyelids), rhinoplasty
   b. Skin: removal of scarring, spider veins, age wrinkles (dermabrasion, laser treatment, chemical peel)
   c. Breast: augmentation, reduction (may be helpful to reduce back strain)
   d. Fatty tissue reduction: abdominoplasty, liposuction

5. **Psychiatric** issues must be considered, especially in patients who repeatedly request “upgrades”

NEXT
STEP

Genitourinary reconstruction or gender reassignment requires a careful preoperative evaluation to determine true gender of patient, genetic causes, realistic outcomes, expectations, and psychiatric issues.

Table 9-3 Common Types of Skin Grafts and Tissue Flaps Used in Wound Repair

Type	Description	Common Donor Sites	Indications
Split-thickness graft	Skin graft composed of epidermis and part of dermis	Abdomen, thighs, buttocks	Skin replaceme to cover extens (contracts over
Full-thickness graft	Skin graft composed of epidermis and full dermis	Above ears (for face), forearm, groin	Defects on face
Composite graft	Skin grafts that also contain other tissues (cartilage, nail bed, fat)	Fingertip, ear, etc.	Site-specific ar tion
Fasciocutaneous flap	Skin and subcutaneous tissue with attached vascular supply	Forehead, groin, deltopectoral region, thighs	Large defects v supply requirin
Muscle flap	Transferred muscle that either includes skin (myocutaneous flap) or requires additional skin graft	Tensor fascia lata, gluteal muscles, sartorius, rectus abdominis, latissimus dorsi	Areas requiring ized tissue, exp severe radiatio

QUESTIONS

1. A 47-year-old man presents to the emergency department with a complaint of itchiness. He has a history of a shellfish allergy and 30 minutes ago accidentally ate a dish that was made with shrimp. His temperature is 98.6 F, heart rate is 70/min, blood pressure is 130/80 mm Hg, respiratory rate is 16/min, and oxygen saturation is 99% on room air. Physical examination is unremarkable except for a diffuse rash with wheals and surrounding erythema. Which of the following is the next best step?

   A. IM epinephrine
   B. Oral diphenhydramine
   C. IV famotidine
   D. Topical high potency corticosteroid
   E. Skin biopsy

2. A 30-year-old man presents to the clinic with a complaint of a rash. The rash started 2 weeks ago and has spread diffusely throughout his body. The rash is pruritic and papular with umbilicated centers. What is the next best step in managing this patient?

   A. Topical corticosteroids
   B. Reassurance
   C. Antihistamines
   D. Dermatology referral
   E. HIV testing

3. A 60-year-old woman presents to the office due to a rash over the last 4 days. The rash is very painful and diffuse involving mostly the trunk as well as the mouth and lips. The rash appears as several bullae with separation of the superficial layer of skin with light touch. What is the most likely diagnosis?

   A. Bullous pemphigoid
   B. Urticaria
   C. Porphyria
   D. Staphylococcal scalded skin syndrome
   E. Pemphigus vulgaris

4. A 28-year-old female was recently diagnosed with epilepsy and started on phenytoin. She now presents to the emergency department with a diffuse rash involving her trunk and extremities as well as her mouth and lips. On examination, the rash is a desquamating rash with diffuse erythema and bullae. What is the best next step?

   A. IV antibiotics
   B. IV corticosteroids
   C. Transfer to a burn center
   D. Admit to the ICU
   E. Debride the rash

5. A 66-year-old female presents with blisters and bullae over her face and dorsum of her hands as well as increased hair growth. She describes the rash as itchy. She denies any fever, body aches, or trouble breathing. Vital signs are unremarkable. What other coexisting disease should you be concerned about?

   A. Lupus
   B. Ulcerative colitis
   C. Rheumatoid arthritis
   D. Hepatitis C
   E. HIV

6. A 4-year-old boy in day care presents with discoloration to skin over the back. It is described as slightly itchy. Vital signs are within normal limits. On examination, there are multiple patches of hypopigmentation. What is the best treatment option?

   A. Topical hydrocortisone
   B. Topical ketoconazole
   C. Oral griseofulvin
   D. Oral acetaminophen
   E. Topical acyclovir

7. A 74-year-old male presents with a lesion to his left leg. He noticed it around 6 months ago and recently feels that it has progressed in size. On examination, the lesion is irregularly shaped with different colors and has increased in size to 7 mm. What is the recommended treatment for this patient's condition?

   A. Topical corticosteroids
   B. UV light therapy
   C. Surgical excision
   D. Oral methotrexate
   E. Reassurance

8. A 55-year-old male presents to the emergency department with a painful rash along his back for 2 days. Vital signs are within normal limits. On examination is an erythematous, vesicular rash along half his back in a dermatomal distribution. What is this patient most at risk for?

   A. Superimposed bacterial infection
   B. Blindness
   C. Postherpetic neuralgia

D. Bell palsy
E. Stroke

9. A 40-year-old male presents to the clinic with a complaint of an itchy scalp. He denies any fever or vomiting. On examination, there is a diffuse rash along the scalp and upper face with yellow, greasy plaques. What is the recommended treatment?

A. Oral diphenhydramine
B. Topical corticosteroids
C. Ketoconazole shampoo
D. Topical ketoconazole
E. Oral corticosteroids

10. A 68-year-old female with a history of type 2 diabetes mellitus presents to the emergency department with left anterior leg redness and swelling for 1 week. Temperature is 101.5 F, heart rate is 101/min, and blood pressure is 110/60 mm Hg. On examination, there left leg is warm, red, and indurated. There is no rapid progression or crepitus. Pulses are intact and equal on both sides. What is the next best step in the management of this patient?

A. Oral cephalexin and discharge
B. Oral clindamycin and discharge
C. General surgery consult
D. IV vancomycin and admit
E. IV piperacillin/tazobactam and vancomycin and admit

10
Pediatrics

I. Pediatric Cardiology

A. Fetal Circulation

1. Gas exchange occurs in uteroplacental circulation.
2. Fetal Hgb has greater O_2 affinity than adult Hgb and pulls O_2 from maternal blood.
3. Umbilical arteries carry deoxygenated blood to placenta; umbilical veins carry oxygenated blood from placenta to portal system.
4. Changes occurring after birth:
   a. Lung expansion causes a **decrease in pulmonary vascular resistance,** increased pulmonary blood flow, leading to an increase in relative blood oxygenation.
   b. A decreasing serum level of prostaglandin E_2 results in **ductus arteriosus closure**; umbilical cord clamping results in end of placental circulation and an increase in systemic vascular resistance.
   c. This increased vascular resistance, in turn, induces **ductus venosus closure** and umbilical artery and vein constriction.
   d. Left atrial (LA) pressure increases (because of increased pulmonary blood flow) and umbilical circulation decreases, causing a decrease in IVC pressure.
   e. Decrease in IVC and right atrial (RA) pressures leads to **foramen ovale closure**.

B. Ventricular Septal Defect (VSD)

1. Opening in ventricular septum allowing shunting of blood (see Figure 10-1A)
2. **Most common** congenital heart defect
3. **H/P** = asymptomatic if small; frequent respiratory infections, failure to thrive, dyspnea, shortness of breath, heart failure symptoms with larger defects; pansystolic murmur at lower left sternal border, loud pulmonic S_2, systolic thrill
4. **ECG** = left ventricular hypertrophy (LVH), right ventricular hypertrophy (RVH); frequently normal
5. **Radiology** = echocardiogram shows shunt
6. **Treatment** = follow small defects; diuretics or ACE-I are useful for decreasing fluid volume and vascular resistance in patients with large shunts; repair large defects soon (before Eisenmenger syndrome develops)
7. **Complications** = if untreated, Eisenmenger syndrome develops (irreversible); increased risk of endocarditis

C. Atrial Septal Defect (ASD)

1. Opening in atrial septum allowing movement of blood between atria (see Figure 10-1B)
2. Initially, blood flow is left-to-right across defect. Most common heart defect in Down Syndrome
3. **H/P** = possibly asymptomatic; large defects can cause cyanosis, heart failure symptoms, dyspnea, fatigue, or failure to thrive; strong impulse at lower left sternal border, **wide fixed split S_2**, systolic ejection murmur at upper left sternal border
4. **ECG** = right axis deviation
5. **Radiology** = echocardiogram shows blood flow between atria, dilated right ventricle (RV), and large heart; CXR shows increased pulmonary vascular markings caused by pulmonary hypertension (HTN)
6. **Treatment** = small defects do not need repair but require **antibiotic prophylaxis** before surgery or dental work; surgical closure for symptomatic infants or when pulmonary blood flow is twice that of systemic blood flow
7. **Complications** = untreated ASD leads to right-to-left shunt (i.e., **Eisenmenger syndrome**), RV dysfunction, pulmonary HTN, arrhythmias

Quick HIT

Atrial septal defect (ASD) has a **fixed** split S_2; VSD does not.

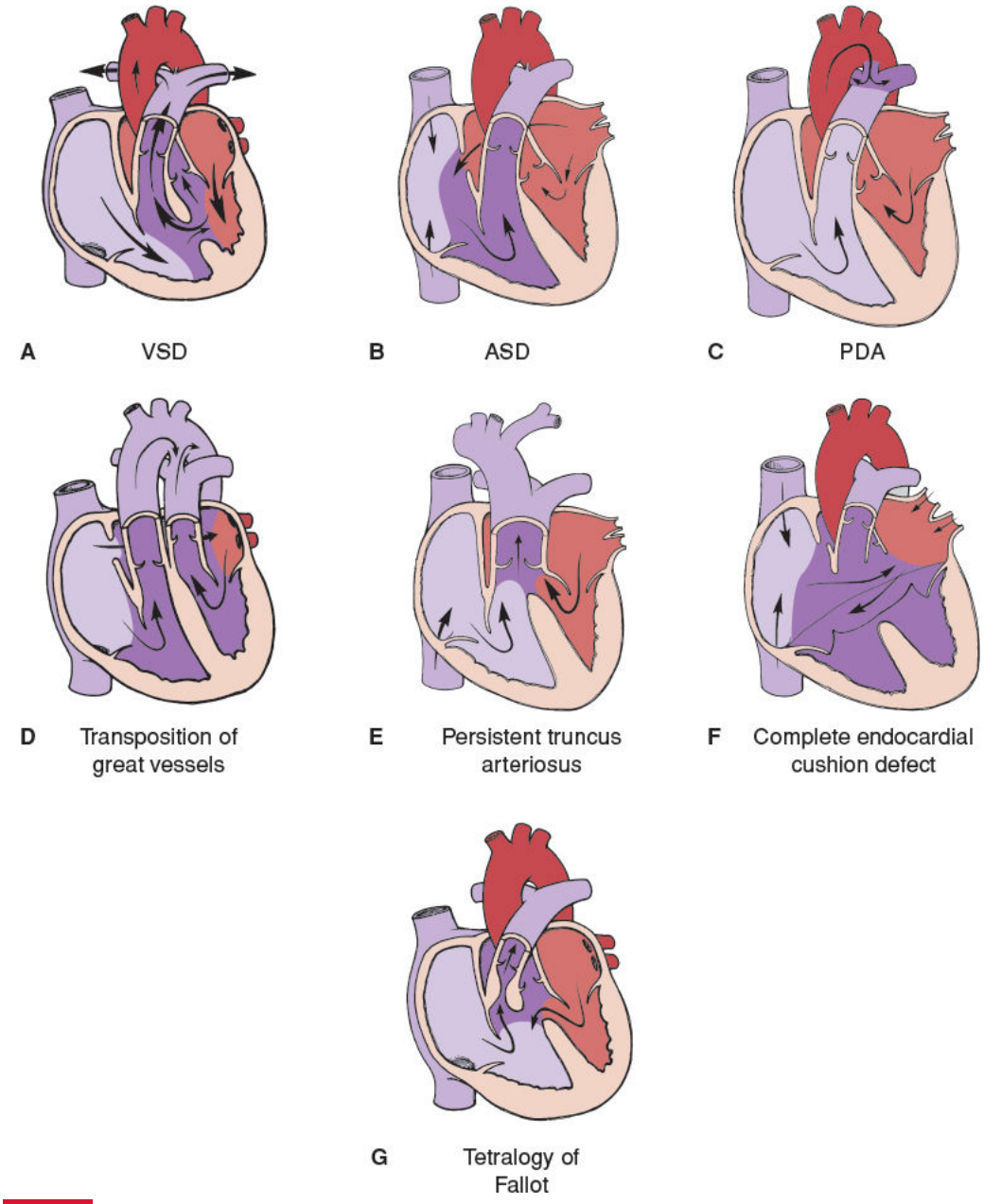


FIGURE **10-1**

Common congenital heart defects.
A: Ventricular septal defect (VSD)—the *arrows* depict shunting of blood predominantly from the left to right ventricle. **B:** Atrial septal defect (ASD)—the *arrows* depict shunting of blood from the left to right atrium. **C:** Patent ductus arteriosus (PDA)—the *arrows* depict shunting of blood from the aorta to pulmonary arteries. **D:** Transposition of the great vessels—the aorta arises from the right ventricle, and the pulmonary artery arises from the left ventricle. Shunting can occur between the great vessels via a PDA. **E:** Persistent truncus arteriosus—single vessel exits both ventricles (with VSD) and gives rise to both systemic and pulmonary circulation. **F:** Complete endocardial cushion defect—ASD, VSD, and single atrioventricular canal. **G:** Tetralogy of Fallot—combination of VSD, right ventricular outflow obstruction, aorta overriding the ventricular septum, and right ventricular hypertrophy.

Quick HIT

Patients with ASD are more susceptible to oxygen desaturation at **high altitudes** and decompression sickness during **deep sea diving**.

D. Patent Ductus Arteriosus (PDA)

1. Failure of ductus arteriosus to close after birth (see Figure 10-1C)
2. Left-to-right shunt (aorta to pulmonary artery)
3. **Risk factors** = **prematurity,** high altitude, first-trimester maternal rubella, maternal prostaglandin administration; females > males
4. **H/P** = possibly asymptomatic; heart failure symptoms, dyspnea; wide pulse pressure, continuous "machinery" murmur at second left intercostal space, loud S_2, bounding pulses
5. **ECG** = possible LVH
6. **Radiology** = possible cardiomegaly on CXR; echocardiogram shows large LA and left ventricle (LV); angiography confirms diagnosis

7. **Treatment** = **indomethacin** induces closure; surgical closure if unresponsive

MNEMONIC

Treatment for a PDA may be remembered with the mnemonic Come **In** and **Close** the Door: (indomethacin **closes** a PDA).

E. Persistent Truncus Arteriosus

1. Failure of aorta and pulmonary artery to separate during development results in a single vessel that supplies systemic and pulmonary circulation (see Figure 10-1E)
2. **H/P** = cyanosis after birth; dyspnea, fatigue, failure to thrive; heart failure symptoms soon develop; harsh systolic murmur at lower left sternal border, loud S_1 and S_2, bounding pulses
3. **ECG** = likely LVH, RVH
4. **Radiology** = angiography or echocardiogram used for diagnosis; CXR may show boot-shaped heart, no pulmonary artery, and large aorta arching to right side
5. **Treatment** = surgical correction

MNEMONIC

To remember cyanotic congenital heart diseases, use the **5 Ts** mnemonic:

- **T**runcus arteriosus
- **T**ransposition of the great vessels
- **T**ricuspid atresia
- **T**etralogy of Fallot
- **T**otal anomalous pulmonary venous return

F. Transposition of the Great Vessels

1. Parallel pulmonary and systemic circulations; aorta connected to RV; pulmonary artery connected to LV (see Figure 10-1D)
2. Cause is poorly understood but is likely linked to cardiac septal development in the truncus arteriosus
3. Incompatible with life (fetus is stillborn) unless comorbid PDA or VSD
4. **Risk factors** = Apert syndrome, Down syndrome, cri-du-chat syndrome, trisomy 13 or 18
5. **H/P** = cyanosis after birth; cyanosis worsens as PDA closes; loud S_2
6. **Radiology** = narrow heart base, abnormal pulmonary markings on CXR; echocardiogram used for diagnosis
7. **Treatment** = **keep PDA open with prostaglandin E;** balloon atrial septostomy to widen VSD; prompt surgical correction

***Quick* HIT**

A PDA is necessary for survival with transposition of the great vessels and outflow tract lesions (severe aortic stenosis, coarctation of the aorta, hypoplastic left heart).

MNEMONIC

Prostaglandin E_1 keeps **P**DA **P**atent.

G. Tricuspid Atresia

1. Failure of tricuspid valve to form, preventing blood flow from the RA to the RV; usually accompanied by ASD, VSD, and RV hypoplasia
2. **H/P** = usually presents immediately after birth with cyanosis, holosystolic murmur from the VSD
3. **Radiology** = echocardiography shows the defect(s)
4. **Treatment** = surgical correction

H. Tetralogy of Fallot

1. VSD, RVH, overriding aorta, RV outflow obstruction (see Figure 10-1G)
2. **Risk factors** = Down syndrome, cri-du-chat syndrome, trisomy 13 and 18
3. **H/P** = early cyanosis, dyspnea, fatigue; children squat for relief during hypoxemic episodes; systolic ejection murmur at left sternal border, RV lift, single S_2
4. **ECG** = right axis deviation

5. **Radiology** = echocardiogram or cardiac catheterization used for diagnosis; boot-shaped heart seen on CXR
6. **Treatment** = prostaglandin E to maintain PDA; O_2, propranolol, IV fluids, morphine, knee-to-chest positioning during cyanotic episodes; surgical correction

I. Total Anomalous Pulmonary Venous Return

1. Pulmonary veins fail to empty into the LA and instead empty into the systemic venous circulation (most commonly the left brachiocephalic vein); incompatible with life unless the foramen ovale or ductus arteriosus remains patent
2. **H/P** = presents as neonate with cyanosis, respiratory failure, shock; may have systolic and diastolic murmur, hepatomegaly from RV heart failure
3. **Radiology** = echocardiogram or angiography used for diagnosis
4. **Treatment** = surgical correction

J. Endocardial Cushion Defect

1. Malformation of atrioventricular valves, atrial septum, and/or ventricular septum during fetal development causes a variety of valvular and septal defects (see Figure 10-1F)
2. **Complete defect** has ASD, VSD, and a single atrioventricular canal
3. **Incomplete defect** has ASD and minor atrioventricular valve abnormalities
4. Found in **20% of children with Down syndrome**
5. **H/P** = incomplete form resembles presentation for ASD; complete form causes heart failure symptoms, pneumonitis; murmurs consistent with particular defect
6. **ECG** = left axis deviation
7. **Radiology** = echocardiogram or cardiac catheterization used for diagnosis
8. **Treatment** = surgical correction

K. Kawasaki Disease

1. Second most common vasculitis in children
2. Necrotizing inflammation of large, medium, and small vessels
3. Most commonly seen in **young children**
4. Coronary vasculitis develops in 25% of patients, leading to possible aneurysm, MI, or sudden death; one of the leading causes of acquired heart disease in children
5. **H/P** = fever >5 days, **C**onjunctivitis, maculopapular **R**ash, cervical **A**denopathy (greater than 1.5 cm), **S**trawberry tongue (lip swelling, erythema), edema, eventual desquamation of **H**ands and feet
6. **Labs** = elevated ESR, low albumin levels, sterile pyuria, thrombocytosis, possible autoantibodies to endothelial cells
7. **Radiology** = echocardiogram can detect coronary artery aneurysms (particularly useful when performed with dobutamine stress test); angiography can detect coronary vessel irregularities
8. **Treatment** = ASA, IV γ-globulin; frequently self-limited

L. Henoch–Schönlein Purpura

1. Most common vasculitis in children
2. IgA immune complex–mediated vasculitis affecting arterioles, capillaries, and venules
3. Usually seen in children between 3 and 15 years of age
4. **H/P** = **recent upper respiratory infection (URI)**; **palpable purpura** on the buttocks and lower extremities, abdominal pain and GI bleeding, polyarticular arthritis/arthralgias, hematuria
5. **Labs** = no testing required for diagnosis; urinalysis (to rule out renal involvement) may show hematuria, proteinuria, casts; biopsy of purpura demonstrates **IgA deposition**; similar findings in renal biopsy
6. **Treatment** = frequently self-limited; use corticosteroids for severe GI symptoms or renal involvement
7. **Complications: intussusception**, acute kidney injury

II. Pediatric Pulmonary Concerns

A. Croup

1. Acute inflammation of larynx caused by **parainfluenza virus types 1 and 2**; less commonly by parainfluenza virus type 3, respiratory syncytial virus (RSV), influenza virus, rubeola, adenovirus, or *Mycoplasma pneumoniae*
2. Most common between 3 months and 5 years of age
3. **H/P** = nasal congestion, **barking cough**, dyspnea, **inspiratory stridor**; fever, mild pharyngeal erythema, lymphadenopathy; respiratory distress in severe cases
4. **Radiology** = neck radiographs may show subglottic narrowing of airway (i.e., **steeple sign**) (see Figure 10-2)
5. **Treatment** = **supportive** care (e.g., hydration, humidified air, rest, analgesia); mild cases are treated with steroids (oral, intramuscular, or intravenous) and severe cases (stridor at rest) are treated with aerosolized epinephrine (in addition to steroids) for rapid decrease in swelling; in severe cases, the child should be admitted for observation

MNEMONIC

Remember the symptoms of severe cases of croup by the 3 **S**s: **S**eal-bark cough, **S**ubglottic swelling, and **S**tridor.

NEXT
STEP

If child develops stridor at rest and has no significant improvement, hospitalization and respiratory monitoring are needed.

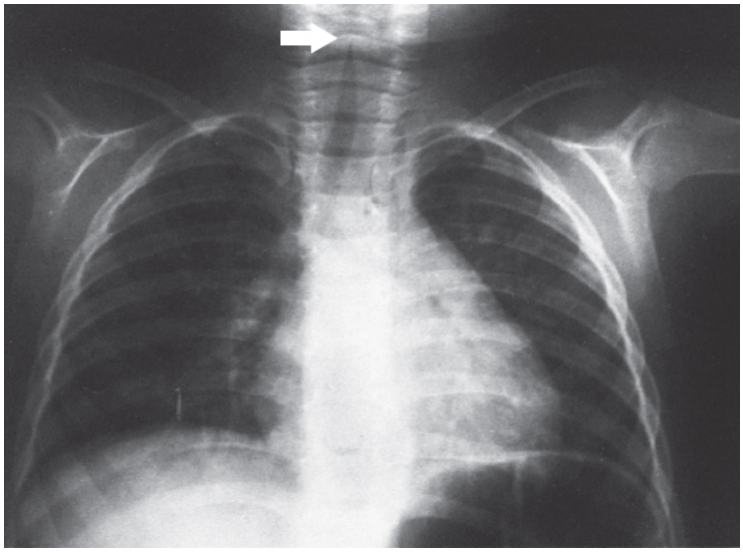


FIGURE **10-2**
Chest x-ray of a child with croup demonstrating subglottic narrowing of the airway (*arrow*), which is reminiscent of the shape of a steeple (steeple sign).
(From Wolfson, A. B., Cloutier, R. L., Hendey, G. W., Ling, L. J., Schaider, J. J., & Rosen, C. L. [2015]. *Harwood-Nuss & Clinical Practice of Emergency Medicine* [6th ed., p. 1220]. Philadelphia, PA: Wolters Kluwer; with permission.)

B. Epiglottitis

1. Rapidly progressive infection of epiglottis and surrounding tissues that can cause airway obstruction
2. Used to be more common in children from 2 to 7 years of age but due to successful *Haemophilus influenzae type b* (Hib) vaccination efforts, incidence has decreased; now more common in older children and adults
3. Historically most commonly caused by **Hib** infection; now associated with streptococcal or other *H. influenzae* bacteria
4. **H/P** = **dysphagia**, drooling, soft stridor, **muffled voice,** anxiety from symptoms; sudden high fever, inspiratory retractions; child may lean forward with hands on knees to aid breathing; erythematous and swollen epiglottis
5. **Labs** = culture from swab of epiglottis can determine causative bacteria (should only be performed if patient is intubated)
6. **Radiology** = neck radiographs show swollen, opacified epiglottis that partially obstructs the airway (i.e., **thumbprint sign, vallecula sign**); laryngoscope (only used in controlled situations) can visualize red and swollen epiglottis (see Figure 10-3)
7. **Treatment** = keep child calm; admit for close observation and respiratory monitoring; unless airway obstruction is mild, **intubate**, ideally in a controlled setting (i.e., operating room, with anesthesia/surgery), to maintain airway patency; antibiotics (ceftriaxone) for 7 to 10 days; airway obstruction preventing intubation requires emergent tracheostomy

Quick **HIT**

In cases of suspected epiglottitis, examine the patient's throat **only** in a setting in which prompt intubation is possible because examination of the patient's throat can lead to additional throat irritation and resulting occlusion.

Quick **HIT**

Widespread use of the **Hib vaccine** has greatly decreased the incidence of epiglottitis.

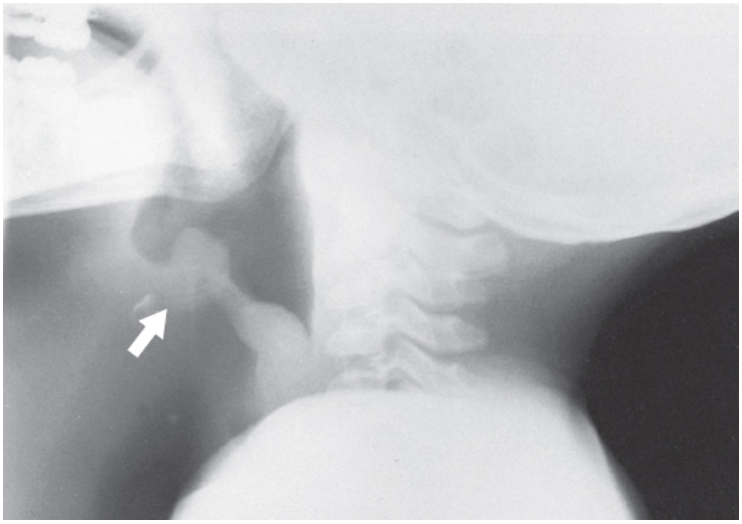


FIGURE **10-3**

Lateral chest x-ray of a child with epiglottitis demonstrating a swollen epiglottis (*arrow*) that resembles a thumbprint (thumbprint sign). (From Wolfson, A. B., Cloutier, R. L., Hendey, G. W., Ling, L. J., Schaider, J. J., & Rosen, C. L. [2015]. *Harwood-Nuss & Clinical Practice of Emergency Medicine* [6th ed., p. 1219]. Philadelphia, PA: Wolters Kluwer; with permission.)

C. Bronchiolitis

1. Viral infection of bronchioles caused by **RSV** (most cases) or parainfluenza virus type 3 (less common)
2. Most commonly occurs in winter and spring; usually found in children <2 years of age
3. **H/P** = nasal congestion, cough, **respiratory distress; wheezing**, fever, tachypnea, crackles, prolonged expiration, hyperresonance to percussion
4. **Radiology** = CXR shows hyperinflation of lungs and patchy infiltrates, but is not required for diagnosis
5. **Treatment** = nasal suction, adequate hydration, humidified air; inhaled bronchodilators (e.g., β_2-agonists, epinephrine) and systemic glucocorticoids are not indicated; children with respiratory distress or hypoxemia should be admitted for observation and respiratory support
6. **Complications** = respiratory distress leading to respiratory failure in severe cases; increased risk of developing asthma

D. Pertussis

1. Bacterial respiratory infection, also known as "**whooping cough,"** caused by ***Bordetella pertussis***
2. Before vaccinations, used to be common in children less than 10 years of age
3. **H/P** = unimmunized patients infected with pertussis have a long manifestation period with three different phases than can last up to 3 months
   a. Catarrhal phase: 1 to 2 weeks with nonspecific symptoms, mild cough, rhinorrhea, conjunctival injection, and may have a mild fever
   b. Paroxysmal phase: After second week of illness, starts with episodes of paroxysmal **cough** followed by an inspiratory "whooping" sound, emesis, syncope
   c. Convalescent phase: Lasts about 2 weeks with a gradual decrease in frequency and severity of cough
4. **Labs** = respiratory culture, PCR testing; complete blood count (CBC) is nonspecific but may show marked leukocytosis with lymphocytosis
5. **Treatment** = supportive care, macrolides (erythromycin) may shorten duration if started early and decreases incidence of spreading infection; also given as postexposure prophylaxis
6. **Complications** = pneumonia, **apnea in infants** (require hospitalization due to high risk)

Quick HIT

Apnea may be the only manifestation of pertussis in an infant.

E. Respiratory Distress Syndrome of the Newborn

1. Preterm infants (e.g., 24 to 37 weeks' gestation and especially before 30 weeks' gestation) have **surfactant deficiency** because of lung immaturity that leads to decreased lung compliance, atelectasis, and respiratory failure
2. **H/P** = **presentation within 2 days of birth;** cyanosis, nasal flaring, expiratory grunting, intercostal retractions, respiratory rate >60 breaths/min, crackles, decreased breath sounds
3. **Labs** = ABG shows increased CO_2, decreased O_2; amniotic fluid analysis (see Figure 10-4) not usually helpful but may guide treatment between 34 and 37 weeks' gestation by determining fetal lung maturity with the amniotic lecithin:sphingomyelin ratio (always treat for <34 weeks, treatment typically unnecessary for >37 weeks)
4. **Radiology** = CXR shows bilateral atelectasis with **ground-glass** appearance and decreased lung volumes
5. **Treatment** = maternal administration of corticosteroids before initiation of labor helps to speed fetal lung maturation; neonatal intensive care unit (NICU) admission appropriate for close observation; supplemental O_2, positive airway

pressure, and **surfactant replacement** therapy form the mainstays of therapy; intubation should be performed for any neonate not responding to treatment or requiring high levels of O_2 to maintain adequate SaO_2

6. **Complications** = pulmonary air leaks (pneumothorax, pneumomediastinum), bronchopulmonary dysplasia, increased risk of developing **asthma** in childhood compared with other children

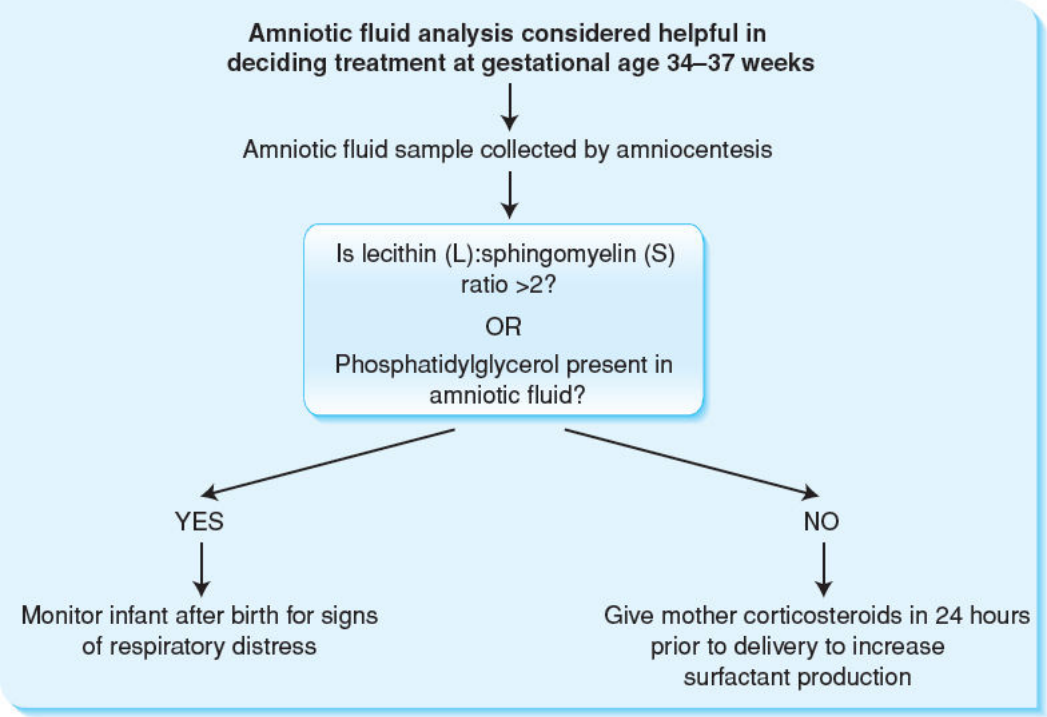


FIGURE **10-4**
Amniotic fluid analysis protocol used to determine fetal lung maturity.

F. Meconium Aspiration Syndrome (MAS)

1. Aspiration of meconium (i.e., fetal stool passed into amniotic sac) predelivery, causing obstruction of airways and pneumonia
2. **H/P** = **meconium-stained amniotic fluid** seen during delivery; cyanosis, intercostal retractions; distended chest, tachypnea
3. **Labs** = consider blood culture to rule out sepsis
4. **Radiology** = CXR shows atelectasis, areas of hyperinflation, or pneumothorax
5. **Treatment** = suction mouth and nose at birth; supplemental O_2; intubate for worsening respiratory distress; surfactant therapy may be useful for improving respiratory function in some cases; consider empiric antibiotic therapy if concerned for development of pneumonia; tracheal intubation for suctioning is no longer recommended in infants with MAS
6. **Complications** = pulmonary HTN can develop if not promptly treated; increased risk of developing asthma during childhood

G. Cystic Fibrosis (CF)

1. Autosomal recessive disorder caused by defect in chloride-pumping channel in exocrine glands; ducts of exocrine glands (e.g., lungs, pancreas, reproductive glands) become clogged with thick secretions
2. Presents in childhood and is universally fatal, but proper treatment may allow survival into 30s and 40s
3. Affects both pulmonary (recurrent infections, chronic sinusitis) and gastrointestinal systems (pancreatic enzyme deficiencies, malabsorption)
4. **Risk factors** = whites at higher risk than other races
5. **H/P** = **recurrent pulmonary infections** (e.g., *Pseudomonas*, *Staphylococcus aureus*), dyspnea, hemoptysis, chronic sinusitis, cough, meconium ileus at birth, steatorrhea, failure to thrive; cyanosis, digital clubbing, esophageal varices, rectal prolapse
6. **Labs** = decreased serum Na; **sweat test** shows increased Na and increased Cl (>60 mEq/L in children, >80 in adults); genetic testing can locate mutation in CF transmembrane conductance regulator (CFTR) gene in suspected cases or in carriers of the gene considering pregnancy
7. **Treatment** = deoxyribonuclease (DNase) aids in decreasing the viscosity of secretions; chest physical therapy helps to clear secretions; bronchodilators, nonsteroidal anti-inflammatory drugs (NSAIDs), antibiotics for any suspected pulmonary exacerbation or infection; supplemental pancreatic enzymes and vitamins A, D, E, and K given for malabsorption

Quick HIT

CF is the most common fatal autosomal recessive disorder in the United States.

III. Pediatric GI Disorders

A. Tracheoesophageal Fistula

1. Malformation of trachea and esophagus resulting in tract formation between structures (see Figure 10-5)
2. Frequently associated with esophageal atresia
3. **H/P** = coughing and cyanosis during feeding, food may fill blind pouch, abdominal distention, possible history of aspiration pneumonia
4. **Radiology** = chest radiograph following nasogastric tube insertion demonstrates malformation (tube in lung or blind pouch)
5. **Treatment** = surgical repair

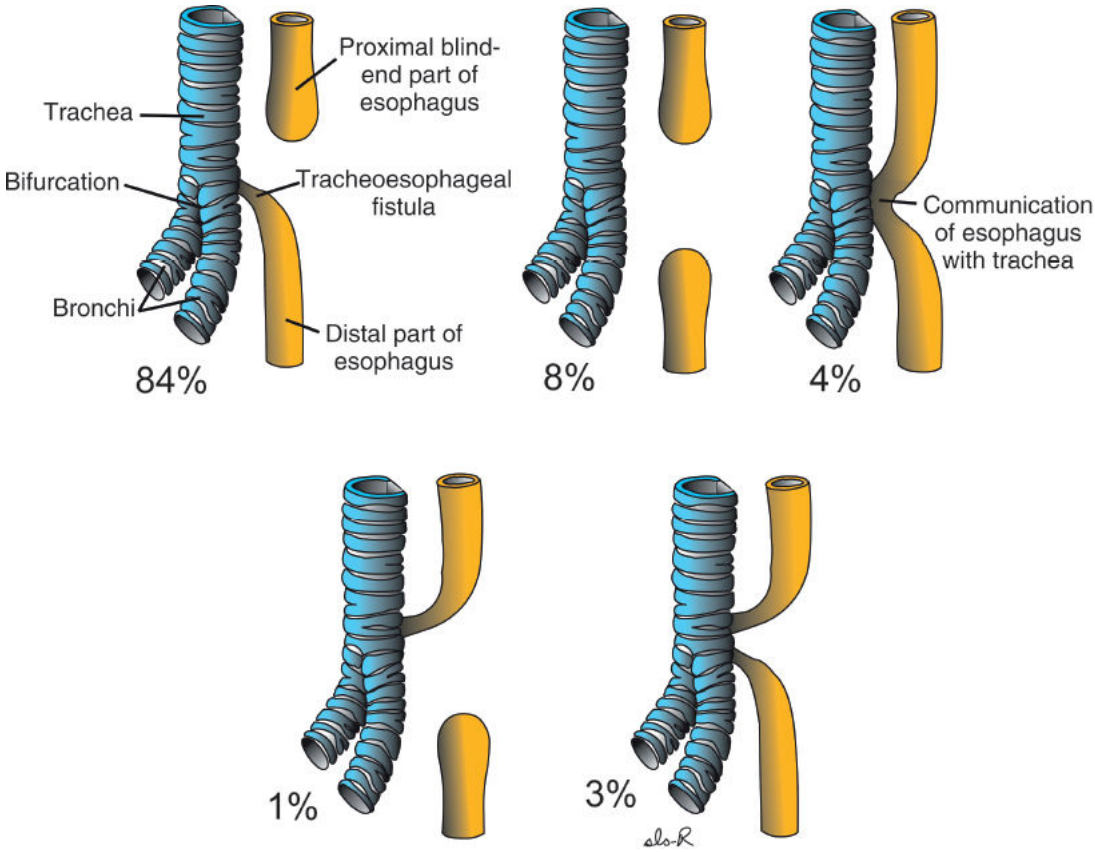


FIGURE 10-5
Variations of tracheoesophageal fistulas.
(Modified from Sadler, T. W. [2012]. *Langman's Medical Embryology* [12th ed., p. 212]. Baltimore, MD: Wolters Kluwer Health; with permission.)

B. Pyloric Stenosis

1. Hypertrophy of pyloric sphincter causing obstruction of gastric outlet
2. **H/P** = symptoms begin a few weeks after birth; nonbilious emesis, **projectile emesis**; **palpable epigastric olive-sized mass**
3. **Labs** = hypochloremic, hypokalemic metabolic alkalosis
4. **Radiology** = barium swallow shows thin pyloric channel (i.e., **string sign**); US shows increased pyloric muscle thickness (see Figure 10-6)
5. **Treatment** = pyloromyotomy

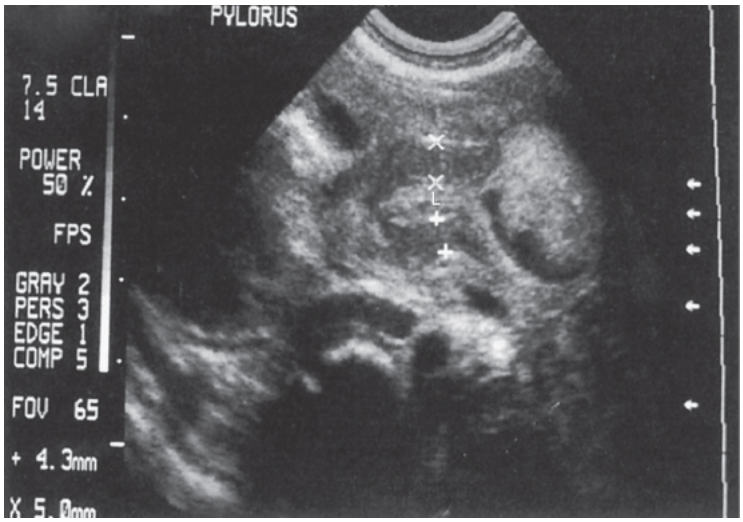


FIGURE **10-6**

Abdominal ultrasound demonstrating pyloric stenosis.
Note the thin pyloric lumen (*L*) and the thickened pyloric musculature (defined by region between ×'s and +'s).
(From Daffner, R. H., & Hartman, M. [2013]. *Clinical Radiology: The Essentials* [4th ed., p. 298]. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; with permission.)

C. Necrotizing Enterocolitis

1. Idiopathic mucosal necrosis and epithelial cell sloughing
2. **Risk factors** = preterm birth, low birth weight
3. **H/P** = bilious vomiting, lethargy, poor feeding, diarrhea, **hematochezia**; abdominal distention, abdominal tenderness; signs of shock in severe cases
4. **Labs** = metabolic acidosis, decreased Na^+
5. **Radiology** = abdominal radiograph shows bowel distention, **air in bowel wall**, portal vein gas, or free air under the diaphragm
6. **Treatment** = TPN, IV antibiotics, broad-spectrum antibiotics, nasogastric suction, surgical resection of affected bowel

D. Hirschsprung Disease

1. Absence of bowel autonomic innervation causing bowel spasm and obstruction
2. **H/P** = vomiting, **obstipation**, failure to pass stool; abdominal distention
3. **Labs** = bowel biopsy shows **absence of ganglia**
4. **Radiology** = abdominal x-ray (AXR) demonstrates dilated bowel; barium enema shows proximal dilation (megacolon) with distal narrowing
5. **Treatment** = colostomy and resection of affected area

E. Intussusception

1. **Telescoping of bowel into adjacent segment** of bowel, leading to obstruction; most frequently proximal to ileocecal valve
2. **Risk factors** = Meckel diverticulum, Henoch–Schönlein purpura (associated with ileoileal intussusception), adenovirus infection, CF
3. **H/P** = sudden abdominal pain that lasts <1 minute and is episodic; pallor, sweating, vomiting, bloody mucus in stool (i.e., **currant jelly stool**); abdominal tenderness; **palpable, sausage-like abdominal mass**
4. **Labs** = increased white blood cell (WBC)
5. **Radiology** = AXR to rule out pneumoperitoneum, may show bowel obstruction; US (first line) or computed tomography (CT) may detect abnormal bowel; usually ileocecal; barium enema will show obstruction
6. **Treatment** = barium enema with air contrast may reduce defect; surgery required for refractory cases
7. **Complications** = bowel ischemia (appendix particularly susceptible), perforation during reduction with air contrast enema

Quick HIT

Intussusception is the most common cause of bowel obstruction in the **first 2 years of life.**

F. Meckel Diverticulum

1. Common **remnant of vitelline** duct that exists as **outpouching of ileum** and may contain **ectopic tissue**
2. **H/P** = asymptomatic; occasionally presents with painless rectal bleeding, **intussusception**, diverticulitis, or abscess formation
3. **Radiology** = gastric mucosa may be detected by technetium radionuclide scan (i.e., **Meckel scan**)
4. **Treatment** = surgical resection if symptomatic

Quick HIT

Intussusception in an adult is considered cancer until proven otherwise and usually will require surgical reduction.

G. Malrotation With Volvulus

1. Congenital malformation (malrotation of the intestine during fetal development) increases the risk of intestinal torsion with bowel ischemia and **obstruction** (volvulus)
2. **H/P** = neonates present with **bilious vomiting** (most common presenting sign), abdominal distention, peritonitis, shock
3. **Radiology** = plain AXR may show "**double bubble**" sign, obstruction pattern, or free air if perforation is present; upper GI contrast series show **"corkscrew"** or **"beak"** appearance of duodenum
4. **Treatment** = emergent surgery (exploratory laparotomy), antibiotics, fluids resuscitation

Quick HIT

Meckel diverticulum rule of 2s—males **2 times** more common than females, occurs within **2 ft** of ileocecal valve, **2 types** of ectopic tissue (gastric, pancreatic), found in **2%** of the population, most complications occur before **2** years of age.

Quick HIT

Any neonate with bilious vomiting needs emergent surgery consult because malrotation with volvulus should be suspected until proven otherwise.

H. Neonatal Jaundice

1. Hyperbilirubinemia in the newborn may be due to **physiologic, hepatic,** or **hematologic** causes
   a. Physiologic (**common**): **physiologic under secretion,** breastfeeding failure
   b. Increased hemolysis: maternal–fetal ABO incompatibility, hereditary RBC abnormalities, glucose-6-phosphate dehydrogenase (G6PD) deficiency
   c. Bilirubin overproduction without hemolysis: hemorrhage, maternal–fetal transfusion
   d. Hepatic abnormalities: Gilbert syndrome, Crigler–Najjar syndrome, biliary atresia
2. Physiologic causes frequently resolve within 2 weeks.
3. **Kernicterus** is deposition of bilirubin in the basal ganglia and hippocampus and may cause permanent damage; results from extremely high serum bilirubin and is typically only seen with hepatic abnormalities
4. **H/P** = jaundice, scleral icterus; lethargy, high-pitched cry, seizures, and apnea seen with kernicterus
5. **Labs** = frequently indirect hyperbilirubinemia (due to hemolysis); jaundice developing with initial 24 hours after birth, total bilirubin >15 mg/dL, or direct bilirubin >2 mg/dL suggests nonphysiologic cause
6. **Treatment** = phototherapy used for physiologic jaundice lasting several days; suspected nonphysiologic causes should be worked up and may require exchange transfusion; intravenous immunoglobulin may reduce need for exchange transfusion in cases of maternal–fetal blood type incompatibility

I. Failure to Thrive

1. Children below third percentile weight for age or failure to gain weight appropriate for age
2. May be due to underlying illness or neglect
3. **H/P** = look for leads to organic causes; screen for abuse
4. **Labs** = urinalysis, CBC, blood culture, urine culture, serum electrolytes, CF testing, and caloric intake records may be helpful in making diagnosis
5. **Treatment** = high-calorie diet, treat underlying disorder; educate parents in proper nutrition and feeding; contact social support services in cases of neglect or abuse

NEXT
STEP

Always look for signs of abuse and neglect in a child with failure to thrive.

IV. Pediatric Genitourinary Concerns

A. Wilms Tumor

1. Malignant tumor of renal origin presenting in **children <4 years of age**
2. **Risk factors** = family history, neurofibromatosis, other genitourinary abnormalities
3. **H/P** = weight loss, nausea, vomiting, dysuria, polyuria; palpable abdominal or flank mass, HTN, fever
4. **Labs** = measure BUN, Cr, and CBC to assess kidney function

5. **Radiology** = CT or US shows renal mass; CXR and CT can show metastases
6. **Treatment** = surgical resection or nephrectomy, chemotherapy, and possible radiation; good prognosis without extensive involvement

B. Urethral Displacement

1. Urethral opening on top (i.e., epispadias) or underside (i.e., hypospadias) of penis associated with other penile anatomic abnormalities
2. **H/P** = defect apparent on examination and during urination
3. **Treatment** = surgical correction (ideally during infancy); do not circumcise before surgical correction
4. **Complications** = may contribute to infertility

C. Enuresis

1. Nocturnal bed-wetting seen in young children
2. Seen in all children; **most cases resolve by age 4 years**; rare cases associated with disease
3. **H/P** = **almost always nonpathologic**; unusual findings in history and examination should prompt further workup
4. **Treatment** = education, enuresis alarms, dietary modifications (no fluids near bedtime); desmopressin or imipramine used in refractory cases

D. Undescended Testes (Cryptorchidism)

1. Testes lying in abdominal cavity and not consistently located within scrotum
2. **H/P** = empty scrotal sac, testes inconsistently found in scrotum
3. **Treatment** = exogenous hCG administration or orchiopexy before age 5 years to reduce risk of cancer and allow testicular development
4. **Complications** = testicular cancer (risk reduced but not eliminated by surgical correction), infertility

E. Posterior Urethral Valves

1. Abnormal folds of tissue in the distal prostatic urethra, causing bladder outlet obstruction and weak urinary stream
2. **H/P** = often diagnosed on prenatal US; weak urinary stream, urinary tract infection (UTI); abdominal distention
3. **Imaging** = ultrasound reveals thick-walled bladder, bilateral hydronephrosis, and/or megaureter; voiding cystourethrogram (VCUG) shows elongation and dilation of the posterior urethra during voiding
4. **Treatment** = cystoscopic transurethral ablation of abnormal tissue or urinary diversion (vesicostomy)

V. Pediatric Endocrine Concerns

A. Congenital Hypothyroidism

1. Caused by severe iodide deficiency (#1 cause in underdeveloped countries), thyroid agenesis (#1 cause in developed countries), or hereditary disorder of thyroid hormone synthesis
2. If untreated, leads to abnormal mental development and growth delay (cretinism)
3. **H/P** = frequently asymptomatic if mother has normal thyroid function; poor feeding, lethargy, large fontanelles that remain open, thick tongue, constipation; umbilical hernia, poor growth, hypotonicity, dry skin, hypothermia, jaundice
4. **Labs** = decreased T_4, increased TSH
5. **Radiology** = x-ray shows poor bone development; thyroid scan shows decreased uptake with malformed thyroids and increased uptake with iodide deficiency
6. **Treatment** = levothyroxine started soon after birth to avoid permanent developmental delays

Quick **HIT**

Prolonged jaundice is frequently the first sign of congenital hypothyroidism.

B. Glucose-6-Phosphatase Deficiency

1. One of multiple disorders of glycogen storage (Table 10-1)
2. Also known as **type 1 glycogen storage disease** or von Gierke disease, results in impaired conversion of glycogen to glucose and accumulation of glycogen in different organs
3. **H/P** = presents during first months of life (3 to 4 months), **hepatomegaly, seizures, doll-like** facial appearance, thin extremities
4. **Labs** = low glucose, elevated lactic acid, elevated lipids, elevated uric acid
5. **Treatment** = dietary changes, restricted intake of fructose and galactose, maintain normal glucose levels

Table 10-1 Types of Glycogen Storage Disorder

Type	Enzyme Affected	Characteristics	Treatment
I (von Gierke disease)	Glucose-6-phosphatase deficiency	Hepatomegaly, **hypoglycemia, seizures, doll-like facial appearance**, thin extremities	Special diet, **avoi tose, and sucros**
II (Pompe disease)	Lysosomal α-glucosidase deficiency	Cardiomegaly, hypotonia, respiratory distress	Enzyme replacem alfa)
III (Cori disease)	Glycogen debranching enzyme deficiency	Mostly affects liver and muscle; mild hypoglycemia	High-protein diet, transplant
IV (Anderson Disease)	Glycogen branching enzyme (Mutation in GBE-1 gene result in glycogen branching deficiency; autosomal recessive inheritance)	Growth delay in childhood, enlarged liver, progressive cirrhosis of the liver (which may lead to liver failure), may affect muscles and heart in late-onset type	Liver transplantat
V (McArdle disease)	Muscle glycogen phosphorylase deficiency	**Skeletal muscle** affected; cramps, myalgias, fatigue	**Sucrose supple**

Quick HIT

Glucose-6-phosphatase deficiency should not to be confused with glucose-6-phosphate dehydrogenase deficiency (G6PD), which predisposes to red blood cell breakdown and is triggered by infections, medications, and stress.

VI. Pediatric Hematologic and Oncologic Concerns (Not Addressed in Other Sections)

A. Hemolytic Disease of the Newborn

1. If Rh^+ fetal cells enter circulation of Rh^- mother, **anti-Rh antibodies** may develop.
2. Antibodies do not affect pregnancy with initial Rh interaction but cause severe fetal RBC hemolysis in subsequent pregnancies with Rh^+ fetuses (i.e., fetal hydrops). Hemolysis will likely cause death of fetus.
3. **Risk factors** = Rh^- mother with any history of fetal–maternal hemorrhage (e.g., abortion, amniocentesis, third-trimester bleeding).
4. **Treatment** = administration of Rho(D) immune globulin (**RhoGAM**) within 72 hours of delivery of initial Rh^+ fetus or at any time maternal and fetal blood may have mixed will prevent development of anti-Rh antibodies and protect future pregnancies by suppressing maternal formation of anti-Rh antibodies; intrauterine fetal transfusion may be required if condition develops in utero.

B. Fanconi Anemia

1. Autosomal recessive disorder associated with **bone marrow failure**, pancytopenia, and increased risk of leukemia
2. **H/P** = fatigue, dyspnea on exertion, frequent infections; frequently associated with **short stature**, **abnormal skin pigmentation** (café au lait spots or hypopigmented areas), horseshoe kidney, and thumb abnormalities
3. **Labs** = decreased Hgb, Hct, platelets, and WBCs; increased serum α-fetoprotein; bone marrow biopsy shows hypocellularity; chromosome analysis detects multiple strand breakage
4. **Treatment** = antibiotics, transfusions, bone marrow or hematopoietic stem cell transplantation, hematopoietic growth factors; androgens and corticosteroids can increase bone marrow activity
5. **Complications** = death in childhood is common from bone marrow failure or leukemia

C. Diamond–Blackfan Anemia

1. Congenital **pure RBC anemia** likely caused by a defect in erythroid progenitor cells
2. **H/P** = fatigue, dyspnea, cyanosis, and pallor detected early in life; craniofacial abnormalities, thumb abnormalities, heart murmurs, intellectual disability, hypogonadism
3. **Labs** = decreased Hgb, decreased Hct, decreased reticulocyte count, increased MCV; bone marrow biopsy shows decreased activity but increased presence of erythropoietin
4. **Treatment** = transfusions, corticosteroids, bone marrow transplant

D. Neuroblastoma

1. Tumors of neural crest cell origin that may arise in adrenal glands or sympathetic ganglia
2. **Risk factors** = neurofibromatosis, tuberous sclerosis, pheochromocytoma, Beckwith–Wiedemann syndrome, Turner syndrome, low maternal folate consumption
3. **H/P** = abdominal distention and pain, weight loss, malaise, bone pain, diarrhea; abdominal mass, HTN, possible Horner syndrome, proptosis, movement disorders, hepatomegaly, fever, periorbital bruising
4. **Labs** = possible increased vanillylmandelic and homovanillic acids in 24-hour urine collection
5. **Radiology** = CT may locate adrenal or ganglion tumor
6. **Treatment** = surgical resection, chemotherapy, radiation
7. **Complications** = poor prognosis if presenting after 1 year of age; metastasizes to bone and brain

Quick HIT

Prognosis for neuroblastoma is good if diagnosed before 1 year of age.

E. Rhabdomyosarcoma

1. Tumor of striated muscle in children
2. **H/P** = painful soft tissue mass with swelling; large tumors frequently cause mass effect on nearby structures
3. **Labs** = biopsy is diagnostic
4. **Radiology** = CT or magnetic resonance imaging (MRI) shows extent of tumor
5. **Treatment** = surgical debulking, radiation, chemotherapy

Quick HIT

Rhabdomyosarcoma is the **most common soft tissue sarcoma** in children.

VII. Pediatric Neurologic Issues

A. Febrile Seizures

1. Childhood seizures between 6 and **60 months (5 years)** associated with **fever**
2. Occur in absence of central nervous system (CNS) infection or lesion, metabolic abnormality, or history of prior afebrile seizures
3. **H/P** = fever (temperature >100.4°F/38°C) with rapid rise in temperature; tonic-clonic seizure lasting <15 minutes; usually **family history** of febrile seizures
4. Classified as simple versus complex febrile seizures
   a. Simple
      (1) Generalized tonic-clonic seizure
      (2) Last less than 15 minutes
      (3) No more than 1 episode per 24-hour period
      (4) Return to baseline after seizure
   b. Complex (any of the following)
      (1) Focal seizure
      (2) Last longer than 15 minutes
      (3) Multiple seizures in 24 hours
      (4) Prolonged postictal state or focal deficit
5. **Labs** = usually not necessary in simple febrile seizures; labs ordered depend on underlying cause of fever (e.g., if suspected UTI, order U/A); LP should be performed if meningitis is suspected and considered in children <12 months of age that are not fully immunized. If complex, may require further tests
6. **EEG** = not routinely warranted for simple febrile seizures, usually normal, unless atypical seizure
7. **Treatment** = confirm respiratory stability; antipyretics; observe for return to baseline; treat underlying illness; atypical seizures should receive more in-depth workup, consider including blood laboratory studies, EEG, and MRI
8. **Complications**
   a. Thirty-five percent of patients have recurrent febrile seizures, but there is little increase in lifetime risk of epilepsy.
   b. Complex febrile seizures are more likely to recur, occur over longer periods of time, and carry an increased risk of **epilepsy**.

Quick HIT

Febrile seizures are the most common seizures in **children**.

B. Childhood Hydrocephalus

1. Hydrocephalus in children caused by either obstruction of CSF circulation in fourth cerebral ventricle (i.e., **noncommunicating**) or dysfunction of subarachnoid cisterns or arachnoid villi (i.e., **communicating**)

2. **H/P** = **increased head growth**, bulging fontanelles, and dilated scalp veins in infants; lethargy, vomiting, poor appetite, irritability, headache, diplopia, papilledema, poor skull suture fusion in older children
3. **Labs** = LP should be performed if infection is suspected
4. **Radiology** = US, CT, or MRI will show expanded ventricles
5. **Treatment** = acetazolamide or furosemide can be used temporarily to relieve symptoms; surgical shunting usually required for most cases
6. **Complications** = increased risk of epilepsy; increased risk of bacterial infection with shunting; 50% mortality before 3 years of age if untreated

Quick HIT

Antipyretics, despite being part of treatment, have not been shown to decrease the risk of febrile seizures.

NEXT
STEP

Do **not** give ASA to young children as an antipyretic because of risk of Reye syndrome.

C. Tay–Sachs Disease

1. Autosomal recessive disorder caused by absence of hexosaminidase A (i.e., enzyme required for lipid ganglioside metabolism)
2. **Risk factors** = **Ashkenazi Jews**, French Canadians
3. **H/P** = poor development after first few months of life, decreased alertness, hyperacute hearing; **cherry red spots** on **retina** on funduscopic examination, progressive paralysis, vision loss, change in mental status
4. **Labs** = decreased hexosaminidase A activity; DNA analysis confirms diagnosis
5. **Treatment** = supportive care; genetic screening may aid parents with future childbearing decisions
6. **Complications** = death within first few years of life

Quick HIT

Arnold–Chiari malformation type II and Dandy–Walker malformations are anatomic defects of the skull and ventricular system associated with hydrocephalus in children.

D. Neural Tube Defects

1. Failure of neural tube closure during gestation leading to a spectrum of defects involving CNS formation
2. **Types of defects**
   a. **Spina bifida occulta:** most benign type; defect in **closure of dorsal vertebral arches** above spinal cord (usually lumbosacral junction)
   b. **Meningocele:** larger defect with herniation of meninges through dorsal vertebral defect; soft mass may form in midline superficial to defect
   c. **Myelomeningocele:** severe defect with herniation of meninges and spinal cord through defect; frequent neurologic deficits, including bowel and bladder incontinence, flaccid paralysis, poor sensation, LMN signs, hydrocephalus
   d. **Anencephaly:** severe disorder with failure of cranial neural tube to close; absence of forebrain, meninges, and portions of skull; death occurs within days of birth
3. **Risk factors** = anticonvulsant use or **poor folate intake** during pregnancy (both result in low maternal serum folate), diabetes mellitus (DM)
4. **H/P** = symptom severity depends on defect severity; patients with mild spina bifida may have tuft of hair over defect and may be asymptomatic. More severe neural tube defects have more severe neurologic and developmental abnormalities
5. **Labs** = increased amniotic α**-fetoprotein** and **acetylcholinesterase** during gestation (measured in properly timed quadruple screen)
6. **Radiology** = US during pregnancy may detect defects
7. **Treatment**
   a. Surgical repair of all but mild defects needed.
   b. Shunting frequently needed for meningocele and myelomeningocele to resolve hydrocephalus.
   c. Fetal surgery is developing as a potential treatment for lower neural tube defects diagnosed in utero.
   d. Pregnant women and women trying to conceive should be given folate supplementation to reduce risk of defects.
8. **Complications** = increased risk of UTI and CNS infection; hydrocephalus in severe defects; children with severe defects may require lifelong care; survival time for anencephaly is typically for only a few days following birth

E. Cerebral Palsy (CP)

1. Disorders of motor function resulting from CNS damage during in utero or infantile development; most cases result from **perinatal complications**
2. **Risk factors** = **prematurity**, intrauterine growth restriction, **birth trauma**, neonatal seizures or cerebral hemorrhage, **perinatal asphyxia**, multiple births, intrauterine infection (chorioamnionitis)

3. Types
   a. **Spastic:** spastic paresis of multiple limbs
   b. **Dyskinetic:** choreoathetoid, dystonic, or ataxic movement disorder
4. **H/P**
   a. Patients with spastic CP have multiple limbs with increased tone, increased DTRs, weakness, gait abnormalities, and frequent intellectual disability.
   b. Patients with dyskinetic CP have choreoathetoid, dystonic, or ataxic movements that worsen with stress as well as difficulty speaking (i.e., dysarthria).
   c. Both types of CP can include hyperactivity, seizures, or limb contractures.
   d. Some patients may exhibit symptoms of both types.
5. **Radiology** = MRI may be useful for detecting causative lesions
6. **Treatment**
   a. Pharmacologic therapy (e.g., botulinum toxin, dantrolene, baclofen, benzodiazepines), physical therapy, bracing, and surgery can be used to alleviate contractures and improve function.
   b. Social and psychological support will be needed to help parents coordinate the many services needed for chronic care.

Quick HIT

Spastic CP is caused by damage of **pyramidal** tracts. **Dyskinetic** CP results from **extrapyramidal** pathology.

F. Retinoblastoma

1. Malignant tumor of retina in children and the most common **intraocular** tumor in children
2. Some cases have a genetic link that increases risk of tumor for both eyes
3. **H/P** = rarely, patients experience decrease in vision or eye inflammation; ophthalmologic examination may detect poor red light reflex in affected eye (i.e., **leukocoria**) or white retinal mass (see Figure 10-7)

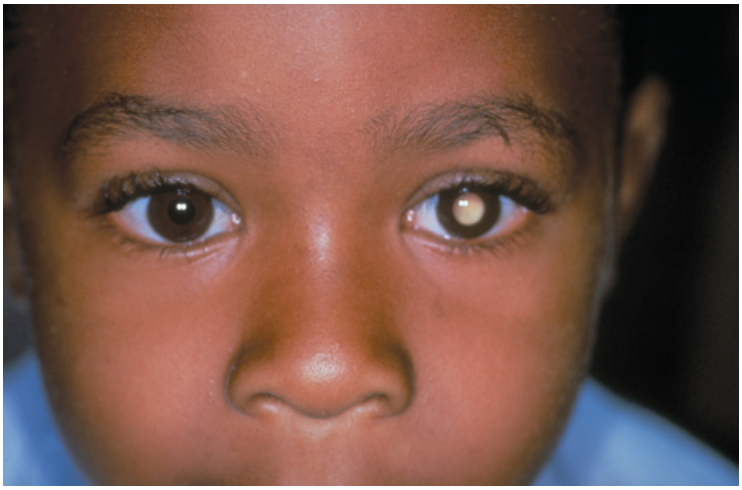


FIGURE 10-7
Leukocoria in a child with a left-eye retinoblastoma.
(From Rubin, R., & Strayer, D. S. [2012]. *Rubin's Pathology* [6th ed., p. 1413]. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; with permission.)

4. **Labs** = mutation of RBI gene apparent on genetic testing
5. **Radiology** = US and CT detect size and extent of tumor; finding of calcified mass with normal globe size on CT is needed before therapy can be initiated
6. **Treatment**
   a. Enucleation performed for large tumors with no vision potential
   b. Radiation can be used for bilateral tumors or tumors near optic nerve
   c. Cryotherapy or laser photocoagulation used for smaller tumors
   d. Chemotherapy used for metastases or vision salvage
7. **Complications** = good prognosis if metastasis has not occurred; risk of vision loss is high if tumor is adjacent to cornea

G. Infantile Botulism

1. Paralysis after presynaptic cholinergic blockade caused by *Clostridium botulinum* toxin; infant's GI tract is colonized with *C. botulinum*, which produces the **toxin in vivo**
2. Usually from spore ingestion after exposure to **dust/soil** or **raw honey**
3. **H/P** = presents with **constipation, weak cry,** poor feeding, hypotonia, decreased gag reflex, lethargy, respiratory difficulty
4. **Labs** = stool sample for botulinum toxin, electromyogram; but neither is required before starting treatment if diagnosis is suspected

5. **Treatment**
   a. Protect the airway, respiratory support if necessary
   b. **Botulism immune globulin intravenous**
6. **Complications** = respiratory failure, death (if untreated)

Quick HIT

Honey in children less than 1 year of age is contraindicated due to risk of infantile botulism.

VIII. Pediatric Orthopedics

A. Developmental Dysplasia of the Hip (DDH)

1. Perinatal displacement of the femoral head from acetabulum disrupting normal development of the hip joint
2. Occurs because of poor development of acetabulum in utero
3. **Risk factors** = female > male, firstborn children, babies delivered in breech presentation, oligohydramnios
4. **H/P**
   a. Positive Barlow and Ortolani maneuvers (provocation of hip dislocation or reduction)
   b. Knees at unequal heights when hips and knees flexed (i.e., Galeazzi sign)
   c. Trendelenburg gait (i.e., sagging of opposite hip)
   d. Asymmetric skin folds
5. **Radiology** = **ultrasound**; x-ray
6. **Treatment** = **Pavlik harness** used in children <6 months of age; closed or open reduction and spica casting performed in children 6 months to 2 years of age; open reduction performed after age 2 years; correction may not be performed after age 8 years because of reduced benefit
7. **Complications** = permanent hip dysplasia results from inadequately treated cases; likelihood of successful treatment and normal hip development improves with earlier treatment

B. Slipped Capital Femoral Epiphysis (SCFE)

1. Separation through growth plate of femoral epiphysis from metaphysis
2. **Risk factors** = **adolescent, obese,** black race, hypothyroidism
3. **H/P** = thigh and knee pain; limp, limited internal rotation and abduction of the hip; hip flexion produces obligatory external hip rotation
4. **Radiology** = x-rays indicate posterior and medial displacement of the femoral head from the femoral metaphysis; need anteroposterior and frog-leg views for full evaluation
5. **Treatment** = surgical pinning, weight-bearing restrictions following repair if unstable (unable to bear weight on presentation), prophylactic pinning of normal contralateral side performed in cases of hypothyroidism
6. **Complications** = increased risk of avascular necrosis (AVN) and premature osteoarthritis if treatment is not performed early

C. Legg–Calvé–Perthes Disease

1. AVN of capital femoral epiphysis most common between 3 and 8 years of age
2. **H/P** = gradual progressive limp, insidious onset of pain, decreased range of motion
3. **Radiology** = x-ray shows asymmetric hips; affected femoral head appears small with sclerotic bone and widened joint space
4. **Treatment** = containment of hip within acetabulum via bracing or surgical means; **acetabular reconstruction performed in cases of permanent hip dysplasia**
5. **Complications** = 50% untreated cases recover fully; increased risk of hip complications in adulthood, including osteoarthritis, progressive AVN, and need for early arthroplasty in cases of permanent dysplasia

D. Osgood–Schlatter Disease

1. Inflammation of the bone–cartilage interface of the tibial tubercle (i.e., osteochondritis)
2. Most common in young boys during pubertal growth spurt
3. **H/P** = pain at involved site that worsens with activity
4. **Treatment** = stretching exercises, NSAIDs

E. Club Foot

1. Inversion of foot, plantar flexion of ankle, and adduction of forefoot
2. **H/P** = child who is slow to walk, limp; obvious defect on examination
3. **Treatment** = **serial casting** of foot in correct position; surgery required in longstanding cases to release contractures and modify bone alignment

F. Physeal Fractures

1. Fractures involving the growth plate of growing bones; described by Salter–Harris classification system (see Table 10-2)

2. Most heal uneventfully, but some will result in impairment of bone growth at site of injury
3. **H/P** = pain at site of injury; possible gross deformity, swelling, warmth at fracture site; growth disturbance with limb inequality seen in cases of permanent physeal damage
4. **Radiology** = x-ray demonstrates fracture at site of injury; premature closure of physis seen in cases of growth disturbance
5. **Treatment** = adequate reduction and immobilization, fixation for unstable fractures; growth disturbance may require limb-lengthening procedures, excision of closed portion of physis, or epiphysiodesis of contralateral physis (i.e., surgical disturbance of physis) to achieve equal limb size

Table 10-2 Salter–Harris Classification of Physeal Fractures

Type	Description	Prognosis
I	Physeal separation without extension into adjacent bone	Good with adequate reduction, quick healing
II	Partial physeal separation with proximal extension into metaphysis	Good; rare growth disturbance
III	Partial physeal separation with distal extension into epiphysis	Poor unless accurate reduction; fixation usually required to maintain stability
IV	Fracture extends through metaphysis, physis, and epiphysis	Perfect reduction must be achieved; guarded prognosis even with good reduction
V	Crush injury of physis	High likelihood of partial growth arrest

G. Clavicular Fracture

1. **Most common** fracture in children (e.g., birth trauma, falls)
2. **H/P** = pain overlying midshaft clavicle, most common fracture sustained during birth
3. **Treatment** = no treatment needed in neonates; figure-of-eight sling

H. Nursemaid Elbow

1. Radial head subluxation that occurs via pulling and lifting on the hand (e.g., yanking the child out of danger by his or her arm)
2. **H/P** = child with painful arm who will not bend elbow, history of recent accidental pull of forearm, elbow/forearm maintained in pronation and adduction
3. **Treatment** = manual reduction via supination of the forearm with flexion of the elbow from 0 to 90 degrees or manual reduction via hyperpronation of the forearm

I. Rickets

1. **Impaired calcification** of bone in children caused by deficient vitamin D intake, absorption, or metabolism (i.e., hypocalcemic types) or impaired phosphate absorption (i.e., hypophosphatemic type)
2. Called **osteomalacia** in adults
3. Results from lack of sunlight and/or poor diet in absence of renal or metabolic defects
4. Epiphyseal cartilage becomes hypertrophic without calcification
5. **H/P** = bone pain, delayed walking; **bowed legs**, kyphoscoliosis, proximal limb weakness, decreased height, softened skull bones; fractures that result from minimal trauma in adults
6. **Labs** = increased alkaline phosphatase (all types), decreased phosphorus (all types), decreased calcium (hypocalcemic), decreased (hypocalcemic) or increased (hypophosphatemic) 25-hydroxyvitamin D3 and 1,25-dihydroxycholecalciferol, increased parathyroid hormone (hypocalcemic)
7. **Radiology** = x-rays will demonstrate widening of physes, bowing of long bones, translucent lines in bones, flattening of skull, and enlarged costal cartilages
8. **Treatment** = phosphorus supplementation for all types, vitamin D supplementation for poor intake, 1,25-dihydroxycholecalciferol for impaired vitamin absorption or metabolism

J. Scoliosis

1. Resting lateral **curvature** of the spine with associated rotatory deformity
2. Curve is at risk of progressing during periods of rapid growth; risk of curve progression increases with size of curve
3. Initially, mainly a **cosmetic** issue; progressive curvature interferes with activities
4. Severe cases result in decreased pulmonary function
5. **H/P** = asymmetry of back musculature and palpable curve of the spine that are augmented when patient bends at the waist; possible pulmonary compromise in severe cases
6. **Treatment** = observation for small curves; bracing for moderate curves in young patients; surgery for more severe curves or curves in older patients
7. **Complications** = severe curves can cause restrictive respiratory disease by limiting lung expansion

K. Juvenile Idiopathic Arthritis (JIA)

1. Nonmigratory arthropathy affecting one or more joints for >3 months
2. Classified as pauciarticular, polyarticular, or systemic, depending on the constellation of symptoms (see Table 10-3)
3. **H/P** = arthralgias of joints involved, morning stiffness; fever; additional findings depend on subtype

4. **Labs** = vary with subtype
5. **Radiology** = x-rays may demonstrate osteopenia and subchondral sclerosis around **involved joints**
6. **Treatment** = varies with subtype but usually consists of NSAIDs, methotrexate, or corticosteroids

Quick HIT

Becker muscular dystrophy is similar to Duchenne muscular dystrophy, except symptoms are less severe and progression occurs more slowly.

L. Duchenne Muscular Dystrophy

1. X-linked disorder resulting from deficiency of **dystrophin** (subsarcolemmal cytoskeletal protein)
2. **Most common** lethal muscular dystrophy
3. Onset at 2 to 6 years of age
4. **H/P** = progressive clumsiness, easy fatigability, **difficulty standing up and walking,** waddling gait, positive **Gower maneuver** (i.e., must push on thighs with hands to stand up); weakness occurs in proximal muscles before distal muscles; **pseudohypertrophy** occurs in calf muscles from fatty infiltration
5. **Labs** = increased CK; muscle biopsy shows muscle fiber degeneration and fibrosis and basophilic fibers; immunostaining for dystrophin (**absent** in disease) is diagnostic
6. **EMG** = polyphasic potentials and increased fiber recruitment
7. **Treatment** = physical therapy, corticosteroids, pulmonary support, ACE-I decrease cardiac afterload
8. **Complications** = progressive cardiac issues, scoliosis, and flexion contractures; death commonly occurs by 20 years of age because of respiratory issues

Table 10-3 Variants of Juvenile Idiopathic Arthritis

	Pauciarticular	Polyarticular	Systemic
Joints involved	Fewer than four joints; large joints **except hips**	Five or more joints; hips less common	Any number
Age of presentation	2–3 yrs	2–5, 10–14 yrs	Any age <17 yrs
Joint symptoms	Insidious swelling and decreased range of motion	Symmetric joint involvement, spine involvement, hand deformities, dactylitis	Acute significant pain, p follow fevers, neck stiff occasional jaw involvem
Extraosseous symptoms	30% cases have **uveitis** or iridocyclitis	Growth retardation, fever, rare iridocyclitis	**Spiking fevers**, **macu** hepatosplenomegaly, **ly** pericarditis, growth reta
Labs	Weakly positive ANA	Mildly increased ESR, mildly decreased Hgb, weakly positive ANA in younger ages, positive RF in older ages	Increased WBC, anemia negative ANA, rarely po
Treatment	NSAIDs; methotrexate for chronic cases	NSAIDs, methotrexate, sulfasalazine, or etanercept	NSAIDs, methotrexate, cytotoxic drugs
Prognosis	Most cases resolve in <6 mo; uncommon chronic arthritis	60% patients enter remission within 15 yrs; higher rate of severe chronic arthritis than pauciarticular; worse prognosis with older onset	Highly variable course; achieve eventual remiss minority have chronic di
Complications	Blindness from iridocyclitis, leg length discrepancy, rare chronic disease with progressive arthritis	Chronic arthritis, leg length discrepancy	Leg length discrepancy, arthritis, amyloidosis

ANA, antinuclear antibody; ESR, erythrocyte sedimentation rate; Hgb, hemoglobin; NSAIDs, nonsteroidal anti-inflammatory drugs; RF, rheumatoid f blood cell.

M. Transient Synovitis of the Hip

1. **Benign inflammation** of the joint that causes pain and limping; usually in children between 3 and 8 years of age
2. Preceded by URI or viral illness

3. **H/P** = **well appearing,** atraumatic, no (or low grade) fever, recent preceding illness, **limping but able to bare weight,** hip slightly flexed and externally rotated, affects just one side
4. **Labs** = normal (or minimally elevated) WBC, sed rate, and CRP
5. **Radiology** = US may show mild uni- or bilateral joint effusions
6. **Treatment** = conservative, pain management with NSAIDs, and return to activity as tolerated
7. **Complications** = excellent prognosis with full recovery within 1 week

N. Septic Hip

1. Bacterial infection of the joint space and synovial fluid of the hip; due to direct inoculation or **hematogenous spread**
2. Usually seen in children between 3 and 6 years of age
3. ***Staphylococcus aureus*** is the most common organism in all ages
4. **H/P** = **ill appearing, fever, nonweight bearing,** hip slightly flexed and externally rotated
5. **Labs** = elevated WBC and inflammatory markers (ESR and CRP**), synovial fluid >50,000/mm^3**
6. **Radiology** = joint effusion seen on ultrasound
7. **Treatment** = emergent orthopedic consult, joint aspiration, antibiotics
8. **Complications** = AVN of the femoral head, hip instability, osteoarthritis, sepsis

IX. Development and Health Supervision

A. Physical Growth

1. Characteristics of growth (i.e., weight, height, and head circumference) fall in a normal range; deviations from this range suggest abnormal growth, disease processes, or environmental concerns
2. Pediatrician should keep a record of growth on a chart
3. **Weight**
   a. Initial loss of weight (~10% of birth weight) in first few days after birth is normal; birth weight is regained by 2 weeks of age.
   b. Birth **weight doubles** by ~**6 months, triples** at ~**12 months,** and **quadruples** at ~**24 months**.
   c. From age 2 years to adolescence (age 13 years), annual weight gain is ~5 lb.
   d. Inadequate weight gain can result from **poor food intake** (including poor feeding and abuse), chronic vomiting or diarrhea, **malabsorption,** neoplasm, or **congenital diseases** (e.g., cardiac, endocrine).
   e. Weight <5th percentile on growth charts or a consistently low weight for a given height suggests **failure to thrive**.
   f. **Psychosocial** or **economic** factors are the most common cause of failure to thrive; however, always consider **organic** causes.
   g. The prevalence of **childhood obesity** (body mass index matched for age and gender >95th percentile) has steadily increased in the United States and is associated with rapid growth, sleep apnea, HTN, **SCFE,** precocious puberty, increased incidence of skin infections, social dysfunction, and earlier development of DM.
4. **Height**

NEXT
STEP

Be sure to collect a thorough **family history** while assessing growth or developmental delays to help distinguish a **hereditary** cause from an **environmental** one.

Quick **HIT**

Weight is the most sensitive and earliest finding in failure to thrive as it is usually affected prior to height, which in turn is affected prior to head circumference.

   a. **Height** (or birth length) is increased by 50% at ~1 year of age, **doubles** at ~**4 years of age,** and **triples** at ~**13 years of age**.
   b. Annual height gain from age 2 years to adolescence is ~2 in/yr.
   c. Greater-than-normal height can be associated with familial tall stature, precocious puberty, gigantism, hyperthyroidism, Klinefelter syndrome, Marfan syndrome, or obesity.
   d. Lower-than-normal height can be associated with familial short stature, neglect, Turner syndrome, constitutional growth delay, chronic renal failure, asthma, CF, inflammatory bowel disease (IBD), immunologic disease, growth hormone deficiency, hypothyroidism, glucocorticoid excess, skeletal dysplasias, or neoplasm.
5. **Head circumference**
   a. Measured during first 1 to 3 years of life.
   b. ~5 cm growth during age 0 to 3 months, ~4 cm in 3 to 6 months, 2 cm in 6 to 9 months, and 1 cm in 9 to 12 months.
   c. Macrocephaly can be associated with cerebral metabolic diseases (e.g., Tay–Sachs, maple syrup urine disease), neurocutaneous syndromes (e.g., neurofibromatosis, tuberous sclerosis), hydrocephalus, increased intracranial pressure, skeletal dysplasia, acromegaly, or intracranial hemorrhage.

d. Microcephaly can be associated with fetal toxin exposure (e.g., **fetal alcohol syndrome**), chromosomal trisomies, congenital infection (**TORCH** infections), cranial anatomic abnormalities, metabolic disorders, or neural tube defects.

6. Trend of growth abnormalities helps suggest certain pathologies
   a. Normal growth rate that declines **after birth** suggests **postnatal** onset.
   b. Growth that is **abnormal from the time of birth** suggests **prenatal** onset (e.g., genetic abnormalities, intrauterine pathology).
   c. Growth that is in low-normal range but eventually becomes closer to the mean suggests **constitutional growth delay**.
   d. Growth that is **consistently** low-normal suggests genetic short stature (i.e., compare with parents).
7. **H/P**
   a. Look for other symptoms and signs that suggest a particular disease.
      (1) Malabsorption: diarrhea
      (2) DM: hyperglycemia
      (3) Congenital heart disease: cyanosis, etc.
      (4) Signs of abuse: bruising, abnormal parent–child interaction
      (5) Psychosocial abnormalities: inattentiveness, apathy
      (6) Growth should be assessed at **each health visit** to confirm normal patterns and catch abnormalities early.
8. **Labs** = should be directed at diagnosis of a specific disease when clinical suspicion exists (e.g., for DM, blood glucose; for congenital heart disease, arterial blood gas, etc.)
9. **Treatment** = **t**reat underlying disorder

Quick HIT

It is **legally imperative** that **all suspected** cases of child abuse are **well documented** and **reported** to the appropriate authorities.

Quick HIT

Ages for developmental milestones are **guidelines.** It is normal for milestones to occur at an appropriate **range of ages**, and parents should be reassured that milestones occur within such a range and not at concrete ages.

B. Developmental Milestones

1. **Social, physical**, and **intellectual** achievements are reached by children at characteristic ages (see Table 10-4).
2. Absence or delay of milestones can suggest developmental delays.
3. Some delays are hereditary, but multiple or significant delays are a cause for concern.
4. Multiple or persistent delays can result from intellectual disability, genetic disorders (e.g., fragile X syndrome, trisomy 21), language or hearing disorders, child abuse, or psychiatric conditions (e.g., attention deficit hyperactivity disorder [ADHD], autism).
5. Certain reflexes are prevalent during infancy but naturally disappear by **6 months** of age; absence or persistence of infantile reflexes beyond 6 months (especially with a history of perinatal complications or suspected congenital malformation) may suggest CNS pathology (see Table 10-5).

Table 10-4 Important Developmental Milestones During Childhood

Age	Social/Cognitive	Gross Motor	Fine Motor	Lang
2 mo	Social smile	Lifts head 45 degrees	Eyes follow object to midline	Coos
4 mo	Laughs Aware of caregiver Localizes sound	Lifts head 90 degrees	Eyes follow object past midline	
6 mo	Differentiates parents from others Stranger anxiety	Rolls over Holds self up with hands Sits without support	Grasps/rakes Attempts to feed self	Babbl
9 mo	Interactive games Separation anxiety (9–15 mo)	Crawls Pulls to stand	Grasps with thumb	First v
12 mo	Separation anxiety (9–15 mo)	Walks with help	Pincer grasp Makes tower of two blocks	~5–10
18 mo	Parallel play	Walks well Walks backward	Makes tower of four blocks Uses cup or spoon	10–50 2-wor
2 yrs	Dresses self with help	Runs Climbs stairs (initially 2 feet/step, then 1 foot/step)	Makes tower of six blocks	50–75 3-wor
3 yrs	Magical thinking Gender identity (2–3 yrs)	Climbs/descends stairs	Makes tower of nine blocks Able to draw circle	
4 yrs	Plays with others	Hops on 1 foot	Able to draw line image (+); later able to draw closed line drawing (Δ)	250+ 4-wor
6 yrs	Able to distinguish fantasy from reality	Skips	Draws a person	Fluent

Table 10-5 Childhood Reflexes and Their Relation to CNS Pathology

Reflex	Description	Time of Disappearance (months)	Area of CNS Associate Persistence or Disappe
Moro	Extension of head causes extension and flexion of limbs; startle reflex	3	Medulla, vestibular nuclei
Grasp	Placing finger in palm causes grasping	3	Medulla, vestibular nuclei
Rooting	Rubbing cheek causes turning of mouth to stimuli	3	Medulla, trigeminal nuclei
Tonic neck	When head turned, arm on faced side extends and arm on opposite side flexes (fencing reflex)	3	Medulla, vestibular nuclei
Placing	Rubbing foot dorsum causes foot to step up	2	Cortex

CNS, central nervous system.

C. Childhood Health Maintenance

1. Periodic physician visits are important during childhood to assess **growth**, detect growth and developmental **delays,** provide **vaccinations, screen** for certain disease processes, and provide **anticipatory guidance** (see Table 10-6).

a. Visits 2 weeks after birth and at 1 month of age
b. Visits at 2 months old, then every 2 months (2, 4, 6 months) until 6 months old
c. Visits every 3 months from age 6 to 18 months (6, 9, 12, 15, 18 months)
d. Visits at age 2 years and annually thereafter

2. Screening during visits should address common medical concerns (e.g., vision, hearing, dentition, diseases in high-risk populations).
3. Anticipatory guidance should address **nutrition, development, daily care, accident prevention,** and **behavioral issues**.
4. Vaccinations should be given at appropriate visits (see Table 10-7).
   a. Contraindications for vaccines include severe allergies to prior vaccine dose or vaccine components and live vaccines (varicella, MMR, rotavirus, oral polio) in immunocompromised patients.
   b. Current fever or mild illness is **not** absolute contraindications to vaccine administration.
   c. If newborn is premature, vaccines are administered based on chronologic age, not gestational age.

Quick HIT

Haemophilus influenzae type b (Hib) vaccine is **unnecessary** in previously unvaccinated children **>5 years** because of the low risk of severe infection at this age and older. **Asplenic** children should **always** receive Hib and pneumococcal vaccines regardless of their age.

Quick HIT

History of **SCID** and prior **intussusception** are **contraindications** for vaccination with rotavirus vaccine.

D. Adolescence

1. Period of **rapid physical, psychosocial,** and **sexual growth** and maturity leading into adulthood; encompasses time between 10 and 19 years of age.
2. Puberty typically begins **12 to 24 months earlier in females** (age 9 to 10 years in girls and 9 to 11 years in boys); development of puberty before these ages is considered **precocious** puberty.

NEXT
STEP

Because of adolescents' desire for independence and need for good self-esteem, adolescent patients should be approached in a **nonjudgmental** fashion to perform an accurate history and physical examination.

Table 10-6 Screening Performed and Anticipatory Guidance Discussed During Regular Childhood Health Visits

Visit	Screening	Nutrition	Daily Care	Accident Prevention	Be
Newborn/ 1 wk	Phenylketonuria, hypothyroidism, genetic metabolic disorders (maple syrup urine disease, cystic fibrosis, etc.) in high-risk patients; hearing; visual mobility and reflexes	Breast or bottle feeding	Crying, **sleep position** ("back to bed"), bathing	Smoke detectors, baby furniture, car seats	Par
1 mo	Visual mobility and reflexes	Breast or bottle feeding, fluoride supplements	Sleep, bowel, and bladder habits	Sun exposure	Imp con
2 mo	Visual mobility and reflexes		Sleep, bowel habits	Close supervision, risks with ability to roll over	
4 mo	Visual mobility and reflexes	**Solid foods** (iron-fortified cereal, pureed fruits, and vegetables) introduced at 4–6 mo of age	Teething	Keeping small objects out of reach	Voc
6 mo	Visual mobility and reflexes	Cup training, daily caloric needs, finger foods, avoidance of milk or juice at bedtime	Shoes	Preparation for increased mobility ("childproofing" the house), electrical socket covers, stair and door gates	Stra sep
9 mo	Hgb/Hct; visual mobility and reflexes	Iron supplementation, self-feeding, spoon training	Tooth care, favorite toys	Aspiration risks	Con disc
12 mo	Visual mobility and reflexes; lead exposure; PPD in high-risk areas	Bottle weaning, eating at table, whole cow's milk		Poisoning risks, stair safety, burns	Spe rein

15 mo	Hgb/Hct; visual mobility and reflexes	Family meals			Toil tan list
18 mo	Visual mobility and reflexes	Reinforcement of utensil use	Nightmares, bedtime regimens	Supervised play, dangerous toys	Dis toil
2 yrs	Lead exposure; visual mobility and reflexes	Avoiding unhealthy snacks, encouraging eating during meals	Transition from crib to bed, toothbrush training		Tod exp par oth
3 yrs	Visual acuity; cholesterol (if family history of high cholesterol or CAD) Routine dental checkups begin at 2–3 yrs	Healthy diet	Regular sleep schedule, **TV/ media limitation**	Water safety, animal safety	Day (ear wor chil con con
4 yrs	Hearing; lead exposure; visual acuity; PPD (if high-risk group); urinalysis	Meals as time for family bonding	Self-dental care	Pedestrian and bicycle safety, car seat or seat belt, dangers of strangers, guns, fires, poisons, teach phone number	Cho day sch
6 yrs	Lead exposure; visual acuity	Avoidance of excess weight; obesity prevention counseling	Exercise, hygiene, school activities	Swimming	Allo lea me
10 yrs	Hearing; visual acuity			Hazardous activities, drug use (including alcohol and tobacco)	Frie pub
12 yrs	Hearing; visual acuity; PPD (if high-risk group); Pap smear only if sexually active (girls)		Adequate sleep, school and extracurricular activities	Sexual responsibility	Boo issu
14 yrs and older	Hearing; Hgb/Hct (girls); visual acuity; STD screening (if sexually active)	Weight maintenance	School and activities	Risk-taking behavior, driving, sexual responsibility	Dat car issu

Note: Anticipatory guidance from **prior** visits should be **reviewed**, when appropriate.
CAD, coronary artery disease; Hgb/Hct, hemoglobin and hematocrit; PPD, purified protein derivative of tuberculin (TB test); STD, sexually transmitt

Table 10-7 Vaccination Schedule and Contraindications During Well-Child Health Visits (2018 Recommendations)

Vaccine	Age										
	Birth	1 mo	2 mo	4 mo	6 mo	12 mo	15 mo	18 mo	24 mo	4–6 yr	11–1
HepB[a]	HepB	HepB			HepB						
Rota[b]			Rota	Rota	Rota						
DTaP[c]			DTaP	DTaP	DTaP		DTaP			DTaP	Tdap (≥
Hib[d]			Hib	Hib	Hib	Hib					
PCV[e]			PCV	PCV	PCV	PCV					
IPV[f]			IPV	IPV	IPV					IPV	
Influenza[g]					Annual vaccination (IIV) 1 or 2 doses						Ar
MMR[h]						MMR				MMR	
VZV[i]						VZV				VZV	
HepA[j]						HepA × 2					
MCV4[k]											MC
HPV[l]											HPV

[a]Hepatitis B (HepB); contraindications: allergy to yeast or anaphylaxis following prior dose.
[b]Rotavirus (Rota); contraindications: anaphylaxis following prior dose, severe combined immunodeficiency (SCID), history of intussusception.
[c]Diphtheria, tetanus, acellular pertussis (DTaP); tetanus booster (Td) given in adolescence; contraindications: encephalopathy or anaphylaxis follow
[d]*Haemophilus influenzae* type b (Hib); contraindications: anaphylaxis following prior dose.
[e]Pneumococcal vaccine (PCV); contraindications: anaphylaxis following prior dose.
[f]Inactivated polio vaccine (IPV); contraindications: pregnancy (or pregnant female at home) and anaphylaxis following prior dose.
[g]Influenza vaccine (IIV); contraindications: anaphylaxis following prior dose.
[h]Measles, mumps, rubella (MMR); contraindications: pregnancy (or pregnant female at home), immunocompromise, thrombocytopenia, hematologi anaphylaxis following prior dose.
[i]Varicella-zoster vaccine (VZV); contraindications: allergy to neomycin, anaphylaxis following prior dose, immunosuppression, pregnancy (or pregna moderate or severe illness.
[j]Hepatitis A (HepA); given in two doses at least 6 months apart; contraindications: anaphylaxis following prior dose.
[k]Meningococcal vaccine (MCV4); possible rare association with Guillain-Barré syndrome.
[l]Human papilloma virus vaccine (HPV); given as three doses over 6-month period.

Table 10-8 Tanner Stages for Male Genital and Pubic Hair Development

Tanner Stage	Penile/Testicular Development	Pubic Hair Development
1	Prepubertal; small genitals	Prepubertal; no hair growth
2	Testicular and scrotal enlargement with skin coarsening	Slight growth of fine genital and axillary hair
3	Penile enlargement and further testicular growth	Further growth of hair
4	Further penile glans enlargement and darkening of scrotal skin	Hair becomes coarser and spreads over much of pubic region
5	Adult genitalia	Coarse hair extends from pubic region to medial thighs

3. Physical changes are classified by Tanner stages (see Table 10-8; also refer to Chapter 12).
4. Psychosocial issues
   a. Early adolescence (10 to 13 years) is typified by concrete thinking and early independent behavior.
   b. Middle adolescence (14 to 16 years) is typified by emergence of **sexuality** (e.g., sexual identity, sexual activity), an increased **desire for independence** (e.g., conflict with parents, need for guidance, self-absorption), and abstract thought.
   c. Late adolescence (17 to 21 years) is typified by increased self-awareness, increased confidence in own abilities, a more open relationship with parents, and cognitive maturity.

d. Adolescents are at an increased risk for **risk-taking behaviors** (e.g., drug use, unprotected sexual activity, violence), **depression, suicidal ideation, homicide,** and **eating disorders**.

5. **H/P**

> ***Quick*** **HIT**
>
> **Confidentiality** between a physician and patient must be maintained during adolescence **unless life-threatening** concerns are involved (e.g., suicidal ideation, homicidal ideation, life-threatening disease), and this right may need to be stressed to parents.

a. History during visits should address **risk factors** (e.g., sexually transmitted diseases [STDs], violence, abuse), substance use, mood, physical changes, nutritional habits, menstrual issues (girls), and **concerns of patient**.
b. Examination should focus on sexual maturation, dermatologic issues (e.g., acne, sun exposure, nevi), appropriate height and weight growth, and scrotal masses (i.e., detection of testicular cancer in boys).
c. Additional medical screening should include that for HTN, obesity, DM, and hyperlipidemia.

6. **Treatment**
a. Most teenagers proceed through adolescence without serious incidents even though accidents are the number one cause of death in this age group.
b. Risk-taking behavior can result in STDs and drug addiction that need to be treated appropriately.
c. Emphasis should be placed on maintaining a good physician–patient relationship while addressing risk prevention.

E. Child Abuse

1. Actions or acts of omission that result in harm or potential harm to a child.
2. Suspect child abuse if history does not correlate with findings or child's developmental age.
3. Children at higher risk include newborns as well as children with developmental delay and intellectual disabilities.
4. Can be **physical (nonaccidental trauma), sexual, psychological, neglect.**
5. Physical findings that suggest nonaccidental trauma include:
a. **Retinal hemorrhages**
b. Specific types of fractures (**posterior rib fractures, metaphyseal corner fractures, fractures at various stages of healing**)
c. Bruises in unusual places or patterns (inner thighs, face, neck)
d. Burns with clear demarcations or shaped like specific objects (cigarettes, irons)
e. Subdural hematomas
6. Most common cause of death in pediatric nonaccidental trauma is **head injury**, followed by abdominal injuries.
7. Management includes complete physical evaluation with adequate treatment, proper documentation, and reporting to Child Protective Services.
8. Tests: **skeletal survey** (for old or acute injuries), **head CT/abd/pelvic** if suspected acute injuries**, ophthalmology consult (**to evaluate for retinal hemorrhages).
9. May require hospitalization for complete evaluation or safety reasons.

X. Immune Disorders

A. Congenital immune Deficiencies Are Uncommon and Can Result From Defects in T Cells And/Or B Cells, Phagocytic Cells, or Complement (See Table 10-9)

B. H/P = Frequent and **Recurrent Infections** Beginning After 3 Months of Age, Including Diseases Caused by Opportunistic Pathogens; Wound Healing May be Impaired (Delayed Umbilical Cord Stump Separation, Think **Leukocyte Adhesion Deficiency**)

Table 10-9 Types of Congenital Immunodeficiency Disorders

Disease	Description	Diagnosis	Treatm
T-Cell Disorders			
DiGeorge syndrome	Chromosomal deletion in 22q11.2 resulting in **thymic and parathyroid hypoplasia, congenital heart disease**, tetany, and abnormal facial structure; recurrent viral and fungal infections occur because of insufficient T cells	**Tetany** and **facial abnormalities** on examination; decreased serum calcium; evidence of congenital heart disease; chest radiograph may show absence of thymic shadow; genetic screening can detect chromosomal abnormality	Calciun thymic marrow surgica abnorm prophyl be help
Chronic mucocutaneous candidiasis	Persistent infection of skin, mucous membranes, and nails by *Candida albicans* from T-cell deficiency; frequent associated adrenal pathology	Poor reaction to cutaneous *C. albicans* anergy test; possible decreased IgG	Antifun fluconа
B-Cell Disorders			
X-linked agammaglobulinemia	Abnormal B-cell differentiation resulting in low B cell and antibody levels; X-linked disorder with **boys** experiencing recurrent bacterial infections after 6 mo of age	**No B cells in peripheral smear**; low total immunoglobulin levels	IVIG, ap ics, sup care
IgA deficiency	Specific IgA deficiency because of abnormal immune globulin production by B cells; patients have increased incidence of respiratory and gastrointestinal infections	**Decreased IgA** with **normal** levels of **other immune globulins**	Prophyl IVIG wi of anap
Hyper IgM disease	Defect in T-cell CD40 ligand resulting in poor interaction with B cells, low IgG, and excessive IgM; infection by **encapsulated bacteria** (pulmonary and gastrointestinal)	Decreased IgG and IgA, **increased IgM**; possible decreased Hgb, Hct, platelets, and neutrophils	IVIG, pr ics; bor
Common variable immunodeficiency	Autosomal disorder of B-cell differentiation resulting in low immune globulin levels; patients experience increased respiratory and gastrointestinal infections beginning in second decade of life; associated with increased risk of **malignant neoplasms** and **autoimmune disorders**	Low immune globulin levels; poor response to vaccines; decreased CD4:CD8 T-cell ratio; family history shows **both men and women affected**	IVIG, ap

Combined B- and T-Cell Disorders			
Severe combined immunodeficiency syndrome (SCID)	Absent T cells and abnormal antibody function resulting in **severe immune compromise**; patients experience significant recurrent infections by all types of pathogens from an early age; **frequently fatal at an early age**	Significantly decreased WBCs, decreased immune globulins	IVIG, ar **row tra or atte** should
Wiskott–Aldrich syndrome	X-linked disorder of immune development resulting in significant susceptibility to **encapsulated** bacteria and opportunistic pathogens; associated with **eczema** and **thrombocytopenia**	Recurrent infections in presence of **eczema** and **easy bleeding**; decreased platelets, decreased IgM with normal or high other immune globulins; genetic analysis detects abnormal WASP gene	**Splene** prophyl marrow
Ataxia–telangiectasia	Autosomal recessive disorder causing **cerebellar dysfunction, cutaneous telangiectasias**, increased risk of cancer, and impaired WBC and IgA development	**Telangiectasias** and **ataxia** develop after 3 yrs of age; recurrent pulmonary infections begin a few years later; decreased WBCs, decreased IgA	IVIG an biotics treatme limit di
Phagocytic Cell Disorders			
Chronic granulomatous disease	Defect in which neutrophils **cannot digest** engulfed bacteria, resulting in recurrent bacterial and fungal infections	Cutaneous, pulmonary, and perirectal abscess formation; chronic lymphadenopathy; genetic analysis detects causative genetic mutations	Prophyl γ-interf bone m
Hyper-IgE disease (Job syndrome)	Defect in neutrophil chemotaxis, T-cell signaling, and overproduction of IgE resulting in **chronic dermatitis, recurrent skin abscesses**, and pulmonary infections; patients commonly have coarse facial features and retained primary teeth	Increased IgE, increased eosinophils; defective chemotactic response of neutrophils on stimulation	Prophyl hydrati
Chediak–Higashi syndrome	Autosomal recessive **dysfunction of neutrophils** resulting in recurrent *Staphylococcus aureus*, streptococcal, gram-negative bacteria, and fungal infections; associated with **abnormal platelets, albinism**, and **neurologic dysfunction**	Large granules seen in granulocytes on peripheral smear	Prophyl bone m
Leukocyte adhesion deficiency (types 1 and 2)	Inability of neutrophils to leave circulation because of abnormal leukocyte integrins (type 1) or E-selectin (type 2); recurrent bacterial infections of upper respiratory tract and skin, delayed separation of umbilical cord; short stature, abnormal facies, and cognitive impairment seen in type 2 disease	Increased serum neutrophils; defective chemotactic response of neutrophils upon stimulation	Prophyl bone m needed type 2 fucose
Complement Disorders			
Complement deficiencies	Multiple inherited deficiencies of one or more complement components, resulting in recurrent bacterial infections and **predisposition to autoimmune disorders (e.g., SLE)**	Hemolytic complement test results are abnormal and indicate problem in pathway; direct testing of components can detect exact deficiency	Approp treat au as need

Hct, hematocrit; Hgb, hemoglobin; IVIG, intravenous immune globulin; SLE, systemic lupus erythematosus; WBC, white blood cell.

C. **Labs** = CBC detects general WBC abnormalities; determination of specific WBCs affected (T cells, B cells, neutrophils, etc.) and peripheral blood smear can help determine precise cell-type abnormality

D. **Treatment** = antibiotics (both prophylactic and therapeutic) are required to treat infections; severe immune deficiencies may require immunotherapies or bone marrow transplant

E. **Complications** = recurrent infections, poor wound healing; death frequently occurs **before third decade of life** (younger for more severe deficiencies) because of body's inability to combat pathogens

Quick HIT

Presentation of immune disorders does not occur immediately after birth because newborns retain **maternally derived antibodies** for ~3 months.

Quick HIT

Most pregnancies with a 45XO karyotype end in spontaneous abortion.

XI. Genetic Disorders (Chromosomal Pathology)

A. Sex Chromosome Disorders

1. Diseases caused by an abnormal number of sex chromosomes in the genetic karyotype (see Table 10-10)
2. In females, sex chromosome abnormalities are usually less severe than autosomal disorders because **X chromosome inactivation** attempts to restore the normal number of active chromosomes and because Y chromosomes contain relatively **few** genes
3. **Labs** = karyotyping will reveal an abnormal number of sex chromosomes
4. **Treatment**
   a. Turner syndrome requires regular cardiovascular assessments and estrogen and progestin replacement.
   b. Special education or behavior counseling may be needed for mental impairments.

Quick HIT

It was previously believed that males with an XYY genotype were at a higher risk for violent and antisocial behavior, but this trend has been disproved. They have the same rate of criminal activity as 46XY individuals with similar intelligence levels.

Quick HIT

Previously known as mental retardation, **intellectual disability** is now the preferred term due to known social stigma. The term *mental retardation* may still be seen in older literature or public policies.

Table 10-10 Common Sex Chromosome Disorders

Condition	Karyotype	History and Physical
Turner syndrome	45XO or mosaicism	Female with **short stature, infertility**, abnormal genital formation, increased incidence of renal and cardiac defects (**coarctation of aorta**), craniofacial abnormalities (protruding ears, **neck webbing**, low occipital hairline)
Klinefelter syndrome	47XXY	Male with **testicular atrophy**, tall and thin body, gynecomastia, infertility, mild intellectual disability, and psychosocial adjustment abnormalities
XYY	47XYY	Male with tall body (>6 ft), significant acne, mild intellectual disability
XXX	47XXX	Female with increased incidence of intellectual disability, menstrual abnormalities

B. Trisomies

1. Syndromes that occur because of **autosomal nondisjunction** or **genetic translocation** during sex cell production that result in extra copies of autosomal genetic material (see Table 10-11)

Quick HIT

Down syndrome is the most common cause of **congenital** intellectual disability when both genders are considered.

2. **Labs**

Quick HIT

Nearly all trisomies result from nondisjunction during meiosis of **maternal** germ cells.

a. Karyotyping can detect extra chromosomes, and genetic screening can detect translocations.
b. Prenatal quadruple screen can help detect potentially affected fetuses, and amniocentesis may be used to confirm the diagnosis.

3. **Treatment**

Quick HIT

The risk of trisomy increases exponentially in women after 35 years of age.

a. Appropriate care for associated medical conditions
b. Special education or selective environment used to handle intellectual disability
c. Surgical correction of anatomic defects, when appropriate
d. Genetic counseling and prenatal preparation recommended for parents
e. Degree of mental impairment determines ability to function in society or need for constant care

Table 10-11 Autosomal Trisomies

Condition	Incidence	History and Physical
Trisomy 21 (Down syndrome)	~1/700 births (**increases with maternal age**)	**Mental retardation**, craniofacial abnormalities (protruding tongue, flat nose, small ears), vision and hearing loss, broad hands with simian crease, cervical spine instability, increased space between first and second toes; increased risk of **duodenal atresia** and other GI abnormalities, **Alzheimer disease**, ALL, and **cardiac defects**; usually survive into fourth decade of life or longer
Trisomy 18	1/6,000 births (**increases with maternal age**)	Severe mental retardation, small mouth, limb abnormalities (malposition, **rocker-bottom feet**, overlapping fingers on grasp), cardiac defects, GI abnormalities; frequently fatal within first year
Trisomy 13	1/5,000 births (**increases with maternal age**)	Cleft lip and palate, cardiac defects, CNS defects, severe mental retardation, rounded nose, **polydactyly**; frequently fatal within first year

ALL, acute lymphoblastic leukemia; CNS, central nervous system; GI, gastrointestinal.

C. Deletion Syndromes

1. Diseases that result from deletion of all or part of an **autosomal** chromosome (see Table 10-12)
2. Usually severe disorders because of importance of missing genetic material
3. **Labs** = high-resolution chromosome banding and fluorescence in situ hybridization techniques are useful for detecting small defects; karyotyping may detect substantial defects
4. **Treatment** = supportive care; genetic counseling recommended for parents
5. **Complications** = early mortality can result from associated abnormalities or diseases and not from deletions directly

Quick HIT

Fragile X syndrome is the most common cause of familial intellectual disability in **men.**

Table 10-12 Common Deletion Syndromes

Syndrome	Deletion	History and Physical
Cri-du-chat	Entire 5p chromosome arm	**High-pitched, cat-like cry**, small head, low birth weight, intellectual disability; early mortality can result from failure to thrive
Wolf–Hirschhorn	4p16 to end of arm	Intellectual disability, multiple **cranial abnormalities**, seizures
Prader–Willi	15q11–15q13 (deletion of **paternal** allele)	**Overeating, obesity**, decreased muscular tone in infancy, intellectual disability, small hands and feet; obesity-related complications can decrease lifespan
Angelman	15q11–15q13 (deletion of **maternal** allele)	**Puppet-like movement, happy mood, unprovoked laughter**, intellectual disability, ataxia, seizures
Velocardiofacial	22q11	**Cleft palate**, cardiac defects, mild intellectual disability, significant overbite, **speech disorders**, T-cell deficiency, hypocalcemia, association with DiGeorge syndrome; early mortality can result from associated cardiac complications or DiGeorge syndrome
Williams	7q11.23	**"Elfin facies"** (short, upturned nose; long philtrum, wide mouth), short stature, **intellectual disability**, cheerful/friendly personality, **cardiac defects** (supravalvular stenosis)

D. Fragile X Syndrome

1. X-linked chromosomal disorder associated with intellectual disability in males; females may be carriers and rarely show any effects of the abnormal gene
2. End of X chromosome appears fragile and does not condense normally because of a high number of terminal CGG codon repeats
3. **H/P** = large face with **prominent jaw** and **large ears**; mild hand and foot abnormalities, large testicles (i.e., macroorchidism); **intellectual disability**, hyperactivity, possible seizures
4. **Labs** = genetic screening detects hundreds of CGG repeats at end of X chromosome (number of repeats increases with each generation when inherited from a woman but not from a man); prenatal DNA analysis can be performed in mothers with a positive family history
5. **Treatment** = appropriate genetic counseling for parents; special education and monitoring will likely be needed by affected males

MNEMONIC

Remember the differences between Prader–Willi syndrome and Angelman syndrome by the mnemonics **POP** and **MAMA:**

- **P**rader–Willi
- **O**vereating
- **P**aternal

and

- **M**aternal
- **A**ngelman
- **M**ood (happy)
- **A**nimated movements

XII. Pediatric Infectious Disorders

A. Neonatal Conjunctivitis

1. Conjunctivitis during the first month of life
2. Incidence is low because of standard prophylaxis provided at birth (erythromycin ointment)
3. Etiology and initial management are based on history (prenatal and birth) and time of onset
   a. **Chemical** conjunctivitis: 0 to 1st day of life, mild discharge, erythema
   b. **Gonococcal (GC)** conjunctivitis: 2nd to 7th day of life, copious, purulent discharge
   c. **Chlamydial** conjunctivitis: 5th to 14th days of life, usually watery discharge but can be purulent. Risk of concomitant chlamydial pneumonia
4. **Labs** = if the child is ill appearing or GC conjunctivitis is suspected, requires full septic workup (CBC, blood culture, CSF culture, etc.), ocular discharge culture; if chlamydial infection suspected and child well appearing, start with ocular Gram stain and culture
5. **Treatment** = eye irrigation; GC conjunctivitis requires admission and IV antibiotics; chlamydial conjunctivitis can be treated with oral macrolides

B. Acute Otitis Media

1. Infection of the middle ear; common in children less than 6 years of age; incidence decreases with age
2. Most common reason for children to receive antibiotics
3. **H/P** = acute onset of ear pain, fever, **bulging TM, poor mobility** with pneumatic otoscopy, TM erythema, **middle ear effusion**
4. **Labs** = not required; clinical diagnosis
5. **Treatment** = analgesics, **high-dose amoxicillin** is first line, if failure with first line or history of multiple ear infections, high-dose amoxicillin-clavulanate
6. **Complications** = hearing loss, TM perforation, mastoiditis, temporal abscess

C. Scarlet Fever

1. Fever and rash associated with some streptococcal pharyngitis infection
2. Skin eruption is a delayed-type skin reaction due to prior exposure to **group A Strep (*Streptococcus pyogenes*)** exotoxin
3. **H/P** = **fever,** diffuse papular, erythematous rash, described as "**sandpaper**" like, **strawberry tongue,** desquamation of palms and soles
4. **Labs** = rapid strep test, throat culture
5. **Treatment** = treat as streptococcal pharyngitis, antibiotics (penicillin or amoxicillin)
6. **Complications** = rheumatic heart disease, poststreptococcal glomerulonephritis

D. Roseola Infantum

1. Also known as exanthema subitum
2. Caused by human herpes virus-6 **(HHV-6)**
3. **H/P** = preceded by 3 to 5 days of high fever and then the rash starts as fever resolves; erythematous macules and papules, distributed in the face, neck, trunk, and proximal extremities; associated with **febrile seizures** during febrile phase
4. **Treatment** = supportive care

E. Rubeola (Measles)

1. Caused by measles virus; tends to affect preschool children and nonimmunized adults
2. Recent outbreaks due to increase in number of nonimmunized children
3. **H/P** = **fever**, **cough**, **coryza, conjunctivitis, Koplik** spots (clustered white to bluish-white lesions on the buccal mucosa, usually opposite to the second molar), erythematous rash that starts at the hairline and chest and extremities
4. **Labs** = PCR testing
5. **Treatment** = supportive care, **vitamin A,** isolation precautions, notify health department
6. **Complications** = pneumonia, encephalitis acute otitis media

F. Rubella (German Measles)

1. Also known as the “three-day measles”
2. **H/P** = starts with mild URI, fever, and then maculopapular rash that begins in the face and spreads to the trunk; associated with **posterior, cervical, and occipital adenopathy**, **Forchheimer spots** (small red spots on the soft palate)
3. **Labs** = PCR testing
4. **Treatment** = supportive care

G. Erythema Infectiosum (Fifth Disease)

1. Caused by ***Parvovirus B19***
2. **H/P** = fever, malaise, sore throat, and then an erythematous rash on the face, more marked on the cheeks (hence the name **slapped cheek fever**)
3. **Treatment** = supportive care
4. **Complications** = **fetal hydrops** (when exposed in utero), **aplastic anemia** (especially in sickle cell disease patients)

H. Urinary Tract Infection

1. Should always be considered in children less than 2 years of age with fever and any other child with urinary symptoms
2. Second most common bacterial infection in children, after otitis media
3. ***Escherichia coli*** is the most common organism
4. **Risk factors** = age <12 months, temperature ≥39°C, fever >2 days, non-black race, **female**, **uncircumcised male**
5. **H/P** = hematuria, vomiting, high fever, irritability
6. **Labs** = urinalysis and urine culture
7. **Treatment** = antibiotics, cephalosporins are first line
8. **Complications** = pyelonephritis, renal scarring, urosepsis

XIII. Pediatric Psychiatric Disorders

A. Autism Spectrum Disorder

1. Severe, persistent impairment in **social communication and interpersonal interactions** as well as restricted, **repetitive patterns of behavior and interests;** generally, presents in early childhood
2. **H/P**
   a. Impaired social interactions: impaired use of nonverbal behaviors, failure to develop peer relationships, failure to seek social interaction, lack of social reciprocity
   b. Impaired communication: developmental language delays, poor initiation or sustenance of conversation, repetitive language, poor eye contact, lack of imaginative or imitative play for age
   c. Restricted behavior: inflexible routines, preoccupation with a restricted pattern of interest, repetitive motor mannerisms, preoccupation with parts of objects
3. **Treatment**
   a. Behavior, speech, and social psychotherapy with peers and family may help improve social interaction.
   b. Aggressive, irritable behavior can be treated with atypical antipsychotics

Quick HIT

Most children with ADHD continue to the diagnostic criteria for ADHD in adulthood.

B. Attention Deficit Hyperactivity Disorder

1. Disorder of **inattention** and **hyperactivity** in school-aged children that causes problems in multiple settings (e.g., both at home and at school)
2. **Risk factors** = two to four times more common in males than females
3. **H/P**
   a. **Inattention: decreased attention span, difficulty following instructions,** carelessness in tasks, easily losing items, forgetfulness, poor listening, easy distractibility, difficulty organizing activity, avoidance of tasks requiring prolonged focus
   b. **Hyperactivity and impulsivity:** fidgetiness, inability to remain seated at times when prolonged sitting is required, constantly "on the go," excessive talking, difficulty waiting turn to speak, interrupts others, answers questions before they are completed
   c. Diagnosis requires child to have **six** inattention symptoms **or six** hyperactivity or impulsivity symptoms that **limit ability to function** in social, educational, or organized settings. Several symptoms must have been evident before 12 years of age
4. **Treatment**
   a. Behavioral therapy is often recommended first line and may be combined with pharmacotherapy.
   b. Atomoxetine or stimulants (e.g., methylphenidate, dexmethylphenidate, amphetamine, dextroamphetamine) improve ability to focus and control behavior.
   c. α_2-Adrenergic agonists and TCAs may be used in refractory cases.

C. Tourette Syndrome

1. Chronic tic disorder beginning in childhood; associated with ADHD and OCD
2. **H/P** = **multiple motor** (e.g., blinking, twitching, etc.) and **vocal** (e.g., sounds, words) tics that occur every day and worsen with stress; location, frequency, and severity of tics change over time; diagnosis requires presence of tics for >1 year and beginning before patient is 18 years of age
3. **Treatment** = behavioral therapy may reduce tics; low-dose fluphenazine, pimozide, or tetrabenazine may reduce tic occurrence; SSRIs and α_2-agonists are useful in treating comorbid behavioral disorders

Quick HIT

Coprolalia (vocal **tics** of repeated obscenities) is seen only in a **minority (40%)** of cases of Tourette syndrome.

D. Conduct Disorder

1. Repetitive disruptive and antisocial behavior that violates others' rights and social norms
   a. May have onset during either childhood or adolescence.
   b. Individuals over 18 years of age are more likely to meet criteria for antisocial personality disorder.
2. **H/P** = **aggressive behavior** toward people or animals, **destruction of property, deceitfulness** or theft, **violation of serious rules**
3. **Treatment** = psychotherapy involving family and parent management training; psychostimulants are helpful when comorbid ADHD is diagnosed; mood stabilizers may be used in severe cases

Quick HIT

Oppositional defiant disorder is similar to conduct disorder in that patients exhibit aggressive, argumentative, or vindictive behavior, but illegal and destructive behavior do not occur.

QUESTIONS

1. A 10-month-old boy is brought to your clinic for a schedule routine visit. He was born at 36 wGA, by vaginal delivery without complications. Based on prior visits, he has had a normal development. His vaccine status is up-to-date. On examination, you notice the child is playing with toys, calm, however starts to cry when mother leaves the room. He starts to crawl to get back to his mother. When you give him a stick, he can grab it and transfer it from one hand to another. He responds to his name and babbles; however, mother states he has not said his first word. How would you describe the child's current development?

	Social/Cognitive	Gross Motor	Fine Motor	Language
A.	Delayed	Normal	Normal	Normal
B.	Normal	Delayed	Normal	Normal
C.	Normal	Normal	Delayed	Normal
D.	Normal	Normal	Normal	Normal

2. A 6-month-old baby girl is brought in to the office for routine vaccination. Child was born premature and required hospitalization at 4 months of age after she was found with intussusception. Mother denies any reactions to prior vaccines. Vital signs are T: 38.1, RR: 26, Pulse: 140, Saturation: 100% at RA. She has a mild runny nose but otherwise normal examination. Mother states she had a mild fever 1 day ago but has otherwise been feeding normally and acting appropriately. Which vaccines should be administered in this child?

   A. DTaP, Hib, PCV, rotavirus
   B. DTaP, Hib, PCV
   C. DTaP, Hib
   D. DTaP, Hib, varicella
   E. DtaP, Hib, PCV, varicella
   F. None

3. A 2-year-old female is brought in to the ED after an episode of suspected seizure. Parents describe the episode as generalized shaking for about 5 minutes. After the shaking stopped, she was "sleepy" and then started crying. Parents have noticed foul-smelling urine during the last 2 days. Mother has a history of febrile seizures. Vaccines are up-to-date. Now the child is smiling, playful, and alert. Her vital signs are as follows: heart rate 140/min, blood pressure 80/54 mm Hg, respiratory rate is 24/min, saturation 98%, temperature 39.3°C. Pupils are reactive bilaterally, tympanic membranes are normal, throat is normal, no nuchal rigidity or meningeal signs, capillary refill is less than 2 seconds. What tests should you order in this patient?

   A. CBC
   B. Lumbar puncture
   C. Urinalysis
   D. No further testing

4. A 2-month-old male is brought to the ED due to episodes of turning blue. Mother states he has been having coughing episodes and then his face and lips turn blue. She denies any fever, irritability, lethargy, decrease in feeding, or decrease in number of wet diapers. Child was born at term, vaginal delivery with no complications. Physical examination is normal except for a mild cough. Which infection is most likely to be associated with this presentation?

   A. Pertussis
   B. Infantile botulism
   C. GBS
   D. Neonatal herpes

5. A 4-year-old girl is brought to the ED due to limping. Mother states that since this morning she is refusing to walk normally. One week ago, she had some cough and congestion that resolved on its own. She denies any trauma, fever, nausea, vomiting, or other symptoms. Vital signs are T: 37.8, RR: 18, pulse: 98, saturation: 100% at RA. On examination, the child is well appearing, limping but able to put weight on both extremities, with no swelling, redness, or significant tenderness over hip, knees, or legs. WBC: 8,000, sed rate: 5 mm/hr, CRP: 0.01 mg/dL. What is the most likely management of this patient?

   A. Hip joint needle aspiration
   B. Ibuprofen and reassessment
   C. Emergent orthopedic consult
   D. Leg splint

6. A 7-month-old baby boy is brought by his mother to the pediatrician's office for a routine checkup. Mother denies any recent illness or changes in baby's behavior. On examination he has a normal growth curve, normal milestones development. On physical examination you find a pansystolic murmur at lower left sternal border with a loud S_2. What is the most likely diagnosis?

   A. Atrial septal defect
   B. Pulmonic stenosis
   C. Ventral septal defect (VSD)
   D. Patent ductus arteriosus

7. A 4-year-old female is brought for evaluation due to abdominal pain. Pain started this morning and is described as intermittent episodes with associated nonbilious vomiting. She denies any fever, diarrhea, dysuria, sore throat, or other symptoms. On examination, ears, nose, and throat are normal, as well as lungs. Abdominal examination is normal except for periumbilical tenderness without rebound or guarding. While examining the lower extremities you notice multiple small red/bluish spots that are nonblanching that extend up to lower buttocks. What is a likely cause of the patient's abdominal pain?

   A. Streptococcal pharyngitis
   B. Intussusception
   C. Appendicitis
   D. Pneumonia

11
Neurologic Disorders

I. Normal Neurologic and Neurovascular Function

A. Cerebral Vasculature

1. The circle of Willis is a system of collateral vessels that supplies all regions of the brain (see Figure 11-1).
2. Symptoms seen with a stroke can be used to determine the site of insult based on association with a particular region of the brain (see Table 11-1).

Quick HIT

The anterior communicating artery is the most common site of intracranial aneurysm formation.

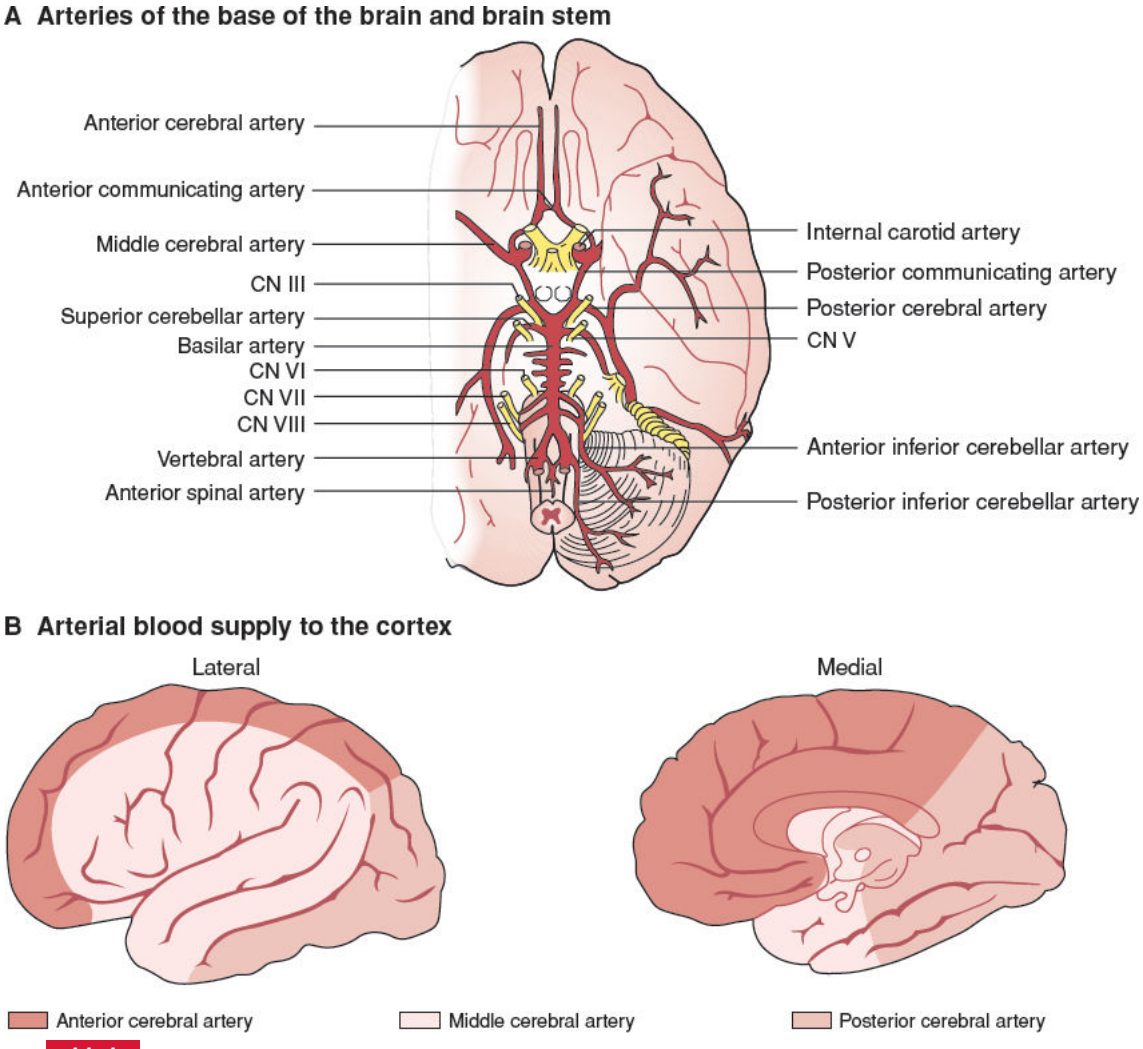


FIGURE 11-1

Arteries of the brain including the circle of Willis and their anatomic relationship to selected cranial nerves.
CN, cranial nerve.
(From Mehta, S., Milder, E. A., Mirachi, A. J., & Milder, E. [2006]. *Step-Up: A high-yield, systems-based review for the USMLE step 1* [3rd ed., p. 32]. Philadelphia, PA: Lippincott Williams & Wilkins.)

Table 11-1 Regions of the Brain Supplied by Vessels in the Circle of Willis

Artery	Region of Brain Supplied
Anterior cerebral artery (ACA)	Medial and superior surfaces and frontal lobes
Middle cerebral artery (MCA)	Lateral surfaces and temporal lobes
Posterior cerebral artery (PCA)	Inferior surfaces and occipital lobes
Basilar artery	Midbrain, brainstem (pons)
Anterior inferior cerebellar artery (AICA)	Brainstem (pons) and parts of cerebellum
Posterior inferior cerebellar artery (PICA)	Brainstem (medulla) and parts of cerebellum

B. Neurologic Organization

1. Sensory and motor neurons are organized into distinct tracts in the spinal cord (see Figure 11-2; Table 11-2).
2. Lesions of the spinal cord cause symptoms that are dependent on the lesion location (see Table 11-3).
3. Cranial nerves (CNs) have distinct functions within the head and neck (see Table 11-4).

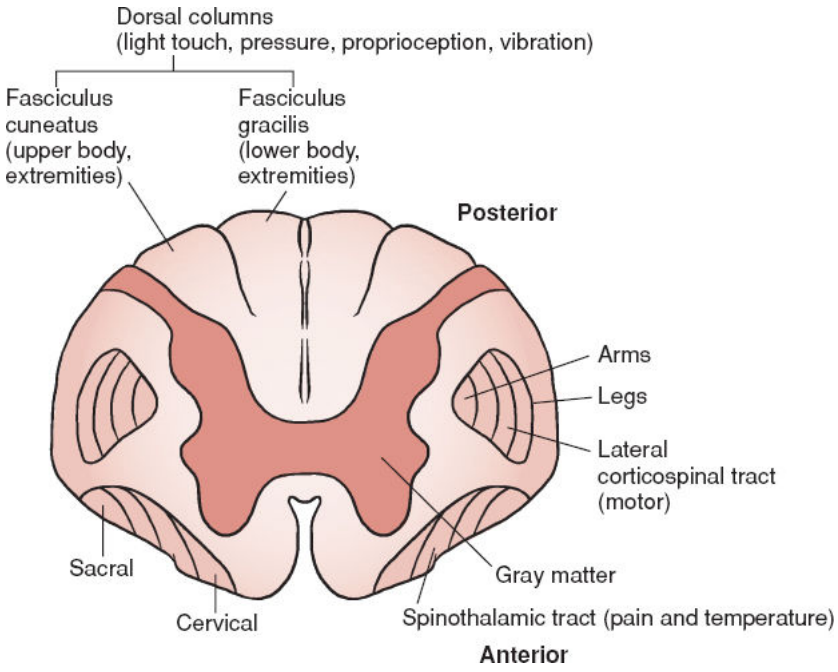


FIGURE 11-2
Primary neuronal pathways of the spinal cord in a thoracic cross-section.

Table 11-2 Primary Sensory and Motor Tracts of the Spinal Cord

Pathway	Location	First-Order Neurons	Second-Order Neurons	Func
Dorsal columns	Posterior spinal cord	Enter at ipsilateral dorsal horn, ascend in fasciculus gracilis and cuneatus, synapse in nucleus gracilis and cuneatus	Decussate at medulla, ascend as medial lemniscus	**Two-natio** sense
Spinothalamic tract	Anterior spinal cord	Originate in dorsal root ganglion, synapse in dorsolateral tract of Lissauer	Decussate in ventral white commissure, ascend in lateral spinothalamic tract	**Sens temp**
Corticospinal tract	Lateral spinal cord	Descend from internal capsule and midbrain, decussate in medullary pyramids, descend in corticospinal tract, synapse in ventral horn through interneurons	Exit cord through ventral horn	**Volu** striat

Table 11-3 Common Lesions of the Spinal Cord

Condition	Tracts Affected	Symptoms
Amyotrophic lateral sclerosis (ALS)	Corticospinal tract, ventral horn	Spastic and flaccid paralysis
Poliomyelitis	Ventral horn	Flaccid paralysis
Tabes dorsalis (**tertiary syphilis**)	Dorsal columns	Impaired proprioception, pain
Spinal artery syndrome	Corticospinal tract, spinothalamic tract, ventral horn, lateral gray matter (**dorsal columns spared**)	Bilateral loss of pain and temperature (one level below lesion), bilateral spastic paresis (below lesion), bilateral flaccid paralysis (level of lesion)
Vitamin B_{12} deficiency	Dorsal columns, corticospinal tract	Bilateral loss of vibration and discrimination and bilateral spastic paresis affecting legs before arms
Syringomyelia	Ventral horn, ventral white commissure	Bilateral loss of pain and temperature (one level below lesion), bilateral flaccid paralysis (level of lesion)
Brown-Séquard syndrome	**All** tracts on one side of cord	Ipsilateral loss of vibration and discrimination (below lesion), ipsilateral spastic paresis (below lesion), ipsilateral flaccid paralysis (level of lesion), contralateral loss of pain and temperature (below lesion)

Table 11-4 Cranial Nerves and Their Functions

Nerve	Type	Function/Innervation
Olfactory (CN I)	Sensory	Smell
Optic (CN II)	Sensory	Sight
Oculomotor (CN III)	Motor	Medial, superior, inferior rectus muscles; inferior oblique muscle, ciliary muscle, sphincter muscle of eye
Trochlear (CN IV)	Motor	Superior oblique muscle of eye
Trigeminal (CN V)	Both	Sensation of face; muscles of mastication
Abducens (CN VI)	Motor	Lateral rectus muscle of eye
Facial (CN VII)	Both	Taste (anterior two-thirds of tongue); muscles of facial expression, stapedius muscle, stylohyoid muscle, digastric muscle (posterior belly); lacrimal, submandibular, sublingual glands
Vestibulocochlear (CN VIII)	Sensory	Hearing, balance
Glossopharyngeal (CN IX)	Both	Taste (posterior one-third of tongue), pharyngeal sensation; stylopharyngeus muscle; parotid gland
Vagus (CN X)	Both	Sensation of trachea, esophagus, viscera; laryngeal, pharyngeal muscles; visceral autonomics
Accessory (CN XI)	Motor	Sternocleidomastoid and trapezius muscles
Hypoglossal (CN XII)	Motor	Tongue

CN, cranial nerve.

II. Neurologic Infection

A. Bacterial Meningitis

1. Infection of meningeal tissue in brain or spinal cord; common bacterial agents differ depending on patient age (see Table 11-5)
2. Infection is usually caused by hematogenous spread, local extension, or cerebrospinal fluid (CSF) exposure to bacteria (e.g., neurosurgery)
3. **Risk factors** = ear infection, sinusitis, immunocompromise, neurosurgery, maternal group B streptococci infection during birth
4. **History and physical (H/P)**
   a. Headache, **neck pain**, photophobia, malaise, vomiting, confusion, fever.
   b. **Brudzinski** sign (i.e., neck flexion in supine patient prompts reflexive hip flexion) and **Kernig** sign (i.e., painful knee extension occurs with hip flexion in supine patient) are not reliable tests.
   c. Petechiae are seen in *Neisseria meningitidis* infection.
   d. Change in mental status, seizures, decreased consciousness seen with worsening infection.
   e. Symptoms in children may be nonfocal.

Quick HIT

Haemophilus influenzae has been significantly reduced as a cause of meningitis owing to childhood **vaccination**.

Quick HIT

Young children with meningitis frequently have **negative** Brudzinski and Kernig signs.

5. **Labs** = increased white blood cell count (WBC); blood cultures frequently positive; lumbar puncture (LP) useful for differentiating causes of meningitis from each other and from healthy patients; CSF culture may determine exact agent (see Table 11-6)
6. **Radiology** = computed tomography (CT) or magnetic resonance imaging (MRI) may be helpful for ruling out other pathologies
7. **Treatment** = initially cephalosporins (third generation) and vancomycin until specific etiology is identified, then agent-specific antibiotics; close contacts of patient should be given **rifampin or ciprofloxacin for prophylaxis** in cases of *Neisseria* infection (rifampin for *Haemophilus influenzae* infection in children without prior vaccination)
8. **Complications** = seizures, increased intracranial pressure (ICP), subdural effusion, empyema, brain abscess, hearing loss, mental impairment

NEXT
STEP

Neurologic examination must be performed before LP. With signs of **increased intracranial pressure** (**ICP**) (papilledema, focal neurologic deficits, pupil asymmetry), do **not** perform LP because of increased risk of **uncal herniation**.

Table 11-5 Common Causes of Meningitis by Age Group

Age	Most Common Agent	Other Common Agents
Newborn	Group B streptococci	*Escherichia coli, Listeria, Haemophilus influenzae*
1 mo–2 yrs	*Streptococcus pneumoniae*, *Neisseria meningitidis*	Group B streptococci, *Listeria, H. influenzae*
2–18 yrs	*N. meningitidis*	*S. pneumoniae*, *Listeria*
18–60 yrs	*S. pneumoniae*	*N. meningitidis*, *Listeria*
60+ yrs	*S. pneumoniae*	*Listeria*, gram-negative rods

Table 11-6 CSF Findings for Different Causes of Meningitis

Status	WBCs	Pressure	Glucose	Protein
Healthy patient	<5	50–180 mm H_2O	40–70 mg/dL	20–45 mg/dL
Bacterial infection	↑↑ (PMNs)	↑↑	↓	↑
Fungal infection or tuberculosis	↑ (Lymphocytes)	↑↑	↓	↑
Viral infection	↑ (Lymphocytes)	↑	Normal	Normal

CSF, cerebrospinal fluid; PMNs, polymorphonuclear cells; WBCs, white blood cells; ↑, mild increase; ↓, decrease; ↑↑, significant increase.

B. Viral Meningitis (Aseptic Meningitis)

1. Meningitis caused by viral infection by enterovirus, echovirus, herpes simplex virus (HSV), lymphocytic choriomeningitis virus, mumps virus
2. **H/P** = nausea, vomiting, headache, neck pain, photophobia, malaise; fever, rash; symptoms generally **milder** than for bacterial meningitis
3. **Labs** = LP helpful for diagnosis; viral culture will confirm etiology
4. **Treatment** = empiric antibiotics may be started until viral cause is confirmed; supportive care usually sufficient for confirmed viral cases

NEXT
STEP

Treat fungal meningitis with amphotericin B, and treat tuberculosis meningitis with the combination of isoniazid, ethambutol, pyrazinamide, and rifampin.

C. Encephalitis

1. Inflammation of brain parenchyma caused by **viral** infection (e.g., varicella-zoster virus, HSV, mumps virus, poliovirus, rhabdovirus, Coxsackievirus, arbovirus, flavivirus, measles) or immunologic response to viral infection
2. **H/P**
   a. Malaise, headache, vomiting, neck pain, decreased consciousness; **change in mental status**, focal neurologic deficits (e.g., hemiparesis, pathologic reflexes, nerve palsy), fever
   b. Skin lesions seen with HSV
   c. Parotid swelling seen with mumps
   d. Flaccid paralysis with maculopapular rash seen in West Nile virus
3. **Labs**

Quick HIT

Common arboviruses include St. Louis and California strains. Common flaviviruses include **West Nile** and Japanese strains.

   a. LP shows increased WBCs and normal glucose.
   b. Culture generally not reliable.
   c. Serologic testing may be useful to identify viral cause.
   d. Brain biopsy can provide definitive diagnosis but is generally impractical.
4. **Radiology** = CT or MRI may show inflamed region of brain with effusion
5. **Treatment** = maintain normal ICP, supportive care; HSV treated with acyclovir

Quick HIT

In young children, encephalitis may be caused by **Reye syndrome** (reaction in children with viral infection who are given aspirin [ASA]).

D. Brain Abscess

1. Collection of pus in brain parenchyma resulting from extension of local bacterial infection, head wound, or hematogenous spread of bacteria
2. **H/P** = **headache**, neck pain, nausea, vomiting, malaise; fever, change in mental status, focal neurologic deficits, papilledema, seizures
3. **Labs** = brain biopsy or culture of abscess material performed during surgical drainage can be used to confirm bacterial identity
4. **Radiology** = **MRI** or CT may show “ring-enhancing lesion”; CT-guided biopsy can be performed to collect material for culture
5. **Treatment** = empiric antibiotics until specific agent identified; corticosteroids; **surgical drainage**

E. Poliomyelitis

1. Poliovirus (a picornavirus) infection of brain and motor neurons
2. Nearly eradicated through polio vaccine given in childhood
3. **H/P** = possibly asymptomatic; headache, neck pain, vomiting, sore throat; fever, **normal sensation, muscle weakness** that may progress to paralysis in severe cases
4. **Labs** = **positive polio-specific antibody**; LP consistent with viral meningitis; viral culture helpful for diagnosis
5. **Treatment** = with supportive care, most patients recover fully; assisted respiration may be required if respiratory muscles are affected

Quick HIT

Poliomyelitis may rarely occur after **oral** polio vaccine administration, so inactivated intramuscular polio vaccine is now more commonly used.

F. Rabies

1. Rhabdovirus transmitted to humans by **bite of infected animal**
2. Causes severe encephalitis with neuronal degeneration and inflammation

3. **H/P** = malaise, headache, restlessness, **fear of water ingestion** (secondary to laryngeal spasm); progressive cases exhibit severe central nervous system (CNS) excitability, **foaming at mouth**, very painful laryngeal spasms, and **alternating mania and stupor**
4. **Labs**
   a. Suspected animal should be caught and tested or observed for signs of rabies.
   b. If the animal appears to be infected, it should be killed and the brain should be tested for presence of virus and **Negri bodies** (i.e., round eosinophilic inclusions in neurons).
   c. Viral testing in humans (CSF, skin, serum) with symptoms is confirmatory of disease.
5. **Prophylaxis** = clean wound area thoroughly; administer rabies immunoglobulin and vaccine to patient if animal was infected or if rabies suspicion is high
6. **Complications** = **100% mortality** without treatment

Quick HIT

Tension headaches are the **most common** type of headache in adults.

III. Headache (See Table 11-7)

A. Head pain that may be a primary disorder (migraine, cluster, tension) or secondary to other pathologies (hemorrhage, encephalopathy, meningitis, temporal arteritis, neoplasm)

B. Trigeminal Neuralgia

1. Head and **facial pain** in trigeminal nerve distribution possibly caused by compression or irritation of trigeminal nerve root
2. **H/P** = sudden severe pain in distributions of maxillary and mandibular branches; "trigger zone" stimulation may induce pain
3. **Radiology** = MRI may identify lesions related to nerve compression
4. **Treatment** = **carbamazepine**, baclofen, phenytoin, gabapentin, valproate, clonazepam, or other **anticonvulsants**; surgical decompression of nerve may be helpful

NEXT
STEP

Any sudden onset of severe headache or focal neurologic deficits should be further examined using **CT without contrast** or MRI to rule out hemorrhage.

Table 11-7 Primary Headache Disorders

Variable	Migraine	Cluster	T
Patients	10–30 yrs of age, **female** > male	Young **men**	F
Pathology	Poorly understood; likely due to neuronal dysfunction	Poorly understood, likely extracerebral cause	P
Precipitating factors	Stress, oral contraceptives, **menstruation**, exertion, foods containing tyramine or nitrates (chocolate, cheese, processed meats)	Alcohol, vasodilators	S
Pain characteristics	Unilateral, throbbing	Severe, unilateral, **periorbital**, recurrent ("in clusters" over time)	B o
Other symptoms	**Nausea, vomiting**, preceding aura (visual abnormalities), photophobia	**Horner syndrome** (ptosis, miosis, anhidrosis), lacrimation, nasal congestion	A
Duration	4–72 hrs	30 min–3 hrs	V
Treatment	NSAIDs, ergots, sumatriptan; IV antiemetics useful for severe cases; prophylaxis includes tricyclic antidepressants, β-blockers, calcium channel blockers, ergots	100% O_2, ergots, sumatriptan; prophylaxis similar to that for migraines	N s ti

IV, intravenous; NSAIDs, nonsteroidal anti-inflammatory drugs.

IV. Cerebrovascular and Hemorrhagic Diseases

A. Transient Ischemic Attack (TIA)

1. **Definition**
   Classic time-based definition: Acute focal neurologic deficits that last **<24 hours** and are caused by temporarily impaired vascular supply to brain (e.g., emboli, aortic stenosis, vascular spasm)
   Tissue-based definition: transient episode of neurologic dysfunction caused by focal brain, spinal cord, or retinal ischemia, **without** acute infarction
2. **Risk factors** = hypertension (HTN), diabetes mellitus (DM), coronary artery disease (CAD), tobacco, hyperlipidemia, hypercoagulable states
3. **H/P**
   a. Sudden appearance of focal neurologic deficits, including weakness, paresthesias, brief unilateral blindness (i.e., amaurosis fugax) or other vision abnormalities, impaired coordination, vertigo.
   b. Carotid bruits suggest carotid atherosclerosis.
   c. Harsh systolic murmur suggests aortic stenosis.

Quick HIT

Most TIAs last <1 hour and are recurrent.

4. **Radiology** = ultrasound (US) may quantify degree of carotid or aortic stenosis; MRI or CT may demonstrate areas of brain ischemia; magnetic resonance angiography (MRA) or CT angiography (CTA) may locate intracranial vascular defects; echocardiography may be useful to determine if septic emboli, mural thrombus, or patent foramen ovale are causes of the condition
5. **Treatment**
   a. Any patient with disease attributable to atherosclerosis should be given **antiplatelet** (e.g., ASA) and **antilipid** (e.g., statins) therapy
   b. **Carotid endarterectomy or angioplasty** performed for carotid narrowing >60% in asymptomatic men, >50% in symptomatic men, and >70% in symptomatic women
   c. β-Blockers, valvuloplasty, or valve replacement used in treatment of aortic stenosis
   d. Long-term anticoagulation used for arrhythmias
   e. Treat other underlying disorders

Quick HIT

Atherosclerosis of carotid, basilar, or vertebral arteries is the most common cause of **thrombotic** ischemic stroke.

B. Stroke (Cerebrovascular Accident [CVA])

1. Acute focal neurologic deficit **lasting >24 hours** caused by ischemia of brain via **impaired perfusion** (i.e., ischemic stroke) or **hemorrhage** (i.e., hemorrhagic stroke)
2. Ischemic stroke may be **thrombotic** (i.e., obstruction of supplying artery by clot) or **embolic** (i.e., blockage of supplying artery by embolization of distant thrombus)
3. **Risk factors** = increased age, family history, obesity, DM, HTN, tobacco use, atrial fibrillation (Afib)
4. Area of neurologic deficit is dependent on location of stroke (Table 11-8)
5. **H/P**

Quick HIT

The **middle cerebral artery** is the most common artery involved in **embolic ischemic** stroke. Most emboli originate in the heart, aorta, carotid, or intracranial arteries.

   a. Sudden appearance of focal neurologic deficit lasting >24 hours.
   b. Constellation of symptoms depends on location of pathology.
   c. Stable findings indicate stable stroke, but progressive findings indicate evolving stroke.
   d. Thorough serial neurovascular examinations are important to determine the region of involvement and evolution.

Table 11-8 Common Stroke Locations and Corresponding Signs and Symptoms

Location of Stroke	Signs and Symptoms
ACA	Contralateral lower extremity and trunk weakness
MCA	Contralateral face and upper extremity weakness and decreased sensation, bilateral visual abnormalities, aphasia (if dominant hemisphere), neglect, and inability to perform learned actions (if nondominant hemisphere)
PCA	Contralateral visual abnormalities, blindness (if bilateral PCA involvement)
Lacunar arteries	Focal motor or sensory deficits, loss of coordination, difficulty speaking
Basilar artery	Cranial nerve abnormalities, contralateral full body weakness and decreased sensation, vertigo, loss of coordination, difficulty speaking, visual abnormalities, coma

ACA, anterior cerebral artery; MCA, middle cerebral artery; PCA, posterior cerebral artery.

Table 11-9 Inclusion and Exclusion Criteria for IV tPA for Acute Ischemic Stroke

Inclusion Criteria	Exclusion Criteria

• Diagnosis of ischemic stroke causing measurable neurologic deficit
• Onset of symptoms <3–4.5 hrs before start of treatment
• Age ≥18 yrs
	• Significant head trauma or prior stroke in previous 3 mo
	• Symptoms suggest subarachnoid hemorrhage
	• Arterial puncture at noncompressible site in previous 7 days
	• History of previous intracranial hemorrhage
	• Intracranial neoplasm, arteriovenous malformation, or aneurysm
	• Recent intracranial or intraspinal surgery
	• Elevated BP (systolic >185 mm Hg or diastolic >110 mm Hg)
	• Active internal bleeding
	• Acute bleeding diathesis, including but not limited to:
	  • Platelet count <100,000/mm^3
	  • Heparin use within 48 hrs, with an elevated aPTT greater than the upper limit of normal
	  • INR >1.7 or PT >15 s
	  • Current use of direct thrombin inhibitors or direct factor Xa inhibitors with elevated sensitive laboratory tests (such as a PTT, INR, platelet count, and ECT, TT, or appropriate factor Xa activity assays)

6. **Radiology** = **CT without contrast** or MRI useful to differentiate ischemic from hemorrhagic stroke; MRA or CTA may be helpful for locating ischemic cause
7. **Electrocardiogram (ECG)** = detection of new-onset arrhythmia or history of Afib seen on prior ECG may be useful in determining cause
8. **Treatment**

NEXT
STEP

Do **not** treat HTN immediately following stroke unless it is extreme (>220/120 mm Hg) or if patient has CAD in order to **maintain cerebral perfusion**.

a. Acute treatment of ischemic stroke:
   (1) Thrombolytic therapy is standard of care and should be administered within 3 to 4.5 hours of onset of symptoms, if patient has no exclusion criteria (Table 11-9). For patients who are >80 years old, have ever had a history of stroke and diabetes, or ANY anticoagulant use even if INR <1.7, the time window is limited to 3 hours from symptom onset.
   (2) In selected acute stroke patients within 24 hours of last known normal who have a large vessel occlusion in the anterior circulation and meet other imaging eligibility criteria, mechanical thrombectomy is recommended.
   (3) DO NOT lower blood pressure in the acute setting unless BP >220/120 OR there is a concurrent hypertensive emergency such as aortic dissection. Doing so is detrimental to the cerebral perfusion pressure (CPP), which becomes directly dependent on the systemic BP during a stroke due to loss of autoregulation (CPP = MAP − ICP).
   (4) Aspirin should be administered within 48 hours unless the patient has a true aspirin allergy or there is evidence of bleeding on the initial non-contrast CT.
   (5) Anticoagulation such as heparin is NOT indicated for most ischemic strokes.
   (6) Lipid-lowering drugs should be started after the acute stages of stroke in addition to optimization of blood pressure control.

b. Acute treatment of intracerebral hemorrhage (ICH). ICH is a medical emergency; 15% to25% have a significant decline within the first several hours
   (1) ABCs: airway, breathing, circulation
   (2) Maintain systolic blood pressure ≤140 to 160 mm Hg

(3) Emergency reversal of coagulopathy
   (a) Warfarin: reverse with vitamin K, fresh frozen plasma (FFP), prothrombin concentrate complex (PCC) for more severe cases
   (b) Direct thrombin inhibitors (e.g., dabigatran): reverse with antidote idarucizumab or PCC
   (c) Factor Xa inhibitors: reverse with antidote andexanet alfa or PCC
(4) Mannitol or hypertonic saline for mass effect or herniation
(5) Ventriculostomy for severe intraventricular hemorrhage/hydrocephalus
(6) Craniotomy for large cerebellar or temporal intracranial hemorrhage

C. Parenchymal Hemorrhage

1. Bleeding within brain parenchyma caused by HTN, arteriovenous malformation (AVM), brain aneurysm, or stimulant abuse
2. **H/P** = headache, nausea, vomiting; change in mental status, focal motor or sensory deficits, possible seizure
3. **Radiology** = CT without contrast used to localize and determine extent of bleeding; MRA or CTA may be useful for locating site of bleed
4. **Treatment** = supportive care, maintain normal ICP; surgical decompression for large hemorrhages to reduce risk of herniation; surgical repair of AVMs or aneurysms frequently required
5. **Complications** = significant supratentorial bleeding can cause transtentorial (uncal) herniation (brainstem damage) and CSF flow obstruction (leading to hydrocephalus and brainstem compression); large hemorrhages are frequently fatal

Quick HIT

Berry aneurysms are associated with **autosomal dominant polycystic kidney disease** and **Ehlers–Danlos syndrome**.

Quick HIT

Patients may describe the headache in SAH as the **"worst headache of my life."**

D. Subarachnoid Hemorrhage (SAH)

1. Bleeding between the pia and arachnoid meningeal layers because of rupture of **arterial aneurysm** (i.e., berry aneurysm), AVM, or trauma
2. **H/P** = **sudden severe headache**, neck pain, nausea, vomiting; fever, loss of (or decreased) consciousness, possible seizure
3. **Labs** = LP shows red blood cells, xanthochromia (i.e., yellowish discoloration of CSF), and increased pressure
4. **Radiology** = CT without contrast shows blood in the subarachnoid space or can be normal especially after 6 hours since symptom onset; MRA or angiography can localize site of bleeding (see Figure 11-3)
5. **Treatment** = prevent increase in ICP (raise head of bed, administer mannitol), treat HTN, reverse anticoagulation, administer anticonvulsants, perform interventional radiologic or surgical clipping or embolization of aneurysm or AVM
6. **Complications** = recurrence of bleeding, arterial vasospasm, hydrocephalus; permanent neurologic damage or death may result

Quick HIT

Patients with imminent rupture of a berry aneurysm may have multiple, although less severe, sentinel headaches in the preceding weeks.

Quick HIT

The most common cause of epidural hematoma is damage to the **middle meningeal artery** from blunt trauma.

Quick HIT

An epidural hematoma may appear to cross the brain midline on CT; subdural hematomas do not.

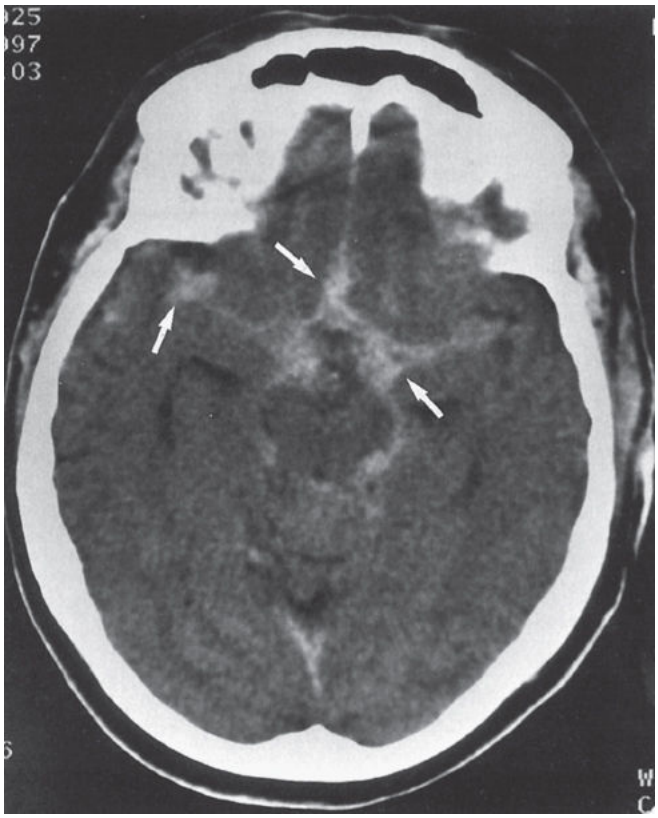


FIGURE 11-3
Subarachnoid hemorrhage seen on computed tomography (CT) scan without contrast; blood is evident in the subarachnoid space (*white arrows*).
(From Daffner, R. H. [2007]. *Clinical radiology: The essentials* [3rd ed., p. 477]. Philadelphia, PA: Lippincott Williams & Wilkins.)

E. Epidural Hematoma

1. Collection of blood between dura and skull caused by arterial hemorrhage
2. **H/P** = possible initial **"lucid interval"** between start of bleeding and onset of symptoms for a few hours or less with no change in consciousness; severe headache, decreased consciousness, nausea; hemiparesis, hemiplegia, seizures, pupil abnormalities (i.e., "blown" pupil)
3. **Radiology** = CT without contrast shows **convex** hyperdensity compressing the brain at site of injury; adjacent skull fracture may be apparent in traumatic cases (see Figure 11-4)

NEXT
STEP

If SAH is suspected despite a **negative** CT, perform an LP.

Quick **HIT**

A **declining red blood cell (RBC) count over successive collection tubes** can occur in a traumatic LP and can help differentiate it from subarachnoid hemorrhage.

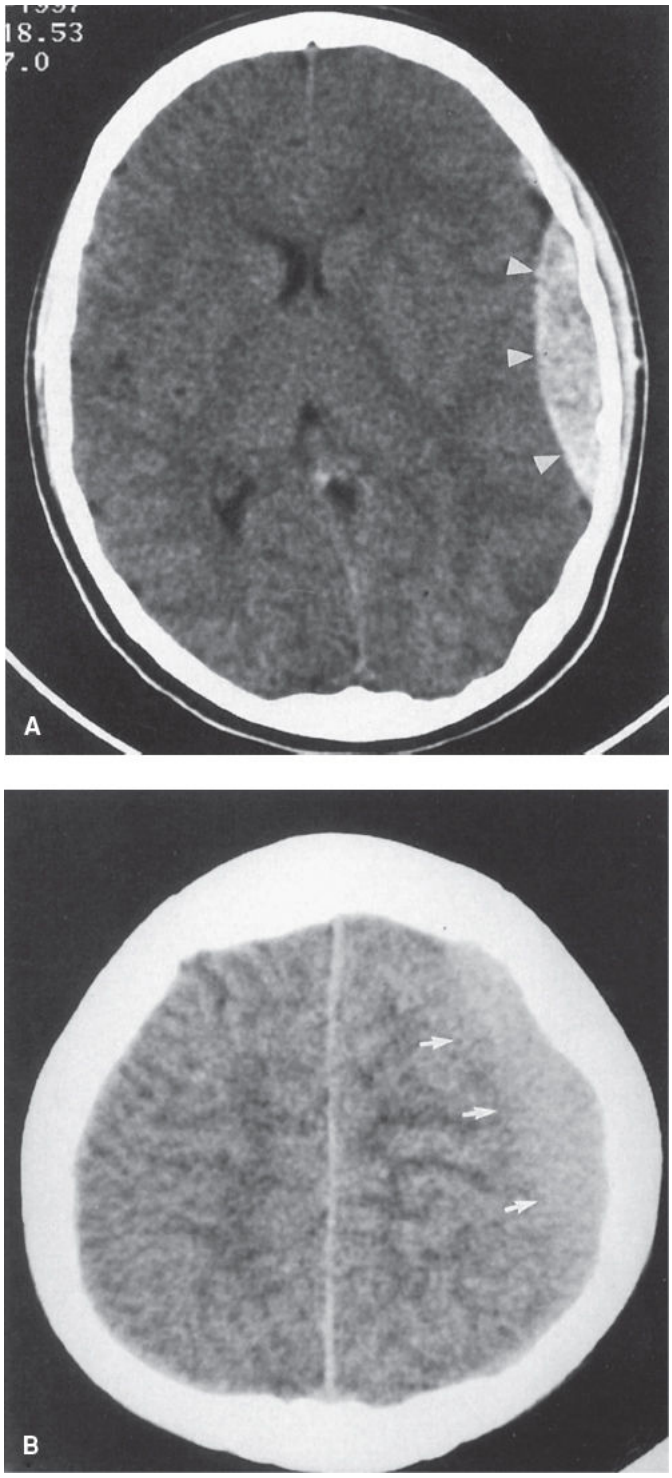


FIGURE 11-4
A: Epidural hematoma. Note convex hyperdensity caused by blood (*white arrows*). B: Subdural hematoma. Note faint concave hyperdensity caused by blood (*white arrows*).

4. **Treatment** = **emergent** drainage of hematoma either under radiographic guidance or by surgical burr hole; stabilization of ICP and blood pressure
5. **Complications** = permanent neurologic injury or death usually results without prompt treatment

NEXT
STEP

With mental status changes seen in an elderly patient with a history of **falls**, perform a workup for subdural hematoma.

F. Subdural Hematoma

1. Collection of blood between the dura and arachnoid meningeal layers caused by rupture of bridging veins following trauma

2. **H/P**
   a. **Slowly progressive** headache (days to weeks); change in mental status, contralateral hemiparesis, increased deep tendon reflexes (DTRs)
   b. Large hematomas can cause transtentorial herniation with decreased consciousness and pupil abnormalities
3. **Radiology** = CT without contrast shows **concave** hyperdensity compressing the brain that does **not** cross midline (see Figure 11-4)
4. **Treatment** = surgical drainage or supportive therapy depending on size of bleed and extent of neurologic deficits

NEXT
STEP

Do **not** perform an LP in patients with **mass lesion or subdural/epidural hematoma** because of increased risk of herniation.

V. Seizure Disorders

A. Causes of Seizures

1. Sudden change in neurologic activity (e.g., behavior, movement, sensation) caused by excessive synchronized discharge of cortical neurons in a limited (focal) or generalized distribution of the brain.
2. **Epilepsy** is a condition of **recurrent** seizures.
3. Common causes of seizures vary with age (see Table 11-10).

Table 11-10 Common Causes of Seizures by Age Group

Age Group	Causes
Infants	Hypoxic injury Metabolic defects Genetic or congenital abnormality Infection
Children	Idiopathic Infection Fever Trauma
Adults	Idiopathic Metabolic defects Drugs or drug withdrawal Trauma Neoplasm Infection Cerebrovascular disease Psychogenic
Elderly	Stroke or cerebrovascular disease Metabolic defects Drugs or drug withdrawal Infection Trauma Neoplasm

Table 11-11 Types of Seizures

Type	Involvement	History and Physical	Electroe
Simple partial	Focal cortical region of brain	**Focal** sensory (paresthesias, hallucinations) or motor (repetitive or purposeless movement) deficit; **no loss of consciousness**	Distinct fo abnormali
Complex partial	Focal cortical region (most commonly **temporal** lobe)	**Hallucinations** (auditory, visual, olfactory), **automatisms** (repeated coordinated movement), déjà vu, impaired consciousness, postictal confusion	Focal abn ral lobe
Generalized convulsive (tonic, clonic, tonic–clonic, myoclonic, atonic)	Bilateral cerebral cortex	Sustained contraction of extremities and back (**tonic**), repetitive muscle contraction and relaxation (**clonic**), brief contraction period followed by repetitive contraction–relaxation (**tonic–clonic**), brief repetitive contractions (**myoclonic**), or loss of tone (**atonic**); loss of consciousness, incontinence, significant postictal confusion, possible unilateral weakness lasting several hours (rarely days) after seizure (Todd paralysis)	**Generali** malities
Absence	Bilateral cerebral cortex	**Brief** (few seconds) episodes of **impaired consciousness**, normal muscle tone, possible eye blinking, no postictal confusion; more common in **children**	Generalize ond **spike**

B. Types of Seizures

1. Classified according to electrical activity and extent of brain involvement (see Table 11-11)
2. Electroencephalogram (EEG) used to measure cortical neuron activity and differentiate types of seizures
3. **Treatment**
   a. Anticonvulsants are the mainstay of therapy (see Table 11-12).
   b. One medication used initially, but additional drugs can be added for better control.
   c. Drug withdrawal may be considered after an extended seizure-free period, but more than half of the patients will have a recurrence.
   d. Surgery is a consideration for resectable sources of abnormal activity (more common in partial seizures).
   e. Vagal nerve stimulation can be considered in a patient failing other therapies.

Quick HIT

Generalized seizures involve **the entire cortex**. Partial seizures involve **focal** neurologic deficits and can progress to **secondary** generalization (as distinguished from primary generalized seizures).

C. Status Epilepticus

1. **Repetitive** or **unremitting seizures** without any period of regained consciousness
2. Caused by withdrawal of anticonvulsants, alcohol withdrawal, trauma, pre-existing seizure disorder, metabolic abnormalities
3. **H/P** = uninterrupted seizures or recurrent seizures without recovery between episodes lasting ≥**5 minutes**
4. **Labs** = complete blood count (CBC), glucose, electrolytes, toxicology, liver function tests (LFTs), blood urea nitrogen (BUN), creatinine, and hCG may be useful to determine underlying cause
5. **EEG** = shows prolonged abnormal electrical activity
6. **Treatment**
   a. Maintain airway, breathing, circulations (ABCs).
   b. **Intravenous (IV) benzodiazepines** used to end seizure activity, phenytoin given to prevent recurrence.
   c. Refractive seizure activity can be treated with phenobarbital or pentobarbital.
   d. Treat underlying disorder.
7. **Complications** = >20% mortality if not controlled promptly

NEXT
STEP

Delay CT and EEG during status epilepticus until patient is stabilized.

MNEMONIC

Remember the common signs of Parkinson disease by the mnemonic **SMART:**

Shuffling gait

Mask-like facies

Akinesia

Rigidity ("cogwheel")

Tremor (resting)

Table 11-12 Anticonvulsant Medications Used in Epilepsy Treatment

Drug	Current Indications	Adverse Effects
Mechanism: Inhibition of voltage-dependent sodium channels		
Carbamazepine	Monotherapy for partial or generalized convulsive seizures	Nausea, vomiting, hyponatremia, Stevens–Johnson syndrome, drowsiness, vertigo, blurred vision, leukopenia
Phenytoin	Monotherapy for partial or generalized convulsive seizures, **status epilepticus**	Gingival hyperplasia, androgenic, lymphadenopathy, Stevens–Johnson syndrome, confusion, blurred vision
Lamotrigine	Partial seizures, second-line drug for tonic–clonic seizures	Rash, nausea, Stevens–Johnson syndrome, dizziness, sedation
Oxcarbazepine	Monotherapy for partial or generalized convulsive seizures	Hyponatremia, rash, nausea, sedation, dizziness, blurred vision
Zonisamide	Second-line drug for partial and generalized seizures	Somnolence, confusion, fatigue, dizziness
Mechanism: Inhibition of neuronal calcium channels		
Ethosuximide	**Absence** seizures	Nausea, vomiting, drowsiness, inattentiveness
Mechanism: Enhanced GABA activity		
Phenobarbital, pentobarbital	Nonresponsive status epilepticus	Drowsiness, general cognitive depression, vertigo, nausea, vomiting, rebound seizures
Benzodiazepines	**Status epilepticus**	Drowsiness, tolerance, rebound seizures
Tiagabine	Second-line drug for partial seizures	Dizziness, fatigue, nausea, inattentiveness, abdominal pain
Mechanism: Inhibition of sodium channels and enhanced GABA activity		
Valproate	Monotherapy or second drug for partial and generalized seizures	Hepatotoxicity, nausea, vomiting, drowsiness, tremor, weight gain, alopecia
Mechanism: Inhibition of NMDA-glutamate receptors and enhanced GABA activity		
Topiramate	Second-line drug for partial and generalized seizures	Weight loss, cognitive impairment, heat intolerance, dizziness, nausea, paresthesias, fatigue
Mechanism: Unknown		
Gabapentin	Monotherapy or second-line drug for partial seizures	Sedation
Levetiracetam	Monotherapy for partial seizures, second-line drug for partial or generalized seizures	Fatigue, somnolence, dizziness

GABA, γ-aminobutyric acid; NMDA, *N*-methyl-d-aspartate.

VI. Degenerative Neurologic Disorders

A. Parkinson Disease

1. Idiopathic dopamine depletion, loss of dopaminergic striatal neurons in the substantia nigra, and Lewy body (eosinophilic cytoplasmic inclusions in neurons) formation leading to abnormal cholinergic input to cortex
2. Similar syndrome may be induced by 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP, a side product in illicit opioid production) intoxication
3. **H/P** = **resting tremor** (i.e., "pill-rolling" tremor of hands), decreased or slowed voluntary movement (i.e., bradykinesia), mask-like facies, **shuffling gait**, involuntary acceleration of gait following initiation, **"cogwheel"** rigidity (i.e., increased tone of agonist and antagonist muscles), memory loss, difficulty initiating movement, postural instability
4. **Treatment**
   a. Dopaminergic agonists (e.g., levodopa, carbidopa, bromocriptine, amantadine), monoamine oxidase type B (MAO-B) inhibitors (e.g., selegiline), anticholinergic agents (e.g., benztropine), amantadine (see Table 11-13).

b. Deep brain electrical stimulation has emerged as a viable option in disease not responsive to medication alone.

Table 11-13 Medications Used in Treatment of Parkinson Disease

Drug	Mechanism	Indications	Adverse Effects
Levodopa	Dopamine precursor	Initial therapy	Nausea, vomiting, anorexia, hallucinations, mood chang, chronic use
Carbidopa	Dopamine decarboxylase inhibitor that reduces levodopa metabolism	Combined with levodopa to augment effects	Reduces adverse effects of smaller dosage
Bromocriptine	Dopamine receptor agonist	Increases response to levodopa in patients with declining response	Hallucinations, confusion, cardiotoxicity
Selegiline	Monoamine oxidase type B inhibitor	Early disease; may help delay need to start levodopa	Nausea, headache, confus
Amantadine	Increases synthesis, release, or reuptake of dopamine	More effective against rigidity and bradykinesia	Agitation, hallucinations
Antimuscarinic agents (e.g., benztropine)	Block cholinergic transmission	Adjuvant therapy	Mood changes, dry mouth, confusion, hallucinations,

Quick HIT

Signs of **UMN** disease include spasticity, increased DTRs, positive Babinski sign. Signs of **LMN** disease include flaccid paralysis, decreased DTRs, fasciculations, negative Babinski sign.

B. Amyotrophic Lateral Sclerosis (ALS)

1. Progressive loss of upper motor neurons (UMNs) and lower motor neurons (LMNs) in brain and spinal cord, involving degeneration of anterior horn cells and corticospinal tract
2. **H/P** = asymmetric **progressive weakness** in face (e.g., tongue, dysphagia) and limbs with **normal sensation**, possible change in personality or impaired judgment; increase or decrease in DTRs, spasticity, positive Babinski sign, flaccid paralysis, and fasciculations seen in limbs
3. **Labs** = blood tests used to rule out other pathologies
4. **Electromyogram (EMG)** = demonstrates widespread muscular denervation and motor block
5. **Radiology** = CT or MRI may be helpful to rule out neurologic lesions
6. **Treatment** = riluzole may slow progression; supportive care (e.g., respiratory support, pain control)
7. **Complications** = half of the patients die within 3 years of diagnosis secondary to respiratory failure

Quick HIT

Clinical diagnosis of ALS requires LMN signs in at least two extremities and UMN signs in one region.

C. Huntington Disease

1. Autosomal dominant disease caused by multiple cytosine-adenine-guanine (CAG) repeats on chromosome 4; higher numbers of CAG repeats lead to earlier onset of disease
2. Characteristic signs include movement and mental dysfunction starting in middle age
3. **H/P** = progressive, rapid irregular involuntary movement of extremities (**chorea**); dementia (e.g., irritability, antisocial behavior); possible seizures
4. **Labs** = genetic analysis will detect chromosome 4 abnormality
5. **Radiology** = CT or MRI shows caudate nucleus atrophy
6. **Treatment** = dopamine antagonists may improve chorea; genetic screening can be used in asymptomatic family members with proper counseling
7. **Complications** = usually fatal in <20 years from diagnosis

Quick HIT

Huntington disease has **100%** genetic penetrance but does not become symptomatic until **middle age**.

D. Multiple Sclerosis (MS)

1. Progressive demyelinating disease of brain and spinal cord with possible autoimmune etiology
2. Most patients are **women** 20 to 40 years of age

MNEMONIC

Remember that **MS** affects the **M**yelin **S**heath and is more common in **MS** (women) than in MR (men).

3. **H/P**
   a. **Variable** initial presentation with multiple neurologic complaints (e.g., vertigo, vision abnormalities, paresthesias, weakness, urinary retention) that are difficult to explain through one cause.
   b. Symptoms may progress slowly with several remissions and become worse during stressful events (e.g., infection, childbirth, trauma, heat).
   c. Late symptoms and signs include worsening vision, poor movement control, difficulty speaking (i.e., dysarthria), sensory abnormalities, postural and positional instabilities (i.e., cerebellar signs), spasticity, increased DTRs, and positive Babinski sign.
4. **Labs** = LP shows CSF with increased protein, mildly increased WBCs, oligoclonal bands, increased IgG
5. **Radiology** = MRI shows multiple asymmetric **white matter lesions**
6. Diagnosis is made considering both clinical and radiographic evidence
7. **Treatment** = corticosteroids, methotrexate, and avoidance of stress may help decrease length of exacerbations; interferon-β and glatiramer acetate decrease frequency of exacerbations; supportive care for worsening neurologic dysfunction
8. **Complications** = progressive neurologic abnormalities with residual deficits; many patients become chronically disabled

NEXT
STEP

Highly suspect MS in a **young woman** with a confusing constellation of neurologic symptoms. Perform MRI to look for white matter lesions and LP to look for oligoclonal bands.

E. Syringomyelia

1. Posttraumatic cystic degeneration of spinal cord from an unknown mechanism
2. Syrinx cavity (i.e., centralized channel within spinal cord) expands and compresses adjacent neural tissue
3. **H/P** = loss of pain and temperature sensation, flaccid paralysis, decreased DTRs, fasciculations
4. **Radiology** = MRI shows syrinx expansion
5. **Treatment** = surgical decompression; shunting may be needed for recurrent cases; supportive care

VII. Peripheral Motor and Neuromuscular Disorders

A. Myasthenia Gravis

1. Autoimmune disorder characterized by antibodies that bind to acetylcholine (ACh) receptors at the neuromuscular junction and block normal neuromuscular transmission, resulting in easy fatigability
2. Often associated with thymoma and thyrotoxicosis
3. Most common in **young adult women**
4. **H/P** = **periodic weakness** and muscle fatigue that worsen throughout day; ptosis, diplopia (i.e., double vision), dysarthria; in severe cases, patients have dyspnea
5. **Labs** = **positive ACh receptor antibodies**; when edrophonium is administered, symptoms improve (i.e., Tensilon test); nerve stimulation and EMG are helpful in making diagnosis
6. **Treatment** = anticholinesterase agents (e.g., neostigmine, pyridostigmine), thymectomy, immunosuppressive agents (e.g., prednisone, azathioprine), plasmapheresis, IV immunoglobulin for refractory cases

Quick **HIT**

Lambert–Eaton syndrome is a paraneoplastic disorder (e.g., **small cell lung cancer**) with similar presentation to myasthenia gravis. It occurs because of antibodies to presynaptic Ca^{2+} channels and is treated with immunosuppressive agents and plasmapheresis.

B. Guillain–Barré Syndrome

1. Autoimmune demyelinating disorder of peripheral nerves associated with recent **viral infection**, surgery, or vaccination (rare)
2. **H/P**

a. Rapidly progressive **bilateral weakness** initially in distal extremities in **"stocking glove"** distribution and extending proximally with **decreased sensation** and possible absent DTRs; possible severe neuropathic pain
b. Recent history of viral infection, vaccination, or surgery
c. Blood pressure, heart rate, or core temperature may be labile
d. Severe cases may include respiratory muscle weakness

3. **Labs** = LP shows increased protein with normal pressure and glucose
4. **EMG** = consistent with widespread demyelination
5. **Treatment** = self-resolving within 1 month; plasmapheresis or IV immunoglobulin may accelerate resolution; patients must be watched for signs of **respiratory failure**; adequate analgesia for neuropathic pain
6. **Complications** = respiratory failure requires intubation and ventilation; most patients recover fully

Table 11-14 Common Hyperkinetic Disorders

Disorder	Movement	Associated Diseases	Treatment
Essential tremor	Fixed oscillation of hands or head	Idiopathic	β-Blockers, p pam; thalamc stimulation ir
Chorea	Rapid **flinching** distal limb and facial movements	**Hyperthyroidism**, stroke, **Huntington disease**, SLE, levodopa use, rheumatic fever	Treat the und
Athetosis	Writhing, snake-like movement in extremities	**Cerebral palsy**, encephalopathy, Huntington disease, Wilson disease	Treat underly
Dystonia	**Sustained** proximal limb and trunk contractions	Wilson disease, **Parkinson disease**, Huntington disease, encephalitis, neuroleptic use **(tardive dyskinesia)**	Carbidopa, le toxin, treat ur
Hemiballismus	**Flinging** of proximal extremities	Stroke (subthalamic nucleus)	Haloperidol
Tics	**Repetitive** brief involuntary movement (blinking, grimacing) or sound (grunting, sniffing, throat clearing)	**Tourette syndrome**, obsessive-compulsive disorder, attention deficit hyperactivity disorder	Fluphenazine nazine

SLE, systemic lupus erythematosus.

NEXT
STEP

If myasthenia gravis is diagnosed in a patient, always perform a chest CT to look for a **thymoma**.

***Quick* HIT**

Edrophonium is a short-acting anticholinesterase agent, making it ideal for myasthenia gravis testing but ineffective for therapy.

C. Facial Nerve Palsy (Bell Palsy)

1. Facial weakness (usually unilateral) affecting both the **upper and lower face**; may be due to HSV reactivation (most common), herpes zoster, Lyme disease, AIDS, sarcoidosis, tumors, diabetes; many "idiopathic" are thought to be due to undiagnosed HSV
2. **H/P** = sudden onset of **unilateral facial muscle weakness**/paralysis (**asymmetrical smile**, drooling, ptosis, inability to close the eye, **inability to raise eyebrow**)
3. **Treatment** = supportive care (artificial tears, patch the eye at night to prevent injury); high-dose **glucocorticoids** (e.g., prednisone) for 1 week; patients presenting with severe disease may benefit from valacyclovir in addition to prednisone

***Quick* HIT**

A peripheral facial nerve palsy will cause paralysis of the upper face, unlike a cortical stroke. The facial nerve nucleus receives bilateral projections from the cortex to control the upper face, so a unilateral cortical stroke will not cause paralysis of the upper face.

D. Hyperkinetic Disorders

1. Abnormal involuntary movement associated with specific neurologic diseases or other causes
2. Described by pattern of movements (see Table 11-14)

Quick HIT

Glioblastoma is the most common primary brain tumor in **adults**. **Astrocytoma** is the most common brain tumor in **children**. **Medulloblastoma** is the most common *malignant* brain tumor in children.

VIII. Neoplasms

A. Primary CNS Neoplasms

1. Brain tumors that are not caused by distant metastases; more common in young and middle-aged adults
2. Tumors in **adults** tend to be **above** the tentorium (i.e., fold of dural meninges that separates cerebellum below from cortex above); tumors in **children** tend to be **below** the tentorium

Quick HIT

Metastatic brain tumors are **more common** than primary tumors.

   a. The three most common primary CNS tumors in adults are glioblastoma, meningioma, and schwannoma.
   b. The three most common primary CNS tumors in children are astrocytoma (benign), medulloblastoma (malignant), and ependymoma (may be malignant).
3. Symptoms result from focal compression (i.e., mass effect) of tumor (e.g., hydrocephalus, increased ICP, venous obstruction)
4. **H/P** = headache, vomiting, lethargy; focal neurologic abnormalities, change in mental status, possible seizures; blown pupil seen if herniation occurs
5. **Labs** = biopsy under CT guidance of detected lesion used for diagnosis
6. **Radiology** = MRI or positron emission tomography (PET) scan detects lesion
7. **Treatment** = surgical resection (if possible), radiation, chemotherapy; corticosteroids may decrease cerebral edema; anticonvulsants used for seizure prophylaxis

Quick HIT

Most metastases to the brain are **supratentorial**.

B. Metastatic CNS Neoplasms

1. Tumors that have metastasized to brain from distant site; lung, renal cell carcinoma, melanoma, breast, and colorectal cancer are most common primary tumors
2. **H/P** = symptoms similar to presentation for primary tumors; headache, vomiting, lethargy; focal neurologic abnormalities, change in mental status, seizures
3. **Labs** = biopsy confirms origin of tumor
4. **Radiology** = MRI is most commonly used tool to detect lesions
5. **Treatment** = treat original tumor; surgical resection for single metastasis, palliative radiation
6. **Complications** = poor prognosis

NEXT
STEP

If an intracranial tumor is the initial lesion detected, workup should include a full search for a source neoplasm (full body CT, blood cancer antigens, etc.).

C. Neurofibromatosis Type 1 (NF1) (von Recklinghausen Disease)

1. Autosomal dominant disorder (NF1 gene on chromosome 17) with multiple neurologic tumor and dermatologic manifestations
2. Neurofibromatosis type 2 is a rare autosomal dominant disorder linked to chromosome 22, characterized by the development of bilateral **acoustic neuromas**
3. At least two of the following required for diagnosis:
   a. >Five **café-au-lait macules** >15 mm diameter
   b. >One **neurofibroma** or one plexiform neurofibroma (i.e., tumors with mix of Schwann cells, fibroblasts, and mast cells)

c. Axillary or inguinal freckling
d. Optic glioma (i.e., tumor of optic nerve)
e. >One iris hamartoma (i.e., **Lisch nodules**)
f. Bone lesions (e.g., cortical thinning of long bones, sphenoid dysplasia)
g. First-degree relative with NF1

4. **H/P**
   a. Initial signs are freckling, **café-au-lait spots, Lisch nodules, neurofibromas**, and **bone abnormalities** evident in the first few years of life.
   b. Severe functional limitations are seen in movement and gait, caused by nonunion of bone fragments (i.e., pseudoarthrosis) and fractures during development.
   c. Short stature and scoliosis may be evident.
   d. Visual abnormalities may result from compression of optic nerve by glioma.
   e. Possible cognitive impairments, seizures, or peripheral neuropathic signs.
5. **Labs** = genetic testing detects abnormal gene
6. **Radiology** = MRI shows multiple areas of increased signal intensity in brain and increased brain volume
7. **Treatment** = therapy directed at maintaining function and treating complications
8. **Complications** = increased risk of malignant CNS tumors, developmental delays, mental retardation, peripheral neuropathy, pheochromocytoma, vision abnormalities, severe bone abnormalities, seizures

IX. Sleep and Loss of Consciousness

A. Sleep

1. **Normal sleep cycles**
   a. Stage N1 sleep is light sleep with fast θ waves on EEG.
   b. Stage N2 sleep is intermediate sleep with sleep spindles and K-complexes on EEG.
   c. Stage N3 is deep sleep with slow δ waves on EEG.
   d. Rapid eye movement (REM) sleep occurs every 90 to 120 minutes and is characterized by REMs, dreams, and low-voltage, high-frequency EEG pattern.a

> ***Quick*** **HIT**
>
> 40%–50% of sleep is spent in stage N2. **Benzodiazepines** increase stage N2 sleep, decrease stage N3, and do not reproduce normal sleep architecture.

2. **Sleep apnea**
   a. Hypoventilation during sleep secondary to pulmonary obstruction or decreased neurologic respiratory drive (see Chapter 6, **Pulmonary Disorders**)
3. **Narcolepsy**
   a. Persistent excessive daytime sleepiness regardless of prior sleep quality
   b. **H/P** = possible sudden loss of muscle tone (i.e., cataplexy), vivid dreams, sleep paralysis; **hypersomnia** (i.e., sudden occurrence of sleep) may occur suddenly during the daytime
   c. **Labs** = polysomnography may show multiple arousals and decreased latency until REM sleep
   d. **Treatment** = modafinil (preferred), methylphenidate, or pemoline help prevent hypersomnia; tricyclic antidepressants may help prevent cataplexy; establishing regular sleep schedule with short naps improves wakefulness

B. Syncope

1. Acute transient loss of consciousness frequently related to inadequate blood supply to the brain
2. Common causes include **cardiac dysfunction** (e.g., aortic stenosis, bradycardia, decreased stroke volume), vasovagal response, hypotension, **hypoglycemia**, seizures, and cerebrovascular ischemia
3. **H/P** = possible prodrome of light-headedness, nausea, and weakness preceding loss of consciousness (i.e., fainting); few generalized spasms may be observed; **patient quickly regains consciousness** (although seizure patients may display postictal sleepiness); hypotension, arrhythmias, and neurologic deficits may be detected following the episode
4. **Labs** = glucose levels should be measured; **orthostatics** or tilt testing (i.e., patient response is measured with rapid posture changes), with or without β-blocker infusion, can help diagnose cardiovascular cause; echocardiography or stress testing may be useful
5. **ECG** = useful for diagnosing cardiac causes; ambulatory monitoring may be used to measure extended periods of time
6. **EEG** = useful for detecting epileptic causes
7. **Radiology** = MRI, MRA, or angiography may detect vascular abnormalities
8. **Treatment** = treat underlying cause

C. Coma (See Figure 11-5)

1. Condition in which patient is **unresponsive to stimuli** and **unable to be aroused**; associated with bilateral cortical or brainstem reticular activating system dysfunction
2. Can result from cerebral hemorrhage, tumor, abscess, sedating drugs (e.g., alcohol, benzodiazepines, narcotics), hypoglycemia, metabolic dysfunction, hypothermia, hepatorenal failure, or psychogenic causes

3. **H/P** = patient unresponsive to stimuli; pertinent history and physical examination helpful for determining cause; CN examination particularly helpful for determining level of injury
4. **Labs** = CBC, electrolytes, BUN and creatinine, glucose, LFTs, coagulation factors, toxicology, CSF analysis, EEG, or arterial blood gas is helpful for diagnosis
5. **Radiology** = CT or MRI may detect intracranial cause (e.g., hemorrhage, tumor)
6. **Treatment** = maintain ABCs; prevent increase in ICP (hyperventilation, mannitol, elevate head); treat underlying cause

Quick HIT

A patient in a **persistent vegetative state** has normal sleep cycles, an inability to perceive and interact with the environment, and preserved autonomic function for **>1 month**. Recovery is unlikely if these symptoms last **>3 months**.

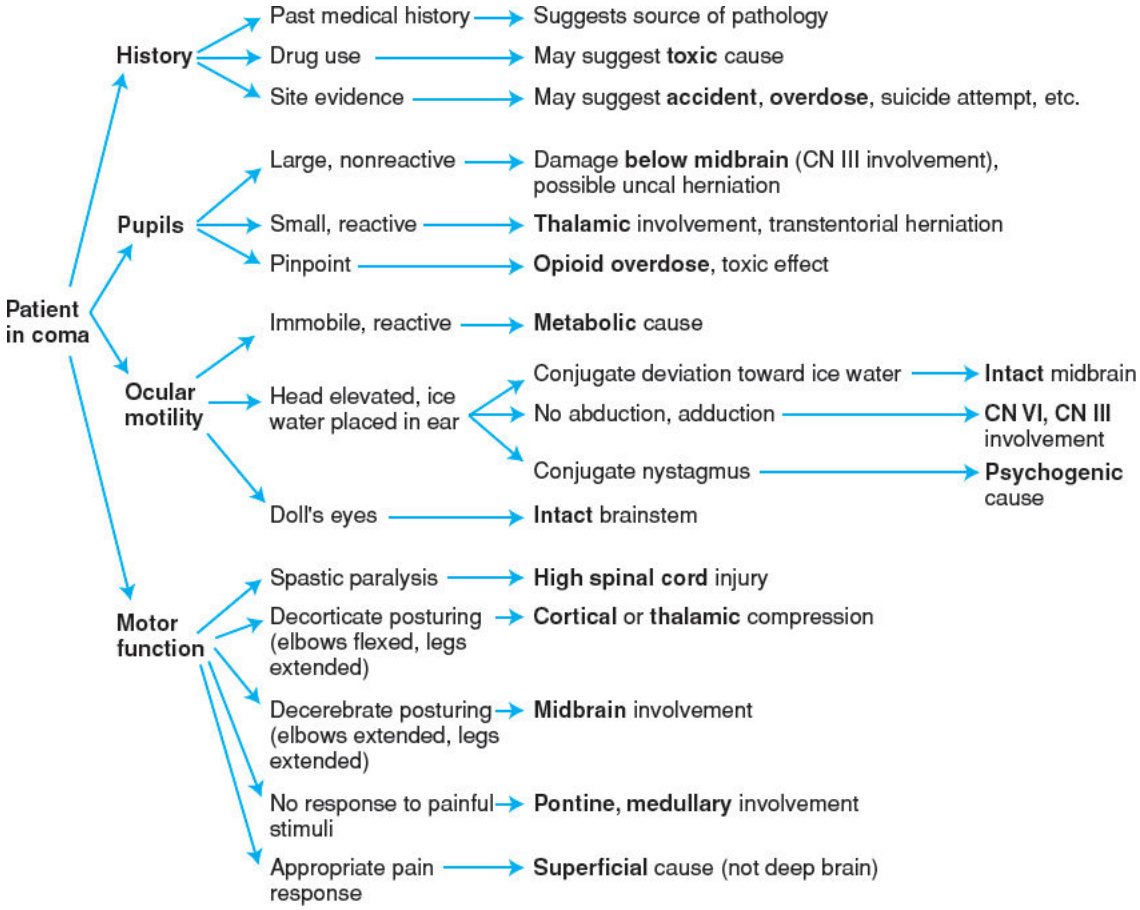


FIGURE 11-5
Approach to the patient in a coma.

X. Ophthalmology

A. Normal Eye Function

1. Retinal artery and vein are vasculature for the retina; vascular pathology affects vision (e.g., occlusion, DM retinopathy)
2. Nerves
   a. Optic nerve (CN II) responsible for vision.
   b. Trochlear nerve (CN IV) controls superior oblique muscle (downward medial gaze, inward eye rotation).
   c. Abducens nerve (CN VI) controls lateral rectus muscle (abduction).
   d. Oculomotor nerve (CN III) controls all other eye muscles.
   e. Medial longitudinal fasciculus (MLF) maintains conjugate gaze when one eye abducts.
   f. Specific distortions in vision result from neuronal injury depending on site of insult (see Figure 11-6; Table 11-15).

B. Common Vision Abnormalities

1. Types of visual irregularity are caused by abnormal eye shape, gaze alignment, or eye focal orientation (see Table 11-16).
2. Usually correctable through lenses, visual training, or surgery.

Quick HIT

Conjunctivitis facts:

- Adenovirus is the most common cause.
- Typically highly contagious and can be spread by contact with towels or linens or by close contact
- Can be caused by *Neisseria gonorrhoeae* and *Chlamydia trachomatis* after sexual contact
- Can occur in the perinatal period if mother is infected with *N. gonorrhoeae* or *C. trachomatis*

C. Eye Inflammation and Infection

1. **Conjunctivitis**
   a. Inflammation of eye mucosa secondary to bacterial (e.g., *Staphylococcus aureus*, *Streptococcus pneumoniae*) or viral infection or allergic reaction
   b. **H/P** = mildly painful eye, **inflamed conjunctiva**, possible lymphadenopathy, pruritic eye when caused by allergy; purulent discharge often seen with bacterial infection (but can also be seen with viral or allergic conjunctivitis)
   c. **Labs** = Gram stain and culture of discharge may indicate bacterial cause
   d. **Treatment** = self-limited; topical sulfonamides or erythromycin reduce duration of bacterial infection; antihistamines improve symptoms caused by allergic reaction; fastidious handwashing decreases community spread of infection

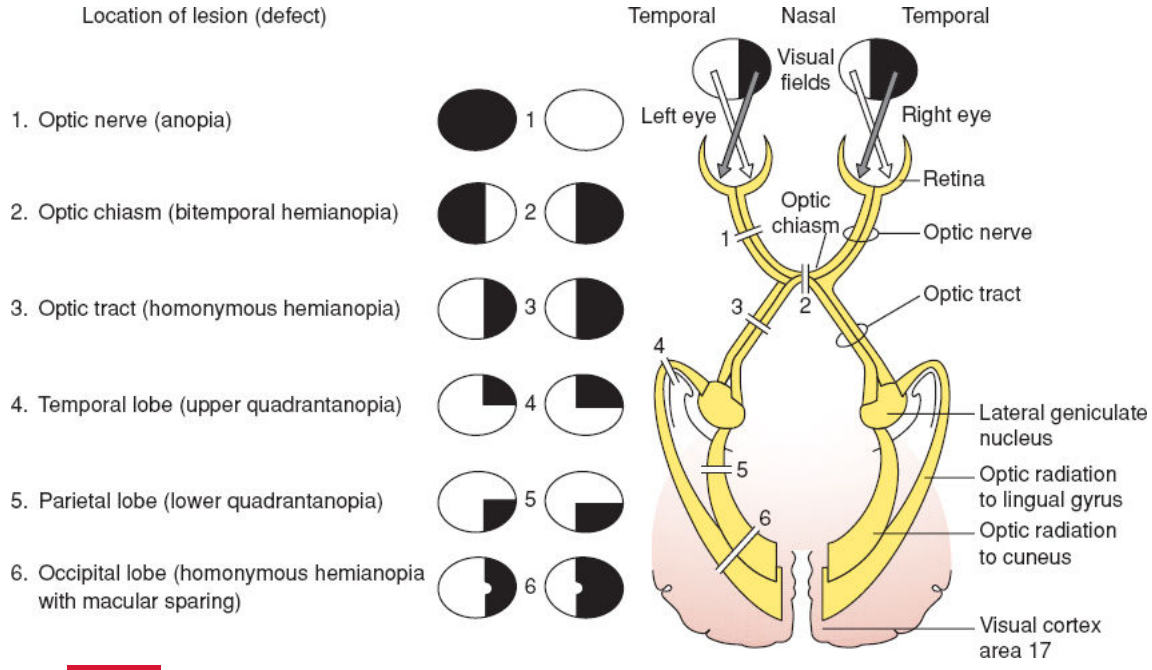


FIGURE **11-6**
Visual field defects resulting from neuronal injury.
(From Mehta, S., Milder, E. A., Mirachi, A. J., & Milder, E. [2006]. *Step-Up: A high-yield, systems-based review for the USMLE step 1* [3rd ed., p. 40]. Philadelphia, PA: Lippincott Williams & Wilkins.)

Table 11-15 Common Pupil and Gaze Abnormalities

Abnormality	Presentation	Cause
Argyll Robertson pupil	Accommodation to near objects, nonreactive to light	Syphilis, SLE, DM
Marcus Gunn pupil	Light in affected pupil causes minimal bilateral constriction, light in normal pupil causes normal bilateral constriction	Afferent nerve defect
Horner syndrome	Ptosis, miosis, anhidrosis	Sympathetic trunk lesion (e.g., Pancoast tumor)
Adie pupil	Minimally reactive dilated pupil	Abnormal innervation of iris
Internuclear ophthalmoplegia	With lateral gaze, there is absent ipsilateral eye adduction	MLF lesion, MS

DM, diabetes mellitus; MLF, medial longitudinal fasciculus; MS, multiple sclerosis; SLE, systemic lupus erythematosus.

Table 11-16 Common Vision Abnormalities

Disorder	Cause	History and Physical	Treatment
Myopia	Refracting power of eye is too great, causing image focal point to be anterior to retina	Blurred vision, vision quality worsens as objects move farther away	Corrective lenses, l
Hyperopia	Refracting power of eye is insufficient, causing image focal point to be posterior to retina	Blurred vision, vision quality worsens as objects move closer	Corrective lenses, l
Astigmatism	Asymmetric cornea surface, causing inconsistent refraction of light	Blurred vision	Corrective lenses
Strabismus	Deviation of eye unable to be overcome by normal motor control	Gaze for each eye is in different directions, double vision, progressive blindness	Vision training, surg to achieve bilateral
Amblyopia	Developmental defect in neural pathways of eye	Poor visual acuity, spatial differentiation in affected eye	Correct visual acuit and patch the unaf use of the affected

2. **Uveitis**
   a. Inflammation of iris, choroids, and ciliary bodies caused by infectious (e.g., viral, syphilis), autoimmune (e.g., ankylosing spondylitis, **juvenile idiopathic arthritis**), or inflammatory (e.g., ulcerative colitis, Crohn disease) conditions
   b. **H/P**
      (1) **Anterior uveitis:** pain and photophobia; slit lamp examination shows inflammation of eye and keratin deposits on cornea
      (2) **Posterior uveitis:** mild vision abnormalities; slit lamp examination shows eye inflammation and retinal lesions
   c. **Treatment** = topical antibiotics if caused by infection; topical or systemic corticosteroids if not caused by infection; treat underlying condition

D. Cataracts

1. **Clouding** of lens leading to progressive vision loss
2. **Risk factors** = trauma (caustic substances), DM, corticosteroid use, age, low education, alcohol use, tobacco use
3. **H/P** = progressive hazy and blurred vision occurring over months to years; examination reveals opacity of lenses and decreased red reflex
4. **Treatment** = lens replacement surgery

Quick HIT

Open-angle glaucoma is the **most common** type of glaucoma.

E. Glaucoma

1. Increased intraocular pressure (IOP) leading to loss of vision
2. **Open-angle glaucoma**
   a. **Gradual** bilateral increase in IOP
   b. **Risk factors** = increased age, increased IOP, blacks, DM, myopia, family history
   c. **H/P** = initially asymptomatic; gradual loss of visual fields (from **peripheral to central**), halos seen around lights, headache, and poor adaptation to changes in light; **cupping** of optic disc seen on funduscopic examination
   d. **Labs** = IOP testing (i.e., tonometry) shows increased pressure over several tests performed at 2- to 4-week intervals
   e. **Treatment**
      (1) Topical β-blockers (e.g., timolol) and α-adrenergic agonists decrease aqueous humor production; prostaglandin analogs, α-adrenergic agonists, and cholinergic agonists (e.g., pilocarpine) increase aqueous humor removal.
      (2) Laser surgery improves aqueous humor drainage in refractory cases.
      (3) Prevention is important for all at-risk patients, who should receive **regular ophthalmologic examinations**.
   f. **Complications** = progressive, permanent vision loss
3. **Closed-angle glaucoma**
   a. **Acute** increase in IOP secondary to narrowing of anterior chamber angle and obstructed drainage of aqueous humor from eye
   b. **Risk factors** = increased age, Asian, hyperopia, dilated pupils (e.g., low-light environments, optometry examination dilation)
   c. **H/P** = severe eye pain, blurred vision, halos seen around lights, nausea, and vomiting; eye is inflamed and **hard** with a **dilated** and nonreactive pupil

d. **Labs** = tonometry demonstrates increased IOP (>21 mm Hg)
e. **Treatment**
   (1) Timolol, apraclonidine, and pilocarpine eye drops to lower pressure acutely.
   (2) Oral/IV acetazolamide or IV mannitol may also be given. Laser iridotomy should be performed to prevent recurrence (frequently performed on unaffected eye as prophylaxis).
f. **Complications** = rapid permanent vision loss

NEXT
STEP

Any patient who requires **frequent changes of lens prescriptions** should be suspected of having glaucoma and pressure testing should be performed.

Quick **HIT**

Closed-angle glaucoma is usually **unilateral**.

NEXT
STEP

Never induce additional pupil dilation during examination of patient with suspected closed-angle glaucoma because it will acutely worsen the condition.

F. Macular Degeneration

1. Atrophic (slow) or exudative (rapid) degeneration of retina, leading to **retinal fibrosis** and **permanent vision loss**
2. **Risk factors** = white, tobacco use, family history, increased age, prolonged sunlight exposure, HTN; female > male
3. **H/P** = painless, gradual loss of vision (**central to peripheral**) at all distances; loss of retinal pigmentation (atrophic type) and hemorrhage (exudative type) in macular region and possible retinal detachment seen on funduscopic examination
4. **Radiology** = fluorescein angiography may show neovascular membranes and retina
5. **Treatment** = dietary supplementation with vitamin C, vitamin E, β-carotene, copper, and zinc may slow progression; intravitreal ranibizumab may help treat exudative lesions near the fovea; laser photocoagulation of discrete lesions may delay progression
6. **Complications** = treatment effectiveness is limited; gradual progression to severe vision loss

Quick **HIT**

Macular degeneration is the most common cause of **bilateral** vision loss in the elderly.

G. Retinal Detachment

1. Separating of retina from adjacent epithelium, leading to acute vision loss
2. **Risk factors** = trauma, cataract surgery, myopia, family history
3. **H/P** = painless acute loss of vision (**"window shade pulled over eye"** or **numerous "floaters"**); pigmented fragments or gray retina floating in vitreous humor seen on funduscopic examination
4. **Treatment** = laser photocoagulation or cryotherapy to halt tear progression and reattachment of retina (may not fully restore loss of vision)

H. Retinal Vessel Occlusion

1. Occlusion of retinal artery or vein resulting in sudden loss of vision
2. Most commonly caused by atherosclerosis, DM, HTN, **thromboembolic disease** (see Figures 11-7 to 11-9)
3. **H/P**
   a. Retinal **artery** occlusion: sudden painless loss of vision; funduscopic examination shows **cherry red** spot in fovea and poor arterial filling
   b. Retinal **vein** occlusion: more gradual painless loss of vision; funduscopic examination shows **cotton wool spots**, edema, **retinal hemorrhages**, and dilated veins
4. **Treatment**
   a. Thrombolysis of arterial occlusion should be performed within 8 hours of onset.
   b. Acetazolamide and O_2 administration also used to decrease congestion and increase perfusion for arterial occlusion.
   c. Laser photocoagulation may be useful for venous occlusion.
5. **Complications** = without prompt treatment, permanent vision loss results

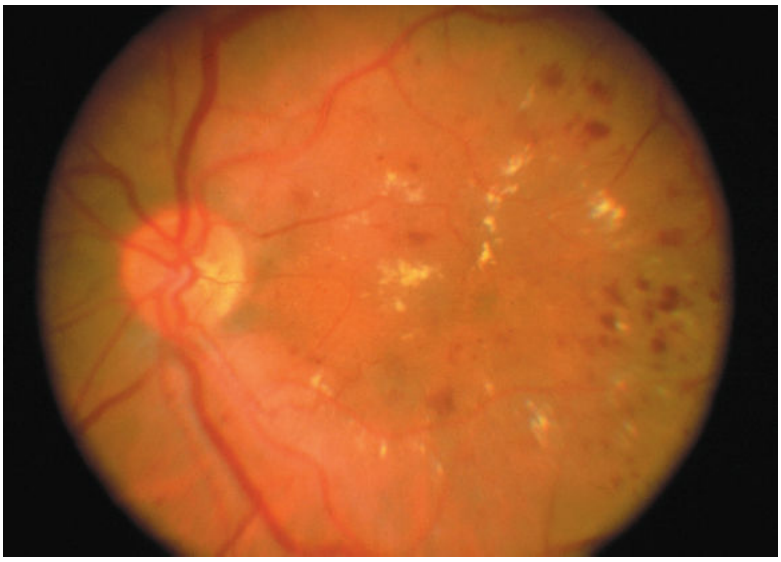


FIGURE 11-7
Diabetic retinopathy.
Note yellowish lipid exudates and multiple small retinal hemorrhages.
(From Rubin, R., & Strayer, D. S. [2012]. *Rubin's pathology* [6th ed., p. 1403]. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; with permission.)

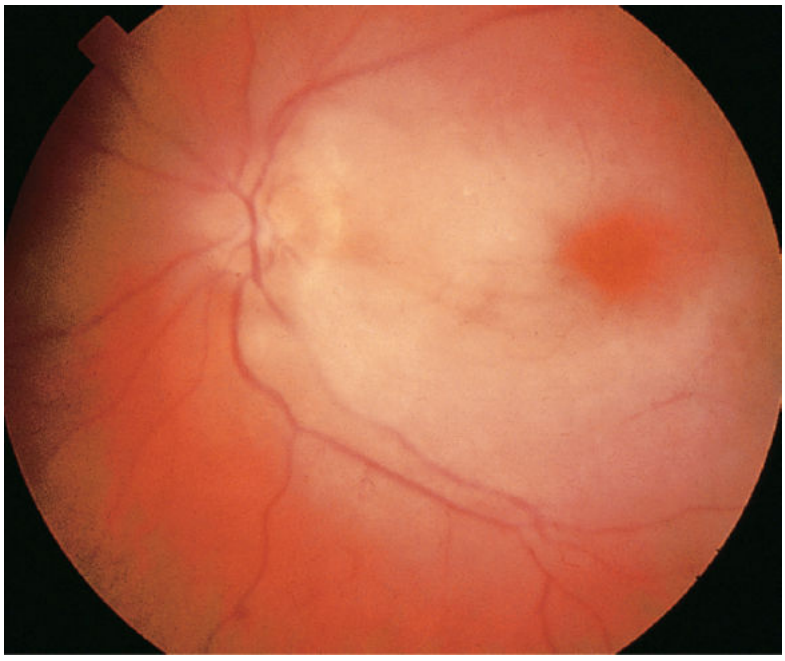


FIGURE 11-8
Retinal artery occlusion.
Note generalized retinal edema and presence of cherry red spot.
(From Gold, D. H., & Weingeist, T. A. [2001]. *Color atlas of the eye in systemic disease* [Figure 75-2]. Philadelphia, PA: Lippincott Williams & Wilkins; with permission.)

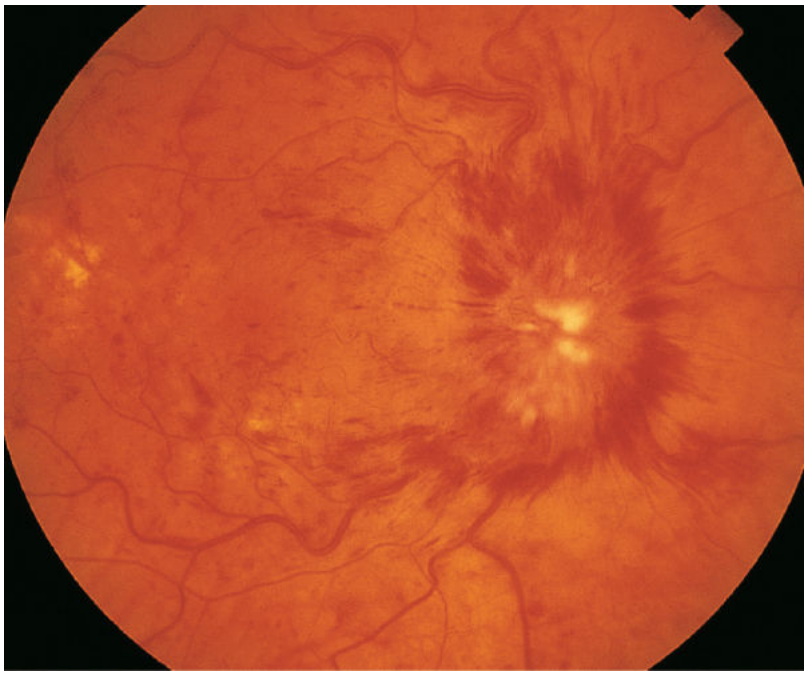


FIGURE 11-9
Retinal vein occlusion.
Note edematous retina, retinal hemorrhages, cotton wool spots, and venous dilation.
(From Gold, D. H., & Weingeist, T. A. [2001]. *Color atlas of the eye in systemic disease* [Figure 29-1]. Philadelphia, PA: Lippincott Williams & Wilkins; with permission.)

XI. Audiovestibular Disorders

A. Otitis Media

1. Infection of middle ear caused by ***S. pneumoniae***, *H. influenzae*, *Moraxella catarrhalis*, ***Streptococcus pyogenes***, or viruses
2. Increased risk in children secondary to shorter and more horizontal ear canal than in adults; pacifier use; hypertrophic tonsillar tissue
3. **H/P** = ear pain, decreased hearing; fever, bulging tympanic membrane with **decreased mobility**, poor light reflex; possible bloody discharge with perforation (i.e., otorrhea)
4. **Treatment**
   a. Initially observation and supportive care
   b. For unresolved cases, amoxicillin for 10 days; resistant strains may require amoxicillin- clavulanic acid or stronger cephalosporins
   c. Recurrent cases may require surgical placement of tympanic tubes to assist in middle ear drainage
5. **Complications** = mastoiditis, meningitis, hearing loss, sigmoid sinus thrombosis, or brain abscess can occur in untreated cases

B. Otitis Externa ("Swimmer's Ear")

1. Infection of ear canal most commonly caused by *S. aureus*, *Pseudomonas*, or *Staphylococcus epidermidis*; frequently associated with water in ears (e.g., swimming)
2. **H/P** = painful, swollen ear with possible white discharge; **ear canal** is red and **swollen**; tenderness of pinna
3. **Treatment** = topical polymyxin, neomycin, and hydrocortisone; oral cephalosporins or ciprofloxacin can be used for *Pseudomonas* infection or infection that spreads to involve skull; topical drying agents after water exposure to prevent recurrent infection

C. Benign Paroxysmal Positional Vertigo (BPPV)

1. Vertigo (i.e., abnormal feeling of rotational movement leading to poor balance and coordination) caused by a dislodged otolith in the inner ear that interferes with semicircular canal stabilization
2. **H/P**
   a. Brief, episodic vertigo that can occur with certain head movements and is accompanied by nausea and vomiting.
   b. Nystagmus may be seen during episodes.
   c. **Dix–Hallpike maneuver** (i.e., moving from sitting to supine while quickly turning head to side) induces symptoms and confirms diagnosis.
3. **Radiology** = CT or MRI can rule out intracranial lesion
4. **Treatment** = physical maneuvers designed to free otolith from semicircular canal can alleviate recurrent episodes

D. Ménière Disease (Endolymphatic Hydrops)

1. Vertigo caused by distension of endolymphatic compartment of inner ear
2. **H/P** = acute vertigo lasting **several hours**, nausea, vomiting, decreased hearing, feeling of ear fullness, tinnitus (ringing in ears)
3. **Labs** = audiometry shows **low-frequency hearing loss**
4. **Treatment** = anticholinergics, antiemetics, and antihistamines improve exacerbations; salt restriction and thiazide diuretics may reduce frequency of episodes; surgical decompression needed in refractory cases
5. **Complications** = progressive hearing loss

E. Acoustic Neuroma (Acoustic Schwannoma)

1. Benign tumor of Schwann cells of CN VIII that can lead to hearing loss secondary to nerve compression
2. **H/P** = hearing loss, dizziness, tinnitus; unilateral facial palsy; decreased sensation may be seen on examination
3. **Labs** = audiometry shows sensorineural hearing loss
4. **Radiology** = MRI can localize tumor
5. **Treatment** = surgical excision
6. **Complications** = large tumors can compress cerebellum or brainstem

Quick HIT

Conductive hearing loss:

- Pathology occurs along conductive pathway from outer ear to inner ear
- Audiometry shows **preserved bone** conduction, but air conduction shows consistently low hearing threshold (abnormal Rinne test).

Sensorineural hearing loss:

- Pathology in neural pathways from ear to brain
- Audiometry shows both **impaired bone** and **air conduction** (asymmetric Weber test, normal Rinne test)

XII. Dementia and Delirium

A. Alzheimer Disease

1. Slowly progressive dementia characterized by neurofibrillary tangles, neuritic plaques, amyloid deposition, and neuronal atrophy; **most common** cause of dementia
2. **Risk factors** = increased age, family history, trisomy 21; female > male
3. **H/P** = progressive **short-term memory loss**, depression, **confusion**, inability to complete complex movements or tasks; severe cases have personality changes and delusions
4. **Labs** = nondiagnostic but can be used to rule out other causes of dementia
5. **Radiology** = CT or MRI shows cortical atrophy
6. **Treatment** = cholinesterase inhibitors (e.g., donepezil, rivastigmine, galantamine) may slow progression; memantine may improve symptoms in moderate disease; occupational therapy helpful to prolong independence
7. **Complications** = median survival following diagnosis is 3 years because of comorbidity

NEXT
STEP

Distinguish dementia from Alzheimer disease from that caused by multiple cortical infarcts with MRI. Multiple small lesions or infarcts will be apparent on MRI when the cause is **vascular**.

B. Frontotemporal Dementia (Pick Disease)

1. Dementia characterized by intracellular inclusions of tau protein (Pick bodies) plus atrophy of the frontal and temporal lobe
2. **H/P**
   a. **Behavioral variant** = behavior and personality changes (e.g., inappropriate social behavior and personal conduct) followed by progressive dementia
   b. **Aphasia variant** = dementia plus progressive nonfluent aphasia
3. **Labs** = nondiagnostic
4. **Radiology** = CT or MRI shows bilateral frontal atrophy (especially in the behavioral variant)
5. **Treatment** = SSRIs, trazodone, or atypical antipsychotics may help control the behavioral symptoms; cholinesterase inhibitors are not beneficial

C. Dementia With Lewy Bodies

1. Dementia characterized by intracellular cortical inclusions called Lewy bodies (eosinophilic inclusions of the protein α-synuclein)

2. **H/P** = fluctuating cognition, impaired attention, visual hallucinations, syncope, frequent falls; limb rigidity, bradykinesia or akinesia, gait disturbance
3. **Labs** = nondiagnostic
4. **Radiology** = CT and MRI show nonspecific generalized cortical atrophy
5. **Treatment** = behavioral therapy; cholinesterase inhibitors may be beneficial; levodopa- carbidopa can be used for disabling parkinsonian symptoms

Quick HIT

Dementia with Lewy bodies may cause movement symptoms similar to Parkinson disease, which is characterized by Lewy bodies in the substantia nigra and other structures.

MNEMONIC

Remember the signs of normal pressure hydrocephalus by the **3 Ws**:

Wacky (cognitive impairment)

Wet (incontinence)

Wobbly (gait abnormalities)

D. Normal Pressure Hydrocephalus

1. Collection of excess CSF in cerebral ventricles and spinal thecal sac; may follow **SAH**, chronic meningitis, or other disease of impaired CSF resorption
2. **H/P** = cognitive impairment, incontinence, gait abnormalities
3. **Labs** = LP shows normal pressure, but removal of CSF can cause improvement in symptoms
4. **Radiology** = MRI shows enlarged cerebral ventricles, white matter lesions, and aqueduct atrophy
5. **Treatment** = ventriculoperitoneal shunting

E. Delirium

1. Altered state of consciousness
   a. Most commonly secondary to:
      (1) **Drugs** (e.g., alcohol, corticosteroids, benzodiazepines, antipsychotics, anticholinergics, antihistamines, etc.)
      (2) Infection, **hypoxia**, or CNS abnormalities
   b. It is frequently quickly reversible once the underlying cause is identified and treated
2. **H/P**
   a. Key features (see Table 11-17)
      (1) Altered level of consciousness with inattentiveness and confusion
      (2) Change in cognition is not caused by pre-existing dementia
      (3) Changes in cognition develop quickly and fluctuate over the course of the day
      (4) Changes are related to disease, medication, or drug use
      (5) Psychomotor agitation or retardation, disturbance of sleep patterns.
      (6) Emotional instability
3. **Labs** = should address potential metabolic or pharmacologic causes
4. **Radiology** = CT can be used to assess CNS insult
5. **Treatment**
   a. Treat underlying cause
   b. Reorientation through observation, reassurance, normalization of sleep–wake cycles, and decreasing excess stimuli improves behavior.
   c. Avoid restraints because they frequently exacerbate delirium (use only if patient is at danger of harming self).
   d. Antipsychotics (e.g., haloperidol) can be used to decrease agitation acutely.

Quick HIT

Elderly patients are particularly susceptible to delirium during inpatient stays.

Quick HIT

Delirium differs from "**sundowning**," the deterioration of behavior during evening hours in patients with dementia, in that it occurs in patients without a history of dementia and can be linked to a medical or substance-related cause.

Table 11-17 Comparison of Delirium and Dementia

Characteristics	Delirium	Dementia
Onset	Acute	Gradual
Daily course	Fluctuating cognitive function and behavior	Generally consistent; sundowning
Level of consciousness	Decreased	Normal
Orientation	Aware of self; impaired for time and place	Generally impaired
Thought production	Disorganized, flight of ideas	Impoverished
Psychotic features	Delusions, hallucinations	Minimal
Memory	Short-term impairment	Short- and long-term impairment
Prognosis	Reversible	Usually irreversible

NEXT
STEP

Do **not** use **benzodiazepines** or **anticholinergics** in the treatment of delirium or dementia-related agitation because they can **worsen** symptoms.

QUESTIONS

1. An 82-year-old woman on warfarin for atrial fibrillation presents with left-sided hemiplegia, an NIHSS of 11, with onset of symptoms 3 hours and 40 minutes ago. Should this patient receive tPA?

   A. Yes
   B. No

2. A 67-year-old woman presents due to contralateral paresis and sensory loss in the face and arm about 25 minutes ago. Where is the lesion?

   A. ACA
   B. MCA
   C. PCA
   D. Not localizable based on information given

3. In which of the following seizure types is consciousness preserved?

   A. Complex partial seizures
   B. Absence seizures
   C. Generalized tonic–clonic seizures
   D. Simple partial seizures

4. A 9-year-old boy is diagnosed with absence seizures. What is the first-line treatment (drug) of choice?

   A. Valproic acid
   B. Phenytoin
   C. Lorazepam
   D. Ethosuximide

5. Which of the following medications is used in the treatment of amyotrophic lateral sclerosis?

   A. Riluzole
   B. Methylprednisolone
   C. Cyclophosphamide
   D. Bromocriptine

6. Hyperprolactinemia causes all of the following except:

   A. Amenorrhea
   B. Galactorrhea
   C. Gynecomastia
   D. Increased libido

7. What is the mechanism by which donepezil works to mitigate the slow cognitive decline associated with Alzheimer?

   A. Reversible acetylcholinesterase inhibitor
   B. Dopamine agonist
   C. Selective serotonin reuptake inhibitor
   D. Dopamine antagonist

12
Gynecologic and Breast Disorders

I. Menstrual Physiology

A. Gynecologic Development

1. Reproductive changes driven by follicle-stimulating hormone (FSH) and luteinizing hormone (LH) levels (see Table 12-1, Figure 12-1).
2. Secondary sexual characteristics are caused by androgens.
3. Tanner stages describe breast and pubic hair development during puberty (see Table 12-2).

Table 12-1 Gynecologic Development by Age

Age	Hormone Levels	Characteristics
Fetal to 4 yrs	High intrauterine FSH and LH that peak at 20-wk gestation and decrease until birth FSH and LH increase again from birth until 6 mo of age then gradually decrease to low levels by age 4 yrs	All oocytes formed and partially matured by 20-wk gestation Tanner stage 1 characteristics
4–8 yrs	Low FSH, LH, and androgen levels caused by GnRH suppression	Tanner stage 1 characteristics Any sexual development considered precocious
8–11 yrs	LH, FSH, and androgen levels begin to increase	Initial pubertal changes, including early breast development and pubic and axillary hair growth
11–17 yrs	Further increase of LH, FSH, and androgens to baseline mature levels Hormones secreted in pulsatile fashion (higher at night) caused by sleep-associated increase in GnRH secretion	Puberty Progression through Tanner stages Development of secondary sexual characteristics and growth spurt Menarche in females (beginning of menstrual cycles) and further oocyte maturation
17–50 yrs (females)	LH and FSH follow menstrual cycle Gradual increase in FSH and LH with ovarian insensitivity	Menstrual cycles Mature sexual characteristics
≥50 yrs (females)	LH and FSH levels increase with onset of ovarian failure	Perimenopause: menstrual cycles become inconsistent (oligomenorrhea) Menopause: menstrual cycles cease (amenorrhea)

FSH, follicle-stimulating hormone; GnRH, gonadotropin-releasing hormone; LH, luteinizing hormone.

Quick HIT

The mean age of menarche is 13 years in the United States and tends to occur earlier in blacks than in whites.

Quick HIT

Order of events of normal female puberty: adrenarche (adrenal androgen production), gonadarche (activation of gonads by FSH and LH), thelarche (appearance of breast tissue), pubarche (appearance of pubic hair), growth spurt, menarche (onset of menses).

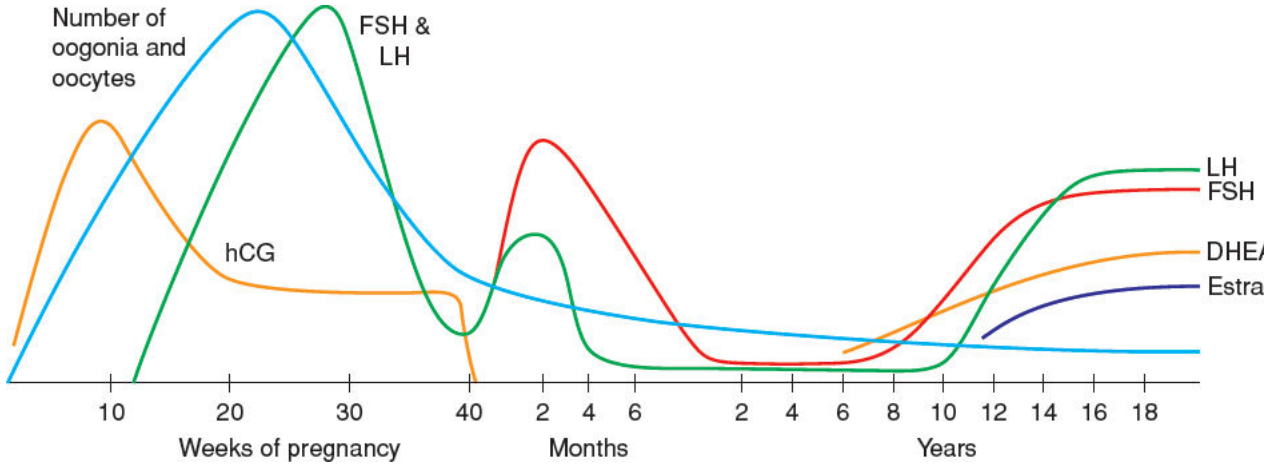


FIGURE **12-1**

Changes in hormone and oogonia (egg) levels with gestation and age.
DHEA, dehydroepiandrosterone; FSH, follicle-stimulating hormone; hCG, human chorionic gonadotropin; LH, luteinizing hormone.
(From Fritz, M. A., & Speroff, L. [2011]. *Clinical gynecologic endocrinology and infertility* [8th ed., p. 939]. Philadelphia, PA: Lippincott Williams & Wilkins; with permission.)

Table 12-2 Tanner Stages for Female Breast and Hair Development

Tanner Stage	Breast Development	Pubic Hair Development
1	Prepubertal: raised papilla (nipple) only	Prepubertal: no hair growth
2	Breast budding, areolar enlargement	Slight growth of fine labial hair
3	Further breast and areolar enlargement	Further growth of hair
4	Further breast enlargement: areola and papilla form secondary growth above level of breast	Hair becomes coarser and spreads over much of pubic region
5	Mature breast: areola recedes to level of breast while papilla remains extended	Coarse hair extends from pubic region to medial thighs

B. Precocious Puberty

1. Development of pubertal changes in girls <8 years
2. Because of **early activation of the hypothalamic–pituitary–gonadal axis** (central precocious puberty) or autonomous excess secretion of sex steroids (pseudoprecocious puberty)
3. Types
   a. **Isosexual**
      (1) Premature sexual development appropriate for gender
      (2) Can be complete (i.e., all sexual characteristics develop prematurely) or incomplete (i.e., only one sexual characteristic develops prematurely)
   b. **Heterosexual**
      (1) Virilization/masculinization of girls or feminization of boys
      (2) In girls, most commonly results from congenital adrenal hyperplasia (CAH), exposure to exogenous androgens, or androgen-secreting neoplasm
4. **H/P**
   a. Complete isosexual: normal pubertal changes take place but at **earlier-than-normal age**
   b. Incomplete isosexual: premature breast budding (i.e., **thelarche**), axillary hair growth, or pubic hair growth (i.e., **pubarche**) may take place
5. **Labs**

***Quick* HIT**

Precocious puberty in boys occurs <9 years and is most commonly caused by adrenal hyperplasia.

***Quick* HIT**

Central nervous system lesions or **traumas** are causes of isosexual precocious puberty in approximately 10% of cases.

   a. Increased LH and FSH with additional release following administration of gonadotropin-releasing hormone (GnRH) suggest central precocious puberty; low LH and FSH with no response to GnRH suggest pseudoprecocious puberty.

b. Increased estrogen in the presence of low LH and FSH suggests ectopic hormone production (neoplasm) or consumption of exogenous estrogen; significantly high levels of adrenal steroids may be seen with neoplasm or CAH.
c. Increased thyroid-stimulating hormone (TSH) with low thyroxine (T_4) and triiodothyronine (T_3) suggests precocious puberty in response to chronic hypothyroidism.

6. **Radiology** = magnetic resonance imaging (MRI) or computed tomography (CT) with contrast may detect cerebral or adrenal lesions
7. **Treatment**
   a. **GnRH analogs** are useful for LH and FSH suppression in central precocious puberty.
   b. Precocious puberty secondary to ectopic hormone secretion should be treated by locating and removing the source of the hormone.
   c. Precocious puberty caused by CAH should be treated with cortisol replacement (see Chapter 8, **Endocrine Disorders**).
   d. Complete precocious puberty with an onset close to the expected start of puberty may not require treatment.
   e. Incomplete precocious puberty requires only observation to make sure that it does not become complete precocity.
8. **Complications** = short stature (bones fuse at early age); social and emotional adjustment issues

C. Normal Menstrual Cycle (See Figure 12-2)

1. LH, FSH, estrogen, progesterone, and human chorionic gonadotropin (hCG) all play roles in the menstrual cycle (see Table 12-3).
2. **Follicular phase**
   a. Begins at first day of menses (i.e., menstruation).
   b. **FSH** stimulates **growth** of **ovarian follicle** (granulosa cells), which in turn secretes estradiol.
   c. **Estradiol** induces **endometrial proliferation** and further increases FSH and LH secretion from positive feedback of pituitary.
3. **Luteal phase**
   a. **LH** surge induces **ovulation**. Ovulation is the transition from the follicular phase of the menstrual cycle to the luteal phase. Cervical mucus immediately before ovulation is copious, thick, and clear, which is an indication of LH surge.
   b. Residual follicle (i.e., **corpus luteum**) secretes estradiol and progesterone to **maintain endometrium** and induce development of secretory ducts.
   c. High estradiol levels inhibit FSH and LH.
   d. If the egg is **not** fertilized, corpus luteum degrades, progesterone and estradiol levels decrease, and the **endometrial lining degrades** (i.e., menses).
4. **Fertilization**

Table 12-3 Roles of Hormones Involved in the Menstrual Cycle

Hormone A	Effects
Luteinizing hormone (LH)	Midcycle **surge** induces **ovulation** Regulates cholesterol conversion to pregnenolone in ovarian theca cells as initial step in estrogen synthesis
Follicle-stimulating hormone (FSH)	Stimulates **development** of **ovarian follicle** Regulates ovarian granulosa cell activity to control estrogen synthesis
Estrogens (estradiol, estriol)	Stimulates **endometrial proliferation** Aids in follicle growth Induces LH surge High levels inhibit FSH secretion Principal role in sexual development
Progesterone	Stimulates **endometrial gland development** Inhibits uterine contraction Increases thickness of cervical mucus **Increases basal body temperature** Inhibits LH and FSH secretion; maintains pregnancy **Decrease** in levels leads to **menstruation**
Human chorionic gonadotropin (hCG)	Acts like LH after implantation of fertilized egg **Maintains corpus luteum viability** and progesterone secretion

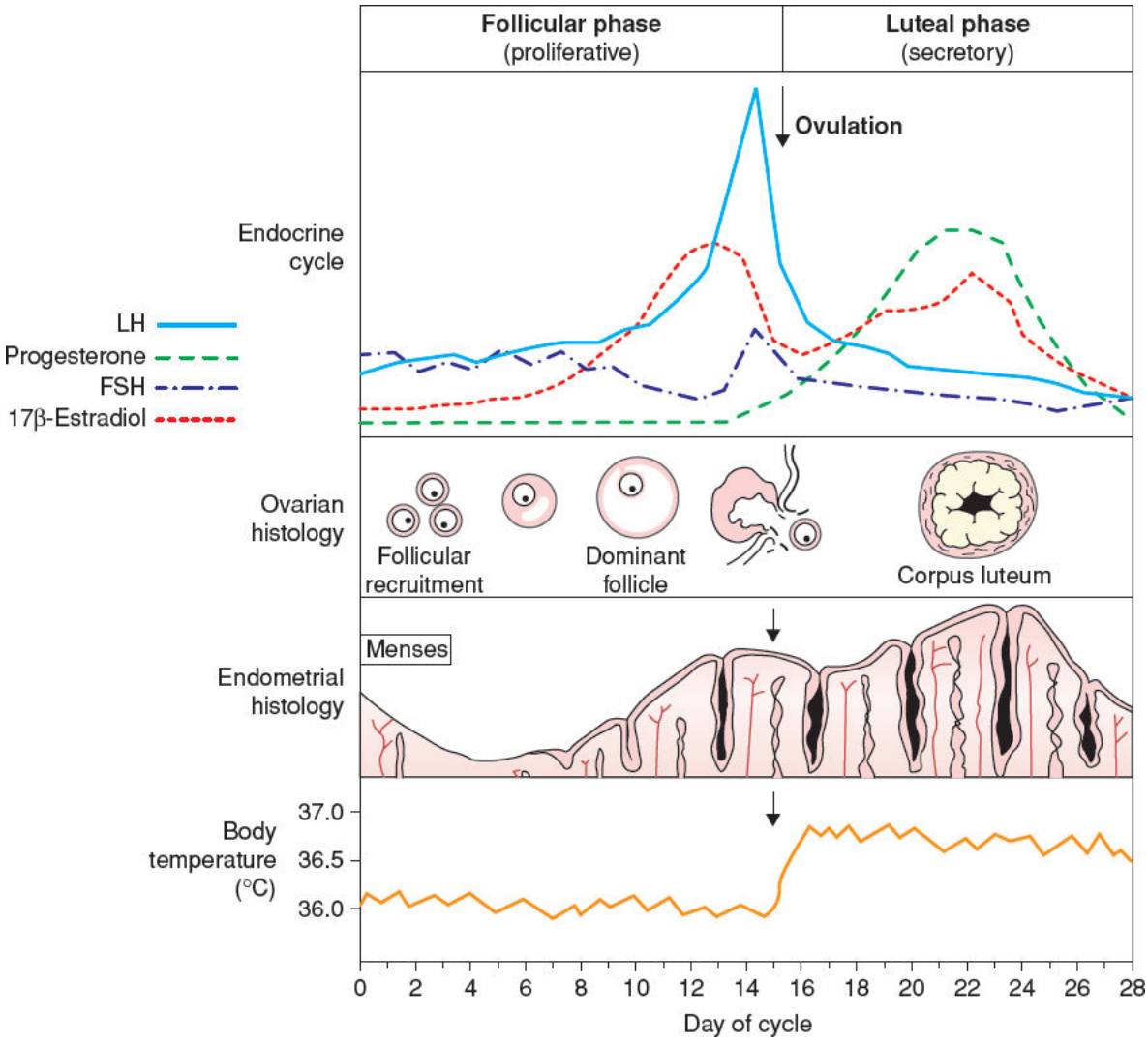


FIGURE **12-2**

Hormone levels during the menstrual cycle with appropriate ovarian, endometrial, and basal body temperature responses.
FSH, follicle-stimulating hormone; LH, luteinizing hormone.
(Modified from Mehta, S., Milder, E. A., Mirachi, A. J., & Milder, E. [2006]. *Step-Up: A high-yield, systems-based review for the USMLE step1* [3rd ed., p. 196]. Philadelphia, PA: Lippincott Williams & Wilkins.)

a. If the egg is fertilized, it will implant in the endometrium.
b. Endometrial tissue secretes **hCG to maintain the corpus luteum.**
c. Corpus luteum continues to secrete progesterone until sufficient production is achieved by a developing placenta (~8 to 12 weeks).

Quick HIT

One year of amenorrhea is required for a diagnosis of menopause.

D. Menopause

1. **Permanent** end of menstruation because of **ceasing of ovarian function** in later middle age (~51.5 years)
2. Premature menopause is defined as ovarian failure before age 40 years (more likely with history of tobacco use, radiation therapy, chemotherapy, autoimmune disorders, or abdominal or pelvic surgery)
3. During evolution of menopause (i.e., **perimenopausal** period), ovarian response to FSH and LH decreases, whereas FSH and LH levels increase and estrogen levels fluctuate
4. **H/P** = **hot flashes** (secondary to thermoregulatory dysfunction), breast pain, sweating, **menstrual irregularity** with eventual **amenorrhea,** possible menorrhagia, fatigue, anxiety, irritability, depression, **dyspareunia** (caused by vaginal wall atrophy and decreased lubrication), urinary frequency, dysuria, change in bowel habits, sleep disturbances, decreased libido, cognitive decline; examination detects vaginal atrophy
5. **Labs** = increased FSH, increased LH, decreased estradiol
6. **Treatment**
   a. Lubricating agents to treat dyspareunia (i.e., painful intercourse); short-term topical vaginal estrogen used in cases of significant vaginal symptoms
   b. The first-line treatment for hot flashes is weight loss
   c. Calcium, vitamin D, bisphosphonates, and exercise to prevent osteoporosis

d. Selective estrogen receptor modulators, such as raloxifene and tamoxifen, may serve a role in reducing osteoporosis and cardiovascular risks
e. Hormone replacement therapy poses an increased risk for breast cancer and deep vein thrombosis

7. **Complications** = osteoporosis, coronary artery disease, dementia

Quick HIT

Topical estrogen use is contraindicated in any patient with a history of breast cancer.

Quick HIT

Increased risk of **osteoporosis** in menopausal women is caused by **decreased estrogen** production by the ovaries.

Quick HIT

Risk factors for osteoporosis are advanced age, postmenopausal, low body weight, white or Asian, smoking, ETOH, and vitamin D deficiency.

II. Contraception

A. Methods of contraception attempt to prevent pregnancy (see Table 12-4).

B. The various forms of contraception are each associated with certain side effects.

C. Method Choice

1. Should consider likelihood of patient compliance.
2. Side effects must be tolerated by patient.
3. Certain methods may be contraindicated for comorbid medical conditions.

Table 12-4 Methods of Contraception

Method	Description	Effectiveness[a] Ideal (%)	Effectiveness[a] Typical (%)	Side Effects
Hormonal Methods				
Oral contraceptive pills (OCPs) (combined formulation)	• Estrogen–progestin combination of pills that inhibits follicle development and ovulation, changes endometrial quality, and increases cervical mucus viscosity to prevent fertilization and implantation	99	92	• Possible nausea, h mood changes • Increased risk of D • Contraindicated fo women with a hist gen-related cancer hypertriglyceridem
Oral contraceptive pills (progestin formulation)	• Progestin-only pills that change endometrial quality and increase cervical mucus viscosity to prevent fertilization and implantation • May be an option for women with contraindication for estrogen	98	88–91	• Increased breakthr • Must be taken at s to maximize effica
Medroxyprogesterone acetate (Depo-Provera)	• Progestin analog injected by health care provider every 3 mo that inhibits ovulation and endometrial development	99	97	• Nausea, headache porosis • Irregular bleeding
Progestin implant	• Subcutaneous implant that slowly releases progestin over ~3 yrs (similar activity to progestin-only pill)	100[b]	100[b]	• Irregular bleeding,
Transdermal contraceptive patch	• Transdermal delivery of estradiol and progestin analog to act in similar manner to OCPs • Patch must be changed weekly	99	99	• Risk of patch detac • Nausea, headache • Irregular bleeding, • Less effective in h because of diffusio • Increased risk of D

Intravaginal ring	• Ring inserted intravaginally that releases ethinyl estradiol over 3 wks to prevent ovulation (less estrogen than OCPs) • Replaced each mo	99	92	• Withdrawal bleedi discomfort, headac • Increased risk of D
Emergency contraception	• Regimen of estradiol and progestin taken within 72 hrs of unprotected intercourse or intercourse with failed contraception method (e.g., broken condom) to prevent ovulation or inhibit fertilization • Levonorgestrel (plan B) • Copper intrauterine device (IUD) inserted within 4–5 days of intercourse interferes with sperm function • Mifepristone (RU 486) interrupts new pregnancy	>90	>90	• Nausea, headache that seen with OCI • Menstrual bleedin 1 wk of administra
Barrier Methods				
Condom	• Barrier (most frequently latex) placed over penis and left in place until withdrawal following ejaculation • Frequently used with spermicide • Polyurethane condoms are produced for those with latex allergy	98	85	• Risk of condom bre • Latex significantly other materials (wi tion of polyurethar • Risk of latex allerg
Diaphragm or cervical cap	• Barrier inserted into vagina before intercourse to cover cervix • Used with spermicide and left in place for several hrs after intercourse	94	84	• Inconvenient • Frequent poor com • Increased risk of U
Contraceptive sponge	• Polyurethane sponge implanted with spermicide that releases spermicide over 24 hrs after insertion to inhibit fertilization	91[c]	80[c]	• Possible increased syndrome
Spermicide alone	• Insertion of spermicidal jelly or cream into vagina immediately before intercourse	82	71	• Correct usage and achieve consistent
Sexual Practice Methods				
Abstinence	• Not engaging in intercourse	100	100	• None
Rhythm method	• Recording occurrence of menses, daily basal body temperature, and cervical mucus to determine timing of cycle, occurrence of ovulation, and period of fertility	95	83	• May be useful in d
Withdrawal method	• Withdrawal of penis from vagina immediately before ejaculation	96	73	• Decreased pleasur • Difficult to conduct
Lactation	• Unprotected intercourse during active postpartum lactation period	98	95	• Only able to be per breastfeeding, <6 and amenorrheic (p contraception rate
Intrauterine Devices				
Copper IUD	• Object inserted into uterus by physician with slow release of copper to prevent fertilization and interfere with sperm transportation • Left in place, 10 yrs • May be placed soon after intercourse as emergency contraception (90% decrease in pregnancy rate)	99	99	• Small risk of spont uterine perforation • Menorrhagia
Progestin-releasing IUD	• Object inserted into uterus by physician with slow release of progestin to prevent fertilization, interfere with sperm transportation, and inhibit ovulation • Left in place ~5 yrs	99	99	• Small risk of spont uterine perforation

Surgical Methods				
Sterilization	• Cutting of vas deferens in men (vasectomy) or tubal ligation in women to prevent fertilization	~100	~100	• May be difficult to • Increased risk of e in cases of failure ligation reversal

[a]As defined by pregnancy rate with 1 yr of use (6 mo for lactation).
[b]Only one efficacy study performed; no pregnancies occurred in study.
[c]Effectiveness decreases to 80%/60% in women with prior vaginal birth history.
DVT, deep venous thrombosis; UTI, urinary tract infection.

III. Menstrual Disorders and Issues

A. Amenorrhea

1. Absence of menstruation
   a. **Primary:** absence of menses (**never** has happened) with normal secondary sexual characteristics by a 16 year old or absence of both menses and secondary sexual characteristics by a 13 year old
   b. **Secondary:** absence of menses for 6 months or for >3 cycles in patient with **prior history of menses**
2. **Etiology**
   a. Primary: hypothalamic or pituitary dysfunction, anatomic abnormalities (e.g., absent uterus, vaginal septa), **chromosome abnormalities** with gonadal dysgenesis
   b. Secondary: pregnancy, ovarian failure, hypothalamic or pituitary disease, uterine abnormalities (e.g., Asherman syndrome), polycystic ovary syndrome (PCOS), anorexia nervosa, malnutrition, thyroid disease, medications (hormonal contraception, dopamine antagonists)
   c. Primary ovarian insufficiency (hypergonadotropic hypogonadism): cessation of ovarian function before 40 years old
3. **H/P**
   a. History should address occurrence of any previous menstruation periods (e.g., primary or secondary amenorrhea), exercise and eating habits (e.g., substantial exercise or inadequate eating), family history, medications, androgenous symptoms (e.g., facial hair, voice deepening), and known comorbidity.
   b. Examination should note Tanner stages (see Table 12-2) and should check for normal sexual anatomy.

Quick HIT

Amenorrhea athlete's triad is amenorrhea, osteoporosis, eating disorder.

Quick HIT

Asherman syndrome (uterine synechiae) is intrauterine adhesions resulting from a surgical procedure or possibly infection.

4. **Labs**
   a. β-**hCG test** used to rule out pregnancy (see Figure 12-3)
   b. TSH, LH, FSH, and PRL
   c. Increased **prolactin** suggests prolactin-secreting tumor
   d. FSH and LH levels measure hypothalamic–pituitary activity
   e. Increased androgens (e.g., testosterone, dehydroepiandrosterone [DHEA]) suggest PCOS
   f. **Progestin challenge** (i.e., patient is observed for bleeding after 5-day administration of progesterone) and **estrogen–progesterone challenge** (i.e., patient is observed for bleeding after administration of estrogen and progesterone) can help detect anatomic abnormalities (bleeding indicates normal outflow tract), hormonal abnormalities, or hypothalamic–pituitary activity

NEXT
STEP

β-**hCG pregnancy test** is always the first step in the workup of any type of amenorrhea.

NEXT
STEP

If testicles are present in an XY patient with androgen insensitivity syndrome, they should be **removed** at an early age because of increased risk of **testicular cancer**.

5. **Treatment**
   a. Modify behaviors (e.g., eating disorders, exercise) to allow menstruation.
   b. Anatomic abnormalities require surgical correction.
   c. Hypothalamic–pituitary dysfunction may be treatable by GnRH or gonadotropin replacement.
   d. Prolactinoma may be treated with dopamine agonists.
   e. Hormone replacement therapy may be considered in ovarian failure.
   f. Lysis of adhesions and estrogen administration performed for Asherman syndrome.
   g. Thyroid dysfunction and Cushing syndrome treated according to specific pathology.
   h. In some untreatable patients with appropriate anatomy, pregnancy may be accomplished through egg donation, in vitro fertilization, and hormone modulation.
6. **Complications** = patients with genetic disorders or ovarian failure may be unable to achieve normal menstrual cycles

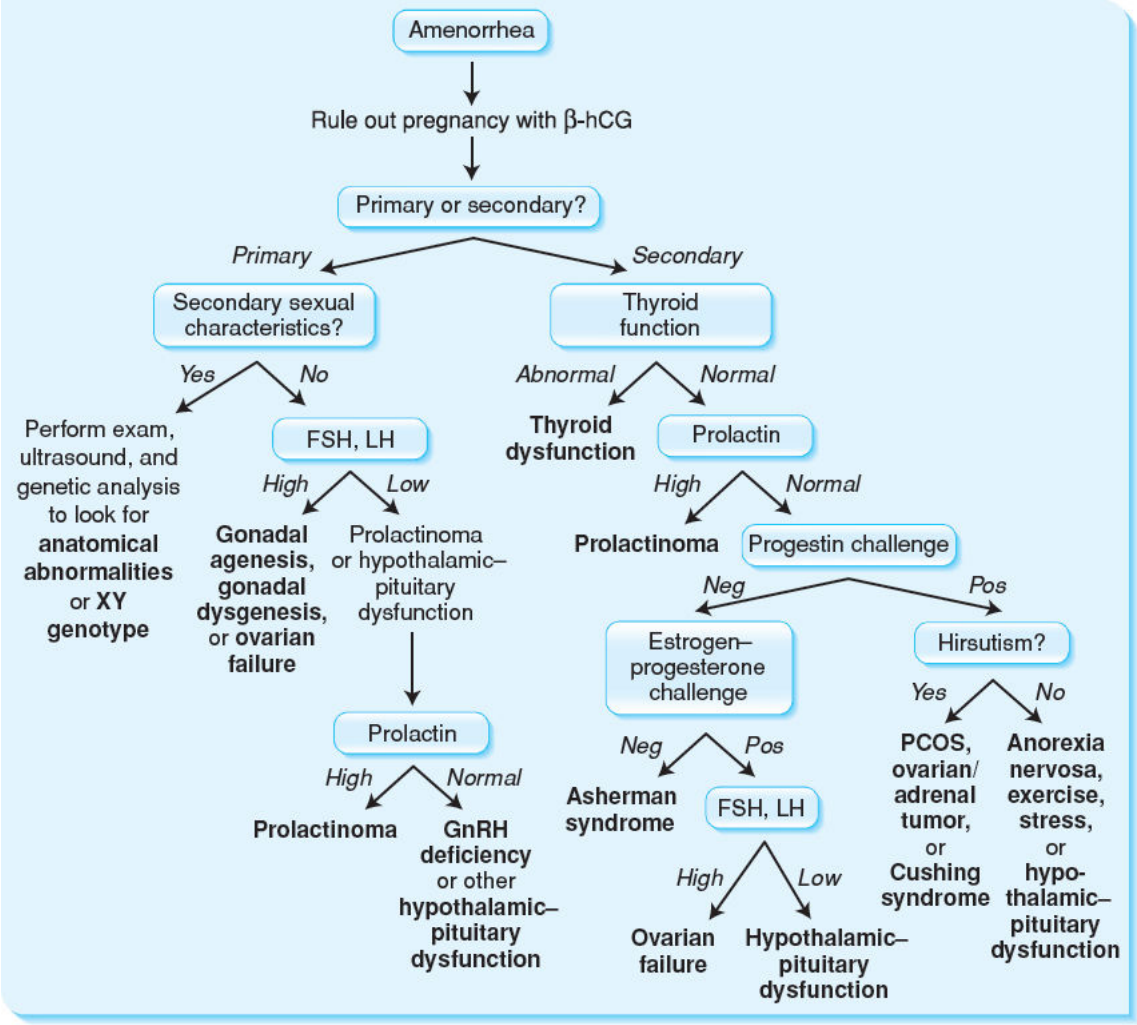


FIGURE **12-3**
Approach to the patient with amenorrhea.
FSH, follicle-stimulating hormone; GnRH, gonadotropin-releasing hormone; β-hCG, human chorionic gonadotropin; LH, luteinizing hormone; Neg, negative; PCOS, polycystic ovary syndrome; Pos, positive.

Quick HIT

Primary dysmenorrhea symptoms occur in the **beginning** of menstruation and resolve over several days; **secondary** dysmenorrhea symptoms often begin **midcycle** before the onset of menstruation and increase in severity until the conclusion of menstruation.

B. Dysmenorrhea

1. Periodic pain associated with menses that may be primary (without pelvic pathology) or secondary (caused by endometriosis, pelvic inflammatory disease [PID], uterine fibroids, ovarian cysts, or adenomyosis)
2. **Risk factors** = menorrhagia, menarche <12 years, body mass index <20, PID, sexual assault, smoking, premenstrual syndrome (PMS)
3. **H/P** = crampy lower abdominal pain associated with menstruation, nausea, vomiting, headache, diarrhea; mild abdominal tenderness
4. **Labs** = β-hCG and blood and vaginal cultures are helpful to rule out pregnancy and infection
5. **Radiology** = ultrasound (US) may be used to detect ovarian and uterine lesions; hysteroscopy or laparoscopy may be needed to detect intrauterine pathology, intra-abdominal pathology, or endometriosis
6. **Treatment** = nonsteroidal anti-inflammatory drugs (NSAIDs) or oral contraceptive pills (OCPs) for primary disorders; treat underlying infection or uterine disease

Quick HIT

Mittelschmerz is recurrent mild and unilateral mid cycle pain prior to ovulation. These episodes of pain last hours to days.

C. Premenstrual Syndrome (PMS) and Premenstrual Dysphoric Disorder (PMDD)

1. Syndromes seen in women with normal functioning ovaries that precede menses (luteal phase) and are characterized by multiple pain, mood, and autonomic symptoms; mood symptoms are more severe in PMDD
2. Most women with menstrual cycles experience some symptoms, but **5% to 10% of women** have severe symptoms that **interfere with daily life**
3. **Risk factors** (for severe symptoms) = family history
4. **H/P** = weight gain, headache, abdominal or pelvic pain, abdominal bloating, change in bowel habits, food cravings, mood lability, depression, fatigue, irritability; breast tenderness, edema, abdominal tenderness, acne
5. **Treatment** = exercise, vitamin B_6, NSAIDs, OCPs, progestins; SSRIs ± alprazolam may improve mood symptoms in both PMS and PMDD

NEXT
STEP

Any woman of childbearing age with abdominal pain must be given a β-hCG pregnancy test to rule out **ectopic pregnancy**.

D. Endometriosis

1. Presence of **endometrial tissue outside the uterus** (e.g., ovaries, broad ligament); ectopic tissue follows same menstrual cycle as normal tissue
2. Retrograde menstruation, vascular/lymphatic spread of endometrial tissue from uterus to pelvic cavity, or iatrogenic spread of endometrial tissue (e.g., during cesarean section) are most plausible causes of condition
3. **Risk factors** = family history, **infertility,** nulliparity (i.e., no history of childbirth), low body mass index
4. **H/P** = dysmenorrhea, dyspareunia, painful bowel movements (i.e., dyschezia), **pelvic pain** that peaks 1to 2 weeks before menses, possible infertility; uterine or adnexal tenderness; palpable adhesions on uterus or ovaries
5. **Labs** = **biopsy** of lesions shows **endometrial tissue;** β-hCG and urinalysis are helpful to rule out pregnancy and urinary tract infection; CA-125 marker frequently increases but is not a highly sensitive test
6. **Radiology** = **laparoscopy** will show **"powder-burn"** lesions and cysts on involved areas and is an optimal diagnostic tool
7. **Treatment**
   a. Recording a journal of symptoms is useful for defining treatment.
   b. OCPs, progestins, danazol, or GnRH agonists may supply symptomatic relief.
   c. Laparoscopic ablation may successfully remove lesions while maintaining fertility potential.
   d. Hysterectomy, lysis of adhesions, or salpingo-oophorectomy may be required in severe cases. Surgical pathology after hysterectomy provides the definitive diagnosis.
8. **Complications** = fertility may not be achieved despite pharmacologic or laparoscopic intervention

NEXT
STEP

If a patient suspected of having PMS or PMDD has mood symptoms **throughout** her menstrual cycle, initiate a psychiatric workup for a mood disorder. Evaluate by asking the patient to keep a symptom/menstrual diary for 2 to 3 menstrual cycles. Menstrual-related symptoms should **only** occur in the **second half** of the cycle.

Quick HIT

Endometriosis is the **most common** cause of **female infertility** and may be responsible for up to 50% of cases.

E. Abnormal Uterine Bleeding

1. **Irregular** menstruation, excessive menses (i.e., menorrhagia), or **increased duration** of menses that may be the result of a variety of causes (e.g., uterine fibroids, endometrial cancer or hyperplasia, hypothalamic–pituitary dysfunction, bleeding diathesis [e.g., von Willebrand disease–impaired platelet aggregation], threatened abortion, molar pregnancy, ectopic pregnancy)
2. **H/P** = Uterine bleeding that does not follow usual menstrual cycle or occurs in postmenopausal women. Menses with **<24-day or >35-day intervals, lasting >7 days, or blood loss >80 mL** (more than one menstrual pad every 2 hours), **or irregular frequency** are considered abnormal
3. **Labs** = β-hCG, complete blood count (CBC), coagulation studies, TSH, FSH, and LH; Papanicolaou (Pap) smear and endometrial biopsy (obtained during dilation and curettage [D&C]) used to rule out cancer; STI testing
4. **Radiology** = US may detect uterine lesions; hysteroscopy frequently indicated to visualize lesions and perform D&C
5. **Treatment** = treat underlying disorder (e.g., coagulopathies, thyroid disease, infection). OCPs can be used for cycle irregularity. Endometrial ablation for severe or recurrent bleeding

Quick HIT

Adenomyosis is endometrial tissue that invades the myometrium, causing symmetric uterine enlargement, uterine tenderness, cyclical pelvic pain, heavy menses. Often presents as chronic pelvic pain in a woman over 40 years old.

F. Polycystic Ovary Syndrome (PCOS)

1. Hypothalamic–pituitary disease characterized by **anovulation** or **oligoovulation** (manifested as amenorrhea/oligomenorrhea), **androgen excess,** and **polycystic ovaries.**
2. **Excess LH secretion** induces overproduction of androgens by ovaries.
3. Some patients with PCOS may have hyperinsulinemia, which induces androgen production and increases risk of insulin resistance.
4. **Excess androgens** produced by ovaries and adrenals are converted to estrogen, which induces further ovarian androgen production.
5. LH/FSH imbalance results in absence of LH surge which inhibits follicle maturation and oocyte release (amenorrhea and infertility).
6. Hirsutism results from an increase in androgens.
7. **H/P** = **metabolic syndrome** (obesity, diabetes mellitus, hypertension), **hirsutism, acne,** menstrual dysfunction, infertility, bilateral ovarian enlargement on bimanual examination.
8. **Labs** = increased **LH, LH:FSH ratio >2**, increased DHEA, increased total testosterone; positive progestin challenge.
9. **Radiology** = US shows **enlarged ovaries** with **multiple cysts.**
10. **Treatment** = exercise and weight loss, OCPs, metformin, spironolactone, clomiphene (for fertility).
11. **Complications** = infertility; increased risk for DM, hypertension, ischemic heart disease, ovarian torsion, and endometrial cancer.

Quick HIT

PCOS is the **most common** cause of androgen excess in women.

Quick HIT

Ovarian cysts are not the cause of disease in PCOS but are a result of androgen hypersecretion.

Quick HIT

Patients with **PCOS** are at an increased risk for **endometrial cancer** secondary to chronically **high estrogen** levels.

IV. Common Gynecologic Infections

A. Vaginitis

1. Vaginal infection caused by overgrowth of normal bacteria (*Gardnerella vaginalis*), protozoans (*Trichomonas*), or fungus (*Candida albicans*)
2. **Risk factors** = DM, human immunodeficiency virus (HIV), unprotected sex, multiple partners, young age at first intercourse, douching, intrauterine device (IUD) use, smoking

3. **H/P** = vaginal **irritation** or **pruritus**, vaginal discharge; examination detects vaginal inflammation with characteristic findings depending on cause (see Table 12-5, Figure 12-4)
4. **Labs** = **wet mount** (i.e., smear of vaginal fluid examined under microscope) with saline or potassium hydroxide (KOH) and **vaginal pH** testing useful to distinguish cause; smell a fishy odor when KOH is added to the vaginal discharge on a slide ("whiff test")
5. **Treatment** = metronidazole (*G. vaginalis* or *Trichomonas*), clindamycin (*G. vaginalis*), or fluconazole (*C. albicans*)

Quick HIT

Lactobacilli are a common normal bacteria whose presence on a wet mount does **not** suggest infection.

Table 12-5 Common Infection Causes of Vaginitis

	Bacterial Vaginosis		
Characteristics	***Gardnerella Vaginalis***	***Trichomonas Vaginalis***	***Candida Albicans***
Physical examination	Mild vaginal inflammation	Vaginal and cervical inflammation, **cervical petechiae**	Significant vaginal inf
Discharge	Profuse, thin, white, fishy odor	Malodorous, frothy, **greenish**	Thick, white, **"cottag**
Wet mount (saline)	**Clue cells** (epithelial cells with multiple attached bacteria)	**Motile trichomonads**	Normal
Wet mount (KOH)	Fishy or amine odor (positive whiff test)	Possible fishy odor	**Pseudohyphae**
Vaginal pH	>4.5 (high)	>4.5 (high)	**3.5–4.5** (normal)
Treatment	Metronidazole	Metronidazole (also **treat partner**)	Topical clotrimazole, m or oral fluconazole (si

KOH, potassium hydroxide.

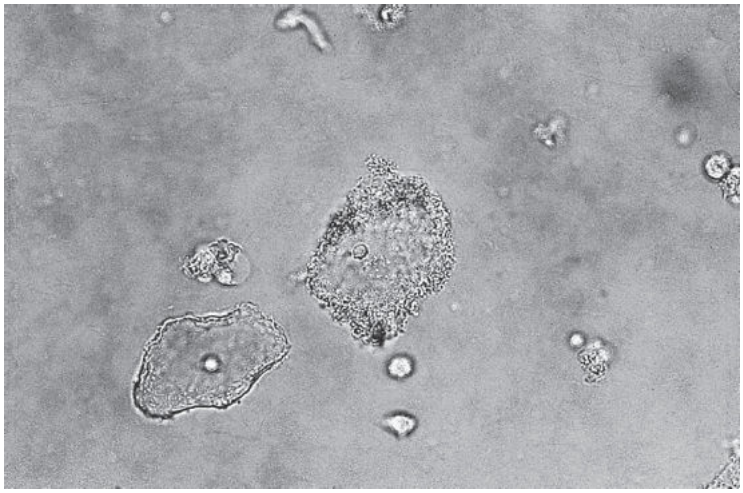


FIGURE **12-4**
Vaginal wet mount (saline preparation) showing clue cell with multiple bacteria attached to the border.
A normal epithelial cell is adjacent to the clue cell (1,000 × magnification).
(From Fleisher, G. R., Ludwig, S., Henretig, F. M., Ruddy, R. M., & Silverman, B. K. [2005]. *Textbook of pediatric emergency medicine* [5th ed., Figure 94-8]. Philadelphia, PA: Lippincott Williams & Wilkins; with permission.)

Quick HIT

Treatment of **partners** is **unnecessary** for ***G. vaginalis*** or ***C. albicans*** but is **required** with ***Trichomonas*** infection (metronidazole).

B. Toxic Shock Syndrome

1. Severe systemic reaction to *Staphylococcus aureus* exotoxin associated with **prolonged tampon** use, prolonged intravaginal contraception use, or postpartum or postabortion infection

2. **H/P** = vomiting, diarrhea, sore throat, headache; high fever, generalized macular rash; severe cases develop **hypotension,** shock, respiratory distress, and **desquamation of palms and soles**
3. **Labs** = vaginal fluid culture shows *S. aureus*; decreased platelets, increased alanine aminotransferase (ALT) and aspartate aminotransferase (AST), and increased blood urea nitrogen (BUN) and creatinine in progressing cases
4. **Treatment**
   a. Remove tampon or other intravaginal objects.
   b. Supportive care for hypotension; pressors may be required.
   c. Clindamycin or penicillinase-resistant β-lactam antibiotics (e.g., oxacillin, nafcillin); vancomycin required for methicillin-resistant strains.

V. Sexually Transmitted Infections

A. Cervicitis

1. Infection of cervical columnar epithelium caused by ***Neisseria gonorrhoeae*** or ***Chlamydia trachomatis.***
2. Urethra, oral cavity, or rectal area can also become infected through sexual contact.
3. **H/P** = dyspareunia, dysuria, bleeding after intercourse, **purulent vaginal discharge** (milder for *Chlamydia*), dysuria; disseminated gonorrhea presents as pustular dermatitis, migratory asymmetric polyarthralgia, and tenosynovitis.
4. **Labs**
   a. Gram stain of cervical scraping shows gram-negative diplococci with *N. gonorrhoeae* (usually nothing seen with *Chlamydia* infection).
   b. Culture on Thayer-Martin agar detects *N. gonorrhoeae*.
5. **Enzyme immunoassays** are useful for detecting both pathogens.

Quick HIT

Chlamydia infection is **the most common reportable STD** because it can be **asymptomatic** (especially in men) and frequently goes unrecognized.

6. **DNA probes** (NAAT) and **DNA amplification** testing of cervical fluid (i.e., PCR) are highly sensitive.
7. **Treatment** = ceftriaxone for *N. gonorrhoeae*, doxycycline (not in pregnancy) or azithromycin for *Chlamydia;* both antibiotics often given together because of **frequent dual infection**; sexual partners must be treated to reduce risk of reinfection
8. **Complication** = PID, septic arthritis

Quick HIT

Clinical cervicitis with negative Gram stain and cultures is highly suggestive of ***Chlamydia*** infection.

B. Pelvic Inflammatory Disease (PID)

1. Progressive *N. gonorrhoeae* or *Chlamydia* infection resulting in involvement of ovaries, uterus, fallopian tubes, or peritoneal cavity
2. Less frequently caused by *Bacteroides*, *Escherichia coli*, or streptococci
3. **Risk factors** = multiple sexual partners, unprotected intercourse, prior PID, douching, young age at first intercourse
4. **H/P** = lower abdominal pain, nausea, vomiting, dysuria; purulent cervical discharge, abdominal tenderness, fever, **cervical motion tenderness,** adnexal tenderness, possible abdominal guarding. Infection can extend into the abdomen and cause inflammation of the liver capsule, called perihepatitis or Fitz-Hugh–Curtis disease

Quick HIT

Barrier contraception use can **reduce** risk of PID.

5. **Labs**
   a. Increased WBC, increased ESR
   b. Gram stain, culture, immunoassays useful for identifying agent
   c. **Culdocentesis** (i.e., aspiration of intraperitoneal fluid from cul-de-sac posterior to uterus) yields pus
6. **Radiology** = transvaginal US may detect inflamed and enlarged uterus, tubo-ovarian abscess, or free fluid (technique used for diagnosis less now than in the past); laparoscopy may visualize inflamed tissue
7. **Treatment** = empiric antibiotics until specific agent identified (doxycycline, ceftriaxone, cefoxitin); treat as inpatient if high fevers or young age; treat sexual partners
8. **Complications** = **infertility** due to adhesions, chronic pelvic pain, **tubo-ovarian abscess**, increased risk of ectopic pregnancy

Quick HIT

Patients with PID may exhibit the **"chandelier sign"**: Palpating the cervix during pelvic examination may be so painful that they almost jump off of the examination table.

C. Syphilis

1. Disease caused by the spirochete *Treponema pallidum* (only transmitted by sexual contact or from mother to child)
2. **H/P** = varies according to stage of disease

NEXT
STEP

Suspect **tubo-ovarian abscess** in a patient with PID who also has signs of **sepsis** or **peritonitis**. Inpatient treatment is required with intravenous (IV) hydration, IV antibiotics, and surgical drainage.

   a. **Primary**
      (1) One to 13 weeks after exposure (average **3 weeks**)
      (2) Solitary **chancre** (i.e., firm papule that evolves into **painless ulcer**) forms near area of contact and heals spontaneously within 9 weeks
      (3) Bilateral inguinal lymphadenopathy
   b. **Secondary** = headache, malaise; fever, **maculopapular rash** on palms and soles, lymphadenopathy, papules in moist areas of body (i.e., condyloma lata)
   c. **Latent** = asymptomatic, lasting several years
   d. **Tertiary**
      (1) One-third of untreated patients progress beyond latent stage in 1 to 30 years after infection
      (2) Granulomatous lesions (i.e., **gummas**) of skin, bone, and liver
      (3) Loss of two-point discrimination and proprioception secondary to dorsal column degeneration (i.e., **tabes dorsalis**), Argyll Robertson pupils
3. **Labs**

Quick HIT

RPR and VDRL may become negative following syphilis treatment, but FTA-ABS will remain positive for life.

Quick HIT

Treponema pallidum cannot be cultured.

   a. VDRL and rapid plasma regain (RPR) are 80% sensitive screening tests. False positives are common early in infection.
   b. Fluorescent treponemal antibody absorption (FTA-ABS) or microhemagglutination assay for antibodies to treponemes (MHA-TP) used to confirm diagnosis.
   c. Spirochetes may be seen with dark-field microscopy analysis of swabs of lesions.
   d. Examination of cerebrospinal fluid (CSF) should be performed to confirm tertiary syphilis in patients with neurologic findings.
4. **Treatment** = **penicillin G**, doxycycline, or tetracycline; IV penicillin G used in severe tertiary cases. Obtain RPR in 2 to 4 weeks to establish baseline titers. Adequate treatment defined as fourfold titer decrease in titers at 6 to 12 months
5. **Complications** = gummatous destruction of skin, bones, and liver; cardiovascular syphilis (aortic regurgitation, aortitis); neurosyphilis (cerebral atrophy, tabes dorsalis, meningitis)

D. Genital Herpes: disease caused by herpes simplex virus type 2 (most cases) or type 1 (less common). Painful, multiple, small vesicles with erythematous base, mild lymphadenopathy (see Chapter 9, **Dermatology**)

E. Molluscum Contagiosum (See Chapter 10, Dermatology)

F. Human Papillomavirus (HPV)

1. More than 100 types of papillomavirus may be associated with **genital warts** (types 6 and 11) or **cervical cancer** (types 16 or 18 in 70% of cases)
2. **H/P** = frequent small pink papules at site of contact; infection caused by HPV types 6 or 11 can cause larger exophytic cauliflower-like warts on genital region
3. **Labs**
   a. An abnormal Pap smear should prompt HPV testing and colposcopy to look for lesions (see Figure 12-5).
   b. Application of acetic acid to lesions will turn them white during examination.
   c. Biopsy of lesions can be used to confirm infection and determine virus type through HPV DNA analysis.

4. **Treatment** = podophyllin, trichloroacetic acid, topical 5-fluorouracil, α-interferon injection of large lesions, cryotherapy, or laser therapy
5. **Prevention** = vaccination for types 6, 11, 16, and 18 of females aged 11 to 26 and males aged 9 to 21
6. **Complications** = vaginal scarring for removal of large lesions, possible **increased risk** of **cervical cancer** depending on viral type

Quick HIT

HPV typing after an abnormal Pap smear is important to assess cervical cancer risk.

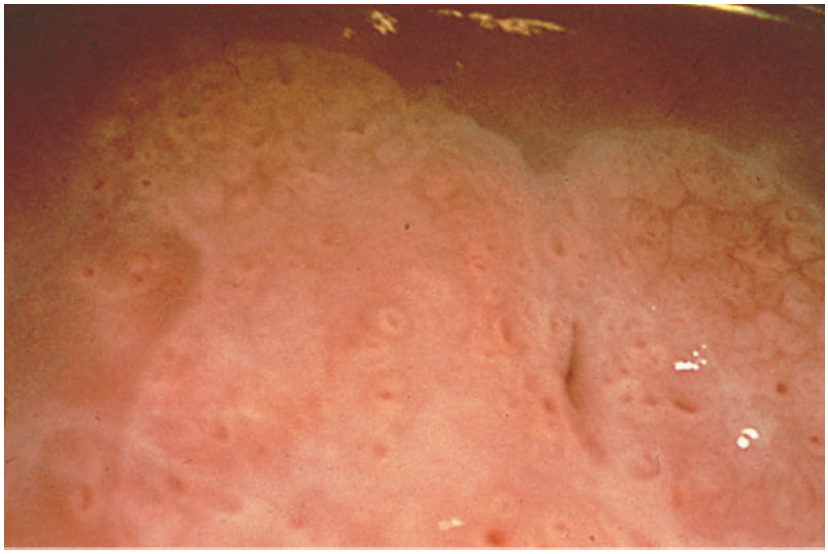


FIGURE 12-5
Colposcopy view of the cervix with multiple lesions consistent with HPV

G. Chancroid

1. Highly contagious disease caused by *Haemophilus ducreyi* seen most commonly in tropical or subtropical regions or in immunocompromised patients
2. **H/P** = within 2 weeks of contact, small papule forms in area of contact and transforms into **painful ulcer** with grayish base and foul odor; possible inguinal lymphadenopathy that can cause **significant inguinal swelling** (i.e., bubo formation)
3. **Labs** = Gram stain of tissue at ulcer edge shows gram-negative rods
4. **Treatment** = ceftriaxone, erythromycin, or azithromycin

MNEMONIC

Remember the characterization of genital ulcers by the mnemonic **S**ome **G**irls **L**ove **L**icorice, but **F**ellows **H**ate **C**andy: **S**yphilis, **G**ranuloma inguinale, and **L**ymphogranuloma venereum = pain**L**ess. Pain**F**ul = **H**erpes simplex and **C**hancroid.

H. Lymphogranuloma Venereum

1. Disease caused by L1, L2, or L3 serotypes of *C. trachomatis* (differentiated from cervicitis); more common in developing nations
2. **H/P**
   a. Within 2 weeks of contact, malaise, headache, fever, and formation of papule at site of contact that becomes **painless ulcer** that heals after a few days
   b. After 1 month, **significant inguinal buboes** develop (more common in men than in women)
3. **Labs** = immunoassays for *Chlamydia* may be helpful for diagnosis
4. **Treatment** = tetracycline, erythromycin, or doxycycline

I. Granuloma Inguinale

1. Disease caused by infection by *Klebsiella granulomatis*
2. **H/P**
   a. Papule on external genitalia forms several weeks after contact and rapidly becomes **painless ulcer** with granulation tissue (**beefy red base**) and **irregular borders**.
   b. Mild lymphadenopathy can occur.
3. **Labs** = lesion biopsy on Giemsa stain shows **Donovan bodies** (i.e., gram-negative, red-encapsulated intracellular bacteria)

4. **Treatment** = doxycycline or trimethoprim-sulfamethoxazole for 3 weeks

VI. Gynecologic Neoplasms

A. Uterine Fibroids (Uterine Leiomyoma)

1. **Benign** uterine masses composed of smooth muscle within myometrium; generally, regress after menopause
2. **Risk factors** = nulliparity, African American heritage, diet high in meats, alcohol consumption, family history
3. **H/P** = possibly asymptomatic; possible **menorrhagia, pelvis pressure or pain,** constipation, urinary frequency, or **infertility;** palpable mass on examination
4. **Radiology** = transvaginal US or hysteroscopy used to locate or visualize mass
5. **Treatment**
   a. Follow **asymptomatic** fibroids with US to detect **abnormal growth**
   b. **GnRH agonists** reduce uterine bleeding and fibroid size but are only recommended as temporary therapy (reduce fibroid size before surgery or as temporizing measure before imminent menopause)
   c. **Myomectomy** indicated for resection of symptomatic fibroids in women wishing to maintain fertility and **hysterectomy** in patients for whom fertility is not a concern
   d. **Uterine artery embolization** following a pelvic MRI to rule out other soft tissue pathologies may be performed to selectively infarct small fibroids in women wishing to avoid surgery but carries a high likelihood of impaired fertility

Quick HIT

Uterine fibroids do **not** continue to grow after menopause (because of estrogen sensitivity and decreased postmenopausal estrogen levels).

Quick HIT

Endometrial cancer **not related** to excess endogenous or exogenous estrogen exposure carries a **worse** prognosis than estrogen- related tumors.

Quick HIT

Indications for endometrial biopsy include postmenopausal bleeding, >45 years old with abnormal uterine bleeding, <45 years old with uterine bleeding and unopposed estrogen exposure, HNPCC, and atypical glandular cells on Pap smear.

B. Endometrial Cancer

1. Adenocarcinoma of uterine tissue most commonly related to **exposure to high estrogen levels**; most common in postmenopausal women
2. **Risk factors** = unopposed exogenous estrogen, chronic anovulation (PCOS), obesity, nulliparity, DM, hypertension, family history, increased age (postmenopausal), high-fat diet, colon cancer (hereditary nonpolyposis colon cancer [HNPCC])
3. **H/P** = heavy menses, irregular or midcycle bleeding, or **postmenopausal bleeding,** with possible abdominal pain; uterus is usually nontender, ovaries or uterus may feel fixed in position if tumor has local extension
4. **Labs** = endometrial biopsy (or examination of cells collected during D&C) shows hyperplastic abnormal glands with vascular invasion; **increased CA-125** tumor marker (not specific for endometrial cancer and not always increased) is useful in monitoring response to therapy
5. **Radiology** = CXR and CT can be used to detect metastases; transvaginal US may detect masses and can be used to measure endometrial wall thickness
6. **Treatment** = **total abdominal hysterectomy** with **bilateral salpingo-oophorectomy** (TAH-BSO) and lymph node sampling, adjuvant radiation therapy, chemotherapy
7. **Complications** = metastases; 96% 5-year survival rate for localized disease; 25% 5-year survival rate with metastases

NEXT
STEP

Although **atrophic vaginitis** is the **most common cause** of vaginal **bleeding** in postmenopausal women (80% cases), endometrial cancer must be ruled out for any postmenopausal woman presenting with this complaint (perform **endometrial biopsy**).

C. Cervical Cancer

1. Squamous cell cancer (80% cases), adenocarcinoma (15% cases), or mixed adenosquamous carcinoma (5% cases) of the cervix that results from progression of **cervical dysplasia**
2. **Risk factors** = smoking, OCPs, early first intercourse, tobacco, **HPV** (types 16, 18, 31, or 33), multiple sexual partners, high-risk sexual partners, history of STIs
3. Cervical dysplasia
   a. Precancerous squamous cell lesions of the cervix that progress to invasive cervical cancer in 1% to 22% of cases depending on cellular grade
   b. Usually detected by Pap smear or liquid-based cytology (abnormal cells seen on cytology)
   c. Cellular grading classified by Bethesda system (see Table 12-6)
4. **H/P** = usually asymptomatic in early stages; possible vaginal bleeding (postcoital or spontaneous), pelvic pain, or cervical discharge; cervical mass may be palpated; invasive cancer can be frequently seen on cervical examination
5. **Labs** = detected by **Pap smear**; punch biopsy of visible lesions; cone biopsy determines invasion extent
6. **Radiology** = CT, MRI, or US may be useful for determining extent of disease
7. **Treatment**
   a. Cervical dysplasia: treatment based on cellular grade (see Table 12-6)
   b. Invasive carcinoma
      (1) Lesions with microscopic invasion <5 mm should be treated with TAH or conization (i.e., cone-shaped endocervical resection) if patient desires to maintain fertility.
      (2) Small lesions with close surgical margins should be treated with postoperative chemotherapy.
      (3) Visibly invasive lesions or those that involve the uterus but do not extend to the pelvic wall or lower third of the vagina should be treated by radical hysterectomy with lymphadenectomy or radiation therapy plus cisplatin-based chemotherapy.
      (4) Lesions with extension to parametrial tissue, pelvic wall, lower third of the vagina, or adjacent organs or any lesions with metastases should be treated with radiation therapy and chemotherapy.
   c. **Complications** = 5-year survival is >90% for microscopic lesions; 65% to 85% for visible lesions limited to the uterus; 40% for lesions extending beyond the uterus; and 20% for metastatic lesions

Quick HIT

All women should receive **Pap smears** beginning at **21 years of age**, and most guidelines recommend stopping at age 65 years. Women 21 to 29 years of age should be screened **every 3 years.** Women ≥30 years may have HPV testing every 5 years in addition to the Pap smear cytology.

Table 12-6 Bethesda Classification of Cervical Squamous Cell Dysplasia and Appropriate Therapy

Grade	Characteristics	Treatment
Atypical squamous cells of undetermined significance (**ASCUS**)	Cellular abnormalities not explained by reactive changes; not suggestive of intraepithelial lesions	HPV screening/typing; if high risk type, do colposcopy with biopsy or close surveillance with repeat Pap smear in 12 mo; if HPV-negative returns to routine screening
Atypical squamous cells, cannot exclude HSIL (**ASC-H**)	Cellular abnormalities not explained by reactive changes; HSIL cannot be excluded	HPV screening; endocervical biopsy (colposcopy); repeat Pap smear in 6 and 12 mo; repeat HPV testing in 12 mo
Low-grade squamous intraepithelial lesion (**LSIL**) (a.k.a. CIN 1)	Mild cellular dysplasia	Repeat Pap smear in 6 and 12 mo; repeat HPV testing in 12 mo; excision by loop electrocautery excision procedure (LEEP) or conization or laser ablation may be performed
High-grade squamous intraepithelial lesion (**HSIL**) (a.k.a. CIN 2 or 3)	Moderate or severe cellular dysplasia including carcinoma in situ	Excision by LEEP or conization or laser ablation; repeat cervical cytology every 6 mo
Squamous cell carcinoma	Highly atypical cells with stromal invasion	Varies with degree of invasion and extent of involvement

CIN, cervical intraepithelial neoplasia; HPV, human papillomavirus.

D. Benign Ovarian Tumors

1. Benign ovarian lesions of functional ovarian cell, epithelial cell, or germ cell origin (see Table 12-7)
2. **H/P**
   a. Lower abdominal pain (more common with functional tumors or tumor torsion), nausea, vomiting, abdominal fullness (only after significant growth)
   b. Palpable ovarian mass on bimanual examination, abdominal tenderness, fever
3. **Labs** = frequently **increased CA-125;** biopsy of tumor used to determine benign or malignant nature
4. **Radiology** = US used to evaluate type of mass (cystic or solid) and quality of mass (irregular, multiple thick septations, smooth edges)
5. **Treatment** = observation common for functional cysts; oophorectomy performed for benign neoplasms; TAH-BSO considered for postmenopausal women

6. **Complications** = tumor torsion, tumor rupture with hemorrhage

Quick HIT

CA-125 is useful only in **postmenopausal** women as an indicator for ovarian cancer. Increased CA-125 is also seen in endometriosis, leiomyomata, and SLE.

Table 12-7 Common Types of Benign Ovarian Masses

Tumor	Origin	Characteristics	History and Physical	Treatmen
Follicular cyst	Ovarian follicle	**Granulosa** cells, cystic (~3 cm diameter), occur in first 2 wks of cycle and **may regress** over menstrual period	Abdominal pain and fullness; palpable tender mass on bimanual examination Peritoneal signs if torsion or rupture occurs	**Observati** tomy if mas or for incre cancer
Corpus luteum cyst	Corpus luteum	**Theca** cells, cystic or hemorrhagic corpus luteum, usually larger and firmer than follicular cyst, more common in later wks of cycle	Abdominal pain; palpable tender mass on bimanual examination Greater risk of torsion or rupture with significant bleeding than follicular cyst	**Observati** tomy if mas or for incre cancer; rup hemorrhag hemostasis
Mucinous or serous cystadenoma	Epithelial tissue	May resemble endometrial or tubal histology, cystic with serous or mucinous contents, may form calcifications **(psammoma bodies), may become extremely large**	Frequently asymptomatic until significant growth has occurred Palpable mass on bimanual examination that may be palpable during abdominal examination if large	Unilateral s tomy; TAH-BSO if
Endometrioma	Endometrium	Spread of endometriosis to involve ovary, similar behavior to other sites of endometriosis	Frequently asymptomatic Abdominal pain, dyspareunia, infertility Tender palpable mass	OCPs, GnRI progestins, lessen sym or oophore required be rence rate
Benign cystic teratoma (i.e., dermoid cyst)	Germ cells	Composed of **multiple dermal tissues** including hair, teeth, and sebaceous glands	Frequently asymptomatic Oily contents released during rupture can cause peritonitis Increased risk of ovarian torsion	Cystectomy preservatio 1–2% unde transforma salpingo-oo
Stromal cell tumor	Granulosa, theca, or Sertoli–Leydig cells	Secrete hormones appropriate to cells of origin, malignant potential	**Precocious puberty** (granulosa theca cell tumors) or **virilization** (Sertoli–Leydig cell tumors) Postmenopausal bleeding	Unilateral s tomy; TAH- pausal

GnRH, gonadotropin-releasing hormone; OCPs, oral contraceptive pills; TAH-BSO, total abdominal hysterectomy with bilateral salpingo-oophorecto

E. Ovarian Cancer

1. Cancer of ovaries most commonly of epithelial (65% cases) or germ cell (25% cases) origin; most cases are diagnosed only after considerable growth
2. **Risk factors** = **family history,** infertility, nulliparity, **BRCA1** or **BRCA2** gene mutations
3. **H/P**
   a. Usually **asymptomatic or minimally symptomatic until late in disease course**
   b. Abdominal pain, fatigue, weight loss, change in bowel habits, menstrual irregularity; ascites, mass may be palpated on bimanual examination
4. **Labs** = **increased CA-125** (80% of cases) in epithelial tumors; α-fetoprotein, hCG, and lactate dehydrogenase (LDH) may be increased in germ cell tumors

5. **Radiology** = US used to detect mass; MRI or CT useful to determine extent of involvement
6. **Treatment**
   a. Epithelial tumors
      (1) TAH-BSO, pelvic wall sampling, and appendectomy; adjuvant chemotherapy frequently prescribed
      (2) Tumor debulking with resection of involved bowel, liver, omentum, spleen, and lymph nodes performed for extensive disease with metastases
      (3) Single oophorectomy may be performed for tumors detected early in patients wanting to maintain fertility
   b. Germ cell tumors
      (1) Unilateral salpingo-oophorectomy performed for limited disease
      (2) Surgical debulking performed for extensive tumors
      (3) Chemotherapy typically administered postoperatively
7. **Complications** = 5-year survival improves with early detection, but because tumor is frequently in advanced stages by time of detection, prognosis is often poor

Quick HIT

US findings of cystic mass, smooth lesion edges, and few septa are more consistent with **benign** ovarian tumors. Findings of irregularity, nodularity, multiple septa, and pelvic extension are more suggestive of **malignancy**.

Quick HIT

Surgical resection is vital to establishing an accurate cytologic diagnosis of a suspected ovarian malignancy.

Quick HIT

Bartholin duct cyst is a soft mobile nontender cystic mass found at the 4- or 8- o'clock position at the base of the labium majus. These cysts may become infected and evolve into an abscess that requires I&D.

VII. Disorders of the Vulva and Vagina

A. Vaginitis. See Common Gynecologic Infections

B. Lichen Planus

1. Chronic, inflammatory, skin dystrophy
2. **H/P** = vulvar irritation, burning, pruritus, bleeding, dyspareunia. Glazed, reticular, erythematous lesions of the vulva with ulcerations. Vagina may become obliterated
3. **Treatment** = supportive therapy and topical high potency corticosteroids

C. Lichen Sclerosus

1. Chronic inflammatory condition of anogenital region in premenstrual and postmenopausal women. Premalignant lesion for vulvar squamous cell carcinoma
2. **H/P** = intense pruritus, dyspareunia, dysuria, painful defecation
   a. Polygonal white plaques involving the vulva and perianal area which spares the vagina.
   b. Perianal skin may have figure 8 appearance.
3. **Diagnosis** = punch biopsy
4. **Treatment** = high-dose topical corticosteroids (clobetasol)

Quick HIT

In lichen sclerosus, the vulvar skin appears thin and wrinkles like "cigarette paper."

D. Vestibulodynia

1. Constellation of symptoms limited to the vulvar vestibule.
2. **H/P** = severe pain on vestibular touch or penetration, tenderness, and erythema
3. **Treatment** = TCAs

E. Genito-Pelvic Penetration Disorder (Vaginismus)

1. **Risk factors** = sexual trauma, lack of sexual knowledge, and history of abuse.
2. **H/P** = pain with vaginal penetration, distress or anxiety over symptoms, no other medical cause. Pain may be limited to sex but may include pain with tampon use or pelvic examinations.
3. **Treatment** = relaxing of the vaginal muscles through Kegel exercises or desensitization therapy.

Quick HIT

Squamous cell cancer of the vagina is located in the upper ⅓ of the posterior vaginal wall and is associated with HPV 16 or 18.

F. Vaginal Cancer presents as malodorous vaginal discharge; postmenopausal or postcoital vaginal bleeding; and an irregular mass, plaque, or ulcer on the vagina.

Quick HIT

Clear cell adenocarcinoma of the vagina is associated with in utero exposure to diethylstilbestrol.

VIII. Disorders of the Breast

A. Breast Abscess

1. Local infection of breast tissue caused by *S. aureus* or streptococcus (superficial infections) or anaerobic bacteria (subareolar infections) (see Table 12-8)
2. Most are related to **breastfeeding;** more common in smokers
3. **H/P** = painful mass in breast; fever, palpable red and warm breast mass, breast tenderness, purulent drainage from mass or from nipple
4. **Labs** = increased WBCs
5. **Radiology** = US helps to locate abscess within breast
6. **Treatment** = antibiotics; incision and drainage of fluctuant masses; continue breastfeeding
7. **Complications** = fistula formation with recurrent abscesses; high recurrence rate

Quick HIT

Monthly **self-breast examinations** after each menstrual period are the best way to distinguish **developing lesions** from **monthly variations** in breast tissue make-up but have not been shown to decrease mortality.

Table 12-8 Management of Palpable Mass

Age	Management
Adolescents	Reassurance and reevaluation after 1–2 menstrual cycles
Age <30 yrs old	Targeted US ± diagnostic mammogram Simple cysts require aspirations and follow-up in 2–4 mo Complex cysts or solid mass require image-guided core biopsy Core biopsy: solid, stromal masses Excisional biopsy: large or suspicious masses FNA: cystic or small masses
Age >30 yrs old	Mammography ± US Core biopsy: suspicious for malignancy

B. Fibrocystic Changes

1. Increased number of benign cysts and fibrous tissue found in women of child-bearing age that varies in size during menstrual cycle
2. **H/P** = multiple bilateral small tender breast masses, possible mild breast pain preceding menses, symptoms improve after menses; breast examination detects mobile masses that **vary in size during menstrual cycle**
3. **Labs** = biopsy (performed when atypical lesions suspected) shows epithelial hyperplasia
4. **Radiology** = mammograms (yearly imaging starting by age 40 years) should be used to identify and follow lesions; US useful for detecting large cystic lesions
5. **Treatment** = caffeine and dietary fat reduction, OCPs, progesterone, or tamoxifen may improve symptoms in confirmed benign lesions

Quick HIT

Suspicious lesions on mammogram are those with **hyperdense regions** or **calcifications**.

C. Fibroadenoma

1. Most common benign breast tumor (proliferative process in single duct); more common in **women <30 years of age**

2. **H/P** = **solitary**, firm spherical, and **mobile mass** with **well-defined edges**; size may vary during menstrual cycle, estrogen sensitive
3. **Labs** = biopsy (FNA or open) confirms benign nature
4. **Radiology** = US, mammogram, or MRI can determine location of mass and determine if solid or cystic
5. **Treatment** = surgical excision or US-guided cryotherapy
6. **Complications** = recurrence is common

Quick HIT

Nonbloody nipple discharge is consistent with a **noncancerous** pathology and frequently does **not** require excision.

D. Intraductal Papilloma

1. Benign lesions of ductal tissue that may have malignant potential
2. **H/P** = **bloody or nonbloody discharge,** breast pain; palpable mass behind areola
3. **Labs** = excisional biopsy used to rule out cancer
4. Treatment = surgical excision

Quick HIT

1% of all cases of breast cancer occur in **males**.

E. Breast Cancer

1. Malignant neoplasms of the breast arising from either ductal (80% of cases, more aggressive) or lobular (20% of cases, less aggressive, more difficult to detect) tissue (see Table 12-9)
2. **Risk factors** = family history (first-degree relative), BRCA1 or BRCA2 gene mutations, ovarian cancer, endometrial cancer, prior breast cancer, increased estrogen exposure, early menarche, late menopause, nulliparity, late first pregnancy (35 years of age), increased age, obesity, alcohol, diethylstilbestrol (DES), industrial chemicals or pesticides, radiation exposure
3. **H/P** = painless breast lump, possible nipple discharge, palpable solid and immobile breast lump (when of sufficient size), peau d'orange (i.e., lymphatic obstruction causing lymphedema and skin thickening that makes breast look like an orange peel), possible nipple retraction

Quick HIT

Hormone replacement therapy has been linked to an **increased** incidence of breast cancer caused by exogenous estrogen administration.

Quick HIT

The **upper outer quadrant** is the most common site of breast cancer.

Table 12-9 Features of Breast Cancer Variants

Variant	Characteristics	History and Physical
Ductal carcinoma in situ (DCIS)	Malignant cells in ducts **without stromal invasion**; possible calcifications; unifocal; higher risk of subsequent invasive cancer than LCIS	Usually asymptomatic, possible nipple discharge or palpable lump
Lobular carcinoma in situ (LCIS)	Malignant cells in lobules **without stromal invasion**; no calcifications; can be multifocal; lower risk of invasion than DCIS, but **increased risk of contralateral malignancy**	Incidental finding, asymptomatic
Invasive ductal carcinoma	Malignant cells in ducts with stromal invasion and microcalcifications; **fibrotic response** in surrounding breast tissue; **most common** form of invasive breast cancer (80% of cases)	Firm palpable mass, skin dimpling, nipple retraction, peau d'orange, or nipple discharge
Invasive lobular carcinoma	Malignant cells in breast lobules with insidious infiltration and **less fibrous response**; more frequently **bilateral** or **multifocal** than ductal carcinoma; slower metastasis; greater association with hormone replacement therapy	Firm palpable mass, skin dimpling, nipple retraction, peau d'orange, or nipple discharge; may be more subtle than ductal carcinoma
Paget disease of the breast	Malignant adenocarcinoma cells infiltrate the epithelium of the nipple and areola; indicates carcinoma (usually ductal) in the deeper breast parenchyma	Scaly, eczematous, or ulcerated lesion on the nipple and areola; may be preceded by pain, burning, or itching
Inflammatory carcinoma	Subtype of ductal carcinoma characterized by **rapid progression** and **angioinvasive** behavior; **poor prognosis**	Breast pain, tender breast, erythema, warmth, peau d'orange, lymphadenopathy
Medullary carcinoma	Well-circumscribed mass; **rapid growth**; better prognosis than ductal carcinoma	**Soft**, well-circumscribed mass
Mucinous carcinoma	Well-circumscribed mass; **slow growth**; more common in older women; better prognosis than ductal carcinoma	**Gelatinous**, well-circumscribed mass
Tubular carcinoma	Slow-growing malignancy of well-formed **tubular** structures invading the stroma; patients typically in late 40s; excellent prognosis	Rarely detected before mammography

4. **Labs**
   a. **Biopsy** is indicated for any palpable breast mass or suspicious mammography findings.
      (1) FNA can be performed on palpable lesions or through US localization.
      (2) Core biopsy provides a better definitive histologic diagnosis and can determine if a lesion is invasive.
      (3) Needle localization under US guidance may be performed on nonpalpable lesions with calcifications to localize a mass for open biopsy.
   b. Testing for estrogen and progesterone receptors in tumor helps guide treatment.
5. **Radiology** = **mammography** is principal screening method; US can be used to differentiate cystic from solid lesions and to localize masses to guide intervention; MRI may be useful to determine extent of lesion; bone scan and CT can be used to identify metastases

Quick **HIT**

Most breast cancers are detected through an **abnormal screening mammogram**, but **20%** of breast cancers are not detected on mammogram (typically in upper outer quadrant of breast).

6. **Treatment**
   a. Carcinoma in situ
      (1) **Ductal carcinoma in situ** (DCIS): **lumpectomy** + radiation; mastectomy considered for high-risk individuals
      (2) **Lobular carcinoma in situ** (LCIS): **close observation** + selective estrogen receptor modulators tamoxifen and raloxifene; prophylactic bilateral mastectomy for women who do not desire lifelong observation
      (3) Hormone receptor positive breast cancer: tamoxifen
   b. Invasive carcinoma
      (1) **Early focal cancers: lumpectomy** + radiation
      (2) **Multifocal** lesions or patients with prior breast radiation: mastectomy
      (3) **Axillary spread: sentinel lymph node biopsy;** positive sentinel node biopsy indicates need for axillary node dissection at time of tumor resection
      (4) **node-positive cancers**, tumors >1 cm, and tumors with aggressive histology: hormone therapy
      (5) **node negative/positive cancers: chemotherapy; trastuzumab** (anti-HER2/neu receptor antibody) used in patients with the appropriate receptors
   c. Advanced cancer
      (1) Chemotherapy and hormone therapy used for locally advanced lesions with extension beyond breast
      (2) Surgical resection and/or radiation therapy can be performed after systemic therapy has decreased tumor size
      (3) Metastases treated with systemic therapy; surgical resection or radiation therapy can be performed for solitary lesions
   d. Inflammatory breast cancer
      (1) Best survival rates when mastectomy, radiation therapy, and chemotherapy are all utilized

7. **Complications**
   a. Tumors not responding to surgery and radiation are unlikely to be cured
   b. Metastases to bone, thoracic cavity, brain, and liver
   c. Tumors with positive estrogen or progesterone hormone receptors or HER2/neu protein receptors and those seen in older patients have a better prognosis
   d. Lymphedema

NEXT
STEP

FNA of a solid breast mass carries a **20%** chance of a **false-negative** finding, so any negative FNA of a solid breast mass requires a more definitive biopsy.

Quick **HIT**

Presence of **positive axillary lymph nodes** and **large tumor size** carries a **worse prognosis** in breast cancer.

Quick **HIT**

Patients with BRCA1 or BRCA2 gene mutations should be followed very closely to look for breast or epithelial ovarian cancer and may want to consider prophylactic mastectomies and oophorectomies.

QUESTIONS

1. A 31-year-old nulligravid woman presents to clinic for evaluation of chronic pelvic pain. The pain began 10 months ago and worsens before menstruation. The patient denies abnormal vaginal discharge, menorrhagia, and fever. She is sexually active and uses condoms intermittently for contraception. Her temperature is 37.1° C and her blood pressure 120/80 mm Hg. Physical examination reveals thickening of the uterosacral ligaments and decreased uterine mobility. Urine β-hCG is negative. Transvaginal ultrasound is normal. Which of the following diagnostic tests would most likely yield a definitive diagnosis in this patient?

   A. CT scan of the abdomen and pelvis
   B. Endometrial biopsy
   C. Laparoscopy
   D. Pap smear
   E. Serum CA-125

2. A 27-year-old woman presents to the office for evaluation for infertility. Despite frequent unprotected sexual intercourse with her husband for the past 18 months, the couple has been unable to conceive. Menarche was at age 12. The patient's menstrual cycles are irregular and her last menstrual period was 2 months ago. Her husband's semen analysis was normal. Physical examination reveals acne of the face and terminal hairs on the upper lips. Pelvic examination reveals normal female external genitalia and mobile uterus without adnexal masses. Urine pregnancy test is normal. Which of the following is the appropriate treatment for this patient's infertility?

   A. Dopamine agonist
   B. Levothyroxine
   C. Progesterone
   D. Selective estrogen modulator
   E. Surgery

3. A 22-year-old woman presents to clinic due to amenorrhea for the last 6 months. Menarche was at age 13 and previously occurred at 28 to 30-day intervals, lasting 5 days. The patient denies tobacco, alcohol, and illicit drug use. The patient is a Track and Field state champion. She is not sexually active. Blood pressure 120/78 mm Hg and pulse is 56/min. BMI is 19 kg/m^2. On pelvic examination, the uterus is small and mobile and there are no adnexal masses. Urine pregnancy test is negative. Which of the following is the patient at increased risk of acquiring?

   A. Cold intolerance
   B. Galactorrhea
   C. Hot flashes
   D. Insulin resistance
   E. Osteoporosis

4. A previously healthy 26 year old presents to the emergency department with right upper quadrant pain that began 4 days ago. The pain is progressively worsening and worsens with inspiration. The patient endorses purulent cervical discharge, fever, and vomiting. She denies changes in her stool. She is sexually active and does not use barrier contraception. She is not taking any medications. She denies tobacco, alcohol, and recreational drug use. Temperature is 102° F, blood pressure is 110/80 mm Hg, and pulse is 106/min. BMI is 22 kg/m^2. Physical examination reveals no rash. Bowels are normoactive and there is tenderness of the upper right quadrant and the lower abdomen. There is no rebound tenderness or guarding. There is no costovertebral angle tenderness. Urine β-hCG is negative. Which of the following is the most likely diagnosis in this patient?

   A. Acute cholecystitis
   B. Acute viral hepatitis
   C. Pelvic inflammatory disease
   D. Ruptured ectopic pregnancy
   E. Ruptured ovarian cyst

5. A 35-year-old woman, G1P1, comes to clinic for evaluation for contraception. The patient would like to begin combined oral contraceptives. She was diagnosed with essential hypertension last year which is well controlled on hydrochlorothiazide. She denies tobacco, alcohol, and illicit drug use. BMI is 23 kg/m^2; blood pressure is 128/75 mm Hg. Physical examination is normal. Combination oral contraceptives would most likely cause what in this patient?

   A. Endometrial hyperplasia
   B. Fibrocystic change of the breast
   C. Hyperandrogenism
   D. Ovarian cancer
   E. Worsening hypertension

13
Obstetrics

I. Normal Pregnancy Physiology

A. Embryonic and fetal development begins with fertilization and takes approximately 38 weeks until fetal maturity occurs (see Figure 13-1).

1. Gestational age is calculated from the mother's last menstrual period (LMP), which began roughly 14 days prior to fertilization. Therefore, **gestational age** is 2 weeks older than the **embryonic age.**
2. Naegele's rule can be used to estimate delivery date by taking LMP, adding 7 days, subtracting 3 months, and adding 1 year (LMP + 7 days – 3 months + 1 year).

Quick HIT

Teratogens will either **kill** the fetus or will have **no effect** within the **initial 2 weeks** of gestation. They can cause **abnormal organ formation** between **2 and 12 weeks.**

Quick HIT

Pseudocyesis (false pregnancy) is the somatization of stress, which alters the hypothalamic–pituitary–ovarian axis resulting in the signs and symptoms of pregnancy in nonpregnant, nonpsychotic women.

B. Normal Changes in Maternal Physiology During Pregnancy

1. Several physiologic changes occur in the mother in response to the maintenance of fetal viability (see Table 13-1).
2. Normal changes in maternal physiology affect every organ system.

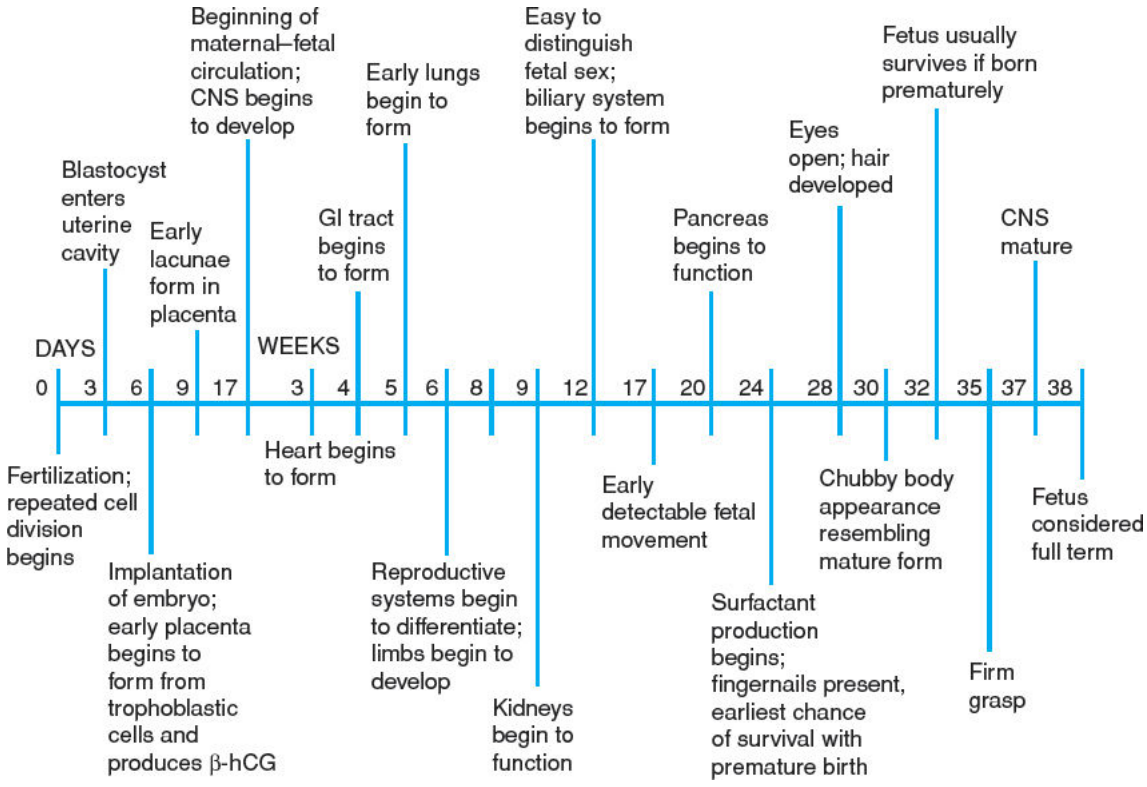


FIGURE 13-1
Timeline of fetal development during gestation.
β-hCG, β-human chorionic gonadotropin; CNS, central nervous system; GI, gastrointestinal. Dates are given using embryonic age, not gestational age.

Quick HIT

Low-risk activity during pregnancy:

- **Moderate intensity exercise** is **encouraged** during pregnancy to improve maternal feelings of well-being, reduce symptoms caused by positional effects of the fetus, and promote healthy blood sugar levels.
- Sexual intercourse can be continued during pregnancy unless the mother is considered at high risk for spontaneous abortion, premature labor, or placenta previa.

Table 13-1 Normal Changes in Maternal Physiology During Pregnancy

Anatomy/System	Changes
Cardiovascular	• Cardiac output increases 40% with associated increases in SV (10%–30%) and HR (12–18 bpm) • Systolic murmur may be heard because of increased cardiac output • Myocardial O_2 demand increases • Systolic and diastolic blood pressures decrease slightly • Uterus displaces heart slightly superiorly
Respiratory	• Uterus displaces diaphragm superiorly and causes decrease of residual volume, functional residual capacity, and expiratory reserve volume • Total body O_2 consumption increases 20% • Tidal volume increases 40% with associated increase in minute ventilation because of stimulation by progesterone • Pco_2 decreases to ~30 mm Hg (chronic respiratory alkalosis with metabolic compensation) • Progesterone stimulates respiratory drive thus increasing minute ventilation and tidal volume
Renal	• Renal plasma flow and glomerular filtration rate increase 40% • Decrease in BUN and creatinine • Increased renal protein excretion • Increased renal loss of bicarbonate to compensate for respiratory alkalosis • Blood and interstitial fluid volumes increase
Endocrine	• Nondiabetic hyperinsulinemia with associated mild glucose intolerance • Production of human placental lactogen contributes to glucose intolerance by interfering with insulin activity • Fasting triglycerides increase • Cortisol increases • Thyroid-binding globulin (TBG) and total T_4 increase, but free T_4 is unchanged • TSH decreases slightly during early pregnancy (but still within normal limits)
Hematologic	• Hypercoagulable state • Increased RBC production • Hematocrit decreases because of increased blood volume
Gastrointestinal	• Increased salivation • Decreased gastric motility

bpm, beats per minute; BUN, blood urea nitrogen; HR, heart rate; RBC, red blood cell; SV, stroke volume; T_4, thyroxine.

II. Assessment of Gestational Age

A. First trimester: Ultrasound (US) with crown–rump length is the most accurate method of determining gestational age. From weeks 7 to 14, gestation accuracy is +/–3 to 5 days.

B. Second trimester: Fetal abdominal circumference, biparietal diameter, femur length, and head circumference are all used to determine gestational age. Gestational age measurements during the second trimester are accurate +/–1 to 2 weeks.

C. After 20 weeks: fundal height is used to estimate gestational age. Fundal height measurements are accurate +/–3 weeks. Uterine fibroids and obesity affect the accuracy of fundal height measurements.

III. Prenatal Care

A. Nutrition

1. Maternal nutritional demands alter during pregnancy to support both the mother and the developing fetus.
2. Some nutrients are specifically required to reduce the risk of birth defects (e.g., folate, iron) (see Table 13-2).
3. Ideal weight gain
   a. 28 to 40 lb in women with a body mass index (BMI) <19.8
   b. 25 to 35 lb for BMI 19.8 to 26 (~2 lb in first trimester, 0.75 to 1 lb/wk in second and third trimesters)
   c. 15 to 25 lb for BMI >26

d. Inadequate weight gain can result in fetal growth restriction and preterm delivery while too much weight gain can result in gestational diabetes, fetal macrosomia, and cesarean.

4. Fish (methylmercury contamination) and caffeine (increased risk of spontaneous abortion) consumption should be limited during pregnancy.

Quick HIT

Daily caloric intake during pregnancy should be approximately **2,500** kcal.

Table 13-2 Important Increased Nutritional Demands During Pregnancy

Substance	Increased Need	Reason for Need	Effects of Insufficie
Folate	0.4–0.8 mg/day (should be started 4 wks before attempted conception)	Normal fetal neural tube development	Neural tube defects
Calcium	1,000–1,300 mg/day (50% increase)	Lactation reserves Increased utilization by fetus	Impaired maternal bone Hypertension Premature birth, low bi
Iron	30 mg/day (100% increase)	RBC production	Maternal anemia Premature birth, low bi Maternal cardiac compl
Protein	60 g/day (30% increase)	Additional needs of maternal, fetal, and placental tissue	Impaired fetal and plac
Fluids	Adequate hydration important	Increased total maternal–fetal fluid volume	Relative dehydration

RBC, red blood cell.

Quick HIT

Women at risk for poor nutrition during pregnancy include those who are teenagers, have a lower socioeconomic status, adhere to diets with certain food avoidances, are underweight, or who smoke, are alcoholics, or are drug abusers.

Quick HIT

Although the full-integrated test is the most sensitive screening test for trisomies with the lowest rate of false-positive findings, it is not routinely performed because abnormal first trimester results frequently prompt the decision to abandon the second trimester tests and perform a more invasive test to find a definitive answer.

B. Prenatal Visits

1. **Good prenatal care** is vital to healthy fetal development; its goals are to prevent or manage conditions that may be harmful to the mother or fetus.
2. Maternal weight (to monitor weight gain), urinalysis (to detect urinary tract infection [UTI] and gestational diabetes mellitus [GDM]), blood pressure, fundal height (to estimate fetal growth), and fetal heart sounds (confirms fetal viability) are evaluated at each visit.
3. Initial visit includes detailed history, physical, and **risk assessment.**
4. Education should be provided to the patient concerning weight gain, nutrition, drug and substance abstinence, animal handling or avoidance, seat belt use, concerning symptoms and signs, scheduling of care and tests, childbirth and breastfeeding classes, and confidentiality issues.
5. Labs and US are performed at certain time points during gestation to detect infection and fetal abnormalities (see Table 13-3).
6. Screening lab tests that are not routinely performed at the first prenatal visit but should be considered in patients at risk: purified protein derivative (PPD) (for TB), red blood cell (RBC) indices, hemoglobin (Hgb) electrophoresis (anemias), hexosaminidase A (Tay–Sachs), phenylalanine levels (phenylketonuria), hepatitis C serology, toxoplasmosis screening, and cystic fibrosis genetic screening.
7. **Leopold maneuvers** (i.e., external abdominal examination) can be performed in the third trimester to determine fetal presentation.

8. Specialized tests are performed in women with increased risk for congenital abnormalities (e.g., **>35 years of age**, history of spontaneous abortion, teratogen exposure, diabetes mellitus [DM], history of fetal demise) (see Table 13-4 and Table 13-5).

Quick HIT

Maternal serum α-fetoprotein levels:

- This screening test is **only valid** if performed during the correct gestational window (**16 to 18 weeks' gestation**).
- **High** levels are associated with an increased risk of **neural tube defects,** abdominal wall defects, and multiple gestations.
- **Low** levels are associated with increased risk of **trisomies 21** and **18**.

Table 13-3 Common Screening Labs Performed During Pregnancy

Length of Gestation	Labs or Study Performed
Initial visit	CBC Blood antibody and Rh typing Pap smear Gonorrhea/chlamydia screening Urinalysis RPR or VDRL Rubella and varicella antibody titer Hepatitis B surface antigen HIV screening (with maternal consent)
16–18 wks	Quadruple screen[a] (maternal serum α-fetoprotein, hCG, unconjugated estriol, maternal serum inhibin A) to look for trisomies 21 and 18 and neural tube defects
18–20 wks	US dating of pregnancy and assessment for gross fetal abnormalities
24–28 wks	1-hr glucose challenge to screen for gestational DM H/H
32–37 wks	Cervical culture for *Neisseria gonorrhoeae* and *Chlamydia trachomatis* (selected populations) Group B streptococcus screening

[a]See Table 13-4 for description of quadruple screen.

CBC, complete blood count; DM, diabetes mellitus; hCG, human chorionic gonadotropin; Rh, rhesus factor; RPR, rapid plasma reagin; US, ultrasound; VDRL, Venereal Disease Research Laboratories.

Table 13-4 Prenatal Assessment for Congenital Diseases in High-Risk Pregnancies

Test	Description	Indications
Quadruple screen	Maternal serum α-fetoprotein, estriol, hCG, and maternal serum inhibin A levels measured to assess risk for neural tube defects and trisomies 18 and 21	• Performed in all pregnant women at 16–18 wks gestation • Frequently initial marker for fetal complications
Full-integrated test	US measurement of nuchal translucency and serum measurement of pregnancy-associated plasma protein A (PAPP-A) in first trimester and quadruple screen in second trimester; lowest false-positive rate for noninvasive tests	• Women who present in first trimester who desire noninvasive testing with the lowest false-positive risk
Amniocentesis	Transabdominal needle aspiration of amniotic fluid from amniotic sac after 16 wks gestation to measure amniotic α-fetoprotein and determine karyotype (detects neural tube defects and chromosome disorders with greater sensitivity than triple screen alone)	• Abnormal quadruple screen, women >35 yrs of age, risk of Rh sensitization • Carries an excess 0.5% risk of spontaneous abortion over normal risks for abortion
Chorionic villi sampling	Transabdominal or transcervical aspiration of chorionic villus tissue at 9–12 wks gestation to detect chromosomal abnormalities	• Early detection of chromosomal abnormalities in higher-risk patients (advanced age, history of children with genetic defects)
Percutaneous umbilical blood sampling	Blood collection from umbilical vein after 18 wks gestation to identify chromosomal defects, fetal infection, Rh sensitization	• Late detection of genetic disorders, pregnancies with high risk for Rh sensitization

hCG, human chorionic gonadotropin; Rh, rhesus factor; US, ultrasound.

Table 13-5 Interpretation of Full-Integrated Test and Quadruple Screen

	Full-Integrated Test (First Trimester)		Quadruple Screen (Second Trimester)			
Genetic Disorder	**PAPP-A**	**NT**	**AFP**	**uE3**	**hCG**	**Inh A**
Trisomy 21 (Down syndrome)	↓	↑	↓	↓	↑	↑
Trisomy 18	↓↓	↑	↓	↓↓	↓↓	↔
Trisomy 13	↓↓	↑	↔	↔	↔	↔

AFP, α-fetoprotein; hCG, human chorionic gonadotropin; Inh A, Inhibin A; NT, nuchal translucency; PAPP-A, pregnancy-associated plasma protein A; uE3, estriol.

IV. Medical Complications of Pregnancy

A. Gestational Diabetes Mellitus

1. **New-onset** glucose intolerance that begins during pregnancy (after 24 weeks)
2. **Risk factors** = family history of DM, >25 years of age, obesity, prior history of GDM, previous macrosomic infant, prior polyhydramnios, recurrent abortions, prior stillbirth, prior macrosomia, hypertension (HTN), African or Pacific Islander heritage, corticosteroid use, polycystic ovarian syndrome (PCOS)
3. **History and physical (H/P)** = usually asymptomatic
4. **Labs** = fasting glucose >126 mg/dL or **abnormal glucose tolerance test** performed at 24 to 28 weeks' gestation, screening is done earlier if patient has risk factors (see Figure 13-2)
5. **Treatment**
   a. Strict glucose control through **diet** and **exercise**
   b. Diet should consist of evenly distributed carbohydrates, protein, and fat over three meals and two to four snacks/day
      (1) 40 kcal/kg/day in women with BMI <22
      (2) 30 kcal/kg/day in women with BMI 22 to 27
      (3) 24 kcal/kg/day in women with BMI 27 to 29
      (4) 12 to 15 kcal/kg/day in women with BMI >29
      (5) Self-monitoring of glucose performed to determine therapy efficacy
   c. Insulin should be used in patients failing nonpharmacologic therapy to keep fasting glucose <90 mg/dL and 1-hour postprandial glucose <120 mg/dL
   d. Metformin and glyburide are also used
   e. Periodic fetal US and nonstress tests (discussed later) performed to assess fetal well-being
   f. Cesarean section may be indicated for macrosomic babies
6. **Complications**
   a. Fetal: macrosomia (i.e., baby of abnormally large size), polyhydramnios, delayed pulmonary maturity, uteroplacental insufficiency (resulting in intrauterine growth restriction [IUGR] or intrauterine fetal demise)
   b. Perinatal or postnatal: traumatic delivery, delayed neurologic maturity, fetal respiratory distress syndrome, hypoglycemia (secondary to therapy; can also occur after delivery), hypocalcemia

Quick HIT

Gestational DM occurs in 1%–6% of pregnancies.

NEXT
STEP

Gestational DM occurs most frequently in the **second** or **third trimesters.** If mother presents with signs of DM earlier in pregnancy, suspect nongestational (type I or II) DM.

B. Pregestational Diabetes Mellitus

1. DM that exists **before** pregnancy; patient may or may not be aware of disease
2. **H/P** = consistent with typical presentation of DM (see Chapter 8, Endocrine Disorders); patients more likely to have significant hyperglycemia, postpartum hyperglycemia, and low BMI

NEXT
STEP

Continue glucose assessment after birth because maternal glucose needs will change suddenly for patients with gestational DM and because the mother has a low risk of remaining diabetic after pregnancy.

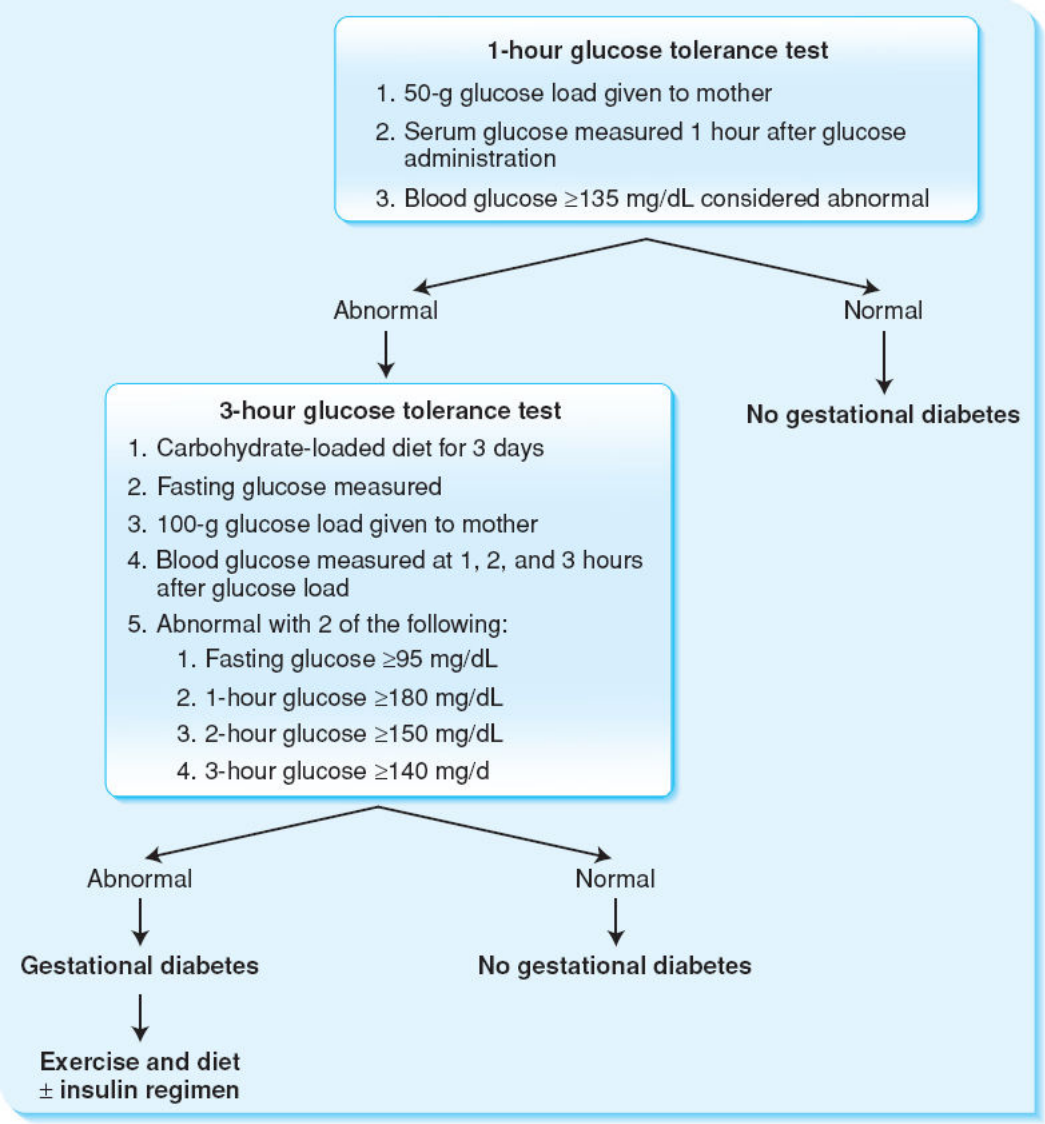


FIGURE **13-2**
Screening for gestational diabetes mellitus performed at 24 to 28 weeks' gestation.

3. **Labs** = increased serum glucose (prior to and during pregnancy), increased Hgb A1c with poor control; detection of anti-insulin and anti-islet cell antibodies is diagnostic for type I DM.
4. **Treatment**
   a. Try to control glucose with diet and exercise
   b. Insulin used for glucose control in type I and in type II DM not adequately controlled with lifestyle modification
   c. Fetal US and echocardiogram (especially third trimester) used to identify cardiac, neurologic, and growth abnormalities
   d. Early delivery after fetal lung assessment and corticosteroid administration recommended for poor glucose control or maternal complications
5. Complications
   a. Maternal: preeclampsia, renal insufficiency, retinopathy, diabetic ketoacidosis, hyperosmolar hyperglycemic state (HHS)
   b. Fetal: cardiac defects (especially transposition of the great vessels, tetralogy of Fallot), neural tube defects, sacral agenesis, renal agenesis, polyhydramnios, macrosomia, IUGR, intrauterine fetal demise

C. Preeclampsia

1. Pregnancy-induced **HTN** with **proteinuria** and/or evidence of end organ damage that develops after 20 weeks' gestation in 5% of pregnancies owing to an unknown cause

2. **Risk factors** = HTN, **nulliparity, prior history of preeclampsia,** <15 or >35 years of age, multiple gestation (e.g., twins), vascular disease, chronic HTN or renal disease, DM, obesity, African American ancestry
3. **H/P**
   a. Asymptomatic in mild cases
   b. **Edema** in **hands** and **face,** rapid weight gain, headache, epigastric abdominal pain, visual disturbances, hyperreflexia
   c. Severe features are SBP >160 or diastolic blood pressure (DBP) >110, platelets <100,000, increased creatinine (<1.1), increased transaminases, pulmonary edema, visual or cerebral symptoms
   d. **Blood pressure ê140/90** mm Hg during pregnancy in a patient who was formerly normotensive, requires two measurements at least 4 hours apart
4. **Labs**
   a. Urinalysis shows 2+ proteinuria on dipstick, >300 mg protein/24 hrs, or protein creatinine ratio >0.3
   b. Decreased platelets, normal or mildly increased creatinine, increased alanine aminotransferase (ALT) and aspartate aminotransferase (AST), decreased glomerular filtration rate (GFR)
   c. Fetal nonstress test and amniocentesis (less commonly) can be useful to assess fetal well-being

Quick HIT

The only definitive cure for preeclampsia is **delivery.**

5. **Treatment**
   a. If near term, **induce delivery.**
   b. If mild and far from term, prescribe restricted activity, frequent maternal examinations for worsening symptoms, protein assessments, and fetal nonstress tests twice per week.
   c. If severe and far from term, closely monitor in inpatient setting and maintain blood pressure <155/105 mm Hg with DBP >90 using antihypertensive medications (labetalol frequently used), give intravenous (IV) **$MgSO_4$ for seizure prophylaxis,** closely monitor maternal and fetal health, and induce delivery as soon as fetus is considered viable.
   d. Continue antihypertensive medications and $MgSO_4$ postpartum and continue close observation for symptoms and lab abnormalities before discontinuing medications.
   e. Mothers with pre-existent HTN should be treated pharmacologically for HTN >140/95 mm Hg; labetalol or methyldopa is used initially, and a long-acting calcium channel blocker (e.g., nifedipine, amlodipine) may be added as a second agent.
6. **Complications** = **eclampsia,** seizures, stroke, IUGR, pulmonary edema, maternal organ dysfunction, oligohydramnios, preterm delivery; hemolysis, elevated liver enzymes, and low platelet counts (HELLP) syndrome can also cause abruptio placentae, renal insufficiency, encephalopathy, and disseminated intravascular coagulation (DIC)

Quick HIT

Do not use angiotensin-converting enzyme inhibitors (**ACE-I**) or angiotensin receptor blockers (ARBs) to stabilize blood pressure in pregnancy because of risk of **teratogenic** effects.

Quick HIT

HELLP syndrome is a form of preeclampsia with poor fetal prognosis and 1% maternal mortality characterized by **H**emolysis, **E**levated **L**iver enzymes, and **L**ow **P**latelets.

D. Eclampsia

1. Progression of preeclampsia leading to **maternal seizures** that can be severe and fatal for both mother and child if untreated
2. **H/P** = headaches, visual disturbances (scotomata), and upper abdominal pain frequently precede onset of **seizures**
3. **Labs** = findings similar to preeclampsia
4. **Treatment**
   a. Treatment is similar to that for preeclampsia, with **delivery** being the definitive solution; labor should be induced as soon as stable.
   b. Use **$MgSO_4$** and **IV diazepam** to control seizures.
   c. Stabilize patient with sufficient O_2 and blood pressure control (labetalol or hydralazine).
   d. **Continue** $MgSO_4$ and antihypertensive medications for **48 hours** following delivery because **25% of seizures** occur within 24 hours postpartum.
5. **Complications** = risk of maternal (<2%) and fetal (6% to 12%) death; 65% risk of preeclampsia and 2% risk of eclampsia in subsequent pregnancy

NEXT
STEP

Do not confuse **eclampsia** with **epilepsy.** Know the patient's history before making a diagnosis because induced delivery **will not** cure the **epileptic** patient.

Quick HIT

Anticonvulsant use in pregnancy:

- Patients with epilepsy should be kept on their regular anticonvulsant medication during pregnancy but should be given supplemental folate.
- Diazepam can be used to break active seizures (80% effective).

E. Maternal Asthma (Pre-Existing)

1. Severe maternal asthma is associated with preeclampsia, spontaneous abortion, intrauterine fetal demise, and IUGR
2. **H/P** = course of disease frequently does not change during pregnancy from prior severity, but exacerbations may be less tolerated by the mother because of normal physiologic respiratory changes of pregnancy
3. **Treatment**
   a. Treat mild intermittent asthma with short-acting β-agonists (e.g., albuterol) as needed (also used as needed for all more severe variants)
   b. Treat mild persistent asthma with a short-acting β-agonist plus a low-dose inhaled corticosteroid.
   c. Treat moderate persistent asthma with either a medium-dose inhaled corticosteroid or combination of low-dose inhaled corticosteroid plus a long-acting β-agonist (e.g., salmeterol).
   d. Treat severe persistent asthma with a high-dose inhaled corticosteroid plus a long-acting β-agonist.
4. **Complications** = increased risk of preeclampsia, spontaneous abortion, intrauterine fetal death, and IUGR in untreated severe disease; oral corticosteroid use may be associated with IUGR and cleft palate (although unproved)

F. Maternal Nausea and Vomiting

1. Most pregnant women experience nausea and vomiting in the **first trimester** of pregnancy (i.e., morning sickness); most cases improve by the second trimester.
2. Most likely caused by increases in hCG or imbalance of progesterone and estrogen
3. **H/P** = nausea and vomiting that occurs frequently and may be daily; typically occurs in first trimester and improves after 16 weeks' gestation
4. **Treatment** = maintenance of hydration status, avoidance of large meals, elevating head in bed; antacids following meals may be helpful in worse cases

Quick HIT

Hyperemesis gravidarum is severe nausea and vomiting that affects 1% of pregnant women. It may be complicated by electrolyte abnormalities, weight loss, and ketonuria. It is treated with hospitalization, fluids, and antiemetics.

G. Maternal Deep Venous Thrombosis (DVT)

1. Risk of DVT **increases** during pregnancy because of **venous stasis** and relative **increase** in **circulating clotting** factors
2. **H/P** = similar presentation to that in nonpregnant patients (see Chapter 1, **Cardiovascular Disorders**); clinical diagnosis may be more difficult in pregnant patients because edema is also common in absence of DVT
3. **Radiology** = US and Doppler studies are safe means of finding thrombosis
4. **Treatment**
   a. At diagnosis, IV heparin dosed to maintain partial thromboplastin time (PTT) at two times normal, or low–molecular-weight heparin (LMWH) (e.g., enoxaparin) dosed to achieve consistent antifactor Xa levels 0.5 to 1.2 U/mL at 4 hours after injection
   b. At discharge, patients should be switched to subcutaneous LMWH.
   c. If possible, discontinue anticoagulation 24 to 36 hours prior to delivery; patients at high risk may be switched to IV unfractionated heparin until 6 hours prior to delivery.
   d. Anticoagulants should be continued following delivery for 6 weeks (warfarin or enoxaparin can be used postpartum).
5. **Complications** = pulmonary embolus; heparin therapy can be complicated by hemorrhage or thrombocytopenia

Quick HIT

Warfarin has teratogenic effects and should **not** be used during pregnancy but is safe to use during breastfeeding.

NEXT
STEP

Stop all anticoagulation during active labor until 6 hours after delivery to prevent severe hemorrhage.

H. Maternal UTIs

1. UTIs are **more common** during pregnancy because of maternal immunosuppression, outflow obstruction, and decreased ureteral peristalsis (secondary to increased progesterone).
2. **H/P** = similar symptoms to nonpregnant patients (e.g., dysuria, urinary frequency, urgency) or asymptomatic
3. **Labs** = urinalysis shows white blood cells (WBCs) and nitrites; urine culture shows bacteria
4. **Treatment** = amoxicillin, nitrofurantoin, or cephalexin × 3 to 7 days; recurrent cases or pyelonephritis may require longer therapy

Quick **HIT**

Fluoroquinolones should not be used for treatment of UTI because of teratogenic effects.

I. Maternal Drug Use

1. Several prescribed and illicit drugs can have a negative effect on pregnancy (see Table 13-6 and Table 13-7)

Table 13-6 Recreational Drug Use and Associated Risks to Mother and Fetus During Pregnancy

Drug	Maternal Risks	Fetal Risks
Marijuana	Minimal	IUGR, prematurity
Cocaine	**Arrhythmia,** myocardial infarction, subarachnoid hemorrhage, seizures, stroke, abruptio placentae	**Abruptio placentae,** IUGR, prematurity, facial abnormalities, delayed intellectual development, fetal demise
Ethanol	Minimal	**Fetal alcohol syndrome** (mental retardation, IUGR, sensory and motor neuropathy, facial abnormalities), spontaneous abortion, intrauterine fetal demise
Opioids	**Infection** (from needles), narcotic withdrawal, premature rupture of membranes	Prematurity, IUGR, meconium aspiration, neonatal infections, **narcotic withdrawal** (may be fatal)
Stimulants	Lack of appetite and **malnutrition,** arrhythmia, withdrawal depression, hypertension	IUGR, congenital heart defects, cleft palate
Tobacco	**Abruptio placentae, placenta previa**, premature rupture of membranes	Spontaneous abortion, prematurity, **IUGR,** intrauterine fetal demise, impaired intellectual development, higher risk of neonatal respiratory infections
Hallucinogens	Personal endangerment (poor decision making)	Possible developmental delays

IUGR, intrauterine growth restriction.

Table 13-7 Common Medications that Carry Teratogenic Risks

Medication	Teratogenic Risks
ACE-I	Renal abnormalities, decreased skull ossification
Aminoglycosides	CN VIII damage, skeletal abnormalities, renal defects
Carbamazepine	Facial abnormalities, IUGR, mental retardation, cardiovascular abnormalities, neural tube defects
Chemotherapeutics (all drug classes)	Intrauterine fetal demise (~30% pregnancies), severe IUGR, multiple anatomic abnormalities (palate, bones, limbs, genitals, etc.), mental retardation, spontaneous abortion, secondary neoplasms
Diazepam	Cleft palate, renal defects, secondary neoplasms
DES	Vaginal and cervical cancer later in life (adenocarcinoma)
Fluoroquinolones	Cartilage abnormalities
Lithium	Ebstein anomaly
Phenobarbital	Neonatal withdrawal
Phenytoin	Facial abnormalities, IUGR, mental retardation, cardiovascular abnormalities
Retinoids	CNS abnormalities, cardiovascular abnormalities, facial abnormalities, spontaneous abortion
Sulfonamides	Kernicterus (bile infiltration of brain)
Tetracycline	Skeletal abnormalities, limb abnormalities, teeth discoloration
Thalidomide	Limb abnormalities
Valproic acid	Neural tube defects (~1% pregnancies), facial abnormalities, cardiovascular abnormalities, skeletal abnormalities
Warfarin	Spontaneous abortion, IUGR, CNS abnormalities, facial abnormalities, mental retardation, Dandy–Walker malformation

ACE-I, angiotensin-converting enzyme inhibitors; CN, cranial nerve; CNS, central nervous system; DES, diethylstilbestrol; IUGR, intrauterine growth restriction; OCPs, oral contraceptive pills.

Table 13-8 Congenital Infections and Effects upon the Fetus and Neonates

Maternal Infection	Possible Fetal/Neonatal Effects	Diagnosis	Treatment
Toxoplasmosis	Hydrocephalus, intracranial calcifications, chorioretinitis, microcephaly, spontaneous abortion, seizures	• Possible mononucleosis-like illness • Amniotic fluid PCR for *Toxoplasma gondii* or serum antibody screening may be helpful for diagnosis	• Pyrimethamine, sulfad • Mother should avoid g litter boxes, and unpas
Rubella	Increased risk of spontaneous abortion, skin lesions **("blueberry muffin baby"), congenital rubella syndrome** (IUGR, deafness, cardiovascular abnormalities, vision abnormalities, CNS abnormalities, hepatitis) if disease transmission occurs	• Early prenatal IgG screening	• Mother should be imm ing to become pregnar • No treatment if infecti pregnancy • No proved benefit from globulin
Rubeola (measles)	Increased risk of prematurity, IUGR, and spontaneous abortion; **high risk** (20% if term birth, 55% if preterm) **of neonatal death** if disease transmission occurs	• Clinical diagnosis in mother confirmed by IgM or IgG antibodies after rash develops	• Mother should be imm to become pregnant • Immune serum globuli infection develops dur • Vaccine is contraindica attenuated virus carrie
Syphilis	Neonatal anemia, deafness, hepatosplenomegaly, pneumonia, hepatitis, osteodystrophy, rash followed by hand/foot desquamation; 25% neonatal mortality	• Early prenatal RPR or VDRL • Confirm with FTA-ABS	• Penicillin (if allergic de
Cytomegalovirus	IUGR, chorioretinitis, **CNS abnormalities,** mental retardation, vision abnormalities, deafness, hydrocephalus, seizures, hepatosplenomegaly	• Possible mononucleosis-like illness • IgM antibody screening or PCR of viral DNA within first few weeks of life	• No treatment if infecti pregnancy • Ganciclovir may decre • **Good hygiene** reduce

Herpes simplex	Increased risk of prematurity, IUGR, and spontaneous abortion; high risk of **neonatal death** or **CNS abnormalities** if disease transmission occurs	• Clinical diagnosis confirmed with viral culture or immunoassays	• Delivery by cesarean section to av disease transmission if active lesio or if primary outbreak • Acyclovir may be beneficial in neon
Hepatitis B	Increased risk of prematurity, IUGR; increased risk of neonatal death if acute disease develops	• Prenatal surface antigen screening	• Maternal **vaccination**; vaccinatior nate and administration of immune shortly after birth
HIV	Viral transmission in utero (5% risk), **rapid progression** of disease to AIDS	• Early prenatal maternal blood screening (consent required)	• **AZT** significantly reduces vertical t sion risk • Continue prescribed antiviral regim avoid efavirenz, didanosine, stavud nevirapine
Gonorrhea/ chlamydia	Increased risk of spontaneous abortion; neonatal sepsis, **conjunctivitis**	• Cervical culture and immunoassays	• Erythromycin given to mother or ne
Varicella-zoster	Prematurity, **encephalitis, pneumonia,** IUGR, **CNS abnormalities,** limb abnormalities, blindness; high risk of neonatal death if birth occurs during active infection	• IgG titer screening in women with **no known history of disease** • IgM and IgG antibody titers can confirm diagnosis in neonates	• Varicella immune globulin given to mother within 96 hours of exposure neonate if born during active infect • Vaccine is contraindicated during p (live-attenuated virus carries risk of fe
Group B streptococcus	Respiratory distress, pneumonia, **meningitis,** sepsis	• Antigen screening after 34 wks of gestation	• IV β-lactams or clindamycin during infected neonates
Parvovirus B19	Decreased RBC production, hemolytic anemia, hydrops fetalis	• IgM antibody screening or PCR of viral DNA	• Monitor fetal hemoglobin by PUBS intrauterine transfusion for severe a

AIDS, acquired immunodeficiency syndrome; AZT, zidovudine; CNS, central nervous system; FTA-ABS, fluorescent treponemal antibody absorption test; HIV, hu immunodeficiency virus; Ig, immunoglobulin; IUGR, intrauterine growth restriction; IV, intravenous; PCR, polymerase chain reaction; PUBS, percutaneous umbil sampling; RBC, red blood cell; RPR, rapid plasma reagin; VDRL, Venereal Disease Research Laboratories.

2. **H/P** = a complete drug history should be taken to assess all potential fetal risks
3. **Treatment**
   a. Appropriate counseling and education for drug abuse
   b. Stop teratogenic drugs during pregnancy (unless stopping drug is more harmful than use) and select alternative medications or therapies to treat medical conditions
   c. Careful screening for related domestic abuse

MNEMONIC

Congenital infections are frequently referred to as the TORCH infections:

Toxoplasmosis
Other (varicella-zoster, Parvovirus B19, group B streptococcus, chlamydia, gonorrhea)
Rubella/**R**ubeola/**R**PR (syphilis)
Cytomegalovirus
Herpes simplex/**H**epatitis B/**H**IV

J. Congenital Infections

1. Maternal infections during pregnancy that may have significant negative effects on fetal development or viability (see Table 13-8)
2. Prenatal screening is performed to detect certain infections that are of particular risk to the fetus

V. Obstetric Complications of Pregnancy

A. Ectopic Pregnancy

1. Implantation of zygote **outside of uterus;** most commonly occurs in **ampulla of fallopian tube** (95% of cases) but can also occur on ovary, cervix, or abdominal cavity

NEXT
STEP

Any woman of childbearing age who presents with abdominal pain must be given a β-hCG **pregnancy test.**

2. **Risk factors** = **pelvic inflammatory disease,** sexually transmitted diseases, gynecologic surgery, **prior ectopic pregnancy,** multiple sexual partners, smoking
3. **H/P**
   a. **Abdominal pain,** nausea, amenorrhea (due to pregnancy); **scant vaginal bleeding,** possible palpable pelvic mass, cervical motion and adnexal tenderness
   b. In cases of rupture, abdominal pain becomes severe and can be accompanied by hypotension, tachycardia, and peritoneal signs
4. **Labs** = elevated β-hCG (urine or serum) indicates pregnancy; β-hCG in intrauterine pregnancy will double every 48 hours; β-hCG that is **low for time of gestation** should raise suspicion for ectopic pregnancy
5. **Radiology**
   a. Transabdominal and transvaginal US should be able to visualize pregnancy once β-hCG reaches **6,500 mIU/mL** and **1,500 mIU/mL,** respectively.
   b. **Absence of visible intrauterine pregnancy** should raise suspicion. If β-hCG is <1,500 mIU/mL, repeat in 2 days.
   c. US may show free abdominal fluid if rupture has occurred.
6. **Treatment** = unruptured ectopic pregnancy of <6 weeks' gestation is treated with methotrexate to abort pregnancy; longer-term or ruptured ectopic pregnancy treated with IV hydration and **surgical excision** with attempt to preserve fallopian tube (unstable patients should receive emergency surgery)
7. **Complications** = unavoidable fetal death, severe maternal hemorrhage, increased risk of future ectopic pregnancy, infertility, Rh sensitization, **maternal death**

Quick **HIT**

β-hCG is produced by the syncytiotrophoblast. β-hCG preserves the corpus luteum in early pregnancy in order to maintain progesterone secretion until the placenta takes over progesterone production.

Quick **HIT**

The most common causes of vaginal bleeding in **early** pregnancy are **ectopic pregnancy,** threatened or inevitable **spontaneous abortion, physiologic** bleeding (related to implantation), and **uterine–cervical pathology.**

B. Spontaneous Abortion (Miscarriage) (See Table 13-9)

1. **Nonelective** termination of pregnancy **<20 weeks'** gestation (see Table 13-9)
   a. First-trimester spontaneous abortions are usually the result of **fetal chromosomal abnormalities** (especially trisomies).
   b. Second-trimester spontaneous abortions are usually caused by infection, **cervical incompetence, uterine abnormalities,** hypercoagulable state, poor maternal health, or **drug use** (prescription or recreational).
2. **Risk factors** = **increased maternal age,** multiple prior births, prior spontaneous abortion, uterine abnormalities, smoking, alcohol, nonsteroidal anti-inflammatory drugs (NSAIDs), cocaine, excessive caffeine use, certain maternal infections, low folate level, autoimmune disease
3. **H/P** = history should focus on prior abortions, birth history, prior gynecologic infections, and family history of congenital diseases; vaginal bleeding, and possible open cervical os seen on examination
4. **Labs** = β-hCG used to assess gestational age and track progress of pregnancy
5. **Radiology** = US used to assess fetal viability
6. **Treatment** = depends on type of spontaneous abortion (see Table 13-9)

Quick **HIT**

Spontaneous abortions occur in up to 25% of pregnancies.

Table 13-9 Types of Spontaneous Abortions

Abortion Type	Threatened	Missed	Inevitable	Incomplete
Sign/Symptoms				
Uterine bleeding	In initial 20 wks of gestation	Present or with pain	Initial 20 wks + pain	Initial 20 wks
Cervical os	Closed	Closed	Open	Open
Uterine contents expelled	None	None	None	Some
Diagnosis	US detects **viable** fetus, **cervix is closed**	US detects **nonviable** intrauterine fetus	**Viable** fetus, **cervix is dilated**	Based on history of expelled products of conception
Treatment	Bed rest, limited activity	Expectant management, misoprostol, or D&C; also give Rho(D) immune globulin	Same as missed abortion	Same as missed abortion

D&C, dilation and curettage; US, ultrasound.

C. Intrauterine Fetal Demise

1. Intrauterine fetal death that occurs **after 20 weeks' gestation** and before the onset of labor
2. Caused by **placental** or **cord abnormalities** secondary to maternal cardiovascular or hematologic conditions, maternal HTN, **infection,** poor maternal health, or fetal congenital abnormalities, often there is no known cause
3. **H/P** = pregnant patient notes no fetal activity; uterus small for length of gestation, no fetal movement, no fetal heart tones
4. **Radiology** = US shows nonviable intrauterine fetus with no heart activity
5. **Treatment** = oxytocin, misoprostol (prostaglandin E_1), or prostaglandin E_2 can be used to induce labor and delivery; dilation and evacuation (D&E) might be used to remove fetus if <24 weeks' gestation
6. **Complications** = **DIC** if fetus is retained for prolonged amount of time
7. Evaluation of fetal demise involves fetal autopsy, examination of placenta, and karyotype

D. IUGR

1. Fetal growth that lags behind gestational age (<10th percentile)
2. Types
   a. **Symmetric**
      (1) 20% of cases
      (2) Overall decrease in fetal size (global growth lag)
      (3) Early in pregnancy
      (4) Most commonly caused by **congenital infection, chromosomal abnormalities,** or maternal drug use (illicit or therapeutic)
   b. **Asymmetric**
      (1) 80% of cases
      (2) Decreased abdominal size with preservation of head and extremities (head sparing growth lag)
      (3) Late in pregnancy
      (4) Caused by multiple gestation, **poor maternal health,** or uteroplacental insufficiency (HTN, GDM, smoking)
3. **H/P** = fundal height is at least **3 cm smaller** than expected for gestational age (beginning at 20 weeks' gestation, distance in centimeters from pubis to top of fundus should equal gestational age in weeks)
4. **Radiology**
   a. US shows head circumference: abdominal circumference and femur length: abdominal circumference ratios **increased** in **asymmetric** IUGR and were **normal** in **symmetric** IUGR.
   b. US can be used to estimate fetal weight.
   c. US frequently detects oligohydramnios.
   d. Doppler US studies may detect decreased fetal, umbilical, or maternal blood flow.
5. **Treatment**
   a. Fetal growth should be followed with US.
   b. Nutritional supplementation, maternal O_2 therapy, and maternal bed rest may aid fetal growth.
   c. Delivery should be induced if fetal growth slows further, maternal health worsens, or tests show fetal distress.
   d. Maternal antenatal corticosteroids help to speed fetal lung maturation in mothers expected to deliver early.

Quick HIT

The initial US finding for IUGR is frequently an **abdominal circumference <10th percentile** for gestational age.

E. Oligohydramnios

1. **Deficiency** of **amniotic fluid** in gestational sac (amniotic fluid index <5 cm)
2. Associated with **IUGR,** fetal stress, HTN, placental insufficiency, fetal renal abnormalities, or poor fetal health
3. Significance of timing
   a. **First trimester:** frequently results in **spontaneous abortion**
   b. **Second trimester:** may be due to **fetal renal abnormalities,** maternal cause (e.g., preeclampsia, renal disease, HTN, collagen-vascular disease), or placental thrombosis
   c. **Third trimester:** associated with **premature rupture of membranes** (PROM), preeclampsia, abruptio placentae, or idiopathic causes
4. **H/P** = possibly asymptomatic; fundal height may be small for gestational age
5. **Radiology** = US used to determine amniotic volume and perform fetal assessment; amniotic fluid index will be <5 cm, with no pockets at least 2 cm in size
6. **Treatment** = expectant management if fetus responds well to tests of well-being; induce delivery of viable fetus if risk of fetal demise is significant (poor response of fetus to tests of well-being); hydration and bed rest may improve amniotic volume
7. **Complications** = spontaneous abortion, intrauterine fetal demise; abnormalities in limb, facial, lung, and abdominal development caused by **compression**

F. Polyhydramnios

1. **Excess** of amniotic fluid in gestational sac (amniotic fluid index >25 cm)
2. Can result from insufficient swallowing of amniotic fluid (e.g., esophageal atresia) by fetus or increased fetal urination related to **maternal diabetes,** multiple gestation, fetal anemia, or chromosomal abnormalities
3. **H/P** = fundal height may be larger than expected for gestational age
4. **Radiology** = US used to assess amniotic fluid volume; amniotic fluid index will be >25 cm or will show one pocket of at least 8 cm
5. **Treatment** = only administered if mother is uncomfortable or if a threat of preterm labor exists; pregnancies of <32 weeks' gestation treated with amnioreduction and indomethacin (tapered dosing); pregnancies >32 weeks' gestation treated with amnioreduction alone
6. **Complications** = preterm labor, PROM, fetal malpresentation, maternal respiratory compromise

Quick HIT

Excessive amniotic fluid frequently **reaccumulates** following percutaneous drainage.

G. PROM

1. Spontaneous **rupture of amniotic sac** with spillage of amniotic fluid **before** onset of labor
2. **Risk factors** = vaginal or cervical infection, cervical incompetence, poor maternal nutrition, prior PROM

Quick HIT

Internal manual examination should **not** be performed by the physician in cases of PROM because of an **increased risk of introducing infection** into the vaginal canal.

3. **H/P** = loss of amniotic fluid from vagina; amniotic fluid may be seen pooling in vagina on visual examination
4. **Labs** = **microscopic examination** of vaginal fluid will show **"ferning"** if amniotic fluid is present; vaginal fluid will turn **nitrazine paper blue** in presence of amniotic fluid; vaginal fluid should be cultured to detect infection
5. **Radiology** = US should be used to confirm oligohydramnios and to assess volume of residual amniotic fluid and fetal position
6. **Treatment**
   a. If PROM occurs at <32 weeks' gestation, give corticosteroids (to hasten fetal lung maturation), prophylactic antibiotics (for group B streptococcus) and magnesium sulfate (for neuroprotection); labor should be induced once amniotic fluid analysis indicates fetal lung maturity.
   b. If PROM occurs at 32 to 34 weeks' gestation, amniotic fluid analysis is performed to determine fetal lung maturity; labor is induced if lung maturity has occurred; corticosteroids and antibiotics are administered if lungs are immature until induction at 34 weeks. If there are signs of infection (maternal fever and fetal tachycardia) or fetal compromise, deliver with antibiotics and corticosteroids.
   c. If PROM occurs after 34 weeks' gestation, antibiotics are administered and delivery is induced.

Quick HIT

Fetal lung maturity can be quantified by measuring lecithin (L) and sphingomyelin (S) levels in amniotic fluid and determining the **LS ratio** (**L:S >2** with the presence of phosphatidylglycerol [PG] in amniotic fluid **suggests lung maturity**).

H. Preterm Labor

1. Onset of labor **<37 weeks'** gestation (regular contractions that cause cervical changes)
2. **Risk factors** = **multiple gestation, PROM,** infection, placenta previa, abruptio placentae, **previous preterm labor,** polyhydramnios, cervical incompetence (cervical surgery), poor nutrition, stressful environment, **smoking,** substance abuse, or lower socioeconomic status
3. **H/P** = constant low back pain, cramping, signs of labor (painful contractions in the setting of cervical change) **<37 weeks' gestation**
4. **Labs** = urine, vaginal, and cervical cultures performed to detect infection
5. **Radiology** = US used to assess amniotic fluid volume and fetal well-being and verify gestational age
6. **Treatment**
   a. At <34 weeks' gestation
      (1) Expectant management (even if PPROM)
      (2) Hospitalization, hydration, and activity restriction
      (3) **Tocolytic therapy** (with **$MgSO_4$, terbutaline,** indomethacin, or nifedipine) for 48 hours
      (4) Glucocorticoids (betamethasone or dexamethasone) for 48 hours to mature fetal lungs
      (5) Give empiric ampicillin for prophylaxis against group B streptococcus if delivery is imminent or if there is evidence of active infection.
   b. At >34 weeks' gestation
      (1) Expectant management if lung maturity is proven
      (2) Active management if there is an indication for delivery (e.g., nonreassuring fetal testing, infection, maternal threat)
      (3) Tocolysis and glucocorticoids are of no proven benefit beyond 34 weeks
      (4) Give empiric ampicillin if delivery is imminent
7. **Complications** = increased risk of neonatal complications and fetal respiratory distress syndrome with shorter gestational age

Quick **HIT**

Although not used to diagnose labor, ultrasound can measure cervical length. A cervical length >35 mm is associated with a very low risk of preterm birth; a cervical length <15 mm has high risk of preterm birth.

I. Placenta Previa

1. **Implantation** of placenta **near or over the internal cervical os,** frequently associated with vaginal bleeding
2. Types (see Figure 13-3)
   a. **Low implantation:** placenta implanted in lower uterus but does not infringe on cervical os until dilation occurs
   b. **Partial** placenta previa: placenta partially covers os
   c. **Complete** placenta previa: placenta completely covers os

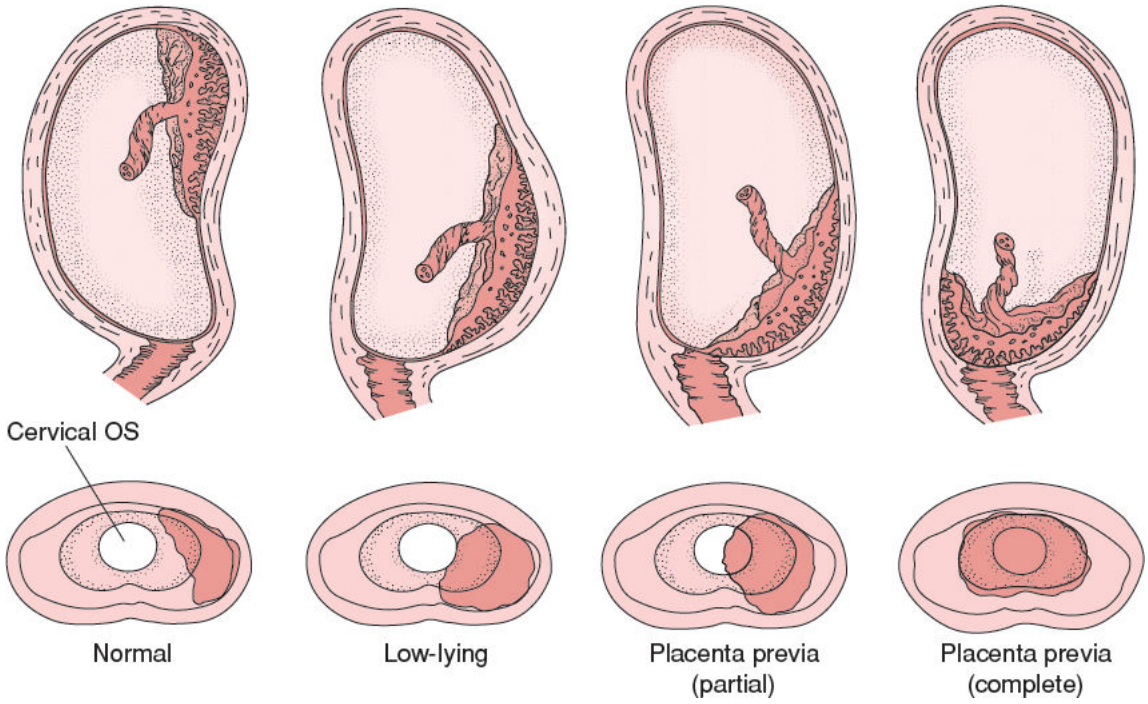


FIGURE **13-3**
Uterine profiles and cross sections demonstrating normal placental implantation and examples of low-lying placenta, partial placenta previa, and complete placenta previa.
(Modified from Simpson, K. R., & Creehan, P. A. [2014]. *Perinatal nursing* [4th ed., p. 146]. Philadelphia, PA: Lippincott Williams & Wilkins; with permission.)

3. **Risk factors** = multiparity (i.e., prior pregnancy), increased maternal age, **prior placenta previa, prior cesarean section or other uterine surgery,** multiple gestation, uterine fibroids, history of abortion, smoking
4. **H/P** = **painless** vaginal bleeding in **third trimester** (30th week of gestation is most common time of onset), no digital cervical examination if suspected
5. **Radiology** = US determines location of placenta (transvaginal or translabial US more sensitive)
6. **Treatment**
   a. Bed rest in cases of minor inconsistent bleeding; inpatient admission with maternal and fetal monitoring for active bleeding; give Rho(D) immune globulin to Rh-negative mothers for any bleeding in the third trimester.
   b. **Tocolytics** can be used to delay delivery and reduce maternal bleeding risk in cases of a preterm fetus with **immature lungs** and **mild maternal bleeding.**
   c. When delivery is indicated, perform by **cesarean section.**
   d. Vaginal delivery can be performed with a low-lying placenta.
7. **Complications** = severe hemorrhage, IUGR, malpresentation, PROM, vasa previa (fetal vessels overlie the os and increase risk for fetal exsanguination); 1% of cases result in **maternal death**

Quick HIT

Placenta previa and **abruptio placentae** are the most common causes of vaginal bleeding **after 20 weeks'** gestation. Bleeding in **placenta previa** is **painless,** and bleeding in **placental abruption** is **painful**.

Quick HIT

Do not perform a sterile vaginal examination in a patient with painless third trimester bleeding until placenta previa is ruled out.

J. Abruptio Placentae

1. Premature separation of the placenta from uterine wall before delivery leading to **significant maternal hemorrhage**
2. **Risk factors** = **HTN,** prior abruptio placentae, trauma, **tobacco use,** cocaine use, PROM, multiple gestation, multiparity
3. **H/P** = **painful** vaginal bleeding in **third trimester,** back pain, abdominal pain; pelvic and abdominal tenderness, **increased uterine tone;** hypotension occurs with severe hemorrhage
4. **Radiology** = US **inconsistently** shows separation of placenta from uterus
5. **Treatment**
   a. Bed rest in inpatient setting for very mild cases.
   b. Delivery typically occurs rapidly secondary to uterine irritation, but **cesarean section** should be performed in cases of **hemodynamic instability.**
   c. Transfusion is frequently required for significant hemorrhage.

6. **Complications** = DIC; **severe hemorrhage** that increases risk of maternal death; **fetal demise** occurs in 20% of cases; increased risk of abruption in future pregnancies; can cause fetal hypoxia

Quick HIT

Benign low back pain in pregnancy radiates to the thighs, worsens with activity, and improves with rest.

K. Multiple Gestations

1. Any pregnancy in which **more than one fetus** develops at the same time
2. More likely to occur with fertility drug use
3. Types
   a. **Monozygotic:** division of zygote resulting in development of identical fetuses; fetuses may or may not share amnion or chorion
   b. **Dizygotic:** fertilization of more than one egg by different sperm resulting in development of dissimilar (i.e., fraternal) fetuses and separate amnions
4. Increased incidence of complications
   a. Maternal: HTN, DM, **preeclampsia, preterm labor**
   b. Fetal: **malpresentation,** placenta previa, abruptio placentae, PROM, **IUGR,** birth trauma, cerebral palsy, respiratory distress syndrome
5. **H/P** = fundal height large for gestational age; more than one fetal heart tone may be detected
6. **Radiology** = US detects 2+ gestational sacs
7. **Treatment**
   a. Close maternal follow-up (weekly or biweekly) starting at 24 weeks' gestation
   b. Activity restriction, frequent assessment of fetal growth with US, and weekly nonstress tests starting at 36 weeks' gestation
   c. Preterm labor should be halted with tocolytic therapy
   d. Vertex–vertex (i.e., both heads downward) presentations may be delivered vaginally, but breech–vertex or breech–breech presentations require cesarean section; vertex–breech (first twin is head down, second is breech) presentation may often attempt vaginal delivery.

Quick HIT

Conjoined twins only occur in cases of monozygotic twinning.

Quick HIT

If the umbilical cords for multiple fetuses are fused, **twin–twin transfusion syndrome** can result, in which one twin is **inadequately** perfused, leading to an increased risk of fetal complications.

Quick HIT

The average delivery time for twins is 36 weeks' gestation.

VI. Labor and Delivery

A. Assessment of Fetal Well-Being

1. Tests of fetal activity, heart rate, and responses to stress used to confirm fetal well-being and to detect fetal distress
2. **Nonstress test**
   a. Used often during **prenatal assessment** and into labor.
   b. Mother reclines in left lateral decubitus position.
   c. Fetal heart rate is monitored with external fetal heart rate and uterine contraction monitors. Must be measured for at least 40 minutes to account for the fetal sleep cycle.
   d. **Effects of fetal movement on heart rate** are noted.
   e. Normal ("reactive") test is considered to be two or more 15-bpm accelerations of fetal heart rate lasting at least 15 seconds, each within 20 minutes.
   f. An external sound device (vibroacoustic stimulator) can be attached to the mother's abdomen to encourage fetal activity and shorten the time of the test.
   g. Nonreactive test prompts the performance of a biophysical profile.

Quick HIT

Normal fetal heart rate is 120–160 bpm.

Quick HIT

A fetal **nonstress test** and **biophysical profile** are easy ways to assess fetal well-being and risk of fetal demise because of a stressful environment.

3. **Biophysical profile**
   a. Performed in follow-up to nonreactive nonstress test
   b. **Nonstress test repeated** and US assessment performed
   c. US used to measure **amniotic fluid index** (i.e., total linear measurement in centimeters of largest amniotic fluid pocket detected in each of four quadrants of amniotic sac), **fetal breathing rate, fetal movement, fetal tone** (i.e., extension of fetal spine or limb with return to flexion)
   d. Scoring system applied to nonstress test results and all US measurements; if test component satisfies criteria, it is given 2 points; if it does not meet criteria, it is assigned 0 points (no 1-point scores allowed)
      (1) Reactive nonstress test (2 points)
      (2) Amniotic fluid index = 5 to 23 cm (2 points)
      (3) 1+ episode of rhythmic breathing lasting 20 seconds within a 30-minute period (2 points)
      (4) 2+ episodes of discrete fetal movement within a 30-minute period (2 points)
      (5) 1+ episodes of spine and limb extension with return to flexion (2 points)
   e. **Reassuring** profile is a score of **8 or 10** and suggests minimal risk of fetal asphyxia; **lower** score suggests **fetal distress**

Table 13-10 Types of Decelerations Seen on Fetal Heart Rate Tracings

Deceleration	Appearance	Cause	Treatment
Early	Decelerations begin and end **with** uterine contractions	Head compression	• None required • **Not a sign of**
Late	Begin **after** initiation of uterine contraction and end **after** contraction has finished	**Uteroplacental insufficiency,** maternal venous compression, maternal hypotension, or abruptio placentae; **may suggest fetal hypoxia**	• Test fetal blood diagnose hypo • Recurrent late hypoxia direct
Variable	**Inconsistent** onset, duration, and degree of decelerations	Umbilical cord compression	Change mother's

4. **Contraction stress test**
   a. Used late in pregnancy or during labor to assess uteroplacental dysfunction
   b. Fetal heart rate is recorded with external fetal monitor or fetal scalp electrode.
   c. **Beat-to-beat variability** of ~5 bpm, **long-term heart rate variability,** and occasional **heart rate accelerations** (2+ accelerations of 15 bpm lasting at least 15 seconds within a 20-minute period) are **reassuring** signs.
   d. **Decelerations** of heart rate from baseline may indicate fetal head compression, umbilical cord compression, or fetal hypoxia (see Table 13-10, Figure 13-4).
5. **Fetal scalp blood sampling**
   a. Performed when a consistently abnormal fetal heart rate tracing seen
   b. Normal fetal blood pH is reassuring; **decreased pH** and **hypoxemia** and increased lactate indicate **fetal distress**
6. **Fetal scalp monitoring**
   a. Monitor attached to fetal scalp to track pulse oximetry and perform continuous fetal heart rate monitoring and electrocardiogram (ECG)
   b. Should be used only in pregnancies >36 weeks' gestation with vertex presentation

Quick HIT

During the last few weeks of gestation, a woman may experience multiple **false** (Braxton–Hicks) **contractions** not associated with true labor.

B. Stages of Labor

1. Labor (i.e., contractions with cervical change and effacement) typically begins at 37 to 42 weeks' gestation and involves four stages of progression (see Table 13-11).
2. Nulliparous and multiparous women proceed through labor at different rates.

C. Induction of Labor

1. Intervention (**oxytocin,** misoprostol, etc.) to initiate uterine contractions or speed progress of labor
2. Indications
   a. Maternal: preeclampsia, DM, stalled stage of labor, chorioamnionitis
   b. Fetal: prolonged pregnancy (i.e., >40 to 42 weeks), IUGR, PROM, some congenital defects
3. Contraindications to induction of labor are need for cesarean section, prior uterine surgery, fetal lung immaturity, malpresentation, acute fetal distress, active genital herpes, and placenta or vasa previa
4. Likelihood of vaginal delivery following induction predicted by measuring fetal station and cervical dilation, effacement, consistency, and position (i.e., Bishop score) (see Table 13-12)
   a. Greater cervical dilation and effacement, softer cervix, more anterior cervical position, and greater station are associated with greater likelihood of vaginal delivery (i.e., higher Bishop score).
   b. Lower Bishop score is associated with higher likelihood of cesarean delivery (30% rate of cesarean delivery if Bishop score <3 after induction, 15% if >3).

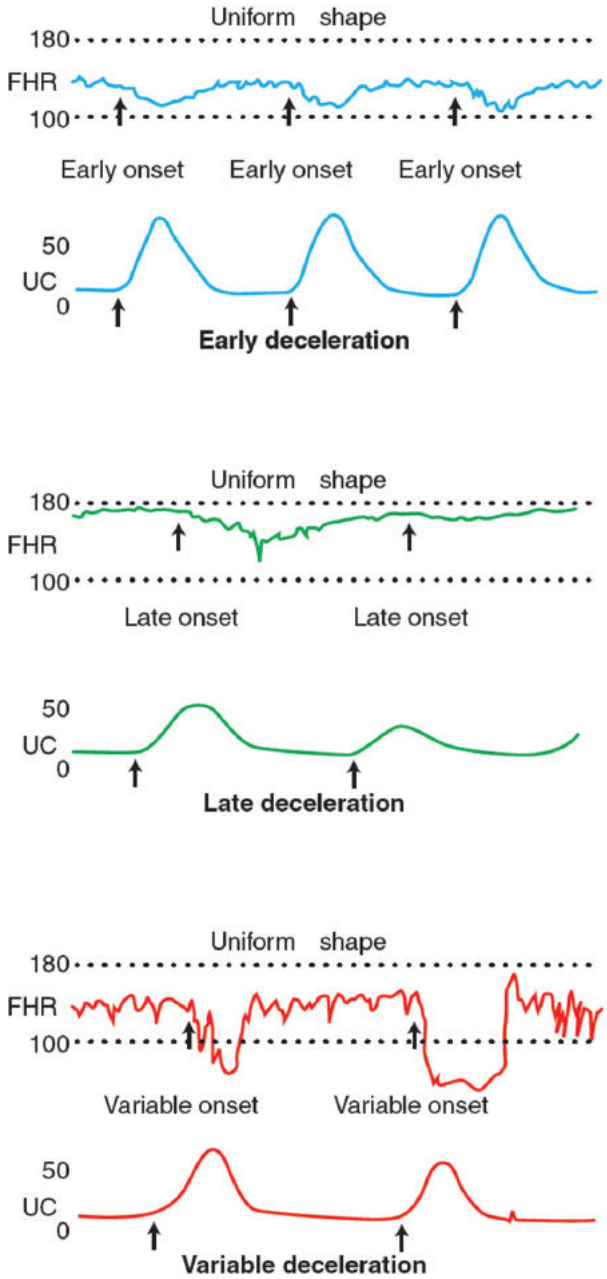


FIGURE 13-4

Examples of fetal heart and uterine tone tracings for early, late, and variable decelerations of fetal heart rate (FHR) following uterine contraction (UC). The *arrows* represent the beginning of a uterine contraction.
(Modified from Hon, E. [1973]. *An introduction to fetal heart rate monitoring*. Los Angeles, CA: University of Southern California. Also see Feibusch, K. C., Miroiu, M. Y., Breaden, R. S., Bader, C., & Gomperts, S. N. [2002]. *Prescription for the boards: USMLE Step 2* (3rd ed.). Philadelphia, PA: Lippincott Williams & Wilkins.)

D. Malpresentation

1. **Normal** fetal presentation (i.e., cephalic or vertex) is with fetal head down, chin tucked, and occiput directed toward birth canal.

2. **Face** (i.e., full hyperextension of neck) presentation occurs rarely and usually undergoes normal vaginal delivery if chin is anterior.
3. **Brow** (i.e., partial hyperextension of neck) presentation occurs very rarely and requires cesarean delivery if the head does not spontaneously correct to a normal presentation.
4. **Breech presentation** is the most common **malpresentation** (Figure 13-5).
   a. **Frank breech:** 75% of cases; hips flexed and knees extended
   b. **Complete breech:** hips and knees flexed
   c. **Footling (incomplete) breech:** one or both legs extended
   d. **Risk factors** = prematurity, multiple gestation, polyhydramnios, uterine anomaly, placenta previa
   e. **H/P** = abdominal examination (i.e., Leopold maneuvers) detects fetal head in abdomen, vaginal examination may detect presenting part
   f. **Radiology** = US confirms fetal orientation
   g. **Treatment** = most cases will resolve before labor; **external cephalic version** may be applied to abdomen at 37 weeks' gestation to attempt repositioning of fetus (up to 75% effective); cesarean section performed in most cases
   h. **Complications** = cord prolapse, head entrapment, fetal hypoxia, abruptio placentae, birth trauma

Quick HIT

Presentation at birth:

- Vertex presentation is position at time of delivery in >95% of pregnancies.
- Before 28 weeks' gestation, **25%** of pregnancies are in **breech** presentation, but **most** will assume **vertex** presentation by the time of birth.

Table 13-11 Stages of Labor

Stage	Beginning/End	Activity	Management	Du Nulliparous
1	• Latent phase: start of uterine contractions until 6-cm cervical dilation and complete effacement • Active phase: 6-cm cervical dilation until near 10-cm cervical dilation with consistent progression • Deceleration phase: transition from active phase to second stage of labor	• Latent phase: cervical effacement and gradual dilation • Active phase: regular uterine contractions, quick progression of cervical dilation (1.2 cm/hr for nulliparous, 1.5 cm/hr for multiparous) and effacement • Deceleration phase: slowdown of dilation and effacement shortly before engagement of fetal head in pelvis	• Monitor fetal heart rate and uterine contractions, assess progression of cervical changes periodically during active phase	<20 hrs (2/3 latent, 1/3 active
2	Full (10-cm) cervical dilation until delivery	Fetal descent through birth canal driven by uterine contractions	Monitor fetal heart rate and movement through birth canal	<3 hrs (<4 hrs w epidural)
3	Delivery of neonate until placental delivery	Placenta separates from uterine wall up to 30 min after delivery of neonate and emerges through birth canal, uterus contracts to expel placenta and prevent hemorrhage	Uterine massage, examination of placenta to confirm no intrauterine remnants	0–30 min
4	Initial postpartum hour	Hemodynamic stabilization of mother	Monitor maternal pulse and blood pressure, look for signs of hemorrhage	1 hr

E. Cesarean Section

1. Delivery of fetus through incision in uterine wall

Table 13-12 Bishop Scoring System[a]

Score	0	1	2	3
Dilation (cm)	0	1–2	3–4	5–6
Effacement (%)	0–30	40–50	60–70	>70
Station (cm)[b]	–3	–2	–1, 0	+1, +2
Cervical consistency	Firm	Medium	Soft	
Cervical position	Posterior	Middle	Anterior	

[a]From Bishop, E. H. (1964). Pelvic scoring for elective induction. *Obstetrics and Gynecology, 24*, 266–268.
[b]Distance of presenting body part above (2) or below (1) ischial spines.

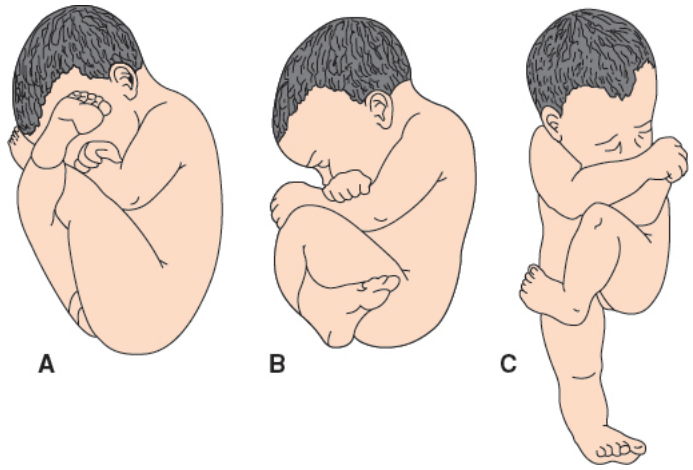


FIGURE 13-5
Examples of frank (A), complete (B), and incomplete (C) variations of breech presentation.
(Modified from Beckmann, C. R. B., Ling, F. W., Herbert, W. N. P., et al. [2014]. *Obstetrics and gynecology* [7th ed., p. 104]. Baltimore, MD: Lippincott Williams & Wilkins; with permission.)

2. Types
   a. **Vertical:** vertical incision in anterior muscular portion of the uterus (i.e., classic) or lower uterine segment (i.e., low vertical); chosen when fetus lies in transverse presentation, adhesions or fibroids prevent access to lower uterus, hysterectomy is scheduled to follow delivery, cervical cancer is present, or in postmortem delivery to remove living fetus from dead mother
   b. **Low transverse:** transverse incision in lower uterine segment; decreased risk of uterine rupture, bleeding, bowel adhesions, and infection (**preferred** to classic technique and performed more commonly)

Quick HIT

Risk of maternal mortality is similar for elective cesarean section and vaginal delivery, but emergency cesarean section carries a higher risk of mortality.

3. Indications
   a. Maternal: **eclampsia, prior uterine surgery, prior classic cesarean section,** cardiac disease, birth canal obstruction, maternal death, cervical cancer, active genital herpes, HIV
   b. Fetal: **acute fetal distress, malpresentation,** cord prolapse, macrosomia
   c. Combined maternal and fetal: **failure to progress in labor,** placenta previa, abruptio placentae, cephalopelvic disproportion
4. In subsequent pregnancies, vaginal delivery can be attempted only if **transverse** cesarean section was performed
5. If **vertical** incision has been used previously, repeat cesarean delivery must be performed because of risk of uterine rupture
6. **Complications** = hemorrhage, infection and sepsis, thromboembolism, injury to surrounding structures; future pregnancies are at increased risk of placenta previa, placenta accreta, and miscarriage

Quick HIT

Breast milk is considered the ideal infant nutrient because it contains important **IgA antibodies** for the newborn, is in **sufficient supply,** is **cost free,** and enhances mother–infant bonding.

F. Normal Puerperium and Postpartum Activity

1. Care of the newborn
   a. Immediate suction of mouth and nose to aid in breathing and to prevent aspiration.
   b. Neonate is dried and wrapped in clothes to prevent heat loss.
   c. Umbilical cord is clamped and cut; blood sample is taken from cord to measure blood gases and blood type.
   d. Onset of respiration within 30 seconds is confirmed; if spontaneous respiration does not begin, resuscitation must be initiated.
   e. Tracheal injection of synthetic or exogenous surfactant may be given in cases of lung immaturity.
   f. Apgar score is performed at 1 minute and 5 minutes after birth; a score of 7+ at 1 minute and 9+ at 5 minutes is reassuring (see Table 13-13).

Quick HIT

Early breast milk (**colostrum**) is rich in proteins, fat, and minerals and contains IgA; after 1 week postpartum, breast milk contains proteins, fat, water, and lactose.

2. Maternal changes
   a. Uterus decreases in size and cervix becomes firm over 3 weeks.
   b. Uterine discharge (i.e., lochia) is red during initial days after birth but becomes paler and white by 10th day postpartum.
   c. Vaginal wall gradually becomes firmer.
   d. Total peripheral resistance increases rapidly because of elimination of uteroplacental circulation; diuresis causes significant weight loss in 1st week postpartum; cardiac output gradually returns to normal.
   e. Mother may feel mild depression for few days after delivery (i.e., "postpartum blues"); most cases resolve without complications.
   f. Menstruation returns 6 to 8 weeks postpartum in nonnursing mothers.
   g. Ovulation and menstruation may not occur for several months in nursing mothers (98% effective in preventing pregnancy for 6 months after delivery if breastfeeding regularly).

Table 13-13 Apgar Scoring System for Determining Neonatal Well-Being

	Score		
Sign	**0**	**1**	**2**
Color	Blue, pale	Pink torso, blue extremities	Pink
Heart rate	None	<100 bpm	>100 bpm
Response to stimulation	None	Grimace	Strong cry
Muscle tone	Poor	Some movement	Active movement
Respirations	None	Poor, weak cry	Good, strong cry

Adapted from Apgar, V. (1953). A proposal of a new method of evaluation of the newborn infant. *Current Researches in Anesthesia and Analgesia, 32,* 261–267.

G. Postpartum Hemorrhage (PPH)

1. Blood loss >500 mL/24 hrs following vaginal delivery or >1,000 mL/24 hrs after cesarean section is abnormal.
2. Because of **uterine atony** in most cases (more likely after multiple gestation, prolonged labor, and chorioamnionitis)
3. Can also result from **birth canal trauma, retained placental tissue, uterine inversion,** or **coagulopathy** (e.g., DIC)
4. **H/P** = excessive postpartum bleeding from genital tract; soft, boggy uterus palpable with uterine atony; vaginal examination may detect lacerations; examination of placenta after birth should detect any missing segments
5. **Radiology** = US may show retained placental tissue (thick endometrial stripe or echogenic mass on US)
6. **Treatment**
   a. Uterine massage and oxytocin administration help increase uterine tone and decrease hemorrhage. Methylergonovine (contraindicated in HTN) and carboprost (contraindicated in asthma) are other uterotonic agents.
   b. Surgical repair of lacerations should be performed.
   c. Dilation and curettage (D&C) may successfully remove retained placental tissue.
   d. IV fluids and manual replacement of the uterus if uterine inversion is the cause of PPH.
   e. Hysterectomy may need to be performed in severe or refractory cases.

Quick HIT

Retained placental tissue causes the most substantial volume of postpartum bleeding.

VII. Gestational Trophoblastic Disease

A. Hydatidiform Mole

1. Benign neoplasms of trophoblastic cells (i.e., cells that make up placenta) that infrequently become malignant; **benign** trophoblastic neoplasms make up **80%** of trophoblastic disease
2. Types
   a. Complete: 46 XX or 46 XY genotype; completely derived from father (empty egg penetrated by two sperm)
   b. Incomplete: 69 XXY, 69 XXX, or 69 XYY genotype; fertilization of egg by two sperm; may be associated with abnormal fetus

NEXT
STEP

Highly suspect a molar pregnancy if **preeclampsia** occurs in the **first half** of pregnancy, and perform an US to confirm diagnosis.

3. **Risk factors** = low socioeconomic status, extremes of maternal age (teen, >40 years), history of prior molar pregnancy, Asian heritage, smoking
4. **H/P** = heavy or irregular painless vaginal bleeding during **first** or **second** trimester, hyperemesis gravidarum, dizziness, anxiety; large fundal height for gestational age, expulsion of **"grape-like" vesicles** from vagina, no fetal movement or heart tones detected
5. **Labs** = β-hCG is much **higher** than expected for gestational age
6. **Radiology** = US detects **"snowstorm"** pattern in uterus (anechoic, cystic spaces) without presence of gestational sac
7. **Treatment** = D&C to remove neoplasm; follow β-hCG for 1 year (levels should gradually decrease); avoid pregnancy for 6 months to 1 year
8. **Complications** = malignant gestational trophoblastic neoplasm (20% of cases), choriocarcinoma (5% of cases, suggested by continued high β-hCG following D&C)

NEXT
STEP

High β-hCG is seen in both **hydatidiform mole** and **multiple gestations;** differentiate the conditions with US.

B. Choriocarcinoma

1. **Malignant** trophoblastic neoplasm that arises from hydatidiform moles (50% of cases) or following abortion, ectopic pregnancy, or normal pregnancy
2. **H/P** = vaginal bleeding and possible hemoptysis, dyspnea, headache, dizziness, or rectal bleeding; enlarged uterus on examination with bleeding seen from cervical os
3. **Labs** = increased β-hCG
4. **Radiology** = US detects uterine mass with mix of hemorrhagic and necrotic areas and possible parametrial invasion; computed tomography (CT) may detect metastases
5. **Treatment** = hysterectomy of disease limited to uterus; chemotherapy routinely administered; patient with early limited disease wishing to maintain fertility may choose chemotherapy alone; follow β-hCG to track cure; avoid pregnancy for 1 year after therapy
6. **Complications** = **metastases** to lungs, brain, liver, kidneys, or gastrointestinal tract; good prognosis unless presence of brain or liver metastases; frequently missed diagnosis if not caused by progression from molar pregnancy

QUESTIONS

1. A 22-year-old woman, G2P1, at 38 weeks comes to the hospital due to nausea and vomiting. The patient also complains of lower abdominal pain. She reports continuous clear vaginal discharge over the past 48 hours and vaginal spotting. Temperature is 102° F, blood pressure is 110/62, and pulse is 102/min. The abdomen is nontender and without guarding. The uterus is diffusely tender. The cervix is 2 cm dilated and there is clear fluid pooled in the posterior fornix. Fetal heart monitoring reveals a rate of 165/min, moderate variability, and no accelerations of decelerations. Contractions occur every 8 minutes. Which of the following is the most likely diagnosis in this patient?

   A. Acute appendicitis
   B. Bacterial cervicitis
   C. Chorioamnionitis
   D. Pelvic inflammatory disease
   E. Uterine rupture

2. A 37-year-old woman, G1 P0, at 39 weeks' gestation delivers a 4.2 kg healthy boy via forceps-assisted vaginal delivery. During delivery, there is avulsion of the cord and the placenta is manually extracted. An ultrasound after extraction shows a thin endometrial stripe. Thirty minutes after delivery, the patient soaks her perineal pad. On bimanual examination, 400 mL of blood is expressed from the uterus. The uterus is soft and 4.5 cm above the umbilicus after expression of clotted blood. Which of the following is the most likely cause of this patient's bleeding?

   A. Placenta accreta
   B. Retained placenta
   C. Uterine atony
   D. Uterine inversion
   E. Uterine rupture

3. A 25-year-old woman, G2P1, at 12 weeks' gestation presents to the emergency department for vaginal bleeding and severe abdominal pain. The bleeding started 5 hours ago. The patient endorses lightheadedness upon standing. Temperature is 99.1°F, blood pressure is 89/65, pulse is 112/min, and respirations are 19/min. On pelvic examination, large clots are seen in the vagina. There is active bleeding from an open cervical os. Hemoglobin is 8.2 g/dL. Transvaginal ultrasound reveals an 11-week fetus in the lower uterine segment with no cardiac activity detected. Fluid resuscitation is begun. Which of the following is the most appropriate next step in management of this patient?

   A. Expectant management
   B. Hysterectomy
   C. Misoprostol
   D. Oxytocin
   E. Suction curettage

4. A 35-year-old, G5P4, at 32 weeks presents to the emergency department due to blurred vision, right upper quadrant (RUQ) abdominal pain, headache, and swelling of the face and fingers. Temperature is 98.2°F, blood pressure is 142/95, pulse is 80/min, respirations are 16/min. Labs show thrombocytopenia, and elevated AST, ALT, and lactate dehydrogenase. Which of the following is the most likely diagnosis?

   A. Abruptio placenta
   B. Acute viral hepatitis
   C. Appendicitis
   D. Intrahepatic cholestasis of pregnancy
   E. Immune thrombocytopenic purpura
   F. Severe preeclampsia

5. A 23-year-old, G1P0, presents to clinic for prenatal visit. The patient does not know when her last menstrual period occurred, but she estimates it to be about 6 months ago. Which of the following is the most accurate method for determining gestational age?

   A. First trimester ultrasound
   B. Fundal height
   C. Head circumference
   D. Last menstrual period
   E. Second trimester ultrasound

14
Psychiatric Disorders

I. Psychotic Disorders

A. Schizophrenia

1. Severe psychosis that causes significant limitations in functional ability; typically begins in late adolescence or early adulthood
2. **Risk factors** = family history, maternal malnutrition, or illness during pregnancy; significantly higher rate in homeless and indigent patients likely secondary to their inability to function in society due to the disease ("downward drift")
3. Diagnosis requires presence of two or more symptoms (see a to e below) for at least 1 month within a 6-month period and impaired social function for >6 months
   a. **Delusions** (false beliefs about self or others which persist despite proof to the contrary)
   b. **Hallucinations** (sensory perception in the absence of external stimuli; e.g., hearing voices, "seeing things")
   c. **Disorganized thoughts or speech** (e.g., circumstantiality, tangentiality, loose associations, "word salad," neologisms)
   d. **Disorganized or catatonic behavior**
   e. **Negative symptoms** (e.g., social withdrawal, flat affect, avolition, apathy, anhedonia, poverty of speech, "thought blocking")
4. **Treatment**
   a. **Antipsychotics** (also known as neuroleptics) are the mainstay of therapy (see Table 14-1). Complications from antipsychotics include neuroleptic malignant syndrome and serotonin syndrome, and need to be recognized and distinguished from anticholinergic syndrome and malignant hyperthermia (see Table 14-2).
   b. Psychotic exacerbations may require hospitalization.
   c. Psychotherapy may be helpful in teaching the patient how to recognize symptoms.
5. **Complications**
   a. Generally poor prognosis, with gradual deterioration over several years in ability to function in society.
   b. Patients with predominantly negative symptoms and/or poor support systems have a worse prognosis.

Quick HIT

Functional ability generally refers to a patient's ability to live independently, perform normal activities of daily living, and function as a contributing member of society.

Quick HIT

High-potency antipsychotics have **more extrapyramidal** side effects and **fewer anticholinergic** side effects. Low-potency antipsychotics have **fewer extrapyramidal** side effects and **more anticholinergic** side effects.

Table 14-1 Antipsychotic Medications

Drug	Mechanism	Indications	Adverse Effe
Low-potency neuroleptics (chlorpromazine, thioridazine)	Block **D_2 dopamine** receptors	• Strong positive symptoms • Frequently second-line drugs for maintenance therapy	**Anticholinergi** sion, constipatic hypotension)
High-potency neuroleptics (fluphenazine, haloperidol, loxapine, thiothixene, trifluoperazine)	Block **D_2 dopamine** receptors	• Strong positive symptoms • **Emergency control** of psychosis or agitation • Frequently second-line drugs for maintenance therapy	**Extrapyramida** parkinsonism, a **tardive dyskin** tinemia, **neurol syndrome**, few effects
Atypical antipsychotics (aripiprazole, clozapine, olanzapine, quetiapine, risperidone, ziprasidone)	Block **dopamine** and **serotonin** receptors	• **First-line** drugs for maintenance therapy for psychotic disorders • Clozapine is the most effective antipsychotic but is reserved for refractory psychosis because of risk of agranulocytosis	Anticholinergic **clozapine** carri **locytosis;** fewe traditional neur

Table 14-2 NMS Versus Serotonin Syndrome Versus Anticholinergic Toxidrome Versus Malignant Hyperthermia

	NMS	SS	Anticholinergic OD	MH
Trigger	D2 blocking antipsychotics, antiemetics	SSRIs, SNRIs, TAs, MAOIs	Antinicotinic and antimuscarinic agents	Volati succi
Onset	Gradual > abrupt	Abrupt > gradual	abrupt	abrup
Course	Prolonged, days to wks	Rapidly resolving	Rapidly resolving	
Neuromuscular findings	**"Lead-pipe rigidity"**	**Myoclonus,** tremor, shivering increased tone in lower extremities	Normal or relaxed muscle tone, occasional myoclonic jerking	"Rigo entire
Reflexes	↓	↑	Normal	↓
Pupils	Mydraisis	Normal	Mydraisis "Blind as bat"	Norm
BP	↑	↑	↑	↑
Mental status	Restlessness, agitation		Confusion, visual, auditory and sensory hallucinations "Mad as a hatter"	
Skin	Diaphoretic	Diaphoretic	"Dry as a bone"	Diaph
Bowel sounds	↑	Normal	↓ Ileus	↓
Adjunct pharmacologic treatment	Cyproheptadine, methylserigide	Bromocriptine, amantadine, dantrolene, ECT	Physostigmine	Dantr

Reproduced with permission from Ganti, L., & Goldstein, J.N. (2018). *Neurologic emergencies: How to do a fast, focused evaluation of any neurolo* Switzerland : Springer International Publishing AG.

B. Other Psychotic Disorders

1. **Schizophreniform disorder—**psychosis characterized by at least two of the symptoms listed for schizophrenia, with a duration of at least 1 month but **fewer than 6 months**

2. **Brief psychotic disorder**—psychosis characterized by at least one of the symptoms listed for schizophrenia (except negative symptoms), with a duration of at least 1 day but **less than 1 month**
3. **Delusional disorder**—psychosis characterized by one or more delusions present for at least 1 month, but does not meet the criteria for schizophrenia; no impairment of functioning apart from the ramifications of the delusion(s)
4. **Schizoaffective disorder—psychosis** characterized by at least two of the symptoms listed for schizophrenia **concurrent with a major depressive or manic episode;** hallucinations or delusions must be present apart from the mood episode

Quick HIT

Major depressive disorder (MDD) and mania may rarely cause psychosis, but the patient is never psychotic apart from the mood episode. In schizoaffective disorder, the psychosis **must** be present apart from the mood symptoms.

II. Mood Disorders

A. Major Depressive Disorder (MDD)

1. Experience of significant depression that:
   a. Lasts >2 weeks and impacts social and/or occupational function
   b. Is not attributable to drug use or medical conditions
      (1) Drugs that cause depressive symptoms include alcohol, benzodiazepines, antihistamines, traditional neuroleptics, glucocorticoids, and interferon-α.
      (2) Medical conditions that cause depressive symptoms include hypothyroidism, hyperparathyroidism, Parkinson disease, stroke, and brain tumors.
2. Following resolution, depressive episodes have a 50% chance of recurring.
3. Pathology may be due to low serotonin, norepinephrine, and dopamine activity in the central nervous system (CNS).
4. Diagnosis requires presence of **five of the following symptoms,** including either depressed mood or anhedonia (i.e., loss of interest in previously pleasurable activity) **lasting >2 weeks:**
   a. **Depressed mood**
   b. **Anhedonia**
   c. Change in sleep patterns (e.g., insomnia, hypersomnia)
   d. Feelings of guilt/worthlessness
   e. Fatigue
   f. Inability to concentrate
   g. Changes in appetite or weight
   h. Psychomotor retardation or agitation (i.e., impaired motor ability related to mental state)
   i. Thoughts about death (**suicidal ideation)**

NEXT STEP

Tardive dyskinesia is a complication of antipsychotic medications characterized by **repetitive facial movements** (e.g., chewing, lip smacking) beginning **after several months** of therapy. It should be treated by stopping the offending drug if the patient's condition allows, but it may be **irreversible**.

NEXT STEP

Neuroleptic malignant syndrome is:

- An uncommon complication of antipsychotic medications that starts within **days** of usage and carries a high mortality rate.
- Characterized by "FEVER": **Fever, Encephalopathy, Vitals unstable, Elevated enzymes (CPK), Rigidity of muscles.**
- Treated by immediately **stopping** the drug, giving antipyretics, correcting electrolytes abnormalities, and administering a dopamine agonist such as **dantrolene**.

5. Subtypes of MDD
   a. **MDD with atypical features** is major depression characterized by:
      (1) **Mood reactivity**
      (2) Hyperphagia (increased appetite and weight gain)
      (3) Hypersomnia
      (4) Psychomotor retardation ("leaden paralysis")
      (5) **Hypersensitivity to rejection** is common

b. **MDD with seasonal pattern** is depression that occurs in a regular pattern corresponding to certain seasons, usually fall and winter, due to decreased exposure to sunlight. Treat with phototherapy.
c. **MDD with peripartum onset** is depression that begins during pregnancy or within 4 weeks of delivery.
d. **MDD with psychotic features** is depression associated with delusions, hallucinations, or other psychotic symptoms.

6. **Treatment**
   a. Psychotherapy (i.e., cognitive or behavioral counseling and instruction designed to provide insight into condition and modify behavior)
   b. Pharmacologic therapy (may be combined with psychotherapy) (see Table 14-3)
   c. Electroconvulsive therapy (ECT) can be used for refractory or severe cases to decrease frequency of major depressive episodes

Quick HIT

MDD with atypical features is the most common subtype of major depression.

B. Persistent Depressive Disorder

1. Symptoms of **depression on more days than not** for >2 years. May include:
   a. Chronic major depression
   b. Chronic mild depression that does not meet the criteria for MDD
2. **H/P** = diagnosis requires **dysphoria** (depressed mood) plus at least two other depressive symptoms for most days for >2 years
3. **Treatment** = pharmacotherapy with or without psychotherapy

MNEMONIC

Remember the characteristics of manic episodes by the mnemonic **DIG FAST:**

- **D**istractibility
- **I**nsomnia
- **G**randiosity
- **F**light of ideas
- **A**ctivity (goal-oriented)
- Pressured **S**peech
- **T**aking risks/**T**houghtlessness

C. Bipolar Disorder

1. Cyclic episodes of **depression** and **mania** (or hypomania) that impair the patient's ability to function; patient is able to function normally between episodes

Table 14-3 Antidepressant Medications

Drug/Class	Mechanism	Indications	Adverse Effect
SSRIs (e.g., citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline)	Inhibit presynaptic serotonin reuptake	**First-line** treatment for depression; anxiety	**Sexual dysfunct** of suicidal ideatio serotonin syndrom administration bef
SNRIs (e.g., desvenlafaxine, duloxetine, venlafaxine)	Inhibit reuptake of both serotonin and norepinephrine	First-line treatment for depression with comorbid neurologic pain; second-line treatment for patients failing SSRIs	Nausea, dizziness, sexual dysfunctior risk of serotonin s
TCAs (e.g., amitriptyline, clomipramine, desipramine, doxepin, imipramine, nortriptyline)	Inhibit reuptake of norepinephrine	Second- or third-line treatment for depression; can be useful in patients with comorbid neurologic pain	Easy to overdose a **only five times t** (due to cardiac QT that causes arrhyt weight gain, sexu **anticholinergic**
MAOIs (e.g., isocarboxazid, phenelzine, selegiline, tranylcypromine)	Inhibit monoamine oxidase activity to inhibit deamination of serotonin, norepinephrine, and dopamine and increase levels of these substances	Infrequently used to treat depression due to side effect profile, dietary restrictions, and drug–drug interactions	Dry mouth, indiges **dizziness;** consur ing **tyramine** (che can cause **hyperte**
Norepinephrine-dopamine reuptake inhibitor (bupropion)	Inhibit reuptake of dopamine and norepinephrine	Depression with **fatigue** and difficulty concentrating or comorbid ADHD; smoking cessation	Insomnia, weight **lowered seizure dysfunction**
Serotonin modulators (e.g., nefazodone, trazodone, vilazodone)	Inhibit reuptake of serotonin; and some direct actions on serotonin receptors	Depression with significant insomnia	Hypotension, naus **priapism;** seizure
Tetracyclic antidepressant (mirtazapine)	Block α_2-receptors and serotonin receptors to increase adrenergic neurotransmission	Depression with insomnia and/or anorexia	Dry mouth, sedati **lation**
St. John's wort (*Hypericum perforatum*)	Decrease reuptake of serotonin and, to a lesser extent, norepinephrine and dopamine	Used as first-line agent in Europe, but considered an **alternative therapy** in the United States	GI distress, dizzine interactions comm

ADHD, attention deficit hyperactivity disorder; GI, gastrointestinal; HTN, hypertension; MAOIs, monoamine oxidase inhibitors; SNRIs, selective reuptake inhibitors; SSRIs, selective serotonin–reuptake inhibitors; TCAs, tricyclic antidepressants.

a. **Manic episode**
   (1) Elevated, expansive, or irritable mood lasting at least 1 week
   (2) Three or more of the following symptoms: grandiosity, pressured speech, **decreased need for sleep,** flight of ideas, **easy distractibility, increased goal-oriented activity,** increased risky pleasurable activity
   (3) Episodes cause **significant impairment** of ability to function
b. **Hypomanic episode**
   (1) Elevated, expansive, or irritable mood lasting at least 4 days
   (2) Three or more of the symptoms of mania (see above)
   (3) Episode does not cause significant impairment of ability to function

2. Types
   a. Bipolar I: at least **one manic episode;** episodes of major depressive are common but are not required for the diagnosis
   b. Bipolar II: at least **one hypomanic episode** and at least **one major depressive episode**
   c. When present, depressive episodes are identical to those seen with MDD
3. **Treatment**
   a. Patients should be hospitalized if psychotic or judged to be a risk to themselves or others until they can be stabilized.
   b. **Mood stabilizers** (e.g., lithium, valproate, lamotrigine, carbamazepine), which may be used alone or in combination with **atypical antipsychotics** (e.g., aripiprazole, quetiapine, risperidone), are used to control and prevent manic and

hypomanic episodes and to treat depression.

c. Lithium is frequently the first-line drug for long-term treatment of mania.
   (1) Mechanism is unknown but likely involves inositol triphosphate activity.
   (2) Adverse effects include tremor, nephrogenic diabetes insipidus, hypothyroidism, teratogenesis (Ebstein anomaly), renal insufficiency, weight gain.

NEXT
STEP

A history of **mania** must be ruled out by a thorough history in a patient suspected of having MDD before antidepressants are prescribed. **Antidepressants** given to a patient with **bipolar disorder** who is **not** taking mood stabilizers can induce a **manic episode**.

D. Cyclothymic Disorder

1. Rapid cycling of mild manic symptoms and mild depression lasting >2 years without a period of normal mood >2 months
2. Mood symptoms impair the ability to function, but criteria for major depression, mania, or hypomania are not met
3. **Treatment** = psychotherapy or mood stabilizers

III. Anxiety Disorders

A. Panic Disorder

1. Experience of recurrent, spontaneous panic attacks with associated fear that these episodes will occur; typically begins in late adolescence.
2. **H/P**
   a. **Recurrent, unexpected panic attacks** that last up to 30 minutes and consist of extreme anxiety, feelings of impending danger, chest pain, shortness of breath, palpitations, diaphoresis, nausea, dizziness, paresthesias, chills or hot flashes, fear of losing control, or fear of dying.
   b. Diagnosis requires a history of recurrent episodes plus a **persistent fear that attacks will happen again,** or maladaptive change of behavior designed to avoid the attacks.
3. **Treatment**
   a. Cognitive behavioral therapy may help alleviate fear between attacks and decrease panic attack occurrence.
   b. Selective serotonin–reuptake inhibitors (SSRIs) and serotonin–norepinephrine reuptake inhibitors (SNRIs) are used for long-term therapy in patients with frequent attacks.
   c. Benzodiazepines can be used to break acute attacks (see Table 14-4).

Table 14-4 Anxiolytic Medications

Drug	Mechanism	Indications	Adverse Effe
Benzodiazepines (e.g., alprazolam, clonazepam, diazepam, lorazepam)	Increase GABA inhibition of neuronal firing	Alprazolam has a rapid onset and short half-life and is particularly useful to break panic attacks; clonazepam and diazepam are more useful for prolonged therapy	Sedation, confu symptoms may confusion, inso frequent use), a
Buspirone	Unclear, but related to serotonin and dopamine receptors	Anxiety disorders in which abuse or sedation is a concern	Headaches, diz

GABA, γ-aminobutyric acid.

B. Generalized Anxiety Disorder

1. Excessive, **persistent** anxiety and worry that occur more days than not for >6 months and impairs ability to function.

Quick **HIT**

It is **very difficult** to commit suicide using an overdose of benzodiazepines because their lethal dose is >1,000 times the therapeutic dose. **Flumazenil** is a benzodiazepine antagonist that can reverse the effects of an overdose.

2. **Epidemiology** = women twice as likely affected than men. Typically begins in early adulthood.
3. **H/P**
   a. Diagnosis requires excessive anxiety for most days, impairment of ability to function, and three of the symptoms listed below for >6 months.

b. Symptoms include restlessness or feeling “on edge,” fatigue, inability to concentrate, irritability, muscle tension, sleep disturbance.

4. **Treatment** = cognitive behavioral therapy; SSRIs or SNRIs; buspirone is considered safer for long-term therapy than benzodiazepines (see Table 14-4) because of the chronic nature of the anxiety and the risk of benzodiazepine dependence.

C. Social Anxiety Disorder

1. Excessive fear or anxiety about **social situations** in which the individual is exposed to scrutiny by others, which is out of proportion to the actual threat that the social situation poses
2. **H/P** = social situations (e.g., performances, conversations) cause anxiety that can be mild or severe (i.e., panic attacks); patients avoid these situations and have a persistent fear of being embarrassed
3. **Treatment**
   a. Cognitive behavioral therapy.
   b. β-Blockers can be used in mild cases to prevent tachycardia when engaging in an anxiety-provoking situation.
   c. SSRIs frequently are effective at reducing anxiety and permitting social interactions.
   d. Benzodiazepines are an alternative option for reducing acute anxiety.

D. Specific Phobia

1. Fear of a **particular object, activity,** or **situation** that causes the patient to avoid feared subject; typically begins in childhood
2. **H/P** = encountering feared subject incites panic attack, the patient makes great effort to avoid feared subject and realizes that behavior is irrational; some patients may experience vasovagal response (i.e., fainting) during episodes
3. **Treatment** = psychotherapy involving systematic desensitization through repeated exposure, relaxation techniques, hypnosis, or insight modification

IV. Obsessive-Compulsive and Related Disorders

A. Obsessive-Compulsive Disorder (OCD)

1. Presence of obsessions and/or compulsions that cause impairment in function and affect daily life. Patients have varying degrees of insight into their condition. Associated comorbidities include mood disorders (~70%), obsessive compulsive personality disorder, and tics (~30%).
   a. **Obsessions** are recurrent, persistent thoughts or urges that are intrusive and unwanted and that cause anxiety or distress.
   b. **Compulsions** are repetitive, ritualized behaviors (e.g., hand-washing), or mental acts (e.g., reciting specific words, counting) that are aimed at reducing or preventing the anxiety or distress caused by obsessive thoughts. Resisting the urge to engage in these compulsions results in increased anxiety.

Quick HIT

OCD is distinct from obsessive- compulsive personality disorder (OCPD). For OCD patients the obsessions and compulsions are **unwanted** and **distressing (ego-DYStonic).** For OCPD, the behaviors are perceived desirable, as they have to do with control and perfectionism (**ego-SYNtonic**).

2. **H/P**
   a. Diagnosis requires presence of obsessions or compulsions that significantly affect daily life.
   b. Stressful events can exacerbate compulsive behaviors.
   c. Patients are aware of compulsive behaviors but feel unable to control them.

Quick HIT

OCD has a significant genetic component, with mean age of onset at age 20 and equal prevalence in men and women.

3. **Treatment** = cognitive behavioral therapy and pharmacologic therapy (SSRIs, SNRIs) help limit and control behavior. Patients often seek help for the consequences of their OCD such as chafed hands from excessive handwashing.

B. Body Dysmorphic Disorder

1. Preoccupation with a perceived defect in physical appearance that limits ability to function; typically begins in adolescence
2. Patient performs repetitive behaviors (e.g., mirror checking, excessive grooming) related to the concerns about his or her appearance
3. Higher prevalence in survivors of child abuse, first-degree relatives of patients with OCD, and in cosmetic surgery patients

4. **H/P** = patient imagines physical defect in distinct body region, frequently presents to dermatologist or plastic surgeon to "improve" defect, and continues to imagine defect following treatment
5. **Treatment**
   a. Psychotherapy addressing self-perception
   b. Antidepressants may help in refractory cases
   c. Avoid performing needless surgery

C. Hoarding Disorder

1. Patient has difficulty discarding or parting with possessions, even if they have no real value; discarding possessions results in significant distress.
2. Accumulation of possessions results in excessive clutter and potentially dangerous/unhealthy living conditions.
3. **Treatment** = cognitive behavioral therapy targeted at hoarding. Generally very difficult to treat.

V. Stress- and Trauma-Related Disorders

A. Adjustment Disorder

1. Behavioral and emotional symptoms in response to a specific **stressful event or situation** (e.g., death in family, assault, divorce), occurring within 3 months of the event and causing **significant impairment** of ability to function
2. **H/P**
   a. **Distress out of proportion** of what is expected following a stressful event, inability to concentrate, **self-isolation,** change in sleep patterns, change in appetite.
   b. May be characterized as adjustment disorder with depressed mood, with anxiety, with mixed anxiety and depressed mood, with disturbance of conduct, etc.
   c. Symptoms **begin within 3 months** of stressful event and **end 6 months after** end of stressor.
3. **Treatment** = cognitive behavioral therapy; antidepressants or anxiolytics can be used if psychotherapy alone is unable to effect normal daily functioning

Quick HIT

Acute stress disorder starts within 1 month of the trigger event and resolves within 1 month. Adjustment disorder starts within 3 months of trigger event and resolves within 6 months.

B. Posttraumatic Stress Disorder (PTSD)

1. Complex syndrome of symptoms that occurs following **psychological trauma** (exposure to actual or threatened death, serious injury, or sexual violation)
   a. The event can be directly experienced by the patient, witnessed in person, or experienced by a close family member or friend.
   b. Symptoms typically begin within a few months of the event, and must last **at least 1 month.**
2. **H/P**
   a. Intrusion symptoms in which the individual reexperiences the traumatic event (e.g., **intrusive memories; recurrent, distressing dreams; flashbacks;** psychological distress; or physiologic reactions to internal or external cues that resemble the event)
   b. **Avoidance** of activities or settings associated with the event
   c. **Persistent negative alterations in cognition or mood** associated with the event (e.g., amnesia of certain aspects of the event, exaggerated negative beliefs about self or others, blaming self for the event, anhedonia, feelings of **detachment,** increased state of arousal, survivor guilt, social withdrawal)
3. **Treatment** = cognitive behavioral therapy, alone or in combination with SSRI or SNRI; atypical antipsychotics may be beneficial for symptoms refractory to SSRIs or SNRIs. Prazosin, an α-1 receptor antagonist, is helpful to decrease nightmares and hypervigilance

VI. Somatic Symptom and Related Disorders

A. Conversion Disorder

1. Also known as functional neurologic symptom disorder.
2. Development of **sensory** or **voluntary motor deficits** without a recognized medical or neurologic condition to cause the deficits. Onset is abrupt.
3. **H/P** = symptoms may include weakness/paralysis, tremor, dystonia, gait disturbance, dysphagia, dysphonia/dysarthria, seizures, numbness/paresthesias, visual or hearing disturbance, or any combination thereof.
4. **Treatment** = Simply presenting the diagnosis and educating the patient about the psychogenic nature of the deficit may lead to spontaneous resolution of symptoms in 40% to 50% of cases; second-line treatments include cognitive behavioral therapy and physical therapy; SSRIs and SNRIs are sometimes helpful.

Quick HIT

"La belle indifference" a French phrase for "beautiful indifference" is characteristic of conversion disorder. Patients are seemingly aloof to their loss of function or neurologic symptom.

Quick HIT

Malingering is the falsification of disease in order to obtain some benefit or reward, such as being excused from work or school, obtaining narcotics, pursuing legal action, etc. More common in men.

B. Somatic Symptom Disorder

1. One or more somatic symptoms which may or may not be due to a recognized medical condition, but which are distressing or disruptively to daily life; accompanied by **anxiety about health** and persistent worry about the seriousness of the symptoms. Patients have a tendency to "doctor-shop" resulting unnecessary diagnostic testing and medical procedures.
2. While the specific symptoms may change over time, the worry and impaired psychosocial functioning are persistent, lasts >6 months.
3. **H/P** = somatic symptoms may include:
   a. Pain symptoms
   b. Sexual symptoms (e.g., erectile dysfunction, decreased libido)
   c. Neurologic symptoms
   d. Gastrointestinal symptoms (e.g., vomiting, diarrhea)
4. **Treatment** = tricyclic antidepressants (TCAs) and SSRIs are beneficial, as is cognitive behavioral therapy. Set patient up with a single primary care doctor.

Quick HIT

In contrast to patients with conversion disorder, patients with somatic symptom disorder are very distressed by their health symptoms.

C. Illness Anxiety Disorder

1. **Preoccupation with having or acquiring a serious illness** in the **absence of significant somatic symptoms,** accompanied by:
   a. A high level of anxiety about health
   b. Performance of excessive health-related behaviors (such as repeatedly checking for evidence of a serious illness)
2. **Treatment**
   a. Regular physician visits help to alleviate fears.
   b. Cognitive behavioral therapy and SSRIs are beneficial.

NEXT
STEP

Münchausen syndrome *by proxy* is a disorder in which **parents** try to make their **children** appear to have a certain disease. It is considered **child abuse** and must be reported to the appropriate authorities.

D. Factitious Disorder (Münchausen Syndrome)

1. Falsification of physical or psychological signs or symptoms of a disease or injury in the absence of obvious reward or clear benefit to the patient
2. **H/P**
   a. Patient reports symptoms or signs of a given disease and attempts to induce disease process (e.g., self-injections of insulin or excrement, attempts to become infected by a pathogen, induction of vomiting/diarrhea, etc.)
   b. Patient may deny intentional production of symptoms; may wander from one physician to another
3. **Treatment**
   a. Patient denial makes treatment difficult.
   b. No unnecessary therapies should be administered.
   c. Attempt to limit medical care to one physician and one hospital.
   d. If patient is willing, psychotherapy may be beneficial.

Quick HIT

The difference between factitious disorder and malingering is that there is no clear benefit or secondary gain for the patient in factitious disorder.

VII. Eating Disorders

A. Anorexia Nervosa

1. Eating disorder characterized by:
   a. **Distorted body image** (patients believe that they are overweight)
   b. Intense **fear of gaining weight**
   c. **Reduced caloric intake** relative to energy requirements and **refusal to maintain a normal body weight;** may involve fasting, excessive exercise, purging, etc.
2. **Risk factors** = adolescence, high socioeconomic status; 90% of cases are women
3. **H/P** = low body weight (generally <85% ideal body weight), fixation on prevention of weight gain, severe body image disturbance, amenorrhea, cold intolerance, hypothermia, dry skin, lanugo hair growth (i.e., fine, short hair similar to that in the newborn), bradycardia. Osteoporosis may be present. Patients often have comorbid depression
4. **Treatment**
   a. Inpatient treatment is frequently required to aid in weight gain.
   b. Psychotherapy that focuses on body image, weight gain; sufficient caloric intake is needed to maintain long-term control.
   c. Pharmacologic therapy has not been proved beneficial.
5. **Complications** = electrolyte abnormalities, arrhythmias (especially ventricular types), refeeding syndrome

NEXT
STEP

Patients with anorexia nervosa should be screened for **depression,** and SSRIs should be included in treatment if depression is diagnosed.

Quick **HIT**

Anorexia nervosa carries a 6% 10-year mortality rate caused by disease complications or suicide.

Quick **HIT**

Refeeding syndrome results from the sudden shift from fat to carbohydrate metabolism in severe anorexics who resume eating and is characterized by **hypophosphatemia, hypomagnesemia,** and **hypocalcemia**. Complications can include **cardiovascular collapse, rhabdomyolysis, confusion,** and **seizures**.

B. Bulimia Nervosa

1. Eating disorder characterized by:
   a. **Binge eating** (inappropriate high caloric intake within a short period of time, which the patient often perceives as uncontrollable)
   b. **Inappropriate compensatory behaviors** (e.g., purging, strict caloric restriction, excessive exercise) following binges, to prevent weight gain
   c. **Unhealthy preoccupation with weight and body shape;** these patients generally maintain a normal (not low) body weight
2. **H/P**
   a. Bingeing–compensation episodes occur at least once a week for >3 months.
   b. Physical examination may reveal **dental enamel erosion** (from repeated vomiting), scars on hands (from inducing vomiting), parotid enlargement/inflammation (which may elevate serum amylase), and oligomenorrhea.
3. **Treatment** = nutritional counseling; psychotherapy (cognitive behavioral therapy) directed at body image and reduction of bingeing–compensation cycles; SSRIs or TCAs help in behavior modification. FDA-approved medication for bulimia is Fluoxetine.

C. Binge Eating Disorder

1. Eating disorder characterized by uncontrollable **episodes of binge eating** without inappropriate compensatory behaviors.
   a. On average, binges occur at least once a week for >3 months.
   b. Patients are often overweight or obese due to excessive caloric intake.
2. **Treatment** = psychotherapy (cognitive behavioral therapy and intrapersonal therapy) is first line and is generally more effective than pharmacotherapy; SSRIs may be used.

VIII. Personality Disorders

A. Persistent pattern of inner experience and behavior that deviates significantly from cultural norms

1. Manifested through perception of others, affect, interpersonal relationships, and impulse control
2. Is **persistent** and **inflexible** despite situation
3. Leads to impaired ability to function
4. Typically begins in late adolescence
5. Is not attributable to drug use, medical condition, or other psychiatric disorder
6. Generally difficult to treat as patients have no insight or awareness that they need help

Quick HIT

A patient who exhibits mild signs of a personality disorder but is able to function normally in society is said to have a **personality trait** and may not require treatment.

B. Clusters (See Table 14-5)

1. Classification system of personality disorders:
   a. Cluster A: odd or eccentric (“weird”). Includes schizoid, schizotypal, and paranoid.
   b. Cluster B: dramatic or emotional (“wild”). Includes histrionic, narcissistic, borderline, and antisocial.
   c. Cluster C: anxious or fearful (“wimpy or worried”). Includes avoidant, dependent, and obsessive compulsive.
2. Personality disorders not meeting criteria for any of the defined variants are classified as “personality disorder not otherwise specified (NOS).”

Table 14-5 Personality Disorders

Disorder	Characteristics	Treatment
Cluster A		
Paranoid	Persistent distrust and suspicion of others, others' actions consistently interpreted as harmful or deceptive, reluctant to share information, frequent misinterpretation of comments, frequent angry reactions, common suspicions of partner fidelity	Supportive, nonjudgmental psychotherapy, low-dose antipsychotics
Schizoid	Inability to form close relationships, social detachment, emotionally restricted, anhedonia, flat affect, lack of sexual interests	Antipsychotics initially to resolve behavior, supportive psychotherapy focusing on achieving comfortable interactions with others
Schizotypal	Paranoia, ideas of reference, eccentric and inappropriate behavior, social anxiety, disorganized speech, odd beliefs	Supportive psychotherapy focusing on recognition of reality, low-dose antipsychotics or anxiolytics
Cluster B		
Antisocial	Aggressive behavior toward people and animals, destruction of property, illegal activity, pathologic lying, irritability, risk-taking behavior, lack of responsibility, lack of remorse for actions; patient >18 yrs of age, history of conduct disorder prior to 15 yrs of age; more common in men	Structured environment, psychotherapy with defined limit-setting may be helpful in controlling behavior
Borderline	Unstable relationships, feelings of emptiness, fear of abandonment, poor self-esteem, impulsivity, mood lability, suicidal ideation, inappropriate irritability, paranoia, splitting (seeing others as either all good or all bad); much more common in women	Extensive psychotherapy using multiple techniques combined with low-dose antipsychotics, SSRIs, or mood stabilizers
Histrionic	Attention-seeking, inappropriate seductive or theatrical behavior, emotional lability, shallow relationships, dramatic speech, uses appearance to draw attention to self, easily influenced by others, believes relationships more intimate than they are	Long-term psychotherapy focusing on relationship development and limit-setting
Narcissistic	Grandiosity, fantasies of success, manipulation of others, expectation of admiration, arrogance, sense of entitlement, believes self to be "special," lacks empathy, envious of others	Psychotherapy focusing on acceptance of shortcomings
Cluster C		
Avoidant	Fear of criticism and embarrassment, social withdrawal, fear of intimacy, poor self-esteem, reluctance to try new activities, preoccupied by fear of rejection, inhibited by feelings of inadequacy	Psychotherapy (initially individualized, then group therapy later) focusing on self-confidence combined with antidepressants or anxiolytics
Dependent	Difficulty making decisions, fear of responsibility, difficulty expressing disagreement, lack of confidence in judgment, need for others' support, fear of being alone, requires constant close relationships	Psychotherapy focusing on developing social skills and development of decisive behavior
Obsessive compulsive	Preoccupied with details, perfectionistic, excessively devoted to work, inflexible in beliefs, miserly, difficulty working with others, hoarding of worthless objects, stubbornness	Psychotherapy focusing on accepting alternative ideas and working with others

SSRIs, selective serotonin–reuptake inhibitors.

IX. Substance Abuse

A. Substance use disorder: problematic substance (e.g., alcohol, drug) use that results in significant functional impairment or stress; formerly labeled "substance abuse" or "substance dependence"; symptoms may include:

1. Consumption of larger amounts of the substance than intended
2. Significant energy spent obtaining, using, or recovering from the substance
3. Tolerance
4. Cravings
5. Persistent desire or unsuccessful attempts to quit or cut down on substance use

NEXT
STEP

Use the **CAGE** questionnaire to screen for alcohol abuse. More than one "yes" response to any of these conditions should raise suspicion for excessive use:

- Desire to **Cut down** on usage
- **Annoyance** over others' suggestions to stop usage
- **Guilt** over usage
- Drug use on waking (i.e., **Eye-opener**)

B. Intoxication: reversible CNS effect of a substance following usage (see Table 14-6)

C. Physical dependence: physical adaptation to repetitive substance use in which abrupt cessation or antagonist use causes a withdrawal syndrome (see Table 14-6)

D. Psychological dependence: perceived need for a given substance because of its associated positive effects or because of fear of effects from lack of use

E. Patients who successfully change habits or behaviors frequently progress through the following stages of change:

1. **Precontemplation**—no acknowledgment that a problem exists or that a change needs to be made (i.e., denial)
2. **Contemplation**—admitting the need to change at some unspecified point in the future, but no immediate plans for change
3. **Preparation**—making concrete plans to deal with problem
4. **Action**—implementing changes
5. **Maintenance**—making sure changes are continued

Table 14-6 Characteristics of Substance Abuse

Substance	Intoxication	Withdrawal	Complications of Chronic Use	Treatn
Alcohol	**Decreased inhibition,** slurred speech, **impaired coordination,** inattentiveness, decreased consciousness, retrograde amnesia	Diaphoresis, **tachycardia,** anxiety, nausea, vomiting, tremor, **delirium tremens** (seizures, delirium), tactile hallucinations	**Malnutrition** (vitamin B_{12}, thiamine), encephalopathy (Wernicke-Korsakoff), **accidents,** suicide, **cirrhosis,** GI bleeding, aspiration pneumonia; higher incidence of abuse in patients with other psychiatric disorders	Supple support or **grou** trexone disulfira ant nau taken b sumptic prevent during v
Amphetamines (methamphetamine, methylphenidate, etc.)	**Hyperactivity,** psychomotor agitation, **pupillary dilation,** tachycardia, HTN, psychosis	Anxiety, depression, increased appetite, fatigue	Psychosis, depression, fatigue, parkinsonian symptoms	Rehabil antipsy epines
Benzodiazepines (alprazolam, etc.)	Sedation, amnesia, slurred speech, decreased coordination	Anxiety, insomnia, tremor, **seizures**	Memory loss	Rehabil anticon
Caffeine	**Insomnia,** restlessness, tremor, anxiety, tachycardia	Headaches, fatigue, inattentiveness	GI irritation, fatigue, inattentiveness	Gradua
Cocaine	**Euphoria,** tachycardia, psychomotor agitation, pupillary dilation, hypertension, paranoia, **grandiosity**	Sedation, **depression,** psychomotor retardation, fatigue, anhedonia	Arrhythmias, **sudden cardiac death,** stroke, suicidal ideation, inattentiveness	Reducti antipsy azepine counsel

Hallucinogens (LSD, mescaline, ketamine)	**Hallucinations,** delusions, anxiety, paranoia, tachycardia, pupillary dilation, tremors	Minimal	Psychosis, "flashbacks"	Remove danger until int antipsy
Marijuana	**Euphoria,** paranoia, psychomotor retardation, impaired judgment, increased appetite, **conjunctival injection,** dry mouth	Irritability, depression, insomnia, nausea, tremor	**Amotivational syndrome,** infertility, depression, psychosis	Rehabil antipsy
Nicotine (and other substances found in tobacco and cigarettes)	Restlessness, nausea, vomiting, abdominal pain	Insomnia, weight gain, irritability, inability to concentrate, nervousness, headaches	Smoking (but not necessarily nicotine) increases the risk of various **cancers, COPD,** respiratory infections, atherosclerosis	Counse (patch) **nicotin** for ciga **vareni**
Opioids	**Euphoria**, slurred speech, **pupillary constriction,** inattentiveness, decreased consciousness, respiratory depression	Depression, anxiety, **stomach cramps, nausea, vomiting,** diarrhea, myalgias	Constipation, increased risk of **bloodborne infection** with IV drug use	**Metha** inpatien counsel prevent naloxon nist use with sig depress
Phencyclidine (PCP)	Euphoria, impulsiveness, **aggressive behavior, nystagmus** (**vertical** and horizontal), hyperreflexia	**Sudden violent behavior,** variable levels of consciousness	Psychosis, memory deficits, impaired cognitive function, inability to retrieve words	Isolated after re cation, antipsy

COPD, chronic obstructive pulmonary disease; GI, gastrointestinal; HTN, hypertension; IV, intravenous; LSD, lysergic acid diethylamide.

QUESTIONS

1. A 22-year-old medical student is brought in by his mother for “anxiety.” Although she has had concerns for more than a year, she reports that he seems increasingly more vigilant over the last few months, and expressing that he feels that “people” are watching him. He explains the reason for this is because they know he has the secrets to the Universe. She notes he seems more withdrawn, doesn’t interact with his friends as he used to, and appears to be “listening” to sources not visibly present. Earlier this week, she received a phone call from the dean of student affairs, who was concerned about his poor performance in school. On examination, you observe a young man who has flat speech, who appears disheveled despite clean clothes. His speech is disorganized, with a few random words you haven’t heard before, but his procedural memory is intact. He is oriented to person, place, and time.
   What is this patient’s most likely diagnosis?

   A. Schizophreniform disorder
   B. Generalized anxiety disorder
   C. Brief psychotic disorder
   D. Schizophrenia
   E. Major depressive disorder

2. A 24-year-old woman presents to your emergency department with palpitations and chest pain. She appears to be in extremis and yells “doctor, help me! I’m dying!” On examination, she is tachycardiac, and diaphoretic. She complains of nausea, dizziness, and parasthesias. After about 20 minutes and 1 mg of lorazepam, she becomes more calm, and tells you that she’s had a lot of early-life stressors, and has actually had these episodes of “dying” a few times before. She explains it has come to the point where she spends most of her time “waiting” for the next episode to occur. Your colleague notes he has seen her several times in the past few months for similar complaints. Her workup today, as in the past, is negative for acute coronary syndrome, thyrotoxicosis, and thromboembolism. What is the next step in the management of this patient?

   A. Start her on daily alprazolam and refer her for cognitive behavioral therapy (CBT)
   B. Start her on a daily β-blocker and refer her for CBT
   C. Start her on a daily SSRI and refer her for CBT
   D. These “attacks” are episodic; thus give her a prescription for alprazolam as needed

3. A 41-year-old woman with a history of major depressive disorder presents to your emergency department as an overdose due to suicide attempt. She got into an altercation with her significant other and took a handful of her antidepressant pills with a shot of vodka. She has a history of depression for many years, and has been on various different antidepressants. She also has a history of prior suicide attempts both by drug overdose and hanging. She is alert, and cooperative on examination. Her pulse is 100, BP 140/70, respiration 18/min, pulse oximetry 100% on room air, and afebrile. She is 5 ft 3 in and has a BMI of 20 kg/m^3. Which of the following abnormalities might you expect to see in this patient?

   A. Serology positive for human leukocyte antigen-DR2
   B. Enlarged lateral ventricles on CT scan of the head
   C. Decreased concentration of 5-hydroxyindoleacetic acid (5-HIAA) in cerebrospinal fluid analysis
   D. Increased sensitivity to lactate infusion
   E. Delayed REM sleep on nighttime polysomnography

4. A 19-year-old thin female (BMI 16.0 kg/m^2) presents to your clinic stating she feels depressed. She is not suicidal or homicidal. She explains she works very hard, attending school, and holding down a part-time job, and also exercises 3 hours every single day. She is concerned that she is overweight, which is why she exercises religiously. She enjoys dance and cooking. In fact, she spends a lot of time talking about food. She reports feeling cold often. On examination, you note a thin female, with very fine hair, and calluses on the dorsum of her right hand. Her last menstrual period was more than a year ago. Which of the following therapeutic approaches would be most helpful in this patient?

   A. Cognitive behavioral therapy (CBT)
   B. Dronabinol capsules
   C. Involuntary psychiatric hospitalization
   D. Levothyroxine therapy
   E. Referral to gynecology

5. A 15-year-old girl is brought in to the pediatric emergency department by her mother who states her daughter has been “irrationally upset” after her boyfriend broke up with her. Whereas, previously her daughter had been an “A” student who was very active in student government and engaged in numerous school activities, nowadays she barely comes out of her room. The patient’s mother became alarmed when her daughter said: “what is the point of living anyway.” When you interview the patient, you note that she appears withdrawn, makes poor eye contact, and upon direct questioning states she has been contemplating suicide via drug overdose. She specifically talks about the large Tylenol bottle in her mother’s bathroom cupboard. She states she has been close a few times, but didn’t do it because she knows her mom would be very sad. She begs you not to tell her mom about her suicidal thoughts. What should be the next course of action?

   A. Refer for prompt pediatric psychiatry appointment, preferably next day
   B. Refer for family therapy, as mother and daughter need to work things out
   C. Start patient on fluoxetine for major depressive disorder
   D. Inform the mother about the patient’s suicidal thoughts and hospitalize the patient
   E. Inform the mother about the patient’s suicidal thoughts and hospitalize once parental consent from both parents is obtained

15
Epidemiology and Ethics

I. Research Studies

A. Study Requirements

1. Subjects in a study must be **representative of the population** that the study seeks to examine.
2. The study must contain a **sufficient number of subjects** to make it statistically significant.
3. Subjects must give **informed consent,** except under special circumstances approved by an institutional review board (IRB) (e.g., trauma patients).
4. Proper **controls** should be included in studies that examine the efficacy of a given treatment.

Quick HIT

Investigator and observational bias may be avoided by **double- blinding** a study.

Quick HIT

Confounding variables are factors that affect **both** the experimental and control groups to interfere with the relationship **between** these groups.

Table 15-1 Study Designs Used in Clinical Research

Study Type	Description	Conclusions	Advantages
Case series	• Report of characteristics of a disease by examining multiple cases	Hypothesis for risk factors	• May be easy to complete • Provides insight into poorly understood conditions
Cross-sectional survey	• **Survey** of large number of people at one time to assess exposure and disease prevalence	Hypothesis for risk factors; disease prevalence	• Can be used as estimate for disease **prevalence** following exposure
Case control study	• Retrospective comparison of patients with a **disease** with healthy controls; frequency of certain exposures in both groups is considered	**Odds ratio**	• Can examine **rare diseases** or those with **long course** in short amount of time • Can study multiple types of exposure • May examine small group size
Cohort study	• Examines a group of subjects **exposed** to a given situation or factor • Can be **prospective** (exposed group identified and followed over time) or **retrospective** (examines exposed group in whom disease has already occurred)	**Relative risk**	• Able to examine **rare exposures** • Can study multiple effects of exposure
Randomized clinical trial	• **Prospective comparison of experimental** treatment with **placebo** controls and **existing** therapies • **Double-blinded** to avoid bias • Patients **randomized** into study groups	Effectiveness of experimental treatment compared with controls and existing therapies	• **Gold standard** for testing therapies • Can be controlled for several confounders
Meta-analysis	• **Pooling** of multiple studies examining a given disease or exposure	Depends on original study type	• Larger study size • Can resolve conflicts in literature

Table 15-2 Types of Bias in Clinical Studies

Types of Bias	Description	Consequences
Enrollment (selection)	**Nonrandom** assignment of subjects to study groups	Results of study not applicable to general population
Investigator	Subjective interpretation of data by **investigator** deviates toward **"desired"** conclusions	Results of study incorrectly resemble proposed hypothesis
Lead time	Screening test provides **earlier diagnosis** in studied group compared with controls but has **no effect on time of survival**	Time from diagnosis to outcome gives the false appearance of increased time of survival; time from disease occurrence to outcome actually remains the same regardless of screening
Length	Screening test **detects** several **slowly** progressive cases of a disease and **misses rapidly** progressive cases	Effectiveness of screening test is overstated
Observational	Subjects may respond to subjective questions in a different way than normal because **awareness** of the study changes their perception of the examined issue	Effectiveness of therapy is not accurately depicted by study group
Publication	Studies that show a difference between groups are **more likely to be published** than studies that do not show a difference	Data available for meta-analyses may not include studies that support the null hypothesis
Recall	Errors of memory within subjects because of **prior confounding experiences**	Patients with negative experiences are more likely to recall negative details
Self-selection	Patients with a certain **medical history** may be more likely to participate in a study related to their condition	Subjects are not representative of the general population and introduce confounding variables

5. The interests of the patient must take priority over the interests of the study (study must be approved by IRB), and researchers must follow data to determine if a study carries any risk to the subjects at any point during its course.
6. Subject confidentiality must be maintained, and subjects must consent to the release of personal information.

B. Study Designs (See Table 15-1)

C. Bias (See Table 15-2)

II. Biostatistics

A. Rates of Disease

1. Incidence
   a. Number of new cases that occurs at a given time within a population (i.e., likelihood of developing that condition in that period of time)
   b. $\text{Incidence} = \frac{(\#\text{ of new cases of a disease in a given time})}{(\text{total population at risk})}$
2. **Prevalence**
   a. Number of individuals with a certain condition at a given time
   b. $\text{Prevalence} = \frac{(\#\text{ of existing cases of a disease})}{(\text{total population})}$
3. **Case fatality rate**
   a. Percentage of people with a given disease who die within a certain amount of time
   b. $\text{Fatality rate} = \frac{(\text{people who die from a disease in a given time})}{(\#\text{ of cases of disease during a given time})}$

B. Risk of Disease

1. **Relative risk (RR)**
   a. Probability of getting a disease in a group exposed to a specific risk factor compared to the probability of getting that disease in an unexposed group
   b. $\text{RR} = \frac{(\text{probability of disease in exposed population})}{(\text{probability of disease in unexposed population})} = \frac{A/(A+B)}{C/(C+D)}$ (see Table 15-3)
   c. **RR** value
      (1) **>1** suggests a **positive** relationship between exposure and disease
      (2) **<1** suggests a **negative** relationship between exposure and disease
      (3) = **1** suggests **no** relationship between exposure and disease
2. **Odds ratio (OR)**
   a. Odds of exposure among patients with a disease compared with odds of exposure among patients without a disease
   b. Estimate of relative risk if prevalence is low
   c. $\text{OR} = \frac{A/C}{B/D} = \frac{A \times D}{B \times C} = \frac{A/B}{C/D}$ (see Table 15-3)

Quick HIT

Relative risk is determined through **cohort** studies.

Quick HIT

Odds ratio is determined through **case control** studies.

Quick HIT

The OR is most accurate as an estimate of RR in cases of **rare diseases**.

Table 15-3 Calculation of Disease Risk

		Disease	
		Yes	No
Exposure	Yes	A	B
	No	C	D

Relative risk (RR) $= \frac{A/(A+B)}{C/(C+D)}$; **Odds ratio (OR)** $= \frac{A/C}{B/D} = \frac{A \times D}{B \times C} = \frac{A/B}{C/D}$

3. **Attributable risk (AR)**
   a. Difference in rates of disease between exposed and unexposed populations
   b. AR = (rate of disease in exposed population) – (rate of disease in unexposed population)
4. **Absolute risk reduction (ARR)**
   a. Difference in rate of disease when treated with a specific intervention
   b. ARR = (rate of disease in control group) – (rate of disease in intervention group)
5. **Number needed to treat (NNT)**
   a. Number of patients that have to be treated in order to prevent one negative outcome
   b. NNT = $1/ARR$

C. Statistics of Diagnostic Tests

1. **Sensitivity**
   a. Probability that a screening test will be **positive** in **patients with a disease**
   b. Sensitivity $= \frac{A}{A+C}$ (see Table 15-4)
   c. Most acceptable screening tests are typically >80% sensitive.
   d. **False-negative findings** occur in patients with a disease and a negative test; approximated by (1 – sensitivity).
2. **Specificity**
   a. Probability that a test will be **negative** in **patients without a disease**
   b. Specificity $= \frac{D}{B+D}$ (see Table 15-4)
   c. Most acceptable confirmatory tests are typically >85% specific.
   d. **False-positive findings** occur in patients without a disease and a positive test; approximated by (1 – specificity).

Quick HIT

Screening tests seek reliable detection of a disease in a patient without incorrectly diagnosing disease in people without the disease (ideally **both high sensitivity and high specificity**).

Quick HIT

Confirmatory tests are used to **validate** that a patient with a positive test truly has a disease.

Table 15-4 Analysis of Diagnostic Tests

		Disease	
		Yes	No
Test	Positive	A	B
	Negative	C	D

Sensitivity $= \frac{A}{A+C}$; **Specificity** $= \frac{D}{B+D}$; **Positive predictive value (PPV)** $= \frac{A}{A+B}$;

Negative predictive value (NPV) $= \frac{D}{C+D}$

3. **Positive predictive value (PPV)**
   a. Probability that a patient with a positive test has a disease
   b. PPV $= \frac{A}{A+B}$ (see Table 15-4)

4. **Negative predictive value (NPV)**
   a. Probability that a patient with a negative test does not have a disease
   b. $\text{NPV} = \frac{D}{C+D}$ (see Table 15-4)
5. **Likelihood ratios**
   a. Odds that a person with a disease will test positive compared to the odds that a nondiseased person will test positive (positive likelihood ratio) or odds that a nondiseased person will test negative compared with the odds that a diseased person will test negative (negative likelihood ratio)
   b. Measures performance of diagnostic tests while eliminating dependence on disease prevalence
   c. $\text{Positive likelihood ratio} \div (\text{PLR}) = \frac{(\text{sensitivity})}{(1 - \text{specificity})}$
   d. $\text{Negative likelihood ratio (NLR)} = \frac{(1 - \text{sensitivity})}{(\text{specificity})}$
6. **Accuracy**
   a. Performance of diagnostic tests considering only number of true results
   b. $\text{Accuracy} = \frac{A+D}{A+B+C+D}$

Quick HIT

A disease with a:

- **High** prevalence will be associated with a high **positive** predictive value in a screening test.
- **Low** prevalence will be associated with a high **negative** predictive value in a screening test.

D. Types of Error

1. **Null hypothesis:** states that no association exists between exposure and disease or treatment and response
2. **Type I error:** null hypothesis is rejected even though it is true (false-positive)
3. **Type II error:** null hypothesis is not rejected even though it is false (false-negative)
4. Risk of these errors decreases with increasing sample size (therefore increasing power)

Quick HIT

The **null hypothesis** suggests that **no association** exists between exposure and disease or treatment and response.
The **alternative hypothesis** suggests that **an association does exist**.

E. Statistical Significance

1. Statistically detectable difference between groups
2. Probability value (***p*-value**)
   a. Chance of a type I error occurring for a given result
   b. If ***p* <0.05,** the null hypothesis can be rejected (i.e., a significant relationship exists between groups)

F. Power

1. Ability of a study to detect an actual difference between two groups
2. Studies with insufficient power may state two groups are equal when they are actually significantly different (i.e., occurrence of a type II error)

III. Ethics

A. Rights of the Patient

1. **Confidentiality**
   a. All information regarding the patient must be kept **private** between the **physician** and the **patient**.
   b. The Health Insurance Portability and Accountability Act (HIPAA)
      (1) All patient account handling, billing, and medical records must be designed to maintain patient confidentiality.
      (2) Exchange of patient information can occur only between care providers involved with the care of the patient in question.
   c. Confidentiality is **not mandated** when the patient:
      (1) Allows the physician to share information with designated others (family, etc.)
      (2) Has a disease that is legally reportable (reported only to appropriate public officials)
      (3) Is considered to be **suicidal** or **homicidal**
      (4) Has suffered a gunshot or other type of penetrating wound from an assault
      (5) Is an adolescent with a condition that is potentially harmful to self or others

Quick HIT

Confidentiality should be maintained in **adolescents** seeking contraception, treatment for sexually transmitted diseases (**STDs**), or treatment for **pregnancy** (this point may need to be clarified with parents).

2. **Public reporting**
   a. Reporting of several diseases to a public health department is required by law (including **HIV, STDs,** hepatitis, Lyme disease, several foodborne illnesses, meningitis, rabies, and **tuberculosis**).
   b. Impaired ability to drive, **child abuse,** and **elder abuse** must be reported to authorities (exact legal requirements vary from state to state).
3. **Informed consent**
   a. **Before any procedure or therapy,** the patient must be made aware of the indications, risks, and potential benefits of a proposed treatment; alternative treatments and their risks and the risks of refusing treatment must also be described.
   b. Informed consent or parental consent for minors is not required for emergent therapy (i.e., **implied consent**).
   c. If a patient is not capable of making a decision, a designated surrogate decision maker is required for nonemergent care.
4. **Full disclosure**
   a. Patients have the right to be made aware of their medical status, prognosis, treatment options, and medical errors in their care.
   b. If a family requests that a physician withhold information from the patient, physicians must deny the request unless it is determined that disclosing information would significantly harm the patient.

Quick HIT

The patient should be made aware that certain diseases or conditions must be reported.

B. Patient Decision Making

1. **Capacity**
   a. "Capacity" means that the patient has the mental ability to make decisions regarding his or her medical care. A patient that lacks capacity might be declared "incompetent" by the legal/judicial system.
   b. To be judged competent, a patient must:
      (1) Not be diagnosed as presently psychotic or intoxicated
      (2) Have an **understanding** of his or her **medical situation**
      (3) Be capable of making decisions that are in agreement with his or her history of values
   c. Medical decisions for nonemancipated minors (i.e., <18 years of age) are made by a minor's parents unless legally ruled not to be in the best interests of the child.

Quick HIT

A **competent** patient can change his or her mind regarding accepting therapy **at any time**.

2. **Durable power of attorney**
   a. Legal documentation that designates a **second party** (e.g., family member) **as a surrogate decision maker** for medical issues
   b. Designated individual should be able to make decisions **consistent with the patient's values**
   c. Not valid in all U.S. states (e.g., NY)

Quick HIT

Parents' decisions regarding their children can be legally **overruled** if they are considered **harmful** to the children.

3. **Living will**
   a. Written document that details a patient's wishes in specific medical situations (e.g., resuscitation, ventilation, extraordinary maintenance of life)
   b. May be less flexible than durable power of attorney

C. End-of-Life Issues

1. **Do-not-resuscitate (DNR) order**
   a. A type of advanced directive document that details care in cases of coma, cardiac arrest, severe dementia, and terminal illness
   b. DNR can refuse all nonpalliative therapies or can only restrict use of specific therapies (e.g., ventilation, cardiopulmonary resuscitation, feeding tubes, antibiotics, etc.).

2. **Life support**
   a. Competent patients can request having supportive measures withdrawn at any time.
   b. Wishes for life support (or withholding it) can be described in a living will or DNR.
   c. Physicians can remove respiratory care in cases in which **no living will** exists and the patient is **incapable** of voicing a decision **if** the **family** and the **physician** believe that removal of care is **consistent** with **what the patient would want**.
3. **Physician-aided death**
   a. Physician-assisted suicide occurs when a physician **supplies** a patient with a means of ending his or her life.
   b. Euthanasia is the **active administration by a physician** of a lethal agent to a patient to end suffering from a condition.
   c. Physician-assisted suicide (also known as "medical aid in dying") is currently legal only in California, Colorado, District of Columbia, Hawaii, Montana, Oregon, Vermont, and Washington and euthanasia is illegal in the rest of United States.
4. **Death**
   a. **Brain death** is defined as the irreversible **absence** of all brain activity (including the brainstem) in a patient lasting >6 hours.
   b. **Heart death** is considered the inability to restore a spontaneous heartbeat in an asystolic patient.
      (1) Absence of cephalic (i.e., cranial nerve) reflexes (e.g., gag, corneal, and caloric reflexes)
      (2) Apnea when patient is off the ventilator for a duration considered sufficient to produce a normal hypercarbic drive
      (3) Absent brainstem-evoked responses, absent cerebral circulation on radiologic testing, or persistent isoelectric EEG
      (4) Patient appearance cannot be explained by a medical condition that mimics death
      (5) Absence of hypothermia or intoxication
   c. Either brain death or heart death can be used to define formal patient death (both are not required).
   d. **Hypothermic** patients must be warmed to normal body temperature before death can be declared.

Quick **HIT**

The absence of electroencephalogram (EEG) activity does **not** define brain death but may help prompt a brain death workup.

Quick **HIT**

Brain death statutes in the United States differ by state and institution.

5. **Organ donation**
   a. Patients can declare themselves as organ donors before death (e.g., living will, driver's license).
   b. Hospitals receiving payments from Medicare are required to approach the family of the deceased regarding organ donation.
   c. Patients and families can define exactly what organs are to be donated.
   d. Organs may be judged unsuitable for donation in cases of widespread or uncured **neoplasm, sepsis,** compromised organ function, organ-specific infection or disease, hypothermia, HIV infection, age >80 years, hemoglobinopathy, or **prolonged ischemia**.

Quick **HIT**

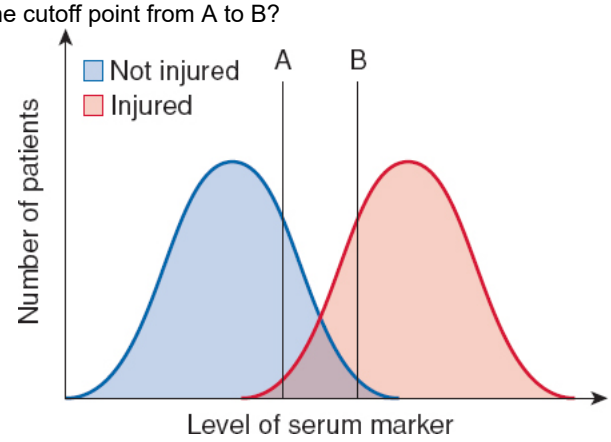
Conditions that can mimic brain death include metabolic encephalopathy, hypothermia, intoxication, locked-in syndrome, and Guillain–Barré syndrome.

Quick **HIT**

Physicians are not required to supply therapies that are irrational for the current condition or when the maximal therapy has already failed.

QUESTIONS

1. The department of defense laboratory isolates a serum marker for traumatic brain injury. The following curves are generated from the data of their international multicenter study. The positive/negative cutoff value is set at point A. What is the effect of moving the cutoff point from A to B?



A. The sensitivity of the test will increase
B. The specificity of the test will increase
C. There is no effect on the sensitivity or specificity of the test
D. More information is needed

2. As part of a widespread public health initiative, a new drug is introduced into a community that prolongs survival in patients with colon cancer. What changes in prevalence and incidence would be expected over the next few years?

A. The incidence will increase, but the prevalence will remain unchanged
B. The prevalence will increase but the incidence will remain the same
C. Both the incidence and prevalence will increase
D. Both the incidence and prevalence will decrease

3. An investigator conducts a large study and finds that coffee consumption of three or more cups a day is strongly associated with myocardial infarction. He calculates the odds ratio to be 5, with a 95% CI of 4.7 to 5.3. As a coffee lover, this finding alarms him. His coinvestigator notes that cigarette smoking is also significantly associated with myocardial infection, and as he likes to smoke while having his coffee, he wonders if smoking is a confounder here. Which of the following are characteristics of confounders?

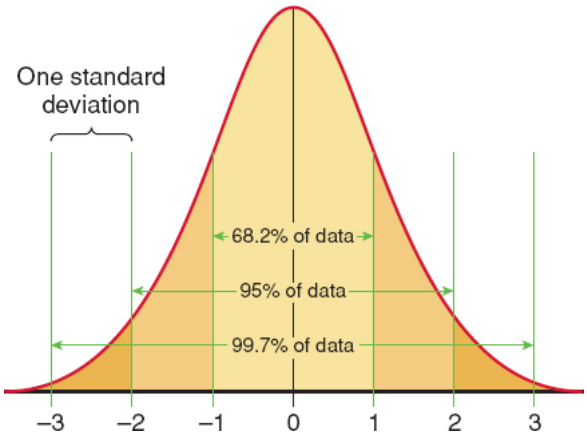
A. It must be associated with both the exposure and the outcome (disease)
B. It should be highly prevalent in the population
C. It should be evenly associated between those who have the outcome of interest (disease) and those who do not
D. None of the above are characteristics of confounders

4. An investigator studies whether initial emergency department blood pressure is associated with increased risk of death after stroke. The blood pressure measurements for all patients who come to the ED with an acute ischemic stroke are recorded, and patients are followed for 90 days. Which of the following best describes the study design?

A. Case control study
B. Cohort study
C. Randomized controlled trial
D. Meta-analysis

5. An investigator is interested in the distribution of mean arterial pressures in patients with TIA. The values are normally distributed with a mean of 90 mm Hg, and a standard deviation of 10 mm Hg. The investigator can therefore conclude that >99% of patients should have MAP values in which range?

A. 80 to 100 mm Hg
B. 75 to 95 mm Hg
C. 70 to 110 mm Hg
D. 60 to 120 mm Hg
E. Cannot be determined from the information given


One standard deviation
68.2% of data
95% of data
99.7% of data
−3
−2
−1
0
1
2
3

ANSWERS

1 Cardiovascular Disorders

1. **Correct answer is B.** Recommend lifestyle modifications and recheck in 2 months. The initial recommendation is not to start medications until three separate readings are reported. Start with weight loss, exercise, salt restriction, smoking and alcohol cessation.
2. **Correct answer is D.** Lisinopril. The use of ACE inhibitors for HTN in diabetic patient is recommended due to data suggesting it delays damage to the kidneys caused by both DM and HTN.
3. **Correct answer is D.** Simvastatin. About 1% of patients on statin medications will develop elevation of transaminases (LFTs) and may require cessation of therapy. A smaller number may develop transient and rarely clinical myositis. In reality any lipid-lowering therapy may elevate LFTs, however the most used and most linked to this event are the “statins.”
4. **Correct answer is B.** False. Nitroglycerin, a potent vasodilator, may also improve the symptoms of esophageal spasm. For this reason, it should not be used to rule in or rule out someone of having myocardial ischemia or CAD.
5. **Correct answer is B.** False. A stress test is used to determine reversible or transient ischemia in intermediate- or moderate-risk patients. It is used to detect high-grade flow-limiting lesions. Thus, a patient can have a negative stress test and still have an acute MI from a new plaque rupture/occlusion.
6. **Correct answer is C.** An arrhythmia (Vfib/Vtach). Despite all the others can be potentially life-threatening events after a myocardial infarction, they tend to happen days or months after the event. The earliest and deadliest would be an arrhythmia.
7. **Correct answer is C.** Multifocal atrial tachycardia. This rhythm strip shows multiple different morphology P waves. This condition is seen commonly on chronic lung disease conditions and is frequently asymptomatic.
8. **Correct answer is B.** Atrial flutter. This rhythm strip shows the classic sawtooth pattern of atrial flutter. Flutter (like atrial fibrillation) is seen more commonly in older patients and patients with chronic heart conditions.
9. **Correct answer is D.** Brain natriuretic peptide. This hormone is released in increasing amounts with dysfunction or expansion of the left ventricle.
10. **Correct answer is B.** False. β-Blockers should not be used during acute exacerbations of patients with congestive heart failure. Use of this medication in the acute phase may contribute to further decompensation. However, this drug should be initiated on patients with congestive heart failure upon discharge if no contraindications.

11. **Correct answer is A.** Aortic stenosis. The findings of syncope, fatigue, and crescendo–decrescendo murmur should be considered to represent aortic stenosis until proven otherwise. Additional findings may include acute congestive heart failure, chest pain, and a wide pulse.
12. **Correct answer is C.** Valve replacement. The management of aortic stenosis is best achieved by valvular replacement to avoid worsening heart failure, continued syncope, or sudden death.
13. **Correct answer is C.** Rheumatic fever. Acute rheumatic fever should be considered in any patient presenting with fever, migratory arthritis, swollen joints, and subcutaneous nodules, or any patient presenting with 2 major or 1 major + 2 minor of the Jones criteria (see Acute rheumatic fever section).
14. **Correct answer is C.** Hypertrophic cardiomyopathy. This is a concerning presentation of exertional syncope. Together with the history of sudden cardiac death in the family, and the findings in the ECG this presentation should be worrisome for hypertrophic cardiomyopathy. The treatment includes β-blockers, hydration, avoidance of exertion, and an implantable defibrillator due to risk of arrhythmias.
15. **Correct answer is D.** Both B and C. Patients with acute pericarditis may present with some of the classic symptoms like fever, and friction rub on examination. ECG findings usually confirm diagnosis with diffuse ST elevations and PR depression.
16. **Correct answer is A.** Post-viral myocarditis. This presentation may be difficult to diagnose. However, with normal blood work, a negative CT scan of the chest, and prior normal cardiac examination it suggests myocarditis as the most likely cause after her viral syndrome.
17. **Correct answer is C.** Cardiogenic shock. This patient has a presentation consistent with worsening of already present heart failure. Evidence of being afebrile, moist mucous membranes, and peripheral edema rules out hypovolemic shock.
18. **Correct answer is B.** Hypovolemic shock. This patient presents after a motor vehicle accident with shock. Due to the injuries described and physical examination findings this is a presentation of traumatic hypovolemic shock until proven otherwise.
19. **Correct answer is D.** Abdominal vascular ultrasound. This patient appears to have a stable examination for an initial screening examination such as an ultrasound to evaluate for aortic aneurysm.
20. **Correct answer is D.** All of the above. Of the listed they are all possible risk factors for development of a deep venous thrombosis.

2 Gastrointestinal Disorders

1. **Correct answer is B.** Achalasia. This patient has no other risk factors for cancer or history of scleroderma symptoms. Adenocarcinoma is the second

most common cause of achalasia. Scleroderma can be a secondary cause of achalasia.

2. **Correct answer is C.** Gastroesophageal reflux disease. The symptoms described on this obese male correlate most likely with GERD. Heartburn is a frequent complaint after food ingestion. It can improve with position changes. ECG and chest x-ray are not bad alternatives as initial workup to rule out major disease processes.
3. **Correct answer is C.** Hepatitis A. This is a classic presentation of transient acute viral hepatitis A. This is most commonly spread from contaminated food sources (shellfish) or fecal–oral routes. This type of hepatitis tends to be self-limited and requires mainly supportive care.
4. **Correct answer is D.** *C. difficile*. This patient is likely suffering from antibiotic-induced diarrhea due to suppression of normal gut/colonic flora. This condition by itself can be challenging to resolve and treat, sometimes requiring hospital admission.
5. **Correct answer is A.** Acute gastritis. This patient is likely suffering from an acute gastric superficial irritation caused by over the counter pain medication (possibly NSAIDs) for his dental pain.
6. **Correct answer is B.** Gastric ulcer, *H. pylori*. This patient presents with a positive urea breath test and symptoms soon after eating. This is diagnostic of *H. pylori* infection and gastric location. The treatment usually consists of dual antibiotic therapy and anatacid medications. Duodenal ulcer symptoms happen 2 to 4 hours after eating.
7. **Correct answer is A.** Crohn disease. Crohn's affects young patients and classically presents with multisystemic symptoms including arthritis and diarrhea. Perianal fissures and fistulas are common. It classically shows cobblestoning and skipped lesions on colonoscopy. Treatment includes steroids, immunosuppressive agents, and occasionally antibiotics.
8. **Correct answer is C.** Diverticulitis. The location of tenderness, fever, elevated white blood cell count, and constipation should prompt evaluation of diverticulitis until proven otherwise.
9. **Correct answer is D.** Insulinoma. Frequent or recurrent unexplained hypoglycemia should prompt investigation for an endocrine pancreatic cancer.
10. **Correct answer is A.** Pancreatitis. This patient is likely suffering from pancreatitis due to chronic alcoholism. This commonly presents with epigastric pain radiating to the back. It is important to rule out other conditions like myocardial infarction and aortic dissection when evaluating for pancreatitis.
11. **Correct answer is D.** Abdominal ultrasound. On a patient presenting with nausea, vomiting, abdominal pain, and a positive Murphy sign in physical examination the next best study to perform is an abdominal or RUQ ultrasound to evaluate for cholelithiasis/cholecystitis.
12. **Correct answer is C.** Ascending cholangitis. This is a classic presentation of cholangitis presenting with Charcot triad of fever, jaundice, and RUQ pain.

This specific case included Reynolds pentad with the inclusion of hypotension/shock and AMS to the other symptoms of the triad.

13. **Correct answer is A.** Cirrhosis. This patient is likely suffering from alcohol-related liver disease progressing to cirrhosis due to continued hepatic inflammation and necrosis. Patients with cirrhosis will have impaired function of liver-produced coagulation factors and may progress to portal hypertension.
14. **Correct answer is D.** Wilson disease. This condition presents with green-brown copper deposits in cornea, psychiatric disturbances, jaundice, and hepatomegaly due to impaired copper secretion. Without treatment, this may progress to cirrhosis and hepatic failure.
15. **Correct answer is B.** Abdominal ultrasound. This child is suffering from pyloric stenosis, classically presenting with dehydration and hypochloremia. A less-invasive study may be an abdominal ultrasound which will show increase in muscle thickness. Barium swallow may diagnose but is more invasive in a nontolerating child.
16. **Correct answer is C.** Necrotizing enterocolitis. Premature children are at risk of this idiopathic mucosal necrosis. This condition may present with bilious vomiting, hematochezia, abdominal distension, and pneumatosis intestinalis (air in bowel). Surgical resection is usually needed.

3 Hematology and Oncology

1. **Correct answer is B.** Obtain hemoccult test. This patient is likely suffering from acute blood loss. Having history of atrial fibrillation suggests patient is likely on anticoagulation. If no obvious source of bleeding is elicited by history the most likely source is often gastrointestinal.
2. **Correct answer is D.** Vitamin deficiency. Strict vegetarians are at risk of anemia due to lack of vitamin B_{12} intake from diet (lack of meat or fish). Pregnancy is a risk for microcytic anemia (iron deficiency).
3. **Correct answer is B.** *S. pneumoniae*. Patients with sickle cell suffer from autosplenectomy in early childhood due to frequent splenic infarctions. This leads to functional asplenia and risk of infection by encapsulated organisms, such as Strep sp.
4. **Correct answer is D.** Parvovirus. Among the many risks patients with sickle cell possess, they have increased risk of aplastic crises when coinfected by Parvovirus B19. Salmonella predisposes to osteomyelitis due to autosplenectomy.
5. **Correct answer is C.** Epinephrine. This is a presentation of a classic anaphylactic reaction, the treatment of which is epinephrine. All other medications are adjunct treatments, but not first line in the treatment of anaphylaxis.

6. **Correct answer is D.** Type IV. This patient is suffering from a delayed T-cell antigen and macrophage reaction, causing an allergic contact dermatitis. This same reaction is used for testing of antigen-mediated response of PPD testing.
7. **Correct answer is A.** *Escherichia coli*. This is a classic presentation of hemolytic uremic syndrome (HUS) in children, caused by E. coli 0157:H7 infection; likely source of diarrhea symptoms.
8. **Correct answer is C.** von Willebrand disease. This is the most common inherited bleeding disorder; characterized by frequent mucosal bleeding (epistaxis, gums, menorrhagia, etc.).
9. **Correct answer is D.** Contact sports. This case is likely infectious mononucleosis caused by Epstein–Barr virus. Patients suffering from this may have an enlarged spleen and should avoid contact sports for at least 1 month to avoid spleen rupture.
10. **Correct answer is B.** *Pneumocystis jiroveci*. A patient with a CD4 count of less than 200 is at increased risk of opportunistic infections like PCP. Usual findings include bilateral “batwing” infiltrates, elevated LDH, and hypoxia. Treatment is TMP-SMX and steroids.
11. **Correct answer is D.** Polycythemia vera. Patients with this condition will present with elevated Hgb, platelets, and large RBCs in blood work; many of the classic symptoms begin after age 60 and include pruritus after warm baths and headaches.
12. **Correct answer is A.** Multiple myeloma. Patients may present with pathologic fractures. Classic x-ray findings include punch out lesions in long bones and skull.

4 Selected Topics in Emergency Medicine, Critical Care, and Surgery

1. **Correct answer is C.** Intubation and transfer. This patient has significant second-degree burns involving face, joints, and circumferential extremities adding to a body surface area of >10%. In addition, any burn to the face that includes facial hairs should be concerning for airway edema and respiratory compromise. Patients with these findings should be transferred to a burn center for adequate care. Blisters should not be excised. Topical antibiotics are an option, but this case requires more management.
2. **Correct answer is C.** Heat stroke. This patient is suffering from heat stroke. Patients will have markedly elevated temperatures, neurologic symptoms including confusion, visual changes, nausea, or syncope. This may be difficult to differentiate from meningitis or infectious causes without an adequate history. Without prior symptoms other than prolonged heat exposure, this would be difficult to diagnose.

3. **Correct answer is C.** Glucagon. This is a case of β-blocker overdose as evidenced by bradycardia, hypotension, hypoglycemia, and the historical evidence of missing blood pressure control medication. Activated charcoal is only effective in acute ingestions (<1 hour). Naloxone is the treatment for opioid overdose. Gastric lavage is almost always NOT recommended. Flumazenil is the treatment of iatrogenic or acute (not on chronic users) benzodiazepine overdose.
4. **Correct answer is D.** Atropine, pralidoxime. This is a classic presentation of organophosphate intoxication. Patients present with diarrhea, urination, miosis, salivation, bradycardia, sweating. Of note, atropine should be given until secretions dry up. Option A is the treatment of salicylate overdoses. Option B describes treatment of β-blocker/calcium channel blocker overdoses.
5. **Correct answer is D.** Consider fibrinolytic therapy, thrombectomy, admit. This is a patient suffering from acute ischemic stroke. The patient has measurable deficits. Recent studies show that patients with acute stroke (<3 hours onset) may benefit from fibrinolytic therapy or in certain instances mechanical thrombectomy. A simple admission and consult to neurology may delay the recommended care for this patient. Aspirin is a medication that can be given early in patients who fail inclusion criteria for fibrinolytic administration.
6. **Correct answer is C.** Endotracheal intubation. This patient is suffering from acute multisystem trauma. A patient who presents after a traumatic event with airway compromise should be assessed immediately and prepared for endotracheal intubation. Delay in this management may present with catastrophic results. On a patient with profuse secretions or bleeding bag-valve masks may increase the risk of aspiration. A C-collar should never be removed until the cervical spine is cleared from injury with imaging or clinical examination. The focused assessment of ultrasonography in trauma is not a part of the primary survey in trauma assessments.
7. **Correct answer is B.** Acute. This patient is suffering from an acute rejection reaction. This type of rejection happens 6 days to a year after the transplant is received. On occasions immunosuppressive agents may help. See Table 7-10.

5 Musculoskeletal Disorders

1. **Correct answer is D.** Wrist splinting. This patient presented with classic signs and symptoms of carpal tunnel, including a positive Tinel sign. Initial treatment should include wrist splinting and activity modifications. NSAIDs and other interventions should follow these two.
2. **Correct answer is C.** Knee dislocation. This patient suffered a dashboard injury to his left lower extremity that caused an initial deformity and self-

reduced prior to arrival. Popliteal artery injury is one of the most concerning complications of posterior knee dislocation.

3. **Correct answer is C.** Cauda equina syndrome. This patient presents with classic findings of cauda equina syndrome including urinary retention (bladder distension), saddle anesthesia (thigh numbness), and incontinence.
4. **Correct answer is B.** Radiation therapy. Radiation should be the first step in management of cord compression caused by a solid tumor on a patient with a history of cancer. Surgical repair is an option for refractory cases of radiation therapy and steroids.
5. **Correct answer is D.** Estrogen deficiency. This patient's advanced age is the strongest risk factor based on given information. The amount of wine consumed should not be a significant risk factor (risk increases with excessive use). Obesity is not a risk factor, but rather low body weight is one.
6. **Correct answer is A.** Calcium and vitamin D. This patient is suffering from Paget disease of bone as characterized by thickening of skull. Headaches are a common complaint. Bone scan would reveal uptake on affected areas. Calcium and vitamin D intake should be increased in this disease and the addition of bisphosphonates should be considered.
7. **Correct answer is A.** Synovial fluid analysis. Despite the history of gout this patient is at risk of septic arthritis based on the current presentation of fever, tachycardia, and gradual onset of symptoms. Synovial fluid should be collected and sent. Serum uric acid levels are unreliable for differentiating acute gout flares versus septic arthritis.
8. **Correct answer is D.** Salmonella sp. Patients with sickle cell have higher risk of infections with encapsulated organisms, including Streptococcus sp. However, when the risk of infection is related to osteomyelitis, Salmonella is the most likely cause in sickle cell.
9. **Correct answer is C.** Bamboo spine. This is a description of a patient with ankylosing spondylitis. The MVC mechanism is unlikely to have caused major trauma, including bilateral facet dislocation. The pencil in cup deformity is seen in psoriatic arthritis.
10. **Correct answer is B.** Anti-citrullinated peptide antibodies (ACPA). Rheumatoid arthritis is sometimes difficult to diagnose. RF, ACPA, and ANA tests may all be positive. Of these, the most specific for RA is ACPA.
11. **Correct answer is B.** Osteosarcoma. This patient has classic appearance of osteosarcoma as evidenced by painful bony mass with sunburst appearance on x-ray. This typically happens in distal femur, proximal tibia, or proximal humerus. Ewing sarcoma tends to happen at an earlier age, x-ray shows destructive onion skin lesions, and blood work shows anemia, elevated WBCs, and increased ESR.
12. **Correct answer is D.** Follow-up outpatient. This patient has a benign bone tumor (osteochondroma) as evidenced by x-ray with no lytic or destructive lesions and a continuous growth in bone. The other options are management options for malignant tumors.

6 Pulmonary Disorders

1. **Correct answer is D: IV cefepime, IV azithromycin, IV vancomycin, and admit.** This is a patient on chronic dialysis and is diagnosed with pneumonia, therefore meeting criteria for health care–associated pneumonia (HCAP). Patients hospitalized >2 days within 90 days; on IV antibiotics or chemotherapy within 30 days; residing in a nursing home within 90 days; receiving wound care, tracheostomy care, or ventilator care within 30 days; or are on chronic dialysis within 30 days are at risk for HCAP. Patients with HCAP require admission with antibiotic coverage covering MRSA and double coverage for pseudomonas.
2. **Correct answer is D: Granulomatosis with polyangiitis (Wegener).** This is a rare disease characterized by granulomatous inflammation and necrosis of the lungs and other organ systems caused by a systemic vasculitis that affects mainly the lungs and kidneys. It is classically associated with chronic sinusitis and nasopharyngeal ulcerations. Labs will reveal renal involvement and a positive c-ANCA level. Biopsy will show noncaseating granulomas. Treatment is with cytotoxic therapy and corticosteroids.
3. **Correct answer is E: IM epinephrine.** After nebulized albuterol, ipratropium, steroids, and magnesium, IM epinephrine or terbutaline should be considered in a severe, acute asthma exacerbation. If the patient is still struggling, it is recommended to initiate a trial of bilevel positive airway pressure noninvasive ventilation (BiPAP) and if the patient is still declining then intubation may be needed.
4. **Correct answer is B: Needle decompression.** This is a patient with a traumatic tension pneumothorax. He had decreased breath sounds, hypotension, and tracheal deviation, which are all classic clinical features due to increased compression of the mediastinum and impaired right ventricular filling. Without immediate needle decompression, death is imminent. Classically, needle decompression should be performed over the 2nd or 3rd intercostal space at the midclavicular line, followed by definitive chest tube placement. Tension pneumothorax is a clinical diagnosis that should not be delayed by imaging.
5. **Correct answer is A: Reassurance.** This patient is a low-risk patient with bronchitis. A chest x-ray is likely unnecessary in the presence of a normal examination. Antibiotics are usually ineffective in bronchitis, as the most common cause is viral. Supportive treatment such as antitussive agents and mucolytics may help treat symptoms.
6. **Correct answer is B: Start inhaled beclomethasone.** This patient has mild persistent asthma which is defined as bronchodilator use >2 times/wk and nocturnal awakening >every 2 weeks. The addition of a low-dose inhaled corticosteroids is recommended in addition to short acting β_2-agonist inhalers as needed. Leukotriene inhibitors such as montelukast can be considered, but the next best step is starting the patient on an inhaled corticosteroid such as beclomethasone.

7. **Correct answer is A: CT angiogram of the chest.** This is a patient with likely pulmonary embolism given the patient's cancer history, tachycardia, tachypnea, and hypoxia. The best and most rapid test for diagnosis is a CT angiogram.
8. **Correct answer is B: Pneumonia.** Since the pleural:serum protein and LDH ratio is greater than 0.5 and 0.6, respectively, this indicates an exudative effusion, with pneumonia as the only exudative process listed. CHF, cirrhosis, and kidney disease are all examples of diseases that cause transudate effusions.
9. **Correct answer is D:** *Streptococcus pneumoniae*. The most common pneumonia in adults as well as those with sickle cell disease is from *S. pneumoniae*. Pseudomonas is associated with immunocompromised patients as well as patients with cystic fibrosis. Mycoplasma is associated with young adults and a positive cold agglutinin test. *Klebsiella* is common in alcohols and patients at high risk for aspiration. Group B streptococcus is commonly seen in neonates and infants.
10. **Correct answer is A: Chest x-ray.** Any patient with a positive PPD for TB should undergo questioning and chest x-ray imaging to look for active disease. This will determine treatment with multidrug treatment or with single therapy for latent TB.

7 Genitourinary Disorders

1. **Correct answer is C.** Oral trimethoprim-sulfamethoxazole and discharge home. This is a patient with pyelonephritis given the urine results and systemic symptoms (vomiting). Most patients with uncomplicated pyelonephritis can be discharged home with oral antibiotics such as a fluoroquinolone, cephalosporin, or trimethoprim-sulfamethoxazole. Oral nitrofurantoin is only indicated in urinary tract infections. IV antibiotics would be appropriate higher-risk patients (sepsis, pregnancy, elderly, immunosuppression).
2. **Correct answer is B.** Pain control, IV antibiotics, and urology consultation. This patient has a likely infected kidney stone which can lead to sepsis if not treated urgently with antibiotics and decompression. Urology should be consulted early for definitive management.
3. **Correct answer is B.** Postinfectious glomerulonephritis. This patient like has postinfectious glomerulonephritis secondary to group A streptococcus. This is evident by hematuria and proteinuria as well as hypertension and peripheral edema. Interstitial nephritis is associated with eosinophiluria and WBC casts. Acute tubular necrosis is associated with granular casts. Nephrotic syndrome would present similarly with edema and proteinuria; however, it is usually not associated with RBC casts.

4. **Correct answer is A.** IV normal saline bolus. This is an elderly patient in prerenal failure, which is illustrated by the clinical history as well as a BUN:creatinine ratio >20. Prerenal failure is caused by hypoperfusion to the kidneys, commonly caused by dehydration, but can also be caused by different etiologies of shock as well as vascular issues such as renal artery stenosis. IV normal saline is indicated to treat the underlying cause.
5. **Correct answer is A.** IV calcium gluconate. This patient presents with hyperkalemia causing cardiac disturbance, which can lead to a serious dysrhythmia. Calcium gluconate or chloride must be given immediately to stabilize the cardiac membrane and prevent dysrhythmia. Insulin and dextrose and sodium bicarbonate shift potassium into the cell. Nebulized albuterol encourages potassium uptake by the cells. Sodium polystyrene sulfonate binds potassium and removes it through the GI tract. Furosemide may help with excretion of potassium. All of these can be given, but they do not have the same effect of rapid cardiac membrane stabilization by calcium.
6. **Correct answer is C.** Refractory fluid overload. Emergent dialysis is indicated in refractory hyperkalemia, severe metabolic acidosis, refractory fluid overload, and symptomatic uremia.
7. **Correct answer is B.** Emergency urology consult. This patient has testicular torsion and requires emergent urology consultation. Manual detorsion in an open book orientation, medial to lateral can be attempted. Ultrasound can be performed, but should not delay consultation or surgery as this is a time-sensitive diagnosis. X-ray and urinalysis have no role in making the diagnosis.
8. **Correct answer is B.** Lumbar puncture. Patients with polycystic kidney disease are at an increased risk of intracranial aneurysms and subarachnoid hemorrhage. A subarachnoid hemorrhage cannot be ruled out by a brain CT; therefore, a lumbar puncture is indicated to help rule this out. The gold standard for diagnosis is a cerebral angiogram, but this is more time consuming and may have more risks to the patient.
9. **Correct answer is B.** IM ceftriaxone and oral doxycycline. This is a sexually active patient with epididymitis. Gonorrhea and chlamydia are common causes for epididymitis; therefore, in those who are sexually active, treatment is recommended. Patients who are not sexually active and/or are low risk for gonorrhea and chlamydia can be treated with fluoroquinolones.
10. **Correct answer is D.** Oral ciprofloxacin for 4 weeks. This patient presents with classic prostatitis. Treatment requires 4 to 6 weeks of oral fluoroquinolones or TMP-SMX. Treatment geared towards gonorrhea and chlamydia should be initiated in high-risk individuals.

8 Endocrine Disorders

1. **Correct answer is B.** Propranolol. Patient has symptoms of thyroid storm with low TSH and elevated free T4. Although radioablation, PTU, and hydrocortisone are part of the treatment of thyrotoxicosis and thyroid storm, treatment should start with β-blockers as they block adrenergic effects and also block peripheral conversion of T4 to T3. Patient has a history of DM and has elevated glucose levels which may eventually require management; however, the patient is not in DKA (no anion gap and glucose is less than 250 mg/dL) and does not require emergent treatment with insulin.
2. **Correct answer is C.** C-Peptide. Patient has episodes of recurrent hypoglycemia, which could be due to exogenous insulin administration or an insulinoma. C-peptide is usually elevated in insulinomas while decreased in exogenous insulin administration, despite elevated insulin levels. Urine metanephrines may be helpful in the diagnosis of pheochromocytomas; however, recurrent hypoglycemia is not a typical presentation. Also note that insulinomas can be found in MEN type I, with pituitary adenomas and parathyroid adenomas, not pheochromocytomas (Table 8-10). Disorders of prolactin would not explain hypoglycemia episodes. While hypothyroidism can cause hypoglycemia, it is usually seen in the setting of high TSH, and low T3 and T4. An isolated finding of low T3 with normal TSH and T4 (known as euthyroid sick syndrome) is not usually associated with recurrent hypoglycemia.
3. **Correct answer is A.** Aldosterone. The patient is in shock with hypoglycemia, hyponatremia, and hyperkalemia, findings seen in congenital adrenal hyperplasia (CAH). 21-hydroxylase deficiency is the most common cause of CAH. As explained with the pathway on Figure 8-6, these patients have low levels of aldosterone (explains hyponatremia and hyperkalemia) and cortisol (explains hypoglycemia and shock), with elevated DHEA and testosterone levels.
4. **Correct answer is B.** Decreased urine calcium. The patient has symptoms of hypercalcemia, likely due to primary hyperparathyroidism. An increase of PTH causes a decrease in urine calcium secretion and an increase in vitamin D production (Figure 8-3).
5. **Correct answer is A.** β-hCG. Although patient has symptoms suggestive of hyperprolactinemia, a known side effect of haloperidol, pregnancy should be ruled out first as it is more common. Prolactin and FSH levels, as well as an MRI, may be appropriate tests once pregnancy has been ruled out.
6. **Correct answer is A.** The patient has findings consistent with Cushing syndrome, likely due to chronic steroid used for her rheumatoid arthritis. Although it may seem unrelated to her current complaint, it is important to know that patients with Cushing syndrome have a higher risk of cardiovascular disease due to hypertension, hyperlipidemia, and other factors. Patients with Cushing syndrome can suffer from hyperglycemia and weakness with decreased muscle mass. Her hip pain may be due to avascular necrosis, fractures, or infection and it should be evaluated and treated accordingly.

9 Dermatology

1. **Correct answer is B.** Oral diphenhydramine. These patient symptoms are consistent with an allergic reaction secondary to shellfish. Symptoms can include urticaria, pruritus, angioedema, and anaphylaxis. For those with only urticaria or pruritus antihistamines alone is indicated as well as discontinuing of the offending agent. IM epinephrine is indicated in severe reactions causing airway angioedema or anaphylaxis.
2. **Correct answer is E.** HIV testing. This patient is likely suffering from molluscum contagiosum, which is a viral skin infection caused by poxvirus. It is very common in children and often benign. In adults with diffuse involvement, immunocompromising conditions, such as HIV must be considered.
3. **Correct answer is E.** Pemphigus vulgaris. This patient has classic pemphigus vulgaris, which is an autoimmune disorder caused by antibodies to adhesion molecules on the epidermis leading to diffuse bullae and separation of the epidermis from the dermis with light touch (Nikolsky sign). This is a life-threatening disorder requiring hospitalization and corticosteroids.
4. **Correct answer is C.** Transfer to a burn center. This patient has toxic epidermal necrolysis which is a life-threatening inflammatory reaction to medications and some infections. Offending agents should be stopped and patients should be treated in a burn center setting with wound care. There are no medications proven to treat the illness, therefore corticosteroids and antibiotics are not indicated. IV fluids are important as patients become easily dehydrated due to the desquamation.
5. **Correct answer is D.** Hepatitis C. This is a case of porphyria cutanea tarda which is a disorder of heme synthesis commonly associated with hepatitis C. It is characterized by blistering and bullae to sun-exposed areas, classically the dorsum of the hands.
6. **Correct answer is B.** Topical ketoconazole. This is a case of tinea versicolor, a fungal infection caused by Malassezia. Patients will present with patches of discolored, hypopigmented skin. Usually they are asymptomatic, however, sometimes there can be pruritus. Treatment is with topical antifungals, such as topical ketoconazole.
7. **Correct answer is C.** Surgical excision. This patient has a lesion suspicious for melanoma. Remember the ABCDE features of melanoma (Asymmetry, Border irregularity, Color variation, Diameter, and Enlargement).
8. **Correct answer is C.** Postherpetic neuralgia. Postherpetic neuralgia is the most common complication of herpes zoster, where pain can persist for several months. Treatment for this is often with tricyclic antidepressants or gabapentin.
9. **Correct answer is C.** Ketoconazole shampoo. This is a case of seborrheic dermatitis, which is a chronic hyperproliferation of the epidermis, commonly effecting the scalp and upper face leading to yellow, greasy plaques. Treatment consists of shampoo containing selenium or ketoconazole.

10. **Correct answer is E.** IV piperacillin/tazobactam and vancomycin and admit. This is a patient with cellulitis who is at high risk due to diabetes and meets sepsis criteria. For severe cellulitis, coverage of both streptococcus **and MRSA is indicated.**

10 Pediatrics

1. **Correct answer is D.** This child has normal development. At 10 months of age, a child should be able to play; however may start to show signs of separation anxiety. He will start to crawl and may be able to stand with a pull. On fine motor, he should be able to grasp with thumb and transfer objects from hand to hand. Although they may start stating their first words around 9 months (like “mama” and “dada”), remember that milestones occur in a range of ages and he is still within that range. Most proper action in this case would be to offer reassurance to parents.
2. **Correct answer is B.** DTaP, Hib, PCV. Vaccines scheduled for 6 months of age are rotavirus, DTaP, Hib, and PCV. However, history of intussusception is a contraindication of rotavirus vaccine administration due to risk of developing intussusception. Although vaccinations in this case could be delayed for a couple of weeks until the child is fever free; remember that a mild febrile illness is not a contraindication for vaccination. The first shot of varicella vaccines is not given until the child is 12 months old.
3. **Correct answer is C.** Urinalysis. The patient presents with a simple febrile seizure episode. She is in the right age group and mother has history of febrile seizures. The most important aspect is reassurance, treating the fever, and treating the underlying illness. Due to foul-smelling urine, urine infection should be considered. Given the child is back to baseline, has no meningeal signs, fully immunized, and is older than 1 year, a lumbar puncture is not required as there are no concerns for meningitis now. CBC and blood culture are not required in a simple febrile seizure, especially in a well-appearing child.
4. **Correct answer is A.** Pertussis. An infection from *Bordetella pertussis* may present as episodes of apnea/cyanosis or “staccato” cough in a neonate. Apnea may be the only presentation, without any fever, and you should have a high index of suspicion. Infantile botulism presents with weak cry, decreased feeding, constipation. GBS and neonatal herpes can cause neonatal sepsis, which is also in the differential; however baby has an otherwise normal examination except for cough, making pertussis more likely.
5. **Correct answer is B.** Ibuprofen and reassessment. The patient has a mild limp but can bare weight, has no fever, and has a normal WBC, sed rate, and CRP. This presentation is consistent with transient synovitis of the hip. Management consists of NSAIDs and outpatient follow-up. If patient had elevated inflammatory markers, nonweight bearing, or high fever, septic arthritis needs to be ruled out and requires hip US, orthopedic consult, needle

aspiration, and antibiotics. With no trauma and no signs of fracture, a splint is not indicated.

6. **Correct answer is C.** Ventral septal defect (VSD). VSD is the most common congenital heart defect and it can be asymptomatic if defect is small. It may be heard on physical examination as a pansystolic murmur at lower left sternal border and loud pulmonic S_2. Pulmonic stenosis is heard as a systolic ejection murmur on the second to third left intercostal space and is associated with tetralogy of Fallot. ASD can be heard as a wide fixed split S_2, systolic ejection murmur at upper left sternal border. A PDA causes a continuous “machinery” murmur at second left intercostal space.
7. **Correct answer is B.** Intussusception. The patient’s rash is suggestive of HSP and a known complication of HSP is intussusception which could be the cause of her intermittent abdominal pain. Streptococcal pharyngitis, appendicitis, and pneumonia can also be present with abdominal pain; however, pain is not usually intermittent and they do not present with this type of rash.

11 Neurologic Disorders

1. **Correct answer is B.** No. Patients who present in the 3 to 4.5 hour window have additional exclusion criteria to those who present within 3 hours, and these include age >80, a history of diabetes and stroke, and being on an anticoagulant, regardless of INR level. This patient is older than 80, and is on warfarin, so tPA would be contraindicated.
2. **Correct answer is A.** ACA. This patient has a classic ACA lesion. See Table 11-8.
3. **Correct answer is D.** Simple partial seizures. Consciousness is impaired in all of the above seizure types except for simple partial seizures. See Table 11-11.
4. **Correct answer is D.** Ethosuximide. Ethosuximide is first-line treatment for absence seizures. It is an inhibitor of neuronal calcium channels. Common comorbidities seen with absence seizures are ADHD and anxiety. Absence seizures are characterized by automatisms such as eyelid twitching, and there is no response to vocal or tactile stimulation during an absence seizure. Once the seizure is done, patients are back to normal; they are not drowsy, there is no postictal period. Absence seizures can be provoked by hyperventilation.
5. **Correct answer is A.** Riluzole. Riluzole is a glutamate inhibitor that is used to treat amyotrophic lateral sclerosis. It does not cure the disease but has been shown to delay the onset of ventilator dependence or tracheostomy in selected patients and may increase survival by approximately 2 to 3 months.
6. **Correct answer is D.** Increased libido. Hyperprolactinemia causes amenorrhea, galactorrhea, gynecomastia, and decreased libido.

Antipsychotics cause hyperprolactinemia by blocking dopamine activity in tuberoinfundibular pathway.

7. **Correct answer is A.** Reversible acetylcholinesterase inhibitor. Donepezil is used to treat dementia related to Alzheimer disease. It does not cure Alzheimer disease, but it may improve memory, awareness, and the ability to function.

12 Gynecologic and Breast Disorders

1. **Correct answer is C.** Laproscopy. Endometriosis is the presence of endometrial tissue outside the uterus. It presents as cyclical pelvic pain that peaks 1 to 2 weeks before menses. Dysmenorrhea, dyspareunia, and dyschezia may also be present. Endometriosis is also a very common cause of female infertility. Although CA-125 is frequently elevated in this condition, laparoscopy showing “powder burn lesions” and cysts is the best diagnostic tool.
2. **Correct answer is D.** Selective estrogen modulator. Polycystic ovary syndrome (PCOS) is a hypothalamic–pituitary–ovarian (HPO) disease marked by anovulation or oligoovulation, androgen excess, and polycystic ovaries. In patients with PCOS, there is increased peripheral conversion of testosterone to estrogen in adipose tissue. Elevated serum estrogen levels inhibit HPO axis by negative feedback. LSH/FSH imbalance results in absence of LH surge which inhibits follicle maturation and oocyte release. Clomiphene, an antiestrogen, promotes follicle stimulation and maturation to allow pregnancy.
3. **Correct answer is E.** Osteoporosis. Functional hypothalamic amenorrhea is decreased levels of gonadotropin-releasing hormone (GnRH), LH secretion, and serum estrogen secondary to a deficiency in caloric intake. This is an example of the female athlete triad: low caloric intake, oligomenorrhea/amenorrhea, and low bone density.
4. **Correct answer is C.** Pelvic inflammatory disease. Pelvic inflammatory disease is progressive *N. gonorrhoeae* or *Chlamydia* infection involving the ovaries, uterus, fallopian tubes, and cavity. PID presents as fever, vaginal discharge, and cervical motion and uterine tenderness. PID can be complicated by perihepatitis (Fitz-Hugh–Curtis disease) which occurs when infection extends into the abdominal cavity causing inflammation of the liver capsule. Perihepatitis presents as right upper quadrant pain that worsens on inspiration.
5. **Correct answer is E.** Worsening hypertension. Combined estrogen–progestin oral contraceptive pills (OCPs) increase risk of hypertension, venous thromboembolism, hepatic adenoma, myocardial infarction, and stroke. Women who have hypertension and who take OCPs should be monitored for worsening of hypertension.

13 Obstetrics

1. **Correct answer is C.** Chorioamnionitis or intra-amniotic infection is a complication of premature rupture of membranes which occurs before the onset of regular contractions and prolonged membrane ruptures (>18 hours). Chorioamnionitis presents as nausea, vomiting, and uterine tenderness. Diagnosis requires the presence of maternal fever and at least one of the following: fetal tachycardia, maternal tachycardia, maternal leukocytosis, or purulent amniotic fluid.
2. **Correct answer is C.** The most common cause of primary postpartum hemorrhage is uterine atony. Atony is a result of uterine fatigue, overdistension, or oxytocin unresponsiveness. The uterus fails to contract and is soft and enlarged. Operative vaginal delivery and hypertension are risk factors for uterine atony.
3. **Correct answer is E.** Inevitable abortion presents as heavy vaginal bleeding, abdominal pain, dilated cervix, and a nonviable intrauterine gestation in the lower uterine segment on ultrasound. If the patient is hemodynamically unstable surgical management is the treatment. Expectant management or misoprostol is used in hemodynamically stable patients.
4. **Correct answer is F.** Preeclampsia is new-onset hypertension, proteinuria, and/or signs of end organ damage after 20 weeks' gestation. In a patient with preeclampsia, the presence of one or more of the following indicates severe preeclampsia: systolic blood pressure ≥160 mm Hg or diastolic blood pressure ≥110 mm Hg on two occasions at least 4 hours apart, visual disturbance, hepatic abnormality, thrombocytopenia, renal abnormality, or pulmonary edema. Appendicitis can present with RUQ pain in late pregnancy (choice C) due to the gravid uterus pushing up on the abdominal contents, but one would not expect to see the other signs or laboratory abnormalities. Similarly, acute viral hepatitis and intrahepatic cholestasis of pregnancy could present with RUQ pain, but one would not expect to see visual disturbances or hypertension.
5. **Correct answer is A.** Ultrasound dating with fetal crown–rump length measurement in the first trimester is the most accurate way to estimate gestational age.

14 Psychiatric Disorders

1. **Correct answer is D.** Schizophrenia. DSM-5 criteria for schizophrenia include two or more of the following for at least one month: (1) Delusions; (2) Hallucinations; (3) Disorganized speech; (4) Grossly disorganized or catatonic behavior; (5) Negative symptoms. (The five As of negative symptoms are Anhedonia, Affect [flat], Alogia, Avolition, Attention [poor]) The patient has the classic features of delusions (his having secrets to the

Universe), hallucinations (“listening” to voices), and disorganized speech. He also demonstrates several negative symptoms, including flat affect, and anhedonia as manifested by lack of interest in socialization. Schizophreniform disorder (choice A) is differentiated from Schizophrenia in that the former only lasts between 1 and 6 months, whereas our patient has been having symptoms for at least a year. A brief psychotic disorder (choice C) only lasts less than 1 month. Generalized anxiety disorder (choice B) does not have associated psychotic symptoms such as delusions and hallucinations with it. Although anhedonia and avolition are associated with major depressive disorder (Choice E) disorganized thought and psychosis are not.

2. **Correct answer is C.** Start her on a daily SSRI and refer her for CBT. This patient is having panic attacks characterized by dizziness, palpitations, paresthesia, nausea, abdominal distress, chest pain, sweating, shaking, and fear of losing control. Panic attacks can often look like life-threatening events. In the acute setting, a benzodiazepine such as lorazepam is helpful to abort the attack. However, benzodiazepines have very high addiction potential, and thus are not recommended for chronic therapy. Alprazolam in particular is a short-acting benzodiazepine and is thus particularly prone to cause withdrawal in patients. Thus choices A and D are inappropriate. β-Blockers (choice B) prevent the tachycardia associated with panic attacks, but since patients with panic attacks are not tachycardic when not having an episode, they are not helpful for chronic therapy. β-Blockers are more commonly used for the treatment of generalized anxiety disorder and performance anxiety. The first-line treatment for panic attacks is SSRI plus CBT. Only a minority of patients have full remission of symptoms, even with treatment.
3. **Correct answer is C.** Decreased concentration of 5-hydroxyindoleacetic acid (5-HIAA) in cerebrospinal fluid analysis. Serotonin (5-HIAA) concentration is decreased in patients with depression. Choice A (HLA-DR2 positivity) is associated with narcolepsy rather than depression. Choice B (enlarged ventricles) are seen with schizophrenia. Increased sensitivity to lactate (choice D) can trigger panic attacks, but is not characteristic of depression.
4. **Correct answer is A.** Cognitive-behavioral therapy (CBT). This patient has the classic signs and symptoms of anorexia nervosa. She is underweight and yet concerned about being overweight. She enjoys cooking for others, even though she hardly eats. The fine hair is lanugo. The calluses on the dorsum of her hand could be from self-induced vomiting, which she should be asked about. The most appropriate therapy for her is CBT, to help her understand her illness, and participate in getting better. Choice B, dronabinol capsules may help her gain weight temporarily, but if she does not have insight into her problem, she will only increase her efforts to keep her weight down. Choice C, involuntary psychiatric hospitalization, is not appropriate because the patient is not suicidal or homicidal. Choice D, levothyroxine therapy, would be appropriate for hypothyroidism. Although the patient reports feeling cold often, we do not know that she has actual hypothyroidism. Rather, the feeling cold is likely part of her anorexia. Choice E, referral to gynecology,

presumably due to amenorrhea is also not the first step, as her amenorrhea is related to her anorexia, and not a primary gynecologic problem.

5. **Correct answer is D.** Inform the mother about the patient's suicidal thoughts and hospitalize the patient. The patient is severely depressed, as suggested by her anhedonia, and is at imminent risk of self-harm. The patient's safety supersedes confidentiality and building trust/rapport with her. The patient has clearly expressed suicidal thoughts, and has a specific plan with access. Although it is positive that she cares about her mother (doesn't want her to be sad), the patient is still in imminent danger, and needs to be hospitalized for her safety. Ideally this would be done with parental consent, but it is not necessary. The most important thing is the patient's safety, so hospitalization is mandatory, whether or not the patient, or one or both of her parents' consent.

15 Epidemiology and Ethics

1. **Correct answer is B.** The specificity of the test will increase. Moving the cutoff point from A to B means there will be fewer false positives, which means fewer people without the disease will test positive. High sensitivity is better for screening tests, while high specificity is better for a diagnostic or confirmatory test.
2. **Correct answer is B.** Prevalence is the number of cases with a given disease (in this case colon cancer). Since the drug prolongs survival, more people will be alive with colon cancer in the population. The drug would not affect the incidence, which is the occurrence of new cases.
3. **Correct answer is A.** It must be associated with both the exposure and the outcome (disease). A confounder is a variable that "confuses" the relationship between an exposure and an outcome. As such, it needs to be associated with both the exposure and the outcome (choice A). In this case, cigarette smoking is associated with both coffee drinking as well as myocardial infarction. Confounders have no relation to prevalence of the disease or outcome of interest (choice B). If a confounder is evenly distributed between those who have the outcome of interest and those who do not (choice C), then there would be no confounding because it would even out.
4. **Correct answer is B.** Cohort study. A cohort is a group of subjects followed over time. In this case, it is a group of patients, who have all had an acute ischemic stroke and have presented to the ED for it. These patients were followed over time (90 days in this case) to ascertain whether the initial blood pressure was associated with an increased risk of death. From the vignette, one cannot determine whether it is a prospective or retrospective cohort study. This cohort study would be prospective if the blood pressures were collected in real time or at least before the outcome of interest occurred. If, on the other hand, the blood pressure measurements were ascertained via chart review after everyone's 90-day outcome had occurred, then it would be a

retrospective cohort study. This is not a case control study (choice A) because there are no controls (everyone has had a stroke in the group). This is not a randomized controlled trial (choice C) as there is no randomization of the groups, and no intervention. The cohort is simply observed to see whether a correlation exists between initial blood pressure in the ED and death at 90 days. Finally, this is not a meta-analysis (choice D), which involves pooling of data from multiple studies, as it is a single study.

5. **Correct answer is D.** 60 to 120 mm Hg. The figure below depicts the standard deviations in normally distributed data. 68.2% of values will lie within 1 standard deviation of the mean—in this case, +/–10 mm Hg from 90 mm Hg, for a range of 80 to 100 mm Hg (choice A). Ninety-five percent of values would lie within 2 standard deviations of the mean, or +/–2(10) mm Hg from 90 mm Hg for a range of 70 to 110 mm Hg. 99.7% of values would lie within 3 standard deviations of the mean, or +/–3(10) mm Hg from 90 mm Hg, for a range of 60 to 120 mm Hg.

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