Crush the Boards

The Ultimate USMLE Step 2 Review

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Adam Brochert, M.D.
Intern
Department of Internal Medicine
Eastern Virginia Medical School
Norfolk, Virginia

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Branches

- 202 Batavia Chambers, 8 Kumara Kruppa Road, Kumara Park East, **Bangalore** 560 001, Phones: 2285971, 2382956 Tele Fax: 2281761
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  e-mail: jpmedpub@bom7.vsnl.net.in

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Introduction

This book was written because I felt there was not a good, comprehensive, high-yield review book for the USMLE Step 2. The goal of the book is to provide information that has appeared on recent administrations of Step 2. The exam covers a lot of information, but if you know all the concepts in this book, you should do much better than just pass: you should CRUSH THE BOARDS!

Step 2 is the same level of difficulty as Step 1, but the questions are more relevant to the practice of medicine. Step 2 stresses the things that are necessary to be a good first-year resident in the emergency room or a general clinic. Knowing how to diagnose, manage, and treat common conditions is stressed. Not just theory, but practice—in other words, knowing the next step. The other topics that frequently appear on Step 2 are treatable emergency conditions. Remember, these are the situations that you, as a future house officer, may have to diagnose and treat at three o'clock in the morning while on call.

Knowing how to manage exotic or rare conditions is low-yield. It is much more high-yield to know rare complications and presentations of common diseases. Usually, when you are asked about a rare disease, you simply need to recognize it from a classic presentation.

Some information from Step 1 is high-yield for Step 2. Epidemiology and biostatistics are retested, as well as pharmacology and microbiology (which bugs cause which conditions in specific patient populations). Cardiac pathophysiology is high-yield, as is common EKG pathology. The behavioral science/psychiatry questions are also similar to those in Step 1.

Overall, though, Step 2 has a different focus, and that focus is clinical. If a patient presents with chest pain, what would you do? What kinds of questions would you ask the patient? What tests would you order? What medications might you give?

There are also five general tips I would like to pass on to those preparing for Step 2:

1. Always get more history when it is an option, unless the patient is unstable and immediate action is needed.
2. You must know cut-off values for the treatment of common conditions (at what numbers do you treat hypertension and hypercholesterolemia, and at what CD4 counts do you need chemoprophylaxis in HIV?).
3. A presentation may be normal (especially in pediatrics and psychiatry) and need no treatment!
4. Don't forget to study your subspecialties. Just because you never took an ophthalmology rotation doesn't mean there won't be any questions about it on the exam. You don't have

to be an expert, but knowing common and life-threatening diseases in the subspecialties can increase you score substantially.

5. Remember that residency programs don't usually see the breakdown of your score, only those magic 2- and 3-digit overall scores (in other words, don't skip studying a subject because you hate it and aren't going into it).

Studying for Step 2 can seem like an overwhelming task. Given the time constraints of medical students in their clinical years, most need a concise review of the tested topics. It is my hope that CRUSH THE BOARDS will meet your needs in this regard.

Adam Brochert, M.D.

CHAPTER 1

Internal Medicine

HYPERTENSION

Screening for hypertension should be done roughly every 2 years, starting at the age of 3. Whenever a patient comes in for any kind of medical visit or hospitalization, it is standard practice to measure the blood pressure. The current accepted cut-off value is 140/90 mmHg (lower in children). A blood pressure of 145/75 mmHg is still considered hypertension (isolated systolic hypertension) and should be treated if it persists. Both systolic and diastolic hypertension decrease life expectancy. Hypertension is not diagnosed until three separate measurements on three separate occasions are greater than 140/90 mmHg (except in pregnancy, when waiting for a return visit could be devastating). Also, if hypertension is severe (> 210 systolic, > 120 diastolic, or end-organ effects), immediate treatment with medication is warranted:

SYSTOLIC BLOOD PRESSURE (mmHg)	DIASTOLIC BLOOD PRESSURE (mmHg)	CLASSIFICATION	FOLLOW-UP RECOMMENDATION
< 130	< 85	Normal	Recheck in 2 yr
130–139	85–89	High normal	Recheck in 1 yr
140–159	90–99	Stage I (mild)	Confirm within 2 mo
160–179	100–119	Stage II (moderate)	Evaluate/refer to source of care in < 1 mo
180–209	110–119	Stage III (severe)	Evaluate/refer to source of care in < 1 wk
≥ 210	≥ 120	Stage IV (very severe)	Evaluate/refer to source of care immediately

Basic studies and evaluation in a new hypertensive patient include urinalysis, chemistry panel 7, EKG, and hemoglobin/hematocrit. Do not treat hypertension until you have a diagnosis (hypertension on three separate visits)! Once you have a diagnosis, first allow the patient 3–4 months of weight reduction, exercise, and other lifestyle modifications (low salt and cholesterol diet, no alcohol or smoking). If this approach is unsuccessful, only then do you start medication. There are four first-line agents for the treatment of hypertension: beta blockers, thiazide diuretics, angiotensin-converting enzyme (ACE) inhibitors, and calcium channel blockers. Which one you choose is often based on the patient (see table, top of next page):

For **pregnant patients**, use hydralazine and/or alpha-methyldopa. Labetalol is slowly gaining acceptance also. Remember that in patients with preeclampsia, magnesium sulfate lowers blood pressure. For side effects of hypertension medications (high yield), see pharmacology section.

DRUG	GOOD FOR FOLLOWING PATIENTS	BAD FOR FOLLOWING PATIENTS
Diuretics	Black race, elderly age, congestive heart failure, chronic renal failure	Electrolyte problems, pregnancy, gout
Beta blocker	Angina, myocardial infarction, migraines, senile tremor, tachycardia, isolated systolic hypertension, young age, white race	Diabetes, asthma/chronic obstructive pulmonary disease, pregnancy, bradycardia/heart block, claudication
ACE inhibitor	Young age, white race, congestive heart failure*, diabetes (renal protection), impotence with other medications	Electrolyte problems, pregnancy, renovascular hypertension (may cause acute renal failure)
Calcium antagonists	Black race, elderly age, angina, migraines, supraventricular tachycardia, Raynaud's phenomenon, claudication	First-degree heart block, sick sinus, pregnancy

* ACE inhibitors are first-line agents for congestive heart failure, because they have been shown to reduce mortality. Any patient with hypertension and congestive heart failure (and any patient with congestive heart failure) should be put on an ACE inhibitor.

Hypertensive emergencies: usually occur when blood pressure is > 200/100 mmHg. Defined as hypertension with acute end-organ damage (i.e., severe hypertension plus one of the following: acute left ventricular failure, unstable angina, myocardial infarction, or encephalopathy; symptoms include one or more of the following: headaches, mental status changes, vomiting, blurry vision, dizziness, papilledema). Hypertensive emergencies are an exception to the rule of measuring blood pressure 3 times before treating! Use nitroprusside, nitroglycerin, diazoxide, or labetalol emergently.

Secondary hypertension: clues include onset before 30 or after 55 years of age and other suggestive history or lab values. In a young woman, the most common cause is birth control pills (discontinue them), followed by renovascular hypertension due to fibrous dysplasia (renal bruit: use intravenous pyelogram or arteriogram for diagnosis; treat with balloon dilatation or angioplasty). In a young man, think of excessive alcohol intake or exotic conditions (pheochromocytoma, Cushing's syndrome, Conn's syndrome, polycystic kidney disease). In elderly patients with new-onset hypertension, think renovascular hypertension due to atherosclerosis (renal bruit; ACE inhibitor precipitates renal failure). If you suspect secondary hypertension (95% of cases of hypertension are essential, primary, or idiopathic), remember the following hints and tests to order:

1. Pheochromocytoma: urinary catecholamines (vanillylmandelic acid, metanephrine) plus intermittent severe hypertension, dizziness, and diaphoresis
2. Polycystic kidney disease: flank mass, family history, elevated blood urea nitrogen, creatinine
3. Cushing's syndrome: dexamethasone suppression test or 24-hr urine cortisol level
4. Renovascular hypertension: intravenous pyelogram or angiogram; look for bruit
5. Conn's syndrome: high aldosterone, **low renin**
6. Coarctation of the aorta: upper extremity hypertension only, unequal pulses, radiofemoral delay, associated with Turner's syndrome, rib notching on x-ray

Note: lowering blood pressure lowers risk for stroke (hypertension is the most important risk factor), heart disease, myocardial infarction, renal failure, atherosclerosis, and dissecting aortic aneurysm. Coronary disease is the most common cause of death among untreated hypertensive patients. Don't forget to treat isolated systolic or diastolic hypertension if it persists.

Note: Nitroprusside dilates arteries and veins, whereas nitroglycerin is a venodilator only and other medications are arterial dilators only (hydralazine, alpha$_1$ antagonists, calcium channel

blockers). Venodilators reduce preload, whereas arterial dilators reduce afterload (nitroprusside does both).

DIABETES

Universal screening is generally *not* recommended. Screening in patients who are obese, > 45 years old, have a positive family history, or are members of certain ethnic groups (black, American Indian, Hispanic) is more accepted but not uniformly.

Classic symptoms of diabetes are polydipsia, polyuria, polyphagia and weight loss. **Diagnosis** is made by a fasting plasma glucose ≥ 126 mg/dl (after an overnight fast) or a random glucose (no fasting) ≥ 200 mg/dl. If the patient has classic symptoms, one measurement is enough to confirm a diagnosis, but in an asymptomatic patient, the test should be repeated. Rarely, an oral glucose tolerance test (OGTT) is done and DM is diagnosed when levels ≥ 200mg/dl are reached within or at 2 hours after a 75-gm glucose load is administered orally.

Differences between Type I and Type II Diabetes Mellitus

	TYPE I	TYPE II
Age at onset	Most commonly < 30 yr	Most commonly > 30 yr
Associated body	Thin	Obese
Develop ketoacidosis	Yes	No
Develop hyperosmolar state	No	Yes
Level of endogenous insulin	Low to none	Low to high (insulin resistance)
Twin concurrence	< 50%	> 50%
HLA association	Yes	No
Response to oral hypoglycemics	No	Yes
Antibodies to insulin	Yes (at diagnosis)	No
Risk for diabetic complications	Yes	Yes
Islet cell pathology	Insulitis (loss of most B cells)	Normal number, but with amyloid deposits

HLA = human leukocyte antigen.

The **goal of treatment** is to keep postprandial glucose < 200 mg/dl and fasting glucose < 130 mg/dl. Stricter control results in too many episodes of hypoglycemia (look for symptoms of sympathetic discharge and mental status changes)

Important points:

1. Remember the importance of C-peptide in distinguishing between too much exogenous insulin (low C-peptide with accidental overdose in a diabetic or factitious disorder) and an insulinoma (high C-peptide).
2. Because IV contrast agents can precipitate acute renal failure in diabetics and other renal patients, you should use contrast only if absolutely necessary. Make sure that the patient is **well-hydrated** before using contrast agents in diabetics and renal patients to prevent renal damage.
3. Diagnosis of diabetic ketoacidosis(type I diabetes mellitus) requires hyperglycemia, hyperketonemia, and metabolic acidosis. Treatment involves fluids, IV regular insulin, and potassium and phosphorus replacement. Do not use bicarbonate unless the pH is < 7.0. Search for the cause, which often is infection. The mortality rate is about 10%.

4. Diagnosis of nonketotic hyperglycemic hyperosmolar state (type II diabetes mellitus) requires hyperglycemia and hyperosmolarity without ketonemia. Treatment involves fluids, fluids, fluids, IV insulin, and electrolyte replacement. The mortality rate is about 50%.

Long-term complications of diabetes mellitus include atherosclerosis, coronary artery disease, myocardial infarction, retinopathy, and nephropathy. Use of ACE inhibitors helps to prevent nephropathy; 30% of end-stage renal disease is caused by diabetes mellitus. Diabetes is associated with an increased risk of infections, peripheral vascular disease (claudication, atrophy), gangrene (the most common cause for nontraumic amputations is diabetes), and neuropathy.

Peripheral neuropathy (autonomic and sensory) causes many problems in diabetics:

- Gastroparesis (early satiety, nausea; treat with metoclopromide and cisapride)
- Charcot's joints (deformed joints due to lack of sensation; patient puts too much stress on joints)
- Impotence (from autonomic neuropathy as well as peripheral vascular disease)
- Cranial nerve palsies (especially 3,4,6-ocular palsies; usually resolve spontaneously within a few months)
- Orthostatic hypotension (due to lack of effective sympathetic innervation; when patient stands up, heart rate and vascular tone do not increase appropriately to maintain blood pressure)

Note: Diabetics commonly have no chest pain with a myocardial infarction because of neuropathy ("silent" MI).

Diabetics are also prone to **foot infections, ulcers and gangrene** because they cannot feel their feet and blood flow is poor so that infection does not heal well. Patients should wear comfortable, properly fitting shoes and regularly inspect their own feet.

When **retinopathy** becomes proliferative, the treatment is panretinal laser photocoagulation to prevent progression and blindness. All diabetics should be followed once a year by an ophthalmologist to monitor retinal changes.

Know how to use **regular** and **neutral protamine Hagedorn** (NPH) insulin. Regular insulin = 45 minutes until onset, peak action at 3–4 hr, and duration of action for 6–8 hr. NPH insulin = 1–1.5 hr until onset, peak action at 6–8 hr, and duration of about 18–20 hr.

- If patient has high (low) 7 AM glucose, increase (decrease) NPH insulin at dinner the night before.
- If patient has high (low) noon glucose, increase (decrease) AM regular insulin.
- If patient has high (low) 5 PM glucose, increase (decrease) morning NPH.
- If patient has high (low) 9 PM glucose, increase (decrease) dinner time regular insulin.

Somogyi effect vs. dawn phenomenon. The Somogyi effect is the body's reaction to hypoglycemia. If too much NPH insulin is given at dinner time the night before, the 3 AM glucose will be low (hypoglycemia). The body reacts by releasing stress hormones, which cause the 7 AM glucose to be high. Treatment is to *decrease* insulin. The dawn phenomenon is hyperglycemia caused by normal early AM growth hormone secretion. 7 AM glucose is high, without 4 AM hypoglycemia (glucose normal or high at 4 AM). Treatment is to *increase* insulin.

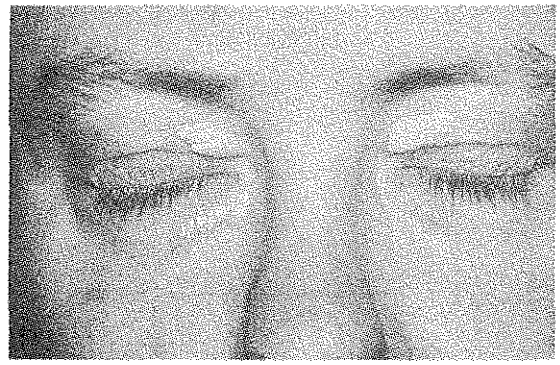
Follow compliance with hemoglobin A1c level, which is an accurate measure of overall control for the previous 3 months. Patients are not afraid to fudge their home test number to please their doctors, and this is the way to catch them.

For surgery, patients with diabetes are allowed nothing by mouth (NPO). Give one-third to one-half of normal insulin dose, then monitor glucose closely through case and postoperatively, using 5% dextrose in water (D5W) and IV regular insulin to maintain glucose control.

Medications in diabetics: Chlorpropamide may cause syndrome of inappropriate secretions of antidiuretic hormone (SIADH). Patients with type I DM are not helped by sulfonylurea medications. Avoid beta blockers, which prevent many of the physical manifestations of hypoglycemia (tachycardia, diaphoresis); therefore, neither you nor the patient will know if the patient is becoming hypoglycemic.

CHOLESTEROL

Measure total cholesterol and high-density lipoprotein (HDL) every 5 years (unless abnormal), starting at age 20 (although this recommendation is not universally accepted). Start earlier if the patient is obese or has a strong family history. Look for xanthelasma (know what it looks like), corneal arcus (in younger patients), lipemic-looking serum, and obesity as markers of possible **familial hypercholesterolemia**. Family members should be tested. Also, look for pancreatitis with no risk factors (e.g., no alcohol, gallstones) as a marker for familial hypertriglyceridemia.



Patient with xanthelasma in all four lids. (From Tasman W, Jaeger EA: The Wills Eye Hospital Atlas of Clinical Ophthalmology. Philadelphia, Lippincott-Raven, 1996, with permission.)

Management of Cholesterol Levels (mg/dL)

NO CHD RISK FACTORS	2 OR MORE CHD RISK FACTORS	INTERVENTION
Total cholesterol < 200	Total cholesterol < 200	Remeasure in 5 years*
Total cholesterol 200–239		Counseling and recheck in 1–2 yr*
Total cholesterol > 239	Total cholesterol > 200	Do fasting lipoprotein analysis (gives LDL)
LDL < 160	LDL < 130	Remeasure in 1 yr (patient meets goals)
LDL 160–189	LDL 130–159	Diet
LDL > 189	LDL > 159	Medications

CHD = coronary heart disease, LDL = low-density lipoprotein.

Note: With evidence of CHD (which includes known coronary artery disease or peripheral vascular disease), use medications when LDL ≥ 130, with a target LDL < 100.

* Unless HDL < 35 mg/dl, in which case you should go ahead and do fasting lipoprotein analysis.

Risk factors for coronary heart disease (LDL and total cholesterol are risk factors for CHD, but do not count them in deciding to treat or not to treat high cholesterol):

- Age (men ≥ 45, women ≥ 55 or with premature menopause and no estrogen replacement therapy)

- Family history of premature CHD (defined as definite myocardial infarction or sudden death in father/first-degree male relative < 55 years old or mother/first-degree female relative < 65 years old)
- Cigarette smoking (> 10 cigarettes/day)
- Hypertension (≥ 140/90 mmHg or on antihypertensive medications)
- Diabetes mellitus
- Low HDL (< 35 mg/dl) (*Note:* HDL ≥ 60 mg/dl is considered to be protective and negates one risk factor.)
- Male sex is also considered a risk factor because men develop coronary heart disease earlier than women (but postmenopausal women quickly catch up with age-matched men). If you give a patient one risk factor for being male, do not give him a second risk factor for age (use one or the other in men).
- Obesity is not an independent risk factor for boards purposes. Stress, physical inactivity and type A personality (look for a hard-driving attorney) are controversial (presumed to be risk factors by some clinicians).
- Hypertriglyceridemia alone is not considered a risk factor, but when associated with high cholesterol causes more coronary heart disease than high cholesterol alone.

Note: Lipoprotein analysis involves measuring total cholesterol, HDL and triglycerides. LDL can then be calculated from the formula LDL = total cholesterol – HDL – (triglycerides/5).

Note: Always give new patients at least 3 months to try lifestyle modifications (decrease calories, cholesterol, and saturated fat in diet; decrease alcohol and smoking; exercise) before initiating drug therapy.

First-line agents are niacin (poorly tolerated but effective) and bile acid-binding resins (e.g., cholestyramine). HMG CoA-reductase inhibitors are the most effective drugs and are considered first-line agents by some, but for board purposes, they are used first only if the other two choices are not appropriate or if patient has extremely high cholesterol (> 300 mg/dl, which is a marker for familial hypercholesterolemia).

Note: High HDL is protective against atherosclerosis and is increased by moderate alcohol consumption (1–2 drinks/day) but not high alcohol intake, exercise and estrogens. HDL is decreased by smoking, androgens, progesterone, and hypertriglyceridemia.

Be aware of **secondary causes of hyperlipidemia:** uncontrolled diabetes mellitus, hypothyroidism, uremia, nephrotic syndrome, obstructive liver disease, excessive alcohol intake (increases triglycerides), and medications (oral contraceptives, glucocorticoids, thiazides, and beta blockers).

Atherosclerosis is involved in about one-half of all deaths in the United States and one-third of deaths between ages 35 and 65. Atherosclerosis is the most important cause of permanent disability and accounts for more hospital days than any other illness (translation: *understand atherosclerosis for the boards*).

SMOKING

Smoking is the single most significant source of preventable morbidity and premature death in the United States. Whenever you are not sure which risk factor to eliminate, smoking is a safe guess.

Important points:

1. Smoking is the best risk factor to eliminate to prevent heart disease-related deaths (responsible for 30–45% of deaths due to coronary heart disease deaths). Risk decreases by 50% within 1 year compared with continuing smokers and decreases to the level of patients who never smoked in 15 years.
2. Smoking also increases risk for the following cancers: lung (90% of cases), oral cavity, esophagus, larynx, pharynx, bladder (50% of cases), kidney, pancreatic, and cervical cancers. Smoking possibly increases stomach cancer also.
3. Chronic obstructive pulmonary disease is often due to smoking. Emphysema almost always is due to smoking (unless the patient is very young or has no smoking history, in which case you should consider alpha$_1$ antitrypsin deficiency). Although the changes of emphysema are irreversible, risk of death still decreases after smoking cessation.
4. When parents smoke, children at increased risk for asthma and upper respiratory infections, including otitis media.
5. Smoking retards healing of peptic ulcer disease, and cessation stops Buerger's disease (Raynaud's symptoms in a young male smoker).
6. Smoking by pregnant woman increases the risk of low birth weight, prematurity, spontaneous abortion, stillbirth, and infant mortality.
7. Smoking cessation preoperatively is the best way to decrease risk of postoperative pulmonary complications.
8. Do not give birth control pills to women over 35 who smoke; do give women smokers postmenopausal estrogen therapy

ALCOHOL

Important points:

1. Alcohol increases the risk for the following cancers: oral, larynx, pharynx, esophagus, liver, and lung. It may increase the risk for gastric, colon, pancreatic, and breast cancer.
2. Alcohol is the most common cause of cirrhosis and esophageal varices.
3. Alcohol is involved in roughly 50% of fatal car accidents, 67% of drownings and homicides, 70–80% of deaths in fires, and 35% of suicides.
4. Always give thiamine before glucose in an alcoholic; if you give them in the reverse order, you may precipitate Wernicke's encephalopathy.

Wernicke's vs. Korsakoff's syndromes. Wernicke's syndrome = ophthalmoplegia, nystagmus, ataxia, and confusion; acute and often reversible; may be fatal. Korsakoff's syndrome = anterograde amnesia and confabulation, chronic and irreversible. Both are due to thiamine deficiency. The most likely cause is damage to the mamillary bodies and thalamic nuclei.

Alcohol withdrawal can be fatal. Treat on an inpatient basis. Use benzodiazepines (chlordiazepoxide and other long-acting benzodiazepines) or, rarely, barbiturates. Gradually taper the dose over days.

Withdrawal stages/symptoms. First comes acute withdrawal syndrome, 12–48 hours after last drink. Symptoms include tremors, sweating, hyperreflexia, and seizures (rum fits). Next is alcoholic hallucinosis, which consists of hallucinations (auditory/visual) and illusions without autonomic symptoms. Finally comes delirium tremens, which usually occurs 2–4 days after the last

drink and involves hallucinations and illusions plus confusion, poor sleep, and autonomic lability (sweating, increased pulse and temperature), which occasionally is fatal. Treat on an inpatient basis.

Stigmata of chronic liver disease in alcoholics: varices, hemorrhoids, caput medusae, jaundice, ascites, palmar erythema, spider angiomas, gynecomastia, testicular atrophy, encephalopathy, asterixis, prolonged prothrombin time, hyperbilirubinemia, spontaneous bacterial peritonitis, hypoalbuminemia, and anemia.

Conditions commonly caused by alcohol include gastritis, Mallory-Weiss tears, pancreatitis (acute and chronic), peripheral neuropathy (via thiamine deficiency), brain damage, and cardiomyopathy (dilated). It also causes testicular atrophy, fatty change in the liver, hepatitis, cirrhosis, hepatocellular liver cancer, Wernicke/Korsakoff syndrome (via thiamine deficiency), cerebellar degeneration, and rhabdomyolysis (acute and chronic).

The best treatment for alcoholism is Alcoholics Anonymous or other support group. Disulfiram also may be tried (patients get sick when they drink because of alcohol dehydrogenase enzyme inhibition).

Alcohol is a definite teratogen. You should be able to recognize **fetal alcohol syndrome:** mental retardation, microcephaly, microphthalmia, short palpebral fissures, midfacial hypoplasia, and cardiac defects. No alcohol is good alcohol during pregnancy. An estimated 1 in 3000 births is affected by fetal alcohol syndrome, which is the most common cause of preventable mental retardation.

Incidence. Alcohol abuse is more common in men. Roughly 10–15% of people abuse alcohol. *Alcoholism has a heritable component* and is especially passed from fathers to sons.

Important points:

1. Skid-row alcoholics commonly develop aspiration pneumonia with weird bugs such as *Klebsiella* species (currant-jelly sputum) and enteric organisms (e.g., anaerobes, *Escherichia coli*, streptococci, staphylococci).
2. Alcohol may precipitate hypoglycemia (but give thiamine first).
3. Alcoholics develop just about every type of vitamin and mineral deficiency; especially common are deficiencies of folate, magnesium, and thiamine.
4. Bleeding varices are treated with stabilization (fluids, blood), then upper endoscopy and sclerotherapy with cauterization, banding, or vasopressin. The mortality rate is high, and rebleeding is common, especially early. Try transjugular intrahepatic portosystemic shunt (TIPS) before portacaval shunting procedures (splenorenal is the most physiologic shunt type).

ACID/BASE STATUS

You must know how to interpret **simple blood gases**, when given pH, O_2, CO_2, and bicarbonate. Here are good basic hints:

1. pH tells you whether you are dealing with acidosis or alkalosis.
2. Look at CO_2. If it is high, the patient has either respiratory acidosis (pH < 7.4) or is compensating for metabolic alkalosis (pH > 7.4). If CO_2 is low, the patient has either respiratory alkalosis (pH > 7.4) or is compensating for metabolic acidosis (pH < 7.4).
3. Look at bicarbonate. If it is high, the patient has either metabolic alkalosis (pH > 7.4) or is compensating for respiratory acidosis (pH < 7.4). If bicarbonate is low, the patient either has metabolic acidosis (pH < 7.4) or is compensating for respiratory alkalosis (pH > 7.4).

Clinical correlation: common causes of different primary disturbances

1. Respiratory acidosis: chronic obstructive pulmonary disease, asthma, drugs (opioids, benzodiazepines, barbiturates, alcohol, and other respiratory depressants), chest wall problems (paralysis, pain), sleep apnea
2. Respiratory alkalosis: anxiety/hyperventilation, aspirin/salicylate overdose
3. Metabolic acidosis: ethanol, diabetic ketoacidosis, uremia, lactic acidosis (sepsis/shock), methanol/ethylene glycol, aspirin/salicylate overdose, diarrhea, carbonic anhydrase inhibitors
4. Metabolic alkalosis: diuretics (except carbonic anhydrase inhibitors), vomiting, volume contraction, antacid abuse/milk-alkali syndrome, hyperaldosteronism
5. Salicylate/aspirin overdose causes two primary disturbances (respiratory alkalosis and metabolic acidosis). Look for coexisting tinnitus and/or hypoglycemia, vomiting, and history of "swallowing several pills." Alkalinization of the urine (with bicarbonate) speeds excretion.
6. In certain patients with chronic lung disease, pH may be alkaline during the day (especially in patients with sleep apnea) because they breathe better when they are awake or have just recovered from an episode of bronchitis. The metabolic alkalosis that usually compensates for respiratory acidosis is no longer compensatory and becomes the primary disturbance (elevated pH and bicarbonate).
7. Sleep apnea, if severe, may cause right-sided heart failure (cor pulmonale).

Treatment. Do not use bicarbonate to treat low pH unless the pH is < 7.0 and other measures have failed (always try saline first).

Note: Beware the asthmatic whose blood gas goes from alkalotic to normal. The patient is probably about to crash and needs intubation.

HYPONATREMIA

Signs and symptoms of hyponatremia are confusion, lethargy, mental status changes, anorexia, seizures, disorientation, cramps, and coma. The first step in determining the cause of true hyponatremia is to look at the volume status:

HYPOVOLEMIC	EUVOLEMIC	HYPERVOLEMIC
Dehydration, diuretics, diabetic ketoacidosis/diabetes mellitus, Addison's disease, hypoaldosteronism	Syndrome of inappropriate secretion of antidiuretic hormone, psychogenic polydipsia, oxytocin use	Congestive heart failure, nephrotic syndrome, cirrhosis, toxemia, renal failure

1. Syndrome of inappropriate secretion of antidiuretic hormone (SIADH) commonly results from head trauma or surgery, meningitis, small cell cancer of lung, postoperative or other painful states, pulmonary infections (pneumonia or tuberculosis), opioids, or chlorpropamide. Treatment is water restriction. Occasionally, when refractive to conservative management, SIADH is treated with demeclocycline (a tetracycline that causes renal diabetes insipidus).
2. With Addison's disease and hypoaldosteronism, potassium is elevated.
3. Hypovolemic hyponatremia should be treated with saline. Euvolemic and hypervolemic hyponatremia should be treated with free water restriction and possibly diuretics for hypervolemia.

4. Never correct hyponatremia rapidly, because you may cause brainstem damage (central pontine myelinolysis). Hypertonic saline is used only when the patient has seizures due to hyponatremia and, even then, only briefly and cautiously. *Normal saline is a better choice 99 times out of 100 for board purposes.*
5. Correct the sodium when the patient has hyperglycemia (once glucose exceeds 200 mg/dl, sodium decreases by 1.6 mEq/L for each increase of 100 mg/dl in glucose). Hyperlipidemia and severe hyperproteinemia may cause a false (spurious) hyponatremia by their osmotic effect.
6. *In a surgical patient*, the most common cause of hyponatremia is inappropriate or excessive fluid administration.
7. Oxytocin administration may cause hyponatremia in pregnant women (oxytocin has an ADH-like effect).

HYPERNATREMIA

The **signs and symptoms** of hypernatremia and hyponatremia are similar: confusion, mental status changes, hyperreflexia, seizures, and coma. **Common causes** include dehydration, inability to drink (paralysis, dementia), diuretics, diabetes insipidus (pituitary or nephrogenic), diarrhea, renal disease, and iatrogenic administration of excessive salt. Sickle cell disease also may cause hypernatremia due to kidney damage that impairs renal concentrating ability. Hypokalemia and hypercalcemia also cause a similar impairment in renal concentrating ability that may mimic diabetes insipidus (DI). **Treatment** involves water replacement. Often the patient is so dehydrated that normal saline may be used at first until the patient is hemodynamically stable; then switch to one-half normal saline (0.45% NaCl). Five-percent dextrose in water should not be used

Pituitary vs. nephrogenic diabetes insipidus. Pituitary DI responds to vasopressin; nephrogenic DI does not. Nephrogenic DI may be caused by medications (lithium, demeclocycline, methoxyflurane, and amphotericin B) and is treated with a thiazide diuretic (*paradoxical effect*). Central DI may be caused by Sheehan's syndrome (postpartum hemorrhage causes shock and pituitary infarction [apoplexy]); look for inability to breast feed and other endocrine deficiencies.

HYPOKALEMIA

Hypokalemia causes **muscular weakness**, including weakness of smooth muscles. The patient may have an ileus and/or hypotension. Muscular weakness may lead to paralysis and ventilatory failure. The most famous (and most tested) effect of hypokalemia, however, is on the heart. EKG findings include loss of T wave, U waves, premature ventricular and atrial contractions and ventricular and atrial tachyarrhythmias.

Changes in pH may cause changes in serum potassium (*alkalosis causes hypokalemia, acidosis* causes hyperkalemia). For this reason, bicarbonate is given to severely hyperkalemic patients. Normalization of deranged pH most likely will correct the potassium derangement automatically (no need to give or restrict potassium).

Important points:

1. The heart is particularly sensitive to hypokalemia when the patient is taking digitalis. Potassium should be watched carefully in all patients taking digitalis, especially if they also take diuretics (a *very* common occurrence).

2. Do *not* replace potassium too quickly! The best method of replacement is oral, but if potassium must be given IV, do not exceed 20 mEq/hr. Monitor the EKG if potassium must be given quickly.
3. If hypomagnesemia is present, it is difficult to correct the hypokalemia unless you also correct the hypomagnesemia.

HYPERKALEMIA

With hyperkalemia, especially if the patient is asymptomatic and the EKG is normal, you should wonder whether the lab specimen is hemolyzed. Hemolysis causes a **false hyperkalemia**. Repeat the test.

Signs and symptoms may include weakness or paralysis, but the most important (and most tested) effects are cardiac. **EKG changes** (in order of increasing potassium value) include tall, peaked T waves; widening of QRS; PR interval prolongation; loss of P waves; and a sine wave pattern. Arrhythmias include asystole and ventricular fibrillation.

Common causes of hyperkalemia include renal failure (acute or chronic), severe tissue destruction, hypoaldosteronism (watch for hyporeninemic hypoaldosteronism in diabetes), medications (potassium-sparing diuretics, beta blockers, nonsteroidal anti-inflammatory drugs, or ACE inhibitors), and adrenal insufficiency (associated with low sodium and low blood pressure). Try stopping all implicated medications.

The **best method of therapy** is oral (decreased intake, sodium polystyrene resin). If, however, potassium is very high (> 6.5) and/or cardiac toxicity is apparent (more than peaked T-waves), immediate IV therapy is needed. First give calcium gluconate, which is cardioprotective, even though it does not change potassium levels. Then give sodium bicarbonate (alkalosis causes potassium to shift inside cells) and glucose with insulin, which also forces potassium inside cells. If the patient has renal failure or initial treatment is ineffective, prepare to institute dialysis emergently.

HYPOCALCEMIA

Hypocalcemia produces **neurologic findings**, the most tested of which is tetany. Tetany is evidenced by tapping on the facial nerve to elicit contraction of the facial muscles (Chvostek's sign) or applying a tourniquet or blood pressure cuff and inflating it to elicit hand muscle (carpopedal) spasms (Trousseau's sign). Other symptoms are depression, encephalopathy, dementia, laryngospasm, and convulsions. EKG shows **QT interval prolongation**.

Common causes:

- DiGeorge's syndrome (tetany shortly after birth, absent thymic shadow)
- Renal failure (because of the kidney's role in vitamin D metabolism)
- Hypoparathyroidism (watch for postthyroidectomy patients; all four parathyroids may have been accidentally removed)
- Vitamin D deficiency
- Pseudohypoparathyroidism (short fingers, short stature, mental retardation, and normal levels of parathyroid hormone [PTH] with end-organ unresponsiveness to PTH)
- Acute pancreatitis
- Renal tubular acidosis

Important points:

1. Hypoproteinemia of any etiology may cause hypocalcemia because the protein-bound fraction of calcium will be decreased. In this instance, however, the patient is asymptomatic, because the ionized (unbound) fraction of calcium is unchanged.
2. Hypomagnesemia of any cause makes it difficult to correct the hypocalcemia until the hypomagnesemia is also corrected.
3. Rickets and osteomalacia are the skeletal effects of vitamin D deficiency in children and adults, respectively.
4. Alkalosis may cause symptoms similar to hypocalcemia because of effects on the ionized fraction of calcium. Treat by correcting the pH.
5. Phosphorus and calcium levels are usually in opposite directions, and derangements in one may cause problems with the other. In renal failure, therefore, you should not only raise calcium but also restrict phosphorus and give PO_4-binding agents, such as aluminum-hydroxide.

HYPERCALCEMIA

Hypercalcemia is **usually asymptomatic** and discovered by routine labs. **When symptoms are present**, remember "bones, stones, groans, and psychiatric overtones" (bone changes such as osteopenia or pathologic fractures; kidney stones and polyuria; abdominal pain, anorexia, constipation, ileus, nausea, vomiting; depression, psychosis, delirium, and confusion). EKG shows **QT interval shortening**.

Causes. Hypercalcemia in outpatients is due most commonly to hyperparathyroidism. In inpatients, the most common cause is malignancy. Other causes include vitamin A or D intoxication, sarcoidosis, thiazide diuretics, familial hypocalciuric hypercalcemia (look for low urinary calcium, which is rare with hypercalcemia), and immobilization. Hyperproteinemia of any cause may cause hypercalcemia because of an increase in the protein-bound fraction of calcium, but the patient is asymptomatic because the ionized (unbound) fraction is unchanged.

Treatment. First, give IV fluids. Once the patient is well-hydrated, give furosemide to cause calcium diuresis (thiazides are *contraindicated*). Other treatments include phosphorus administration (oral; IV is rarely used because it is dangerous), calcitonin, diphosphonates (e.g., etidronate, often used in Paget's disease), plicamycin, prednisone (especially for malignancy-induced hypercalcemia), and gallium nitrate.

Note: Severe prolonged hypercalcemia may cause nephrocalcinosis and renal failure from calcium salt deposits in kidney.

OTHER ELECTROLYTE DISTURBANCES AND FLUID ADMINISTRATION

Hypomagnesemia is seen most often in alcoholics. Signs and symptoms, which include EKG changes and tetany, are similar to those of hypocalcemia. Hypomagnesemia is notorious because it makes hypokalemia and hypocalcemia difficult to correct. Treat with oral replacement.

Hypermagnesemia almost always is iatrogenic in pregnant patients treated for preeclampsia (but may also be seen in patients with renal failure). In patients treated with magnesium sulfate, check for decreased deep-tendon reflexes, hypotension, and respiratory depression.

Treatment includes stopping magnesium sulfate (first step), supportive treatment (intubate if necessary), IV hydration, furosemide, and dialysis as a last resort.

Important points:

1. Hypophosphatemia is seen primarily in patients with diabetic ketoacidosis and alcoholics. Signs and symptoms are neuromuscular disturbances (encephalopathy, weakness), rhabdomyolysis (especially in alcoholics) and anemia with white blood cell and platelet dysfunction.
2. Hyperphosphatemia is seen almost always in patients with renal failure. Treat with phosphate restriction, dialysis, and phosphate-binding resins (aluminum hydroxide).
3. In trauma patients, the fluid of choice is Ringer's lactate; the second choice is normal saline.
4. In hypovolemic patients, use normal saline or Ringer's lactate, regardless of other electrolyte problems.
5. Maintenance fluid in NPO patients is usually 5% dextrose in one-half normal saline. In pediatric patients, use 5% dextrose in one-fourth or one-third normal saline because of renal differences.
6. Add 20 mEq of potassium chloride to each liter of maintenance fluid in an NPO patient (assuming absence of potassium derangements).

VITAMINS AND MINERALS

VITAMIN	SIGNS AND SYMPTOMS OF DEFICIENCY	TOXICITY
A	Night blindness, scaly rash, xerophthalmia (dry eyes), Bitot's spots (debris on conjunctiva), increased infections	Pseudotumor cerebri, bone thickening, teratogenicity
D	Rickets, osteomalacia, hypocalcemia	Hypercalcemia, nausea and vomiting, renal effects
E	Anemia, peripheral neuropathy, ataxia	Necrotizing enterocolitis(infants)
K	Hemorrhage, prolonged prothrombin time	Hemolysis (kernicterus)
B_1 (thiamine)	Wet beriberi (high-output cardiac failure), dry beriberi (peripheral neuropathy), Wernicke and Korsakoff syndromes	
B_2 (riboflavin)	Cheilosis, angular stomatitis, dermatitis	
B_3 (niacin)	Pellagra (**d**ementia, **d**ermatitis, **d**iarrhea), stomatitis	
B_6 (pyridoxine)	Peripheral neuropathy, cheilosis, stomatitis, convulsions in infants, microcytic anemia, seborrheic dermatitis	Peripheral neuropathy (only B vitamin with toxicity)
B_{12} (cobalamin)	Megaloblastic anemia *plus* neurologic symptoms	
Folic acid	Megaloblastic anemia *without* neurologic symptoms	
C	Scurvy (hemorrhages—skin petechiae, bone, gums; loose teeth; gingivitis), poor wound healing, hyperkeratotic hair follicles, bone pain (from periosteal hemorrhages)	

MINERAL	DEFICIENCY SIGNS AND SYMPTOMS (ALSO TOXICITIES)
Iron	Microcytic anemia, koilonychia (spoon-shaped fingernails); toxicity = hemochromatosis
Iodine	Goiter, cretinism, hypothyroidism; toxicity also may cause myxedema
Fluorine	Dental caries (cavities); toxicity = fluorosis with mottling of teeth and bone exostoses
Zinc	Hypogeusia (decreased taste), rash, slow wound healing
Copper	Menke's disease (X-linked, kinky hair, and mental retardation); toxicity = Wilson's disease
Selenium	Cardiomyopathy and muscle pain; toxicity = loss of hair and nails
Manganese	Toxicity equals "manganese madness" in miners of ore
Chromium	Impaired glucose tolerance

Important points:

1. Deficiency of fat-soluble vitamins (A, D, E, K) often is due to malabsorption (e.g., cystic fibrosis, cirrhosis, celiac disease, sprue, duodenal bypass, bile-duct obstruction, pancreas insufficiency, chronic giardiasis). In such patients, parenteral supplements are required if high-dose oral supplements fail.
2. Alcoholics can have just about any deficiency, but check folate, thiamine, and magnesium.
3. Vitamin B_{12} deficiency most commonly is due to pernicious anemia, in which antiparietal cell antibodies destroy the ability to secrete intrinsic factor. Conditions associated with pernicious anemia include hypothyroidism and vitiligo. Schilling's test is used to diagnose the cause of B_{12} deficiency. Removal of the ileum and the tapeworm *Diphyllobothrium latum* also cause B_{12} deficiency.
4. Isoniazid causes B_6 (pyridoxine) deficiency. Patients taking isoniazid (especially young patients) are often given prophylactic B_6 supplements.
5. Anticonvulsants (especially phenytoin) may cause folate deficiency.
6. Vitamin A is teratogenic and any female patient given one of the vitamin A analogs as treatment for acne (e.g., isotretinoin) *must have a negative pregnancy test before medication* is started and must be put on some form of birth control as well as counseled about the risks of teratogenicity if they become pregnant. Periodic pregnancy tests also should be offered.
7. Rickets causes interesting physical findings: craniotabes (poorly mineralized skull and bones that feel like a ping-pong ball), rachitic rosary (costochondral beading with small, round masses on anterior rib cage), delayed fontanelle closure, bossing of the skull, kyphoscoliosis, bowlegs, and knock-knees. Bone changes first appear at the lower ends of the radius and ulna.
8. *Vitamin K is given to all newborns* as prophylaxis against hemorrhagic disease of the newborn. Vitamin K is needed for the synthesis of factors II, VII, IX, and X as well as proteins C and S. Chronic liver disease (cirrhosis) may cause prolongation of the prothrombin time (PT) because of inability to synthesize clotting factors, even in the presence of adequate vitamin K. Treat with fresh frozen plasma; vitamin K is ineffective.

SHOCK

Definition of shock: a state in which blood flow to and perfusion of peripheral tissues is inadequate to sustain life. Although not included in a rigid definition of shock for board purposes, associated findings include hypotension and oliguria/anuria. Tachycardia is also usually present.

Pragmatically speaking, there are **four clinical types of shock:**

1. Hypovolemic
2. Cardiogenic
3. Septic
4. Neurogenic

Your job is to figure out why the patient is in shock while keeping him or her alive. Give fluids while you're thinking. *If the patient doesn't respond to a fluid bolus and you are given the choice,* use invasive hemodynamic monitoring (Swan-Ganz catheter) to help make diagnostic and therapeutic decisions:

TYPE OF SHOCK	CO	PCWP	SVR	SVO_2
Septic (early)	*High*	Low	Low	*High*
Hypovolemic*	Low	Low	*High*	Low
Cardiogenic	Low	*High*	High	Low
Neurogenic	Low	Low	Low	Low

* Also the parameters for late septic shock.

CO = cardiac output, PCWP = pulmonary capillary wedge pressure, SVR = systemic vascular resistance, SvO_2 = systemic venous oxygen saturation.

Associated findings help to differentiate the etiology of shock:

1. Neurogenic shock: history of severe central nervous system trauma or bleed; flushed skin. Heart rate may be normal.
2. Septic shock: fever, white blood cell count changes, skin flushed and warm to the touch, extremes of age. Use broad-spectrum antibiotics after pan-culturing the patient (get blood, sputum and urine cultures plus others if history dictates).
3. Cardiogenic shock: history of myocardial infarction, chest pain, congestive heart failure, or several risk factors for coronary artery disease. The patient has cold, clammy skin and looks pale. Distended neck veins, pulmonary congestion (on exam and x-ray). Patients usually need diuretics—fluid may make them worse!
4. Hypovolemic: history of fluid loss (blood, diarrhea, vomiting, sweating, diuretics, inability to drink water). The patient has cold, clammy skin and looks pale. Fluid loss may be internal, as in a ruptured abdominal aortic aneurysm or spleen, pancreatitis, or after surgery. Other signs include orthostatic hypotension, tachycardia, sunken eyes, tenting of skin, and sunken fontanelle (in children).
5. Anaphylaxis: look for bee stings, peanuts, shellfish, penicillins, sulfas, and other medications. Treat with epinephrine and fluids, administer O_2, intubate if necessary (do a tracheostomy or cricothyroidotomy if laryngeal edema prevents intubation). Antihistamines help only when the reaction is mild. Use corticosteroids when the reaction is prolonged or severe (not first-line drugs for treatment of anaphylaxis). Monitor all patients for at least 6 hours after initial reaction.
6. Pulmonary embolus: look for risk factors for deep vein thrombosis (Virchow's triad: endothelial damage, stasis, hypercoagulable state), history of recent delivery (amniotic fluid embolus), fractures (fat emboli), deep vein thrombosis (positive Homan's sign with painful, swollen leg), and recent surgery (especially orthopedic or pelvic surgery). Patients have chest pain, tachypnea, shortness of breath, parasternal heave, right-axis shift on EKG, and positive V/Q scan. Heparinize to prevent further clotting and emboli.
7. Pericardial tamponade: history of stab wound in left chest, distended neck veins. Do pericardiocentesis emergently.
8. Toxic shock syndrome: classic patient is woman of reproductive age who leaves tampons in place too long. Look for skin desquamation. Caused by *Staphylococcus aureus* toxin.

Note: ABCs (airway, breathing, circulation) come first. Patients in shock often need heroic measures to survive. Intubate at the drop of a hat, and keep NPO, avoid narcotics if possible (mental status changes are often an important clue to impending doom). Monitor EKG, vital signs, Swan-Ganz parameters, urine output, arterial blood gases (ABGs), hemoglobin, and hematocrit.

Note: Most patients in shock need fluid. The standard bolus is 10–20 ml/kg of normal saline (roughly 1–2 L infused as fast as it will go). After the bolus, reassess the patient to determine whether the bolus helped. Do not be afraid to bolus twice if the first bolus has no effect. Of course, you must watch for fluid overload, which may cause congestive heart failure (especially in cardiogenic shock when the patient is already in failure).

IV medications and their use to support blood pressure should be understood:

1. Dobutamine: $beta_1$ agonist used to increase cardiac output by increasing contractility (ICU equivalent of digoxin).
2. Dopamine: low doses hit dopamine receptors in renal vasculature and keep kidney perfused. Higher doses have $beta_1$ agonist effects to increase contractility. Highest doses have $alpha_1$ agonist effects and cause vasoconstriction.
3. Norepinephrine: used for its $alpha_1$ agonist effects; given in hypotension to increase peripheral resistance so that perfusion to vital organs can be maintained. Also has beta agonist effects.
4. Phenylephrine: used for its $alpha_1$ agonist effects.
5. Epinephrine: used for cardiac arrest and anaphylaxis.
6. Milrinone/amrinone: phosphodiesterase inhibitors used in refractory heart failure (*not* first-line agents) because they have a positive inotropic effect.

Note: Remember Addison's disease as a cause of shock, especially in a postoperative patient who has taken steroids in the past year and received no extra steroids perioperatively. Give patient steroids!

For shock in the setting of trauma, see trauma section (Surgery).

CHAPTER 2

Cardiovascular Medicine

CHEST PAIN AND MYOCARDIAL INFARCT

When a patient presents with chest pain, your job is to make sure that the cause is not life-threatening, which usually means that you try to make sure that the patient has not had a myocardial infarction (MI).

Findings that make MI unlikely:

1. Wrong age: in the absence of known heart disease, strong family history, or risk factors for coronary artery disease (CAD), a patient under the age of 40 is extremely unlikely to have had an MI.
2. Risk factors: a 50-year-old marathon runner who eats well and has a high HDL without other risk factors for coronary heart disease is unlikely to have had an MI.
3. Physical characteristics of pain: if the pain is reproducible by palpation, its source is the chest wall, not an MI. Pain should not be sharp and well-localized or related to certain foods.

Findings that elevate suspicion of MI:

1. EKG: after an MI, you should see flipped or flattened T waves, ST segment elevation, and/or Q waves in a segmental distribution (e.g., leads II, III, and aVF for an inferior infarct).
2. Pain characteristics: usually described as crushing, poorly localized substernal pain that may radiate to the shoulder, arm, or jaw; not reproducible on palpation. Pain usually does not resolve with nitroglycerin (as it often does in angina). Pain usually lasts at least a half-hour.
3. Laboratory values: a patient with a possible MI should have serial determinations of creatine kinase (the MB isoenzyme) or troponin I/P (usually drawn every 8 hours times 3 before MI is ruled out). Lactate dehydrogenase (LDH) elevation and flip ($LDH_1 > LDH_2$) also may be used, especially if the patient presents after 24 hours. Aspartate aminotransferase is also elevated but not used clinically for MI. X-ray may show cardiomegaly and/or pulmonary congestion; echocardiography may show ventricular wall motion abnormalities.
4. Physical exam: pulmonary rales in the absence of other pneumonia-like symptoms, distended neck veins, S3 or S4, new murmurs, hypotension, and/or shock should make you think along the lines of an MI. Patients are often diaphoretic, tachycardic, and pale; nausea and vomiting may be present.

5. History: patients with MI often have a history of angina or previous chest pain, murmurs, arrhythmias, or risk factors for CAD. Some are taking heart medications (digoxin, furosemide, antihypertensives, cholesterol medications).

Treatment for an MI involves hospital admission to the intensive care or cardiac care unit with adherence to several basic principles:

1. Early thrombolysis (usually less than 6 hr after pain onset) if the patient meets strict criteria for use; PTCA (percutaneous transluminal coronary angioplasty) may be used if thrombolysis contraindicated.
2. EKG monitoring: if ventricular tachycardia develops, use lidocaine (*do not use* prophylactically).
3. Give O_2 by nasal cannula (maintain O_2 saturation > 90%).
4. Pain control with morphine (which may help with pulmonary edema if present)
5. Nitroglycerin
6. Beta blocker (on which patient should remain for life if no contraindications are present; proven to reduce incidence of second MI)
7. Aspirin (and possibly low-dose heparin)
8. Soft diet or NPO and stool softeners
9. Begin anticoagulation with IV heparin in patients with cardiac thrombus, large area of dyskinetic ventricle, or severe congestive heart failure (CHF).
10. Patients with CHF (ejection fraction < 40%) should be started on an angiotensin-converting enzyme inhibitor, which has been shown to reduce mortality in this setting.

Note: Remember that the patient can reinfarct on the same hospital visit, even with adequate medical management.

Other causes of chest pain and clues to diagnosis:

1. Gastroesophageal reflux disease and peptic ulcer disease: relation to certain foods (spicy, chocolate), smoking, caffeine, lying down; relieved by antacids or acid-reducing medications; positive for *Helicobacter pylori* (peptic ulcer disease only).
2. Stable angina: pain begins with exertion or stress and remits with rest or calming down; relieved by nitroglycerin. EKG shows ST segment depression with pain, then reverts to normal when pain stops; pain lasts less than 20 minutes
3. Chest wall pain (costochondritis, bruised or broken ribs): reproducible on palpation and well localized.
4. Esophageal problems (achalasia, nutcracker or esophageal spasm): difficult differential. Question will probably mention a negative work-up for MI; look for barium swallow (achalasia) or esophageal manometry abnormalities. Treat achalasia with pneumatic dilatation; treat nutcracker/esophageal spasm with calcium channel blockers, then myotomy if calcium channel blockers are ineffective
5. Pericarditis: look for viral upper respiratory infection prodrome. EKG shows diffuse ST segment elevation. Other signs include elevated erythrocyte sedimentation rate and low-grade fever. The most common cause is viral (coxsackie virus); others include tuberculosis, uremia, malignancy, and lupus or other autoimmune diseases.
6. Pneumonia: chest pain due to pleuritis. Patients also have cough, fever, and/or sputum production, with possible sick contacts.

Unstable angina usually presents with normal cardiac enzymes and EKG changes (ST depression) with prolonged chest pain that does not respond to nitroglycerin initially (like MI). Pain often begins at rest. Treat like an MI, but use IV heparin to anticoagulate and consider PTCA emergently if pain does not resolve. Almost all patients have a history of stable angina and CAD risk factors. In strict terms, unstable angina is defined as a change from previous stable angina; thus, if a patient who used to get angina once a week now gets it once a day, he or she has unstable angina.

Variant (Prinzmetal's) angina is rare and associated with anginal pain at rest with **ST elevation** (cardiac enzymes, however, are normal). The cause is coronary artery spasm. Variant angina responds to nitroglycerin; long-term treatment usually is with calcium channel blockers.

Note: 25% of MIs are silent, meaning that they present without chest pain (especially in diabetics, who have neuropathy). Such patients present with CHF, shock, or confusion/delirium (especially elderly patients).

VALVULAR HEART DISEASE

Murmur Characteristics

VALVE PROBLEM	PHYSICAL CHARACTERISTICS (BEST HEARD HERE)	OTHER FINDINGS
Mitral stenosis	Late-diastolic blowing murmur (at apex)	Opening snap, loud S1, atrial fibrillation, LAE, PH
Mitral regurgitation	Holosystolic murmur (radiates to axilla)	Soft S1, LAE, PH, LVH
Aortic stenosis	Harsh systolic ejection murmurs (aortic area, radiates to carotids)	Slow pulse upstroke, S3/S4, ejection click, LVH, cardiomegaly, syncope with angina and CHF
Aortic regurgitation	Early-diastolic decrescendo murmur (apex)	Widened pulse pressure, LVH, LV dilatation, S3
Mitral prolapse	Mid-systolic click/late-systolic murmur	Panic disorder

LAE = left atrial enlargement, PH = pulmonary hypertension, LVH = left ventricular hypertrophy.

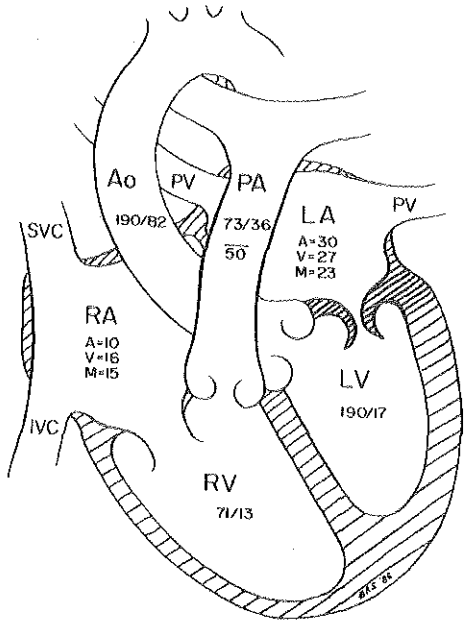
Note: Understanding the pathophysiologic changes associated with longstanding valvular disease has a high yield (e.g., do you understand why mitral stenosis or regurgitation can cause right heart failure?). (See figures, top of next page.)

Use **endocarditis prophylaxis** for people with known valvular heart disease (with mitral valve prolapse, use prophylaxis only if a murmur is heard on physical exam or if the patient has history of endocarditis) or prosthetic valves. For oral surgery, use amoxicillin before and after the procedure (use erythromycin in penicillin-allergic patients). For gastrointestinal or genitourinary procedures, use ampicillin plus gentamicin before and amoxicillin after procedure (substitute vancomycin for penicillin-allergic patients).

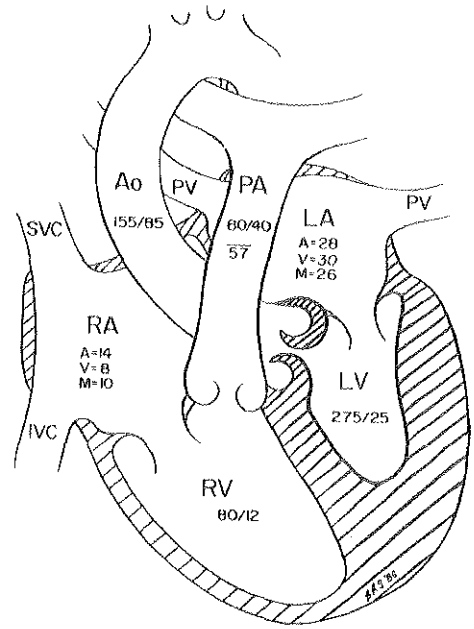
DEEP VEIN THROMBOSIS, PULMONARY EMBOLISM, ANTICOAGULATION

Important points:

1. Remember Virchow's triad (endothelial damage, stasis, and hypercoagulable state) as a clue to the the diagnosis of deep vein thrombosis (DVT).
2. Common causes or situations in which DVT occurs: surgery (especially orthopedic, pelvic, or abdominal), neoplasms, trauma, immobilization, pregnancy, oral contraceptives, disseminated intravascular coagulation, lupus anticoagulant, and deficiency of antithrombin III, protein C, or protein S.



Mitral stenosis: The mitral valve oriface is narrowed, resulting in obstruction to flow out of the atrium and an increase in pressure in the left atrium and pulmonary veins. Pulmonary hypertension develops secondarily. A = A wave, V = V wave, M = mean pressure. (From James EC, Corry RJ, Perry JF: Principles of Basic Surgical Practice. Philadelphia, Hanley & Belfus, 1987, with permission.)



Aortic stenosis: The narrowed aortic valve results in high pressures in the left ventricle, which are transmitted to the left atrium and ultimately resulting in pulmonary hypertension. The left ventricle is hypertrophied due to the chronic pressure overload. (From James EC, Corry RJ, Perry JF: Principles of Basic Surgical Practice. Philadelphia, Hanley & Belfus, 1987, with permission.)

3. DVTs commonly present with unilateral leg swelling, pain or tenderness, and/or Homan's sign (present in 30%).
4. The best way to diagnose DVT is doppler ultrasound or impedance plethysmography. The gold standard is venography, but it is invasive and usually reserved for settings in which the diagnosis is not clear.
5. Superficial thrombophlebitis (erythema, tenderness, edema, and palpable clot in a superficial vein) is *not* a risk factor for pulmonary embolism (PE) and generally is considered a benign condition. *Treat with NSAIDs or aspirin.*
6. In patients with DVT, systemic anticoagulation is necessary. Use IV heparin, followed by gradual crossover to oral warfarin. Patients are maintained on warfarin for at least 3 months, possibly permanently if they experience more than one episode.
7. The best DVT prophylaxis for surgery is pneumatic compression boots and early ambulation; use low-dose heparin if ambulation is not possible. Warfarin is an alternative, especially for orthopedic hip or knee surgery.
8. Pulmonary embolus follows DVT, delivery (amniotic fluid embolus), or fractures (fat emboli). Symptoms include tachypnea, dyspnea, chest pain, hemoptysis (if lung infarct), and hypotension, syncope, and death if severe. Rarely, on a chest x-ray you may see a wedge-shaped defect due to a pulmonary infarct.
9. Left-sided heart clots (from atrial fibrillation, ventricular wall aneurysm, severe congestive heart failure, or endocarditis) that embolize cause arterial-sided infarcts (stroke and renal, GI, and extremity infarcts), *not* PEs. Right-sided clots that embolize (DVTs) cause PEs, *not* arterial emboli. *The exception is a patent foramen ovale, in which the clot may* cross over to the left side of the circulation and cause an arterial infarct.

10. Use V/Q scan to screen for PE. If positive, PE is diagnosed and treated. If indeterminate, use pulmonary angiogram (the gold standard, but invasive). If low probability or negative, it is highly unlikely that the patient has a significant PE.
11. Treat PE with IV heparin to prevent further clots and emboli; then gradually switch to oral warfarin, on which the patient will remain for at least 3 months. If clots recur on anticoagulation or the patient has contraindications to anticoagulation, use inferior vena cava filter (Greenfield filter).
12. Heparin causes thrombocytopenia and arterial thrombosis in some unlucky patients. Discontinue heparin immediately!
13. Heparin is followed by determination of partial thromboplastin time (PTT) (internal pathway), and warfarin is followed by prothrombin time (PT) (external pathway), whereas aspirin affects the bleeding time. In emergencies, reverse heparin with protamine, reverse warfarin with fresh frozen plasma and/or vitamin K, reverse aspirin with platelet transfusion.

Other Factors Affecting Coagulation Tests

DISEASE	PROLONGED TEST	OTHER AIDS TO DIAGNOSIS
Hemophilia A	PTT	Low levels of factor 8; normal PT and bleeding time; X-linked
Hemophilia B	PTT	Low levels of factor 9; normal PT and bleeding time; X-linked
vWF deficiency	Bleeding time and PTT	Normal levels of factor 8; normal PT; autosomal dominant
DIC	PT, PTT, bleeding time	Positive D-dimer or FDPs; postpartum, infection, malignancy; schistocytes, fragmented cells on peripheral smear
Liver disease	PT	PTT normal or prolonged; all factors but factor 8 are low; stigmata of liver disease, no correction with vitamin K
Vitamin K deficiency	PT, PTT (slight)	Normal bleeding time; low levels of factors 2, 7, 9, and 10, proteins C and S; look for neonate (who did not receive prophylactic vitamin K), malabsorption, alcoholism, or prolonged antibiotics (which kill vitamin K-producing bowel flora)

PTT = partial thromboplastin time, PT = prothrombin time, VWF = von Willebrand's factor, DIC = disseminated intravascular coagulation, FDPs = fibrin degradation products.

Note: Uremia causes a qualitative platelet defect. Vitamin C deficiency and chronic corticosteroid therapy may cause a bleeding tendency with normal coagulation tests.

CONGESTIVE HEART FAILURE AND ARRHYTHMIAS

Symptoms and signs of CHF

- Fatigue
- Dyspnea
- Orthopnea (seen in left ventricular failure; patient sleeps on more than one pillow)
- Paroxysmal nocturnal dyspnea (left ventricular failure)
- Peripheral edema (right ventricular failure)
- Jugular venous distention (right ventricular failure)
- Peripheral edema (right ventricular failure)
- S3/S4
- Pulmonary congestion (rales; seen in left ventricular failure)

- Hepatomegaly/ascites (right ventricular failure)
- Chest x-ray abnormalities (cardiomegaly [seen in left or right ventricular failure], Kerley B lines, pulmonary vascular congestion, and bilateral pleural effusions are seen in left ventricular failure)

Treatment: sodium restriction, angiotensin-converting enzyme inhibitor (first-line agents; proved to reduce mortality in CHF), beta blockers (also reduce mortality), diuretics, digoxin (not in hypertrophic obstructive cardiomyopathy or atrioventricular conduction blocks; usually reserved for moderate-to-severe CHF with low ejection fraction), vasodilators (arterial and venous), and IV sympathomimetics (dobutamine, dopamine, amrinone) for inpatients with severe CHF.

Important points:

1. Many factors can precipitate exacerbation of CHF in a previously stable cardiac patient. Noncompliance, myocardial infarction, hypertension, arrhythmias, infections/fever, pulmonary embolism, anemia, thyrotoxicosis, and myocarditis are common causes.
2. Cor pulmonale is right ventricular enlargement, hypertrophy, or failure due to primary lung disease. Common causes are chronic obstructive pulmonary disease and pulmonary embolism. In a young woman (20–40) with no other medical history or risk factors, think of primary pulmonary hypertension, and treat with calcium channel blockers while awaiting heart-lung transplant. Sleep apnea also may cause cor pulmonale (an obese snorer who is sleepy during the day).
3. Patients with cor pulmonale have tachypnea, cyanosis, clubbing, parasternal heave, loud P2, and right-sided S4 in addition to signs and symptoms of pulmonary disease.
4. Restrictive cardiomyopathy usually results from amyloidosis, sarcoidosis, hemochromatosis or myocardial fibroelastosis (ventricular biopsy abnormal in all of these conditions). On the other hand, constrictive pericarditis can be simply treated by removing the pericardium (pericardial knock, calcification of pericardium, normal ventricular biopsy).
5. Dilated cardiomyopathy commonly is due to alcohol, myocarditis, or doxorubicin.

EKG Abnormalities and Their Treatments*

ARRHYTHMIA	TREATMENT AND WARNINGS
Atrial fibrillation	If patient is symptomatic, first slow ventricular rate (digoxin, beta blocker, calcium channel blocker): ▪ If acute (onset < 24 hr), cardiovert with quinidine, procainamide, or direct current cardioversion. ▪ If chronic, first anticoagulate, then cardiovert (if patient returns to atrial fibrillation, continue digoxin and warfarin)
Atrial flutter	Treat like atrial fibrillation.
Heart block:	
First-degree	No treatment, but avoid beta blockers and calcium channel blockers (both slow conduction)
Second-degree	Pacemaker or atropine only for symptomatic patient with Mobitz type I; use pacemaker for all patients with Mobitz type II
Third degree	Pacemaker
WPW syndrome	Use procainamide or quinidine; avoid digoxin and verapamil.
Ventricular tachycardia	Lidocaine
Ventricular fibrillation	Immediate defibrillation
Premature ventricular contractions	Usually not treated; if severe and symptomatic, consider lidocaine.
Sinus bradycardia	Usually not treated; use atropine in severe and symptomatic cases (after myocardial infarction); avoid beta blockers, calcium channel blockers, and other conduction slowers.
Sinus tachycardia	Usually none; correct underlying cause; use beta blocker if patient is symptomatic.

* Always check for electrolyte disturbances as the cause.

WPW = Wolff-Parkinson-White syndrome.

Important points:

1. Sinus tachycardia and atrial fibrillation are common presentations for hyperthyroidism; check level of thyroid-stimulating hormone.
2. Wolff-Parkinson-White syndrome commonly presents in childhood. The patient becomes dizzy or dyspneic or passes out after playing, then recovers and has no other symptoms (transient arrhythmias via accessory pathway). Look for the infamous delta wave.

PEDIATRIC CARDIOLOGY

Congenital Heart Defects

DEFECT	SYMPTOMS, TREATMENT, AND OTHER INFORMATION
Patent ductus arteriosus	Constant, machine-like murmur in upper left sternal border; dyspnea and possible CHF; close with indomethacin (or surgery if indomethacin fails); keep open with prostaglandin E_1; associated with congenital rubella and high altitudes.
Ventricular septal defect	Holosystolic murmur next to sternum; most cases resolve on their own; *most common congenital heart defect.*
Atrial septal defect	Asymptomatic until adulthood; fixed, split S2 and palpitations; most defects do not need correction (unless very large)
Tetralogy of Fallot	(1) Ventricular septal defect, (2) right ventricular hypertrophy, (3) pulmonary stenosis, and (4) overriding aorta; *most common cyanotic congenital heart defect*; look for "tet" spells (squatting after exertion).
Coarctation of aorta	Upper extremity hypertension only; radiofemoral delay; systolic murmur heard over mid-upper back; rib notching on x-ray; associated with Turner's syndrome.

Note: Endocarditis prophylaxis is required for all of these cardiac defects except asymptomatic atrial septal defect.

Important points:

1. A heart rate over 100 beats/min may be normal in children.
2. In the presence of a ventricular septal defect, think about the possibility of fetal alcohol syndrome, TORCH syndrome, or Down syndrome.
3. Hypertrophic obstructive cardiomyopathy classically presents in a young male who passes out on exertion (watch for collapse or sudden death in an athlete) and often is associated with a family history of sudden death. This disorder is considered a diastolic dysfunction and thus is treated with beta blockers to give the heart more time to fill. Positive inotropic agents (e.g., digoxin), diuretics, and vasodilators are *contraindicated*, because they make the condition worse.
4. Oxygen content in the fetal circulation is highest in the umbilical vein and lowest in the umbilical arteries; oxygen content is higher in blood going to upper extremities than in blood going to lower extremities.
5. Understand the changes in the circulation from intra- to extrauterine life. First breaths inflate the lungs and cause decreased pulmonary vascular resistance, which increases blood flow to the pulmonary arteries. This and the clamping of the cord increase left-sided heart pressures, which functionally close the foramen ovale. Increased oxygen concentration shuts off prostaglandin production in the ductus arteriosus, causing gradual closure.

CHAPTER 3

Pulmonology

Chronic obstructive pulmonary disease (COPD) means that the FEV_1/FEV ratio is less than normal (0.75–0.80, usually given value), whereas in **restrictive lung disease**, the FEV_1/FEV ratio is often normal. FEV_1 may be equal in both conditions; it is the FEV_1/FEV ratio that is different.

Emphysema almost always is due to smoking (even if second-hand). In a young person with minimal smoke exposure (< 5 years of smoking), think of $alpha_1$ antitrypsin deficiency.

Asthma: look for wheezing in children. Treat with $beta_2$ agonists in the emergency department. Use steroids if asthma is severe or does not respond to $beta_2$ agonists. Cromolyn is for prophylaxis, not acute attacks. The new leukotriene inhibitors (zafirlukast, zileuton) are used regularly, not usually for acute attacks. Phosphodiesterase inhibitors (theophylline, aminophylline) are older, second-line agents.

Note: Do *not* put patients with asthma or COPD on beta blockers, which block the $beta_2$ receptors needed to open the airways.

Wheezing in children under age 2 is often due to **respiratory syncytial virus**, especially in the winter. Look for coexisting fever.

Important points:

1. Beware the asthmatic who no longer hyperventilates or whose CO_2 is normal or rising (the patient should hyperventilate, which causes low CO_2). Do *not* think that patients who seem calm or sleepy are okay. They are probably crashing and need an immediate arterial blood gas analysis and possible intubation. Fatigue alone is enough reason to intubate an asthmatic.
2. A patient with COPD may normally live at a higher CO_2 and lower O_2; treat the patient, not the lab value. If the patient is asymptomatic and talking to you, the lab value should not make you panic.
3. As a rough rule of thumb, you should prepare to intubate any patient whose CO_2 is > 50 mmHg or whose O_2 is < 50 mmHg, especially if the pH in either case is < 7.30 while the patient is breathing room air. Usually, unless the patient is crashing rapidly, a trial of O_2 by nasal cannula is given first. If this approach does not work or if the patient becomes too tired (use of accessory muscles is a good clue to the work of breathing), intubate.

With a **solitary pulmonary nodule**, the first step is to check for old films. If the lesion has not changed in more than 1 year, it is likely to be benign. Certain clues point to the etiology:

- Immigrant: think tuberculosis (do a skin test).
- Southwest U.S.: think *Coccidioides immitis*.
- Cave explorer, exposure to bird droppings, or Ohio/Mississippi River valleys: think histoplasmosis.
- Smoker over the age of 50: think lung cancer (bronchoscopy and biopsy).
- Person under 40 with none of the above: think hamartoma.

A baseline chest x-ray is standard preoperative evaluation for patients over 60 and patients with known pulmonary or cardiovascular disease, but when to order **pulmonary function tests** is not as clear. Overall, the best indicator of possible postoperative pulmonary complications is preoperative pulmonary function. Overall, the best way to reduce pulmonary postoperative complications is to *stop smoking* preoperatively. Aggressive pulmonary toileting, incentive spirometry, minimal narcotics, and early ambulation help to prevent or minimize postoperative pulmonary complication.

Note: The most common cause of a postoperative fever in the first 24 hours is atelectasis.

Adult respiratory distress syndrome (ARDS): acute lung injury that results in noncardiogenic pulmonary edema, respiratory distress, and hypoxemia. Common causes are sepsis, major trauma, pancreatitis, shock, near drowning, and drug overdose. Look for ARDS to develop within 24–48 hr of the initial insult. Classic symptoms include mottled/cyanotic skin, intercostal retractions, rales/rhonchi, and no improvement of hypoxia with O_2 administration. X-ray shows pulmonary edema with normal cardiac silhouette (no congestive heart failure). Treat with intubation, mechanical ventilation with high percentage of O_2 and positive end-expiratory pressure (PEEP).

The diagnosis of pneumonia usually is based on clinical findings plus elevated white blood cell count and chest x-ray abnormalities. On physical exam, look to differentiate between typical (*Staphylococcus pneumoniae*) and atypical (other bugs) pneumonia, although the distinction is not always clear-cut:

	TYPICAL PNEUMONIA	ATYPICAL PNEUMONIA
Prodrome	Short (< 2 days)	Long (> 3 days)—headache, malaise, other aches
Fever	High (> 102° F)	Low (< 102° F)
Age	> 40 yr	< 40 yr
Chest x-ray	One distinct lobe involved	Diffuse or multilobe involvement
Infective agent	*S. pneumoniae*	Many (e.g., *Haemophilus influenzae*, *Mycoplasma* sp., *Chlamydia* sp.)
Medications*	Penicillin, third-generation cephalosporin	Erythromycin

* Avoid the temptation to pull out the "big gun" antibiotics (very wide spectrum) unless the patient is crashing or unstable.

Certain clinical clues should make you think of certain bugs:

- College student: think *Mycoplasma* sp. (look for cold agglutinins) or *Chlamydia* sp.
- Alcoholic: think *Klebsiella* sp. (currant jelly sputum), *Staphylococcus aureus*, other enteric bugs (aspiration).
- Cystic fibrosis: think *Pseudomonas* sp. or *S. aureus*.
- Immigrant: think tuberculosis.
- COPD: think *H. influenzae*, *Moraxella* sp.

- Patient with known tuberculosis and pulmonary cavitation: think *Aspergillus* sp.
- Patient with silicosis (metal, granite, pottery workers): think tuberculosis.
- Exposure to air conditioner/aerosolized water: think *Legionella* sp.
- HIV/AIDS: think *Pneumocystis carinii* or cytomegalovirus (if shown a picture of koilocytosis).
- Exposure to bird droppings: think *Chlamydia psittaci* or *Histoplasma* sp.
- Child < 1 yr: think respiratory syncytial virus.
- Child 2–5 yr: think parainfluenza (croup) or epiglottitis.

Recurrent pneumonia in a child, if it always occurs in the right middle and/or right lower lobe, is most likely due to **foreign body aspiration** (a foreign body is most likely to go down the right bronchus). It should be a consideration especially if the patient has no other signs of immunodeficiency (e.g., other types of infections, cystic fibrosis symptoms) before or during the episodes.

Sinusitis: usually *S. pneumoniae* or *Haemophilus* sp. Look for purulent (green/yellow) nasal discharge with tenderness over the involved sinus. Associated symptoms are headache and/or toothache (maxillary sinusitis). You cannot transilluminate the sinuses, and an x-ray or CT scan shows opacification of the frontal or maxillary sinuses (order a sinus x-ray to confirm the diagnosis if it has not already been done). Treatment is with penicillin/amoxicillin or erythromycin for 10–14 days.

Note: The most common cause of epistaxis in children is nose-picking (do *not* assume low or defective platelets without evidence.

Respiratory distress syndrome, due to atelectasis from deficiency of surfactant, almost always occurs in premature infants and infants of diabetic mothers. Look for rapid, labored respirations, substernal retractions, cyanosis, grunting, and/or nasal flaring. Arterial blood gases show hypoxemia and hypercarbia, whereas x-ray shows diffuse atelectasis. Treat with O_2, give surfactant, and intubate if needed (often). Complications include intraventricular hemorrhage and pneumothorax/bronchopulmonary dysplasia (acute or chronic mechanical ventilation complications).

Diaphragmatic hernia commonly causes respiratory problems because bowel herniated into the chest pushes on developing lung and causes lung hypoplasia on the affected side. Look for scaphoid abdomen and bowel sounds in the chest (herniated bowel also may be seen on the chest x-ray; 90% are left-sided).

Note: Look for meconium aspiration if the infant is covered with meconium when delivered. Suction the nose first (bulb suction); then suction the oropharynx under direct visualization. Intubate if necessary.

The most common type (85%) of **tracheoesophageal fistula** is an esophagus with a blind pouch proximally and a fistula between a bronchus or the carina and the distal esophagus. Look for a neonate with excessive oral secretions, coughing and cyanosis with attempted feedings, abdominal distention, and aspiration pneumonia. Diagnosis is made by inability to pass a nasogastric tube; contrast x-ray shows the proximal esophagus only. Treatment is early surgical correction.

Cystic fibrosis: autosomal recessive inheritance; the most common lethal genetic disease in white children. Always suspect it in children with rectal prolapse, meconium ileus, esophageal varices, a "salty" taste, recurrent pulmonary infections, and/or failure to thrive. Diagnosis is made by an abnormal increase in the electrolytes of the patient's sweat (sodium and chloride).

Patients also have pancreatic insufficiency (give pancreatic enzyme replacements and fat-soluble vitamin supplements) and infertility (98% of affected males and many females) and may develop cor pulmonale (right heart failure). Look for *S. aureus* and *Pseudomonas* sp. as the causes of the many respiratory infections. Treat with chest physical therapy, annual influenza vaccine, fat-soluble vitamin supplements, pancreatic enzyme replacement, and aggressive treatment of infections with antibiotics.

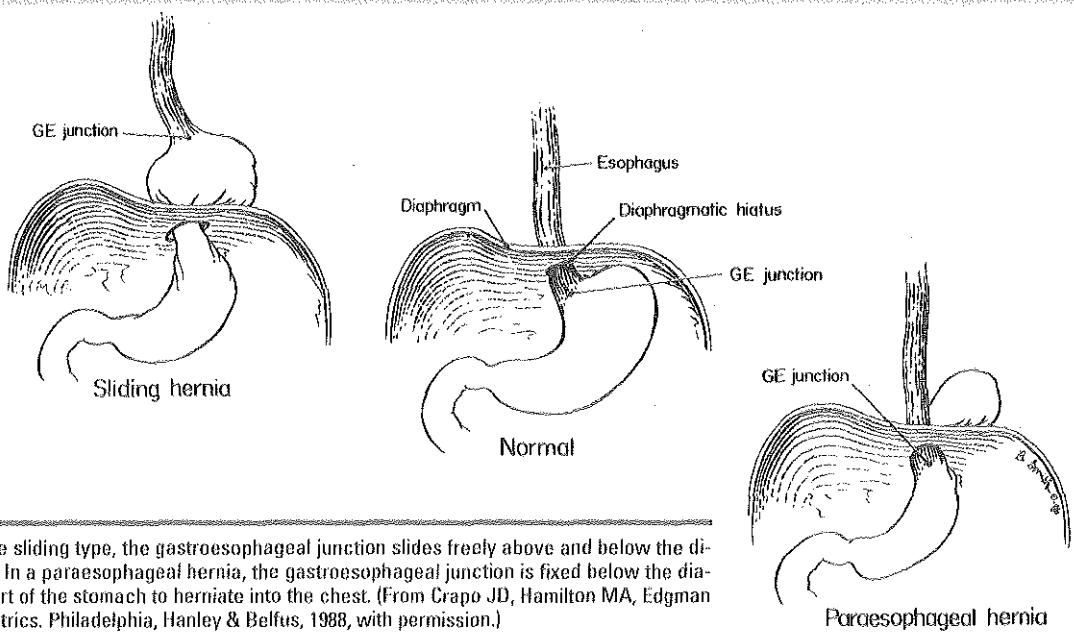
Pleural effusion: if you do not know the cause, always consider thoracentesis and examine the fluid with Gram stain, culture and sensitivity (including tuberculosis culture), cell count with differential, glucose (low in infection), and protein (high in infection).

CHAPTER 4

Gastroenterology

Gastroesophageal reflux disease (GERD) is due to inappropriate, intermittent lower esophageal sphincter (LES) relaxation. The incidence is greatly increased in patients with a hiatal hernia. GERD presents as "heartburn," often related to eating and lying supine. Initial treatment is to elevate the head of the bed and to avoid coffee, alcohol, tobacco, spicy and fatty foods, chocolate, and medications with anticholinergic properties. If this approach fails, antacids, H2-blockers, and proton-pump inhibitors may be tried. Surgery is reserved for severe or resistant cases (Nissen fundoplication). Sequelae of GERD include esophagitis, esophageal stricture (may mimic esophageal cancer), esophageal ulcer, hemorrhage, and Barrett's metaplasia/esophageal adenocarcinoma.

Hiatal hernia, as the term is commonly used, implies a sliding hiatal hernia; that is, the entire gastroesophageal junction moves above the diaphragm, pulling the stomach with it—a common and benign finding. A paraesophageal hiatal hernia means that the gastroesophageal junction stays below the diaphragm, but the stomach herniates through the diaphragm into the thorax. This is an uncommon, serious type of hernia that may become strangulated and should be repaired surgically.



Hiatal hernias. In the sliding type, the gastroesophageal junction slides freely above and below the diaphragmatic hiatus. In a paraesophageal hernia, the gastroesophageal junction is fixed below the diaphragm, allowing part of the stomach to herniate into the chest. (From Crapo JD, Hamilton MA, Edgman S: Medicine & Pediatrics. Philadelphia, Hanley & Belfus, 1988, with permission.)

Peptic ulcer disease presents with chronic, *intermittent, epigastric pain*—*burning*, gnawing, or aching—that is localized and often relieved by antacids or milk. Look for epigastric tenderness. Patients may have occult blood in stool and nausea or vomiting. Peptic ulcer disease is more common in males. The two types are gastric and duodenal.

	DUODENAL	GASTRIC
% of cases	75	25
Acid secretion	*Normal to high*	*Normal to low*
Main etiology	*Helicobacter pylori*	Nonsteroidal anti-inflammatory drugs
Peak age	Forties	Fifties
Blood type	O	A
Eating food	Pain improves, then worsens 2–3 hr later	Pain not relieved or made worse

Important points:

1. Endoscopy is becoming the first-line diagnostic study (upper GI barium study is classically done first) and is more sensitive (but more expensive) than x-ray.
2. Always biopsy any gastric ulcer to exclude malignancy (duodenal ulcers do not have to be biopsied initially).
3. The major complication is perforation. Look for peritoneal signs, history of peptic ulcer disease, or free-air on abdominal x-ray. Treat with antibiotics and laparotomy with repair of perforation:
   - If ulcers are severe, atypical, or nonhealing, think about Zollinger-Ellison syndrome (get gastrin level) or stomach cancer.
   - Diet changes *are not* thought to help heal ulcers (but reduced alcohol or tobacco use may help).
   - Start treatment with antacids, H2 blockers or proton-pump inhibitors, as well as antibiotics to eliminate *H. pylori*. Triple therapy (ampicillin or amoxicillin, metronidazole, and bismuth) is the gold standard, but many regimens are in use.
4. Surgical options should be considered after failure of medical treatment or in patients with complications (perforation, bleeding). Common procedures include antrectomy, vagotomy, and Billroth I and II. After surgery (especially Billroth procedures) watch for dumping syndrome (weakness, dizziness, sweating, nausea or vomiting after eating). Patients also may develop hypoglycemia 2–3 hr after the meal, which causes the same symptoms to recur; afferent loop syndrome (bilious vomiting after a meal relieves abdominal pain), bacterial overgrowth, and vitamin deficiencies (B_{12} and/or iron, causing anemia).
5. Achlorhydria, the absence of hydrogen chloride, is associated with pernicious anemia (antiparietal cell antibodies destroy parietal cells and thus cause achlorhydria and B_{12} deficiency).

Upper versus lower gastrointestinal bleeding (see table, top of next page).

Important points:

1. The first step is to make sure that the patient is stable (ABCs, IV fluids and blood if needed); then get a diagnosis.
2. Endoscopy is usually the first test performed (upper or lower, depending on symptoms). Classically, barium x-ray studies were performed first, but endoscopy is more sensitive.

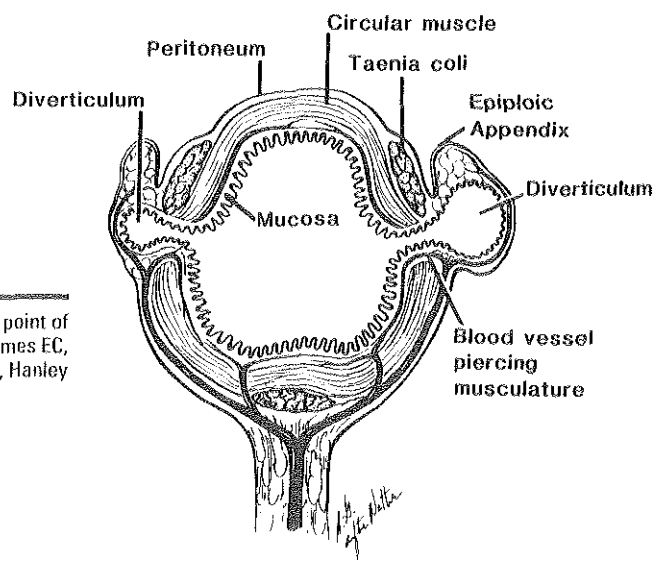
Upper vs. Lower Gastrointestinal Bleeding

	UPPER	LOWER
Location	Proximal to ligament of Treitz	Distal to ligament of Treitz
Common causes	Gastritis, peptic ulcer disease, varices	Vascular ectasia, diverticulosis, colon cancer, colitis/inflammatory bowel disease, hemorrhoids
Stool	Tarry, black stool (melena)	Red blood seen in stool (hematochezia)
Nasogastric tube aspirate	Positive for blood	Negative for blood

- Endoscopically treatable lesions include polyps, vascular ectasias, and varices.
- Radionuclide scans can detect slow or intermittent bleeding if source cannot be found with endoscopy. Angiography can detect more rapid bleeding, and embolization of bleeding vessels can be done with this procedure.

3. Surgery is reserved for severe or resistant bleeding and usually involves resection of affected bowel (usually colon).

Diverticulosis is extremely common, and the incidence increases with age. It is thought to be caused partially by a low-fiber, high-fat diet. Complications are lower GI bleeding (common cause) and diverticulitis (inflammation of a diverticula). Look for lower left quadrant pain and tenderness, fever, diarrhea or constipation, and a white count.



Diverticulosis. Herniation of mucosa between two taeniae. Note the point of weakness where main blood vessel passes into the mucosa. (From James EC, Corry RJ, Perry JF: Principles of Basic Surgical Practice. Philadelphia, Hanley & Belfus, 1987, with permission.)

Diarrhea has multiple etiologies and is best broken down into categories:

1. Systemic causes: any illness can cause diarrhea as a systemic symptom (e.g., hyperthyroidism, infection).
2. Osmotic diarrhea: nonabsorbable solutes remain in the bowel, where they retain water (e.g., lactose or other sugar intolerances, Olestra in potato chips). When the patient stops ingesting the substance (e.g., no more milk or a trial of NPO), the diarrhea stops—an easy diagnosis.
3. Secretory diarrhea: bowel secretes fluid. Causes include bacterial toxins (cholera, some strains of *Escherichia coli*), vasoactive intestinal peptide-secreting tumor (pancreatic islet cell tumor), or bile acids (after ileal resection). Diarrhea continues with NPO status.

4. Malabsorption: causes include celiac sprue (look for dermatitis herpetiformis, and stop gluten in the diet), Crohn's disease, and gastroenteritis. Diarrhea stops with NPO status.
5. Infectious causes: look for fever, white blood cells in stool (not with toxigenic bacteria; only with invasive bacteria such as *Shigella*, *Salmonella*, *Yersinia*, and *Campylobacter* spp.) and travel (Montezuma's revenge caused by *E. coli*). Hikers and stream drinkers may get *Giardia* sp., which presents with steatorrhea (fatty, greasy, malodorous stools that float) due to small bowel involvement and unique protozoal cysts in the stool. Treat with metronidazole.
6. Exudative diarrhea: inflammation in bowel mucosa causes seepage of fluid. Due to inflammatory bowel disease (Crohn's disease or ulcerative colitis) or cancer.
7. Altered intestinal transit: after bowel resections or medications that interfere with bowel function.

Important points:

1. With all diarrhea, watch for dehydration and electrolyte disturbances (e.g., metabolic acidosis, hypokalemia), a common and preventable cause of death in underdeveloped areas.
2. Do a rectal exam, look for occult blood in stool, and examine stool for ova or parasites, fat content (steatorrhea), and white blood cells.
3. If the patient has a history of antibiotic use, think of *Clostridium difficile* and test the stool for *C. difficile* toxin. If the test is positive, treat with metronidazole (if it fails or is not a choice, use vancomycin).
4. Do not forget about diabetic diarrhea, factitious diarrhea (surreptitious laxative abuse, usually by medical personnel), hyperthyroidism, and colorectal cancer as causes of diarrhea.
5. Irritable bowel syndrome (IBS) is a common cause of GI complaints. Patients are anxious or neurotic and have a history of diarrhea aggravated by stress; bloating; abdominal pain relieved by defecation; and/or mucus in the stool. Look for psychosocial stressors in the history and normal physical findings and diagnostic tests. This diagnosis of exclusion requires basic lab tests, rectal and stool examination, and sigmoidoscopy, but because it is *very common*, it is the most likely diagnosis in the absence of positive findings, especially in young adults. IBS is three times more common in females than males.
6. After bacterial diarrhea (especially *E. coli* or *Shigella* sp.) in children, watch for hemolytic uremic syndrome: thrombocytopenia, hemolytic anemia (schistocytes, helmet cells, fragmented red blood cells), and acute renal failure. Treat supportively. Patients may need dialysis and/or transfusions.

Inflammatory bowel disease

Comparison of Crohn's Disease and Ulcerative Colitis

	CROHN'S DISEASE	ULCERATIVE COLITIS
Site of origin	Distal ileum, proximal colon	Rectum
Thickness of pathology	Transmural	Mucosa and submucosa only
Progression	Irregular (skip-lesions)	Proximal, continuous from rectum; no skipped areas
Location	From mouth to anus	Involves only colon; rarely extends to ileum
Change in bowel habits	Obstruction, abdominal pain	Bloody diarrhea
Classic lesions	Fistulas/abscesses, cobblestoning, string sign on barium x-ray	Pseudopolyps, lead-pipe colon on barium x-ray, toxic megacolon
Colon cancer risk	Slightly increased	Markedly increased
Surgery cures bowel disease?	No (may worsen)	Yes (proctocolectomy with ileoanal anastomosis)

Both Crohn's disease and ulcerative colitis may involve uveitis, arthritis, ankylosing spondylitis, erythema nodosum/multiforme, primary sclerosing cholangitis, failure to thrive or grow in children, toxic megacolon (more common in ulcerative colitis; look for markedly distended colon on abdominal x-ray), anemia of chronic disease, and fever. Both are treated with 5-ASA with or without a sulfa drug (e.g., sulfasalazine); steroids are used for severe flare-ups.

Toxic megacolon is classically seen with inflammatory bowel disease and infectious colitis (especially *C. difficile*). It may be precipitated by the use of antidiarrhea medications. Symptoms include high fever, leukocytosis, abdominal pain, rebound tenderness, and a very dilated segment of colon on abdominal x-ray. Toxic megacolon is an emergency. Start treatment by discontinuing all antidiarrhea medications; then place the patient on NPO status, insert a nasogastric tube, and administer IV fluids, antibiotics to cover bowel flora (e.g., ampicillin or cefazolin), and steroids if the cause is inflammatory bowel disease. Go to surgery if perforation occurs (free air on abdominal x-ray).

Liver disease, acute: elevated liver function tests, jaundice, nausea/vomiting, right upper quadrant pain or tenderness, and/or hepatomegaly.

Important points:

1. Alcoholic hepatitis: elevated liver function tests; aspartate aminotransferase levels are more than twice as high as alanine aminotransferase levels in a patient who was just drinking.
2. Hepatitis A: look for outbreaks from food-borne source; no long-term sequelae. Serology: positive IgM antibody to hepatitis A virus during jaundice or shortly thereafter.
3. Hepatitis B: prevention is best treatment (vaccination); acquired through needles, sex, or perinatally. Transfused blood is now screened for hepatitis B, but a history of transfusion years ago is still a risk factor. Use hepatitis B immunoglobulin for exposed neonates and health care workers. Serology: HBsAg-positive with unresolved infection (acute or chronic). HBeAg is a marker for infectivity (HBeAb-positive patients have low likelihood of spreading disease). The first antibody to appear is IgM anti-HBc, which appears during the window phase, when both HBsAg and HBsAb are negative. Positive HBsAb means that the patient is immune (due either to recovery from infection or vaccination) and never appears if the patient develops chronic hepatitis. Sequelae are cirrhosis and hepatocellular cancer (only with chronic infection).
4. Hepatitis C: the new king of chronic hepatitis; most likely cause of hepatitis after a blood transfusion (used to be hepatitis B before blood was screened). More likely than hepatitis B to progress to chronic hepatitis, cirrhosis, and cancer. Serology: antibody to hepatitis C virus shows immunity. New test for HCV RNA detects virus (blood is now screened).
5. Hepatitis D: seen only in patients with hepatitis B; may become chronic with hepatitis B coinfection. Acquired in same ways as hepatitis B. IgM antibodies to hepatitis D antigen show recent resolution of infection; presence of hepatitis D antigen means chronicity.
6. Hepatitis E: similar to hepatitis A (food-and water-borne, no chronic state). Often fatal in pregnant women.
7. Drug-induced: look for acetaminophen, isoniazid (other tuberculosis drugs), halothane, carbon tetrachloride, tetracycline. Stop the drug!
8. Reye's syndrome: develops in a child given aspirin for fever.
9. Acute fatty liver of pregnancy: develops in third trimester. Treat with immediate delivery.
10. Ischemia/shock: history of shock.

11. Idiopathic autoimmune hepatitis: 20–40-year-old women with anti-smooth muscle or antinuclear antibodies and no risk factors or lab markers of other causes for hepatitis. Treat with steroids.
12. Biliary tract disease: see below; look for markedly elevated alkaline phosphatase.

Liver disease, chronic: often due to alcohol, hepatitis, and metabolic diseases (hemochromatosis, Wilson's disease, alpha$_1$ antitrypsin deficiency). Stigmata of chronic liver disease include gynecomastia, testicular atrophy, palmar erythema, spider angiomas on skin, and ascites.

Important points:

1. Alcoholism: positive history, Mallory bodies on histology (not specific).
2. Hepatitis B or C: positive history and serology.
3. Hemochromatosis: primary form is autosomal recessive disease (look for family history) caused by excessive iron that is deposited in liver (cirrhosis, hepatocellular carcinoma), pancreas (diabetes), heart (dilated cardiomyopathy), skin (pigmentation, classically called "bronze diabetes"), and joints (arthritis). Men are symptomatic earlier and more often; women lose iron with menstruation. Treat with phlebotomy. Secondary iron overload also may cause a hemochromatosis-like picture, including anemia from ineffective erythropoiesis (e.g., thalassemia) and excessive iron intake.
4. Wilson's disease: autosomal recessive disease caused by excessive copper. Serum ceruloplasmin is low. Serum copper may be normal, but liver biopsy shows excessive copper. Patients also have central nervous system/psychiatric manifestations (copper deposits in basal ganglia; another name for this disease is hepatolenticular degeneration) and Kayser-Fleischer rings in the eye. Treat with penicillamine (copper chelator).
5. Alpha$_1$ antitrypsin deficiency: younger adult who develops cirrhosis and emphysema without risk factors for either; autosomal recessive inheritance.

Metabolic derangements that accompany liver failure:

1. Coagulopathy: prolonged prothrombin time; in severe cases, partial thromboplastin time may be prolonged. Because the damaged liver cannot use vitamin K, patients must be treated with fresh frozen plasma.
2. Jaundice/hyperbilirubinemia: elevated conjugated and unconjugated bilirubin with hepatic damage (vs. biliary tract disease).
3. Hypoalbuminemia: liver synthesizes albumin.
4. Ascites: due to portal hypertension and/or hypoalbuminemia. Ascites can be detected on physical exam by shifting dullness or a positive fluid wave. Possible complication is **spontaneous bacterial peritonitis**—infected ascitic fluid that leads to sepsis. Look for fever and/or change in mental status in a patient with known ascites. Do a paracentesis, and examine the ascitic fluid for white blood cells (especially neutrophils), Gram stain, culture and sensitivity, glucose (low with infection), and protein (high with infection). Usually caused by *E. coli*, *S. pneumoniae*, or other enteric bugs. Treat with broad-spectrum antibiotics.
5. Portal hypertension: seen with cirrhosis (chronic liver disease); causes hemorrhoids, varices, caput medusae.
6. Hyperammonemia: liver clears ammonia. Treat with decreased protein intake (source of NH_3) and lactulose (prevents absorption of ammonia). Last choice is neomycin (stops bowel flora from making NH_3).

7. Hepatic encephalopathy: mostly due to hyperammonemia; often precipitated by protein, GI bleed, or infection.
8. Hepatorenal syndrome: liver failure causes kidney failure (idiopathic).
9. Hypoglycemia: liver stores glycogen.
10. Disseminated intravascular coagulation: activated clotting factors usually cleared by liver.

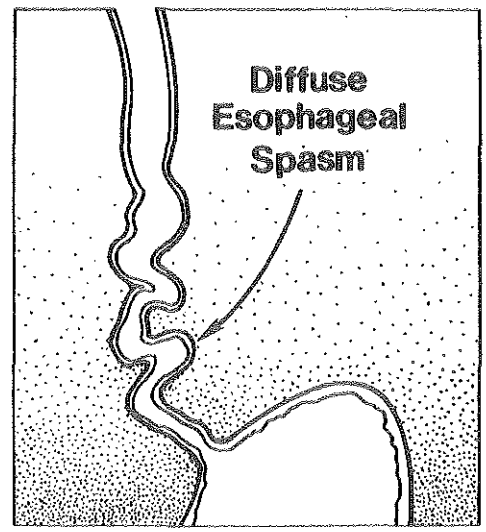
Biliary tract disease: jaundice may be caused by bile duct obstruction. Look for markedly elevated alkaline phosphatase, conjugated bilirubin that is more elevated than unconjugated bilirubin, pruritus, clay-colored stools, and dark urine that is strongly bilirubin-positive. Unconjugated bilirubin is not excreted in the urine because it is tightly bound to albumin.

1. Common bile duct obstruction with gallstone: look for history of gallstones or the four Fs (female, forty, fertile, fat). Ultrasound can often image the stone; if not, use endoscopic retrograde cholangiopancreatography.
2. Common bile duct obstruction from cancer: usually pancreatic cancer, sometimes cholangiocarcinoma or bowel cancers.
3. Cholestasis: often from medications (oral contraceptives, phenothiazines, androgens) or pregnancy.
4. Primary biliary cirrhosis: middle-aged woman with no risk factors for liver or biliary disease, marked pruritus, jaundice, and positive antimitochondrial antibodies; rest of work-up is negative. Cholestyramine helps with symptoms, but no treatment (other than liver transplantation) is available.
5. Primary sclerosing cholangitis: young adults with inflammatory bowel disease (usually ulcerative colitis); presents like cholangitis.
6. Cholangitis: Charcot's triad = fever, right upper quadrant pain, and jaundice. Treat with antibiotics, and remove stones surgically or endoscopically.

Esophageal disorders: dysphagia is usually an esophageal complaint. Patients may present with atypical chest pain.

1. Achalasia: hypertensive lower esophageal sphincter (LES), incomplete relaxation of LES, and loss or derangement of peristalsis. Achalasia is usually idiopathic but may be secondary to Chagas' disease (South America). Patients have intermittent dysphagia for solids and liquids with *no heartburn*. Barium swallow reveals dilated esophagus with distal "bird-beak" narrowing. Diagnosis can be made with esophageal manometry. Treat with calcium channel blockers, pneumatic balloon dilatation, and, as a last resort, surgery (myotomy).
2. Diffuse esophageal spasm/nutcracker esophagus: both have irregular, forceful, painful esophageal contractions that cause intermittent chest pain. Diagnose with esophageal manometry. Treat with calcium channel blockers and, if needed, surgery (myotomy). (See figure, top of next page.)
3. Scleroderma: may cause aperistalsis due to fibrosis and atrophy of smooth muscle. Lower LES becomes incompetent, and patients may develop GERD. Look for positive antinuclear antibody and mask-like facies, other autoimmune symptoms (**CREST** = **c**alcinosis, **R**aynaud's phenomenon, **e**sophageal dysmotility, **s**clerodactyly, **t**elangiectasias).
4. Barrett's esophagus: columnar metaplasia due to acid reflux; must be followed with periodic endoscopy and biopsies to rule out progression to adenocarcinoma.

Pancreatitis: more than 80% of cases are due to alcohol and gallstones. Other causes include hypertriglyceridemia, viral infections (mumps, coxsackie virus), trauma, and medications



Diffuse esophageal spasm. (From James EC, Corry RJ, Perry JF: Principles of Basic Surgical Practice. Philadelphia, Hanley & Belfus, 1987, with permission.)

(steroids, azathioprine). Patients have abdominal pain radiating to the back, nausea and vomiting that does not relieve the pain, leukocytosis, and elevated amylase/lipase. Perforated peptic ulcer disease also may have elevated amylase and presents similarly, but patients have free air on abdominal x-ray and history of peptic ulcer disease.

- Treatment: NPO, nasogastric tube, IV fluids, narcotics (merperidine, not morphine)
- Grey-Turner's sign = blue/black flanks; Cullen's sign = blue/black umbilicus (both are due to hemorrhagic exudate; both indicate severe pancreatitis).
- Complications include pseudocyst (drain surgically if symptomatic), abscess/infection (antibiotics and surgical abscess drainage), and diabetes (with chronic pancreatitis).
- Treat chronic pancreatitis with alcohol abstinence, oral pancreatic enzyme replacement, and fat-soluble vitamin supplements.

Mallory-Weiss tears are superficial esophageal erosions that may cause a GI bleed. They usually are seen with vomiting and retching (alcoholics and bulimics). Diagnosis and treatment are done endoscopically (sclerose any bleeding vessels). Boerhave's tears are full-thickness esophageal ruptures; if not iatrogenic (from endoscopy), they are usually due to vomiting or retching (alcoholics and bulimics). Diagnose with endoscopy or barium enema, and treat with immediate surgical repair and drainage.

Note: With suspected GI perforation, never use barium (which may cause chemical peritonitis). *Use water-soluble contrast instead (e.g., Gastrografin).* The exception is esophageal perforation because the lungs tolerate barium well but develop chemical pneumonitis from water-soluble contrast.

Gastrointestinal malformations seen in children: (see table, top of next page)

Tracheoesophageal fistula: the most common variant (85% of cases) has esophageal atresia with a fistula from the bronchus to the distal esophagus (hence, gastric distention; each breath transmits air to the GI tract). Be able to recognize a sketch of this most common variant. Treat each of the following conditions with surgical repair.

NAME	PRESENTING AGE	VOMIT DESCRIPTION	FINDINGS/KEY WORDS
Pyloric stenosis	0–2 mo	Nonbilious, projectile	M >> F; palpable olive-shaped mass in epigastrium, low potassium, metabolic alkalosis
Intestinal atresia	0–1 wk	Bilious	"Double-bubble" sign, Down syndrome
Transesophageal fistula	0–2 wk	Food regurgitation	Respiratory compromise with feeding, aspiration pneumonia, inability to pass nasogastric tube, gastric distention (air)
Hirschsprung's disease	0–1 yr	Feculent	Abdominal distention, obstipation, no ganglia seen on rectal biopsy, M >> F
Anal atresia	0–1 wk	Late, feculent	Detected by initial exam in nursery, M > F
Choanal atresia	0–1 wk	—	Cyanosis with feeding, relieved by crying; inability to pass nasogastric tube

Other gastrointestinal conditions in children:

NAME	PRESENTING AGE	VOMIT DESCRIPTION	FINDINGS/KEY WORDS
Intussusception	4 mo–2 yr	Bilious	Currant-jelly stools (blood and mucus), palpable sausage-shaped mass; diagnose and treat with barium enema
Necrotizing enterocolitis	0–2 mo	Bilious	Premature babies, fever, rectal bleeding, air in bowel wall; treat with NPO, orogastric tube, IV fluids, antibiotics
Meconium ileus	0–2 wk	Feculent, late	Cystic fibrosis manifestation (as is rectal prolapse)
Volvulus	0–2 yr	Bilious	Sudden onset of pain, distention, rectal bleeding, peritonitis, "bird's beak" on abdominal x-ray; treat with surgery
Meckel's diverticulum	0–2 yr	Varies	Rule of 2s*; GI ulceration or bleeding; use Meckel's scan to detect; treat with surgery
Strangulated hernia	Any age	Bilious	Physical exam detects bowel loops in inguinal canal

* Rule of 2s for Meckel's diverticulum: 2% of population affected (most common GI tract abnormality—remnant of the omphalomesenteric duct), 2 inches long, within 2 feet of ileocolic junction, presents in first 2 years of life. Meckel's diverticulum may cause intussusception, obstruction, or volvulus.

Diaphragmatic hernia: more common in males and on the left side. The main point to know is that bowel herniates into the thorax, compressing and impeding lung development (pulmonary hypoplasia develops). Patients present with respiratory distress and have bowel sounds in the chest/bowel loops in the thorax on chest x-ray.

Omphalocele vs. gastroschisis: omphalocele is in the midline. Sac contains multiple abdominal organs, the umbilical ring is absent, and other anomalies are common. Gastroschisis is to the right of the midline. Only small bowel is exposed (no true hernia sac), the umbilical ring is present, and other anomalies are rare.

Henoch-Schönlein purpura may present with GI bleeding and abdominal pain. Look for history of upper respiratory infection, characteristic rash on lower extremities and buttocks, swelling in hands and feet, arthritis, and/or hematuria/proteinuria. Treat supportively.

Note: Children (more than adults) develop nausea and vomiting and/or diarrhea with any systemic illness. They also may develop inflammatory bowel disease or irritable bowel syndrome and often have GI complaints with anxiety or psychiatric problems (separation anxiety, reluctance to go to school, depression, child abuse).

Neonatal jaundice: may be physiologic or pathologic. The first step is to measure total, direct, and indirect bilirubin. The main concern is kernicterus, which is due to high levels of unconjugated

bilirubin and subsequent deposit into the basal ganglia. Look for poor feeding, seizures, flaccidity, opisthotonos, and/or apnea to accompany severe jaundice.

Physiologic jaundice: in 50% of normal infants; even more common in premature infants. Bilirubin is mostly unconjugated. In preterm infants, bilirubin is < 15 mg/dl, peaks at 3–5 days and may be elevated for up to 3 weeks. In full-term infants, bilirubin is < 12 mg/dl, peaks at 2–4 days, and returns to normal by 2 weeks.

Pathologic jaundice: levels rise higher than normal and continue to rise or fail to decrease appropriately. **Any jaundice present at birth is pathologic.**

1. Breast milk jaundice: breast-fed infants with peak bilirubin of 10–20 mg/dl occurring at 2–3 weeks of age. Treat with temporary cessation of breast feeding (switch to bottle) until jaundice resolves.
2. Illness: infection/sepsis, hypothyroidism, liver insult, cystic fibrosis, and other illnesses may prolong neonatal jaundice and lower the threshold for kernicterus. The youngest, sickest infants are at greatest risk for hyperbilirubinemia and kernicterus.
3. Hemolysis: from Rh incompatibility or congenital red cell diseases that cause hemolysis in the neonatal period. Look for anemia, peripheral smear abnormalities, family history, and higher level of unconjugated bilirubin.
4. Metabolic: Crigler-Najjar syndrome causes severe unconjugated hyperbilirubinemia, Gilbert's disease causes mild unconjugated hyperbilirubinemia, and Rotor and Dubin-Johnson syndromes cause conjugated hyperbilirubinemia.
5. Biliary atresia: full-term infants with clay- or gray-colored stools and high levels of conjugated bilirubin. Treat with surgery.
6. Medications: avoid sulfa drugs in neonates (displaces bilirubin from albumin and may precipitate kernicterus).

Treatment for unconjugated hyperbilirubinemia that persists, rises higher than 15 mg/dl, or rises rapidly is phototherapy to convert the unconjugated bilirubin to a water-soluble form that can be excreted. The last resort is exchange transfusion (do not even think about it unless the level of unconjugated bilirubin is > 20 mg/dl).

Note: Any infant born to a mother with active hepatitis B should get the first immunization shot and hepatitis B immunoglobulin at birth.

CHAPTER 5

Endocrinology

You must understand the **hypothalamic-pituitary axis** so that you can distinguish primary from secondary disorders. In primary endocrine disturbances, the gland itself is malfunctioning (e.g., from tumor, inflammation, enzyme deficiency), but the pituitary and hypothalamus are functioning normally and exhibit the appropriate response to the gland's action. For example, thyroid-stimulating hormone (TSH) is low in Graves' disease, because the thyroid is malfunctioning and overproduces thyroid hormone. The appropriate response is for the pituitary to secrete less TSH because of feedback inhibition. In a secondary endocrine disturbance, the gland is perfectly normal, but the pituitary or hypothalamus is malfunctioning. For example, if the pituitary secretes low levels of TSH or the hypothalamus secretes low levels of thyrotropin-releasing hormone (TRH) in patients with hypothyroidism, the pituitary or hypothalamus is malfunctioning, because it should be secreting high levels of TSH or TRH when the level of thyroid hormone is inadequate.

Hypothyroidism: look for classic symptoms of fatigue, bradycardia, menstrual disturbances (usually menorrhagia), slow speech, cold intolerance, constipation, carpal tunnel syndrome, decreased reflexes, anemia of chronic disease, and/or coarse hair. Hypothyroidism may be associated hypercholesterolemia, which resolves with treatment. Check thyroid function tests (TSH, thyroxine [T_4], free thyroxine index [FTI]). Usually TSH is high, and T_4 (primary) is low. Treat with thyroid hormone (synthetic T_4).

Causes of hypothyroidism:

1. Hashimoto's thyroiditis: most common cause; associated with other autoimmune diseases (e.g., pernicious anemia, vitiligo, lupus). Look for positive antimicrosomal antibodies. Histology shows lymphocyte infiltration of the gland.
2. Subacute thyroiditis: acute viral inflammation with fever and enlarged, **tender** thyroid gland. History of upper respiratory infection or mumps is common. Give NSAIDs for symptom relief. Patients often recover without treatment.
3. After treatment for hyperthyroidism, be aware that it frequently occurs (second most common cause in U.S.).
4. Sick-euthyroid syndrome: any illness may decrease T_4 and/or triiodothyronine (T_3), but TSH is *normal*. The condition is self-limiting, and no treatment is necessary except for the underlying disorder.
5. Iodine deficiency: rare in U.S. May cause cretinism in children (stunted growth and mental retardation).

Hyperthyroidism: symptoms include nervousness, anxiety, insomnia, tachycardia, palpitations, atrial fibrillation, heat intolerance, weight loss, diarrhea, menstrual irregularities (hypomenorrhea), increased appetite, and "thyroid stare." Check thyroid function tests. Usually TSH is low, and T_4 (primary) is high. Exophthalmos and pretibial myxedema are specific for Graves' disease. Treatment begins with antithyroid drugs (propylthiouracil or methimazole). Most patients eventually require further therapy. Use surgery for patients under 25 or pregnant women and radioactive iodine for patients over 40. For patients 24–40, treatment is controversial, and either approach is acceptable. Propranolol is used for thyroid storm (the patient decompensates, physically and mentally, from very high thyroid hormone levels) and symptomatic tachycardia, palpitations, and arrhythmias.

Causes of hyperthyroidism:

1. Graves' disease: by far, most common cause. Exophthalmos and pretibial myxedema are specific for Graves' disease. Patients have *positive thyroid-stimulating immunoglobulins*/thyroid-stimulating antibodies, which activate the TSH receptor. Nontender, diffuse goiter also is present. Whole gland takes up excessive radioactive iodine.
2. Plummer's disease/toxic multinodular goiter: hyperfunctioning nodules cause a lumpy goiter without positive antibodies or exophthalmos/pretibial myxedema. Radioactive iodine uptake is high in nodules, but decreased in the rest of the gland.
3. Toxic adenoma: one nodule is palpable and has high radioactive iodine uptake; the rest of the gland shows decreased uptake (thyroid cancer is rarely hyperfunctional).
4. Thyroiditis: Hashimoto's or subacute thyroiditis may produce a transient hyperthyroidism due to inflammation before converting to hypothyroidism.

Note: In pregnancy and other states (administration of oral contraceptives/estrogens, infections), thyroid-binding globulin (TBG) may be elevated. Although this causes elevation of total thyroid hormone levels, free thyroid hormone is not elevated, and **TSH is normal.** Do not treat. Nephrotic syndrome or large protein losses of any kind and anabolic steroids can decrease TBG (again, TSH is normal and you should not treat).

Hypoadrenalism (Addison's disease, primary adrenal insufficiency): the most common cause is idiopathic (probably autoimmune). Look for increased skin pigmentation, weight loss, dehydration, anorexia, nausea and vomiting, dizziness and syncope, hyponatremia, and hyperkalemia. Under metabolic stress (infection, surgery) *patients may have an adrenal crisis*—abdominal pain, hypotension/cardiovascular collapse, renal shutdown, and death. Treat with hydrocortisone and IV fluids to avoid adrenal crisis. The diagnosis of hypoadrenalism, when not obvious, is done by administering adrenocorticotropic hormone (ACTH) and seeing whether levels of plasma cortisol increase over baseline. *Do not delay giving steroids to do this* test if the patient is doing poorly; the patient may die while you wait for the results.

Secondary adrenal insufficiency: commonly tested disorder, and is most often due to previous taking of steroids. Once patients take steroids for more than 1 month, they may not be able to mount an appropriate increase in ACTH when needed for **up to 1 year!** The classic setting is the patient on steroids who stops taking all medications before surgery, then develops refractory hypotension and electrolyte disturbances after surgery. Give corticosteroids! Other secondary causes of adrenal insufficiency are Sheehan's syndrome (history of post-partum hypotension, inability to breast-feed, and other endocrine insufficiencies) and neoplasms (pituitary adenomas and craniopharyngiomas). In secondary hypoadrenalism, mineralocorticoid (aldosterone) secretion is not affected, because it is not directly under pituitary control; thus, the electrolyte disturbance is not as severe, and there is no skin hyperpigmentation. ACTH is

decreased, as is melanocyte-stimulating hormone (MSH), which is thought to cause the skin hyperpigmentation in primary adrenal insufficiency.

Hyperadrenalism (Cushing's syndrome): usually due to prescribed steroids in the U.S. Look for moon facies, truncal obesity, "buffalo hump", striae, poor wound healing, hypertension, osteoporosis, secondary diabetes or glucose intolerance, menstrual abnormalities, and psychiatric disturbances (depression, psychosis). Cushing's disease is Cushing's syndrome caused by pituitary overproduction of ACTH, which usually is due to a pituitary adenoma. Get an MRI of the brain if levels of ACTH and cortisol are high. Other causes are adrenal neoplasms that produce steroids and small cell cancer of the lung, which may produce ACTH. Treat by curing the neoplasm. Diagnosis is made by first doing a screening test. The best choice is usually a 24-hour urine test for free cortisol; plasma cortisol is not a good test because of wide inter- and intrapatient fluctuation. Then do a dexamethasone suppression test.

Hyperaldosteronism: primary disease is known as Conn's syndrome and is due to an adenoma. Look for hypertension, hypernatremia, hypokalemia and *low* renin. Get a CT scan of the abdomen. Secondary hyperaldosteronism is much more common, and is related to hypertension (especially with renal artery stenosis) and edematous disorders (congestive heart failure, cirrhosis, nephrotic syndrome). Look for hypertension, edema, renal bruit, variable sodium and potassium, and *high* renin. Treat the underlying cause.

Pheochromocytoma: popular on the boards. Look for intermittent hypertension that is very high, wild swings in blood pressure, tachycardia, postural hypotension, headaches, sweating, dizziness, mental status changes, and/or feeling of impending doom. Patients also may have glucose intolerance due to high catecholamines. If you are suspicious, first screen with a 24-hour urine test to look for catecholamines and their break-down products (vanillylmandelic acid [VMA] and/or homovanillic acid [HVA], metanephrines). If the screen is positive, do an abdominal CT, and cut out the tumor after stabilizing the patient with alpha and beta blockers.

Diabetes insipidus (DI): Symptoms include severe polydipsia and polyuria (patients may urinate 25 L/day). When access to water is restricted, patients rapidly develop dehydration and hypernatremia, which may cause death. Giving antidiuretic hormone (ADH) determines whether the cause is central or nephrogenic. Central disease responds to ADH, whereas nephrogenic disease does not.

- Nephrogenic DI: look for medications as cause (lithium, methoxyflurane, demeclocycline). Treat with thiazide diuretics (paradoxical effect; ADH does not help).
- Central DI: look for trauma, neoplasm, or sarcoidosis, although central DI is often idiopathic. Treat with ADH/vasopressin, and treat underlying cause, if possible.

Syndrome of inappropriate secretion of antidiuretic hormone (SIADH): symptoms include hyponatremia as well as low levels of every other electrolyte (and lab value) because of dilution from excessive water retention. Look for medications (morphine, chlorpropamide, oxytocin—be careful in pregnant patients), small cell lung cancer, *postoperative status* (watch for all electrolytes to fall after surgery), trauma, lung infections, and pain. Treat with **water restriction**. For board purposes, *do not* give hypertonic saline, and do *not* try to correct hyponatremia aggressively or quickly. Rapid correction may cause brainstem damage.

Obesity: causes an increased risk of the following problems:

1. Overall mortality (at any age)
2. Insulin resistance/diabetes mellitus

3. Hypertension
4. Hypertriglyceridemia (also weakly associated with hypercholesterolemia)
5. Heart disease/coronary artery disease
6. Gallstones (cholesterol stones)
7. Hypoventilation, pickwickian syndrome, sleep apnea
8. Symptomatic osteoarthritis
9. Cancer, especially endometrial cancer
10. Thromboembolism
11. Varicose veins

CHAPTER 6

Nephrology

Acute renal failure (ARF): progressive rise in creatinine and blood urea nitrogen (BUN), metabolic acidosis, hyperkalemia, and hypervolemia. Symptoms include rales, elevated jugular venous pressure, and dilutional hyponatremia. Three categories:

1. Prerenal: most common example is hypovolemia (dehydration, hemorrhage). Look for BUN/creatinine ratio > 15 or 20. Patients have signs of hypovolemia (e.g., tachycardia, weak pulse, depressed fontanelle). Give IV fluids and/or blood. Other prerenal causes are sepsis (treat the sepsis and give IV fluids), heart failure (give digitalis and diuretics), and liver failure (hepatorenal syndrome; treat supportively).
2. Postrenal: most common example is benign prostatic hypertrophy (BPH). The patient is a man over 50 with BPH symptoms (e.g., hesitancy, dribbling), and ultrasound reveals bilateral hydronephrosis. Treat with catheterization (suprapubic catheterization if necessary) to relieve obstruction and prevent further renal damage; then consider surgery (transurethral prostatectomy [TURP]). Nephrolithiasis is also a possible cause, but stones have to be bilateral to cause renal failure.
3. Renal: acute tubular necrosis is the most common type. Examples of renal causes:
   - IV contrast: do *not* give to diabetics or renal patients if you can avoid it; you may precipitate acute renal failure. If you must give it, give *lots* of hydration.
   - Myoglobinuria/rhabdomyolysis: from strenuous exercise (e.g., marathon), alcohol, burns, muscle trauma, heat stroke, or neuroleptic malignant syndrome. Muscle breaks down and plugs up the renal filtration system. Look for very high levels of creatine phosphokinase (CPK). Treat with hydration and diuretics.
   - Lupus erythematosus: look for malar rash and arthritis. Renal failure is a major cause of morbidity and mortality.
   - Toxins/medications: chronic NSAID use (papillary necrosis), cyclosporine, aminoglycosides, methicillin.
   - Goodpasture's syndrome: due to antiglomerular basement membrane antibodies (linear immunofluorescence pattern on renal biopsy), which also react with the lungs. Look for a young male with hemoptysis, dyspnea, and renal failure. Treat with steroids and cyclophosphamide.
   - Wegener's granulomatosis: also has lung and kidney involvement. Look for nasal involvement (bloody nose, nasal perforation) or hemoptysis and pleurisy as presenting symptoms. Patients have positive antineutrophil cytoplasm antibody (ANCA) titer. Treat with cyclophosphamide.

- *Glomerulonephritis: prototype is post-streptococcal syndrome;* usually seen in children with history of upper respiratory infection or strep throat 1–3 weeks earlier; they present with edema, hypervolemia, hypertension, hematuria, and oliguria. Red blood cell casts on urinalysis clinch the diagnosis. Treat supportively.

Note: In all cases of ARF, dialysis may be required. Indications for dialysis include uremic encephalopathy, pericarditis, severe metabolic acidosis (roughly, pH < 7.25), heart failure, and hyperkalemia severe enough to cause arrhythmia.

Nephrotic syndrome: proteinuria (> 3.5 gm/day), hypoalbuminemia, edema (classic example is morning periorbital edema), and hyperlipidemia/lipiduria. In children, it is usually due to minimal change disease, often after an infection. Measure 24-hour urine protein to clinch the diagnosis, and treat with steroids. Causes in adults include diabetes mellitus, hepatitis B, *amyloidosis, lupus, and drugs (gold,* penicillamine, captopril).

Nephritic syndrome: oliguria, azotemia (rising BUN/creatinine), hypertension, and hematuria. Patients may have some *proteinuria, but not in the nephrotic range.* The usual cause is post-streptococcal glomerulonephritis.

Chronic renal failure (CRF): any of the causes of ARF may cause CRF *if the insult is severe or* prolonged. The majority of cases of CRF are due to diabetes mellitus (number one cause of CRF) and hypertension. Another common cause is polycystic kidney disease (multiple cysts in kidney). Look for positive family history (usually autosomal dominant; autosomal recessive form presents in children), hypertension, hematuria, palpable renal masses, berry aneurysms in the circle of Willis, and cysts in liver.

Metabolic derangements due to CRF:

1. Azotemia—high BUN/creatinine
2. Metabolic acidosis
3. Hyperkalemia—know EKG changes
4. Fluid retention—may cause hypertension, edema, congestive heart failure, and pulmonary edema
5. Hypocalcemia/hyperphosphatemia—vitamin D production impaired; bone loss leads to renal osteodystrophy
6. Anemia—from lack of erythropoietin (synthetic erythropoietin may correct)
7. Anorexia, nausea, vomiting—from build-up of toxins
8. Central nervous system disturbances—mental status changes and even convulsions or coma from toxin build-up
9. Bleeding—due to disordered platelet function, patients may have prolonged bleeding time test
10. Uremic pericarditis—may hear a friction rub
11. Skin pigmentation and pruritus—*skin turns yellowish-brown and itches* due to metabolic byproducts
12. Increased susceptibility to infection—due to decreased cellular immunity

Treatment of CRF: regular dialysis, water-soluble vitamins (removed during dialysis), phosphate restriction/*binders (aluminum or calcium* carbonate), erythropoietin, and hypertension control. The only cure is renal transplant.

Urinary tract infection (UTI): much more common in females. Usually caused by *Escherichia coli* (also by other enteric organisms). Look for urgency, dysuria, suprapubic/low back pain, and low-grade fever. The gold standard for diagnosis is urine culture (at the least, get a midstream sample; best is catheterized sample or suprapubic tap). Urinalysis shows white blood cells, bacteria, positive leukocyte esterase, and/or positive nitrite. Treat with trimethoprim/sulfamethoxazole, amoxicillin, nitrofurantoin, or first-generation cephalosporin for about 1 week.

Important points:

1. In patients less than 5 years old, UTI is a cause for concern because it may be the presenting symptom of a genitourinary malformation. The most common examples are vesicoureteral reflux (VUR) and posterior urethral valves. Get an ultrasound and a voiding cystourethrogram to evaluate any male under 6 with a UTI and any female under 6 with recurrent UTIs or pyelonephritis.
2. Some women get recurrent UTIs related to sex and can be given antibiotics to take afterwards.
3. Conditions that promote urinary stasis (BPH, pregnancy, stones, neurogenic bladder, VUR) or bacterial colonization (indwelling catheter, fecal incontinence, surgical instrumentation) predispose to UTI. They also predispose to ascending UTI (pyelonephritis) and bacteremia/sepsis.
4. Asymptomatic bacteriuria is treated in pregnancy (high risk of progression to pyelonephritis).

Pyelonephritis: almost always from an ascending UTI and due to *E. coli* (> 80% of cases). Patients present with high fever, shaking chills, **costovertebral angle tenderness**/flank pain, and/or UTI symptoms. Urinalysis and urine and blood cultures establish the diagnosis. Treat on an inpatient basis with IV antibiotics while awaiting test results (penicillin or cephalosporin plus aminoglycoside).

Kidney and hematologic disorders in children

	HUS	HSP	TTP	ITP
Most common age	Children	Children	Young adults	Children or adults
Previous infection	Diarrhea (*E. coli*)	URI	None	Viral (especially in children)
Red blood cell count	Low	Normal	Low	Normal
Platelet count	Low	Normal	Low	Low
Peripheral smear	Hemolysis	Normal	Hemolysis	Normal
Treatment	Supportive*	Supportive*	Plasmapheresis, NSAIDs, no platelets†	Steroids, splenectomy if medications fail‡
Kidney manifestations	ARF, hematuria	Hematuria	ARF, proteinuria	None
Key differential points	Age, diarrhea	Rash, abdominal pain, arthritis, melena	CNS changes, age	Antiplatelet antibodies

HUS = hemolytic uremic syndrome, HSP = Henoch-Schönlein purpura, TTP = thrombotic thrombocytopenic purpura, ITP = idiopathic thrombocytopenic purpura, URI = upper respiratory infection, ARF = acute renal failure, CNS = central nervous system, ARF = acute renal failure.

* In HUS and HSP, patients may need dialysis and transfusions.
† Do *not* give platelet transfusions to patients with TTP (may form clots).
‡ Give steroids only if the patient is symptomatic (bleeding) or platelets < 20,000.

Renal stones: present with severe, intermittent, unilateral flank and/or groin pain. Most stones show up on abdominal x-ray and are composed of calcium. Most cases are idiopathic

and should be treated with lots of hydration and pain control (to see if stone will pass). If stone does not pass, it needs to be removed surgically (preferably endoscopically) or by lithotripsy.

Underlying causes of stones:

1. *Hypercalcemia:* due to hyperparathyroidism or malignancy (metastases or squamous cell lung cancer–secreting parathyroid hormone).
2. Infection: from ammonia-producing bugs (*Proteus, Staphylococcus* spp.). Look for **Staghorn calculi**.
3. Hyperuricemia: from gout or from leukemia treatment (allopurinol and IV fluids are given before chemotherapy as preventive measures).
4. Cystinuria/aminoaciduria: suspect if the stone is made of cystine and in repetitive stone-forming patients.

CHAPTER 7

Rheumatology

Arthritis: the large majority of cases are due to osteoarthritis (OA). When in doubt or if you suspect something other than OA, aspirate fluid from the affected joint for examination. Examine the fluid for cell count and differential, glucose, bacteria (Gram stain and culture), and crystals:

	OSTEOARTHRITIS	RHEUMATOID ARTHRITIS	GOUT	PSEUDOGOUT	SEPTIC ARTHRITIS
Usual age/sex	Older adults	Women 20–45	Older men	Older adults	Any age
Classic joints	DIP, PIP, hip, knee	PIP, MCP, wrist	Big toe	Knees, elbows	Knee
Joint fluid white blood cell count	< 2,000	> 2,000	> 2,000	> 2,000	>50,000
% Neutrophils	< 25	> 50	> 50	> 50	> 75

DIP = distal interphalangeal, PIP = proximal interphalangeal, MCP = metacarpophalangeal.

Other key differences/points:

1. OA: few signs of inflammation on exam (lacks hot, red, tender joints seen in all the others of this group). Symptoms include Heberden's (DIP) and Bouchard's (PIP) nodes, worsening of symptoms in evening and after use, and bony spurs. Incidence increases with age. Treat with weight reduction and NSAIDs as needed.
2. Rheumatoid arthritis (RA): positive rheumatoid factor clinches the diagnosis in most patients, but children are often negative. Look for systemic symptoms (fever, malaise, subcutaneous nodules, pericarditis/pleural effusion, uveitis), prolonged morning stiffness, and swan neck and boutonnière deformities. The buzz word is **pannus** (articular cartilage looks like granulation tissue due to chronic inflammation). Treat with NSAIDs, hydroxychloroquine, gold, penicillamine, and steroids (for bad flare-ups).
3. Gout: classically starts with podagra (gout in the big toe). Look for tophi (subcutaneous uric acid deposits, punched-out lesions in bone x-ray) and needle-shaped crystals (often inside leukocytes) with **negative** birefringence. Gout is more common in men than women. Patients should avoid alcohol (may precipitate an attack). Colchicine or NSAIDs (not aspirin, which causes decreased excretion of uric acid by the kidney) are used for acute attacks. Maintenance therapy includes high fluid intake, alkalinization of the urine, and/or probenicid/allopurinol (neither for acute attacks).
4. Pseudogout: rhomboid-shaped crystals with weakly **positive** birefringence.

5. Septic arthritis: synovial fluid has bacteria on Gram stain. *Staphylococcus aureus* is the most common organism, except in sexually active young adults (*Neisseria gonorrhoeae* is most common in this group). Do blood cultures in addition to joint cultures, because the bug usually reaches the joint via the hematogenous route. Do urethral swabs and cultures in appropriate patients.

Other causes of arthritis

1. Psoriasis: in the presence of skin lesions, diagnosis is easy. Arthritis usually affect hands and feet, and the arthritis resembles RA but rheumatoid factor is negative. Treat with NSAIDs, gold, penicillamine, or steroids.
2. Lupus erythematosus or inflammatory bowel disease: other symptoms of the primary disease make diagnosis easy.
3. Ankylosing spondylitis: associated with HLA-B27. Most often a 20–40-year-old man with a positive family history presents with back pain and morning stiffness; the patient may assume a bent-over posture. Sacroiliac joints are primarily affected, and x-rays may reveal a bamboo spine. Patients have other autoimmune-type symptoms, such as fever, elevated erythrocyte sedimentation rate (ESR), and anemia; some develop uveitis. Treatment is exercise and NSAIDs.
4. Reiter's syndrome: also associated with HLA-B27. The classic triad is urethritis (due to *Chlamydia* sp.), conjunctivitis, and arthritis ("can't pee, can't see, can't climb a tree"), but Reiter's syndrome also may follow enteric bacterial infections. Superficial oral and penis ulcers also are common. Diagnose and treat the sexually transmitted disease, and treat sexual partners. NSAIDs are used for arthritis.
5. Hemophilia: recurrent hemarthroses may cause debilitating arthritis. Treat with acetaminophen (avoid aspirin).
6. Lyme disease: look for tick bite, erythema chronicum migrans, and migratory arthritis later. Treat with doxycycline/tetracycline (amoxicillin in pregnant women).
7. Rheumatic fever: look for previous streptococcal pharyngitis. Migratory polyarthritis is one of the major Jones criteria.
8. Sickle cell disease: patients frequently develop arthralgias and avascular necrosis of the femoral head.
9. Trauma
10. Childhood orthopedic problem: slipped capital femoral epiphysis, congenital hip dysplasia, and Legg-Calvé-Perthes disease may cause arthritis as adulthood. Use history (age of onset) and x-rays to determine which disease the patient had as a child.
11. Charcot joint: most commonly seen in diabetes mellitus; also in other neuropathies. Lack of sensation causes patient to overuse or misuse joints, which become deformed and painful. The best treatment is prevention. After even seemingly mild trauma, patients with neuropathy in the area of the trauma need x-rays to rule out fractures.
12. Hemochromatosis/Wilson's disease: both may be associated with arthritis due to deposition of iron/copper.

Autoimmune diseases: affect women of reproductive age unless otherwise specified. For board purposes, classic disease findings differentiate one condition from the other. Almost all patients have systemic signs of inflammation (elevated ESR/C-reactive protein, fever, anemia of chronic disease, fatigue, weight loss).

1. Systemic lupus erythematosus: malar rash, discoid rash, photosensitivity, kidney damage, arthritis, pericarditis/pleuritis, positive antinuclear antibody (ANA), positive anti-Smith antibody, positive Venereal Disease Research Laboratory or rapid plasma reagin test for syphilis, positive lupus anticoagulant, blood-penias (thrombocytopenia, leukopenia, anemia or pancytopenia), neurologic disturbances (depression, psychosis, seizures) and oral ulcers may all be presenting symptoms. Use ANA titer as a screening test, anti-Smith antibody to confirm. Treat with NSAIDs, hydroxychloroquine, and steroids.
2. Scleroderma/progressive systemic sclerosis: look for **CREST** symptoms (**c**alcinosis, **R**aynaud's phenomenon, **e**sophageal dysmotility, **s**clerodactyly, **t**elangiectasia), heartburn and mask-like, leathery facies. Screening test is ANA; confirmatory tests are anticentromere antibody (for CREST) and antitopoisomerase (scleroderma). Steroids may help.
3. Sjögren's syndrome: dry eyes (keratoconjunctivitis sicca) and dry mouth (xerostomia), often associated with other autoimmune disease. Treat with eyedrops and good oral hygiene.
4. Dermatomyositis: polymyositis (see below) plus skin involvement (heliotrope rash around the eyes with associated periorbital edema is classic). Patients classically have trouble rising out of a chair or climbing steps (proximal muscles affected). Muscle enzymes are elevated, electromyography is irregular. Muscle biopsy establishes the diagnosis. Patients have increased incidence of malignancy.
5. Polyarteritis nodosa: associated with hepatitis B infection and cryoglobulinemia. Patients present with fever, abdominal pain, weight loss, renal disturbances, and/or peripheral neuropathies. Lab abnormalities include high ESR, leukocytosis, anemia, and hematuria/proteinuria. Vasculitis involves medium-sized vessels. Biopsy is the gold standard for diagnosis.
6. Wegener's granulomatosis: resembles Goodpasture's syndrome, but instead of antiglomerular antibody, there is a positive ANCA titer. Look for nasal (nose bleeds, nasal perforation), lung (hemoptysis, dyspnea), and kidney (hematuria, acute renal failure) involvement. Treat with cyclophosphamide.
7. Kawasaki's syndrome: affects children less than 5 years old (more common in Japanese and females). Patients present with truncal rash, high fever (lasts > 5 days), conjunctival injection, cervical lymphadenopathy, strawberry tongue, late skin desquamation of palms and soles, and/or arthritis. Patients develop coronary vessel vasculitis and subsequent aneurysms, which may thrombose and cause a myocardial infarction (suspect Kawasaki's disease in any child who has a myocardial infarction). Treat during acute stage with aspirin and intravenous immunoglobulin to reduce the risk of coronary aneurysm development.
8. Takayasu's arteritis: tends to affect Oriental women between 15 and 30 years old. It is called "pulseless disease" because you may not be able to feel the patient's pulse or measure blood pressure on one side. Vasculitis affects the aortic arch and the branches that arise from it. Carotid involvement may cause neurologic signs or stroke, and congestive heart failure is not uncommon. Angiogram shows the characteristic lesions. Treat with steroids and/or cyclophosphamide.
9. Behçet's syndrome: the classic patient is a 20-something man with painful oral and genital ulcers. Patients may also have uveitis, arthritis, and other skin lesions (especially erythema nodosum). Steroids may help.

Fibromyalgia vs. polymyositis vs. polymyalgia rheumatica

	FIBROMYALGIA	POLYMYOSITIS	POLYMYALGIA RHEUMATICA
Classic age/sex	Young adult females	40–60-year-old women	Women > 50 years old
Location	Various	Proximal muscles	Pectoral and pelvic girdles, neck
ESR	Normal	Elevated	Markedly elevated (often > 100)
Muscle biopsy/EMG	Normal	Abnormal	Normal
Classic findings	Anxiety, stress, insomnia, point tenderness over affected muscles, negative work-up	Elevated CPK, abnormal EMG and biopsy, greater risk of cancer	Temporal arteritis, great response to steroids, very high ESR, elderly
Treatment	TCAs, NSAIDs, rest	Steroids	Steroids

ESR = erythrocyte sedimentation rate, EMG = electromyography, CPK = creatine phosphokinase.

Paget's disease: a disease of bone in which bone is broken down and regenerated, often simultaneously; seen in patients > 40 years old, more common in men. Often discovered in an asymptomatic patient through an x-ray; be able to recognize a Pagetoid skull (frontal bossing). Classic sites of involvement are in the pelvis and skull. Watch for a person who has had to buy larger-size hats. Patients may complain of bone pain, osteoarthritis, nerve deafness, or paraplegia. Alkaline phosphatase is **markedly elevated** in the presence of normal calcium and phosphorus. The risk of osteosarcoma is increased in affected bones. Treat with NSAIDs, possibly etidronate or calcitonin for severe disease.

Note: With juvenile RA, rheumatoid factor is often negative. Watch for uveitis (especially in pauciarticular form).

CHAPTER 8

Hematology

Anemia is defined as hemoglobin < 12 mg/dl in women or < 14 mg/dl in men. Symptoms include fatigue, dyspnea on exertion, light-headedness, dizziness, syncope, palpitations, angina, and claudication. Signs include tachycardia, pallor (especially of the sclera and mucous membranes), systolic ejection murmurs (from high flow), and signs of the underlying cause (e.g., jaundice in hemolytic anemia, positive stool guaiac in GI bleed). Medication history is important; many medications can cause anemia through various mechanisms. Classic examples include methyldopa, which causes red blood cell antibodies and hemolysis; chloroquine and sulfa drugs, which cause hemolysis in G-6-PD deficiency; phenytoin, which causes megaloblastic anemia; and chloramphenicol, which causes aplastic anemia. Other important points of the history include blood loss (trauma or surgery, melena, hematemesis), chronic diseases (anemia of chronic disease), family history (e.g., hemophilia, thalassemia, G-6-PD deficiency), and alcoholism (which tends to cause iron, folate, and B_{12} deficiencies as well as GI bleeds).

Steps to diagnosing the cause of anemia:

1. Complete blood count (CBC) with differential and red blood cell (RBC) indices. First and foremost, hemoglobin and hematocrit must be below normal. The mean corpuscular volume (MCV) tells you whether the anemia is microcytic (MCV < 80), normocytic (MCV = 80–100), or macrocytic (MCV > 100).
2. Peripheral smear: Look for classic findings to give you an easy diagnosis. You must know what the following look like:
   - Sickled cells (sickle cell disease)
   - Hypersegmented neutrophils (folate/B_{12} deficiency)
   - Hypochromic and microcytic RBCs (iron deficiency)
   - Basophilic stippling (lead poisoning)
   - Heinz bodies (G-6-PD deficiency)
   - "Bite cells" (hemolytic anemias)
   - Howell-Jolly bodies (asplenic patients)
   - Iron inclusions in RBCs of bone marrow (sideroblastic anemia)
   - Teardrop-shaped RBCs (myelofibrosis)
   - Schistocytes, helmet cells, and fragmented RBCs (intravascular hemolysis)
   - Spherocytes and elliptocytes (hereditary spherocytosis/elliptocytosis)
   - Acanthocytes/spur cells (abetalipoproteinemia)

- Target cells (thalassemia, liver disease)
- Echinocytes and burr cells (uremia)
- Polychromasia (from reticulocytosis; should alert you to possibility of hemolysis)
- Rouleaux formation (multiple myeloma)
- Parasites inside RBCs (malaria, babesiosis)

3. Reticulocyte index (RI) should be > 2% with anemia; otherwise, the marrow is not responding properly. A reticulocyte index > 3% should make you think of hemolysis as the cause (the marrow is responding properly, so it is not the problem). With these three parameters, you can make a reasonable differential diagnosis if the cause is not obvious.

MICROCYTIC	NORMOCYTIC	MACROCYTIC
Normal to elevated RI	**Normal to elevated RI**	***All forms have low RI***
Thalassemia/hemoglobinopathy	Acute blood loss	Folate deficiency
Low RI	Hemolytic (multiple causes)	B_{12} deficiency
Lead poisoning	Medications (antibody-causing)	Medications (methotrexate, phenytoin)
Sideroblastic anemia	**Low RI**	Cirrhosis/liver disease
Anemia of chronic disease (some)	Cancer, dysplasia (e.g., myelophthisic anemia)	
Iron deficiency	Anemia of chronic disease (some)	
	Aplastic anemia	
	Endocrine failure (thyroid, *pituitary*)	
	Renal failure	

Other clues to the presence of hemolytic anemia:

- Elevated lactate dehydrogenase
- Elevated bilirubin (unconjugated as well as conjugated if the liver is working)
- Jaundice
- Low or absent haptoglobin (intravascular hemolysis)
- Positive urobilinogen, bilirubin, hemoglobin in urine (only conjugated bilirubin appears in the urine, and hemoglobin appears only when haptoglobin has been saturated, as in brisk intravascular hemolysis)

Causes of anemia:

1. **Iron deficiency** (hypochromic, microcytic): the most common cause of anemia in the U.S. Look for low iron/ferritin level, elevated total iron-binding capacity (TIBC; also known as transferrin), and low *TIBC saturation*. Rarely patients have a craving for ice or dirt (pica) or Plummer-Vinson syndrome (esophageal web producing dysphagia, iron deficiency anemia, and glossitis). In a patient over 40, rule out colon cancer as a cause of chronic blood loss. Iron deficiency anemia is common in women of reproductive age because of menstrual irregularities. Give iron supplements to all infants except full-term infants who are exclusively breast-fed; giving cow's milk before 1 year of age may cause anemia through GI bleeding. Start iron supplementation at 4–6 months for full-term infants and at 2 months for preterm infants. Iron supplements also are commonly given during pregnancy and lactation because of increased demand. To treat iron deficiency anemia, correct the underlying cause if possible and treat with oral iron supplementation for roughly **6 months**.

2. **Folate deficiency** (macrocytic): commonly seen in alcoholics and pregnant women. All women of reproductive age should take folate supplements to prevent neural tube defects. Rare causes include poor diet (e.g., tea and toast), methotrexate, prolonged course of trimethoprim/sulfamethoxazole, anticonvulsant therapy (especially phenytoin), and malabsorption. Look for macrocytes and hypersegmented neutrophils (even one should make you think of the diagnosis) and low folate levels (serum or RBC). Treat with oral folate.

3. **Vitamin B_{12} deficiency** (macrocytic): most commonly due to pernicious anemia (antiparietal cell antibodies). Remember the physiology of B_{12} absorption and the association with vitiligo and hypothyroidism. Other causes include gastrectomy, terminal ileum resection, diet (strict vegan), chronic pancreatitis, and *Diphyllobothrium latum* (fish tapeworm) infection. Peripheral smear looks the same as in folate deficiency (macrocytes, hypersegmented neutrophils), but the patient has neurologic deficiencies (loss of sensation or position sense, paresthesias, ataxia, spasticity, hyperreflexia, positive Babinski sign, dementia). Look for low serum B_{12}, achlorhydria (no stomach acid secretion, elevated stomach pH), and antibodies to parietal cells. A Schilling test usually determines the etiology. Usual replacement route is intramuscular, because most patients cannot absorb B_{12}.

4. **Thalassemia** (microcytic, hypochromic): must be differentiated from iron deficiency. Iron levels are normal in thalassemia; **iron is contraindicated** because it may cause overload. Look for **elevated hemoglobin A_2** (β-thalassemia only) or hemoglobin F (β-thalassemia only), target cells, nucleated RBCs, diffuse basophilia on peripheral smears, x-ray of the skull showing a "crew-cut" appearance, splenomegaly, and positive family history (more common in blacks, Mediterraneans, Asians). No treatment is required for minor thalassemia; patients often are asymptomatic as they are used to living at a lower level of hemoglobin and hematocrit. Thalassemia major is more dramatic and severe. Treat with as-needed transfusions and iron chelation therapy to prevent hemochromatosis. Diagnosis is made by hemoglobin electrophoresis. There are four gene loci for alpha-chain and only two for beta-chain thalassemia. Alpha thalassemia is symptomatic at birth, or the fetus dies in utero (hydrops); beta thalassemia is not symptomatic until 6 months of age.

5. **Sickle cell anemia:** smear gives it away. Look for very high percentage of reticulocytes. Sickle cell anemia almost always is seen in blacks (8% are heterozygotes in U.S.). Watch for classic manifestations of sickle cell disease:

   - Aplastic crises (due to parvovirus B19 infection)
   - Bone pain (due to microinfarcts; the classic example is avascular necrosis of the femoral head)
   - Dactylitis (hand-foot syndrome; know what it looks like)
   - Renal papillary necrosis
   - Splenic sequestration crisis
   - Autosplenectomy (increased infections with encapsulated bugs)
   - Acute chest syndrome (mimics pneumonia)
   - Pigment cholelithiasis
   - Priapism
   - Stroke

   Diagnosis is made by hemoglobin electrophoresis. Screening is done at birth, but symptoms usually do not appear until around 6 months of age because of lack of adult

hemoglobin production. Treat with prophylactic penicillin (start as soon as the diagnosis is made), proper vaccination (including pneumococcal vaccine at the age of 2 years old), folate supplementation, early treatment of infections, and proper hydration. Sickle crisis is characterized by severe pain in various sites due to RBC sickling. Treat with oxygen, lots of IV fluids, and analgesics (do not be afraid to use narcotics). Consider transfusions if symptoms and/or findings are severe.

6. **Acute blood loss** (normocytic, normochromic): immediately after blood loss, hemoglobin and hematocrit are normal; it takes at least 3–4 hours (often more) for reequilibration. Look for pale, cold skin; tachycardia; and hypotension. Transfuse if indicated, even with normal hemoglobin and hematocrit in the acute setting.

7. **Autoimmune hemolytic anemia** (normocytic, normochromic)—can have multiple etiologies: lupus (or meds that cause lupus, like procainamide, hydralazine, and isoniazid), drugs (classic is methyldopa, also PCN/cephalosporins/sulfas and quinidine), leukemia/lymphoma or infection (classic is *Mycoplasma*, also EBV and syphilis). Coombs' test is positive, may have spherocytes due to incomplete macrophage destruction in extravascular hemolysis

8. **Lead poisoning** (hypochromic, microcytic): classically seen in children. With acute poisoning, look for vomiting, ataxia, colicky abdominal pain, irritability (aggressive, behavioral regression), and encephalopathy, cerebral edema, or seizures. Usually, however, poisoning is chronic and low-level; look for pica (especially paint chips and dust in old buildings, which may still have lead paint); residence in an old or neglected building; residence near a lead-smelting or battery-recycling plant; family members who work at such plants; basophilic stippling; and elevated free erythrocyte protoporphyrin (FEP). Screening asymptomatic children for serum lead level at 1 and 2 years of age is important (screen at 6 months if risk factors are present) because chronic low-level lead exposure may lead to permanent neurologic sequelae. Screen and measure symptomatic lead exposure with serum lead levels (should be < 10 µg/dl). Treat with decreased lead exposure (best and first treatment) as well as as-needed lead chelation therapy (succimer in children, dimercaprol in adults; in severe cases, use dimercaprol plus edetate for children or adults).

9. **Sideroblastic anemia** (microcytic, hypochromic): increased or normal iron, ferritin, and TIBC saturation (which distinguish it from iron deficiency), polychromatophilic stippling, and the classic "ringed sideroblast" in the bone marrow (know what it looks like). Sideroblastic anemia may be related to myelodysplasia or future blood dyscrasia. Manage supportively; in rare cases the anemia responds to pyridoxine. Do not give iron!

10. **Anemia of chronic disease** (microcytic, hypochromic, or normocytic): look for diseases that cause chronic inflammation (rheumatoid arthritis, lupus erythematosus, cancer, tuberculosis). Serum iron is low, but so is TIBC (thus, the % saturation may be nearly normal). Serum ferritin is elevated (because ferritin is an acute-phase reactant, the level should be increased). Treat the underlying disorder to correct the anemia. Do not give iron!

11. **Spherocytosis** (normochromic): look for spherocytes, family history (autosomal dominant), splenomegaly, **positive osmotic fragility test**, and increased mean corpuscular hemoglobin concentration. Treatment often involves splenectomy. Spherocytes also may be seen in extravascular hemolysis, but the osmotic fragility test is normal.

12. **Chronic renal disease:** the kidney produces erythropoietin; thus, you may give erythropoietin in end-stage renal disease to correct the anemia.

13. **Aplastic anemia:** usually idiopathic; may be caused by chemotherapy, radiation, malignancy (especially leukemias), benzene, and medications (chloramphenicol, carbamazepine, phenylbutazone, sulfa drugs, zidovudine, and gold). Look for decreased white blood cells and platelets to accompany anemia. Stop any possible causative medication; then try antithymocyte globulin or bone marrow transplant.
14. **Myelophthisic anemia:** usually due to myelodysplasia/myelofibrosis or malignant invasion and destruction of bone marrow (most common cause). Look for marked anisocytosis (different size), poikilocytosis (different shape), nucleated RBCs, giant and/or bizarre-looking platelets, and teardrop-shaped RBCs on the peripheral smear. A bone marrow biopsy is usually done and may reveal no cells ("dry tap" because marrow is fibrotic) or malignant-looking cells.
15. **G-6-PD deficiency:** X-linked recessive (males affected); most common in blacks and Mediterraneans. Look for sudden hemolysis or anemia after fava bean or drug exposure (antimalarials, salicylates, sulfa drugs), or after infection or diabetic ketoacidosis. Heinz bodies and bite cells also are seen on peripheral smear. Diagnosis is made with RBC enzyme assay. Do *not* perform the assay immediately after hemolysis—you may get a false-negative result because all of the older RBCs already have been destroyed and the younger RBCs are not affected. Treat by avoiding precipitating foods and medications. Discontinue the triggering medication first!
16. **Other causes:** endocrine failure (especially pituitary and thyroid); mechanical valves (which hemolyze RBCs); disseminated intravascular coagulation, thrombotic thrombocytopenic purpura, and hemolytic uremic syndrome (look for schistocytes/RBC fragments and appropriate other findings); other hemoglobinopathies (hemoglobins C and E fairly common); paroxysmal nocturnal or cold hemoglobinuria; *Clostridium perfringens*, malaria, babesiosis, and hypersplenism (always accompanied by splenomegaly and often by low platelets and white blood cells).

Transfusions: always based on clinical grounds. Treat the patient, not the lab value; there is no such thing as a "trigger value" for transfusion. Different blood components have different indications:

1. Whole blood: used only for rapid, massive blood loss or exchange transfusions (poisoning, thrombotic thrombocytopenic purpura)
2. Packed RBCs: used instead of whole blood when the patient needs a transfusion
3. Washed RBCs: free of traces of plasma, whtie blood cells, and platelets; good for IgA deficiency and allergic or previously sensitized patients
4. Platelets: given for symptomatic thrombocytopenia (usually < 10,000/μl)
5. Granulocytes: rarely used for neutropenia with sepsis caused by chemotherapy
6. Fresh frozen plasma: contains all clotting factors; used for bleeding diathesis when one cannot wait for vitamin K to take effect (disseminated intravascular coagulation, severe warfarin poisoning) or vitamin K will not work (liver failure).
7. Cryoprecipitate: contains fibrinogen and factor 8; used in hemophilia, von Willebrand disease, and disseminated intravascular coagulation

The most common cause of **blood transfusion reaction** is lab error. Type O negative can be used when you cannot wait for blood typing or the blood bank does not have the patient's type. If a transfusion reaction occurs, the first step is to *stop the transfusion!* Look for febrile reaction (chills, fever, headache, back pain) from antibodies to white blood cells; hemolytic reaction

(anxiety, discomfort, dyspnea, chest pain, shock, jaundice) from antibodies to RBCs; or allergic reaction (urticaria, edema, dizziness, dyspnea, wheezing, anaphylaxis) to an unknown component in the donor serum. Patients with associated oliguria should be treated with IV fluids and diuresis (mannitol or furosemide). Massive transfusions may lead to bleeding diathesis from thrombocytopenia (look for oozing from puncture/IV sites) and citrate (calcium chelator). Patients also may develop hyperkalemia.

Disseminated intravascular coagulation (DIC): most commonly due to pregnancy and obstetric complications (50%), malignancy (33%), sepsis, and trauma (especially head trauma, prostate surgery, and snake bites). DIC usually manifests as bleeding diathesis. Look for the classic oozing/bleeding from puncture or IV sites, but patients may have thrombotic tendencies. Look for prolonged prothrombin time (PT), parital thromboplastin time (PTT), and bleeding time (BT); positive D-dimer and increased fibrin degradation products; thrombocytopenia; and decreases in fibrin and clotting factors (including factor 8, which is normal in hepatic necrosis). Treat the underlying cause (evacuate uterus, give antibiotics). Patients may need transfusions, fresh frozen plasma, or, rarely, heparin (only in the presence of thrombosis).

Eosinophilia: causes include idiopathic etiology, allergy, eczema, atopy, angioedema, drug reactions, parasitic infections, blood dyscrasias (especially lymphoma), Loffler's syndrome (pulmonary eosinophilia), autoimmune diseases (e.g., lupus erythematosus, rheumatoid arthritis, inflammatory bowel disease), IgA deficiency, and adrenal insufficiency.

Basophilia: think of allergies, neoplasm, or blood dyscrasia.

Bleeding problems: lupus anticoagulant may cause a prolonged PTT but the patient has a tendency toward thrombosis. Look for associated lupus, positive Venereal Disease Research Laboratory or rapid plasma reagin test for syphilis, and/or history of miscarriages. Deficiencies in protein C, protein S, or antithrombin III also may cause increased tendency toward thrombosis. Patients are treated with anticoagulant therapy to prevent deep venous thrombosis, pulmonary embolism, and other complications.

Clotting tests: PT for extrinsic system (prolonged by warfarin), PTT for intrinsic system (prolonged by heparin), and BT for platelet function:

DISEASE	PT	PTT	BT	PLATELET NO.	RBC NO.	OTHER
von Willebrand	Normal	High	High	Normal	Normal	Autosomal dominant (look for family history)
Hemophilia A/B	Normal	High	Normal	Normal	Normal	X-linked recessive; A = low factor 8, B = low factor 9
DIC	High	High	High	Low	Normal/low	Appropriate history, low factor 8 level
Liver failure	High	High	Normal	Normal/low	Normal/low	Jaundice, normal factor 8 level; do not give vitamin K!
Heparin	Normal	High	Normal	Normal/low	Normal	Watch for thrombocytopenia, thrombosis
Warfarin	High	Normal	Normal	Normal	Normal	Vitamin K antagonist (factors 2, 7, 9, and 10)
ITP	Normal	Normal	High	Low	Normal	Watch for preceding upper respiratory infection
TTP	Normal	Normal	High	Low	Low	Hemolysis (smear), CNS symptoms; treat with plasmapheresis; do not give platelets!
Scurvy	Normal	Normal	Normal	Normal	Normal	Fingernail, gum, and bone hemorrhages

DIC = disseminated intravascular coagulation, ITP = idiopathic thrombocytopenic purpura, TTP = thrombotic thrombocytopenic purpura, CNS = central nervous system.

Thrombocytopenia may be caused by idiopathic thrombocytopenic purprua, thrombotic thrombocytopenic purpura, hemolytic uremic syndrome, disseminated intravascular coagulation,

HIV, splenic sequestration, heparin (treat by first stopping heparin), other medications (especially quinidine and sulfa drugs), autoimmune disease, and alcohol. Bleeding from thrombocytopenia is in the form of petechiae, nose bleeds, and easy bruising.

Note: Do not give platelets to a patient with thrombotic thrombocytopenic purpura or heparin-associated thrombocytopenia. They may cause thrombosis.

Vitamin C deficiency (scurvy) may cause bleeding similar to that seen with low platelets (splinter and gum hemorrhages, petechiae); perifollicular and subperiosteal hemorrhages are unique to scurvy. Patients have a poor dietary history (the classic example is hot dogs and soda), myalgias and arthralgias, and capillary fragility. Bleeding is due to collagen problems in vessels. Treat with oral vitamin C.

Bleeding tendency also may be due to inherited connective tissue disorder (Ehlers-Danlos syndrome, Marfan syndrome, pseudoxanthoma elasticum, osteogenesis imperfecta) or **chronic steroid use**, but it is rarely a clinical problem.

CHAPTER 9

Oncology

Blood Dyscrasias

TYPE	AGE (YR)	WHAT TO LOOK FOR IN CASE DESCRIPTION/TRIGGER WORDS
Acute lymphoblastic leukemia	Children (peak = 3–5)	Pancytopenia (bleeding, fever, anemia), history of radiation exposure, Down syndrome
Acute myeloid leukemia	> 30	Pancytopenia (bleeding, fever, anemia), Auer rods, disseminated intravascular coagulation
Chronic myelocytic leukemia	30–50	White blood cell count>50,000, Philadelphia chromosome, blast crisis, splenomegaly
Chronic lymphocytic leukemia	> 50	Male sex, lymphadenopathy, lymphocytosis, infections, smudge cells, splenomegaly
Hairy cell leukemia	Adults	Blood smear (hair-like projections), splenomegaly
Mycosis fungoides/Sézary syndrome	> 50	Plaque-like, itchy skin rash that fails to improve with treatment, blood smear (cerebriform nuclei, also called "butt cells"), Pautrier's abscesses in epidermis
Burkitt's lymphoma	Children	Associated with Epstein-Barr virus (in Africa)
Central nervous system B-cell lymphoma	Adults	Human immunodeficiency virus/AIDS
T-cell leukemia	Adults	Human T-cell leukemia virus-1 is a cause
Hodgkin's disease	15–34	Reed-Sternberg cell, cervical lymphadenopathy, night sweats
Non-Hodgkin's lymphoma	Any age	Small, follicular type has best prognosis; large, diffuse type is worst, GI tract may be location of primary tumor
Myelodysplasia/myelofibrosis	> 50	Anemia, **teardrop cells**, "dry tap" on bone marrow biopsy, high mean corpuscular volume and red blood cell distribution width index, associated with chronic myelocytic leukemia
Multiple myeloma	> 40	Bence-Jones protein (IgG = 50%, IgA = 25%), osteolytic lesions, high calcium
Waldenström's macroglobulinemia	> 40	Hyperviscosity, IgM spike, cold agglutinins (Raynaud's phenomenon with cold sensitivity)
Polycythemia vera	> 40	High hematocrit, hemoglobin, pruritus (especially after hot bath or shower); use phlebotomy
Thrombocythemia	> 50	Platelet count usually > 1,000,000; may have bleeding or thrombosis

Cancer Statistics (See table, top of next page)

Important points:

1. In children and younger adults, leukemia is the most common cancer. Remember, however, that *age* has the most signifigant impact on the incidence and mortality rate of cancer.

OVERALL HIGHEST INCIDENCE		OVERALL HIGHEST MORTALITY	
MALE	FEMALE	MALE	FEMALE
1. Prostate	1. Breast	1. Lung	1. Lung
2. Lung	2. Lung	2. Prostate	2. Breast
3. Colon	3. Colon	3. Colon	3. Colon

The incidence of cancer in the U.S. roughly doubles every 5 years after age 25; therefore, cancer most commonly affects older adults.

2. In most organs, the most common malignancy is *metastatic*. Do not be fooled into saying that hepatocellular cancer is the most common malignancy of the liver if metastatic cancer is a choice. Unless the question specifically asks for a primary tumor, do *not* assume that a primary tumor is the answer.
3. Metastases to the spine can cause cord compression (local spinal pain, reflex changes, weakness, sensory loss, paralysis). Cord compression is an emergency, and the first step is to start high-dose corticosteroids. Then get an MRI. The next step is to treat with radiation. Surgical decompression is used if radiation fails or the tumor is known not to be radiosensitive. Prompt intervention is essential, and outcome is closely linked to pretreatment function.

Genetic predisposition to cancer

DISEASE/SYNDROME	INHERITANCE	TYPE OF CANCER (IN ORDER OF MOST LIKELY)/OTHER INFORMATION
Retinoblastoma	Autosomal dominant	Retinoblastoma, osteogenic sarcoma (later in life)
MEN, type I	Autosomal dominant	Parathyroid, pituitary, pancreas (islet cell tumors)
MEN, type IIa	Autosomal dominant	Thyroid (medullary cancer), parathyroid, pheochromocytoma
MEN, type IIb	Autosomal dominant	Thyroid (medullary cancer), pheochromocytoma, mucosal neuromas
Familial polyposis coli	Autosomal dominant	Hundreds of colon polyps, which *always* become colon cancer
Gardner syndrome	Autosomal dominant	Familial polyposis plus osteomas and soft tissue tumors
Turcot syndrome	Autosomal dominant	Familial polyposis plus central nervous system tumors
Peutz-Jeghers syndrome	Autosomal dominant	Look for perioral freckles and multiple noncancerous GI polyps; increased incidence of noncolon cancer (stomach, breast, ovaries, no increased risk of colon cancer)
Neurofibromatosis, type 1	Autosomal dominant	Multiple neurofibromas, café-au-lait spots; increased number of pheochromocytomas, bone cysts, Wilms' tumor, leukemia
Neurofibromatosis, type 2	Autosomal dominant	Bilateral acoustic neuromas
Tuberous sclerosis	Autosomal dominant	Adenoma sebaceum, seizures, mental retardation, glial nodules in brain; increased renal angiomyolipomas and cardiac rhabdomyomas
Von Hippel-Lindau disease	Autosomal dominant	Hemangiomas in cerebellum, renal cell cancer, cysts in liver and/or kidney
Xeroderma pigmentosum	Autosomal recessive	Skin cancer
Albinism	Autosomal recessive	Skin cancers
Down syndrome	Trisomy 21	Leukemia

MEN = multiple endocrine neoplasia.

Other diseases with increased incidence of cancer are immunodeficiency syndromes, Bloom syndrome, and Fanconi anemia. Breast, ovarian, and colon cancer have well-known familial tendencies (along with some other types of cancer), but rarely can a Mendelian inheritance pattern be demonstrated (yet).

Avoidable risk factors for cancer development

CANCER TYPE	AVOIDABLE RISK FACTOR (GREATEST IMPACT LISTED FIRST)
Lung	Smoking, asbestos (also nickel, radon, coal, arsenic, chromium, uranium)
Mesothelioma	Asbestos
Leukemia	Chemotherapy, radiotherapy, other immunosuppressive drugs, benzene
Bladder	Smoking, aniline dyes (rubber and dye industry), schistosomiasis (in immigrants)
Skin	Ultraviolet light exposure (e.g., sun), coal tar, arsenic
Liver	Alcohol, vinyl chloride (liver angiosarcomas), aflatoxins
Oral cavity	Smoking, alcohol
Pharynx/larynx	Smoking, alcohol
Esophagus	Smoking, alcohol
Pancreas	Smoking
Renal cell	Smoking
Stomach	Alcohol, nitrosamines, nitrites (from smoked meats and fish)
Clear cell cancer	Mothers should avoid diethylstilbestrol (DES) during pregnancy
Colorectal	High-fat and low-fiber diet
Breast	High-fat and low-fiber diet
Cervical	Smoking, sex, high parity
Thyroid	Childhood head, neck,or chest irradiation
Endometrial	Unopposed estrogen stimulation, obesity
All cancer overall	Smoking (second is probably alcohol)

LUNG CANCER

Lung cancer is the number-one cause of overall cancer mortality in the U.S. The incidence is rising in women (due to increased smoking). Look for change in a chronic cough in a smoker. The more pack years of tobacco use, the more suspicious you should be. Patients also may present with hemoptysis, pneumonia, and/or weight loss. Chest x-ray may show pleural effusion; put a needle in the fluid and examine for malignant cells. After chest x-ray, get a tissue biopsy to confirm the diagnosis and define the histologic type. Non-small cell cancer may be treated with surgery if the cancer remains within the lung parenchyma. Small cell cancer is treated with chemotherapy only; early metastases make surgery inappropriate.

Weird and frequently tested consequences of lung cancer:

1. Horner's syndrome: from invasion of cervical sympathetic chain by an apical (Pancoast) tumor. Look for **unilateral** ptosis, miosis, and anhidrosis (no sweating)
2. Diaphragm paralysis: from phrenic nerve involvement
3. Hoarseness: from recurrent laryngeal nerve involvement
4. Superior vena cava syndrome: look for edema and plethora (redness) of the neck and face and central nervous system symptoms (headache, visual symptoms, altered mental status); due to compression of superior vena cava with impaired venous drainage
5. Cushing's syndrome: from adrenocorticotropic hormone production by a small cell carcinoma
6. Syndrome of inappropriate secretion of antidiuretic hormone: from anitdiuretic hormone production by a small cell carcinoma

7. Hypercalcemia: from bone metastases or production of parathyroid hormone by a squamous cell carcinoma
8. Eaton-Lambert syndrome: myasthenia gravis-like disease due to lung cancer that spares the ocular muscles; the muscles become stronger with repetitive stimulation (opposite of myasthenia gravis)

Solitary pulmonary nodule on chest x-ray: the first step is **comparison with previous chest x-rays**. If the nodule has remained the same size for > 2 years, it is not cancer. If no old films are available and patient is older than 35 or has a long smoking history, get a biopsy of the nodule (via bronchoscopy or transthoracic biopsy if possible) for tissue diagnosis. If the patient is younger than 35 or has no smoking history, the cause is most likely infectious (tuberculosis or fungi), hamartoma, or collagen vascular disease. The patient may undergo careful observation and follow-up with repeat chest x-ray.

BREAST CANCER

Incidence: roughly 1 in 10 women will develop breast cancer in their lifetime.

Risk factors for breast cancer:

1. History of breast cancer (biggest risk factor)
2. Family history in first-degree relatives
3. Age (breast cancer is rare before age 30; the incidence increases with age). Greatest risk in women > 75 years old.
4. Early menarche, late menopause, and late first pregnancy or nulliparity (more menstrual cycles = more risk)
5. Atypical hyperplasia of the breast
6. Radiation exposure before age 30
7. Prolonged use of oral contraceptive pills (> 5 years) only if nulliparous or before first pregnancy (controversial)

Signs and symptoms that suggest a mass is breast cancer until proved otherwise: fixation of breast mass to the chest wall or overlying skin, satellite nodules or ulcers on the skin, lymphedema/peau d'orange, matted or fixed axillary lymph nodes, inflammatory skin changes (red, hot skin with enlargement of the breast due to inflammatory cancer), prolonged unilateral scaling erosion of the nipple with or without discharge (may be Paget's disease of the nipple), microcalcifications on mammography, and *any new breast mass in a postmenopausal woman.*

The **conservative approach** is to biopsy every palpable breast mass in women over 35 when in doubt, especially if they have any risk factors. If the board question does not want you to biopsy the mass, it will give you clues that it is not cancer (e.g., bilateral, lumpy breasts that become symptomatic with every menses and have no dominant mass, age < 30).

Important points:

1. In women under 30, breast cancer is extremely rare. With a discrete breast mass in this age group, think of fibroadenoma and observe the patient over a few menstrual cycles before considering biopsy. Fibroadenomas are usually roundish, rubbery-feeling, and freely movable.
2. The most common histologic type of breast cancer is invasive ductal carcinoma.

3. In patients with a palpable breast mass, the decision to do a biopsy is a *clinical* one. A mammogram that looks benign should not deter you from doing a biopsy. On the other hand, a lesion that is detected on mammography and looks suspicious should be biopsied, even if not palpable (needle localization biopsy).
4. Do not do mammograms in women under 35 (breast tissue too dense to see cancer).
5. Tamoxifen (or other endocrine therapy) generally improves survival if the tumor is estrogen receptor-positive (ER+) and even more so if the tumor is also progesterone receptor-positive (PR+).
6. Mastectomy and breast-conserving surgery plus radiation are considered equal in efficacy. In either case, do an axillary node dissection to determine spread to the nodes. If nodes are positive, give chemotherapy.

PROSTATE CANCER

Risk factors:

1. Age (not seen in men < 40 years old; incidence increases with age; 60% of men > 80 have prostate cancer)
2. Race: black > white > Asian

Patients present late, because early prostate cancer is asymptomatic. Look for symptoms suggestive of benign prostatic hypertrophy (hesitancy, dysuria, frequency) with hematuria and/or elevated prostate-specific antigen (PSA) or acid phosphatase. Acid phosphatase is elevated only when the cancer has broken through the capsule; for this reason, it was replaced with the more sensitive PSA as a screening tool. Look for prostate irregularities (nodule) on rectal exam. Patients also commonly present with back pain from vertebral metastases (osteoblastic).

Local prostate cancer is treated with surgery (prostatectomy). Patients with metastases have several options for hormonal therapy: orchiectomy, gonadotropin-releasing hormone agonist (leuprolide), androgen-receptor antagonist (flutamide), estrogen (diethylstilbestrol), and others (e.g., cyproterone). Chemotherapy does not work, and radiation therapy is used for local disease or pain from bony metastases.

COLORECTAL CANCER

Risk factors:

1. Age (incidence begins to increase after age 40; peak incidence between 60–75 years)
2. Family history (especially with familial polyposis or Gardner, Turcot, or Lynch syndrome)
3. Inflammatory bowel disease (ulcerative colitis > Crohn's disease, but both increase risk)
4. Low-fiber, high-fat diet (weak evidence)

Important points:

1. Patients may present with asymptomatic blood in stool (visible streaks of blood on stool or guaiac-positive), anemia with right-sided colon cancer, change in stool caliber ("pencil stool") or frequency (alternating constipation and frequency) with left-sided colon cancer. As with any cancer, look for weight loss.
2. Occult blood in the stool of a patient > 40 years old should be considered colon cancer until proved otherwise. To rule out colon cancer, either do flexible sigmoidoscopy and a

barium enema or do a total colonoscopy. If you see any lesions with a flexible sigmoidoscope or barium enema, you need to do a total colonoscopy with removal and histologic examination of all polyps/lesions. For this reason, most people now start with colonoscopy.

3. Carcinoembryonic antigen (CEA) is often elevated with colon cancer, and a preoperative level is usually measured. After surgery to remove the tumor, CEA should return to normal levels. Periodic monitoring of CEA postoperatively helps to detect recurrence before it is clinically apparent. CEA is not used as a screening tool for colon cancer; it is used only to follow known cancer.
4. Treatment is primarily surgical, with resection of involved bowel. Adjuvant chemotherapy is sometimes done with 5-fluorouracil (5-FU) and levamisole or leucovorin.
5. Colon cancer frequently metastasizes to the liver; if the metastasis is solitary, surgical resection is often attempted. With metastases elsewhere, chemotherapy is the only option. Prognosis is poor.
6. Colon cancer is a common cause of a large bowel obstruction in an adult.

PANCREATIC CANCER

- **Classic presentation:** a smoker in the 40–80-year-old range who has lost weight and is jaundiced. Symptoms may include epigastric pain, migratory thrombophlebitis (Trousseau syndrome, which also may be seen with other visceral cancer), or a palpable, nontender gallbladder (Courvoisier's sign)
- **Epidemiology:** males > females, diabetics > nondiabetics, blacks > whites
- **Surgery** (Whipple procedure): rarely curative; the prognosis is dismal
- **Cell of origin:** ductal epithelium

Islet cell tumors:

1. Insulinoma (beta cell tumor): most common islet cell tumor. Look for two-thirds of Whipple's triad: hypoglycemia (glucose < 50 mg/dl) and central nervous system symptoms due to hypoglycemia (confusion, stupor, loss of consciousness). As *the good doctor*, you will provide the third part of Whipple's triad: give glucose to relieve symptoms. Ninety percent of insulinomas are benign and cured with resection, if possible. In your work-up, take history and check C-peptide first to make sure that the patient is not a diabetic who accidentally took too much insulin or a patient with factitious disorder. C-peptide is high with insulinoma, low with other conditions.
2. Gastrinoma: Zollinger-Ellison syndrome is gastrinoma plus acid hypersecretion and peptic ulcer disease (gastrin causes acid secretion). Peptic ulcers are often multiple and resistant to therapy; they may be in an unusual location (distal duodenum or jejunum). More than one-half are malignant.
3. Glucagonoma (alpha cell tumor): hyperglycemia with high glucagon level and migratory necrotizing skin erythema.

OVARIAN CANCER

Ovarian cancer usually presents late with weight loss, pelvic mass, ascites, and/or bowel obstruction in a postmenopausal woman. Any ovarian enlargement in a postmenopausal woman is cancer until proved otherwise. In women of reproductive age, most ovarian enlargements are

benign. Ultrasound is a good first test to evaluate an ovarian lesion. Treatment includes debulking surgery and chemotherapy; prognosis is usually poor. Most ovarian cancer arises from ovarian epithelium. Serous cystadenocarcinoma, the most common ovarian cancer, often has psammoma bodies on histopathology.

Germ cell tumors make good questions:

1. Teratoma/dermoid cyst: look for a description of the tumor to include skin, hair, and/or teeth/bone; may show up on x-ray.
2. Sertoli-Leydig cell tumor: causes virilization (hirsutism, receding hairline, deepening voice, clitoromegaly).
3. Granulosa/theca-cell tumor: causes feminization and precocious puberty.

Terms worth knowing:

- Meig's syndrome: ovarian fibroma, ascites, and right hydrothorax.
- Krukenberg's tumor: stomach cancer with metastases to both ovaries.

Note: Oral contraceptives have been shown to reduce the incidence of ovarian cancer by 50%; they also reduce endometrial cancer.

CERVICAL CANCER

Papanicolaou smears decrease the incidence and mortality of cervical cancer. Give female patients a Pap smear if they are due, even if they present with an unrelated complaint. Follow up any dysplastic Pap smear with colposcopy-directed biopsies and endocervical curettage. If the Pap smear shows microinvasive cancer, proceed to conization. Frankly invasive cancer needs surgery and/or radiation.

Risk factors for cervical cancer:

1. < 20 years old at first coitus, pregnancy, or marriage
2. Multiple sexual partners (role of human papillomavirus and possibly herpes) or coitus with a promiscuous person
3. Smoking
4. Low socioeconomic status
5. High parity (which protects against endometrial cancer)

Important points:

1. Invasive cervical cancer begins in the transformation zone and usually presents with vaginal bleeding or discharge (may be postcoital, intermenstrual spotting, or abnormal menstrual bleeding).
2. Treat with surgery and/or radiation.
3. Maternal exposure to diethylstilbestrol causes daughters to get clear cell cancer of the cervix or vagina.

UTERINE CANCER

Postmenopausal bleeding is cancer until proved otherwise; endometrial cancer is the most common cancer to present in this fashion (fourth most common cancer in women). Get an endometrial biopsy for any patient with postmenopausal bleeding (as well as a Pap smear and

endocervical curettage). Any woman with unexplained gynecologic bleeding that persists needs a Pap smear, endocervical curettage, and endometrial biopsy.

Risk factors for endometrial cancer:

1. Obesity
2. Nulliparity
3. Late menopause
4. Diabetes mellitus
5. Hypertension
6. Gallbladder disease
7. Chronic, unopposed estrogen stimulation, as in polycystic ovary/Stein-Leventhal syndrome, estrogen-secreting neoplasm (granulosa-theca cell tumor), and estrogen replacement (increases risk of cancer only if taken without progesterone).

Important points:

1. Oral contraceptives have been shown to reduce the incidence of uterine as well as ovarian cancer.
2. Most uterine cancer is adenocarcinoma and spreads by direct extension.
3. Treat with surgery and radiation.

MISCELLANEOUS NEOPLASMS

Brain tumors: in adults two-thirds of primary tumors (metastases are more common than primary tumors) are supratentorial, whereas in children two-thirds are infratentorial (posterior fossa/cerebellar). In either group, look for new-onset seizures, neurologic deficits, or signs of intracranial hypertension (headache, blurred vision, papilledema, projectile nausea and vomiting). In children, also look for hydrocephalus and ataxia. The most common type in adults is glioma (most are intraparenchymal astrocytomas with little or no calcification), followed by meningioma (usually calcified, external to the brain substance). In children, the most common types are cerebellar astrocytoma and medulloblastoma, followed by ependymoma. Treatment is surgical removal, which may be followed by radiation and chemotherapy, depending on the tumor. Important points to remember:

1. A young, obese woman who has headaches, papilledema, and vomiting with a negative CT/MRI has pseudotumor cerebri, not a malignancy.
2. The most common posterior fossa tumors in children are astrocytoma and medulloblastoma; in adults, it is acoustic neuroma (watch for neurofibromatosis).
3. In children, watch for craniopharyngioma (a remnant of Rathke's pouch). It is heavily calcified and shows up on skull x-ray (most likely tumor in children if it shows up on skull x-ray).

Testicular cancer: the most common solid malignancy in men < 30 years old. The main risk factor is cryptorchidism. Transillumination and ultrasound help to distinguish hydrocele (fluid-filled, transilluminates) from cancer (solid). The most common type is seminoma (radiosensitive).

Sarcoma botryoides: female child with a "bunch of grapes" coming out of her vagina.

Pituitary tumors: look for bitemporal hemianopsia (order an MRI if the patient has it). The most common type is prolactinoma (high prolactin levels with galactorrhea and menstrual/sexual dysfunction). Other types may cause Cushing's disease or hyperthyroidism.

Nasopharyngeal cancer: seen in Asians; remember association with Epstein-Barr virus.

Esophageal cancer: weight loss, possible anemia, and complaints that "my food is sticking," which progress to dysphagia for liquids in a chronic smoker and drinker (blacks > whites). Patients present late, because early cancer is asymptomatic. The most common type is squamous cell. Barrett's esophagus (columnar metaplasia of esophageal squamous epithelium due to acid reflux) may give rise to adenocarcinoma of the esophagus, and the incidence is increasing.

Thyroid cancer: the patient presents with a nodule in the thyroid gland. Be suspicious of cancer in any of the following scenarios: "cold nodule" on nuclear scan, male patient, history of childhood irradiation, nodule described as "stony hard,"recent or rapid enlargement, and increased calcitonin level (medullary thyroid cancer—usually in patients with multiple endocrine neoplasia type II). To evaluate a nodule in the thyroid, get thyroid function tests. Thyroid-stimulating hormone is the best screening test; "toxic" or functional nodules are unlikely to be cancer. On a nuclear scan, a "cold" nodule or area of decreased uptake is more suspicious than normal/increased uptake. Consider fine-needle aspiration or open biopsy.

Bladder cancer: look for persistent, painless hematuria. Patients often are smokers or work in the rubber/dye industry (aniline dye exposure). Cystoscopy is usually done first to evaluate a potential bladder cancer.

Liver tumors: hepatocellular cancer is caused by alcohol, hepatitis, and anything else that causes cirrhosis (hemochromatosis is especially known to cause liver cancer). Hepatitis C is more likely to cause cancer in the chronic setting than hepatitis B. For hepatitis B, the best prevention is proper vaccination; for hepatitis C, the best prevention is avoidance of blood transfusions. Alpha-fetoprotein is often elevated and can be measured postoperatively to detect recurrences. Patients have a history of alcoholism, hepatitis, and/or hemochromatosis or other causes of cirrhosis and present with weight loss, right upper quadrant pain, and an enlarged liver. Surgery is the only hope for cure; prognosis is poor. Other tumors of the liver:

1. Hemangioma: the most common primary tumor of the liver; generally left alone. Surgery is done if the patient is symptomatic.
2. Hepatic adenoma: women of reproductive age taking oral contraceptives. Stop the pills! (The cancer may regress.)
3. Cholangiosarcoma: 50% of patients have a history of ulcerative colitis; liver flukes (*Clonorchis*) may be found in immigrants.
4. Angiosarcoma: look for industrial exposure to vinyl chloride.
5. Hepatoblastoma: the main primary liver tumor in children.

Adrenal tumors: may be functional and cause primary hyperaldosteronism (Conn's syndrome) or hyperadrenalism (Cushing's disease). Patients also may have a pheochromocytoma (intermittent, severe hypertension with mental status changes, headaches, and diaphoresis). Check 24-hour urine catecholamines (vanillylmandelic acid, homovanillic acid).

Stomach cancer: risk factors are Japanese race, increasing age, smoking, and consumption of smoked meat. *Helicobacter pylori* also is implicated. Krukenberg's tumor is stomach cancer with bilateral ovarian metastases. Virchow's node is left supraclavicular node enlargement due to visceral cancer spread (classically stomach cancer). If a gastric ulcer is seen on upper GI barium series or endoscopy, it *must* be biopsied to exclude malignancy.

Osteosarcoma: 10–30-year-olds; recognize x-ray findings ("sunburst" appearance in distal femur or proximal tibia).

Carcinoid tumors: the most common location is the small bowel, but carcinoid is the most common appendiceal tumor. The liver breaks down serotonin and other vasoactive secreted substances to make the tumor asymptomatic, but when carcinoid metastasizes to the liver and vasoactive products reach the systemic circulation, symptoms begin (carcinoid syndrome): episodic cutaneous flushing, abdominal cramps, diarrhea, and right-sided heart valve damage. Urinary 5-hydroxyindoleacetic acid (5-HIAA) is increased (a product of serotonin breakdown).

Kaposi's sarcoma: in HIV-positive patients; a vascular skin tumor that starts as a papule or plaque, commonly on the upper body or in the oral cavity. The classic description is a rash that does not respond to multiple treatments.

Skin cancer: ultraviolet light increases risk of basal, squamous, and melanoma skin cancer. The **ABCDs** of melanoma should make you suspicious of malignancy. Biopsy any lesion with any of these characteristics: **a**symmetry, **b**orders (irregular), **c**olor (change in color or multiple colors), or **d**iameter (the bigger the lesion, the more likely that it is malignant). Know the classic appearance of basal cell cancer (pearly, umbilicated, telangiectasias). Basal cell cancer is extremely common and almost never metastasizes. Squamous cancer rarely metastasizes, whereas melanoma commonly metastasizes. Biopsy any suspicious lesion (excisional biopsy).

Wilms' tumor vs. neuroblastoma: both present as flank masses in children at a peak age of around 2 years old. The classic way to differentiate the two (although you should always get a tissue diagnosis to make sure) is intravenous pyelography: neuroblastomas tend not to distort the calyces of the kidney (most come from the adrenal gland), whereas Wilms' tumor arises in the kidney and thus distorts the calyceal architecture. Rarely, neuroblastomas may regress spontaneously (for unknown reasons).

Oral cancer: due to smoking or chewing tobacco and drinking; also look for poor oral hygiene. Oral cancer often starts as leukoplakia (know the appearance), which must be differentiated from oral hairy leukoplakia, which is associated with Epstein-Barr virus and affects HIV-positive patients.

Histiocytosis: CD1-positive, Birbeck granules (cytoplasmic inclusion bodies that look like tennis rackets).

Unicameral bone cyst: expansile, lytic, well-demarcated lesion in the proximal portion of the humerus in children and adolescents. It is benign but may weaken bone enough to cause a pathologic fracture.

Retinoblastoma: leukocoria in a young child (red reflex is white with a penlight) or unilateral exophthalmos; inherited form may be bilateral.

Note: Patients with cancer, like all others, have the right to refuse treatment. However, watch for and treat depression, even in terminal patients.

Tumor markers *101*

MARKER	CANCER(S)	MARKER	CANCER(S)
Alpha-fetoprotein	Liver, testicular (yolk-sac)	Human chorionic gonadotropin	Hydatiform moles, choriocarcinoma
Carcinoembryonic antigen	Colon, pancreas, other GI tumors	CA-125	Ovarian
Prostate-specific antigen	Prostate (early)	S-100	Melanoma, central nervous system/nerve tumors
Acid phosphatase	Prostate (only with extension outside the capsule)	CA 19-9	Pancreas

CHAPTER 10

Infectious Disease

Empiric therapy while awaiting culture and sensitivity results

CONDITION	MAIN BUG(S)	EMPIRIC ANTIBIOTIC(S)
Urinary tract infection	*Escherichia coli*	Trimethoprim-sulfamethoxazole, nitrofurantion, amoxicillin, quinolones
Bronchitis	Viral, *Mycoplasma* sp., *Haemophilus influenzae*	Amoxicillin, erythromycin
Pneumonia—classic type	*Streptococcus pneumoniae, H. influenzae*	Penicillin (for boards), cephalosporin, erythromycin
Pneumonia—atypical	*Mycoplasma* sp., *Chlamydia* sp.	Erythromycin, third-generation cephalosporin
Osteomyelitis	*Staphylococcus aureus, Salmonella* sp.	Antistaphylococcal penicillin,* vancomycin
Cellulitis	Streptococci, staphylococci	Antistaphylococcal penicillin* (covers both bugs)
Meningitis—neonate	Streptococci B, *E. coli, Listeria* sp.	Ampicillin + aminoglycoside, third-generation cephalosporin
Meningitis—child/adult	*S. pneumoniae, Neisseria meningitidis*†	Penicillin/amoxicillin + chloramphenicol, third-generation cephalosporin
Sepsis	Gram-negative, streptococci, staphylococci	Third-generation penicillin/cephalosporin + aminoglycoside, imipenem
Tuberculosis	*Mycobacterium tuberculosis*	Isoniazide + rifampin for 6–12 months, add ethambutol/pyrazinamide in immunocompromised patient
Septic arthritis‡	*S. aureus* Gonococci	Antistaphylococcal penicillin, vancomycin Ceftriaxone, penicillin, spectinomycin
Endocarditis	Staphylococci, streptococci	Antistaphylococcal penicillin (or vancomycin) + aminoglycoside

* Examples: dicloxacillin, methicillin.
† *Haemophilus influenzae* type b is no longer a common cause of meningitis in children because of widespread vaccination. If there is no history of vaccination, *H. influenzae* is the most likely cause of meningitis in a child.
‡ Think of staphylococci if the patient is not sexually active or is monogamous. Think of gonorrhea for younger adults who are sexually active and/or promiscuous.

Empiric antibiotics of choice for different bugs (always use culture sensitivities to guide therapy if available.) (See figure, top of next page.)

Staining hints:

- Gram-positive organisms are blue/purple; gram-negative organisms are red.
- Gram-positive cocci in chains = streptococci
- Gram-positive cocci in clusters = staphylococci
- Gram-positive cocci in pairs (diplococci) = *Streptococcus pneumoniae*
- Gram-negative coccobacilli (small rods) = *Haemophilus* sp.

BUG	ANTIBIOTIC	OTHER CHOICES
Streptococci A or B	Penicillin	Erythromycin
Enterococci	Penicillin + aminoglycoside	Vancomycin + aminoglycoside
Gonococci	Ceftriaxone	Penicillin
Haemophilus sp.	Second- or third-generation cephalosporin	Ampicillin
Bacteroides sp.	Metronidazole	Clindamycin
Treponema sp.	Penicillin	Erythromycin
Escherichia coli	Third-generation cephalosporin	Aminoglycoside
Rickettsia sp.	Tetracycline	Erythromycin
Mycobacterium tuberculosis	Isoniazid/rifampin	Ethambutol, pyrazinamide
Streptococcus pneumoniae	Penicillin	Erythromycin, third-generation cephalosporin
Staphylococci	Antistaphylococcal penicillin	Vancomycin (MRSA)
Meningococcus	Penicillin/ampicillin	Cefotaxime, chloramphenicol
Pseudomonas sp.	Penicillin + aminoglycoside	Aztreonam, imipenem
Mycoplasma sp.	Erythromycin	Tetracycline
Chlamydia sp.	Tetracycline	Erythromycin
Borrelia sp.	Tetracycline	Erythromycin
Klebsiella sp.	Third-generation cephalosporin	Third-generation penicillin + aminoglycoside

MRSA = methicillin-resistant *S. aureus*.

- Gram-negative diplococci = *Neisseria* (gonorrhea, septic arthritis, meningitis) or *Moraxella* sp. (lungs, sinusitis)
- Gram-negative rod that is plump and has thick capsule (mucoid appearance) = *Klebsiella* sp.
- Gram-positive rods that form spores = *Clostridium*, *Bacillus* spp.
- Pseudohyphae = *Candida* sp.
- Acid-fast organisms = *Mycobacterium tuberculosis*, *Nocardia* sp.
- Gram-positive oragnism with sulfur granules = *Actinomyces* sp. (pelvic inflammatory disease in women who use intrauterine devices; rare cause of neck mass/cervical adenitis)
- Silver-staining = *Pneumocystis carinii* (PCP) and cat-scratch disease
- Positive India ink preparation (thick capsule) = *Cryptococcus* sp.
- Spirochete = *Treponema*, *Leptospira* spp. (both seen only on dark-field microscopy), *Borrelia* sp. (regular light microscope)

Pneumonia: look for classic clues to differentiate. The gold standard for diagnosis is sputum culture; do blood cultures, too:

1. *Streptococcus pneumoniae*: most common cause, especially in older adults. Look for rapid onset of shaking chills after an upper respiratory infection, then fever, pleurisy, and productive cough (yellowish-green or rust-colored from blood). X-ray shows lobar consolidation. White blood cell count is high, with large percentage of neutrophils. Give vaccine to patients older than 65 yr, splenectomized patients, patients with sickle cell disease, immunocompromised patients (HIV, malignancy, organ transplant), and all patients with chronic disease (diabetes mellitus, cardiac, pulmonary, renal, or liver disease). For board questions, penicillin is still the empiric drug of choice.
2. *Haemophilus influenzae*: second only to *S. pneumoniae* as most common cause of pneumonia; more common in young children. Resembles *S. pneumoniae* clinically. Treat with

ampicillin/amoxicillin, cephalosporin, or trimethoprim/sulfamethoxazole if gram-negative coccobacilli are seen on sputum Gram stain.

3. *Staphylococcus aureus:* causes hospital-acquired pneumonia and pneumonia in patients with cystic fibrosis (second to *Pseudomonas* sp.), intravenous drug abusers, and patients with chronic granulomatous disease (look for recurrent lung abscesses). Empyema and lung abscesses are relatively common. Cultures usually are positive.
4. Gram-negative organisms: *Pseudomonas* sp. classically is associated with cystic fibrosis; *Klebsiella* sp. is classic cause in skid-row alcoholics and homeless people; enteric gram-negative organisms (e.g., *E. coli*) are common with aspiration, neutropenia and hospital-acquired pneumonia. High mortality rate because of patients affected and severity of pneumonia (abscesses common). Treat empirically with third-generation penicillin/cephalosporin plus aminoglycoside.
5. *Mycoplasma* sp: most common in adolescents and young adults (the classic case is a college student who lives in the dorm and has sick contacts). Called "atypical" penumonia because it is different from *S. pneumoniae*, with long prodrome and gradual worsening of malaise, headaches, dry nonproductive cough, and sore throat. Chest x-ray shows a patchy, diffuse bronchopneumonia (the x-ray classically looks terrible, although the patient does not feel that bad). Look for positive cold-agglutinin antibody titers (may cause hemolysis/anemia). Empiric treatment of "atypical" pneumonia is erythromycin.
6. *Chlamydia pneumoniae:* second only to *Mycoplasma* sp. as cause of pneumonia in adolescents and young adults; presents similarly but has negative cold-agglutinin antibody titers.
7. Viral pneumonia: viruses commonly cause respiratory infections (respiratory syncytial virus, influenza, parainfluenza, adenovirus)
8. *Pneumocystis carinii* pneumonia (PCP) and cytomegalovirus (CMV): always suspect in HIV-positive patients. PCP is more common; bronchoalveolar lavage often is required to obtain the diagnosis. PCP shows up with silver stains—know what it looks like. Treat with trimethoprim/sulfamethoxazole; the alternative is pentamidine. PCP is acquired when the CD4 count is below 200, at which point you should institute PCP prophylaxis in an HIV-positive patient. CMV has intracellular inclusion bodies. Treat with ganciclovir; foscarnet is an alternative.

Classic infectious disease questions:

- Patient stuck with thorn or gardener: *Sporothrix schenckii* (a fungus). Treat with oral potassium iodide or ketoconazole.
- Aplastic crisis in sickle cell disease or other hemoglobinopathy: parvovirus B19
- Sepsis after splenectomy (or autosplenectomy in sickle cell disease): *S. pneumoniae, H. influenzae, N. meningitidis* (encapsulated bugs)
- Pneumonia in the Southwest (California, Arizona): *Coccidioides immitis.* Treat with amphotericin B.
- Pneumonia after cave exploring or exposure to bird droppings in Ohio and Mississippi River valleys: *Histoplasma capsulatum*
- Pneumonia after exposure to a parrot or exotic bird: *Chlamydia psittaci*
- Fungus ball/hemoptysis after tubercular cavitary disease: *Aspergillus* sp.
- Pneumonia in a patient with silicosis: tuberculosis
- Diarrhea after hiking or drinking from a stream: *Giardia lamblia;* cysts in stool; treat with metronidazole

- Pregnant women with cats: *Toxoplasma gondii*
- B_{12} deficiency and abdominal symptoms: *Diphyllobothrium latum*
- Seizures with ring-enhancing brain lesion on CT: *Taenia solium* (cysticercosis)
- Bladder cancer (squamous cell) in Middle East and Africa: *Schistosoma haematobium*
- Worm infection in children: *Enterobius* sp. (positive tape test, perianal itching)
- Fever, muscle pain, eosinophilia, and periorbital edema after eating raw meat: *Trichinella spiralis* (trichinosis)
- Gastroenteritis in young children: rotavirus
- Food poisoning after eating reheated rice: *Bacillus cereus*
- Food poisoning after eating raw seafood: *Vibrio parahaemolyticus*
- Diarrhea after traveling to Mexico: *Escherichia coli* (Montezuma's revenge)
- Diarrhea after antibiotics: *Clostridium difficile*; treat with metronidazole or vancomycin
- Infant paralyzed after eating honey: *Clostridium botulinum* (toxin blocks acetylcholine release)
- Genital lesions in children in the absence of sexual abuse/activity: molluscum contagiosum
- Cellulitis after cat or dog bites: *Pasteurella multocida* (treat cat and dog bites with prophylactic ampicillin)
- Slaughterhouse worker with fever: *Brucella* sp.
- Pneumonia after being in a hotel, near air conditioner or water tower: *Legionella pneumophila*; treat with erythromycin)
- Burn wound infection with blue/green color: *Pseudomonas* sp. (*S. aureus* also common, but without blue-green color)

Syphilis: screen with Venereal Disease Research Laboratory (VDRL) or rapid plasma reagin (RPR) test; if positive, confirm with fluorescent treponemal antibody, absorbed (FTA-ABS) or microhemagglutination *Treponema pallidum* (MHA-TP) test. *Treponema pallidum* also can be seen with darkfield microscopy but not with a Gram stain. Screen all pregnant women with VDRL/RPR. Treatment is penicillin; use erythromycin for penicillin allergy. Three stages:

1. Primary: look for painless chancre that resolves on its own within 8 weeks.
2. Secondary: roughly 6 weeks to 18 months after infection; look for condyloma lata, maculopapular rash (especially involving palms and soles of feet), and lymphadenopathy.
3. Tertiary: occurs years after initial infection; between secondary and tertiary stages is the latent phase, when the disease is quiet and asymptomatic. Look for gummas (granulomas in many different organs), neurologic symptoms and signs (neurosyphilis, Argyll-Robertson pupil, dementia, paresis, tabes dorsalis, Charcot joints), and/or thoracic aortic aneurysms.

Note: Watch for false-positive VDRL/RPR in patients with lupus erythematosus. For other sexually transmitted diseases, see gynecology section.

Infectious rashes (most often in children; supportive treatment only unless otherwise specified):

1. **Measles (rubeola):** look for a reason for patient not to be immunized. Koplik's spots (tiny white spots on buccal mucosa) are seen 3 days after high fever. Other symptoms include cough, runny nose, and conjunctivitis/photophobia. On the next day, the rash (maculopapular) begins on the head and neck and spreads downward to cover the trunk (cephalocaudal progression). Complications include pneumonia (giant-cell pneumonia,

especially in very young and immunocompromised patients), otitis media, and encephalitis (which may be acute or cause subacute sclerosing panencephalitis [SSPE], which usually occurs years later).

2. **Rubella (German measles):** most important because of infection in pregnant women. Screen and immunize any woman of reproductive age *before* she becomes pregnant; the vaccine contraindicated in pregnant women. Rubella is milder than measles with low fever, malaise, tender swelling of the suboccipital and postauricular nodes, and arthralgias. After a 2–3-day prodrome, the rash (maculopapular, faint) starts on the face and neck and spreads to the trunk (cephalocaudal progression). Complications include encephalitis and otitis media.

3. **Roseola infantum (exanthem subitum):** easy to recognize because of progression: high fever (may be > 40° C) with no apparent cause for 4 days (patient may get febrile seizures), then an abrupt return to normal temperature as a diffuse macular/maculopapular rash appears on the chest and abdomen. Rare in children older than 3 years, it is caused by the human herpesvirus type 6 (a DNA virus).

4. **Erythema infectiosum (fifth disease):** classic "slapped-cheek" rash (confluent erythema over the cheeks) appears around the same time as mild constitutional symptoms (low fever, malaise). One day later, a maculopapular rash appears on the arms, legs, and trunk. It is caused by parvovirus B19 (the same virus that causes aplastic crisis in sickle cell disease).

5. **Chickenpox (varicella):** the description and progression of the rash itself should lead to the diagnosis: discrete macules (usually on the trunk) turn into papules, which turn into vesicles that rupture and crust over. These changes occur within 1 day. The lesions appear in successive crops; therefore, the rash is in different stages of progression in different areas. The patient is infectious until the last lesion crusts over. A complication is infection of the lesions (streptococci, staphylococci—erysipelas, cellulitis, sepsis). The patient should be instructed to keep clean to avoid infection. Other complications include pneumonia (especially in very young children and immunocompromised adults), encephalitis, and Reye's syndrome. Do *not* give aspirin to any child with a fever unless the diagnosis requires its use. A Tzanck smear of tissue from the base of a vesicle shows multinucleated giant cells. Varicella zoster immunoglobulin (VZIG) is available for prophylaxis in patients with debilitating illness (e.g., leukemia, AIDS) if you see them within 4 days of exposure or in newborns of mothers with chickenpox. Acyclovir may be used in severe cases. The varicella zoster virus can reactivate years later to cause shingles (zoster), which is characterized by dermatomal distribution of rash. Pain and paresthesias often precede the rash.

6. **Scarlet fever:** look for a history of untreated streptococcal pharyngitis (caused only by *Streptococcus* species that produce erythrogenic toxin), followed by a sandpaper-like rash on the abdomen and trunk with classic circumoral pallor and strawberry tongue. The rash tends to desquamate once the fever subsides. Treat with penicillin to prevent rheumatic fever.

7. **Kawasaki's syndrome** (mucocutaneous lymph node syndrome): rare; usually occurs in patients younger than 5 years. Diagnostic criteria include fever > 5 days (mandatory for diagnosis); bilateral conjunctival injection; changes in the lips, tongue, or oral mucosa (strawberry tongue, fissuring, injection); changes in the extremities (desquamation, edema, erythema); polymorphous truncal rash (usually begins one day after the fever starts); and cervical lymphadenopathy. Also look for arthralgia or arthritis. The most

feared complications involve the heart (coronary artery aneurysms, congestive heart failure, arrhythmias, myocarditis, myocardial infarction). Think of Kawasaki's syndrome in the differential diagnosis of any child who has a myocardial infarction. If suspicion is high, give aspirin and IV immunoglobulin, both of which reduce cardiac lesions. Follow up with echocardiography to detect heart involvement.

8. **Infectious mononucleosis** (Epstein Barr virus [EBV] infection): look for fatigue, fever, pharyngitis, and lymphadenopathy (similar to streptococcal pharyngitis, but malaise tends to be more prolonged and pronounced). To differentiate from streptococcal disease, look for splenomegaly; hepatomegaly; atypical lymphocytes (bizarre forms that may resemble leukemia) with lymphocytosis, anemia, or thrombocytopenia; and positive serology (heterophile antibodies [e.g., monospot test] or specific EBV antibodies: VCA, EBNA). Patients may develop splenic rupture and should avoid contact sports and heavy lifting. Include HIV in the differential diagnosis. Remember the association of EBV with nasopharyngeal cancer and African Burkitt's lymphoma.
9. **Rocky Mountain spotted fever** (*Rickettsia rickettsii* infection): look for history of a tick bite (especially on the East Coast) one week before the development of high fever or chills, severe headache, and prostration or severe malaise. The rash appears roughly 4 days after symptoms on the palms/wrists and soles/ankles, rapidly spreading to the trunk and face (unique pattern of spread). Patients look very sick (disseminated intravascular coagulation, delirium) and require tetracycline and chloramphenicol immediately.
10. **Impetigo:** look for history of skin break (e.g., previous chickenpox, insect bite, scabies, cut). The rash starts as thin-walled vesicles that rupture and form yellowish crusts. The skin often is described as "weeping." Classically, lesions are on the face and tend to be localized. Impetigo is infectious; look for sick contacts. Treat with oral antistaphylococcal penicillin to cover streptococci and staphylococci, the most common causative bugs.

Endocarditis: either acute (fulminant, most commonly caused by *S. aureus*) or subacute (insidious onset, most commonly caused by *Streptococcus viridans*). Look for general signs of infection (e.g., fever, tachycardia, malaise) plus new-onset heart murmur, embolic phenomena (stroke and other infarcts), Osler's nodes (painful nodules on tips of fingers), Roth spots (round retinal hemorrhages with white centers), and septic shock (more dramatic with acute than subacute disease). Diagnosis is made by blood cultures. Empiric treatment is begun with wide-spectrum antibiotics until culture and sensitivity results are known. A third-generation penicillin or cephalosporin plus aminoglycoside is a reasonable choice. Patients more likely to be affected include IV drug abusers (who develop right-sided lesions, although left-sided lesions are much more common in the general population), patients with abnormal heart valves (prosthetic valves, rheumatic valvular disease, congenital heart defects, such as ventricular septal defect or tetralogy of Fallot), and postoperative patients (especially after genitourinary, gastrointestinal, or dental surgery). Hence the need for **prophylaxis** in susceptible people. Any patient with known valvular disease is given oral amoxicillin (erythromycin if the patient is penicillin-allergic) before and after dental procedures (to cover *S. viridans*) and IV ampicillin (vancomycin if the patient is penicillin-allergic) before and amoxicillin/gentamicin before and after gastrointestinal or genitourinary procedures (to cover enterococci). Patients with secundum atrial septal defect (the more common type) as well as patients with mitral valve prolapse and no audible murmur are *not* given endocarditis prophylaxis.

Meningitis: the highest incidence of meningitis is seen in neonates; > 75% of cases are seen in patients younger than 2 years. Thus the decision about when to do a lumbar tap is difficult, because such patients often do not have classic physical findings (Kernig's and Brudzinski's

signs). Look for lethargy, hyper- or hypothermia, poor tone, bulging fontanelle, vomiting, photophobia, altered consciousness, and signs of generalized sepsis (hypotension, jaundice, respiratory distress). Seizures may be seen, but simple febrile seizures also are possible if the patient is between 5 months and 6 years old and has a fever > 102° F in the absence of other signs of meningitis. If seizures occur in the presence of other signs of meningitis or sepsis, proceed to lumbar puncture immediately and begin broad-spectrum antibiotics immediately after the procedure. The most common neurologic sequela of meningitis is hearing loss. All patients need formal hearing evaluation after a bout of meningitis; vision testing also is recommended. Other sequelae include mental retardation, motor deficits/paresis, epilepsy, and learning/behavioral disorders.

- Mumps and measles are possible causes of aseptic (nonbacterial or culture-negative) meningitis. The best prevention is immunization.
- Watch for herpes encephalitis if the mother has herpes simplex lesions at the time of the infant's birth. Look for temporal lobe abnormalities on a CT or MRI scan of the head. Give acyclovir.
- If meningitis is due to *Neisseria* sp., give all contacts rifampin as prophylaxis.
- For cerebrospinal fluid findings in meningitis, see the neurology chapter.

Pediatric respiratory infections: the big three are croup, epiglottitis, and respiratory syncytial virus (RSV)—high yield!

1. Croup/acute laryngotracheitis: look for patient to be 1–2 years old; usually occurs in fall or winter. About 50–75% of cases are due to parainfluenza virus; the other causative agent is influenza. Patients start with symptoms of viral upper respiratory infection (rhinorrhea, cough, and fever) and roughly 1–2 days later develop a "barking" cough, hoarseness, and inspiratory stridor. The "steeple sign" is classic on lateral x-ray of the neck. Treat supportively with a mist tent and racemic epinephrine.
2. Epiglottitis: the patient usually is 2–5 years old. The main cause by far used to be *Haemophilus influenzae* type b, but with widespread vaccination, *H. influenzae* and *S. aureus* are equally frequent. Pick *H. influenzae* if you have to choose. Look for little or no prodrome, with rapid progression to high fever, toxic appearance, drooling, and respiratory distress with no coughing. The "thumb sign" is classic on lateral neck x-ray. Do *not* examine the throat or irritate the patient in any way—you may precipitate airway obstruction. When a case of epiglottitis is presented, the first step is to be prepared to establish an airway (intubate, tracheostomy if needed). Treat with antibiotics (e.g., third-generation cephalosporin).
3. RSV/bronchiolitis: look for 0–18 months old patient; usually occurs in fall or winter. Over 75% of cases are caused by RSV; other causes are parainfluenza and influenza. Patients start with symptoms of viral upper respiratory infection, followed 1–2 days later by rapid respirations, intercostal retractions, and expiratory wheezing. The patient also may have crackles on auscultation of the chest. Diffuse hyperinflation of the lungs is classic on chest x-ray; look for flattened diaphragms. Treat supportively (oxygen, mist tent, bronchodilators, IV fluids). Use ribavarin in patients with severe symptoms or increased risk (cyanosis, other health problems).

Note: Diphtheria (*Corynebacterium diphtheriae*) and pertussis (*Bordetella pertussis*) should be considered if the patient is not immunized. Diphtheria is associated with grayish pseudomembranes (necrotic epithelium and inflammatory exudate) on the pharynx, tonsils, and/or uvula and myocarditis. Pertussis is associated with severe paroxysmal coughing and a high-pitched whooping inspiratory noise (classically called "whooping cough"). Treat both with antibiotics.

Rabies: in the U.S., usually due to bites from bats, skunks, raccoons, or foxes. Vaccination has eliminated dog rabies. The incubation period is usually around 1–2 months. Classic symptoms are hydrophobia and central nervous system signs (paralysis). After a bite, several steps should be taken:

1. Local wound treatment: cleanse thoroughly with soap; do not cauterize or suture the wound.
2. Observe the animal. If possible, capture and observe a dog or cat to see if it develops rabies. If a wild animal (bat, skunk, raccoon, fox) is caught, it should be killed and the tissue examined for rabies.
3. Prophylaxis with rabies immunoglobulin and vaccine:
   - If a captured or killed animal has rabies, definitely give prophylaxis and vaccinate.
   - If a wild animal (bat, skunk, raccoon, fox only) bites and escapes, give prophylaxis and vaccine.
   - If a dog or cat bites and escapes, do *not* give prophylaxis or vaccine *unless* the animal acted strangely and/or bit the patienht without provocation *and* rabies is prevalent in the area (rare).
   - Do *not* give prophylaxis or vaccine for bites by rabbits or other rodents (rats, mice, squirrels, chipmunks).

STREPTOCOCCAL INFECTION

Streptococcus pyogenes (strep A) causes multiple important infections:

1. **Pharyngitis:** look for sore throat with fever, tonsillar exudate, enlarged tender cervical nodes, and leukocytosis. Streptococcal throat culture confirms the diagnosis. Elevated antistreptolysin O (ASO) and anti-DNase titers also are used retrospectively when needed (rheumatic fever, post-streptococcal glomerulonephritis). Treat with penicillin to avoid rheumatic fever and scarlet fever.
   - Rheumatic fever: diagnosis is made by history of streptococcal pharyngitis and Jones criteria, major (migratory polyarthritis, carditis, chorea, erythema marginatum, subcutaneous nodules) and minor (elevated erythrocyte sedimentation rate, C-reactive protein, white blood cell count, and ASO titer; prolonged PR interval; arthralgia). Treat with aspirin; steroids are used for severe carditis (e.g., congestive heart failure). After rheumatic fever, patients need continuous prophylaxis against streptococci (benzathine penicillin intramuscularly every month or orally for compliant patients; erythromycin for penicillin-allergic patient) until age 18 (or longer) plus endocarditis prophylaxis before surgical procedures. Treatment of streptococcal pharyngitis reduces the incidence of rheumatic fever.
   - Scarlet fever: some untreated cases progress to scarlet fever if the streptococcal species produces erythrogenic toxin. Symptoms include red flush in skin (which blanches with pressure, classically with circumoral pallor), truncal rash, strawberry tongue, and late skin desquamation. Kawasaki's syndrome is another cause of this set of symptoms.
   - Post-streptococcal glomerulonephritis: occurs most commonly after a skin infection but may occur after pharyngitis. The patient presents with history of streptococcal infection (by a nephritogenic strain) 1–3 weeks earlier and abrupt onset of hematuria, proteinuria (mild, not in nephrotic range), red blood cell casts, hypertension, edema (especially

periorbital), and elevated BUN/creatinine. Treat supportively: control blood pressure, and use diuretics for severe edema. Treating streptococcal infections does *not* reduce the incidence.

2. **Skin infections:** often occur after a break in the skin due to trauma, scabies, or insect bite. Watch for development of post-streptococcal glomerulonephritis:
   - Impetigo: maculopapules, vesicopustules/bullae, or honey-colored, crusted lesions. Staphylococci are a more frequent cause than streptococci. Definitely think of staphylococci if a furuncle or carbuncle is present; think of streptococci if glomerulonephritis occurs. Infection is contagious; watch for sick contacts. Treat empirically with antistaphylococcal penicillin (e.g., dicloxacillin).
   - Erysipelas: a superficial cellulitis that is red, shiny, swollen, and tender; may be associated with vesicles and bullae, fever, and lymphadenopathy.
   - Cellulitis: involves subcutaneous tissues (deeper than erysipelas). Streptococci are the most common cause, but staphylococci also may be implicated. Treat empirically with antistaphylococcal penicillin or vancomycin to cover both. If *Pseudomonas* sp. is suspected (diabetic foot ulcers, burns, severe trauma), treat with broad-spectrum penicillin plus an aminoglycoside. If *Pasteurella multocida* is suspected (after dog or cat bites), treat with IV ampicillin. If *Vibrio vulnificus* is suspected (fishermen or other salt-water exposure), treat with tetracycline.
   - Necrotizing fasciitis: progression of cellulitis to necrosis and gangrene, crepitus, and systemic toxicity (tachycardia, fever, hypotension). Often multiple organisms (aerobes and anaerobes) are involved. Treat with IV fluids, incision and drainage or debridement, and broad-spectrum antibiotics (broad-spectrum penicillin or cephalosporin plus an aminoglycoside).
3. **Endometritis/puerperal fever:** postdelivery fever and uterine tenderness. Treat with amoxicillin/ampicillin.

Streptococcus agalactiae (strep B): famous as the most common cause of neonatal meningitis and sepsis; acquired from maternal birth canal, in which it is part of the normal flora. Penicillin-sensitive.

Streptococcus viridans: causes subacute endocarditis and dental caries (*Streptococcus mutans*).

Enterococcus faecalis: normal bowel flora; causes endocarditis, urinary tract infection, and sepsis.

Streptococcus pneumoniae: common cause of pneumonia, otitis media, meningitis, sinusitis, and sepsis.

STAPHYLOCOCCAL INFECTION

Staphylococcus aureus: common cause of various infections:

- Abscess (especially in the breast after breast-feeding or in the skin after a furuncle)
- Endocarditis (especially in drug users)
- Osteomyelitis (most common cause except in patients with sickle cell disease)
- Septic arthritis
- Food poisoning (preformed toxin)

- Toxic shock syndrome (preformed toxin, classically in a woman who leaves tampon in place too long and develops hypotension, fever, and a rash that desquamates)
- Scalded skin syndrome (preformed toxin that affects younger children, who often start with impetigo, then desquamate)
- Impetigo
- Cellulitis
- Wound infections
- Pneumonia (often forms lung abscess or empyema)
- Furuncle or carbuncle

Note: Health care workers who are chronic nasal carriers may cause nosocomial infections. Treat carrier with antibiotics. Treat abscesses with incision and drainage, other infections with antistaphylococcal penicillin (e.g., methicillin, dicloxacillin) or vancomycin.

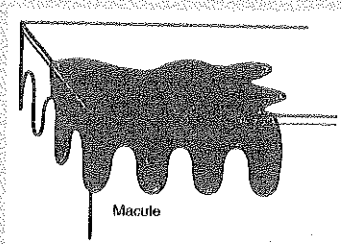
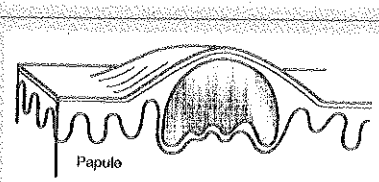
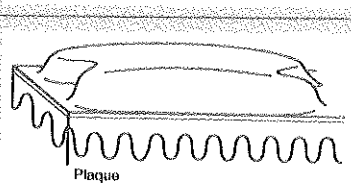
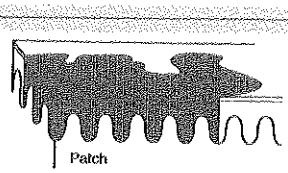
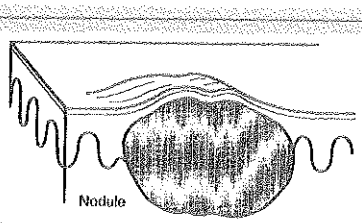
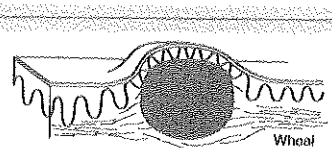
Staphylococcus epidermidis: causes IV catheter infections, infections of prosthetic implants (heart valves, vascular grafts), and sepsis. Treat empirically with antistaphylococcal penicillin or vancomycin.

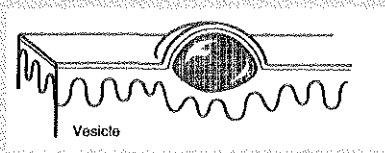
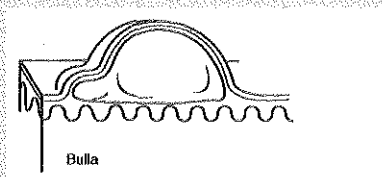
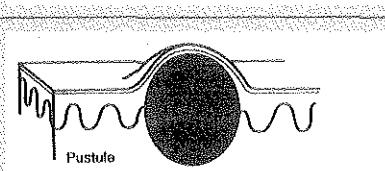
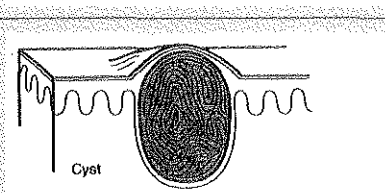
Staphylococcus saprophyticus: common cause of urinary tract infection. Treat empirically with standard urinary tract infection antibiotics.

CHAPTER 11

Dermatology

Common terms to describe skin finding

PRIMARY LESION	DEFINITION	MORPHOLOGY	EXAMPLES
Macule	Flat, circumscribed skin discoloration that lacks surface elevation or depression		Café-au-lait Vitiligo Freckle Junctional nevi Ink tattoo
Papule	Elevated, solid lesion < 0.5 cm in diameter		Acrochordon (skin tag) Basal cell carcinoma Molluscum contagiosum Intradermal nevi Lichen planus
Plaque	Elevated, solid "confluence of papules" (> 0.5 cm in diameter) that lacks a deep component		Bowen's disease Mycosis fungoides Psoriasis Eczema Tinea corporis
Patch	Flat, circumscribed skin discoloration; a very large macule > 1 cm in diameter		Nevus flammeus Vitiligo
Nodule	Elevated, solid lesion > 0.5 cm in diameter; a larger, deeper papule		Rheumatoid nodule Tendon xanthoma Erythema nodosum Lipoma Metastatic carcinoma
Wheal	Firm, edematous plaque that is evanescent and pruritic; a hive		Urticaria Dermographism Urticaria pigmentosa

PRIMARY LESION	DEFINITION	MORPHOLOGY	EXAMPLES
Vesicle	Papule that contains clear fluid; a blister		Herpes simplex Herpes zoster Dyshidrotic eczema Contact dermatitis
Bulla	Localized fluid collection > 0.5 cm in diameter; a large vesicle		Pemphigus vulgaris Bullous pemphigoid Bullous impetigo
Pustule	Papule that contains purulent material		Folliculitis Impetigo Acne Pustular psoriasis
Cyst	Nodule that contains fluid or semisolid material		Acne Epidermoid cyst Pilar cyst

Vitiligo: depigmentation of unknown etiology; associated with pernicious anemia, hypothyroidism, Addison's disease, and diabetic mellitus; may have autoimmune basis. Patients often have antibodies to melanin, parietal cells, or thyroid.

Pruritus: may be a clue to diagnosis of serious and common conditions; seen in obstructive biliary disease, uremia, polycythemia rubra vera (classically after a warm shower or bath), contact or atopic dermatitis, scabies, and lichen planus.

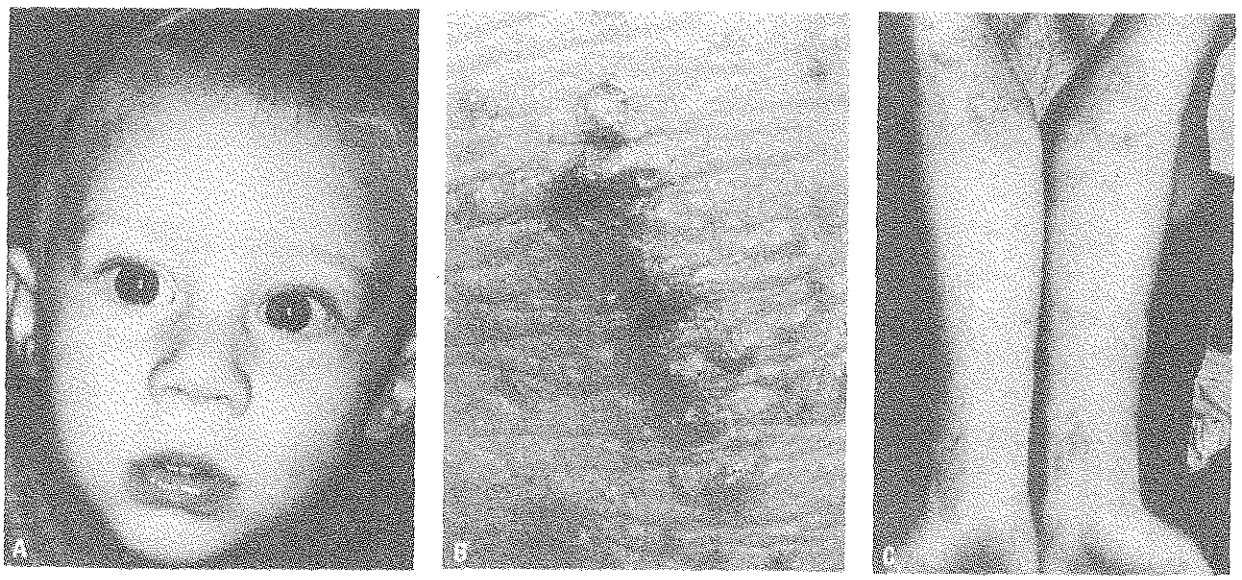
Contact dermatitis: often due to a type IV hypersensitivity reaction; also may be due to irritating or toxic substance. Look for question that mentions new exposure to a classic offending agent (poison ivy, nickel earrings, deodorant). The rash is well circumscribed and found only in the area of exposure; skin is red and itchy and often has vesicles or bullae. Avoidance of the agent is required; patch testing can be done, if needed, to determine the antigen.

Atopic dermatitis: look for family and personal history of allergies (e.g., hay fever) and asthma. This chronic condition begins in the first year of life with red, itchy, weeping skin on the head, upper extremities, and sometimes around the diaper area. The biggest problem is scratching, which leads to skin breaks and possible bacterial infection. Treatment involves avoidance of drying soaps, antihistamines, and topical steroids (see figure, top of next page).

Seborrheic dermatitis: causes the common conditions known as cradle cap and dandruff as well as blepharitis (eyelid inflammation). Look for scaling skin on the scalp and eyelids, and treat with dandruff shampoo.

Fungal skin infections (dermatophyte infections, ringworm), depending on location, are known as:

1. Tinea corporis (body/trunk): look for red ring-shaped lesions that have raised borders and tend to clear centrally while they expand peripherally.



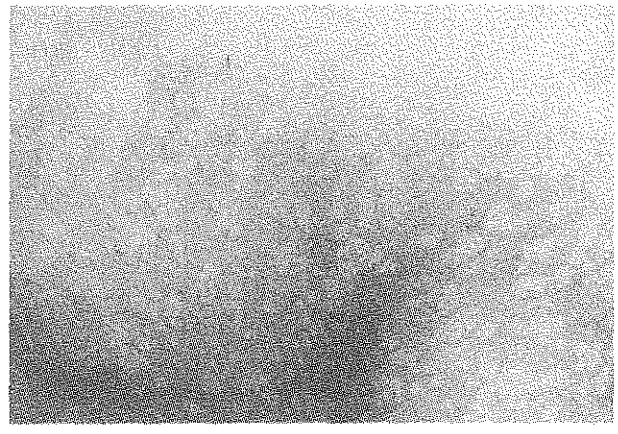
Phases of atopic dermatitis. *A*, Infantile phase. Typical erythematous, oozing, and crusted plaques seen on the cheek of an infant with atopic dermatitis. *B*, Childhood phase. Close-up view of a lichenified, excoriated, crusted, and secondarily infected plaque on the right knee of a 4-year-old girl. *C*, Adolescent or young adult phase. (From Fitzpatrick JE, Aeling JL: Dermatology Secrets. Philadelphia, Hanley & Belfus, 1996, with permission.)

2. Tinea pedis (athlete's foot): look for macerated, scaling web spaces between the toes that often itch and thickened, distorted toenails (onychomycosis). Good foot hygiene is part of treatment.
3. Tinea unguium (onychomycosis): thickened, distorted nails with debris under the nail edges.
4. Tinea capitis (scalp): mainly affects children (highly contagious), who have scaly patches of hair loss and may have an inflamed, boggy granuloma of the scalp (known as a kerion), which usually resolves on its own.
5. Tinea cruris (jock itch): more common in obese males, usually in the crural folds of the upper inner thighs.

Most fungal skin infections are due to *Trichophyton* species. Infections are diagnosed by scraping the lesion and doing a potassium hydroxide (KOH) preparation to visualize the fungus or a culture. Griseofulvin (oral) must be used to treat tinea capitis and onychomycosis; the others can be treated with topical antifungals (e.g., miconazole, clotrimazole, ketoconazole) or griseofulvin, which is better for severe or persistent infections. In tinea capitis, if the hair fluoresces under Wood's lamp, *Microsporum* sp. is the cause; if it does not, the probable cause is *Trichophyton* sp.

Candidiasis: thrush (creamy white patches on the tongue or buccal mucosa that can be scraped off) may be seen in normal children, and candidal vulvovaginitis is seen in normal women, especially when they are pregnant or after taking antibiotics. However, at other times and in different patients, candidal infections may be a sign of diabetes mellitus or immunodeficiency. For example, thrush in an adult male should make you think about the possibility of HIV/AIDS. Treat with local or topical nystatin or imidazoles (e.g., miconazole, clotrimazole); oral therapy (nystatin or ketoconazole) is used for extensive or resistant disease.

Tinea versicolor: Pityrosporon sp. infection that presents most commonly in young adults with multiple patches of various size and color (brown, tan, and white) on the torso. It often becomes noticeable in the summer because the affected areas fail to tan and look white. Diagnose from lesion scrapings (KOH preparation). Treat with selenium sulfide shampoo or topical imidazoles.



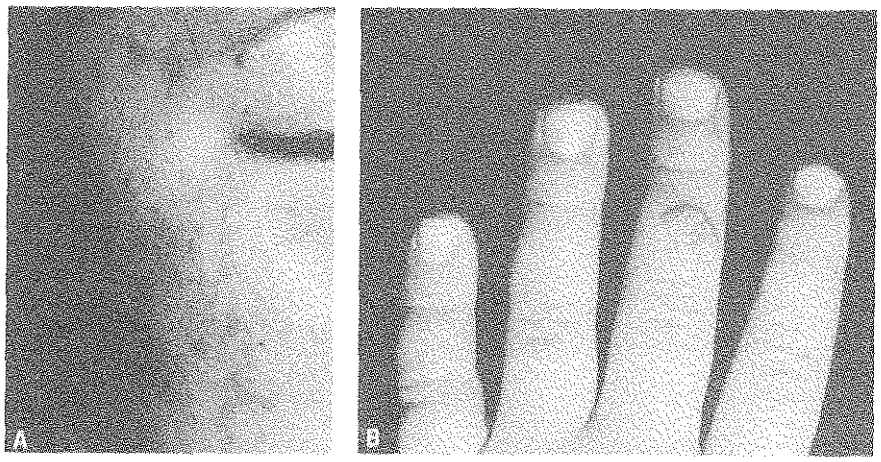
Tinea versicolor demonstrating hypopigmented scaly papules. (From Fitzpatrick JE, Aeling JL: Dermatology Secrets. Philadelphia, Hanley & Belfus, 1996, with permission.)

Scabies: caused by the mite *Sarcoptes scabei*, which tunnels into the skin and leaves visible burrows on the skin (know what they look like), classically in the finger web spaces and flexor surface of the wrists. Facial involvement sometimes is seen in infants. Patients have severe pruritus, and itching may lead to secondary bacterial infection. Diagnosis is made by scraping the mite out of a burrow and viewing it under a microscope. Treat with permethrin cream applied to the whole body. Remember to treat *all* contacts (e.g., the whole family). *Do not* use lindane to treat unless permethrin is not a choice. Lindane used to be the treatment of choice but can cause neurotoxicity, especially in young children.

Lice (pediculosis): lice can infect the head (*Pediculus capitis*, which is common in school-aged children), body (*Pediculus corporis*, which is unusual in people with good hygiene), or pubic area (crabs, caused by *Phthirus pubis* and transmitted sexually). Infected areas tend to itch, and diagnosis is made by seeing the lice on hair shafts. Treat with permethrin cream (preferred over lindane because of lindane's neurotoxicity), and decontaminate sources of reinfection (wash or sterilize combs, hats, bed sheets, clothing).

Warts: caused by human papillomavirus (HPV); infections are most commonly seen in older children, often on the hands. Treatments include salicylic acid, liquid nitrogen, curettage, and others. Genital warts also are caused by HPV (types 16 and 18 are associated with cervical cancer). (See figure, top of next page.)

Molluscum contagiosum: a poxvirus infection that is common in children but also may be transmitted sexually. A child who has genital molluscum may or may not have contracted the infection from sexual contact; autoinnoculation is possible. Do *not* automatically assume child abuse, although it must be ruled out. Diagnosis is made by the characteristic appearance of the lesions (skin-colored, smooth, waxy papules with a central depression [umbilicated] that are roughly 0.5 cm) or by looking at contents of the lesion, which include cells with characteristic inclusion bodies. Usually treated with freezing or curettage.



Some common types of warts. *A*, Flat warts of the face. *B*, Wart of the hand. (From Fitzpatrick JE, Aeling JL: Dermatology Secrets. Philadelphia, Hanley & Belfus, 1996, with permission.)

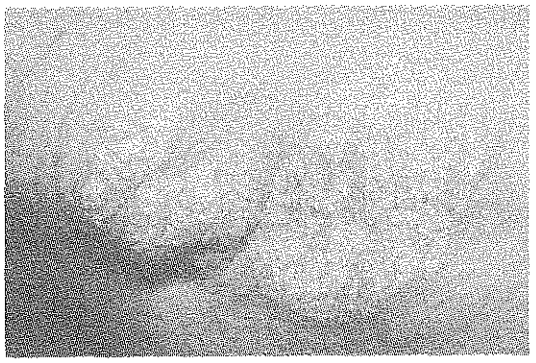
Acne: know the description of acne: comedones (whiteheads, blackheads), papules, pustules, inflamed nodules, superficial pus-filled cysts with possible inflammatory skin changes. *Propionibacterium acnes* is thought to be partially involved in pathogenesis as well as blockage of pilosebaceous glands. Acne has *not* been proved to be related to food (but if the patient relates it to a food, you can try discontinuing it), exercise, or sex/masturbation, but cosmetics may aggravate it. Treatment options are multiple. Start with topical benzoyl peroxide, then try topical clindamycin, oral tetracycline, oral erythromycin (for *P. acnes* eradication), and topical tretinoin. The *last resort* is oral isotretinoin. Isotretinoin is highly effective but teratogenic (pregnancy testing before and during therapy is mandatory) and may cause dry skin and mucosae, muscle and joint pain, and liver function abnormalities.

Rosacea: looks like acne but starts in middle age. Look for rhinophyma (bulbous red nose) and coexisting blepharitis. Treat with topical metronidazole or oral tetracycline. The pathogenesis is unknown, but it is not related to diet.

Hirsutism: most commonly idiopathic, but other signs of virilization (deepening voice, clitoromegaly, frontal balding) indicate an androgen-secreting ovarian tumor. Other causes include corticosteroid administration, Cushing's syndrome, Stein-Leventhal syndrome (polycystic ovary), and drugs (minoxidil and phenytoin).

Baldness: watch out for trichotillomania (psychiatric patients pulling out their hair) and alopecia areata (idiopathic and associated with antimicrosomal and other autoantibodies, lupus, syphilis, or chemotherapy) as exotic causes of irregular, patchy baldness. Male-pattern baldness is considered a genetic disorder that requires androgens to be expressed.

Psoriasis: know what classic lesions look like and how they are described (dry, not pruritic, well-circumscribed, silvery, scaling papules and plaques). Family history is often positive. Psoriasis occurs mostly in whites with onset in early adulthood. Classic lesions are found on the scalp and extensor surfaces of the elbows and knees. Patients may have pitting of the nails and arthritis that resembles rheumatoid arthritis but is rheumatoid factor-negative. Diagnosis is made by appearance, but biopsy can be used for doubtful cases. Treatment is complex but involves exposure to ultraviolet light (e.g. sunlight), lubricants, topical corticosteroids, and keratolytics (coal tar, salicylic acid, anthralin). (See figure, top of next page.)



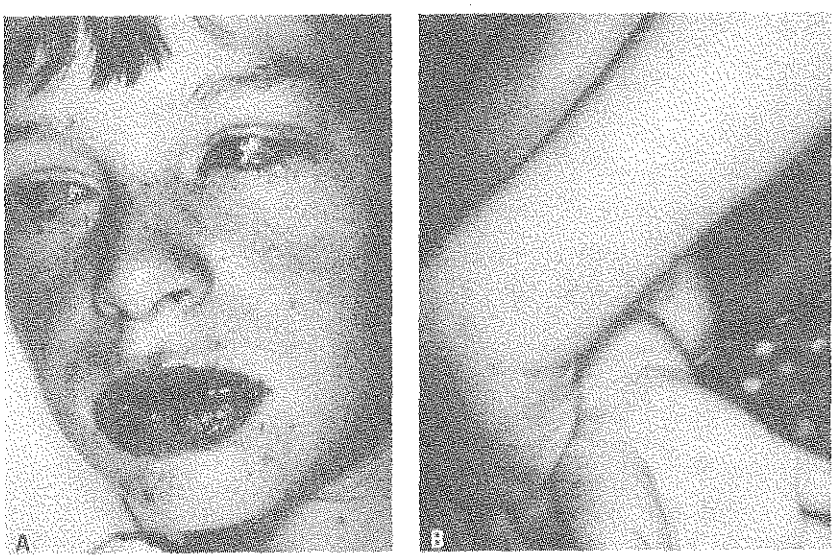
Psoriasis. Elbow involvement of psoriasis vulgaris, *demonstrating typical well-demarcated, red plaques* with silvery scale. (From Fitzpatrick JE, Aeling JL: Dermatology Secrets. Philadelphia, Hanley & Belfus, 1996, with permission.)

Pityriasis rosea: seems to be a popular dermatology question. Pityriasis rosea is seen in adults. Look for a "herald patch" (slightly erythematous, ring-shaped or oval, and scaly patch classically seen on the trunk) followed 1 week later by many similar lesions that tend to itch. Look for lesions on the back with a long axis that parallels the Langerhans' skin cleavage lines, typically in a "Christmas tree" pattern. Pityriasis rosea usually remits spontaneously *in 1 month*. Think about syphilis in the differential diagnosis. Treat with reassurance.

Lichen planus: look for the four Ps (pruritic, purple, polygonal papules) and oral mucosal lesions.

Drug reactions: penicillin, cephalosporins, and sulfa drugs commonly cause rashes; tetracycline and phenothiazines commonly cause photosensitivity.

Erythema multiforme: look for classic target (iris) lesions. Usually caused by drugs or infections (e.g., herpes). The severe form is known as Stevens-Johnson syndrome, which often is fatal. Treat supportively. (See figure below.)



A, Stevens-Johnson syndrome. Typical mucosal inflammation of the mouth, lips, and conjunctiva. *B*, Erythema multiforme or Stevens-Johnson syndrome. The eruption consists of annular and papular erythema over the acral areas. (From Fitzpatrick JE, Aeling JL: Dermatology Secrets. Philadelphia, Hanley & Belfus, 1996, with permission.)

Erythema nodosum: inflammation of the subcutaneous tissue and skin, classically over the shins (pretibial). Tender, red nodules are present. Look for exotic diseases such as sarcoidosis, coccidioidomycosis, and ulcerative colitis as the cause, although more commonly the cause is unknown or due to a streptococcal infection.

Pemphigus: an autoimmune disease of the middle-aged and elderly that presents with multiple bullae, starting in the oral mucosa and spreading to the skin of the rest of the body. Biopsy can be stained for antibody and shows a linear immunofluorescence pattern. Treat with corticosteroids.

Dermatitis herpetiformis: should alert you to the presence of gluten-sensitivity; look for diarrhea and weight loss. Skin has IgA deposits even in unaffected areas. Patients present with intensely pruritic vesicles, papules, and wheals on the extensor aspects of the elbows and knees, possibly on the face and neck. Treat with gluten-free diet.

Decubitus ulcers (bedsores or pressure sores): due to prolonged pressure against the skin. The best treatment is prophylaxis. Periodic turning of paralyzed, bedridden, or debilitated patients prevents bedsores. Cleanliness and dryness also help to prevent this condition, and periodic skin inspection makes sure that you catch the problem early. When missed, the lesions can ulcerate down to the bone and become infected, possibly leading to sepsis and death. Treat major skin breaks with aggressive surgical debridement and antibiotics if signs of infection are present.

Excessive perspiration: think of hyperthyroidism and pheochromocytoma.

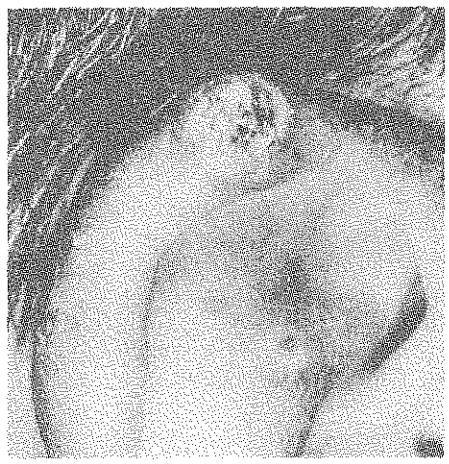
Moles: common and benign, but malignant transformation is possible. *Excise any mole* (or do a biopsy if the lesion is very large) if it enlarges suddenly, develops irregular borders, darkens or becomes inflamed, changes color (even if only one small area of the mole changes color), begins to bleed, begins to itch, or becomes painful. Dysplastic nevus syndrome is a genetic condition with multiple dysplastic appearing nevi (usually > 100); also look for a family history of melanoma. Treat with careful follow-up and excision/biopsy of any suspicious-looking lesions as well as sun avoidance and sunscreen use.

Keratoacanthoma: mainly important because it mimics skin cancer (especially squamous cell cancer). This flesh-colored lesion with a central crater contains keratinous material classically is found on the face. The best way to differentiate it from cancer is that a keratoacanthoma has a *very* rapid onset, and grows to full size in 1–2 months. Such rapid growth almost never occurs with squamous cell cancer. The lesion involutes spontaneously in a few months and requires no treatment. If you are unsure, the best option is a biopsy, but choose observation/keratoacanthoma if the history is classic.

Keloid: an overgrowth of scar tissue after an injury, most frequently seen in blacks. Usually slightly pink and classically found on the upper back, chest, and deltoid area. Also look for keloids to develop after ear piercing.

Basal cell cancer: begins as a shiny papule and slowly enlarges and develops an umbilicated center (which later may ulcerate) with peripheral telangiectasias. Basal cell cancer rarely metastasizes. As with all skin cancer, sunlight exposure increases risk. It is more common in light-skinned people. Treat with excision. Biopsy any suspicious skin lesion in elderly patients.

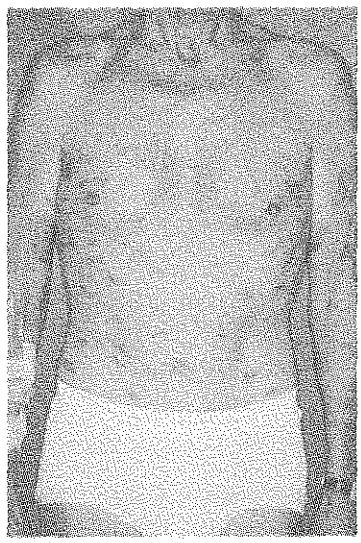
Squamous cell cancer: look for preexisting actinic keratoses (hard, sharp, red, often scaly lesions in sun-exposed areas) or burn scars that become nodular, warty, or ulcerated. Do a biopsy if this happens! Squamous cell cancer in situ is known as Bowen's disease. (See figure, top of next page.)



Squamous cell carcinoma of the ear, demonstrating a nodule with central scale and crust. (From Fitzpatrick JE, Aeling JL: Dermatology Secrets. Philadelphia, Hanley & Belfus, 1996, with permission.)

Malignant melanoma: usually arises from preexisting moles. Remember your **ABCDs**: asymmetry, irregular borders, color change, and increasing diameter). Prognosis is directly related to the depth of vertical invasion. Superficial spreading melanoma tends to stay superficial and has the best prognosis. Nodular melanoma is the worst because it tends to grow downward first. Although uncommon in blacks, melanoma tends to be of the acrolentiginous type. Look for black dots on the palms and soles or under the fingernail. Treat with surgery; if surgery fails, the prognosis is poor.

Kaposi's sarcoma: seen in AIDS patients. Look for classic mucosal lesions or an expanding, strange rash or skin lesion that does not respond to multiple treatments. (See figure below.)



Kaposi's sarcoma. Multiple violaceous plaques are seen on the trunk of an HIV-positive patient. (From Fitzpatrick JE, Aeling JL: Dermatology Secrets. Philadelphia, Hanley & Belfus, 1996, with permission.)

Paget's disease of the nipple: watch for a unilateral red, oozing, and crusting nipple in an adult woman. An underlying breast cancer with extension to the skin must be ruled out.

Stomatitis: watch for deficiencies of B-complex vitamins (riboflavin, niacin, pyridoxine) or vitamin C.

CHAPTER 12
Neurology

Classic cerebrospinal fluid findings in different conditions

CONDITION	CELLS/μl*	GLUCOSE (mg/dl)	PROTEIN (mg/dl)	PRESSURE (mmHg)
Normal cerebrospinal fluid	0–3 (L)	50–100	20–45	100–200
Bacterial meningitis	**> 1000 (PMN)**	< 50	Around 100	> 200
Viral or aseptic meningitis	>100 (L)	Normal	Normal or slightly increased	Normal or slightly increased
Pseudotumor cerebri	**Normal**	Normal	Normal	**> 200**
Guillain-Barré syndrome	0–100 (L)	Normal	**> 100**	Normal
Cerebral hemorrhage†	**Bloody (RBC)**	Normal	> 45	> 200
Multiple sclerosis‡	Normal or slightly increased (L)	Normal	Normal or slightly increased	Normal

* Main cell type is put in parenthesis after the number (L = lymphocytes, PMN = polymorphonuclear neutrophils, RBC = red blood cells).
† Think of subarachnoid hemorrhage, but the same findings also may occur after an intracerebral hemorrhage.
‡ On electrophoresis of cerbrospinal fluid, look for oligoclonal bands due to increased IgG production and an increased level of myelin basic protein (MBP) during active demyelination.

Important points:

1. Do *not* do lumbar puncture in patients with acute head trauma or signs of intracranial hypertension until you have a CT/MRI. You may cause death.
2. Tuberculosis and fungal meningitis have low glucose (< 50) with high cells (> 100), which are predominantly **lymphocytes**. Watch for a positive India ink preparation for *Cryptococcus* sp.

Multiple sclerosis: look for insidious onset of neurologic symptoms in women aged 20–40 with exacerbations and remissions. Common presentations include paresthesias and numbness, weakness and clumsiness, visual disturbances (decreased vision and pain due to optic neuritis, diplopia due to cranial nerve involvement), gait disturbances, incontinence or urgency, and vertigo. Also look for emotional lability or other mental status changes. Internuclear ophthalmoplegia and scanning speech are classic; Babinski's sign may be positive. MRI, the most sensitive diagnostic tool, shows demyelination plaques. Look for increased IgG or oligoclonal bands and possibly myelin basic protein in the cerebrospinal fluid. Treatment is not very effective but includes corticosteroids and interferons.

Guillain-Barré syndrome: look for history of mild infection or immunization roughly 1 week before onset of symmetric, distal weakness, paralysis, or mild paresthesias with loss of deep

tendon reflexes in affected areas. As the ascending paralysis and weakness progress, respiratory paralysis may occur. Patients must be watched carefully; usually spirometry is used to follow inspiratory ability. Intubation may be required. Diagnosis depends on clinical signs and symptoms, analysis of cerebrospinal fluid (usually normal except for **markedly increased protein**), and nerve conduction velocities (slowed). Disease usually stops spontaneously. Plasmapheresis reduces the severity and length of disease. Do not use steroids; you may make the patient worse.

Nerve conduction velocities: slowed by demyelination (Guillain-Barré, multiple sclerosis). Repetitive stimulation can assess fatigability. Myasthenia gravis is characterized by increasing fatigue with stimulation, Eaton-Lambert syndrome by decreasing fatigue with stimulation.

Electromyography (EMG): measures the electrical (contractile) properties of muscle. Lower motor neuron lesions are associated with fasciculations and fibrillations at rest. When the disease is in the muscle itself, no electrical activity is seen at rest (which is normal), but amplitude is decreased with contraction of the muscle.

Syncope: the most common cause (after stress, fear, or other emotional states) is vasovagal. Other causes include cardiac events (especially arrhythmias; get an EKG), transient ischemic attacks (consider carotid artery duplex scan), and neurologic disorders (especially seizures; consider CT or MRI of head if other neurologic symptoms are present).

***Localizing* pathology of the central nervous system**

SYMPTOM/SIGN	*THINK OF THIS AREA*
Decreased or no reflexes, fasciculations	Lower motor neuron disease (or possibly a muscle problem)
Hyperreflexia	Upper motor neuron lesion (cord or brain)
Apathy, inattention, or uninhibited, labile affect	*Frontal lobes*
Broca's (motor) aphasia	Dominant frontal lobe*
Wernicke's (sensory) aphasia	Dominant temporal lobe*
Memory impairment or aggressive sexual behavior	Temporal lobes
Inability to read, write name, or do math	Dominant parietal lobe*
Ignoring one side of body, trouble with dressing	Nondominant parietal lobe*
Visual hallucinations or illusions	Occipital lobes
Cranial nerves 3 and 4	Midbrain
Cranial nerves 5, 6, 7, and 8	Pons
Cranial nerves 9, 10, 11, and 12	Medulla
Ataxia, dysarthria, nystagmus, intention tremor, dysmetria, scanning speech	Cerebellum

* Left side is dominant in >95% of population (99% of right-handed people and 60–70% of left-handed people).

For ***delirious or unconscious* patients in the emergency department** with no history of trauma, think first of hypoglycemia (give glucose), opioid overdose (give naloxone), and thiamine deficiency (*give thiamine before giving glucose* in a suspected alcoholic). Other common causes are alcohol, illicit drugs, prescription medications, diabetic ketoacidosis, stroke, and epilepsy or postictal state.

Delirium vs. dementia (See table, top of next page.)

	DELIRIUM	DEMENTIA
Onset	Acute and dramatic	Chronic and insidious
Common causes	Illness, toxin, withdrawal	Alzheimer's, multiinfarct dementia, HIV/AIDS
Reversible	Usually	Usually not
Attention	Poor	Usually unaffected
Arousal level	Fluctuates	Normal

Important points:

1. Both delirium and dementia may have hallucinations, illusions, delusions, memory impairment (usually global in delirium, whereas remote memory is spared in early dementia), orientation difficulties (time, place, person), and "sundowning" (worsened delirium or dementia at night).
2. In the elderly watch for pseudodementia, which is caused by depression and reversible with treatment.
3. Treatable causes of dementia include vitamin B_{12} deficiency, endocrine disorders (especially thyroid and parathyroid), uremia, syphilis, brain tumors, and normal-pressure hydrocephalus. Treatment of Parkinson's syndrome also may reverse dementia.
4. Watch for thiamine deficiency in alcoholics as the cause of delirium (Wernicke's encephalopathy, which classically presents with ataxia, ophthalmoplegia, nystagmus, and confusion). If untreated, it may progress to Korsakoff's syndrome (memory loss with confabulation; usually irreversible). Give thiamine before glucose in an alcoholic to prevent precipitating Wernicke's encephalopathy.

Causes of headache:

1. Tension headaches: most common cause. Look for long history of headaches and stress plus a feeling of tightness or stiffness, usually frontal or occipital and bilateral. Treat with stress reduction and acetaminophen or NSAID.
2. Cluster headaches: unilateral, severe, tender; occur in clusters. Oxygen may abort an attack acutely.
3. Migraine headache: look for aura, photophobia, nausea and vomiting, and positive family history. Patients may have neurologic symptoms during attacks, which usually begin between ages 10 and 30. Treat and prophylax with antimigraine medication (e.g., sumatriptan).
4. Tumor or mass: look for progressive neurologic symptoms, papilledema, intracranial hypertension (classically with nausea and vomiting, which may be projectile), mental status changes. and headache every day (classically worse in the morning). CT/MRI should be ordered.
5. Pseudotumor cerebri: may mimic tumor or mass; both cause intracranial hypertension, papilledema, and daily headaches that classically are worse in the morning and may be accompanied by nausea and vomiting. Found in young obese females, who are unlikely to have a brain tumor; CT and MRI are negative. Pseudotumor cerebri may cause permanent vision loss. Treatment is usually supportive; weight loss usually helps. Large doses of **vitamin A**, tetracyclines, and withdrawal from corticosteroids are possible causes.
6. Meningitis: look for fever, Brudzinski's or Kernig's sign, cerebrospinal fluid findings (see above).
7. Subarachnoid hemorrhage: "worst headache" of patient's life; may be due to congenital berry aneurysm, rupture, or trauma. Look for grossly bloody cerebrospinal fluid. Treat supportively.

8. Extracranial causes: eye pain (optic neuritis, eyestrain from refractive errors, iritis, glaucoma), middle ear pain (otitis media, mastoiditis), sinus pain (sinusitis), oral cavity pain (toothache), herpes zoster with cranial nerve involvement, and nonspecific (malaise from any illness).

Cranial nerve (CN) lesions:

1. Olfactory (CN 1): rarely important clinically. Kallmann's syndrome is anosmia plus hypogonadism due to deficiency of *gonadotropin-releasing hormone*.
2. Optic (CN 2): you must be able to localize the lesion through the resultant visual deficit (e.g., bitemporal hemianopia due to a lesion at the optic chiasm), as on Step I boards. Most commonly tested are bitemporal hemianopia and monocular loss of vision (see ophthalmology chapter).
3. Oculomotor (CN 3): the cause may be benign (hypertension, diabetes *mellitus*) *or serious* (aneurysm, tumor, uncal herniation). With benign causes the pupil is spared (normal), and no treatment is needed. With serious causes the pupil is dilated and nonreactive ("blown"). Urgent diagnosis and treatment are required.
4. Trochlear (CN 4) and abducens (CN 6): see ophthalmology chapter.
5. Trigeminal (CN 5): innervates muscles of mastication and facial sensation (including the afferent limb of the corneal reflex). Patients may have trigeminal neuralgia (tic douloureux), which is characterized by unilateral shooting pains in the face in older adults and often triggered by activity (e.g., brushing teeth). Treat with carbamazepine and anti-epilepsy medications. If the patient is young and/or female and/or the disease is bilateral, consider *multiple sclerosis. Make sure to rule out* other causes, such as tumor or stroke.
6. Facial (CN 7): innervates muscles of facial expression, taste in anterior two-thirds of tongue, skin of external ear, lacrimal and salivary glands (except parotid gland), and stapedius muscle. Differentiate between upper motor neuron lesions (the forehead is spared on the affected side, and the cause is usually stroke or tumor) and lower motor neuron lesions (the forehead is involved on the affected side, and the cause is usually Bell's palsy or tumor) of the facial nerve. Patients may be unable to close the eye; give artificial tears to prevent corneal ulceration. Patients with Bell's palsy may get hyperacusis due to stapedial muscle paralysis. *If CNs 7 and 8 are affected, think of possible* cerebellopontine angle tumor (e.g., acoustic neuroma, especially in neurofibromatosis).
7. Vestibulocochlear (CN 8): for hearing and balance. Lesions cause deafness, tinnitus, and vertigo. In children, think of meningitis as a cause. In adults, think of toxins and medications (aspirin, aminoglycosides, loop diuretics, cisplatin), tumors (with CN 7 coinvolvement, *think of acoustic neuroma*), *or stroke*.
8. Glossopharyngeal (CN 9): innervates pharyngeal muscles and mucous membranes (afferent limb of gag reflex), parotid gland, taste in posterior third of tongue, skin of external ear, and carotid body and sinus. Look for loss of gag reflex and loss of taste in posterior third of tongue.
9. Vagus (CN 10): innervates muscles of *palate, pharynx, larynx (efferent limb* of gag reflex), taste buds in base of tongue, abdominal viscera, and skin of external ear. Look for hoarseness, dysphagia, and loss of gag or cough reflex. Think of aortic aneurysms or tumors, especially Pancoast lung tumors.
10. Spinal accessory (CN 11): innervates sternocleidomastoid and trapezius muscles. With a *CN 11 lesion, the patient has trouble turning* the head to the opposite side of lesion and shoulder droop.

11. Hypoglossal (CN 12): innervates muscles of the tongue. With a CN 12 lesion, a protruded tongue deviates to the side of the lesion.

Vitamin deficiencies may present with neurologic signs and symptoms:

1. Vitamin B_{12}: dementia, peripheral neuropathy, loss of vibration sense in lower extremities, loss of position sense, ataxia, spasticity, hyperactive reflexes, and positive Babinski's sign
2. Thiamine: peripheral neuropathy, confusion, ophthalmoplegia, nystagmus, ataxia, confusion, delirium, dementia
3. Vitamin E: loss of proprioception/vibratory sensation, areflexia, ataxia, and gaze palsy
4. Vitamin A: vision loss
5. Vitamin B_6: peripheral sensory neuropathy (watch for isoniazid as a cause and give prophylactic B_6 to patients taking isoniazid if given the choice)

Five main types of seizures are tested on boards (although there are others):

1. Simple partial (local, focal) seizures: may be motor (e.g., Jacksonian march), sensory (e.g., hallucinations), or psychic (cognitive or affective symptoms). The key point is that consciousness is *not* impaired. Treat with phenytoin, carbamazepine, or valproate.
2. Complex partial (psychomotor) seizures: any simple partial seizure followed by impairment of consciousness. Patients perform purposeless movements and may become aggressive if restraint is attempted (people who get in fights or kill people are not having a seizure!). The first-line agent is carbamazepine; phenytoin and valproate also are effective.
3. Absence (petit mal) seizures: *never* begin after the age of 20. They are brief (10–30-second duration), generalized seizures in which the main manifestation is loss of consciousness, often with eye or muscle flutterings. The classic description is a child in a classroom who stares off into space in the middle of a sentence (the child is not daydreaming but having a seizure), then 20 seconds later resumes the sentence. There is no postictal state (an important differential point). The first-line agent is **ethosuximide**; valproate also is effective.
4. Tonic clonic (grand mal) seizures: the classic seizures that may have an aura; tonic muscle contraction is followed by clonic contractions, usually lasting 2–5 minutes. Patients often have incontinence and a postictal state (drowsiness, confusion, headache, muscle soreness). Treat with phenytoin, carbamazepine, or valproate.
5. Febrile seizures: between the ages of 6 months and 5 years old, children may have a seizure due to fever. The seizure is usually of the tonic-clonic, generalized type, and no specific seizure treatment is required. Treat the underlying cause of the fever, if possible, and give acetaminophen. Such children do *not* have epilepsy, and the chances of their getting it are just barely higher than in the general population. Make sure that affected children do not have meningitis, tumor, or other serious cause of seizure. The board question will give clues in the case description if you are expected to pursue work-up for a serious condition.

Secondary seizure disorder may be caused by:

- Mass (tumor, hemorrhage)
- Metabolic disorder (hypoglycemia, hypoxia, phenylketonuria, hyponatremia)
- Toxins (lead, cocaine, carbon monoxide)
- Drug withdrawal (alcohol, barbiturates, benzodiazepines, too-rapid anticonvulsant withdrawal)
- Cerebral edema (severe or malignant hypertension; also watch for pheochromocytoma)
- Eclampsia

- Central nervous system infections (meningitis, encephalitis, toxoplasmosis, cysticercosis)
- Trauma
- Stroke

Cysticercosis is due to infection with the larval form of *Taenia solium*, the pork tapeworm, and most often is seen in patients with AIDS and immigrants. On CT scan the lesion often is described as "ring-enhancing." Treat with niclosamide or praziquantel. In secondary seizures of any etiology, treat the underlying disorder and use diazepam, or phenytoin acutely to control seizure.

Note: For all seizures, secure the airway and, if possible, roll the patient onto his or her side to prevent aspiration.

Status epilepticus: when seizures of any type follow one after the other with no intervening periods of consciousness. May occur spontaneously or result from too-rapid withdrawal of anticonvulsants. Treat with IV diazepam, lorazepam, or phenytoin. Remember to protect the airway and intubate if necessary.

Important points:

1. Hypertension may cause seizures or convulsions, headache, and confusion, stupor, or mental status changes.
2. All anticonvulsants are teratogenic, and women need counseling about the risks of pregnancy. Do a pregnancy test before starting an anticonvulsant.

Cerebrovascular disease (stroke, cerebrovascular accident): the most common cause of neurologic disability in the U.S. and the third leading cause of death. Ischemia from atherosclerosis is by far the most common cause; other classic causes include atrial fibrillation with resultant clot formation and emboli to the brain and septic emboli from endocarditis. Treatment for acute stroke in evolution is supportive (e.g., airway, oxygen, IV fluids). Heparin is controversial and should be *avoided* if the patient is hypertensive; it should not be given until a hemorrhagic stroke has been ruled out by CT. The vascular surgery chapter discusses the role of carotid endarterectomy, which is *not* done emergently.

Transient ischemic attack (TIA): focal neurologic deficit that lasts minutes to hours, then resolves spontaneously; often a precursor to stroke. The classic presentation is ipsilateral blindness (amaurosis fugax) and/or unilateral hemiplegia, hemiparesis, weakness, or clumsiness. Get a carotid duplex scan to look for stenosis. Heparin may be given acutely (if not contraindicated), but for long-term therapy use aspirin-antiplatelet medications, or carotid endarterectomy (if carotid stenosis > 70%).

Huntington's disease: autosomal dominant condition that usually begins at 35–50 years of age. Look for choreiform movements (irregular, spasmodic, involuntary movements of the limbs or facial muscles) and progressive intellectual deterioration, dementia, and psychiatric disturbances. Atrophy of the caudate nucleus may be seen on CT/MRI. Treatment is supportive; antipsychotics may help.

Parkinson's disease: classic tetrad of slowness or poverty of movement, muscular rigidity ("lead pipe" and "cog-wheel"), resting "pill-rolling" tremor (which disappears with movement and sleep), and postural instability (shuffling gait and festination). Patients also may have dementia and depression. The mean age of onset is around 60. The cause is loss of dopaminergic neurons, especially in the substantia nigra, which projects to the basal ganglia; the result is decreased dopamine in the basal ganglia. Drug therapy aims to increase dopamine. Options include levodopa/carbidopa, bromocriptine/pergolide, monoamine oxidase-B inhibitors (selegiline), amantidine, anticholinergics (trihexyphenidyl, benztropine), and antihistamines (diphenhydramine).

Note: Antipsychotics may cause Parkinson-like symptoms in schizophrenics. Treat with anticholinergics (benztropine, trihexyphenidyl) or antihistamines (diphenhydramine).

Tremor and chorea: resting tremor generally due to basal ganglia disease (chorea), intention tremor due to cerebellar disease, and hemiballismus (random, violent, unilateral flailing of the limbs) due to a lesion in the subthalamic nucleus. Besides Parkinson's disease, a resting tremor may be due to hyperthyroidism, anxiety, drug withdrawal or intoxication, or a benign (essential) hereditary tremor (usually autosomal dominant; look for a positive family history, and use beta blockers to reduce the tremor). Watch for Wilson's disease (hepatolenticular degeneration) and asterixis (outstretched hands flap slowly and involuntarily) in patients with liver and kidney failure.

Cerebellar disorders: in children, think of brain tumor (cerebellar astrocytoma, medulloblastomas), hydrocephalus (enlarging head in infants younger than 6 months, Arnold-Chiari and Dandy-Walker syndromes), Friedreich's ataxia (autosomal recessive), or ataxia-telangiectasia (the diagnosis is in the name). Friedreich's ataxia starts between 5 and 15 years of age and presents with areflexia, loss of vibration or position sense, and cardiomyopathy. In adults, think of alcoholism, tumor, ischemia or hemorrhage, or multiple sclerosis.

Amyotrophic lateral sclerosis (Lou Gehrig's disease): an idiopathic degeneration of both upper and lower motor neurons that is more common in males. The mean age at onset is 55. The key is to notice a combination of upper motor neuron lesion signs (spasticity, hyperreflexia, positive Babinski's sign) and lower motor neuron lesion signs (fasciculations, atrophy, flaccidity) in the same patient. Treatment is supportive, but 50% of patients die within 3 years of onset.

"Floppy baby"syndrome (infants with hypotonia or flaccidity) may be caused by two disorders:

1. Werdnig-Hoffmann disease: autosomal recessive degeneration of anterior horn cells in the spinal cord and brainstem (lower motor neurons). Most infants are hypotonic at birth, and all are affected by 6 months. Look for a positive family history, long and slowly progressive course of disease. Treatment is supportive.
2. Infant botulism: look for sudden onset and a history of **honey ingestion** (or other home-canned foods). Diagnosis is made by finding *Clostridium botulinum* toxin or organisms in the feces. Treat on an inpatient basis with close monitoring of respiratory status. Patients may need intubation for respiratory muscle paralysis. Spontaneous recovery usually occurs within 1 week.

Peripheral neuropathies have multiple causes:

1. Metabolic: diabetes mellitus (autonomic and sensory neuropathy), uremia, hypothyroidism
2. Nutritional: deficiencies of vitamin B_{12}, B_6 (look for history of isoniazid), thiamine (dry beriberi), or vitamin E
3. Toxins and medications: lead (classic symptom is wristdrop or footdrop; look for coexisting central nervous system or abdominal symptoms) or other heavy metals, isoniazid, vincristine, ethambutol (especially optic neuritis), aminoglycosides (especially CN 8)
4. Postinfection/immunization and autoimmune: Guillain-Barré syndrome, systemic lupus erythematosus, polyarteritis nodosa, scleroderma, sarcoidosis, amyloidosis
5. Trauma: carpal tunnel syndrome (median nerve entrapment at the wrist), pressure paralysis (radial nerve palsy in alcoholics), or fractures. Carpal tunnel syndrome usually is due to repetitive physical activity but may be a presentation of acromegaly or hypothyroidism. Look for positive Tinel and Phalen signs.
6. Infectious: Lyme disease, diphtheria, HIV, tick bite, leprosy

Note: Nerve conduction velocity is slowed with a peripheral neuropathy.

Myasthenia gravis (MG): autoimmune disease that destroys acetylcholine receptors. MG usually presents in women aged 20–40. Look for ptosis, diplopia, and general muscle fatigability, especially toward the end of the day. Diagnosis is made with the Tensilon test. Injection of edrophonium (trade name: Tensilon), a short-acting anticholinesterase, improves muscle weakness. Watch for associated thymomas; most patients with MG improve after removal of the thymus, which is considered part of standard treatment. Most patients have antibodies to acetylcholine receptors in their serum. Treat with long-acting anticholinesterase (pyridostigmine, neostigmine).

Eaton-Lambert syndrome: a paraneoplastic syndrome (classically seen with small cell lung cancer) characterized by muscle weakness, with sparing of the extraocular muscles (MG almost always has prominent involvement of extraocular muscles). Eaton-Lambert syndrome has a different mechanism of disease (impaired release of acetylcholine from nerves) and a *differential* response to repetitive nerve stimulation (MG worsens, Eaton-Lambert improves).

Important points:

1. *Do not forget organophosphate poisoning as a cause for myasthenic-like muscle weakness.* Usually it occurs with agricultural exposure. Symptoms of parasympathetic excess also are present (e.g., miosis, excessive bronchial secretions, urinary urgency, diarrhea). Edrophonium causes worsening of the muscular weakness. Treatment is atropine and pralidoxime.
2. Aminoglycosides in high doses may cause myasthenic-like muscular weakness and prolong the effects of muscular blockade in anesthesia.

Muscular dystrophy: most commonly due to Duchenne muscular dystrophy, an X-linked recessive disorder of dystrophin that usually presents in boys aged 3–7. Look for muscle weakness, markedly elevated creatine kinase, and pseudohypertrophy of the calves (due to fatty and fibrous infiltration of the degenerating muscle). IQ often is less than normal. Gowers' sign is classic (when the patient tries to rise from a prone position, he "walks" the hands and feet toward each other). Muscle biopsy establishes the diagnosis. Treatment is supportive; most patients die by age 20. Other muscular dystrophies:

1. Becker muscular dystrophy: also an X-linked recessive dystrophin disorder, but milder
2. Facioscapulohumeral dystrophy: autosomal dominant disease that affects the areas in the name (face, shoulder girdle) and begins between ages 7 and 20. Life expectancy is normal.
3. Limb-girdle dystrophy: affects pelvic and shoulder muscles; begins in adulthood.
4. Mitochondrial myopathies: interesting because they are inherited mitochondrial defects (passed only from mother to offspring; males cannot transmit). The key phrase is "ragged red fibers" on biopsy specimen. Ophthalmoplegia usually is present.
5. Myotonic dystrophy: autosomal dominant disorder that presents between 20 and 30 years of age. Myotonia (inability to relax muscles) classically presents as **inability to relax the grip** (inability to release a handshake). Look for coexisting mental retardation, baldness, and testicular/ovarian atrophy. Treatment is supportive and includes genetic counseling. Diagnosis is clinical.

Note: *Do not forget the rare glycogen storage diseases (autosomal recessive)* as a cause for muscular weakness (especially McArdle's disease, a deficiency in glycogen phosphorylase that is relatively mild and presents with weakness and cramping after exercise).

CHAPTER 13

Immunology

Types of hypersensitivity reactions:

1. **Type I (anaphylactic):** due to preformed IgE antibodies, which cause release of vasoactive amines (e.g., histamine, leukotrienes) from mast cells and basophils. Examples are anaphylaxis (bee stings, food allergy [especially peanuts and shellfish], medications [especially penicillin and sulfa drugs], rubber glove allergy), atopy, hay fever, urticaria, allergic rhinitis, and some forms of asthma.
   - With chronic type I hypersensitivity (atopy, some asthma, allergic rhinitis), look for eosinophilia, elevated IgE levels, family history, and seasonal exacerbations. Patients also may have allergic "shiners" (bilateral infraorbital edema) and a transverse nasal crease (from frequent nose rubbing). Pale, bluish, edematous nasal turbinates with many eosinophils in clear, watery nasal secretions also are classic.
   - If patients have nasal polyps, do *not* give aspirin; you may precipitate a severe asthmatic attack.
   - Treat anaphylaxis immediately by securing the airway. Laryngeal edema may prevent intubation, in which case do a cricothyrotomy, if needed. Give subcutaneous epinephrine, then an antihistamine. Steroids are sometimes given for severe reactions, but only if other options are not present.
   - Watch for C1 esterase inhibitor (complement) deficiency as a cause of hereditary angioedema. Patients have diffuse swelling of lips, eyelids, and possibly the airway, unrelated to any allergen exposure. The deficiency is autosomal dominant; look for a positive family history. C4 complement is low. Treat acutely as anaphylaxis; androgens are used for long-term treatment to increase liver production of C1 esterase inhibitor.
   - Skin testing may identify an allergen if it is not obvious.
2. **Type II (cytotoxic):** due to preformed IgG and IgM, which react with antigen and cause secondary inflammation. Examples are autoimmune hemolytic anemia (classic causes are methyldopa or penicillin/sulfa drugs) and other cytopenias caused by antibodies, such as idiopathic thrombocytopenic purpura, transfusion reactions, erythroblastosis fetalis (Rh incompatibility), Goodpasture's syndrome (watch for linear immunofluorescence on kidney biopsy), myasthenia gravis, Graves' disease, pernicious anemia, pemphigus, and **hyperacute** transplant rejection (as soon as the anastomosis is made at transplant surgery, the transplanted organ deteriorates in front of your eyes).

Note: With anemia, watch for a positive Coombs' test; in pregnancy, watch for a positive indirect Coombs' test.

3. **Type III (immune complex-mediated):** due to deposits of antigen-antibody complexes (usually in vessels) that cause an inflammatory response. Examples are serum sickness, lupus, rheumatoid arthritis, polyarteritis nodosa, cryoglobulinemia, and glomerulonephritis (e.g., chronic hepatitis).
4. **Type IV (cell-mediated [delayed]):** due to sensitized T lymphocytes, which release inflammatory mediators. Examples include tuberculosis skin test, contact dermatitis (especially poison ivy, nickel earrings, cosmetics, medications), chronic transplant rejection, granulomas.

Human immunodeficiency virus (HIV)/AIDS: initial seroconversion may present as a mononucleosis-type syndrome (fever, malaise, pharyngitis, rash, lymphadenopathy). Keep seroconversion in the back of your mind as a differential diagnosis for any sore throat or Epstein-Barr virus-type presentation. Diagnosis is made with the enzyme-linked immunosorbent assay (ELISA), which, if positive, should be confirmed with a second assay. If the second assay is positive, confirm with a Western blot test. Do all tests before you tell the patient anything! It takes at least 1 month for antibodies to develop; therefore, if a patient comes to you for testing because of recent risk-taking behavior, you should retest the patient in 6 months if the initial test is negative.

Important points:

1. Once the diagnosis of HIV infection is made, the patient should get a CD4 count every 6 months.
2. Antiretroviral therapy should be started when the CD4 count falls below 500 (or sooner).
3. Once the CD4 count is less than 200, start prophylaxis for *Pneumocystis carinii* pneumonia (PCP). Use trimethoprim-sulfamethoxazole (TMP-SMX) or pentamidine (if the patient is allergic to or intolerant of TMP-SMX).
4. Once the CD4 count is less than 100, start prophylaxis for *Mycobacterium avium intracellulare* with rifabutine; consider cryptococcal and candidal prophylaxis with fluconazole.
5. Once CD4 < 200, the patient automatically is considered to have AIDS (even without opportunistic infections).
6. Give measles, mumps, and rubella (MMR) vaccine to HIV-positive patients (the only live vaccine given to HIV patients!).
7. Give pneumococcal, hepatitis B, inactivated polio vaccine, and annual influenza vaccines to all HIV-positive patients.
8. Do annual purified protein derivative test for tuberculosis in HIV-patients; get an annual chest x-ray if the patient is anergic.
9. Do *not* give oral polio vaccine to HIV-positive patients or their contacts.
10. Watch for Kaposi's sarcoma or non-Hodgkin's lymphoma (especially primary B-cell lymphomas of the central nervous system).
11. A positive India ink preparation of the cerebrospinal fluid means *Cryptococcus neoformans* meningitis.
12. Ring-enhancing lesions in the brain usually mean toxoplasmosis or cysticercosis (*Taenia solium*).
13. Other commonly seen HIV sequelae include wasting syndrome (progressive weight loss), dementia, peripheral neuropathies, thrombocytopenia, and loss of delayed hypersensitivity (type IV) on skin testing (anergy).

14. Give pregnant HIV-positive patients zidovudine (AZT), and give the infant AZT for 6 weeks after birth. This protocol reduces mother-to-child transmission from roughly 25% to 8%. The infant may have a positive HIV test for 6–12 months because of maternal antibodies. Retest after 6–12 months. Recent studies indicate that cesarean section also may reduce transmission.
15. HIV-positive mothers should *not* breast-feed, because they can transmit the disease to their infants through breast milk.
16. Use ganciclovir for cytomegalovirus retinitis; foscarnet is the second choice.
17. In any patient with HIV and pneumonia, think of PCP first. Look for severe hypoxia with normal x-ray or diffuse, bilateral interstitial infiltrates. Usually the patient has a dry, nonproductive cough. PCP may be detectable with silver stains (Wright-Giemsa, Giemsa, methenamine silver) of induced sputum; if not, use bronchoscopy with bronchoalveolar lavage and brush biopsy to make the diagnosis.
18. Any adult patient with thrush should make you think of HIV or leukemia.
19. Any young adult who presents with herpes zoster should make you think of HIV.
20. *Cryptosporidium* and *Isospora* spp. are diarrheal infections uniquely seen in HIV-positive patients

Primary immunodeficiencies: because they are rare, your job is simply to recognize the classic case presentation:

1. IgA deficiency: most common primary immunodeficiency. Look for recurrent respiratory and GI infections. IgA is low, and IgG subclass 2 may be low. Do *not* give immunoglobulins; you may cause anaphylaxis due to development of anti-IgA antibodies. Alternatively, in any patient who develops anaphylaxis after immunoglobulin exposure, you should think of IgA deficiency.
2. X-linked agammaglobulinemia (Bruton's agammaglobulinemia): X-linked recessive disorder that affects males. B-cells are low or absent; infections begin after 6 months when maternal antibodies disappear. Look for recurrent lung and sinus infections with *Streptococcus* and *Haemophilus* spp.
3. DiGeorge syndrome: caused by hypoplasia of the third and fourth pharyngeal pouches. Look for **hypocalcemia** and **tetany** (from absent parathyroids) in the first 24–48 hours of life. Also look for absent or hypoplastic thymus and congenital heart defects.
4. Severe combined immunodeficiency (SCID): may be autosomal recessive or X-linked. Many cases are due to adenosine deaminase deficiency (autosomal recessive). Patients have B- and T-cell defects and severe infections in the first few months of life, and cutaneous anergy usually is present. Other signs include an absent or dysplastic thymus and lymph nodes.
5. Wiskott-Aldrich syndrome: X-linked recessive disorder that affects males. Look for classic triad: **eczema, thrombocytopenia** (look for bleeding), and **recurrent infections** (usually respiratory).
6. Chronic granulomatous disease: usually X-linked recessive disorder that affects males. Patients have a defect in reduced nicotinamide adenine dinucleotide phosphate (NADPH) oxidase activity and thus get recurrent infections with catalase-positive organisms (e.g., *Staphylococcus aureus*, *Pseudomonas* sp.). The diagnosis is clinched if the question mentions deficient nitroblue tetrazolium dye reduction by granulocytes. This test measures respiratory burst, which patients lack.

7. Chediak-Higashi syndrome: usually autosomal recessive. Look for giant granules in neutrophils and associated oculocutaneous albinism. The cause is a defect in microtubule polymerization.
8. Complement deficiencies: C5–C9 deficiencies cause recurrent *Neisseria* infections; specific complement component is low.
9. Chronic mucocutaneous candidiasis: a cellular immunodeficiency specific for *Candida* sp. Patients have candidal thrush, scalp, skin, and nail infections and anergy to *Candida* sp. with skin testing. Hypothyroidism is often an associated finding. The rest of immune function is intact.
10. Hyper IgE syndrome (Job-Buckley syndrome): patients get recurrent staphylococcal infections (especially of the skin) and have extremely high IgA levels. They also commonly have fair skin, red hair, and eczema.

CHAPTER 14
Genetics

Questions often ask you to give genetic counseling to a parent or to predict the likelihood of having a second affected child after the first is born with a given disease. Because it is assumed that you know the inheritance pattern of the disease, the following lists should come in handy:

Autosomal dominant: look for affected mother or father who passes the disease to 50% of offspring:

- von Willebrand disease
- Neurofibromatosis: café-au-lait spots, profuse peripheral nerve tumors, acoustic neuroma
- Multiple endocrine neoplasia (MEN) type I and II syndromes
- Achondroplasia: diagnosis by picture of a patient
- Marfan syndrome: tall patient with arachnodactyly, mitral valve prolapse, aortic dissection, lens dislocation
- Huntington's disease
- Familial hypercholesterolemia: look for xanthomas, early coronary artery disease, markedly elevated cholesterol
- Familial polyposis coli
- Adult polycystic kidney disease
- Hereditary spherocytosis
- Tuberous sclerosis: hypopigmented skin macules, seizures, mental retardation, central nervous system hamartomas, rhabdomyomas, renal tumors
- Myotonic dystrophy: muscle weakness with inability to release grip, balding, cataracts, mental retardation, cardiac arrhythmias

Autosomal recessive: look for family history and unaffected parents who pass the disease to 25% of children:

- Sphingolipidoses (e.g., Tay-Sachs disease, Gaucher's disease; exception is Fabry's disease, which is X-linked)
- Mucopolysaccharidoses (e.g., Hurler's disease; exception is Hunter's disease, which is X-linked)
- Glycogen storage diseases (e.g., Pompe's and McArdle's disease.)
- Cystic fibrosis

- Galactosemia: look for congenital cataracts, neonatal sepsis; avoid galactose- and lactose-containing foods
- Amino acid disorders (e.g., phenylketonuria, alkaptonuria)
- Sickle cell disease
- Children's polycystic kidney disease
- Wilson's disease
- Hemochromatosis (usually)
- Adrenogenital syndrome (e.g., 21-hydroxylase deficiency)

X-linked recessive: look for affected fathers to pass the gene only to their daughters, who become carriers but do not get disease. Carrier mothers (family history in male relatives) who pass the gene to their sons, who get the disease:

- Hemophilia
- G-6-P-D deficiency
- Fabry's disease
- Hunter's disease
- Lesch-Nyhan syndrome: hypoxanthine-guanine phosphoribosyltransferase enzyme deficiency. Look for mental retardation and self-mutilation (patients may bite off their own fingers)
- Duchenne muscular dystrophy
- Wiscott-Aldrich syndrome
- Bruton's agammaglobulinemia
- Fragile X syndrome: second most common cause of mental retardation in males (after Down syndrome). Patients have large testes.

Polygenic disorders: relatives are more likely to have disease, but there is no obvious heritable pattern:

- Pyloric stenosis
- Cleft lip and/or palate
- Type II diabetes
- Obesity
- Neural tube defects
- Schizophrenia
- Bipolar disorder
- Ischemic heart disease
- Alcoholism

Chromosomal disorders

- Down syndrome (trisomy 21): most common known cause of mental retardation. The major risk factor is age of the mother (1/1500 offspring of 16-year-old mothers, 1/25 for 45-year-old mothers). At birth look for hypotonia, transverse palmar crease, and characteristic facies. Congenital cardiac defects (especially ventral septal defect) are common, and patients are at increased risk for leukemia, duodenal atresia, and early Alzheimer's disease.

- Edwards syndrome (trisomy 18): more common in females than males. Patients are small for their age and have mental retardation, small head, hypoplastic mandible, low-set ears, and clenched fist with index finger overlapping third and fourth fingers (almost pathognomonic).
- Patau's syndrome (trisomy 13): mental retardation, apnea, deafness, holoprosencephaly (fusion of cerebral hemispheres), myelomeningocele, cardiovascular abnormalities, rocker-bottom feet.
- Turner's syndrome (XO instead of XX): lymphedema of neck at birth, short stature, webbed neck, widely spaced nipples, amenorrhea, and lack of breast development (due to primary ovarian failure). Coarctation of the aorta is common, and patients may have horse-shoe kidneys or cystic hygroma.
- Klinefelter's syndrome (XXY): tall patient with microtestes (< 2 cm in length), gynecomastia, sterility (the classic presentation is for infertility), and decreased IQ.
- Cri-du-chat: due to a deletion on the short arm of chromosome 5; look for **high-pitched cry like a cat** along with severe mental retardation.

CHAPTER 15
Geriatrics

Important points:

1. The most rapid increase in population in the U.S. (percentage-wise) is in people over 65. Within this group, the over-85 subgroup is increasing most rapidly.
2. At age 80 patients have half the lean body mass of a 30-year-old. Because basal metabolic rate depends on lean body mass, elderly patients need fewer calories. They also need more sodium, vitamin B_{12}, vitamin D (and/or calcium), folate, and nonheme iron.
3. Normal changes in elderly: slightly impaired immune response, visual (presbyopia) and hearing (presbycusis) impairment, decreased muscle mass, increased fat deposits, osteoporosis, brain changes (decreased weight, enlarged ventricles and sulci), and slightly decreased ability to learn new material.
4. Normal sexual function changes in men: elderly men take longer to get an erection and have an increased refractory period (after ejaculation it takes longer before the patient can have another erection). Delayed ejaculation is common, and the patient may ejaculate only 1 of every 3 times that he has sex. Impotence and lack of sexual desire are *not* normal and should be investigated. Look for psychological (depression) as well as physical causes. Medications, especially antihypertensives, are notorious culprits.
5. Normal sexual function changes in women: for decreased lubrication, advise water-soluble lubricants. Atrophy of clitoris, labia, and vaginal tissues may cause dyspareunia; treat with estrogen cream. Delayed orgasm is common, but lack of sexual desire is *not* normal and should be investigated (psychological or physical causes).
6. The best prophylaxis for pressure ulcers in an immobilized patient is frequent turning.
7. Sleep changes: elderly people sleep less deeply, wake up more frequently during the night, and awaken earlier in the morning. They take longer to fall asleep (longer sleep latency) and have less stage 3 and 4 and rapid-eye-movement sleep.
8. Depression in the elderly may present as dementia (i.e., pseudodementia). Look for a history that would trigger depression (e.g., loss of a spouse, terminal or debilitating disease).
9. In 1993, 12% of the U.S. population was over age 65.
10. Fifteen percent of people over age 65 suffer from dementia. The most common causes of dementia, in order, are Alzheimer's disease (gradually progressive, neurofibrillary tangles) and multiinfarct (step-wise, risk factors for cerebrovascular accident). Other causes include HIV and Pick's disease.
11. Only 5% of people over the age of 65 live in nursing homes.

CHAPTER 16

Preventive Medicine, Epidemiology, and Biostatistics

PREVENTIVE MEDICINE

American Cancer Society guidelines for cancer screening in asymptomatic patients*

CANCER	PROCEDURE	AGE (YR)	FREQUENCY
Colorectal	Sigmoidoscopy	> 50	After 2 normal exams 1 yr apart, every 3–5 yr
Colorectal	Stool guaiac	> 50	Annually
Colon, prostate	Digital rectal exam	> 40	Annually
Cervical	Pap smear	20–65†	After 2 normal exams 1 yr apart, every 3 yr
Gynecologic	Pelvic exam	20–40	Every 3 yr
		> 40	Annually
Endometrial	Endometrial biopsy	Menopause	Once at menopause
Breast	Breast self-exam	> 20	Monthly
Breast	M.D. physical exam	20–40	Every 3 yr
		> 40	Annually
Breast	Mammography	35–40	Baseline mammography
		40–49	Every 1–2 yr
		> 50	Annually
Lung	Sputum cytology, chest x-ray		Do not do even in high-risk patients
Cancer check-up‡	Health counseling and exam	20–39	Every 3 yr
		> 40	Annually

* The above table is for screening of asymptomatic, normal patients. Do any of these tests at any time if indicated by history and physical exam. Although other committees have their own cancer screening recommendations, you will not get any board questions wrong if you use the above guidelines from the American Cancer Society. The boards generally do not test controversial areas.
† Start Pap smears at < 20 if the patient is sexually active.
‡ Includes examination for cancers of the thyroid, testis, prostate, ovary, lymph nodes, oral region, and skin.

Important points:

1. Colonoscopy is equal to flexible sigmoidoscopy plus barium enema (BE) for colon cancer screening. Colonoscopy is more sensitive and more expensive. Choose flexible sigmoidoscopy + BE over colonoscopy for boards. Double-contrast (air-contrast) BE is superior to single-contrast (no air) BE.

2. In general, urinalysis (screening for urinary tract cancer that results in hematuria), acid phosphatase (prostate cancer), alpha-fetoprotein (liver and testicular cancer), and other serum markers are not appropriate for screening asymptomatic patients with no physical findings, but look for these abnormal lab values to show up in questions as a clue to diagnosis. Prostate-specific antigen (PSA) is becoming popular as a prostate cancer screening test, but does not replace rectal exam.

Immunizations in adults

VACCINE	WHO SHOULD BE VACCINATED AND OTHER INFORMATION
Hepatitis B	Offer to any young adults not immunized Give to high-risk adults: Sexually promiscuous (heterosexual or homosexual) Household contacts and sex partners of HBsAg-positive people Intravenous drug abusers Health care workers and others at occupational risk Hemodialysis patients Hemophiliacs and other blood product recipients International travelers Inmates Anyone who asks for it
Influenza	Given annually to all patients over 65 Patients with chronic pulmonary or cardiovascular disorders Health care workers (to protect patients) Nursing home and chronic care residents Children with asthma Diabetics Renal patients Patients with hemoglobinopathies Patients with immunosuppression (including that due to medications) Children on chronic aspirin therapy (to prevent Reye's syndrome) Women who will be pregnant during the influenza season (winter) Household contacts of high-risk patients (to protect the high-risk patient, not the contact)
Pneumococcal infection	All patients over 65 Patients with chronic cardiovascular or pulmonary disease Diabetics Alcoholics Patients with cirrhosis Patients with cerebrospinal leaks Immunocompromised patients Patients with asplenia or splenic dysfunction (give to patients with sickle cell disease at the age of 2) Patients with malignancy Patients with chronic renal failure or nephrotic syndrome Organ transplant recipients
Rubella	All women of child-bearing age who lack immunity or whose history of immunization is unknown Do not give to a pregnant woman Women should avoid pregnancy for 3 months after vaccination Health care workers (to protect pregnant patients' unborn children!) Do not give to immunocompromised patients (exception: give measles, mumps, and rubella vaccine to HIV-positive patients)
Tetanus	All patients every 10 years Give for all wounds if vaccination history is unknown or if patient has less than 3 shots Give tetanus booster to patients with full vaccination history if more than 10 yr have passed for clean, minor wound or if 5 yr have passed for all other wounds since last booster Give tetanus immunoglobulin only for patients with unknown or incomplete vaccination and nonclean/nonminor wounds
Diphtheria	Given with tetanus; has the same indications

EPIDEMIOLOGY

Per-year rates commonly used to compare groups:

1. Birth rate: live births/1000 population
2. Fertility rate: live births/1000 population of females age 15–45 yr
3. Death rate: deaths/1000 population
4. Neonatal mortality rate: neonatal deaths (in the first 28 days)/1000 live births
5. Perinatal mortality rate: neonatal deaths + stillbirths per 1000 total births
   - The major cause is prematurity
   - The neonatal mortality rate is roughly 6/1000 (higher in blacks)
   - The fetal mortality rate is roughly 9/1000 (higher in nonwhites)
   - The perinatal mortality rate is roughly 15/1000
   - A stillbirth (fetal death) is defined as a prenatal or natal death after 20 weeks' gestation
6. Infant mortality rate: deaths (from 0–1 year old)/1000 live births (the top three causes, in descending order, are congenital abnormalities, low birth weight, and sudden infant death syndrome)
7. Maternal mortality rate: maternal pregnancy-related deaths (deaths during pregnancy or in the first 42 days after delivery)/100,000 live births
   - The top three causes are pulmonary embolism, pregnancy-induced hypertension, and hemorrhage
   - The rate increases with age and is higher in blacks

Important points:

1. Medicare is health insurance for people who are eligible for Social Security (primarily people > 65 years old as well as the permanently and totally disabled and patients with end-stage renal disease). Nursing home care is paid by Medicare only in the short term after a hospital admission; then it is paid by the patient (if the patient has no money, the state usually pays).
2. Medicaid covers the indigent and poor who are deemed eligible by the individual states.

BIOSTATISTICS

Review this section of Step I material for some easy points.

Sensitivity: ability to detect disease. Mathematically, sensitivity is calculated by dividing the number of true positives by the number of people with the disease. Tests with high sensitivity are used for screening. They may have false positives but do not miss many people with the disease (low false-negative rate).

Specificity: ability to detect health (or nondisease). Mathematically, specificity is calculated by dividing the number of true negatives by the number of people without the disease. Tests with high specificity are used for disease confirmation. They may have false negatives but do not call anyone sick who is actually healthy (low false-positive rate). The ideal confirmatory test must have high sensitivity *and* high specificity; otherwise, people with the disease may be called healthy.

The **trade-off between sensitivity and specificity** is a classic statistics question. Understand how changing the cut-off glucose value in screening for diabetes (or changing the value of any of several screening tests) will change the number of true and false negatives and true and false positives. If the cut-off value is raised, fewer people will be called diabetic (more false negatives, fewer false positives), whereas if the cut-off value is lowered, more people will be called diabetic (fewer false negatives, more false positives).

Positive predictive value (PPV): when a test comes back positive for disease, the PPV measures how likely it is that the patient has the disease (probability of having a condition, given a positive test). Mathematically, PPV is calculated by dividing the number of true positives by the number of people with a positive test. PPV depends on the prevalence of a disease (the higher the prevalence, the greater the PPV) and the sensitivity/specificity of the test (e.g., an overly sensitive test that gives more false positives has a lower PPV).

Negative predictive value (NPV): when a test comes back negative for disease, the NPV measures how likely it is that the patient is healthy and does not have the disease (probability of not having a condition, given a negative test). Mathematically, NPV is calculated by dividing the number of true negatives by the number of people with a negative test. NPV depends on prevalence and sensitivity/specificity just like PPV. The higher the prevalence, the lower the NPV. In addition, an overly sensitive test with lots of false positives will make the NPV higher.

Attributable risk: number of cases attributable to one risk factor; in other words, the amount by which you can expect the incidence to decrease if a risk factor is removed. For example, if the incidence rate of lung cancer in the general population is 1/100 and in smokers it is 10/100, the attributable risk of smoking in causing lung cancer is 9/100 (assuming a properly matched control).

Relative risk (RR): compares the disease risk in the exposed population to the disease risk in the unexposed population. RR can be calculated only after prospective or experimental studies; it *cannot* be calculated from retrospective data. RR greater than 1 is clinically significant.

Odds ratio (OR): used only for retrospective studies (e.g., case-control). OR compares disease in exposed and nondisease in unexposed populations with disease in unexposed and nondisease in exposed populations to determine whether there is a difference between the two. Of course, there should be more disease in exposed than unexposed populations and more nondisease in unexposed than exposed populations. OR is a less than perfect way to estimate relative risk.

Get in the habit of drawing a **2 × 2 table** to make calculations easier:

		Disease (+)	Disease (−)
Test (+) or Exposure	(+)	A	B
	(−)	C	D

Sensitivity = A/(A + C)

Specificity = D/(B + D)

PPV = A/(A + B)

NPV = D/(C + D)

Odds ratio = (A × D)/(B × C)

Relative risk = [A/(A + B)] / [C/(C + D)]

Attributable risk = [A/(A + B)] − [C/(C + D)]

Standard deviation (SD): with a normal or bell-shaped distribution, 1 SD holds 68% of values, 2 SD holds 95% of values, and 3 SD holds 99.7% of values. The classic question gives you the mean and standard deviation and asks you what percentage of values will be above a given value; variations on this question are also common. In a normal distribution, the mean = median = mode. The mean is the average, the median is the middle value, and the mode is the most common value. Questions may give you several numbers and ask for their mean, median, and mode.

Skewed distribution: a positive skew is asymmetry with an excess of high values (tail on right, mean > median > mode); a negative skew is asymmetry with an excess of low values (tail on left, mean < median < mode). These are *not* normal distributions; thus, standard deviation and mean are less meaningful values.

Reliability of a test (synonymous with precision): measures the reproducibility and consistency of a test (e.g., the concept of interrater reliability: if two different people administer the same test, they will get the same score if the test is reliable). Random error reduces reliability/precision (e.g., limitation in significant figures).

Validity of a test (synonymous with accuracy): measures the trueness of measurement—whether the test measures what it claims to measure. For example, if you give a valid IQ test to a genius, the test should not indicate that he or she is retarded. Systematic error reduces validity/accuracy (e.g., miscalibrated equipment).

Correlation coefficient: measures the degree of relationship between two values. The range of the coefficient is −1 to +1. The important point in determining the strength of the relationship between the two variables is how far the number is from zero. Zero equals no association whatsoever; positive one (+1) equals a perfect positive correlation (when one variable increases, so does the other); and negative one (−1) equals a perfect negative correlation (when one variable increases, the other decreases). Use the absolute value to give you the strength of the correlation (e.g., −0.3 is a stronger correlation than +0.2).

Confidence interval (CI): when you take a set of data and calculate a mean, you want to say that it is equivalent to the mean of the whole population, but usually they are not exactly equal. The CI (usually set at 95%) says that you are 95% confident that the population mean is within a certain range (usually within 2 SD of the experimental or derived mean). For example, if you sample the heart rate of 100 people and calculate a mean of 80 bpm and a SD of 2, your confidence interval (confidence limits) is written as $76 < X < 84 = 0.95$. This means that you are 95% certain that the mean heart rate of the whole population (X) is between 76 and 84.

Different types of studies (listed in decreasing order of quality and desirability):

1. Experimental: the gold standard, which compares two equal groups in which one variable is manipulated and its effect is measured. Remember to use double-blinding (or at least single-blinding) and well-matched controls.
2. Prospective, longitudinal, cohort, incidence, follow-up: choose a sample and divide it into two groups based on presence or absence of a risk factor and follow the group over time to see what diseases they develop (e.g., follow people with and without asymptomatic hypercholesterolemia to see whether people with hypercholesterolemia have a higher incidence of myocardial infarction later in life). This approach sometimes is called an observational study because all you do is observe. Relative risk and incidence can be calculated. Prospective studies are time-consuming, expensive, and good for common diseases, whereas retrospective studies are less expensive, less time-consuming, and good for rare diseases.

3. Retrospective/case-control: samples are chosen after the fact based on presence (cases) or absence (controls) of disease. Information can then be collected about risk factors; for example, look at people with lung cancer vs. people without lung cancer and see if the people with lung cancer smoke more. An odds ratio can be calculated, but you *cannot* calculate a *true relative risk* or measure incidence from a retrospective study.
4. Case series: good for extremely rare diseases (as are retrospective studies). Case series simply describe the clinical presentation of people with a certain disease and may suggest the need for a retrospective study.
5. Prevalence survey/cross-sectional survey: looks at prevalence of a disease and prevalence of risk factors. When comparing two different cultures, you may get an idea about the cause of a disease, which can be tested with a prospective study (e.g., more colon cancer and higher-fat diet in U.S. vs. less colon cancer and low-fat diet in Japan).

Incidence: the number of new cases of disease in a unit of time (generally 1 year, but any time frame can be used). Incidence rate also equals the absolute risk (to be differentiated from relative or attributable risk).

Prevalence: the total number of cases of disease that exist (new or old).

Important points:

1. The classic question about incidence and prevalence: when a disease can be treated and people can be kept alive longer but the disease cannot be cured, what happens to the incidence and prevalence? Answer: nothing happens to incidence, but prevalence will increase as people live longer. In short-term diseases, such as the flu, incidence may be higher than prevalence, whereas in chronic diseases, such as diabetes mellitus, prevalence is greater than incidence.
2. An epidemic occurs when the observed incidence greatly exceeds the expected incidence.

Comparison of data:

1. Chi-squared test: used to compare percentages or proportions (nonnumeric data, also called nominal data)
2. T-test: used to compare two means
3. Analysis of variance (ANOVA): used to compare three or more means

P-value: the board exam always contains one or more questions about the significance of the p-value. If someone tells you that $p < 0.05$ for a given set of data, there is less than a 5% chance (because 0.05=5%) that these data were obtained by random error or chance. If $p < 0.01$, the chance that the data were obtained by random error or chance is less than 1%. For example, if I tell you that the blood pressure in my controls is 180/100 mmHg but decreases to 120/70 mmHg after administration of drug X and that $p < 0.10$, there is less than a 10% chance that the difference in blood pressure was due to random error or chance. However, there is up to a 9.99999% chance that the result is due to random error or chance. For this reason, $p < 0.05$ is commonly used as the cut-off for statistical significance. Three points to remember: (1) the study may still have serious flaws, (2) a low p-value does not imply causation, and (3) a study that has statistical significance does *not* necessarily have clinical significance. For example, if I tell you that drug X can lower the blood pressure from 130/80 to 128/80, $p < 0.000000000000000001$, you still would not use drug X.

The p-value also ties into the **null hypothesis** (the hypothesis of no difference). For example, in a drug study about hypertension, the null hypothesis is that the drug does not work; any difference

in blood pressure is due to random error or chance. When the drug works beautifully and lowers the blood pressure by 60 points, I have to reject the null hypothesis, because clearly the drug works. When $p < 0.05$, I can confidently reject the null hypothesis, because the p-value tells me that there is less than a 5% chance that the null hypothesis is correct—and if the null hypothesis is wrong, the difference in blood pressure is *not* due to chance and must be due to the new drug. In other words, the p-value represents the chance of making a **type I error** (claiming an effect or difference when none exists, rejecting the null hypothesis when it is true). If $p < 0.07$, there is less than a 7% chance that you are making a type I error if you claim a difference in blood pressure between control and experimental groups. **Type II error** is to accept the null hypothesis when it is false (the hypertension drug works, but you say that it does not).

Power: probability of rejecting the null hypothesis when it is false (a good thing). The best way to increase power is to **increase sample size**.

Experimental conclusions and errors: the exam may give you data and the experimenter's conclusion and ask you to explain why the conclusion should not be drawn or to point out flaws in the experimental design:

1. Confounding variables: an unmeasured variable affects both the independent (manipulated, experimental variable) and dependent (outcome) variables. For example, an experimenter measures number of ashtrays owned and incidence of lung cancer and finds that people with lung cancer have more ashtrays. He concludes that ashtrays cause lung cancer. Smoking tobacco is the confounding variable, because it causes the increase in ashtrays and lung cancer.
2. Nonrandom or nonstratified sampling: city A and city B can be compared but may not be equivalent. For example, if city A is a retirement community and city B is a college town, of course city A will have higher rates of mortality and heart disease if the groups are not stratified into appropriate age-specific comparisons.
3. Nonresponse bias: people fail to return surveys or answer the phone for a phone survey. If nonresponse is a significant percentage of the results, the experiment will suffer. The first strategy is to visit or call the nonresponders repeatedly in an attempt to reach them and get their response. If this strategy is unsuccessful, list the nonresponders as unknown in the data analysis and see if any results can be salvaged. *Never* make up or assume responses!
4. Lead time bias: due to time differentials. The classic example is a cancer screening test that claims to have prolonged survival compared with old survival data, when in fact the difference in survival is due only to earlier detection, *not* to improved treatment or prolonged survival.
5. Admission rate bias: in comparing hospital A with hospital B for mortality due to myocardial infarction, you find that hospital A has a higher mortality rate. But this finding may be due to tougher hospital admission criteria at hospital A, which admits only the sickest patients with myocardial infarction and thus has higher mortality rates, although their care may be superior. The same bias can be found in a surgeon's mortality/morbidity rates if the surgeon takes only tough cases.
6. Recall bias: risk for retrospective studies. When patients cannot remember, they may inadvertently over- or underestimate risk factors. For example, John died of lung cancer, and his angry wife remembers him as smoking "like a chimney," whereas Mike died of a non–smoking-related cause and his loving wife denies that he smoked "much." In fact, both men smoked 1 pack per day.
7. Interviewer bias: due to lack of blinding. A scientist gets big money to do a study and wants to find a difference between cases and controls. Thus, he or she inadvertently labels

the same patient comment or outcome as "no significance" in controls and "serious difference" in treated cases.

8. Unacceptability bias: patients do not admit to embarrassing behavior or claim to exercise more than they do to please the interviewer—or they may claim to take experimental medications when they spit them out.

CHAPTER 17

Psychiatry

Schizophrenia:

1. The diagnostic criteria provide clues: delusions, hallucinations, disorganized speech, grossly disorganized/catatonic behavior, and negative symptoms (flat affect, refusal to talk, avolition, apathy).
2. Time period important: < 1 month = acute psychotic disorder, 1–6 months = schizophreniform disorder, > 6 months = schizophrenia.
3. Positive symptoms: delusions, hallucinations, bizarre behavior, thought disorder (e.g., tangentiality, clanging). These symptoms respond to traditional antipsychotics (haloperidol, chlorpromazine).
4. Negative symptoms = flat affect, alogia (no speech), avolition (apathy), anhedonia, poor attention. These symptoms respond poorly to traditional antipsychotics but may respond to clozapine or risperidone.
5. Good prognosis features: good premorbid functioning (most important); late onset; obvious precipitating factors; married; family history of mood disorders; positive symptoms; good support system.
6. Poor prognosis features: poor premorbid functioning (most important); early onset; no precipitating factors; single, divorced, or widowed; family history of schizophrenia; negative symptoms; poor support system.
7. Typical age of onset: 15–25 years for men (look for someone going to college and deteriorating); 25–35 years for women.
8. Roughly 1% of people have schizophrenia (in all cultures).
9. In the U.S., most schizophrenic patients are born in the winter (not known why).
10. Up to 10% of schizophrenics eventually commit suicide (past attempt is best predictor of eventual success).
11. Antipsychotic medications are the mainstay of therapy, but psychosocial treatment has been shown to improve outcome. Medications are used first, but the best treatment (as in most of psychiatry) is medications plus therapy.

Antipsychotic medications (see table, top of next page)

	HIGH POTENCY	LOW POTENCY	ATYPICAL
Examples	Haloperidol	Chlorpromazine	Clozapine, risperidone
EP side effects	*High incidence*	*Low incidence*	*Low incidence*
ANS side effects*	Low incidence	High incidence	Medium incidence
Positive symptoms	Works well	Works well	Works well
Negative symptoms	Works poorly	Works poorly	Works well

EP = extrapyramidal, ANS = autonomic nervous system.

* ANS side effects include anticholinergic (dry mouth, urinary retention, blurry vision, mydriasis), alpha-1 blockade (orthostatic hypotension), and antihistamine effects (sedation).

Extrapyramidal side effects:

1. Acute dystonia: first few hours or days of treatment. The patient has muscle spasms or stiffness (e.g., torticollis, trismus), tongue protrusions and twisting, opisthotonos, and oculogyric crisis (forced sustained deviation of the head and eyes). Acute dystonia is most common in young men. Treat by giving antihistamines (diphenhydramine) or anticholinergics (benztropine, trihexyphenidyl).
2. Akathisia: first few days of treatment. The patient has a subjective feeling of restlessness. Look for constant pacing, alternate sitting and standing, and inability to sit still. Beta blockers can be tried for treatment.
3. Parkinsonism: first few months of treatment. The patient has stiffness, cogwheel rigidity, shuffling gait, mask-like facies, and drooling. Parkinsonism is most common in older women. Treat by giving antihistamines (diphenhydramine) or anticholinergics (benztropine, trihexyphenidyl).
4. Tardive dyskinesia: after years of treatment. Most commonly, the patient has perioral movements (darting, protruding movements of the tongue, chewing, grimacing, puckering). The patient also may have involuntary, choreoathetoid movements of head, limbs, and trunk. There is no known treatment for tardive dyskinesia. If you have to make a choice when the patient develops tardive dyskinesia, discontinue the antipsychotic and consider switching to clozapine.
5. Neuroleptic malignant syndrome: life-threatening condition that can develop at any time during treatment. The patient has rigidity, mutism, obtundation, agitation, **high fever** (up to 107°F), **high creatine phosphokinase** (often > 5000), sweating, and myoglobinuria. Treatment: **first** discontinue antipsychotic; then provide supportive care for fever and renal shutdown due to myoglobinuria; finally, administer dantrolene (just as in malignant hyperthermia).

Other antipsychotic medication pearls:

1. Dopamine blockade causes increases in prolactin (dopamine is a prolactin-inhibiting factor in the tuberoinfundibular tract), which may cause galactorrhea, impotence, menstrual dysfunction, and decreased libido.
2. Individual antipsychotic side effects: *thioridazine causes retinal pigment deposits;* clozapine causes agranulocytosis (white blood cells counts must be monitored); chlorpromazine causes jaundice and photosensitivity.

Bipolar disorder:

1. Mania is the only symptom required for a diagnosis of bipolar disorder, but a history of depression is common.

2. Look for classic symptoms such as decreased need for sleep, pressured speech, sexual promiscuity, shopping sprees, and exaggerated self-importance or delusions of grandeur.
3. Look for initial onset between 16–30 years old.
4. Lithium and valproic acid are first-line treatments. Choose lithium if both are options; choose carbamazepine if lithium fails. If valproic acid is a choice, choose valproic acid over carbamazepine.
5. Antipsychotics may be needed if the patient becomes psychotic; use at the same time as mood stabilizer.
6. Bipolar II disorder is **hypomania** (mild mania without psychosis that does not cause occupational dysfunction) plus major depression.
7. Cyclothymia is at least 2 years of **hypomania** alternating with depressed mood (no full-blown mania or depression).
8. Lithium causes renal dysfunction (diabetes insipidus), thyroid dysfunction, tremor, and central nervous system effects at toxic levels. Valproic acid causes liver dysfunction, and carbamazepine may cause bone marrow depression.

Suicide:

1. The major risk factors are age > 45 years, alcohol or substance abuse, history of rage or violence, prior suicide attempts, male sex (men commit suicide 3 times more often than women, but women attempt it 4 times more often than men), prior psychiatric history, depression, recent loss or separation, loss of health, unemployment or retirement, and single, widowed, or divorced status.
2. If you have to choose, the best predictor of future suicide is a past attempt.
3. Always ask patients about suicide (it does not make them more likely to commit suicide). If you need to do so, hospitalize acutely suicidal patients against their will.
4. When patients come out of a deep depression, they are at increased risk of suicide. The antidepressant may begin to work, and the patient gets more energy—just enough to carry out suicide plans.
5. Suicide rates are rising the fastest in 15–24-year-olds, but the greatest risk is in people over age 65.

Depression:

1. Patients may not directly say, "I'm depressed." You have to watch for clues: change in sleep habits (classically, insomnia), vague somatic complaints, anxiety, low energy or fatigue, change in appetite (classically, decreased appetite), poor concentration, psychomotor retardation, and/or anhedonia (loss of pleasure).
2. Patients may or may not have obvious precipitating factors in history, such as loss of loved one, divorce or separation, unemployment or retirement, chronic or debilitating disease.
3. Depression is more common in females.
4. Treat with both antidepressants and psychotherapy (combination works better than medications alone).
5. **Adjustment disorder with depressed mood:** when a bad situation occurs, the patient does not handle it well and feels "bummed out" for < 6 months, but does not meet criteria for full-blown depression. For example, the patient gets a divorce, seems to cry a lot for the next few weeks, and leaves work early on most days.

6. **Dysthymia:** depressed mood on most days for more than 2 years, but no episodes of major depression, mania, hypomania, or psychosis.
7. Antidepressants can trigger mania or hypomania, especially in bipolar patients.
8. Tricyclic antidepressants (TCAs; e.g., nortriptyline, amitriptyline) prevent reuptake of norepinephrine and serotonin. They also block alpha-adrenergic receptors (watch for orthostatic hypotension, dizziness, and falls) and muscarinic receptors as well as cause sedation and lower the seizure threshold (especially bupropion, which technically is not a tricyclic). TCAs are dangerous in overdose primarily because of **cardiac arrhythmias**, which may respond to bicarbonate.
9. Selective serotonin reuptake inhibitors (SSRIs; e.g., fluoxetine, paroxetine) prevent reuptake of serotonin only and have less serious side effects (insomnia, anorexia, **sexual dysfunction**).
10. Monoamine oxidase inhibitors (*MAOIs*; e.g., phenelzine, *tranylcypromine*) are older medications and not first-line agents. They may be good for atypical depression (look for hypersomnia and hyperphagia, the opposite of classic depression). When patients eat tyramine-containing foods (especially wine and cheese), they may get a hypertensive crisis. Do not give MAOI at the same time as SSRIs or meperidine; severe reactions may occur, possibly death.
11. Trazodone is famous because it can cause priapism (persistent, painful erection without sexual arousal or desire).

Normal vs. pathologic grief, mourning, bereavement:

1. Initial grief after a loss (e.g., death of a loved one) may include a state of shock, feeling of numbness or bewilderment, distress, crying, sleep disturbances, decreased appetite, difficulty with concentrating, weight loss, and guilt (survivor guilt) **for up to 1 year**—in other words, the same symptoms as depression.
2. It is **normal** to have an illusion or hallucination about the deceased, but a normal grieving person knows that it is an illusion or hallucination, whereas a depressed person believes that the illusion or hallucination is real.
3. **Intense yearning** (even years after the death) and even searching for the deceased are normal.
4. Feelings of worthlessness, psychomotor retardation, and suicidal ideation are not normal expressions of grief; they are signs of depression.

Panic disorder: Look for 20–40-year-old patient who thinks that he or she is dying or having a heart attack but is healthy and has a negative work-up for organic disease. Patients often hyperventilate and are extremely anxious. A common association is agoraphobia (fear of leaving the house). Treat with SSRIs (e.g., fluoxetine).

Generalized anxiety disorder: patients worry about everything (e.g., career, family, future, relationships, money) at the same time. Symptoms are not as dramatic as in panic disorder; patients are just severe worriers. Treat with buspirone (nonaddictive, nonsedating) or benzodiazepines (addictive, sedating).

Simple phobias: for example, to needles, blood products, animals, or heights. Treat with behavioral therapy (flooding, systematic desensitization, biofeedback, mental imagery—know what these terms mean).

Social phobia: a specific simple phobia that is best treated with behavioral therapy. Beta blockers may be used to reduce symptoms before a public appearance that cannot be avoided.

Posttraumatic stress disorder: look for someone who has been through a life-threatening event (Vietnam veteran, victim of severe accident or rape) who recurrently experiences the event in nightmares or flashbacks, tries to avoid thinking about it, and has depression or poor concentration as a result. Treat with group therapy; if you have to choose a medication, use imipramine or phenelzine (MAOI).

Homosexuality and homosexual experimentation are not considered a disease at any age; they are normal variants. Kinky fantasies or occasional kinky activities (a man wearing women's underwear, mild foot fetish) are normal.

Somatoform disorders: patients do *not* behave inappropriately on purpose. Treat with frequent return clinic visits and/or psychotherapy.

1. Somatization disorder: multiple *different* complaints in multiple *different* organ systems over many years with extensive work-ups in the past.
2. Conversion disorder: obvious precipitating factor (fight with boyfriend) followed by unexplainable neurologic symptoms (blindness, stocking-and-glove numbness).
3. Hypochondriasis: patients keep believing that they have the *same* disease despite extensive negative work-up.
4. Body dysmorphic disorder: preoccupation with imagined physical defect (e.g., a teenager who thinks that his or her nose is too big when it is of normal size).

Somatoform disorders vs. factitious disorder vs. malingering:

1. Somatoform disorders: patients do not intentionally create symptoms.
2. Factitious disorders: patients intentionally create their illness or symptoms (e.g., inject themselves with insulin to provoke hypoglycemia) and subject themselves to procedures to assume the role of a patient (no financial or other secondary gain).
3. Malingering: patients intentionally create their illness for secondary gain (e.g., money, to get out of work).

Dissociative fugue/psychogenic fugue: the patient has amnesia and travels, assuming new identity.

Multiple personality disorder: most likely to be associated with childhood sexual abuse.

Adjustment disorder: normal life experience (e.g., relationship break-up, failing grade, loss of job) is not handled well. Patients often are depressed (adjustment disorder with depressed mood) but do *not* meet the criteria for full-blown depression. For example, a high-school girl who breaks up with her boyfriend may mope around the house, crying and not wanting to attend school or go out with her friends for 1 week.

Personality disorders are lifelong disorders with no real treatment, although psychotherapy may be tried:

1. Paranoid: patients think that everyone is out to get them (friends, too) and often start law-suits.
2. Schizoid: the classic loner; no friends and no interest in having friends.
3. Schizotypal: bizarre beliefs (extrasensory perception, cults, superstition, illusions) and manner of speaking but no psychosis.
4. Avoidant: patients have no friends but want them; they are afraid of criticism or rejection and avoid others (inferiority complex).

5. Histrionic: overly dramatic, attention-seeking, and inappropriately seductive; the patient must be the center of attention.
6. Narcissistic: egocentric and lacking empathy; patients use others for their own gain or have a sense of entitlement.
7. Antisocial: most frequently tested personality disorder. Patients have long criminal record (con-men) and torture animals or set fires as children (a history of conduct disorder is required for this diagnosis). They are aggressive, do not pay bills or support children, often lie, and have no remorse or conscience. Strong association with alcoholism or drug abuse and somatization disorder. Most patients are male.
8. Borderline: unstable mood, behavior, relationships (many bisexual), and self-image. Look for splitting (people are all good or all bad and may frequently change categories), suicide attempts, micropsychotic episodes (2 minutes of psychosis), impulsiveness and constant crisis (see Glenn Close in *Fatal Attraction*).
9. Dependent: patients cannot be (or do anything) alone; a wife stays with an abusive husband; highly dependent on others.
10. Obsessive-compulsive: anal-retentive, stubborn; rules more important than objectives; restricted affect, cheap.

Obsessive-compulsive disorder: patients have recurrent thoughts or impulses (obsessions) and/or recurrent behaviors/acts (compulsions) that cause marked dysfunction in occupational and/or interpersonal lives. Look for **washing** (wash hands 30 times a day) and/or **checking rituals** (check to see if door is locked 30 times a day). Onset usually is in adolescence or early adulthood. Treat with SSRIs or clomipramine. Behavioral therapy also may be effective (e.g., flooding).

Narcolepsy: daytime sleepiness; decreased rapid-eye-movement (REM) latency (patients go into REM as soon as they fall asleep); cataplexy (loss of muscle tone, falls); hypnopompic (as patient wakes up) and hypnagogic (as patient falls asleep) hallucinations. Treat with amphetamines.

Note: Patients can be hospitalized against their will if they are a danger to themselves (suicidal or unable to take care of themselves) or others (homicidal).

Many different **psychological tests** are available to aid in a difficult diagnosis; they are not used for a straightforward case. There are two types of tests: objective (multiple choice, scored by a computer) and subjective (no right answer, scored by test giver):

1. Stanford-Binet: objective IQ test for adults.
2. Wechsler Intelligence Scale for Children: objective IQ test for children (4–17 years old).
3. Rorschach test: subjective test in which patients describe what they see in an inkblot.
4. Thematic Apperception Test: subjective test in which the patients describes what is going on in a cartoon drawing of people.
5. Beck Depression Inventory: objective test to screen for depression.
6. Minnesota Multiphasic Personality Inventory: objective test designed to measure personality type.
7. Halstead-Reitan Battery: used to determine the location and effects of specific brain lesions.
8. Luria-Nebraska Neuropsychological Battery: assesses a wide range of cognitive functions and tells you the patient's cerebral dominance (left or right).

CHILD PSYCHIATRY

85% of cases of **mental retardation** are mild (IQ range: 55–70) and are usually idiopathic. Patients often have a reasonable level of independence with assistance or guidance during periods of stress. Fetal alcohol syndrome is the number-one **preventable** cause, whereas Down syndrome is the number-one **overall** cause. Fragile X syndrome (in males) is another common cause of mental retardation.

Autism: usually starts at a very young age. Look for impaired social interaction (isolative, unaware of surroundings), impaired verbal/nonverbal communication (strange words, babbling, repetition), and restricted activities and interests (head banging, strange movements). Autism is usually idiopathic, but look for congenital rubella as a potential cause. See Dustin Hoffman in the movie *Rain Man*.

Learning disorder: impairment in math, reading, writing, speech, language, or coordination, but everything else is normal and no mental retardation is present ("Johnny just can't do math").

Conduct disorder: pediatric form of antisocial disorder. Look for fire setting, cruelty to animals, lying, stealing, and/or fighting. As adults, patients often have antisocial disorder. ***Note:*** Conduct disorder is required to make a diagnosis of antisocial personality disorder in adults.

Attention-deficit hyperactivity disorder (ADHD): as the name implies, affected children are hyperactive and have short attention spans. Males are affected more often than females. Look for a fidgety child who is impulsive and cannot pay attention but is not cruel. Treat with stimulants (paradoxical calming effect) such as methylphenidate (Ritalin) and dextroamphetamine, both of which may cause insomnia, abdominal pain, anorexia, and weight loss or growth suppression.

Oppositional-defiant disorder: negative, hostile, and defiant behavior toward authority figures (parents, teachers). The child misbehaves around adults but behaves normally around peers and is not a cruel, lying criminal.

Separation anxiety disorder: look for a child who refuses to go to school. Basically, affected children think that something will happen to them or their parents if they separate; thus, they will do anything to avoid separation (stomachache, headache, temper tantrums).

Anorexia: look for a female adolescent who is a good athlete and/or student with a perfectionistic personality. Patients have body weight at least 15% below normal, intense fear of gaining weight (or "feel fat" even though emaciated), and amenorrhea (all three are required for diagnosis). Death occurs in roughly 10–15% of patients as a result of complications of starvation and/or bulimia (electrolyte imbalances, cardiac arrhythmias, infections). Some patients are hospitalized against their will for IV nutrition. Roughly one-half of anorexics also have bulimia.

Bulimia: look for a female adolescent who is of normal weight or overweight (unless anorexia coexists). Patients have binge-eating episodes during which they feel a lack of control and then engage in purging behavior (vomiting, laxatives, exercise, fasting). Patients may require hospitalization for electrolyte disturbances. In the classic patient tooth enamel has been eroded because of frequent vomiting; skin may be eroded over the knuckles from putting fingers into the throat.

Tourette's disorder: only 10–30% of patients utter obscenities. Look for males with motor tics (eye-blinking, grunting, throat-clearing, grimacing, barking, or shoulder shrugging) that are exacerbated by stress and remit during activity or sleep. Of interest, Tourette's disorder can be

caused or unmasked by use of stimulants (e.g., for presumed ADHD). Antipsychotics (haloperidol) are used if symptoms are severe. Tourette's disorder tends to be a life-long problem.

Encopresis/enuresis: not a disorder until after age 4 (*encopresis*) or 5 (*enuresis*). This is obviously an important diagnostic point to remember when the mother complains (normal finding if the child is 3 years old). Rule out physical problem (e.g., Hirschsprung's disease, urinary tract infection), then treat with behavioral therapy ("gold star for being good" charts, alarms, biofeedback). Imipramine is used only for refractory cases of enuresis; it is not a first-line agent.

Important points:

1. Depression in children often presents as irritable instead of depressed mood. Depression in the elderly may present as pseudodementia (cognitive decline), which is reversible with treatment.
2. The top three causes of adolescent deaths in order are **accidents**, **homicide**, and **suicide**. Together they account for about 75% of teenage deaths.

DRUGS OF ABUSE

Marijuana: most commonly abused illegal drug. Look for a teenager who listens to rock music, has red eyes, and acts "weird." Other symptoms include "amotivational syndrome" (chronic use may cause laziness and lack of motivation), time distortion and "munchies" (eating binge when intoxicated). No physical withdrawal symptoms are noted, although patients may have psychological cravings. Overdose is not dangerous, although patients may have temporary dysphoria. Marijuana is not a teratogen.

Cocaine: look for sympathetic stimulation (insomnia, tachycardia, mydriasis, hypertension, sweating) with hyperalertness and possible paranoia, aggressiveness, delirium, psychosis, or formications ("cocaine bugs"—patients think that bugs are crawling on them). Overdose can be fatal (arrhythmia, myocardial infarction, seizure, or stroke). On withdrawal, patients become sleepy, hungry (vs. anorexic with intoxication), and irritable, possibly with severe depression. Withdrawal is not dangerous, but psychological cravings usually are severe. Cocaine is teratogenic (vascular disruptions in fetus).

Amphetamines: classically associated with psychotic symptoms (patients may appear to be full-blown schizophrenics), but effects are similar to cocaine.

Opioids: heroin and other opioids cause euphoria, analgesia, drowsiness, miosis, constipation, and central nervous system depression. Overdose can be fatal (respiratory depression); treat with naloxone. Because the drug is usually taken intravenously, there are associated morbidities or mortalities (endocarditis, HIV, cellulitis, talc damage). Withdrawal is not life-threatening, but patients act as though they are going to die. Symptoms include gooseflesh, diarrhea, insomnia, and cramping/pain. Methadone treatment sometimes is given for addicts. Methadone is a longer-acting opioid that allows patients to function by keeping them on a chronic, free, low-dose. Its use is controversial.

Lysergic acid diethylamide (LSD) and mushrooms: symptoms of intoxication include hallucinations, mydriasis, tachycardia, diaphoresis, and perception/mood disturbances. Hallucinations usually are visual rather than auditory, whereas in schizophrenia they are auditory. Overdose is not dangerous (unless the patient thinks that he or she can fly and jumps out a window). No withdrawal symptoms are noted. Patients may get "flashbacks" months to years later (brief feeling of being on drug again, although none was taken) or a "bad trip" (acute

panic reaction or dysphoria). Treat bad trips with reassurance or benzodiazepine/antipsychotic medication (if needed).

Phencyclidine (PCP): LSD/mushroom symptoms in intoxication plus confusion, agitation, and aggressive behavior. Also look for vertical and/or horizontal nystagmus, plus possible schizophrenic-like symptoms (paranoia, auditory hallucinations, disorganized behavior and speech). Overdose can be fatal (convulsions, coma, respiratory arrest). Treat with supportive care and urine acidification to hasten elimination. No withdrawal symptoms are noted.

Inhalants (e.g., gasoline, glue, varnish remover): intoxication causes euphoria, dizziness, slurred speech, a feeling of floating, ataxia, and/or a sense of heightened power. Intoxication usually is seen in younger teenagers (11–15 years). Can be fatal in overdose (respiratory depression, cardiac arrhythmias, asphyxiation) or cause severe permanent sequelae (central nervous system, liver, kidney toxicity, peripheral neuropathy). There is no known withdrawal syndrome.

Benzodiazepines/barbiturates: cause sedation and drowsiness as well as reduced anxiety and disinhibition. Overdose may be fatal (respiratory depression). Treat with flumazenil if symptoms are due to benzodiazepine. Withdrawal also may be fatal (just as with alcohol) because of seizures and/or cardiovascular collapse. Treat withdrawal on an inpatient basis with a long-acting benzodiazepine; gradually taper the dose over several days. Benzodiazepines and barbiturates are especially dangerous when mixed with alcohol (all three are central nervous system depressants).

Note: Caffeine can cause headaches and fatigue in withdrawal.

CHAPTER 18

Gynecology

Pelvic inflammatory disease (PID): look for a female aged 13–35 years with abdominal pain, adnexal tenderness, *and* cervical motion tenderness (all three must be present). PID also requires one or more of the following: elevated erythrocyte sedimentation rate, leukocytosis, fever, purulent cervical discharge, or purulent fluid from culdocentesis. Treat with more than one antibiotic (e.g., cefoxitin/ceftriaxone and doxycycline on outpatient basis; clindamycin and gentamicin on an inpatient basis) to cover multiple organisms (e.g., *Neisseria gonorrhoeae, Chlamydia* sp., *Escherichia coli*). With a history of intrauterine device use, think *Actinomyces israelii*.

Important points:

1. PID is the most common cause of preventable infertility (causes scarring of tubes).
2. Watch for progression to tuboovarian abscess (palpable on exam) and its rupture. Treat with emergent laparotomy with excision of affected tube (unilateral disease) or total abdominal hysterectomy and bilateral salpingo-oophorectomy (bilateral disease)
3. PID is the most likely cause of infertility in a *normally* menstruating woman under age 30.

Vaginal Infections 101:

BUG	FINDINGS	TREATMENT
Candida sp.	"Cottage cheese" discharge, pseudohyphae on KOH preparation, history of diabetes mellitus, antibiotic treatment, pregnancy	Topical antifungal
Trichomas sp.	See bugs swimming under microscope; pale green, frothy, watery discharge, "strawberry" cervix	Metronidazole
Gardnerella sp.	Malodorous discharge; fishy smell on KOH preparation, clue cells	Metronidazole
Human papillomavirus	Venereal warts, koilocytosis on Pap smear	Many (acid, cryotherapy, laser, podophyllin)
Herpes	Multiple shallow, painful ulcers; recurrence and resolution	Acyclovir
Primary syphilis	Painless chancre, spirochete on dark-field microscopy	Penicillin
Secondary syphilis	Condyloma lata, maculopapular rash on palms, serology	Penicillin
Chlamydia sp.	Most common sexually transmitted disease; dysuria, positive culture/antibody test	Doxycycline (see below)
Neisseria gonorrhoeae	Mucopurulent cervicitis; gram-negative bugs on Gram stain	Ceftriaxone (see below)
Molluscum	Characteristic appearance of lesions, intracellular inclusions	Many (curette, cryotherapy, coagulation)
Pediculosis	"Crabs," itching, lice on pubic hairs	Permethrin cream (or Lindane)

KOH = potassium hydroxide.

Important points:

1. Chlamydia is treated with erythromycin if the patient is pregnant. If compliance is an issue (alcoholic, drug-abusing, homeless, or unreliable patient), you can give azithromycin, 1 gm orally all at once, and watch the patient take it.
2. Any patient with gonorrhea is generally treated for presumed chlamydial coinfection (give ceftriaxone and doxycycline).
3. With all infections but *Candida* sp., treat the patient's sexual partners and give counseling (e.g., condoms).
4. All of the above information is similar for men (except candidal infection), but any lesions and discharges are on or come from the penis.

Endometriosis: endometrial glands outside the uterus (ectopic). Patients usually are nulliparous and over 30 with the following symptoms: dysmenorrhea, dyspareunia (painful intercourse), dyschezia (painful defecation), and/or perimenstrual spotting. The most common site is the ovaries (look for tender adnexae in an afebrile patient), followed by the broad or uterosacral ligament (classic signs are nodularities on physical exam and sequela of retroverted uterus), and peritoneal surface. The gold standard of diagnosis is laparoscopy with visualization of endometriosis.

Important points:

1. Endometriosis is the most likely cause of infertility in a menstruating woman over age of 30 (in the absence of a PID history).
2. Treat first with oral contraceptives (danazol and gonadotropin-releasing hormone agonists are second-line agents).
3. Surgery and cautery may be used to destroy endometrioma and improve fertility markedly. In an older patient, consider total abdominal hysterectomy and bilateral salpingo-oophorectomy for severe symptoms.

Adenomyosis: endometrial glands within the uterine musculature. Patients usually are over 40 with dysmenorrhea and menorrhagia; physical exam reveals large, boggy uterus. Do dilatation and curettage (D&C) to rule out endometrial cancer, and consider total abdominal hysterectomy to relieve severe symptoms. Gonadotropin-releasing hormone agonists also may relieve symptoms.

Leiomyoma (fibroids): benign tumors; most common indication for hysterectomy (when they grow too large or cause symptoms). Malignant transformation is rare (< 1%). Look for rapid growth during pregnancy or use of oral contraceptives with regression after menopause (estrogen-dependent). Fibroids may cause infertility; myomectomy may restore fertility. Other symptoms include pain and menorrhagia/metrorrhagia. Anemia due to leiomyoma is an indication for hysterectomy. D&C rules out endometrial cancer and malignant transformation in women > 40. Patients may present with polyp protruding through cervix.

Note: Any sexually active woman of reproductive age with abnormal uterine bleeding should have a pregnancy test first.

Dysfunctional uterine bleeding (DUB): defined as abnormal uterine bleeding not associated with tumor, inflammation, or pregnancy. DUB is the most common cause of abnormal uterine bleeding and is a diagnosis of exclusion. Over 70% of cases are associated with anovulatory cycles (unopposed estrogen). The age of the patient is important. After menarche and just before menopause, DUB is extremely common and, in fact, physiologic. Most other patients

have polycystic ovaries. Always do a D&C to rule out **endometrial cancer** in women over 35. Also get hemoglobin/hematocrit to make sure that the patient is not anemic from excessive blood loss. Uncommon causes of DUB are infections, endocrine disorders (thyroid, adrenal, pituitary/prolactin), coagulation defects, and estrogen-producing neoplasm.

Important points:

1. In the absence of pathology, treat first with NSAIDs (first-line agents for DUB and dysmenorrhea).
2. Oral contraceptives are also a first-line agent for menorrhagia and DUB if the patient does not desire pregnancy and cycles are irregular.
3. Use progesterone only for severe bleeding.

Polycystic ovarian syndrome (PCOS): look for heavy woman who has hirsutism, amenorrhea, and/or infertility. PCOS is the most likely cause of infertility in a woman under 30 with *abnormal* menstruation. Multiple ovarian cysts often are seen on ultrasound. The primary event is androgen excess. The ratio of luteinizing hormone (LH) to follicle-stimulating hormone(FSH) is greater than 2:1. Unopposed estrogen increases the risk for endometrial cancer. Treat with oral contraceptives or cyclic progesterone. If the patient desires pregnancy, use clomiphene.

Infertility:

1. In two-thirds of couples infertility is a female problem; in one-third, it is a male problem.
2. If nothing is apparent after history and physical exam, the first step is semen analysis (cheap, easy, noninvasive). Normal semen has the following properties:
   - Ejaculate volume: > 1 ml
   - Sperm concentration: > 20 million/ml
   - Initial forward motility: > 50% of sperm
   - Normal morphology: > 60% of sperm
3. The next step is documentation of ovulation. History may suggest an ovulatory problem (irregular cycle length, duration, or amount of flow, lack of premenstrual symptoms). Basal body temperature, luteal phase progesterone levels, and/or endometrial biopsy can be done to check for ovulation.
4. Tubal/uterine evaluation is done by a hysterosalpingogram. History may suggest a tubal problem (PID, previous ectopic pregnancy) or a uterine problem (previous D&C may cause intrauterine synechiae, history of fibroids or endometriosis symptoms).
5. Cervical factor may be a cause of infertility and is suggested by a history of cervicitis, birth trauma, or previous cone biopsy. Evaluate cervical mucus, and do a postcoital test.
6. Laparoscopy is a last resort or is done in patients with a history suggestive of endometriosis. Lysis of adhesions and destruction of endometriosis lesions can restore fertility.
7. Medical therapy is usually clomiphene citrate to induce ovulation, but this approach requires that the woman is producing adequate estrogen. If the woman is hypoestrogenic, use human menopausal gonadotropin (hMG), which is a combination of FSH and LH. If these methods fail, use in vitro fertilization.

Secondary amenorrhea: in a previously menstruating, sexually active woman of reproductive age, the diagnosis is pregnancy until proved otherwise (with a negative human chorionic gonadotropin assay). Amenorrhea is not uncommon in hard-training athletes (due to exercise induced depression of gonadotropin-releasing hormone). Watch for amenorrhea as a presenting

symptom for anorexia (amenorrhea required for a diagnosis of anorexia), especially in a ballet dancer or model. Another common cause is PCOS (see above). Secondary amenorrhea also may be due to endocrine disorders (headaches, galactorrhea, and visual field defects may indicate a pituitary tumor), antipsychotics (due to increased prolactin), or previous chemotherapy (which causes premature ovarian failure/menopause). The first step after a negative pregnancy test and no obvious abnormality in the history or physical exam is to **administer progesterone**, which tells you the patient's estrogen status:

- If the patient has vaginal bleeding within 2 weeks, she has sufficient estrogen. Next, check LH. If the level is high, think of PCOS. If it is low or normal, check the prolactin level to rule out pituitary adenoma and the thyroid-stimulating hormone (TSH) level to rule out hypothyroidism (high TSH level causes high prolactin level). If prolactin is high with normal TSH, get an MRI of the brain. If prolactin is normal, look for drug-, stress-, or exercise-induced depression of gonadotropin-releasing hormone. Any of these patients may try clomiphene to become pregnant.
- If the patient does not have vaginal bleeding, she has insufficient estrogen. Check FSH next. If the level is elevated, the patient has premature ovarian failure; check for autoimmune disorder, karyotype abnormalities, and history of chemotherapy. If FSH is low or normal, the patient may have a craniopharyngioma; get an MRI of the brain.

Primary amenorrhea: any female who has not menstruated by age 16 has primary amenorrhea. In the absence of secondary sexual characteristics by age 14 or absence of menstruation within 2 years of developing secondary sex characteristics, patients also should be evaluated.

Important points:

1. The first step is to rule out pregnancy! (Yes, pregnancy can present as primary amenorrhea.)
2. If the patient is older than 14 and has no secondary sexual characteristics, she most likely has a congenital problem.
3. In a phenotypically normal female (normal breast development) with an absence of both axillary and pubic hair, think of androgen insensitivity syndrome. The uterus is absent.
4. In the presence of normal breast development and a uterus, the first step is to get a prolactin level to rule out pituitary adenoma. If prolactin is high, get an MRI. If it is normal, administer progesterone and follow the same procedures as for evaluation of secondary amenorrhea.

When in doubt, follow these steps *in order* to evaluate any amenorrhea:

1. Do a pregnancy test.
2. Administer progesterone.
3. Further testing depends on results of progesterone challenge (bleeding or no bleeding).

Note: Some clinicians may do a TSH and/or prolactin level before a progesterone challenge. For board purposes, choose progesterone challenge over TSH/prolactin levels unless obvious clues point to a TSH or prolactin problem (symptoms of hypothyroidism or pituitary tumor).

Any sexually active woman of reproductive age who has amenorrhea should have a pregnancy test as the first step in evaluation.

Menopause: the average age at menopause is around 50. Patients have irregular cycles or amenorrhea, hot flashes, mood swings, and an elevated FSH level. (See pharmacology chapter.) A bone density test may show osteoporosis and help the patient to make a decision about whether to take hormone replacement therapy. Patients also may complain of dysuria, dyspareunia,

incontinence, and/or vaginal itching, burning, or soreness—symptoms that often are due to atrophic vaginitis in this age group. Look for vaginal mucosa to be thin, dry, and atrophic with increased parabasal cells on cytology. Estrogen, either topical or systemic, improves symptoms.

Breast discharge: first get the patient's history of oral contraceptives, hormone therapies, antipsychotic medications, or hypothyroidism symptoms, all of which can cause discharge. When bilateral and nonbloody, the discharge is *not* due to breast cancer; the cause may be a prolactinoma (check prolactin) or endocrine disorder. A discharge that is unilateral and bloody and/or associated with a mass should raise concern about possible breast cancer. Nipple discharge secondary to carcinoma should contain hemoglobin. Do a biopsy of any mass.

Breast mass in a woman under 35:

1. **Fibrocystic disease:** *bilateral*, multiple, tender (especially premenstrually) *cystic lesions*. Most common of all breast diseases. Generally, no further work-up is needed—just routine follow-up. Progesterone for 1 week at the end of each month or danazol may help to relieve symptoms.
2. **Fibroadenoma:** painless, discrete, sharply circumscribed, rubbery, mobile mass. Most common benign tumor of the female breast. Observe the patient for one or more menstrual cycles in the absence of symptoms. Pregnancy or oral contraceptives may stimulate growth; menopause causes regression (estrogen-dependent). Excision is curative but not required.
3. **Mastitis/abscess:** look for lactating woman with reddish, painful, fluctuant mass. Culture breast milk, discontinue breast-feeding, and start on antistaphylococcal antibiotics (e.g., cloxacillin). Staphylococcal infection is by far the most common cause. If symptoms do not resolve, assume that the patient has an abscess, which requires incision and drainage.
4. **Fat necrosis:** history of trauma.

Note: Do *not* do mammography in women under 35 (breast tissue is too dense to give interpretable films). If suspicious of cancer (exceedingly rare in this age group), proceed directly to biopsy.

Breast mass in a woman 35 or over:

1. **Fibrocystic disease:** as above, but aspiration of cyst fluid and baseline mammography are recommended. If the cyst fluid is nonbloody and the mass resolves after aspiration, the patient needs only reassurance, follow-up, and a baseline mammogram. If the fluid is bloody or the cyst recurs quickly, do a biopsy to rule out cancer.
2. **Fibroadenoma:** get baseline mammogram. Observe briefly if the mass is small *and* seems benign clinically *and* the woman is premenopausal *and* has no risk factors for breast cancer. Otherwise, do a biopsy. Watch out for cystosarcoma phylloides that masquerades as a fibroadenoma.
3. **Fat necrosis:** as above.
4. **Mastitis/abscess:** as above.
5. **Breast cancer:** you may not get a classic presentation of nipple retraction and/or peau d'orange in a nulliparous woman with a strong family history. In a woman 35 or older, you will never be faulted for doing a biopsy of any mass. In the absence of a classic benign presentation (such as trauma to the breast with fat necrosis or bilaterality with premenstrual mastalgia), always consider biopsy. Also get a baseline mammogram. (See oncology chapter.)

Important points:

1. If the patient is postmenopausal (or over age 50) and develops a new lesion, you should proceed directly to biopsy.
2. In patients with a clinically evident breast mass, mammography is a poor test to evaluate the mass, although it should be done in a woman over 35 to have a baseline for future comparison. Mammography is used to detect nonpalpable breast masses (as a screening tool), not to evaluate masses that are already present.
3. Any suspicious lesion found on mammogram should be biopsied, even if it seems benign or is inapparent on physical exam.

Pelvic relaxation/vaginal prolapse: due to weakening of pelvic supporting ligaments. Look for history of several vaginal deliveries, feeling of heaviness or fullness in the pelvis, backache, worsening of symptoms with standing, and resolution with lying down:

1. Cystocele: bladder bulges into the *upper anterior* vaginal wall. Symptoms: urinary urgency, frequency, incontinence.
2. Rectocele: rectum bulges into the *lower posterior* vaginal wall. Major symptom: difficulty with defecating.
3. Enterocele: loops of bowel bulge into the *upper posterior* vaginal wall.
4. Urethrocele: urethra bulges into the *lower anterior* vaginal wall. Symptoms: urinary urgency, frequency, incontinence.

Note: Conservative treatment involves pelvic strengthening exercises and/or a pessary (artificial device to provide support). Surgery is used for refractory or severe cases.

Birth control:

1. The best choice is oral contraceptives if the patient is a candidate and does not desire sterilization. Oral contraceptives do *not* reduce transmission of sexually transmitted diseases.
2. An intrauterine device should be used only in older women, preferably those who are monogamous, because it increases the risk of ectopic pregnancy and PID (look for *Actinomyces* sp.).
3. Condoms are good because they prevent transmission of sexually transmitted diseases.

PEDIATRIC GYNECOLOGY

Ambiguous genitalia: look for adrenogenital syndrome and congenital adrenal hyperplasia, which usually are due to 21-hydroxylase deficiency (90% of cases). Patients are female; males with this disease show precocious sexual development. Patients with 21-hydroxylase deficiency have salt-wasting (low sodium levels), hyperkalemia, hypotension, and elevated 17-hydroxyprogesterone. Treat with steroids and IV fluids immediately to prevent death. No patient with ambiguous genitalia should be assigned a gender until the work-up is complete. A karyotype must be done.

Important points:

1. Any child with a "bunch of grapes" protruding from her vagina probably has sarcoma botryoides, a malignant tumor
2. Premature or precocious puberty is usually idiopathic but may be caused by a hormone-secreting tumor or central nervous system disorder, which must be ruled out. By definition,

the patient must be younger than 8 (9 for males). Treat underlying cause or, if idiopathic, treat with gonadotropin-releasing hormone analog to prevent premature epiphyseal closure and to arrest or reverse puberty until appropriate age.

3. Most cases of vaginitis or vaginal discharge are nonspecific or physiologic. But look for foreign body, sexual abuse (especially with sexually transmitted disease), or candidal infection (as a presentation of diabetes; measure serum glucose and/or check for glycosuria).
4. Imperforate hymen: patient of menarche age with hematocolpos (blood in vagina) that cannot escape (hymen bulges outward). Treatment is surgical opening of the hymen.
5. Vaginal bleeding in the neonate is usually physiologic as a result of maternal estrogen withdrawal and resolves by itself.

CHAPTER 19

Obstetrics

Important points:

1. The most common cause of secondary amenorrhea is pregnancy. *Always* do a pregnancy test first when a patient presents with amenorrhea. Pregnancy also must be ruled out as a cause of primary amenorrhea.
2. A woman may say that she is taking oral contraceptives and still be pregnant. No contraception is 100% effective, especially when you factor in poor compliance.
3. **Signs of pregnancy:** amenorrhea, morning sickness, Hegar's sign (softening and compressibility of the lower uterine segment), Chadwick's sign (dark discoloration of the vulva and vaginal walls), linea nigra, chloasma, auscultation of fetal heart tones, visibility of gestational sac and/or fetus on ultrasound, uterine contractions, weight gain, and palpation/ballottement of fetus.
4. Give all pregnant patients folate to prevent neural tube defects. Ideally, all women of reproductive age should take folate, because it is most effective in the first trimester when most women do not know that they are pregnant. Iron is often given routinely to prevent anemia.
5. Macrosomia (or positive history in previous children) is caused by maternal diabetes mellitus until proved otherwise.

Routine laboratory tests in a pregnant patient:

1. Pap smear: give to every patient at first visit, unless she had a normal Pap smear in past 6 months.
2. Urinalysis: at first visit and every visit (screen for preeclampsia and bacteriuria; not a good screen for diabetes mellitus).
3. Complete blood count: at first visit to see if the patient is anemic (pregnancy may aggravate it).
4. Blood type, Rh type, and antibody screen: at first visit (for identification of possible isoimmunization).
5. Syphilis test: at first visit (mandated in most states) and subsequent visits if the patient is at high risk.
6. Rubella antibody screen: in the absence of a good vaccination history, obtain at first visit (otherwise not needed).

7. Glucose screen: at first visit if the patient has risk factors for diabetes mellitus (obesity, family history, age > 30 years); otherwise, do at 24–28 weeks. Screen with fasting serum glucose *and* serum glucose 1 or 2 hours after an oral glucose load.
8. Serum alpha-fetoprotein (AFP) or triple screen: between 16–20 weeks for older or other high-risk patients. Positive triple screen (low AFP, low estriol, and high human chorionic gonadotropin [HCG]) means likely Down syndrome.
9. Hepatitis B serology, tuberculous skin test, HIV test, *Chlamydia* sp. and gonorrhea cultures, and ultrasound are used only when the patient has a suggestive history or risk factors. If asked, you should do *Chlamydia* sp. and gonorrhea cultures for any pregnant teenager.

Important points:

1. *At every prenatal visit*, listen for fetal heart tones and evaluate uterine size for any **size/date discrepancy**. Uterine size is evaluated by measuring the distance from the symphysis pubis to the top of the fundus in centimeters. Between roughly 20–35 weeks, the measurement in cm should equal the number of weeks of gestation. A discrepancy greater than 2–3 cm is called a size/date discrepancy, and ultrasound should be done to evaluate further. Possible explanations include intrauterine growth retardation and multiple gestation.
2. At 12 weeks' gestation, the uterus enters the abdomen; at roughly 20 weeks, it reaches the umbilicus.
3. Between 16 and 20 weeks, ultrasound is most accurate at estimating fetal age (using the biparietal diameter).

Hydatidiform mole: in a sense, the products of conception become a tumor. Look for preeclampsia before the third trimester; an HCG that does not return to zero after delivery or abortion or that rapidly rises during pregnancy; first- or second-trimester bleeding with possible expulsion of "grapes;" uterine size/date discrepancy; and/or a *"snow-storm"* pattern on ultrasound. Complete moles are 46 XX (all chromosomes from the father) and have no fetal tissue; incomplete moles are usually 69 XXY and contain fetal tissue. Gross appearance suggests a bunch of grapes. Treat with uterine dilatation and curettage, then follow HCG until it falls to zero. If HCG does not fall to zero or rises, the patient has either an invasive mole or choriocarcinoma; in either case, the patient needs chemotherapy (usually methotrexate or actinomycin D).

Intrauterine growth retardation (IUGR): defined as size below the tenth percentile for age. The causes are many and are best understood in broad terms as caused by one of three factors: maternal (e.g., smoking, alcohol or drugs, lupus erythematosus), fetal (e.g., TORCH infections, congenital anomalies) or placental (e.g,. hypertension, preeclampsia). **TORCH** infections consist of **t**oxoplasmosis, **o**ther (congenital syphilis and viruses), **r**ubella, **c**ytomegalovirus, and **h**erpes simplex virus. Do ultrasound on all patients who have a size/date discrepancy greater than 2–3 cm or risk factors for pregnancy problems (e.g., hypertension; diabetes mellitus; renal disease; lupus erythematosus; cigarette, alcohol, or drug use; history of previous problems). Ultrasound parameters measured for IUGR determination include biparietal diameter, head circumference, abdominal circumference, and femur length.

Evaluation of fetal well-being:

1. **Nonstress test (NST):** with the mother resting, fetal heart rate tracing is obtained for 20 minutes. A normal strip has at least two accelerations of the heart rate, each of which is at least 15 bpm above baseline and lasts at least 15 seconds. This is the first screening test to evaluate fetal well-being; it is often done in the context of a biophysical profile.

2. **Biophysical profile (BPP):** includes four measurements:
   - NST (see above).
   - Amniotic fluid index (AFI): measures vertical pockets of amniotic fluid (in cm) in each of the four quadrants. The sum of the highest vertical pocket in each quadrant is used to determine whether oligohydramnios or polyhydramnios is present (AFI < 5 cm = oligohydramnios, AFI > 25 cm = polyhydramnios).
   - Fetal breathing movements: fetus should have at least 30 breathing movements in 10 minutes.
   - Fetal movements: fetus should have at least three body movements (e.g., flexion, body rotation) in 10 minutes.

Note: If the fetus scores low on the BPP, the next test is the contraction stress test. With high-risk pregnancies (e.g., IUGR, diabetes mellitus, hypertension, alcohol or drug use, postterm pregnancy, history of problem pregnancies, maternal or physician concern), the BPP often is done once or even twice a week until delivery.

3. **Contraction stress test (CST):** a test for uteroplacental dysfunction. Give oxytocin, and monitor the fetal heart strip. If late decelerations are seen on the fetal heart strip with each contraction, the test is positive, and usually a cesarean section is done.

Note: In women with antiphospholipid antibodies and previous problem pregnancies, low-dose aspirin may help in subsequent pregnancies. Normally, aspirin and other NSAIDs should be *avoided* in pregnancy; use acetaminophen instead.

Postterm pregnancy: > 42 weeks' gestation. Generally, if gestational age is known to be accurate, labor is induced (e.g., by oxytocin) if the cervix is favorable. If the cervix is not favorable or the dates are uncertain, do twice-weekly NST and BPP. At 43 weeks, most authorities advise induction of labor or cesarean section. Both prematurity and postmaturity increase perinatal morbidity and mortality. Prolonged gestation is common in association with anencephaly and placental sulfatase deficiency.

Normal pregnancy changes: nausea and vomiting (morning sickness), amenorrhea, heavy (possibly even painful) feeling of the breasts, increased pigmentation of the nipples and areolae (and Montgomery tubercles), backache, linea nigra, chloasma, striae gravidarum, *mild* ankle edema, heartburn, and increased frequency of urination.

Alpha-fetoprotein levels:

- Low AFP = Down syndrome, fetal demise, or inaccurate dates.
- High AFP = neural tube defects (e.g., anencephaly, spina bifida), ventral wall defects (e.g., omphalocele, gastroschisis), multiple gestation, or inaccurate dates.
- If AFP or triple screen is positive (at 16–20 weeks), the patient should undergo amniocentesis (also done at 16–20 weeks) for a definitive diagnosis of chromosomal disorders (cell culture) or neural tube defects (amniotic fluid AFP).

Chorionic villus sampling (CVS): can be done at 9–12 weeks (earlier than amniocentesis) and generally is reserved for women with previously affected offspring or known genetic disease. CVS gives women the advantage of first-trimester abortion if a fetus is affected. It is associated with a slightly higher miscarriage rate than amniocentesis and *cannot* detect neural tube defects.

Teratogenic agents (see table, top of next page)

AGENT	DEFECT CAUSED
Alcohol	Fetal alcohol syndrome
Aminoglycoside	Deafness
Aminopterin	Intrauterine growth retardation, central nervous system problems, cleft lip/palate
Antineoplastics	Many
Carbamazepine	Fingernail hypoplasia, craniofacial defects
Cigarettes	Intrauterine growth retardation, low birth weight, prematurity
Cocaine	Cerebral infarcts, mental retardation
Diazepam	Cleft lip/palate
Diethylstilbestrol	Clear cell vaginal cancer, adenosis, cervical incompetence
Isotretinoin*	Central nervous system, craniofacial/ear, and/or cardiovascular defects
Lithium	Cardiac (Ebstein's) anomalies
Oral contraceptives	VACTERL syndrome
Phenytoin	Craniofacial, limb, and/or cardiovascular defects, mental retardation
Progesterone	Masculinization of females
Tetracycline	Yellow or brown teeth
Thalidomide	Phocomelia
Trimethadione	Craniofacial and/or cardiovascular defects, mental retardation
Valproic acid	Spina bifida, hypospadias
Warfarin	Craniofacial defects, intrauterine growth retardation, central nervous system problems, stillbirth

VACTERL = **v**ertebral, **a**nal, **c**ardiac, **t**racheoesophageal, **r**enal, and **l**imb malformations.

* Vitamin A in general is considered teratogenic when recommended intake levels are exceeded.

Important points:

1. Hyperglycemia and diabetes mellitus cause cardiovascular anomalies, cleft lip/palate, caudal regression, neural tube defects, left colon hypoplasia, and macrosomia (early diabetes) or microsomia (long-standing diabetes).
2. *Radiation (> 5 cGy) causes IUGR, central nervous system defects, eye malformations, and future malignancies (especially leukemia).*
3. Drugs that are generally **safe** in pregnancy: acetaminophen (not NSAIDs or aspirin), penicillin, cephalosporins, erythromycin, nitrofurantoin, H_2 blockers, antacids, heparin, hydralazine, methyldopa, labetalol, insulin, docusate.
4. Most **TORCH** intrauterine fetal infections can cause mental retardation, microcephaly, hydrocephalus, hepatosplenomegaly, jaundice, anemia, low birth weight, and/or IUGR:
   - **T**oxoplasma gondii: look for exposure to cats; specific defects include intracranial calcifications, chorioretinitis.
   - **O**ther: varicella zoster (limb hypoplasia and scarring of the skin) and syphilis (rhinitis, saber shins, Hutchinson's teeth, interstitial keratitis, skin lesions).
   - **R**ubella: worst in first trimester (some authorities recommend abortion if the mother contracts rubella in the first trimester). Always check antibody status on first visit if the patient has a poor immunization history. Look for cardiovascular defects (patent ductus arteriosus, ventral septal defect), deafness, cataracts, and microphthalmia.
   - **C**ytomegalovirus: most common; look for deafness, cerebral calcifications, microphthalmia.
   - **H**erpes: look for vesicular skin lesions (with positive Tzanck smears), history of maternal herpes lesions.

Note: With all in utero infections that can cause problems with the fetus, the mother may be asymptomatic (subclinical infection) and the infant may even be asymptomatic at birth, only to develop symptoms later (e.g., learning disability, mental retardation).

5. In untreated HIV-positive patients, transmission to the fetus occurs in roughly 25% of cases. With prenatal zidovudine (AZT) treatment for the mother and administration of AZT to the infant for 6 weeks after birth, HIV transmission is reduced to roughly 10%. A noninfected infant may still be HIV-positive on testing because maternal antibodies can cross the placenta. Within 6 months, the test reverts to negative. HIV-positive mothers should not breast-feed because milk can transmit virus to the infant.
6. When the mother has genital herpes simplex, delay the decision of whether to do a cesarean section until the mother goes into labor. If at the time of true labor she has lesions of HSV, do a cesarean section. If at the time of true labor the mother has no HSV lesions, deliver vaginally.
7. If the mother has hepatitis B, give the infant the first hepatitis B vaccine shot and hepatitis B immunoglobulin at birth.
8. If the mother gets chickenpox in the last 5 days of pregnancy or first 2 days after delivery, give the infant varicella zoster immunoglobulin.
9. In pregnancy, treat chlamydial infection with erythromycin (not tetracycline).
10. Signs of placental separation: fresh show of blood from vagina; umbilical cord lengthens; the fundus rises and becomes firm and globular.
11. After a cesarean section with classical (vertical) uterine incision, the patient must have cesarean sections for all future deliveries because of the increased rate of uterine rupture. After a cesarean section with a lower (horizontal) uterine incision, the patient may deliver future pregnancies vaginally.
12. For the first several days after delivery, it is normal to have some discharge (lochia), which is red on the first few days and gradually turns to a white or yellowish-white color by day 10. If the lochia is foul-smelling, suspect endometritis.

Breast-feeding:

1. If a woman does not want to breast-feed, prescribe tight-fitting bras, ice packs, and analgesia. Bromocriptine and estrogens or oral contraceptives also may be used to suppress lactation.
2. If a woman does breast-feed, watch for mastitis, which usually develops in the first 2 months of breast-feeding. Breasts are red, indurated, and painful; often the patient has a low-grade fever. *Staphylococcus aureus* almost always is the cause. Treat by stopping breast-feeding; obtain milk for culture and sensitivity; and begin antibiotic (penicillinase-resistant penicillin such as cloxacillin) for 7–10 days while awaiting culture results. Evaluate infant for staphylococcal colonization if given the option. If the breast is fluctuant, the condition may have progressed into an abscess, in which case incision and drainage are needed.
3. Breast-feeding is contraindicated in patients with HIV or hepatitis B and in patients who use the following: benzodiazepines, barbiturates, opiates, alcohol, caffeine or tobacco (in large amounts), antithyroid medications, lithium, chloramphenicol, anticancer agents, or ergot and its derivatives (e.g., methysergide).

Important points:

1. **Epidural anesthesia** is the preferred method in obstetric patients. General anesthesia involves a higher risk of aspiration and resulting pneumonia, because the gastroesophageal

sphincter is relaxed in pregnancy and most patients have not been NPO. Spinal anesthesia can interfere with the mother's ability to push and has a higher incidence of hypotension than epidural anesthesia.

2. **Treat asymptomatic bacteriuria** in pregnancy (20% of patients develop cystitis and/or pyelonephritis if untreated because progesterone decreases the tone of the ureters and the uterus compresses the ureters.
3. **Treat group B streptococcal (GBS) carriers only during labor and delivery.** For example, if the patient is GBS-positive at 26–28 weeks, wait until labor and give ampicillin. The goal of treatment is to prevent neonatal sepsis and endometritis.
4. **If a woman has tuberculosis in pregnancy** (positive purified protein derivative [PPD] test and suspicious chest x-ray, plus a positive sputum culture), treat as you would any other patient. If the patient is a known recent PPD converter or has additional risk factors (such as HIV positivity or household contact with an active case of tuberculosis), treat with isoniazid like a nonpregnant patient. Make sure to give the mother vitamin B_6 with isoniazid to prevent nutritional defect in her and the fetus. Avoid streptomycin, which may cause deafness and nephrotoxicity in fetus.
5. Marijuana and lysergic acid diethylamide (LSD) have not been confirmed as teratogens.

Preeclampsia: look for hypertension (in patients with preexisting hypertension, blood pressure should increase by > 30/15 mmHg over baseline); urinalysis with 2+ or more proteinuria; oliguria; swelling or edema of hands and/or face; headache; visual disturbances; and **HELLP** syndrome (**h**emolysis, **e**levated **l**iver enzymes, **l**ow **p**latelets). Preeclampsia often involves right upper quadrant and epigastric pain and develops in the third trimester. The main risk factors (in order of importance) are chronic renal disease, chronic hypertension, family history, multiple gestation, nulliparity, age > 40 (although the classic case is a young woman with her first child), diabetes mellitus, and black race. Treatment is delivery if the patient is at term. If the patient is premature and has mild disease, treat hypertension with hydralazine or labetalol and bed rest. Observe the patient carefully. If the patient has severe disease (oliguria, mental status changes, headache, blurred vision, pulmonary edema, cyanosis, HELLP, blood pressure > 160/110 mmHg, or progression to eclampsia [seizures]), deliver regardless of gestational age because both mother and infant may die.

- Mild ankle edema is normal in pregnancy, but severe ankle edema or hand edema is likely to be preeclampsia.
- If preeclampsia symptoms develop before the third trimester, think of hydatiform mole and/or choriocarcinoma.
- Hypertension plus proteinuria in a pregnant patient is preeclampsia until proved otherwise.
- Preeclampsia plus seizures = **eclampsia**. Eclampsia can be prevented by regular prenatal care. Catch it in preeclamptic stage, and treat appropriately.
- Use magnesium sulfate for eclamptic seizures (also lowers blood pressure). Toxic effects include **hyporeflexia** (first sign of toxicity), respiratory depression, central nervous system depression, coma, and death.
- Do not remeasure very high blood pressure in a pregnant patient. Err on the safe side; assume that it represents preeclampsia and start treatment.
- Do not try to deliver the infant until the mother is stable (do not do a cesarean section while the mother is having a seizure).

- Preeclampsia and eclampsia cause uteroplacental insufficiency, IUGR, fetal demise, and increased maternal morbidity and mortality.
- Preeclampsia and eclampsia are *not* risk factors for future development of hypertension or end-organ effects of hypertension.

Important points:

1. The top causes of maternal mortality are pulmonary embolism, pregnancy-induced hypertension, and hemorrhage (most texts say in that order).
2. When a postpartum mother develops shortness of breath, tachypnea, chest pain, hypotension, and/or disseminated intravascular coagulation, think of amniotic fluid (AF) pulmonary embolism.
3. **Oligohydramnios** = AF < 500 ml, AF index < 5. Causes include IUGR, premature rupture of membranes, postmaturity, and renal agenesis (Potter's disease). Oligohydramnios may cause fetal problems such as pulmonary hypoplasia, cutaneous and skeletal abnormalities due to compression, and hypoxia due to cord compression.
4. **Polyhydramnios** = AF > 2000 ml, AF index > 25. Causes include maternal diabetes mellitus, multiple gestation, neural tube defects (anencephaly, spina bifida), GI anomalies (omphalocele, esophageal atresia), and hydrops fetalis. Polyhydramnios may cause postpartum uterine atony with resultant postpartum hemorrhage and maternal dyspnea (overdistended uterus compromising pulmonary function).

Normal Labor

STAGE	CHARACTERISTICS	NULLIGRAVIDA	MULTIGRAVIDA
First	Onset of true labor to full cervical dilation	< 20 hours	< 14 hours
Latent phase	From 0 to 3–4 cm dilation (slow, irregular)	Highly variable	Highly variable
Active phase	From 3–4 cm to full dilation (rapid, regular)	>1 cm/hr dilation	>1.2 cm/hr dilation
Second	From full dilation to birth of infant	30 minutes to 3 hours	5–30 minutes
Third	From delivery of infant to delivery of placenta	0–30 minutes	0–30 minutes
Fourth	From placental delivery to maternal stabilization	Up to 48 hours	Up to 48 hours

Protraction disorder: occurs once true labor has begun if the mother takes longer than she should, according to the above table. **Arrest disorder** occurs once true labor has begun if no change in dilation (as opposed to the slow change of protraction disorder) occurs over 2 hours or if no change occurs in descent over 1 hour. First, rule out abnormal lie or cephalopelvic disproportion. If everything is okay, treat with labor augmentation (oxytocin, prostaglandin gel, amniotomy). If this approach does not work, manage expectantly and do a cesarean section at the first sign of trouble. The most common cause of failure to progress (protraction or arrest disorder), also known as dystocia (difficult birth), is cephalopelvic disproportion, defined as disparity between the size of the infant's head and the mother's pelvis. Labor augmentation is contraindicated in this setting.

True labor: normal contractions occur at least every 3 minutes, are fairly regular, and are associated with cervical changes (effacement and dilation). **False labor** (Braxton-Hicks contractions) is characterized by irregular contractions with no cervical changes. You may try oxytocin to augment ineffective uterine contractions. Watch out for uterine hyperstimulation (painful, overly frequent, and poorly coordinated uterine contractions), uterine rupture, fetal heart rate

decelerations, and water intoxication (from the antidiuretic hormone-like effect of oxytocin). Treat all of these symptoms by first discontinuing oxytocin infusion (half-life = < 10 minutes). Prostaglandin E_2 (dinoprostone) also may be used locally to induce ("ripen") the cervix and is highly effective in combination with (often before) oxytocin. Prostaglandin E_2 also may cause uterine hyperstimulation. Amniotomy hastens labor but exposes the fetus and uterine cavity to possible infection if labor does not occur.

Contraindications to labor induction and augmentation (similar to contraindications to vaginal delivery):

- Placenta or vasa previa
- Umbilical cord prolapse or presentation
- Prior classic uterine cesarean section incision
- Transverse fetal lie
- Active genital herpes
- Known cervical cancer
- Known cephalopelvic disproportion

Abortion: defined as termination of a pregnancy at < 20 weeks (fetus < 500 gm). The following specific terms also imply that the event occurs at < 20 weeks' gestation:

1. Threatened abortion: uterine bleeding without cervical dilation and no expulsion of tissue. Treat with IV fluids (or blood, if needed), bedrest, pelvic rest, and Rhogam if the patient is Rh-negative. Do dilatation and curettage if the fetus dies.
2. Inevitable abortion: uterine bleeding with cervical dilation and crampy abdominal pain and no tissue expulsion. Treat with IV fluids, Rhogam if the patient is Rh-negative, and dilatation and curettage.
3. Incomplete abortion: passage of some products of conception through the cervix. Treat with IV fluids, Rhogam if the patient is Rh-negative, and dilatation and curettage.
4. Complete abortion: expulsion of all products of conception from the uterus. Treat with serial HCG testing to make sure that HCG drops to zero, do dilatation and curettage, and give Rhogam if the patient is Rh-negative.
5. Missed abortion: fetal death with no expulsion of tissue (often for several weeks). Treat with dilatation and curettage if less than 14 weeks, attempted delivery if greater than 14 weeks. Give Rhogam if the patient is Rh-negative.
6. Induced abortion: intentional termination of pregnancy < 20 weeks; may be elective (requested by patient) or therapeutic (to maintain the health of the mother).
7. Recurrent abortion: two or three successive unplanned abortions. History and physical exam may show:
   - Infectious etiology (*Listeria*, *Mycoplasma*, or *Toxoplasma* spp., syphilis)
   - Environmental (alcohol, tobacco, drugs)
   - Diabetes mellitus
   - Hypothyroidism
   - Systemic lupus erythematosus (especially with positive antiphospholipid/lupus anticoagulant antibodies)
   - Cervical incompetence (watch for history of patient's mother taking diethylstilbestrol during pregnancy and patient with recurrent second-trimester abortions; treat future pregnancies with a cervical cerclage at 14–16 weeks)

- Congenital female tract abnormalities (correct if possible to restore fertility)
- Fibroids (remove them)
- Chromosomal abnormalities (e.g., maternal/paternal translocations)

HCG roughly doubles every two days in the first trimester of pregnancy. An HCG that stays the same or increases only slowly with serial testing indicates a fetus in trouble or fetal demise. A rapidly increasing HCG or one that does not decrease after delivery may indicate a hydatiform mole or choriocarcinoma. The standard HCG home pregnancy test becomes positive roughly 2 weeks after conception.

Transvaginal ultrasound: detects intrauterine gestational sac at roughly 5 weeks, fetal image at 6–7 weeks, and a beating heart at 8 weeks. Use this information in trying to determine the possibility of an ectopic pregnancy. If the patient's last menstrual period (LMP) was 4 weeks ago and the pregnancy test is positive, you cannot rule out a uterine pregnancy with ultrasound. If, however, the patient's LMP was 10 weeks ago and an ultrasound of the uterus shows no gestational sac, think of ectopic pregnancy. If HCG is > 2000 mIU, you should be able to visualize a gestational sac with transvaginal ultrasound.

The major risk factor for ectopic pregnancy is a history of pelvic inflammatory disease (10-fold increase in ectopic pregnancies). Other risk factors include previous ectopic pregnancy, history of tubal sterilization or tuboplasty, pregnancy that occurs with an intrauterine device in place, and diethylstilbestrol exposure (which may cause tubal abnormalities in women exposed in utero).

Classic symptoms of ectopic pregnancy are amenorrhea, vaginal bleeding, and abdominal pain. Patients also have positive HCG test. If you palpate an adnexal mass, you may be palpating an ectopic pregnancy or a corpus luteum cyst, which may coexist with a tubal pregnancy or a threatened abortion (both may have similar symptoms). When in doubt and the patient is doing poorly (hypovolemia, shock, severe abdominal pain, or rebound tenderness), do a laparoscopy for definitive diagnosis and treatment, if necessary. On rare occasions, culdocentesis is done in a stable patient to check for blood in the pouch of Douglas (with a ruptured ectopic pregnancy), but it has a high false-negative rate. When culdocentesis is negative, laparoscopy is still required. Therefore, do *not* choose culdocentesis unless laparoscopy is not a choice.

Tubal pregnancy, if stable and less than 3 cm in greatest diameter, can be treated with salpingostomy and removal, leaving the tube open to heal on its own. If the patient is unstable or the ectopic pregnancy has ruptured or is greater than 3 cm, salpingectomy is required. Give Rhogam after treatment for Rh-negative patients.

Pregnancy and diabetes mellitus:

1. Problems with diabetic mothers in pregnancy: polyhydramnios, preeclampsia, and complications of diabetes.
2. Problems in infants born to diabetic mothers: macrosomia and IUGR; respiratory distress syndrome; cardiovascular, colon, craniofacial, and neural tube defects; caudal regression syndrome (lower half of body incompletely formed), and **postdelivery hypoglycemia** in the fetus (from fetal islet-cell hypertrophy due to maternal and thus fetal hyperglycemia). After birth, the infant is cut off from the mother's glucose and the hyperglycemia goes away, but islet cells still overproduce insulin and cause hypoglycemia. Treat with IV glucose.

3. Treat diabetes mellitus with diet, exercise, and/or insulin (no oral hypoglycemics). Tighter control results in better outcomes for mother and infant. Check HbA1c to determine compliance and glucose fluctuations.
4. In evaluating amniotic fluid to determine fetal lung maturity, phosphatidylglycerol concentration is much better than the lecithin:sphingomyelin ratio when the mother is diabetic.

Fetal heart monitoring: routinely done, but its benefit is controversial. Fetal heart tones can be heard with Doppler at 10–12 weeks and with a stethoscope at 16–20 weeks. At term the normal heart rate is 120–160 bpm. Any value outside this range is worrisome. Know what a basic fetal heart strip with uterine contraction patterns looks like, and know the following abnormalities:

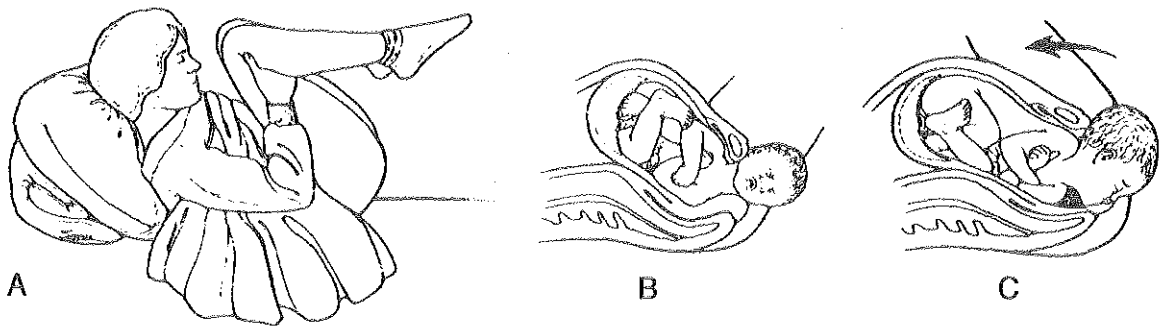
1. Early deceleration: peaks match up (fetal heart deceleration nadir and uterine contraction peak). Early deceleration signifies head compression (probable vagal response) and is *normal*.
2. Variable deceleration: variable with relation to uterine contractions. The most commonly encountered abnormality, variable deceleration signifies cord compression. Place the mother in a lateral decubitus position, administer oxygen by face mask, and stop any oxytocin infusion. If bradycardia is severe (< 80–90 BPM) or does not resolve, measure fetal scalp pH.
3. Late deceleration: fetal heart deceleration comes after uterine contraction. Late deceleration signifies uteroplacental insufficiency and is the most worrisome pattern. First, place the mother in a lateral decubitus position, give oxygen by face mask, and stop oxytocin if it is being given. Next, give a tocolytic ($beta_2$ agonist such as ritodrine or magnesium sulfate) and IV fluids if the mother is hypotensive (especially with epidural anesthesia). If late decelerations persist, measure fetal scalp pH.
4. Short-term variability (beat-to-beat variability): reflects the interval between successive heart beats. The normal value is 5–25 bpm. Variability consistently less than 5 bpm is worrisome, especially when combined with decelerations. Measure fetal scalp pH.
5. Long-term variability: a 1-minute strip normally shows changes in the baseline heart rate. Less than 3 cycles per minute is worrisome, especially when combined with decelerations. Measure fetal scalp pH. *Special warning:* long-term variability is decreased normally during fetal sleep.
6. Fetal tachycardia: > 160 bpm. Poor indicator of fetal distress unless prolonged or marked. Often associated with oxytocin administration, maternal fever, or intrauterine infection.

Note: Any fetal scalp pH < 7.2 is an indication for immediate cesarean delivery. If pH > 7.2, continue to observe.

When **shoulder dystocia** occurs, the first step is McRobert's maneuver (see figure, top of next page). Ask the mother to flex her thighs sharply against her abdomen. This maneuver may free the impacted shoulder. If it does not work, options are limited. A cesarean section is usually the procedure of choice (after pushing the infant's head back up into the birth canal).

Third-trimester bleeding (very high yield): *always* do an ultrasound before a pelvic exam. *Always* do an ultrasound before a pelvic exam (written twice on purpose). The differential diagnosis includes the following:

1. Placenta previa: predisposing factors include multiparity, increasing age, multiple gestation, and prior previa. This condition is why you *always* do an ultrasound before a pelvic exam. Bleeding is painless and may be profuse. Ultrasound is 95–100% accurate in diagnosis.



A, McRobert's maneuver with legs flexed on the maternal abdomen and chest. Angle of inclination of the pelvic area is increased when the legs are flexed *(C)* compared to the legs being extended in lithotomy *(B)*; thus, the shoulder of the infant may become disengaged. (From Ratcliffe SD, Byrd JE, Sakornbut EL: Handbook of Pregnancy and Perinatal Care in Family Practice. Philadelphia, Hanley & Belfus, 1996, with permission.)

Cesarean section is mandatory for delivery, but you may try to admit with bed and pelvic rest and tocolysis if the patient is preterm and stable and the bleeding stops.

2. Abruptio placentae: predisposing factors include hypertension (with or without preeclampsia), trauma, polyhydramnios with rapid decompression after membrane rupture, cocaine/tobacco use, and preterm premature rupture of membranes. Do *not* forget that the patient can have this condition without visible bleeding (blood contained behind placenta). Patients have pain, uterine tenderness, and increased uterine tone with hyperactive contraction pattern. Fetal distress also is present. Abruptio placentae may cause disseminated intravascular coagulation if fetal products enter the maternal circulation. Ultrasound detects only 2% of cases. Treat with IV fluids (and blood if needed) and rapid delivery (vaginal preferred).
3. Uterine rupture: predisposing factors include previous uterine surgery, trauma, oxytocin, grand multiparity (several previous deliveries), excessive uterine distention (e.g., multiple gestation, polyhydramnios), abnormal fetal lie, cephalopelvic disproportion, and shoulder dystocia. Uterine rupture is characterized by *extreme pain* of sudden onset and often associated with maternal hypotension or shock. Fetal parts may be felt in the abdomen, or the abdominal contour may change. Treat with immediate laparotomy and usually hysterectomy after delivery.
4. Fetal bleeding: usually from vasa previa or velamentous insertion of the cord. The major risk factor is multiple gestation (the higher the number of fetuses, the higher the risk). Bleeding is *painless*, and the mother is completely stable while the fetus shows worsening distress (tachycardia initially, then bradycardia as the fetus decompensates). The Apt test is positive on uterine blood and differentiates fetal from maternal blood. Treat with immediate cesarean section.
5. Cervical/vaginal lesions: examples include herpes simplex virus, gonorrhea, chlamydial or candidal infection.
6. Cervical/vaginal trauma: usually from intercourse.
7. Bleeding disorder: rarely presents before delivery (more common after delivery).
8. Cervical cancer: may occur in pregnant patients too!
9. "Bloody show": with cervical effacement, a blood-tinged mucous plug may be released from the cervical canal and heralds the onset of labor. This event is *normal* and a diagnosis of exclusion.

Treatment: in all patients with third-trimester bleeding, start IV fluids and give blood, if needed. Give oxygen, and get complete blood count, coagulation profiles, and ultrasound. Set up fetal and maternal monitoring. Do drug screen if you are suspicious (cocaine causes placental abruption). Give Rhogam if the mother is Rh-negative. The Kleihauer-Betke test quantifies fetal blood in maternal circulation and is used to calculate the dose of Rhogam.

Preterm labor: defined as labor between 20–37 weeks. Treat with lateral decubitus position, bed and pelvic rest, oral or IV fluids, and oxygen administration (all may stop the contractions). Then give a tocolytic ($beta_2$ agonist or magnesium sulfate) if no contraindications are present (heart disease, hypertension, diabetes mellitus, hemorrhage, ruptured membranes, cervix dilated > 4 cm). Patients may be discharged on oral tocolytic. Do not tocolyze the mother if it is dangerous to do so (preeclampsia, severe hemorrhage, chorioamnionitis, IUGR, fetal demise, or fetal anomalies incompatible with survival). Often steroids are given with tocolysis (if the infant is 24–34 weeks old) to hasten fetal lung maturity.

Important points:

1. Quickening (when the mother first detects fetal movements) usually occurs at 18–20 weeks in a primigravida and 16–18 weeks in a multigravida.
2. Order of labor positions: descent, flexion, internal rotation, extension, external rotation, and expulsion
3. IgG is the only maternal antibody that crosses the placenta. An elevated neonatal IgM concentration is never normal, whereas an elevated neonatal IgG often represents maternal antibodies.

Rh incompatibility and hemolytic disease of the newborn: occur when the mother is Rh-negative and the infant is Rh-positive. If both mother and father are Rh-negative, there is nothing to worry about—the infant will be Rh-negative. If the father is Rh-positive, the infant has a 50/50 chance of being Rh-positive. If the potential for hemolytic disease exists, check maternal Rh antibody titers every month, starting in the seventh month. Give Rhogam automatically at 28 weeks and within 72 hours after delivery as well as after any procedures that may cause transplacental hemorrhage (e.g., amniocentesis). An important point is that development of disease requires previous sensitization. In other words, if a nulliparous mother has never received blood products, her first Rh-positive infant will not be affected by hemolytic disease (except in the rare case of sensitization during the first pregnancy from undetected fetomaternal bleeding, which usually occurs later in the pregnancy and can be prevented by Rhogam administration at 28 weeks in most instances). The second Rh-positive infant, however, will be affected—unless you, the astute board taker/physician, administer Rhogam at 28 weeks and within 72 hours after delivery during the first pregnancy. Any history of blood transfusion, abortion, ectopic pregnancy, stillbirth, or delivery can cause sensitization. If you check maternal Rh antibodies and they are strongly positive, Rhogam is worthless, because sensitization has already occurred. Rhogam administration is a good example of primary prevention.

- If not detected and prevented, Rh incompatibility leads to fetal hydrops (edema, ascites, pleural and pericardial effusions).
- Amniotic fluid spectrophotometry gauges the severity of fetal hemolysis.
- Treatment of hemolytic disease involves delivery if the fetus is mature. Check lung maturity with the lecithin:sphingomyelin ratio. Intrauterine transfusion is risky; phenobarbital helps the fetal liver to break down bilirubin by inducing enzymes.
- ABO blood group incompatibility also may cause hemolytic disease of the newborn when the mother is type O and the infant is type A, B, or AB. Previous sensitization is not

required, because IgG antibodies, which can cross the placenta, occur naturally in patients with blood type O. Usually the disease is less severe than with Rh incompatibility, but treatment is the same. Other minor blood antigens also cause a reaction in rare cases.

Summary: Give Rhogam only when the mother is Rh-negative and the father's blood type is unknown or Rh-positive. During routine prenatal care, check for Rh antibodies at the first visit. If the test is positive, do *not* give Rhogam—you are too late. Otherwise, give routinely at 28 weeks and immediately after delivery. Also give Rhogam after an abortion, stillbirth, ectopic pregnancy, amniocentesis, chorionic villus sampling, and any other invasive procedure during pregnancy that may cause transplacental bleeding.

Note: If fetal lungs are immature (lecithin:sphingomyelin ratio < 2:1 or prostaglandin-negative) and the fetus is between 24–34 weeks, corticosteroid administration may hasten lung maturity and thus reduce the risk of respiratory distress syndrome.

Premature rupture of membranes (PROM): rupture of the amniotic sac before the onset of labor. Diagnosis of rupture of the membranes (whether premature or not) is based on history and sterile speculum exam, which will show (1) pooling of amniotic fluid, (2) fern ing pattern when the fluid is placed on a microscopic slide and allowed to dry, and/or (3) positive nitrazine test (nitrazine paper turns blue in presence of amniotic fluid). Ultrasound also should be done to assess amniotic fluid volume (as well as gestational age and any anomalies that may be present). Spontaneous labor often follows membrane rupture. If labor does not occur within 6–8 hours and the patient is at term, labor should be induced. If the cervix is highly unfavorable, you can wait 24 hours to attempt induction. PROM carries an increased risk of infection, both to the mother (chorioamnionitis) and infant (neonatal sepsis, pneumonia, meningitis), usually from group B streptococci, *Escherichia coli*, or *Listeria* sp.

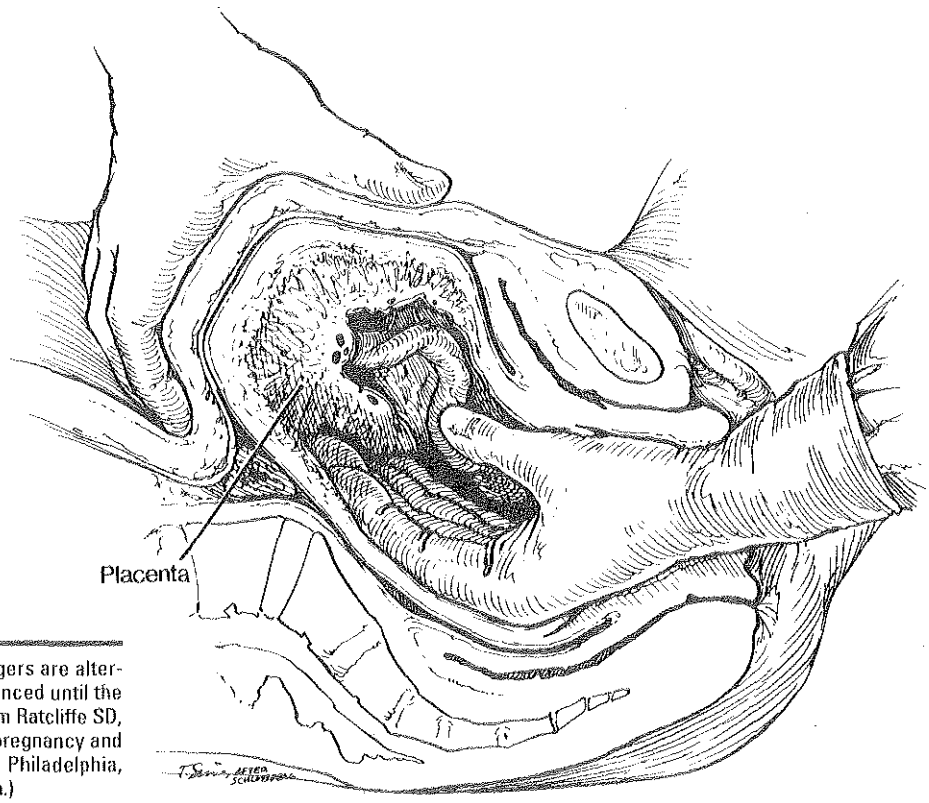
Preterm premature rupture of membranes (PPROM): PROM that occurs before 36–37 weeks. Risk of infection increases with the duration of ruptured membranes. Do a culture and Gram stain of amniotic fluid. If they are negative, treat with pelvic and bed rest and frequent follow-up. If positive for group B streptococci, treat the mother with penicillin, even if she is asymptomatic.

Chorioamnionitis: presents with fever and tender, irritable uterus (usually postpartum but may be antepartum in patients with PROM or PPROM). Do a culture and Gram stain of amniotic fluid, and treat with ampicillin while awaiting culture results.

Postpartum hemorrhage: defined as estimated blood loss > 500 ml during a vaginal delivery (> 1000 ml during cesarean section). The most common cause is uterine atony (75–80% of cases). Hemorrhage also may be caused by lacerations, retained placental tissue (placenta accreta, increta, or percreta), coagulation disorders (e.g,. disseminated intravascular coagulation, von Willebrand disease), low placental implantation, and uterine inversion. The major risk factor for retained placental tissue is previous uterine surgery or cesarean section. Treatment is usually a hysterectomy.

Uterine atony: caused by overdistention of the uterus (multiple gestation, polyhydramnios, macrosomia), prolonged labor, oxytocin usage, grandmultiparity (history of 5 or more deliveries), and precipitous labor (< 3 hr). Treat with dilute oxytocin infusion, and use bimanual compression and massage of the uterus while the infusion is running. If this approach fails, try ergonovine or another ergot drug (contraindicated with maternal hypertension) or prostaglandin $F_{2\alpha}$. If this approach also fails, do a hysterectomy (ligate the uterine vessels if the patient wants fertility).

With **retained products of conception** (which is probably the most common cause of delayed postpartum hemorrhage), remove the placenta manually to stop bleeding; then do curettage in the operating room under anesthesia. If placenta accreta or percreta is present (placental tissue grows into/through the myometrium), a hysterectomy is usually necessary to stop the bleeding.



Manual removal of placenta. The fingers are alternately abducted, adducted, and advanced until the placenta is completely detached. (From Ratcliffe SD, Byrd JE, Sakornbut EL: Handbook of pregnancy and Perinatal Care in Family Practice. Philadelphia, Hanley & Belfus, 1996, with permission.)

With **uterine inversion** (the uterus inverts and can be seen outside the vagina, usually as a result of pulling too hard on the cord), put the uterus back in place manually (anesthesia may be needed) and give IV fluids and oxytocin.

Postpartum fever: defined as temperature >100.4°F (38°C) for at least two consecutive days. Postpartum fever usually is due to endometritis. Important predisposing factors are PROM/PPROM, prolonged labor, frequent vaginal exams during labor, and manual removal of placenta or retained placental fragments (good culture medium). Patients with endometritis have a tender uterus in addition to fever. Anaerobes usually are involved. Treat with broad-spectrum penicillin or cephalosporin; add clindamycin, metronidazole, and gentamicin if the patient is doing poorly. Before antibiotics, do cultures of endometrium, vagina, blood, and urine. Do not forget the easy causes of postpartum fever, such as urinary tract infection or atelectasis and pneumonia, especially after cesarean section.

- If a postpartum fever does not resolve with broad-spectrum antibiotics, there are two main possibilities: progression to pelvic abscess or pelvic thrombophlebitis. Get a CT scan, which will show an abscess. If an abscess is present, it needs to be drained. If no abscess is seen on CT, think of **pelvic thrombophlebitis**, which presents with persistent spiking fevers and lack of response to antibiotics. Give heparin for an easy cure (and diagnosis in retrospect).

- If a postpartum patient goes into shock and you see no bleeding, think of amniotic fluid embolism, uterine inversion, or concealed hemorrhage (e.g., uterine rupture with bleeding into the peritoneal cavity)

Normal physiologic changes in pregnancy:

1. **Laboratory tests:** erythrocyte sedimentation rate is markedly elevated (*worthless* test in pregnancy). Thyroxine and thyroxine-binding globulin increase, but free thyroxine is *normal*. Hemoglobin increases, but plasma volume increases more, so net result is a decreased hematocrit and hemoglobin; BUN and creatinine decrease/GFR increases (high end of normal range for BUN/creatinine indicate renal disease in pregnancy); alkaline phosphatase increases markedly. Mild proteinuria and glycosuria are NORMAL in pregnancy, electrolytes and LFTs remain normal.
2. **Cardiovascular changes:** blood pressure decreases slightly, heart rate increases by 10–20 bpm, stroke volume increases, and cardiac output increases (up to 50%).
3. **Pulmonary changes:** minute ventilation increases because of increased tidal volume with the same or only slightly increased respiratory rate. Residual volume and carbon dioxide decrease (physiologic hyperventilation/respiratory alkalosis).
4. The average **weight gain** in pregnancy is 28 lb (12.5 kg). With a greater weight gain, think of diabetes mellitus. With a smaller weight gain, think of hyperemesis gravidarum or psychological or major systemic disease.

Note: Treat asymptomatic bacteriuria in pregnancy (because of the high rate of progression to pyelonephritis) with penicillin, cephalosporin, or nitrofurantoin.

Hyperemesis gravidarum: intractable nausea and vomiting leading to dehydration and possible electrolyte disturbances. The condition presents in the first trimester, usually in younger patients with their first pregnancy and underlying social stressors or psychological problems. Treat with supportive care, including small, frequent meals and antiemetics (fairly safe in pregnancy). Outpatient treatment sometimes is acceptable unless the patient has severe dehydration and/or electrolyte disturbances, in which case admit for treatment.

Cholestasis of pregnancy: presents with itching, abnormal liver function tests, and/or jaundice during pregnancy. The only treatment is delivery, but cholestyramine may help with symptoms. **Acute fatty liver of pregnancy** is a more serious disorder that presents in the third trimester or after delivery and usually progresses to hepatic coma. Treatment includes IV fluids, IV glucose, and fresh frozen plasma. Vitamin K does not work, because the liver is in temporary failure.

Surgical conditions: Pregnant women can have the same surgical conditions as nonpregnant women. In general, treat the disease regardless of pregnancy. This rule of thumb always works with acute surgical conditions (e.g., appendicitis, cholecystitis). With semiurgent conditions (e.g., ovarian neoplasm), it is best to wait until the second trimester, when the patient is most stable. Purely elective cases are avoided. Appendicitis may present with right upper quadrant pain or tenderness due to displacement of the appendix by the uterus. Do a laparotomy if you are unsure and the patient has peritoneal signs.

Fetal malpresentations: although under specific guidelines some frank and complete breeches may be delivered vaginally, it is acceptable to do a cesarean section for *any* breech presentation. With shoulder presentation or incomplete/footling breech, cesarean section is mandatory. For face and brow presentations, watchful waiting is best, as most convert to vertex presentations; if they do not convert, do a cesarean section.

Multiple gestations: if sex or blood type is different, twins are dizygotic. If the placentas are monochorionic, the twins are monozygotic. These three simple factors differentiate monozygotic from dizygotic twins in 80% of cases. The remaining 20% require HLA-typing studies. Complications of multiple gestations (the higher the number of fetuses, the higher the risk of most of these conditions) include the following:

1. Maternal: anemia, hypertension, premature labor, postpartum uterine atony, postpartum hemorrhage, preeclampsia
2. Fetal: polyhydramnios, malpresentation, placenta previa, abruptio placentae, velamentous cord insertion or vasa previa, PROM, prematurity, umbilical cord prolapse, IUGR, congenital anomalies, increased perinatal morbidity and mortality.
3. With vertex-vertex presentations, you can try vaginal delivery for both infants; with any other combination of presentations, do a cesarean section.

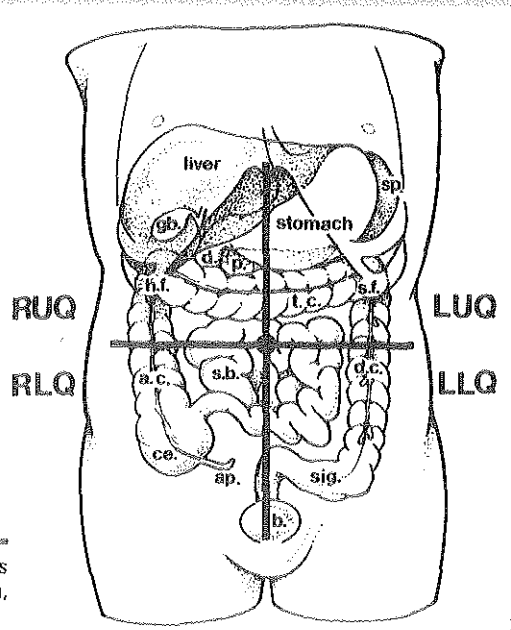
CHAPTER 20

General Surgery

Acute abdomen: an inflamed peritoneum often leads to a laparotomy because it signifies a potentially life-threatening condition (important exceptions to laparotomy are pancreatitis, many cases of diverticulitis, and spontaneous bacterial peritonitis). The best physical confirmations of peritonitis are rebound tenderness and involuntary guarding. Voluntary guarding and tenderness to palpation are softer signs because both are often present in benign diseases. When you are in doubt and the patient is stable, *withhold pain medications* (do *not* mask symptoms before you have a diagnosis), and do serial abdominal exams. If the patient is unstable or worsening, proceed to laparoscopy or laparotomy.

Localization of acute abdomen:

- Right upper quadrant: think of gallbladder (cholecystitis, cholangitis) or liver (abscess)
- Left upper quadrant: think of spleen (rupture with blunt trauma)
- Right lower quadrant: think of appendix (appendicitis)
- Left lower quadrant: think of sigmoid colon (diverticulitis)
- Epigastric: think of stomach (penetrating ulcer) or pancreas (pancreatitis)



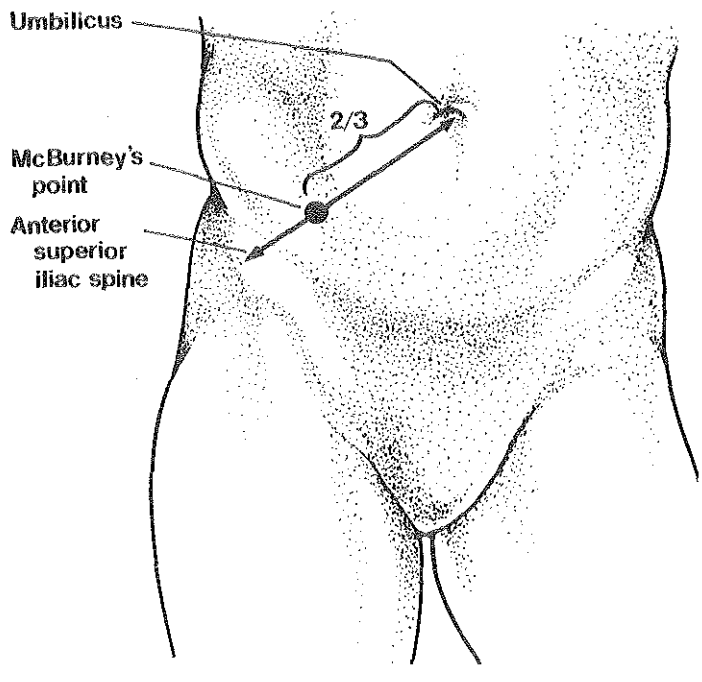
Topographic anatomy (4-quadrant construct) of the abdomen. (From James EC, Corry RJ, Perry JF: Principles of Basic Surgical Practice. Philadelphia, Hanley & Belfus, 1987, with permission.)

Gallbladder disease:

1. Cholecystitis: the classic patient is fat, forty, fertile, female, flatulent and now febrile (especially with gallstones on ultrasound or history of gallstones and/or gallstone-type symptoms, such as postprandial right upper quadrant colicky pain with bloating and/or nausea and vomiting). Look for Murphy's sign. Do a cholecystectomy.
2. Cholangitis: right upper quadrant pain, fever and shaking chills, and jaundice. Patients often have a history of gallstones. Start antibiotics, and do a cholecystectomy.
3. Ultrasound is the best first imaging study for suspected gallbladder disease in the acute abdomen. For cholecystitis, a nuclear hepatobiliary/scintigraphy study (e.g., a hepatoiminodiacetic acid [HIDA] scan) clinches a difficult diagnosis (nonvisualization of the gallbladder).

Splenic rupture: history of blunt abdominal trauma, hypotension/tachycardia, shock, and Kerr's sign. Patients with Epstein-Barr virus infection should not play contact sports. Immunize all patients after splenectomy (see section on immunizations).

Appendicitis: peaks in 10–30-year-olds. The classic history is crampy, poorly localized periumbilical pain followed by nausea and vomiting. Pain then localizes to the right lower quadrant, and patients develop peritoneal signs with worsening of nausea and vomiting. Patients who are hungry and ask for food do not have appendicitis. Remember positive Rovsing's sign and McBurney point tenderness. *Do an appendectomy.*



McBurney's point: usual point of maximal tenderness in right lower quadrant. (From James EC, Corry RJ, Perry JF: *Principles of Basic Surgical Practice*. Philadelphia, Hanley & Belfus, 1987, with permission.)

Diverticulitis: left lower quadrant pain in a patient over 50 is diverticulitis unless you have a good reason to think otherwise. Treat medically with avoidance of oral ingestion (NPO) and broad-spectrum antibiotics. If the disease is recurrent or refractory to medical therapy, consider sigmoid resection.

Pancreatitis: look for epigastric pain in an alcohol abuser or patient with history of gallstones. Pain may radiate to the back, and serum amylase or lipase, if given, is elevated—if they have not been given, order them! Common symptoms include decreased bowel sounds, local ileus (sentinel loop of bowel on x-ray), and nausea and vomiting with anorexia. Treat with narcotics (meperidine, not morphine), NPO, nasogastric tube, IV fluids, and supportive care. Watch for complications of pseudocyst and pancreatic abscess, which may require surgical intervention.

Perforated ulcer: patients often have no history of alcohol consumption or gallstones. X-ray classically shows free air under the diaphragm, and patients have a history of peptic ulcer disease. Treat with surgery.

Small bowel obstruction: symptoms include bilious vomiting (seen early), abdominal distention, constipation, hyperactive bowel sounds (high-pitched, rushing sounds), and pain that usually is poorly localized. X-ray shows multiple air-fluid levels. Patients often have a history of previous surgery; the most common cause of small bowel obstructions in adults is adhesions, which usually develop from prior surgery. In children, think of Meckel's diverticulum or incarcerated hernia. Start treatment with NPO, nasogastric tube, and IV fluids. If symptoms do not resolve or peritoneal signs occur, laparotomy is needed to relieve the obstruction.

Large bowel obstruction: gradually increasing abdominal pain, abdominal distention, constipation, feculent vomiting (seen late). In older patients the most common causes are volvulus and diverticulitis, but colon cancer is a possibility. Treat early with NPO and nasogastric tube. A sigmoid volvulus often can be decompressed with an endoscope. Other causes or refractory cases require surgery to relieve the obstruction. In children, watch for Hirschsprung's disease.

Four types of hernia (all are treated with surgical repair):

1. **Indirect:** *most common type* in both sexes and all age groups. Hernia sac travels through the inner and outer inguinal rings (protrusion begins lateral to the inferior epigastric vessels) and *into the scrotum* because of a patent processus vaginalis (congenital defect).
2. **Direct:** hernia (*no sac*) protrudes medial to the inferior epigastric vessels because of weakness in the abdominal musculature of Hesselbach's triangle.
3. **Femoral:** more common in women. Hernia (no sac) goes through the femoral ring onto the anterior thigh (located *below the inguinal ring*). This type is most susceptible to incarceration and strangulation.
4. **Incisional:** after any wound (especially surgical), a hernia can occur through the site of the incision.

- Incarceration: when herniated organs become trapped and swollen or edematous. Incarcerated hernias are the *most common* cause of small bowel obstruction in a patient who has never had abdominal surgery and the *second most common* cause in patients who have had abdominal surgery.
- Strangulation: the entrapment becomes so severe that the blood supply is cut off; necrosis may occur. Strangulation is a surgical emergency; the patient may present with symptoms of small bowel obstruction and shock.

Important preoperative and postoperative points:

1. Before surgery the patient should avoid oral ingestion for at least 8 hours to reduce the risk of aspiration. For this reason, general anesthesia is dangerous in obstetrics, because patients have *not* been NPO when they go into labor.

2. Spirometry and a *good history* are the best preoperative tests for assessment of pulmonary function. Spirometry evaluates forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), FEV_1/FVC (%), and maximal voluntary ventilation.
3. Use compressive or elastic stockings, early ambulation, and/or low-dose heparin to help prevent deep vein thrombosis and pulmonary embolism. Warfarin often is used for orthopedic procedures.
4. The most common cause of postoperative fever in the first 24 hours is atelectasis. Treat or prevent with early ambulation, chest physiotherapy and percussion, incentive spirometry, and proper pain control. Both too much pain and too many narcotics increase risk of atelectasis.
5. "Water, wind, walk, wound, and weird drugs" helps to recall causes of postoperative fever. Water = urinary tract infection, wind = atelectasis or pneumonia, walk = deep vein thrombosis, wound = surgical wound infection, and weird drugs = drug fever. If daily fever spikes occur, think about an intraabdominal abscess. Order a CT scan to locate; drainage is required.
6. Fascial or wound dehiscence: occurs *5–10 days postoperatively*. Look for leakage of *serosanguinous* fluid from the wound, particularly after the patient coughs or strains, which is often associated with infection. Treat with antibiotics (if secondary to infection) and reclosure of the incision.

TRAUMA

If you spent your free time during your surgery rotation trying to catch up on lost sleep, go back and read a chapter about trauma from a general surgery text. Trauma and its management are high yield for Step II.

ABCDEs are the key to management of patients with trauma. Always do them in order. For example, if the patient is bleeding to death and has a blocked airway, you must choose which problem to address first. The answer is airway management:

A = Airway: provide, protect, and maintain an adequate airway at all times. If the patient can answer questions, the airway is fine. You can use an oropharyngeal airway in uncomplicated cases and give supplemental oxygen. When you are in doubt or the patient's airway is blocked, intubate. *If intubation fails, do a cricothyroidotomy.*

B = Breathing: similar to airway, but even when the airway is patent, the patient may not be breathing spontaneously. The end result is the same: *when you are in doubt or* the patient is not breathing, intubate. If intubation fails, do a cricothyroidotomy.

C = Circulation: if the patient seems hypovolemic (tachycardia, bleeding, weak pulse, paleness, diaphoresis, capillary refill > 2 seconds), give IV fluids and/or blood products. The initial procedure is to start two large-bore IV catheters and give a bolus of 10–20 ml/kg (roughly 1 L) of lactated Ringer's solution (IV fluid of choice in trauma). Reassess the patient after bolus for improvement. Give another bolus if needed.

D = Disability: check neurologic function (Glasgow coma scale).

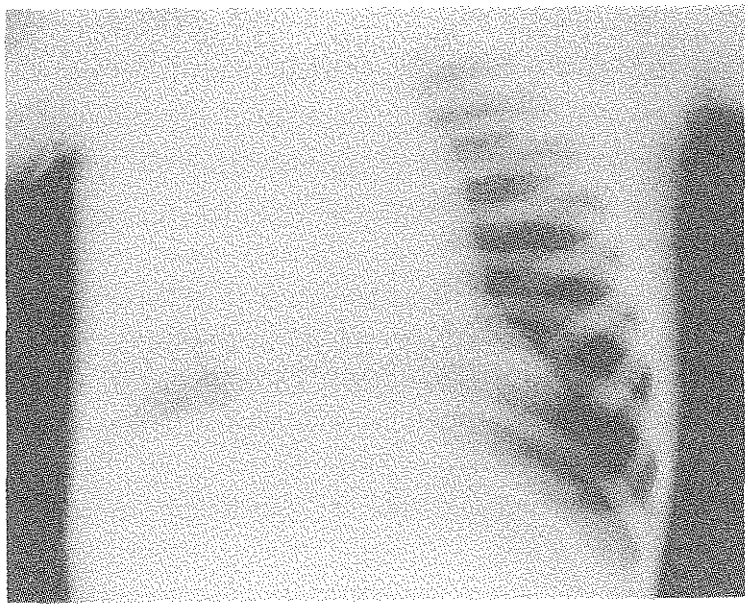
E = Exposure: strip the patient and "*put a finger in every orifice*" so that you do not miss any occult injuries.

Important points:

1. All trauma patients generally get cervical spine, chest, and pelvic x-rays.
2. Evaluate any head trauma with a noncontrast CT (better than MRI for trauma).
3. In **blunt abdominal trauma**, initial findings determine the course of action:
   - If the patient is awake and stable and your exam is benign, observe and repeat the abdominal exam later.
   - If the patient is hemodynamically unstable (hypotension and/or shock that do not respond to a fluid challenge), proceed directly to laparotomy.
   - If the patient has altered mental status, the abdomen cannot be examined, or an obvious sources of blood loss explains the hemodynamic instability, either do a diagnostic peritoneal lavage (DPL) or get a CT scan.
4. In **penetrating abdominal trauma**, the type of injury and initial findings determine the course of action:
   - With any gunshot wound, proceed directly to laparotomy.
   - With a wound from a sharp instrument, management is more controversial. Either proceed directly to laparotomy (the better choice if the patient is unstable) or do a DPL. If the DPL is positive, do a laparotomy; if it is negative, observe and repeat the abdominal exam later.

Six thoracic injuries that can be rapidly fatal and that you should be able to recognize:

1. **Airway obstruction:** no audible breath sounds. Patients cannot answer questions even though they are awake and gurgling. Treat by intubation. If intubation fails, do a cricothyroidotomy (or a tracheostomy in the operating room if time allows).
2. **Open pneumothorax:** open defect in the chest wall that causes poor ventilation and oxygenation. Treat with intubation, positive-pressure ventilation, and closure of the defect in the chest wall. You can use gauze. Tape it *on three sides only* to allow excessive pressure to escape. Otherwise you may convert an open pneumothorax into a tension pneumothorax.
3. **Tension pneumothorax:** usually after blunt trauma. Air forced into pleural space cannot escape and collapses the affected lung, then shifts the mediastinum and trachea to the opposite side of the chest. Know what this condition looks like on x-ray. There are no breath sounds on the affected side, and chest percussion produces a hypertympanic sound. Hypotension and distended neck veins may result from impaired cardiac filling. Treat with needle thoracentesis, followed by insertion of a chest tube. (See figure, top of next page.)
4. **Cardiac tamponade:** the classic history is penetrating trauma to the left chest (where the heart is located). Patients have hypotension (due to impaired cardiac filling), distended neck veins, muffled heart sounds, pulsus paradoxus (exaggerated fall in blood pressure on inspiration), and normal breath sounds. Treat with pericardiocentesis if the patient is unstable (put a catheter in the pericardial sac, and aspirate the blood or fluid). If the patient is stable, you can do an echocardiogram to confirm the diagnosis first.
5. **Massive hemothorax:** loss of more than 1 L of blood into the thoracic cavity. Patients have decreased (not absent) breath sounds in the affected area, dull note on percussion, hypotension/collapsed neck veins (from blood leaving the vascular tree), and tachycardia. Placement of a chest tube causes the blood to come out. Give IV fluids and/or blood before you place the chest tube. If bleeding stops after the initial outflow, get an x-ray to check for remaining blood or pathology and treat supportively. If bleeding does not stop, perform an emergent thoracotomy.

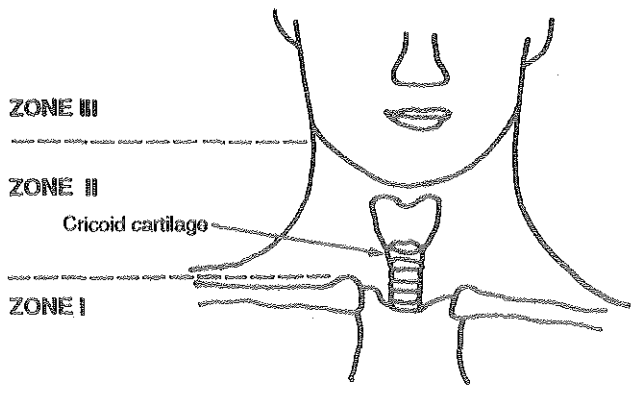


Left tension pneumothorax. (From James EC, Corry RJ, Perry JF: Principles of Basic Surgical Practice. Philadelphia, Hanley & Belfus, 1987, with permission.)

6. **Flail chest:** when several adjacent ribs are broken in multiple places, the affected part of the chest wall may move paradoxically during respiration (in during inspiration, out during expiration). There is almost always an associated pulmonary contusion, which, combined with pain, may make respiration inadequate. When you are in doubt or the patient is not doing well, intubate and give positive pressure ventilation.

Other injuries:

1. **Aortic rupture:** the most common cause of immediate death after an automobile accident or fall from a great height. Look for widened mediastinum on x-ray and appropriate trauma history. Get an angiogram if you are suspicious. Treat with surgical repair.
2. **Diaphragm rupture:** usually occurs on the left because the liver protects the right side. Look for bowel herniated into the chest. Fix surgically.
3. **Neck trauma:** the neck is divided into three zones for trauma:



Neck zones for trauma. (From Markovchick V, Pons P: Emergency Medicine Secrets, 2nd ed. Philadelphia, Hanley & Belfus, 1999, with permission.)

- Zone I: base of the neck (from 2 cm above the clavicles to the level of the clavicles)
- Zone II: midcervical region (2 cm above the clavicle to the angle of the mandible)
- Zone III: the angle of the mandible to the base of the skull
- With zone I and III injuries, do an arteriogram before going to the operating room.
- With zone II injuries, proceed to the operating room for surgical exploration (do *not* do an arteriogram first).
- In the presence of obvious bleeding or a rapidly expanding hematoma, proceed directly to the operating room, no matter where the injury is.

4. **Choking:** leave choking patients alone if they are speaking, coughing, or breathing. If they stop doing all three, do the Heimlich maneuver.
5. **Tooth avulsion:** put the tooth back in place with no cleaning (or rinse it only in saline), and stabilize as soon as possible. The sooner this procedure is done, the better the prognosis for salvage of the tooth.

CHAPTER 21

Ophthalmology

Conjunctivitis causes conjunctival vessel hyperemia. The three main causes are allergic (common), viral (common), and bacterial (rare):

ETIOLOGY	UNIQUE SIGNS/SYMPTOMS	TREATMENT
Allergic	Itching, bilateral, seasonal, long duration	Vasoconstrictors if needed
Viral*	Preauricular adenopathy, highly contagious (history of infected contacts); clear, watery discharge	Supportive, hand washing (prevents spread)
Bacterial	Purulent discharge; more common in neonates	Topical antibiotics

* Number-one cause is adenovirus.

Neonatal conjunctivitis is usually due to one of three causes:

1. Chemical: silver nitrate (or erythromycin) drops are given prophylactically to all newborns to prevent gonorrheal conjunctivitis. The drops may cause a chemical conjunctivitis (with *no* purulent discharge) that develops within 12 hours of instilling the drops and resolves within 48 hours (pick this answer if conjunctivitis occurs in the *first 24 hours of life*).
2. Gonorrheal: look for symptoms of gonorrhea in the mother. The infant has an *extremely purulent* discharge at *2–5 days of age*. Treatment is topical (e.g., erythromycin ointment). Infants that are given prophylactic drops should not get gonorrheal conjunctivitis.
3. Chlamydial (inclusion conjunctivitis): the mother often reports no symptoms. The infant has mild-to-severe conjunctivitis beginning at *5–14 days of age*. Patients must be treated with topical *and* systemic antibiotics (oral erythromycin usually is used) to prevent chlamydial pneumonia (a common complication). Prophylactic eyedrops do *not* effectively prevent chlamydial conjunctivitis.

Important points:

1. If you forget everything else, remember the age at which the three diseases present.
2. Conjunctivitis involves no loss of vision (other than transient blurriness due to tear film debris that resolves with blinking). If loss of vision is present, think of other, more serious conditions.

Glaucoma: best thought of as ocular hypertension with its resultant effects. Risk factors are age > 40, race (black), and family history. Two types:

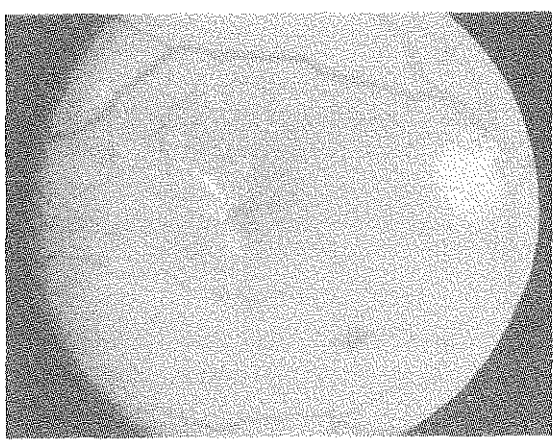
1. **Open angle:** although it is traditional to talk about painful attacks, they are rare. Open-angle glaucoma causes 90% of cases of glaucoma, is *painless*, and does not involve acute attacks.

The only signs are elevated intraocular pressure (usually 20–30 mmHg), a gradually progressive visual field loss, and optic nerve changes (increased cup-to-disc ratio on fundoscopic exam). Treat with several different types of medications (beta blockers, prostaglandin [latanoprost], acetazolamide, pilocarpine) or surgery.

2. **Closed angle:** presents with sudden ocular pain, haloes around lights, red eye, high intraocular pressure (> 30 mmHg), nausea and vomiting, sudden decreased vision, and a fixed, mid-dilated pupil. Treat immediately with pilocarpine drops, oral glycerin, and acetazolamide to break the attack. Then use surgery to prevent further attacks (peripheral iridectomy). In rare cases, anticholinergic medications may cause an attack of closed-angle glaucoma in a susceptible, previously untreated patient. Medications do not cause glaucoma attacks in open-angle glaucoma or patients previously treated surgically for closed-angle glaucoma.

Important points:

1. Steroids, whether topical or systemic, can cause glaucoma and cataracts. Topical steroids can worsen ocular herpes and fungal infections. For board purposes, do not give topical steroids (especially if the patient has a dendritic corneal ulcer stained green by fluorescein).
2. Exposure to ultraviolet light can cause keratitis (corneal inflammation) with resultant pain, foreign body sensation, red eye, tearing, and decreased vision. Patients have a history of welding, using a tanning bed or sunlamp, or snow-skiing ("snow-blindness"). Treat with an eye patch (24 hours), topical antibiotic, and possibly with an anticholinergic (cycloplegic agent that reduces pain).
3. Uveitis is common in juvenile rheumatoid arthritis (especially the pauciarticular form). Patients need periodic ophthalmologic examination to check for uveitis.
4. Cataracts are the most common cause of a painless, slowly progressive loss of vision. Treatment is surgical. Cataracts in a neonate should make you think of TORCH infections or an inherited metabolic disorder (e.g., galactosemia).
5. Know the retinal and fundus changes seen in diabetes (dot-blot hemorrhages, microaneurysms, neovascularization) and hypertension (arteriolar narrowing, copper/silver wiring, cotton wool spots, papilledema with severe hypertension).



Background diabetic retinopathy with exudate, hemorrhages, and edema (dot and blot). (From Vander JF, Gault JA: Ophthalmology Secrets. Philadelphia, Hanley & Belfus, 1998, with permission.)

6. Diabetes is the number-one cause of blindness in adults under 55. Senile macular degeneration (look for macular drusen) is the most common cause of blindness in adults over age 55. Glaucoma is the number-one cause of blindness in blacks of any age and the number-three overall cause of blindness.
7. Treatment for proliferative diabetic retinopathy (with neovascularization) is application of a laser beam to the periphery of the whole retina (panretinal photocoagulation). Focal laser treatment is common for nonproliferative retinopathy with macular edema; the laser is applied only to the affected area.

Be able to differentiate **orbital cellulitis** from **preorbital cellulitis** (preseptal cellulitis). Both may involve swollen lids, fever, chemosis, and a history of facial laceration, trauma, insect bite, or sinusitis. Ophthalmoplegia, proptosis, severe eye pain, or decreased visual acuity indicates orbital cellulitis (a medical emergency). The most common bugs in both are *Streptococcus pneumoniae*, *Haemophilus influenzae* type b, and staphylococci/streptococci with a history of trauma. Complications of orbital cellulitis include extension into the skull, vein thromboses, and blindness. Treat either condition with blood cultures and administration of broad-spectrum antibiotics to cover the likely bugs until culture results are known. Inpatient IV antibiotics are needed for orbital cellulitis.

With **chemical burns** to the eye (acid or alkaline), the key to management is copious irrigation with the closest source of water. The longer you wait, the worse the prognosis. Do *not* get additional history in this instance. Alkali burns have a worse prognosis, because they tend to penetrate more deeply into the eye.

Hordeolum (stye) is a painful, red lump near the lid margin. Treat with warm compresses. **Chalazion** is a painless lump away from the lid margin. Treat with warm compresses. If the compresses do not work, use incision and drainage for both conditions.

Herpes simplex keratitis usually starts with conjunctivitis and a vesicular lid eruption, then progresses to the classic dendritic keratitis (seen with fluorescein—know what this looks like). Treat with topical antivirals (e.g., idoxuridine, trifluridine). Corticosteroids are *contraindicated* with dendritic keratitis, because they may make the condition worse.

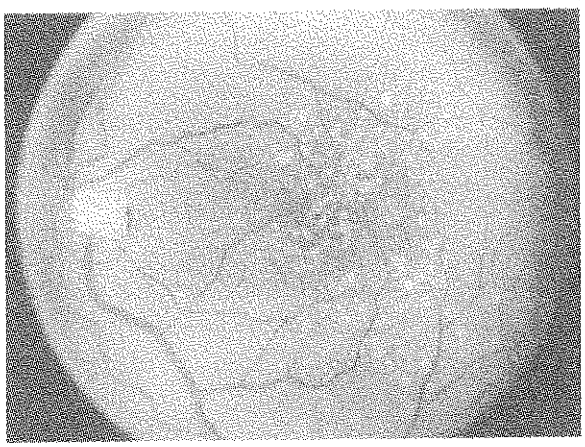
Ophthalmic herpes zoster should be suspected with involvement of the tip of the nose and/or medial eyelid with a typical zoster dermatomal pattern. Treat with oral acyclovir. Complications include uveitis, keratitis, and glaucoma.

Central retinal artery occlusion presents with sudden (within a few minutes), painless, unilateral loss of vision. The fundoscopic appearance is classic (know it!). No treatment is satisfactory. The most common cause is emboli from carotid plaque or the heart, but look for coexisting symptoms of temporal arteritis (elderly patients with jaw claudication, tortuous temporal artery, markedly elevated erythrocyte sedimentation rate, and co-existing polymyalgia rheumatica symptoms of proximal muscle pain and stiffness). If temporal arteritis is suspected, start corticosteroids immediately before confirming the diagnosis with a temporal artery biopsy. The patient may lose vision in the other eye if you wait to confirm the diagnosis.

Central retinal vein occlusion also presents with sudden (within a few hours), painless, unilateral loss of vision. The fundoscopic appearance is classic (know it!). No treatment is satisfactory. The most common causes are hypertension, diabetes mellitus, glaucoma, and increased blood viscosity (e.g., leukemia). Complications (vision loss, glaucoma) are related to neovascularization.

Retinal detachment causes a sudden (instant), painless, unilateral loss of vision. History usually includes "floaters" and seeing flashes of light. Often described as a "curtain or veil coming down in front of my eye." This history should prompt immediate referral to an ophthalmologist. Surgery to reattach the retina may save the patient's sight.

In elderly patients, both **macular degeneration** and **cataracts** cause painless loss of vision, often bilateral, but one side may be worse than the other. Know what the red reflex looks like in a patient with a cataract and what the fundus looks like in a patient with macular degeneration (macular drusen). Treat cataracts with surgery. Macular degeneration currently has no treatment.



Drusen are the byproduct of retinal metabolism and manifest as focal yellow-white deposits deep to the retinal pigment epithelium. They serve as a marker of nonexudative age-related macular degeneration. (From Vander JF, Gault JA: Ophthalmology Secrets. Philadelphia, Hanley & Belfus, 1998, with permission.)

Optic neuritis and **papillitis** present with a fairly quick (over hours to days), painful (unless retrobulbar), unilateral or bilateral loss of vision. If loss of vision bilateral in a 20–40-year-old woman, think of multiple sclerosis; the same applies to internuclear ophthalmoplegia. Worry about tumor if the patient is male and has signs of intracranial hypertension or other neurologic deficits. Lyme disease and syphilis are rare causes. Disc margins may appear blurred on fundoscopic exam, just as in papilledema.

Note: Know your visual pathway lesions and location, just as for Step I (e.g., homonymous hemianopia, bitemporal hemianopia). The most commonly tested example is bitemporal hemianopia, which usually is due to a pituitary tumor.

Ophthalmologic cranial nerve (CN) palsies: usually due to vascular complications of diabetes and hypertension. Most cases resolve on their own within 2 months. In patients under 40, patients with other neurologic deficits or severe pain, and any patient who does not improve within 8 weeks, get an MRI because benign causes are less likely:

1. Oculomotor (CN 3): the eye is down and out and can move only laterally. In cases due to hypertension or diabetes mellitus, the pupil is normal. Close observation is all that is needed; the condition resolves on its own in several weeks. A pupil that is "blown" (dilated, nonreactive) is a medical emergency; the most likely cause is an aneurysm or tumor. Get an MRI and/or magnetic resonance or cerebral angiogram.

2. Trochlear (CN 4): when the gaze is medial, the patient cannot look down.
3. Abducens (CN 6): the patient cannot look laterally with the affected eye.
4. CN 5 and 7 palsies also affect the eye because of corneal drying (loss of corneal blink reflex).

Children with a **"lazy eye"** or **strabismus** (deviation of the eye, usually inward) that persists beyond 3 months need ophthalmologic referral. The condition does not resolve and may cause blindness (amblyopia) in the affected eye. For this reason, visual screening must be done in pediatric patients; the visual system is still developing after birth until the age of 7 or 8. If one eye does not see well or is turned outward, the brain cannot fuse the two different images that it sees and suppresses the bad eye, which will not develop the proper neural connections. Thus, the eye will never see well and cannot be corrected with glasses (neural rather than refractive problem).

Presbyopia: between the ages of 40 and 50 years, the lens loses its ability to accommodate. Patients need bifocals or reading glasses for near vision. Presbyopia is a normal part of aging.

CHAPTER 22

Orthopedic Surgery

Important points:

1. Pelvic fracture is the fracture with the highest mortality rate. Patients can bleed to death. If the patient is unstable, consider heroic measures such as military antishock trousers and external fixator.
2. For any fracture, always do a neurologic and vascular exam distal to the fracture site to see if there is any neurologic or vascular compromise. Either may be an emergency.
3. For any fracture, get two x-ray views (usually anteroposterior and lateral) of the site, and consider x-rays of the joint above and below the fracture site.
4. **Open fracture** (compound fracture): skin is broken over the fracture site. **Closed fracture:** skin is intact over the fracture site.
5. For open fractures (lacerated skin), give antibiotics (cefazolin or cefazolin/gentamicin if the laceration is large or contaminated), do surgical debridement, give tetanus vaccine, lavage fresh wounds (< 8 hours old), and do an open reduction and internal fixation. The main complication in open fractures is infection.

Compartment syndrome: usually occurs after fracture, crush injury, burn, or other trauma or as a reperfusion injury (e.g., after revascularization procedure). The most common site is the calf. Symptoms and signs include pain on passive movement (out of proportion to injury), paresthesias, cyanosis or pallor, firm-feeling muscle compartment, hypesthesia or numbness (decreased sensation and two-point discrimination), paralysis (late, ominous sign), and elevated compartment pressure (> 30–40 mmHg). The diagnosis usually is made clinically without a need to measure pressure. Compartment syndrome is an *emergency*, and quick action can save an otherwise doomed limb. Pulses are *usually palpable* or detectable with Doppler ultrasound. Treatment is an immediate fasciotomy; incising the fascial compartment relieves the pressure. Untreated, the condition progresses to permanent nerve damage and muscle necrosis. The classic clinical scenarios associated with compartment syndrome are supracondylar elbow fractures in children, proximal/midshaft tibial fractures, electrical burns, arterial or venous disruption, and revascularization procedures.

Open vs. closed reduction:

1. Reasons to do open reduction
   - Intraarticular fractures or articular surface malalignment
   - Open (compound) fractures
   - Nonunion or failed closed reduction

- Compromise of blood supply
- Multiple trauma (to allow mobilization at earliest possible point)
- Extremity function requiring perfect reduction (e.g., professional athlete)

2. Closed reduction should be done for all other fractures.

NERVE	MOTOR	SENSORY	WHEN CLINICALLY DAMAGED
Radial	Wrist extension	Back of forearm, back of hand (first 3 digits)	Humeral fracture (wrist drop)
Ulnar	Finger abduction	Front and back of last 2 fingers on hand	Elbow dislocation (claw hand)
Median	Pronation, thumb opposition	Palmar surface of hand (first 3 digits)	Carpal tunnel, humeral fracture
Axillary	Abduction/lateral rotation	Lateral shoulder	Upper humeral dislocation/fracture
Peroneal	Dorsiflexion/eversion	Dorsal foot and lateral leg	Knee dislocation (footdrop)

Important points:

1. To test for anterior cruciate ligament (ACL) integrity, do the anterior drawer test. The knee is placed in 90° of flexion and pulled forward (like opening a drawer). If the tibia pulls forward, the test is positive, and the patient has an ACL tear.
2. Pain in the anatomic snuff-box after trauma (fall on an outstretched hand, especially in young adults) usually is due to a scaphoid bone fracture.
3. After falling on an outstretched hand, the most likely fracture in older adults is a Colles' fracture (distal end of radius).

Lumbar disc herniation: common correctable cause of low back pain

- The most common site is the L5–S1 disc. Herniation affects the S1 nerve root. Look for decreased ankle jerk, weakness of plantarflexors in foot, pain from midgluteal area to the posterior calf, and sciatica with the straight-leg raise test.
- The second most common site is L4–L5. Herniation affects the L5 nerve root. Look for decreased biceps femoris reflex, weakness of foot extensors, and pain in the hip or groin.
- Diagnosis is made by CT/MRI or myelogram.
- Conservative treatment consists of bed rest and analgesics. Surgery (discectomy) is an option if conservative treatment fails.
- Cervical disc disease (classic symptom = neck pain) is less common than lumbar disease. The C6–C7 disc is the most common site. Herniation affects the C7 nerve root. Look for decreased triceps reflex/strength and weakness of forearm extension.

Charcot joints and neuropathic joints are seen most commonly in diabetes mellitus and other conditions causing peripheral neuropathy (e.g., tertiary syphilis). Lack of proprioception causes gradual arthritis and arthropathy and joint deformity. Do x-rays for any (even minor) trauma in neuropathic patients, who may not feel even a severe fracture.

The most common cause of **osteomyelitis** is *Staphylococcus aureus*, but think of gram-negative organisms in immunocompromised patients and IV drug abusers, and *Salmonella* sp. in sickle cell disease. Aspirate the joint and do Gram stain, cultures and sensitivities, blood cultures and complete blood cell count with differential if you are suspicious.

Septic arthritis also is most commonly due to *S. aureus*, but in a sexually active adult (especially if promiscuous), suspect gonococci. Aspirate the joint and do Gram stain, culture and sensitivities, blood cultures and complete blood cell count with differential if you are suspicious.

Important points:

1. With a true posterior knee dislocation, get an angiogram
2. The most common type of bone tumor is metastatic (from the breast, lung, or prostate).
3. The most common cause of a pathologic fracture is osteoporosis (especially in elderly, thin women).
4. A hip dislocation, fracture, or inflammation can refer pain to the knee (classic in children).

Pediatric hip problems

NAME	AGE	EPIDEMIOLOGY	SYMPTOMS/SIGNS	TREATMENT
CHD	At birth	Female, first-born, breech delivery	Barlow's, Ortolani's signs	Harness
LCP disease	4–10 yr	Male, short with delayed bone age	Knee, thigh, and groin pain, limp	Orthoses
SCFE	9–13 yr	Overweight, male, adolescent	Knee, thigh, and groin pain, limp	Surgical pinning

CHD = congenital hip dysplasia, LCP = Legg-Calvé-Perthes disease, SCFE = slipped capital femoral epiphysis.

Note: All three of the above pediatric hip problems may present in an adult as arthritis of the hip. Given the correct history (especially age of onset of symptoms!), you should be able to tell which disorder they had. X-rays may be taken, but history gives it away.

Osgood-Schlatter disease is osteochondritis of the tibial tubercle. It is often bilateral and usually presents in males 10–15 years old with pain, swelling, and tenderness in the knee. Pediatric hip problems (see above) give referred pain to the knee, but the patient has no knee swelling or pain with palpation of the knee. Treat with rest, activity restriction, and NSAIDs. The disease usually resolves on its own.

Scoliosis usually affects prepubertal females and is idiopathic. Treat with a brace unless the deformity is severe (with rapidly progressive respiratory compromise); then consider surgery. Ask the patient to touch her toes, and look at the spine. With scoliosis, a lateral curvature is seen.

CHAPTER 23

Neurosurgery

Whenever **intracranial hemorrhage** is suspected, order a CT without contrast. Blood shows up as white and may cause a midline shift.

1. **Subdural hematoma:** due to bleeding from veins that bridge the cortex and dural sinuses; **crescent-shaped**; common in alcoholics and after head trauma. Patients may present immediately after trauma or up to 1–2 months later. If the question includes a history of head trauma, always consider the diagnosis of a subdural hematoma. Treat with surgical evacuation.
2. **Epidural hematoma:** due to bleeding from meningeal arteries (classically, the middle meningeal artery); **lenticular-shaped**; almost always associated with a skull fracture (classically, fracture of the temporal bone; see below). More than 50% of patients have an ipsilateral "blown" pupil (see below). The classic history is a head trauma with loss of consciousness, followed by a lucid interval of minutes to hours, then neurologic deterioration. Treat with surgical evacuation.
3. **Subarachnoid hemorrhage:** due to blood between the arachnoid and pia mater. The most common cause is trauma, followed by ruptured berry aneurysms. Blood is seen in ventricles and around (but not in) the brain/brainstem. Patients classically present with the "worst headache of my life," although many die before they reach the hospital or may be unconscious. Awake patients have signs of meningitis (positive Kernig's and Brudzinski's signs). Remember the association between polycystic kidney disease and berry aneurysms. Although CT is the test of choice, a lumbar tap shows **grossly bloody cerebrospinal fluid**. Treat with support, anticonvulsants, and observation. Once the patient is stable, do a cerebral angiogram/MR angiogram to look for aneurysms and arteriovenous malformations, which are treated with surgical clipping.
4. **Intracerebral hemorrhage:** results from bleeding into the brain parenchyma. The most common cause is **hypertension**; other causes include arteriovenous malformations, coagulopathies, tumor, and trauma. Two-thirds occur in the basal ganglia. Patients often presents with coma, if awake, they have contralateral hemiplegia and hemisensory deficits. Blood (white) is seen in brain parenchyma and perhaps in the ventricles. Surgery is reserved for large bleeds that are accessible.

After a history of trauma, a **dilated, unreactive ("blown") pupil on only one side** most likely represents impingement of the ipsilateral third cranial nerve and impending uncal herniation due to increased intracranial pressure. Of the different intracranial bleeds, this is most commonly seen with epidural hematomas. Do *not* do a lumbar tap on any patient with a "blown" pupil; you may precipitate uncal herniation and death. First do a CT/MRI.

Basilar skull fracture has four classic signs:

1. Raccoon eyes: periorbital ecchymosis
2. Battle's sign: postauricular ecchymosis
3. Hemotympanum: blood behind the eardrum
4. Cerebrospinal fluid otorrhea/rhinorrhea: clear fluid from the ears or nose

Important points:

1. Skull fractures of the calvarium are seen on CT scan (preferred) or x-ray, generally as a depressed fracture. *Surgical indications* are *contamination* (cleaning and debridement), impingement on brain parenchyma, or open fracture with cerebrospinal fluid leak. Otherwise, fractures may be observed and generally heal on their own.
2. Head trauma also may cause cerebral contusion or shear injury of the brain parenchyma. Neither may show up on a CT scan, but both may cause temporary or permanent neurologic deficits.

Increased intracranial pressure (intracranial hypertension): normal intracranial pressure is 5–15 mmHg). An increase is suggested by bilaterally dilated and fixed pupils. Other symptoms include headache, papilledema, nausea and vomiting, and mental status changes. Look also for the classic and important Cushing's triad (increasing blood pressure, bradycardia, respiratory irregularity). The first step is to put the patient in reverse Trendelenburg (head up) and intubate. Once intubated, the patient should be hyperventilated to rapidly lower the intracranial pressure. This approach decreases intracranial blood volume by causing cerebral vasoconstriction. If the decrease in pressure is not sufficient, mannitol diuresis can be tried to lessen cerebral edema. Furosemide is also used but less effective. Barbiturate coma and decompressive craniotomy (burr holes) are last-ditch measures. Prophylactic anticonvulsants are controversial.

- Cerebral perfusion pressure equals blood pressure minus intracranial pressure. In other words, do *not* treat hypertension initially in a patient with increased intracranial pressure; hypertension is the body's way of trying to increase cerebral perfusion.
- *Never* do a lumbar tap on any patient with signs of increased intracranial pressure until a CT scan is done first. If the CT is negative, you can proceed to a tap, if needed.

Spinal cord trauma: often presents with spinal shock (loss of reflexes, loss of motor function, and hypotension). Get standard trauma x-rays (cervical spine, thorax, pelvis) as well as additional spine x-rays based on physical exam. Also give steroids (proved to improve outcome). Surgery is done for incomplete neurologic injury (some residual function is maintained) with external compression (e.g., subluxation, bone chip).

Spinal cord compression: subacute compression (vs. acute compression in trauma) is often due to metastatic cancer but also may be due to a primary neoplasm or subdural or epidural abscess or hematoma (especially after lumbar tap or epidural/spinal anesthesia in a patient with a bleeding disorder or on anticoagulation). Patients present with local spinal pain (especially with bone metastases) and neurologic deficits below the lesion (hyperreflexia, positive Babinski's, weakness, sensory loss). The first steps in the emergency department are to give high-dose corticosteroids and get a CT/MRI. Then give radiotherapy to metastases from a known primary that is radiosensitive. Alternatively, surgical decompression may be done.

- Prognosis is most closely related to pretreatment function; the longer you wait to treat, the worse the prognosis.
- For hematoma or subdural/epidural abscess (seen especially in diabetics and usually due to *Staphylococcus aureus*), surgery is indicated for decompression and drainage.

Syringomyelia: central pathologic cavitation of the spinal cord, usually in the cervical or upper thoracic region. Syringomyelia is idiopathic but may follow trauma or congenital cranial base malformations (e.g., Arnold-Chiari or Dandy-Walker syndrome). The classic presentation is a bilateral loss of pain and temperature sensation below the lesion in the distribution of a "cape" due to involvement of the lateral spinothalamic tracts. The cavitation in the cord gradually widens to involve other tracts, causing motor and sensory deficits. MRI is the imaging study of choice, and treatment is surgical (creation of a shunt).

Neural tube defects: triangular patch of hair over the lumbar spine indicates spina bifida occulta. More serious defects are obvious and occur most commonly in the lumbosacral region. Meningocele is defined as meninges outside the spinal canal; myelomenigocele, as central nervous system tissue plus meninges outside the spinal canal. Most importantly, giving folate to potential mothers reduces the incidence of neural tube defects.

Hydrocephalus: in children, look for increasing head circumference, increased intracranial pressure, bulging fontanelle, scalp vein engorgement, and paralysis of upward gaze. The most common causes include congenital malformations, tumors, and inflammation (hemorrhage, meningitis). Treat the underlying cause, if possible; otherwise, a surgical shunt is created to decompress the ventricles.

CHAPTER 24

Ear, Nose, and Throat Surgery

Bell's palsy: most common cause of facial paralysis; sudden unilateral onset, usually after an upper respiratory infection. The cause is unknown but may be viral, immune, or ischemic. Patients may have hyperacusis; everything sounds loud because the stapedius muscle in the ear is paralyzed. In severe cases, patients may be unable to close the affected eye; use drops to protect the eye. Most cases resolve spontaneously in about 1 month, although some have permanent sequelae.

Other causes of unilateral facial paralysis:

- Herpes (Ramsay Hunt syndrome): eighth cranial nerve is commonly involved also. Look for vesicles on pinna and inside ear, encephalitis and meningitis may be present.
- Lyme disease: probably the most common cause of bilateral facial nerve palsy.
- Middle ear and mastoid infections
- Meningitis
- Fracture (temporal bone): patients may have Battle's sign and/or bleeding from the ear.
- Tumor: especially in the cerebellopontine angle (acoustic neuroma; consider neurofibromatosis) or glomus jugulare.

Note: Get CT/MRI scans of the head to evaluate if the cause is not apparent or seems suspicious (especially if additional neurologic signs are present) after history and/or physical exam.

Hearing loss: the most common cause is aging (presbycusis); a hearing aid can be used, if needed. History may suggest other causes:

- Exposure to prolonged or intense loud noise
- Congenital TORCH infection
- Ménière's disease: accompanied by severe vertigo, tinnitus, nausea and vomiting; treated with anticholinergics, antihistamines (meclizine), or surgery (if refractory)
- Drugs (aminoglycosides, aspirin, quinine, loop diuretics, cisplatin)
- Tumor (usually acoustic neuroma).
- Labyrinthitis: may be viral or follow/extend from meningitis or otitis media
- Diabetes mellitus
- Hypothyroidism
- Multiple sclerosis
- Sarcoidosis
- Pseudotumor cerebri

Sudden deafness: develops over a few hours; most often due to a viral cause (endolymphatic labyrinthitis from mumps, measles, influenza, chickenpox, adenovirus). Hearing usually returns within 2 weeks, but loss may be permanent. No treatment has proved effective; empiric steroids often are used.

Note: Bacterial meningitis is the most common cause of acquired hearing loss in children. Follow all children with hearing testing after a bout of meningitis.

Vertigo: may be due to the same eighth cranial nerve lesions that cause hearing loss (Menière's disease, tumor, infection, multiple sclerosis). Another common cause is benign positional/paroxysmal vertigo, which is induced by certain head positions and may be accompanied by nystagmus without associated hearing loss. The condition often resolves spontaneously; treatment is not necessary.

Note: Deviated nasal septum or other congenital defects may cause recurrent sinusitis. Treat with surgical correction.

Causes of rhinitis (edematous, vasodilated nasal mucosa and turbinates with clear nasal discharge):

1. Viral (common cold): from rhinovirus (most common), influenza, parainfluenza, coxsackie virus, adenovirus, respiratory syncytial virus, coronavirus, echovirus. Treatment is symptomatic; vasoconstrictors such a phenylephrine are used for short-term treatment but may cause rebound congestion.
2. Allergic (hay fever): associated with seasonal flare-ups, boggy and bluish turbinates, early onset (< 20 years old), nasal polyps, sneezing, pruritis, conjunctivitis, wheezing, asthma, eczema, positive family history, eosinophils in nasal mucus, and elevated IgE. Skin tests may identify an allergen. Treat with avoidance when the antigen (e.g., pollen) is known, antihistamines, cromolyn, and/or steroids for severe symptoms. Desensitization is also an option.
3. Bacterial infection: from *Streptococcus* A, *Pneumococcus*, or *Staphylococcus* spp. Do streptococcal throat culture, and treat with antibiotics if appropriate (sore throat, fever, tonsillar exudate).

The most common cause of **nosebleed** in children is nose-picking (trauma), but watch out for local tumor, leukemia, and other causes of thrombocytopenia (idiopathic thrombocytopenic purpura, hemolytic uremic syndrome). Nasopharyngeal angiofibroma should be suspected in adolescent males with recurrent nosebleeds and/or obstruction but no history of trauma or blood dyscrasias. Leukemia may result in pancytopenia; look for associated fever and anemia.

Neck mass:

1. 75% are benign in children, and 75% are malignant in patients > 40 years old.
2. Causes:
   - Branchial cleft cysts: lateral; often become infected.
   - Thyroglossal duct cysts: midline; elevate with tongue protrusion.
   - Cystic hygroma: lymphangioma; treat with surgical resection.
   - Cervical lymphadenitis: from streptococcal pharyngitis, Epstein-Barr virus (common in adolescents and adults in 20s), cat-scratch disease, *Mycobacterium* sp. (scrofula).
   - Neoplasm: may be lymphadenopathy due to primary (lymphoma) or metastatic neoplasm, or the mass may be the tumor itself.

3. Work-up of unknown cancer in the neck includes *random* biopsy of the nasopharynx, palatine tonsils, and base of the tongue as well as laryngoscopy, bronchoscopy, and esophagoscopy (with biopsies of any suspicious lesions)—the so-called triple endoscopy with triple biopsy.

Otitis externa (swimmer's ear): most commonly due to *Pseudomonas aeruginosa*. Manipulation of the auricle produces pain; the skin of the auditory canal is erythematous and swollen. Patients may have foul-smelling discharge and conductive hearing loss. Treat with topical antibiotics (neomycin, polymyxin B); steroids may reduce swelling.

Otitis media: most commonly due to *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis*. Manipulation of the auricle produces no pain. Patients have earache, fever, erythematous and bulging tympanic membrane (light reflex and landmarks are difficult to see), and nausea and vomiting. Complications include tympanic membrane perforation (bloody or purulent discharge), mastoiditis (fluctuation and inflammation over mastoid process 2 weeks after otitis), labyrinthitis, palsies of cranial nerves VII and VIII, meningitis, cerebral abscess, lateral sinus thrombosis, and chronic otitis media (permanent perforation of tympanic membrane). Patients may get cholesteatomas with marginal perforations; treat with surgical excision. Treat otitis with antibiotics to avoid these complications (amoxicillin, second-generation cephalosporins such as cefuroxime or trimethoprim-sulfamethoxazole).

- Recurrent otitis media is a common pediatric clinical problem (as well as prolonged secretory otitis, a result of incompletely resolved otitis) and can cause hearing loss with resultant developmental problems (speech, cognitive functions). Treatment consists of prophylactic antibiotics or tympanostomy tubes. Adenoidectomy is thought to help in some cases by preventing blockage of the eustachian tubes.
- Infectious myringitis (tympanic membrane inflammation) is caused by *Mycoplasma* sp., *Streptococcus pneumoniae*, or viruses. Otoscopy reveals vesicles on the tympanic membrane. Treat as otitis media (with antibiotics).

Sinusitis: often due to *S. pneumoniae*, *H. influenzae*, and other streptococci or staphylococci. Look for tenderness over affected sinus, headache, and purulent nasal discharge (yellow or green). X-ray shows opacification of the sinus; CT is used to evaluate chronic sinusitis or suspected extension of infection outside the sinus (suggested by high fever and chills). Treat with antibiotics (penicillin/amoxicillin or erythromycin for 2 weeks, up to 6 weeks for chronic cases). Operative intervention for resistant cases (drainage procedure, sinus obliteration). Remember that the frontal sinuses are not well developed until after the age of 10 years.

Otosclerosis: the most common cause of progressive conductive hearing loss in adults (vs. presbyacusis, the most common cause of sensorineural hearing loss in adults). Otic bones become fixed together and impede hearing. Treat with hearing aid or surgery.

Parotid swelling: the most common cause is mumps. The best treatment for mumps and the complication of infertility is prevention through immunization. Parotid swelling also may be due to neoplasm (pleomorphic adenoma is the most common), Sjögren's syndrome, sialolithiasis (more common in the submandibular gland), and sarcoidosis.

Note: After nasal fracture (which you should be able to recognize on x-ray), rule out a septal hematoma, which must be removed to prevent pressure-induced septal necrosis.

CHAPTER 25

Vascular Surgery

Carotid stenosis: the classic presentation is a transient ischemic attack (TIA), especially amaurosis fugax, which is characterized by sudden-onset and transient unilateral blindness, sometimes described as a "shade pulled over one eye." Patients may have a carotid bruit. If a bruit is heard or the patient has a TIA, ultrasound of the carotid arteries should be done to determine the degree of stenosis.

- If stenosis is greater than 70% and the patient has had a TIA/amaurosis fugax or a small, nondisabling stroke, carotid endarterectomy (CEA) should be performed. Patients should not undergo CEA after a stroke that leaves them severely disabled, nor should they undergo CEA during a TIA or stroke in evolution. CEA is an elective, not emergent, procedure.
- If stenosis is less than 70%, whether the patient has symptoms or not, do not do CEA. Treat with daily aspirin instead.
- If the patient has greater than 70% stenosis, with or without symptoms, CEA provides the best long-term prognosis. If the patient is asymptomatic, you have to weigh the risk-benefit ratio more carefully.
- Carotid stenosis is a generalized marker for atherosclerosis. Virtually all patients have significant coronary artery disease; perioperative myocardial infarction is the most common cause of death in patients undergoing vascular surgery. Make sure to evaluate risk factors for atherosclerosis (cholesterol, hypertension, smoking, diabetes mellitus).

Abdominal aortic aneurysm (AAA): look for a pulsatile abdominal mass that may cause abdominal pain. If pain is present, suspect possible rupture of AAA, although even an unruptured AAA may cause some pain. CT scan usually is used for initial evaluation. If the AAA is smaller than 5 cm, follow it with serial ultrasound to make sure that it is not enlarging. If the AAA is larger than 5 cm (or you are told that it is rapidly enlarging), surgical correction should be done.

- A pulsatile abdominal mass plus hypotension = emergent laparotomy (means ruptured AAA, which has a mortality rate of roughly 90%).
- A dissecting AAA, if not ruptured, can be treated conservatively with antihypertensive medications, although an elective repair should be considered if the patient is in good health.

Leriche's syndrome: claudication in the buttocks, buttock atrophy and impotence in men; a classic marker for aortoiliac occlusive disease. Patients usually need an aortoiliac bypass graft.

Claudication: pain the the lower extremity (usually) brought on by exercise and relieved by rest. Claudication is an indicator of severe atherosclerotic disease. Associated physical findings

include cyanosis (with dependent rubor), atrophic changes (thickened nails, loss of hair, shiny skin), decreased temperature, and decreased (or absent) distal pulses. The best treatment is conservative: cessation of smoking, exercise, and control cholesterol, diabetes mellitus, and hypertension. Beta blockers may worsen claudication (due to beta-2 receptor blockade) and should be avoided.

- If the patient progresses to rest pain in the forefoot, which generally occurs at night and is relieved by hanging the foot over the edge of the bed, or cannot continue current lifestyle or work obligations, consider revascularization procedure.
- Severe pain in the foot that has a sudden onset without previous history, trauma, or any associated chronic physical findings is generally more serious, and may represent an embolus (look for atrial fibrillation) or compartment syndrome (commonly occurs after revascularization procedures).
- Claudication and peripheral vascular disease are generalized markers for atherosclerosis. Check patients for other atherosclerosis risk factors.

Mesenteric ischemia: the classic patient has a long history of postprandial abdominal pain, which causes a fear of food and thus leads to extensive weight loss. This diagnosis is difficult because, like all atherosclerotic disease, it presents in patients over 40, who may have other disorders that cause the problem (e.g., peptic ulcer disease, pancreatic cancer, stomach cancer). Look for a history of extensive atherosclerosis (previous myocardial infarctions, cerebrovascular accidents, known coronary artery disease, or peripheral vascular disease with several risk factors), possible abdominal bruit, and a lack of jaundice (which would steer you toward pancreatic cancer). Usually CT scan of the abdomen is negative and should make you more suspicious of ischemia. Patients should be treated surgically with revascularization because of the risks of bowel infarction and malnutrition.

Note: After a penetrating trauma in an extremity (or iatrogenic catheter damage), an arteriovenous fistula may result. Look for bruits over the area or a palpable pulsatile mass (aneurysm). Such fistulas can be left alone if they are small; otherwise, surgical correction is needed.

Venous insufficiency: generally refers to the lower extremities. Patients may have a history of deep vein thrombosis; swelling in the extremity with pain, fatigability, and heaviness, which are relieved by elevating the extremity; and/or varicose veins. Skin pigmentation may increase around the ankles with possible skin breakdown and ulceration. Initial treatment is conservative: elastic compression stockings, elevation with minimal standing, and treatment of any ulcers with cleaning, wet-to-dry dressings, and antibiotics (if cellulitis is present). Patients with varicose veins, localized leg pain with cord-like induration, reddish discoloration, and mild fever have superficial thrombophlebitis (not deep vein thrombosis), which rarely leads to pulmonary embolism. Patients do not need anticoagulation. Treatment is often thrombectomy under local anesthesia; medical treatment (NSAIDs) is used if pain is mild or the patient does not want surgery. Pain generally subsides in a few days on its own.

Subclavian steal syndrome: usually due to left subclavian artery obstruction proximal to the vertebral artery. To get blood to an exercising arm, blood is "stolen" from the vertebrobasilar system; it flows backward into the distal subclavian artery instead of forward into the brainstem. As a result, the patient develops *central nervous system symptoms* (syncope, vertigo, confusion, ataxia, dysarthria) and *upper extremity claudication*. Treat with surgical bypass.

Cervical rib: may compromise subclavian vessel blood flow. Patients may develop upper extremity paresthesias, weakness, and cold temperature (arterial compromise) or edema/venous distention (venous compromise) *without* CNS symptoms. Treat with rib resection.

CHAPTER 26

Urology

Testicular torsion vs. epididymitis

	TESTICULAR TORSION	EPIDIDYMITIS
Age (yr)	< 30 (usually prepubertal)	> 30
Appearance	Testes may be elevated into the inguinal canal; swelling	Swollen testis, overlying erythema, positive urinalysis, urethral discharge, urethritis, prostatitis
Prehn's sign	Pain stays the same or worsens with testicular elevation	Pain decreases with testicular elevation
Treatment	Immediate surgery to salvage testis; orchiopexy of both testes	Antibiotics*

* In men < 50, epididymitis is commonly due to a sexually transmitted disease (chlamydial infection, gonorrhea); treat accordingly. In men > 50, it is commonly due to urinary tract infection bugs; treat with trimethoprim-sulfamethoxazole or ciprofloxacin.

Testicular cancer: usually presents as a painless mass in a young man (age 20–40). The main risk factor is cryptorchidism. Roughly 90% are germ cell tumors, the most common being seminoma. Treatment generally consists of orchiectomy and radiation. If disease is widespread, use chemotherapy. Alpha-fetoprotein is a tumor marker for yolk sac tumors, whereas human chorionic gonadotropin is a marker for choriocarcinoma. Leydig cell tumors may secrete androgens and cause precocious puberty.

Note: Remember mumps as a cause of orchitis (painful, swollen testis, usually unilateral, in a postpubertal male). The best treatment is prophylactic (immunization). Mumps almost never causes sterility because it is usually unilateral.

Benign prostatic hypertrophy (BPH):

1. Symptoms: urinary hesitancy, intermittency, terminal dribbling, decreased size and force of stream, sensation of incomplete emptying, nocturia, urgency, dysuria, frequency.
2. BPH may result in urinary retention, urinary tract infections, hydronephrosis, and even kidney damage or failure in severe cases.
3. Drug therapy is started when the patient becomes symptomatic. Options include alpha-one blockade (prazosin, terazosin, doxazosin) and antiandrogens (gonadotropin-releasing hormone analogs, flutamide, finasteride).
4. Transurethral resection of the prostate (TURP) is used for more advanced cases, especially with repeated urinary tract infections, urinary retention, and hydronephrosis or kidney damage due to reflux. Prostatectomy also may be used but is a more complicated operation.

Note: With acute urinary retention (pain, palpation of full bladder on abdominal exam, history of BPH, no urination in past 24 hours), the first step is to empty the bladder. If you cannot pass a regular Foley catheter, do a suprapubic tap. Then address the underlying cause.

Impotence: most commonly caused by vascular problems. Medications are also a common culprit (especially antihypertensives and antidepressants). Diabetes mellitus may be a vascular (increased atherosclerosis) or neurogenic cause of impotence. Remember **p**oint and **s**hoot: **p**arasympathetics mediate erection, **s**ympathetics mediate ejaculation. Patients undergoing dialysis also are commonly impotent. The history often gives you a clue if the cause of impotence is psychogenic. Look for a normal pattern of nocturnal erections, selective dysfunction (a patient who has normal erections when masturbating but not with his wife), and stress, anxiety, or fear.

In **patients with trauma**, look for signs of urethral injury (high-riding, ballottable prostate, blood at the urethral meatus, severe pelvic fracture, ecchymosis) before trying to pass a Foley catheter. If any of these signs are present, do not try to pass a Foley catheter until you have gotten a retrograde urethrogram to rule out urethral injury. Urethral injury is a contraindication to a Foley catheter.

Hydrocele vs. varicocele: hydrocele represents a remnant of the processus vaginalis (remember embryology?) and transilluminates. It generally causes no symptoms and does not require treatment. A varicocele is a dilatation of the pampiniform venous plexus ("bag of worms," usually on the left), does not transilluminate, disappears in the supine position, and may be a cause of male infertility or pain (in which case it is surgically treated).

Nephrolithiasis:

1. Signs and symptoms include severe flank pain, which often radiates to the groin and is colicky in nature; hematuria; and stone on abdominal x-ray (90% of stones radiopaque).
2. 75% of stones are calcium (look for hypercalcemia and hyperparathyroidism; small bowel bypass also increases oxalate absorption and thus calcium stone formation), 15% are struvite/magnesium-ammonium-phosphate stones (think of infection), 7% are uric acid stones (look for history of gout or leukemia), and 2% are cystine stones (think of cystinuria).
3. Treat stones with lots of hydration, narcotics for pain, and observation. Most stones pass by themselves. If not, do lithotripsy, uteroscopy with stone retrieval, or open surgery (if needed).

Cryptorchidism: arrest of descent of the testicle(s) somewhere between the renal area and the scrotum. The more premature the infant, the greater the likelihood of cryptorchidism. Many arrested testes eventually descend on their own within the first year. After 1 year, surgical intervention (orchiopexy) is warranted to attempt to preserve fertility as well as facilitate future testicular exams (because of increased cancer risk). Cryptorchidism is a major risk factor for testicular cancer (40-fold increased risk), and bringing the testis into the scrotum does not alter the increased risk for testicular cancer. The higher the testicle is found (the further away from the scrotum), the higher the risk of developing testicular cancer and the lower the likelihood of retaining fertility.

Note: The right testicular/ovarian vein drains into the inferior vena cava, whereas the left ovarian/testicular vein drains into the left renal vein.

Renal transplant: an option for patients with end-stage renal disease, unless they have active infections or other life-threatening conditions (e.g., AIDS, malignancy). Lupus and diabetes

mellitus are not contraindications to transplant. Living, related donors are best (siblings or parents), especially when HLA-similar, but cadaveric kidneys are more common because of availability. Before the transplant, perform ABO and lymphocytotoxic (HLA) cross-matching.

- A transplanted kidney is placed in the iliac fossa (for easy biopsy access in case of problems as well as for technical reasons); usually the recipient's kidneys are left in place to reduce morbidity.
- Unacceptable kidney donors: newborns, age over 60, history of generalized or intraabdominal sepsis, history of disease with possible renal involvement (e.g., diabetes mellitus, hypertension, lupus), and history of malignancy.

Rejection:

1. Hyperacute rejection: preformed cytotoxic antibodies against donor kidney (happens with ABO mismatch as well as other preformed antibodies). Classic picture: surgery is complete, vascular clamps are released, and the kidney quickly turns bluish-black. Treat by removing the kidney.
2. Acute rejection: T-cell–mediated rejection that presents during first several months with fever, oliguria, weight gain, tenderness and enlargement of the graft, hypertension, and/or renal function lab derangement. Treat by increasing steroids or using antithymocyte globulin or other immunosuppressants.
3. Chronic rejection: T-cell– or antibody–mediated. Late cause of renal deterioration presenting with gradual decline in kidney function, proteinuria, and hypertension. Treatment is supportive and not effective, but the graft may last several years before it gives out completely. The patient may be retransplanted with a new kidney.
4. Follow creatinine to assess asymptomatic rejection (more reliable than blood urea nitrogen).
5. Immunosuppressive medications: steroids (inhibit interleukin-1 production), cyclosporine (inhibits interleukin-2 production), azathioprine (antineoplastic that is cleaved into mercaptopurine and inhibits DNA/RNA synthesis, which decreases B-cell and T-cell production), antithymocyte globulin (antibody against T-cells), and OKT3 (antibody to CD3 receptor on T-cells).
6. Cyclosporine causes nephrotoxicity, which can be difficult to distinguish from graft rejection clinically. When in doubt, a percutaneous needle biopsy of the graft should be done if the patient is taking cyclosporine, because the two usually can be distinguished histologically. Renal ultrasound also helps to distinguish between the two. Practically speaking, if you increase the immunosuppressive dose, acute rejection should decrease, whereas cyclosporine toxicity stays the same or worsens.
7. Immunosuppression carries the risk of infection (with common as well as the strange bugs that infect patients with AIDS) and increased risk of cancer (especially lymphomas and epithelial cell cancer).

Penile anomalies: hypospadias occurs when the urethra opens on the dorsal side of the penis; epispadias, when the urethra opens on the ventral side of the penis (also associated with extrophy of the bladder). Treat both surgically.

Potter's syndrome: bilateral renal agenesis causes oligohydramnios in utero (the fetus swallows fluid but cannot excrete it), limb deformities, abnormal facies, and hypoplasia of the lungs. It is generally incompatible with life.

CHAPTER 27

Emergency Medicine

Burns may be thermal, chemical, or electrical. Initial management of all burns includes *lots of IV fluids* (use lactated Ringer's solution or normal saline if Ringer's solution is not a choice), removal of all clothes and other smoldering items on the body, copious irrigation of chemical burns, and, of course, the ABCs (airways, breathing, circulation). You should have a very low threshold for intubation; use 100% oxygen until significant carboxyhemoglobin from carbon monoxide inhalation is ruled out.

- Electrical burns: most of the destruction is internal and may lead to myoglobinuria, acidosis, and renal failure. Use *lots* of IV fluids to prevent such complications. The immediate, life-threatening risk with electricity exposure or burns (including lightning and putting the finger in an electrical outlet) is cardiac arrhythmias. Get an EKG.
- Chemical burns: alkali burns are worse than acidic burns, because alkali penetrates more deeply. Treat all chemical burns with copious irrigation from the nearest source (e.g., tap water).

Burned skin is much more prone to infection, usually by *Staphylococcus aureus* or *Pseudomonas* sp. (with *Pseudomonas* sp., look for a fruity smell and/or blue-green color). Prophylactic antibiotics are given topically only. Give tetanus booster to all burn patients unless they received it recently (within the past 5 years). Severity classification:

1. First-degree burns involve epidermis only (painful, dry, red areas with *no* blisters). Keep clean.
2. Second-degree burns involve epidermis and some dermis (painful and swollen, with blisters and open weeping surfaces). Remove blisters; apply antibiotic ointment (e.g., silver nitrate, silver sulfadiazine, neomycin) and dressing.
3. Third-degree burns involve all layers of the skin, including nerve endings (*painless*, dry, and charred). Surgical excision of eschar and skin grafting are required. Watch for compartment syndrome; treat with escharotomy.

Hypothermia: body temperature < 95°F (35°C), usually accompanied by mental status changes and generalized neurologic deficits. If the patient is conscious, use slow rewarming with blankets. If the patient is unconscious, consider immersion in a tub of warm water. It is most important to monitor the EKG for arrhythmias, which are common with hypothermia. You also may see the classic J wave, a small, positive deflection following the QRS complex. Also monitor electrolytes, renal function, and acid-base status.

- With frostnip (cold, painful areas of skin, mild) and frostbite (cold, anesthetic areas of skin, more severe), treat with warming of affected areas using warm water (not scalding hot) and generalized warming (e.g., blankets).

- A patient is not considered dead until "warm and dead"; in other words, do not give up resuscitation efforts until the patient has been warmed.

Hyperthermia: may be due to heat stroke. Look for history of heat exposure and high temperature (>104° F). Treat with immediate cooling (wet blankets, ice, cold water). The immediate threats to life are convulsions (which should be treated with diazepam) and cardiovascular collapse. Rule out infection and other classic culprits:

1. Malignant hyperthermia: look for succinylcholine or halothane exposure. Treat with dantrolene.
2. Neuroleptic malignant syndrome: caused by taking an antipsychotic. First, stop the medication. Second, treat with support (especially lots of IV fluids to prevent renal shutdown from rhabdomyolysis) and dantrolene.
3. Drug fever: idiosyncratic reaction to a medication that usually was started within the past week.

Near-drowning: fresh water is worse than sea water, because fresh water, if aspirated, can cause hypervolemia, electrolyte disturbances, and hemolysis. Intubate such patients if they are unconscious and monitor arterial blood gases if they are conscious. Patients who drown in cold water often do better than those who drown in warm water because of decreased metabolic needs. Death usually results from hypoxia and/or cardiac arrest.

CHAPTER 28

Pediatrics

Milestones: there are a million of them, but concentrate on the common ones. The following table gives rough average ages when milestones are achieved.

MILESTONE	AGE*	MILESTONE	AGE*
While prone, lifts head up 90°	3–4 mo	First words	9–12 mo
Rolls front to back	4–5 mo	Imitates others' sounds	9–12 mo
Sits with no support	7 mo	Cooing	2–4 mo
Voluntary grasp (no release)	5 mo	Ties shoelaces	5 yr
Voluntary grasp with voluntary release	10 mo	Waves "bye-bye"	10 mo
Plays pat-a-cake	9–10 mo	Social smile	1–2 mo
Can build tower of 2 cubes	13–15 mo	Runs well	2 yr
Can build tower of 6 cubes	2 yr	Walks without help	13 mo
Good use of cup and spoon	15–18 mo	Pulls to stand	9 mo
Understands 1-step commands (no gesture)	15 mo	Stranger anxiety	6–9 mo
Separation anxiety	12–15 mo		

* Rough, average ages for milestones are given. The exact age is not as important as the overall pattern when you are looking for dysfunctional development. When in doubt, use a formal developmental test. The age of a premature infant is reduced in the first 2 yr when development is assessed. For example, subtract 3 months from the chronologic age of an infant born prematurely after 6 months' gestation; therefore, the infant is expected to perform at the 6-month-old interval at the age of 9 months.

Screening and preventive care: an important part of well-baby exams that also may provide an answer to a question about a child with a complaint. For example, the mother complains of a 4-year-old child who sleeps 11 hours every night (this is normal). The answer to the question, "What should you do next?" may be to get an objective hearing exam, which is a routine screening procedure in a 4-year-old child. Height, weight, blood pressure, developmental and behavioral assessment, history and physical exam, and anticipatory guidance (counseling and discussion about age-appropriate concerns) should be done at every visit. Remember the following:

1. Metabolic/congenital disorders: all states mandate screening for hypothyroidism and phenylketonuria at birth (within the first month). Most mandate screening for galactosemia and sickle cell disease. If any of the screens are positive, the first step is a confirmatory test to make sure that the screen gave you a true positive.
2. Anticipatory guidance: remember to tell parents the following:
   - Keep the water heater < 110–120°F.
   - Use car restraints.

- Put baby to sleep on the side or back to help prevent sudden infant death syndrome (most common cause of death in children aged 1–12 months).
- Do not use infant walkers (which cause injuries).
- Watch out for small objects (risk of aspiration).
- Do not give cow's milk before 1 year of age.
- Introduce solid foods gradually, starting at 6 months.
- Supervise children in a bathtub or swimming pool.

3. Height, weight and head circumference: head circumference should be measured routinely in the first 2 years, height and weight routinely until adulthood. All are markers of general well-being. The pattern of growth along plotted growth curves (which you need to know how to read) tells you more than any raw number. If a patient has always been low or high compared with peers, this pattern is generally benign. Parents commonly bring in a child with delayed physical growth or delayed puberty, and you must know when to reassure and follow up and when to do further testing and questioning. If a patient goes from a normal curve to an abnormal curve, this is a much more worrisome pattern.
   - Failure to thrive (< 5th percentile for age): most commonly due to psychosocial or functional problems. Watch for child abuse. Organic causes usually have specific clues to trigger your suspicion.
   - Obesity: usually due to overeating; < 5% of cases are due to organic causes (Cushing's or Prader-Willi syndrome).
   - Increased head circumference may mean hydrocephalus or tumor, whereas decreased head circumference may mean microcephaly (e.g., from congenital TORCH infection).
4. Hearing and vision: should be measured objectively once by or at 4 years old. Measure every few years until adulthood, more often if history dictates.
   - After a bout of meningitis, all children should be screened objectively for hearing loss (the most common neurologic complication of meningitis). Hearing screening is also important after congenital TORCH infections, measles and mumps, and chronic middle ear effusions and otitis media.
   - Check the red reflex at birth and routinely thereafter to detect congenital cataracts (usually due to congenital rubella, other TORCH infections, or galactosemia) or retinoblastoma (know what they look like on exam).
   - It is normal for children to have occasional ocular misalignment (strabismus) until 3 months; after that, it should be evaluated further to prevent possible blindness in the affected eye.
5. **Anemia:** routine screening (hemoglobin and hematocrit) is somewhat controversial; traditionally screening was done once in the first year (8–12 months), once between 4–6 years, and once during adolescence. If any risk factors for iron deficiency are present during infancy (prematurity, low birth weight, ingestion of cow's milk before 12 months, low dietary intake, low socioeconomic status), definitely screen the hemoglobin and hematocrit if given the option. Give all infants prophylactic iron supplements; start full-term infants at 4–6 months, preterm infants at 2 months.
6. **Lead:** initial screen at 12 months if risk is low, at 6 months if risk is high (residence in old building, paint chip eater, home near battery-recycling plant). If level is < 10, rescreen at 24 months if risk is low or at 12 months if risk is high. After 2 years old, screen annually only in high-risk patients. If level > 10, closer follow-up and intervention are needed. The best first course of action is to stop the exposure.

7. **Fluoride:** start supplementation in first few years of life if water is inadequately fluoridated (rare) or if the patient is fed exclusively from a premixed, ready-to-eat formula (nonfluoridated water is used in such products). Most children need no supplementation.
8. **Vitamin D:** some authorities still recommend that all breast-fed infants should receive vitamin D; most recommend it only for high-risk patients (inadequate maternal vitamin D intake, little sunlight exposure and/or dark skin, exclusively breast-fed beyond 6 months of age). Start supplements by 6 months. Formula-fed infants do not require vitamin D supplements, which the formula already contains.
9. **Tuberculosis:** screen for tuberculosis immediately if it is suggested by history or annually at any age if risk factors are present (HIV, incarceration). If the only risk factor is living in a high-risk area or immigrant parents, screen once at 4–6 years old and once at 11–16 years old. If no risk factors are present, do not screen.
10. **Urinalysis:** universal screening is not recommended. Do, however, screen for renal disease when a boy < 6 years old develops a urinary tract infection or a girl < 6 years old has repeated urinary tract infections. Get a voiding cystourethrogram and a renal ultrasound.
11. **Immunizations:** when to give normal immunizations is constantly being updated, so the administration schedule for common vaccines is usually given. Special patient populations (pneumococcal vaccine for patients with sickle cell disease or splenectomy) and vaccine contraindications (no measles, mumps, and rubella or influenza vaccine for egg-allergic patients, no live vaccines to pregnant women or immunocompromised patients) are high yield.
12. **Other:** give sexually active adolescents an annual Pap smear and screen for sexually transmitted diseases. The first dental referral should be made around 2–3 years old.

Tanner stages: Stage 1 is preadolescent, stage 5 is adult. Increasing stages are assigned for testicular and penile growth in males and breast growth in females; pubic hair development is used for both sexes. Average age of puberty (when the patient first shows changes from stage 1 status) is 11.5 years in males (the first event usually is testicular enlargement) and 10.5 years in females (the first event usually is breast development).

Delayed puberty: no testicular enlargement in males by age 14, no breast development or pubic hair in females by age 13. The usual cause is **constitutional delay**. Parents often have a similar history. In this normal variant, the growth curve lags behind others of same age but is consistent. Delayed puberty is rarely due to primary testicular failure (Klinefelter's syndrome, cryptorchidism, history of chemotherapy, gonadal dysgenesis) or ovarian failure (Turner's syndrome, gonadal dysgenesis). Other rare causes include hypothalamic/pituitary defects, such as Kallmann's syndrome or tumor.

Precocious puberty: usually idiopathic but may be due to McCune-Albright syndrome (in females), ovarian tumors (granulosa, theca cell, or gonadoblastoma), testicular tumors (Leydig cell), central nervous system disease or trauma, adrenal neoplasm, or congenital adrenal hyperplasia (males only; usually 21-OH deficiency). Most patients with an uncorrectable, idiopathic precocious puberty are given long-acting gonadotropin-releasing hormone agonists to suppress progression of puberty and thus prevent premature epiphyseal closure.

Cavernous hemangioma: first noticed a few days after birth. Lesions increase in size after birth and gradually resolve within first 2 years. The best treatment is to do nothing but observe and follow up.

Caput succedaneum: diffuse swelling or edema of the scalp that crosses the midline and is benign. Cephalhematomas are subperiosteal hemorrhages that are sharply limited by sutures and do not cross the midline. Cephalhematomas are usually benign and self-resolving but rarely may indicate an underlying skull fracture; get an x-ray to rule it out.

Large anterior fontanelle: may indicate hypothyroidism, hydrocephalus, rickets, or intrauterine growth retardation. It usually is closed by 18 months; delayed closure may be due to the same factors.

Important points:

1. Check the umbilical cord at birth for two arteries, one vein, and the absence of the urachus. If there is only one artery, consider the possibility of congenital renal malformations.
2. Female infants may have a milky-white (and possibly blood-tinged) vaginal discharge in the first week of life. This discharge is physiologic and due to maternal hormone withdrawal.

Child abuse: watch for failure to thrive; multiple fractures, bruises, or injuries in different stages of healing; shaken baby syndrome (subdural hematomas and retinal hemorrhages with no external trauma signs); behavioral, emotional, and interaction problems; sexually transmitted diseases; and multiple personality disorder (sexual abuse). Consider abuse whenever the injury does not fit the story. Reporting any suspicion is mandatory; you do not need proof and cannot be sued.

Note: Children have different normal laboratory and physiology values (normal values usually are given): lower blood pressure, higher heart and respiratory rates, and different hemoglobin and hematocrit values (higher at birth, lower throughout childhood). Renal, pulmonary, hepatic, and central nervous system still not fully mature and functional at birth.

APGAR score: commonly done at 1 and 5 minutes. *Do not wait until the 1-minute mark to* evaluate the newborn; you may have to suction or intubate the infant 3 seconds after delivery. The APGAR score includes five categories with a maximal score of 2 points per category and a total maximum of 10 points:

1. Heart rate: 0 = absent, 1 = < 100, 2 = > 100
2. Respiratory effort: 0 = none, 1 = slow, weak cry, 2 = good, strong cry
3. Muscle tone: 0 = limp, 1 = some flexion of extremities, 2 = active motion
4. Reflex irritability (response to stimulation of sole of foot or catheter put in nose): 0 = none, 1 = grimace, 2 = grimace and strong cry, cough, or sneeze
5. Color: 0 = pale, blue, 1 = body pink and extremities blue, 2 = completely pink

Continue to score every 5 minutes until the infant reaches a score of 7 or more (while resuscitating).

Important points:

1. Reye's syndrome may cause encephalopathy and/or liver failure in children taking aspirin. The syndrome usually develops after influenza or varicella infection. Avoid aspirin in children; use acetaminophen instead.
2. Moro and palmar grasp reflex should disappear by 6 months.

CHAPTER 29

Pharmacology

Side effects: bizarre, unique, and fatal side effects are tested as well as common side effects of common drugs.

DRUG	SIDE EFFECT(S)	DRUG	SIDE EFFECT(S)
Trazodone	Priapism	Chloramphenicol	Aplastic anemia, gray baby syndrome
Aspirin	GI bleeding, hypersensitivity	Doxorubicin	Cardiomyopathy
Bleomycin	Pulmonary fibrosis	Busulfan	Pulmonary fibrosis, adrenal failure
Cyclophosphate	Hemorrhagic cystitis	Monoamine oxidase inhibitors	Tyramine crisis (cheese, wine)
Bupropion	Seizures	Hydralazine	Lupus erythematosus
Isoniazid	Vitamin B_6 deficiency, lupus, liver toxicity	Procainamide	Lupus erythematosus
		Minoxidil	Hirsutism
Cyclosporine	Renal toxicity	Aminoglycosides	Hearing loss, renal toxicity
Penicillins	Anaphylaxis, rash with Epstein-Barr virus	Acetaminophen	Liver toxicity (in high doses)
		Chlorpropamide	Syndrome of inappropriate secretion of antidiuretic hormone
Angiotensin-converting enzyme inhibitors	Cough	Oxytocin	Syndrome of inappropriate secretion of antidiuretic hormone
Demeclocycline	Diabetes insipidus		
Lithium	Diabetes insipidus, thyroid dysfunction	Opiates	Syndrome of inappropriate secretion of antidiuretic hormone
Methoxyflurane	Diabetes insipidus	Dideoxyinosine (DDI)	Pancreatitis, peripheral neuropathy
Sulfa drugs	Allergies, kernicterus in neonates	Halogen anesthetic	Malignant hyperthermia
Halothane	Liver necrosis	Succinylcholine	Malignant hyperthermia
Local anesthetic	Seizures	Zidovudine (AZT)	Bone marrow suppression
Phenytoin	Folate deficiency, teratogen, hirsutism	Digitalis	Gastrointestinal disorders, vision changes, arrhythmias
Vincristine	Peripheral neuropathy	Acetazolamide	Metabolic acidosis
Amiodarone	Thyroid dysfunction	Trimethadioine	Terrible teratogen
Valproic acid	Neural tube defects in offspring	Clozapine	Agranulocytosis
Isotretinoin	Terrible teratogen	Selective serotonin reuptake inhibitors (SSRIs)	Anxiety, agitation, insomnia
Thioridazine	Retinal deposits, cardiac toxicity		
Heparin	Thrombocytopenia, thrombosis	Warfarin	Necrosis, teratogen
Vancomycin	Red man syndrome	Niacin	Skin flushing, pruritus
Clofibrate	Increased GI neoplasms	3-Hydroxy-3-methylglutaryl-coenzyme A reductase (HMG CoA Red)	Liver and muscle toxicity
Tetracyclines	Photosensitivity, teeth staining in children		
Quinolones	Teratogens (cartilage damage)	Ethambutol	Optic neuritis
Quinine	Cinchonism (e.g., tinnitus, vertigo)	Metronidazole	Disulfiram-like reaction with alcohol
Morphine	Sphincter of Oddi spasm		
Clindamycin	Pseudomembranous colitis (may be caused by any broad-spectrum antibiotic)	Cisplatin	Nephrotoxicity
		Methyldopa	Hemolytic anemia (Coombs' positive)

The **side effects of diuretics** are high yield. Thiazides cause hyperglycemia, hyperuricemia, hyperlipidemia, hyponatremia, hypokalemic metabolic alkalosis, and hypovolemia. Thiazides also cause *calcium retention* and, because they are sulfa drugs, should be avoided in patients with sulfa allergy. Loop diuretics cause hypokalemic metabolic alkalosis, hypovolemia, ototoxicity, and *calcium excretion*. All loop diuretics except ethacrynic acid are also sulfa drugs. Carbonic anhydrase inhibitors cause *metabolic acidosis*.

Antihypertensives are notorious for causing sedation, depression (the worst is methyldopa), and sexual dysfunction. Beta blockers also cause bradycardia, heart block, and congestive heart failure in susceptible patients. Calcium channel blockers also should be avoided in some cardiac patients for the same reason. Because beta blockers may precipitate asthmatic attacks and mask the symptoms of hypoglycemia, they should be avoided in asthmatics and diabetics. Alpha-one antagonists are notorious for severe first-dose orthostatic hypotension.

The side effects of **psychiatric medications** are also high yield. See psychiatry chapter.

Antidotes

POISONING OR OVERDOSE	ANTIDOTE
Acetaminophen	Acetylcysteine
Cholinesterase inhibitors	Atropine, pralidoxime
Quinidine or tricyclic antidepressants	Sodium bicarbonate (cardioprotective)
Iron	Deferoxamine
Digoxin	Normalize potassium and other electrolytes, digoxin antibodies
Methanol or ethylene glycol	Ethanol
Benzodiazepines	Flumazenil
Beta blockers	Glucagon
Lead	Edetate
Copper/gold	Penicillamine
Opioids	Naloxone
Carbon monoxide	Oxygen (hyperbaric if severe)
Muscarinic receptor blockers	Physostigmine

A few **drug interactions** are high yield. Do *not* give the following drugs together:

1. Monoamine oxidase inhibitors and meperidine (coma)
2. Monoamine oxidase inhibitors and selective serotonin reuptake inhibitors (serotonin syndrome: hyperthermia, rigidity, myoclonus, autonomic instability)
3. Ketoconazole and astemizole/terfenadine (lethal arrhythmias)
4. Aminoglycosides and loop diuretics (enhanced ototoxicity)
5. Thiazides and lithium (lithium toxicity)

Important points:

1. Rifampin is given for prophylaxis in contacts of a patient with *Neisseria meningitidis*.
2. Barbiturates, antiepileptics, and rifampin induce hepatic enzymes; cimetidine and ketoconazole inhibit hepatic enzymes (important for drug-drug interactions).
3. If a patient responds to placebo, it does not mean that the disease is psychosomatic; it means simply that the patient responded to placebo! Normal people with real diseases often have an improvement in symptoms with placebo.

HORMONE REPLACEMENT THERAPY AND ORAL CONTRACEPTIVES

Hormone replacement therapy (HRT) should be considered for all postmenopausal and posthysterectomy women. Observation during therapy is necessary, because estrogen and progesterone are not harmless. Every patient should make the decision on her own after weighing the risks and benefits.

Known benefits of estrogen therapy: decreased osteoporosis, decreased fractures (especially hip fractures), decreased coronary heart disease, reduced risk of all-cause mortality, reduced hot flushes or flashes, and reduced genitourinary symptoms (dryness, urgency, atrophy-induced incontinence, frequency). The decrease in coronary heart disease is probably due to the fact that estrogen increases high-density lipoprotein cholesterol; this beneficial effect is reduced or negated by coadministration of progesterones.

Known risks of estrogen therapy: increased risk of endometrial cancer (eliminated by coadministration of progesterones), increased risk of venous thromboembolism, possible increased risk of breast cancer (not with short-term use) and increased risk of gallbladder disease. The risk of breast cancer may increase after 10 or more years of use, but this risk is controversial.

Other side effects of estrogen therapy: endometrial bleeding, breast tenderness, nausea, bloating, and headaches.

Absolute contraindications to estrogen therapy: unexplained vaginal bleeding, active liver disease, history of thrombophlebitis or thromboembolism, history of endometrial or breast cancer.

Relative contraindications to estrogen therapy: seizure disorder, hypertension, uterine leiomyomas, familial hyperlipidemia, migraines, thrombophlebitis, endometriosis, gallbladder disease.

Important points:

1. Women who take estrogen therapy need an endometrial biopsy and dilatation and curettage at the onset of treatment to rule out hyperplasia and cancer and an evaluation of any unexplained bleeding, even while on therapy, unless they have had a normal evaluation in the past 6 months.
2. The main reason to give progesterone with estrogen is to eliminate the increased risk of endometrial cancer. If a women has no uterus, do not give progesterone.

Oral contraceptives should not be given to women over 35 who smoke or have other cardiovascular risk factors (hypercholesterolemia or untreated hypertension) because of an increased risk of sudden death. Oral contraceptives are the most common cause of secondary hypertension in women, and any patient who is noted to have increased blood pressure should discontinue oral contraceptives and have her blood pressure rechecked at a later date.

Absolute contraindications to oral contraceptives: smoking after age 35, pregnancy (do pregnancy test before prescribing), breast-feeding, active liver disease, hyperlipidemia, uncontrolled hypertension, diabetes mellitus with vascular changes, prolonged immobilization of an extremity, history of thromboembolism or thrombophlebitis, coronary artery disease, stroke, sickle cell disease, estrogen-dependent neoplasm (breast, endometrium), liver adenoma, and history of cholestatic jaundice of pregnancy.

Relative contraindications to oral contraceptives: depression, migraine headaches (may trigger attacks), oligomenorrhea, undiagnosed amenorrhea, gallbladder disease, and heavy cigarette smoking under age 35.

Side effects of oral contraceptives: glucose intolerance (check for diabetes mellitus annually in patients at high risk), depression, edema (bloating), weight gain, cholelithiasis, benign liver adenomas, melasma ("the mask of pregnancy"), nausea, vomiting, headache, hypertension, and drug interactions (drugs such as rifampin and antiepileptics may induce metabolism of oral contraceptives and reduce their effectiveness).

Important points:

1. Because of the risks of thromboembolism, oral contraceptives should be stopped 1 month before elective surgery and not restarted until 1 month after surgery.
2. The risk of breast cancer does *not seem to be increased with oral contraceptives*, except in long-term users (controversial; unlikely to be asked on boards). Cervical neoplasia may be increased, possibly because of the confounding factor of increased sexual relations and number of partners; nonetheless, oral contraceptive users should have at least annual Pap smears.

Other benefits of oral contraceptives: *50% reduction in ovarian cancer*; decrease in the incidence of menorrhagia, dysmenorrhea, benign breast disease, functional ovarian cysts (*often prescribed for the previous four effects*), premenstrual tension, iron-deficiency anemia, ectopic pregnancy, and salpingitis.

ASPIRIN, NONSTEROIDAL ANTI-INFLAMMATORY DRUGS, ACETAMINOPHEN

Effects: aspirin and nonsteroidal anti-inflammatory drugs (NSAIDs) inhibit cyclooxygenase centrally and peripherally, *giving them anti-inflammatory*, antipyretic, analgesic, and antiplatelet properties. Aspirin inhibits cyclooxygenase irreversibly and thus for the life of the platelet, whereas other NSAIDs inhibit cyclooxygenase reversibly. Acetaminophen is mostly central-acting; thus, it is only an analgesic and antipyretic with no platelet or anti-inflammatory effects.

Toxicity:

1. Aspirin may cause GI upset and bleeding, gastric ulcers, and gout. Always consider GI bleeding and ulcer in any patient taking aspirin or NSAIDs.
2. Higher aspirin doses cause tinnitus, vertigo, respiratory alkalosis and metabolic acidosis, hyperthermia, coma, and death.
3. Aspirin can be removed by dialysis in severe overdose.
4. Do not give aspirin to people with nasal polyps. Hypersensitivity reactions are extremely common in this group; look for nasal polyps in anyone with an asthmatic-type reaction to aspirin.
5. People with asthma may have an asthma attack after taking aspirin—even those without nasal polyps.
6. Do not give aspirin to children younger than 8 years with fever or viral infection; it may cause Reye's syndrome (look for encephalopathy and liver dysfunction).

7. Other NSAIDs also cause GI upset, bleeding, and ulcers. Always consider GI bleeding and ulcer in any patient taking aspirin or NSAID.
8. NSAIDs also may cause renal damage (interstitial nephritis and papillary necrosis), especially in patients who take them chronically and have preexisting renal disease.
9. Phenylbutazone can cause fatal aplastic anemia and agranulocytosis and should not be used chronically.
10. Acetaminophen causes liver toxicity in high doses due to depletion of glutathione. Treat with acetylcysteine.

Note: New NSAID/prostaglandin E_1 combinations help to prevent GI damage.

Low-dose aspirin has been proved to be of benefit in reducing the risk of stroke in patients with a transient ischemic attack or previous stroke, in reducing the risk of myocardial infarction in patients who have had a previous myocardial infarction and patients with stable or unstable angina who have not had a myocardial infarction. Many also recommend daily aspirin for patients with known coronary artery disease. Generally, use of aspirin for primary prevention of myocardial infarction or stroke in a patient with no definite history of myocardial infarction, angina, or coronary artery disease is not appropriate. Studies have not shown a clear benefit, and there may be an increased risk of hemorrhagic stroke and/or sudden death. If the patient has a history of liver or kidney disease, peptic ulcer disease, GI bleeding, poorly controlled hypertension, or bleeding disorder, the risks of aspirin prophylaxis may outweigh the benefits.

Important points:

1. Give aspirin to any patient in the emergency department with unstable angina, myocardial infarction, or transient ischemic attack.
2. Stop aspirin 1 week before surgery, other NSAIDs on the day before surgery.

CHAPTER 30

Radiology

Screening and/or confirmatory radiologic tests for suspicion of different diseases

CONDITION	SCREENING (OR ONLY) TEST TO ORDER	CONFIRMATORY TEST	COMMENTS
Skull fracture (depressed)	Computed tomography (CT) scan		
Head trauma	CT without contrast		Observe if mild
Intracranial hemorrhage	CT without contrast		
Acute stroke	CT without contrast		
Multiple sclerosis	Magnetic resonance imaging (MRI) of brain		
Brain tumor/metastases	CT or MRI with contrast		
Pneumonia	Chest x-ray		
Chest trauma	Chest x-ray		
Chest mass	CT scan		
Hemoptysis	Chest x-ray	Bronchoscopy	
Pulmonary embolism	Ventilation/perfusion scan (nuclear scan)	Pulmonary arteriogram	
Aortic aneurysm/dissection	CT with contrast		
Aortic tear (trauma)	Angiogram		
Carotid stenosis	Duplex ultrasound		
Esophageal obstruction	Barium x-ray or endoscopy	Endoscopy	
Esophageal tear	Barium x-ray or endoscopy	Endoscopy	
Bowel perforation	Chest and abdominal x-rays (free air)	Laparoscopy	
Hematemesis	Endoscopy		
Peptic ulcer disease	Upper GI series or endoscopy	Endoscopy	
Abdominal trauma	CT or diagnostic peritoneal lavage (see emergency medicine chapter)	Laparoscopy	
Abdominal aortic aneurysm	CT with contrast		Follow with ultrasound
Abdominal abscess	CT with contrast		
Cholelithiasis	Ultrasound		
Choledocholithiasis	Ultrasound	ERCP	
Cholecystitis	Ultrasound	HIDA scan (nuclear hepatobiliary study)	
Intestinal obstruction	Abdominal x-ray (supine and upright)		
Appendicitis	Abdominal x-ray, then ultrasound	Laparoscopy	Clinical diagnosis
Nephrolithiasis	Abdominal x-ray, then ultrasound	Intravenous pyelogram	

Table continued on following page.

CONDITION	SCREENING (OR ONLY) TEST TO ORDER	CONFIRMATORY TEST	COMMENTS
Ovarian pathology	Ultrasound	Laparoscopy	
Diverticulitis	Barium enema (*not* acutely)	CT	No scope acutely!
Upper GI bleeding	Upper GI series or endoscopy	Endoscopy	
Lower GI bleeding	Barium enema or endoscopy	Endoscopy	
Unknown GI bleed	Nuclear medicine bleeding study *or* angiography (brisk bleed)	Laparotomy	
Hydronephrosis	Intravenous pyelogram initially, ultrasound to follow		
Hematuria (persistent)	Intravenous pyelogram	Cystoscopy or CT	
Fibroid uterus	Ultrasound		
Pelvic mass (female)	Ultrasound	CT	
Bone metastases	Bone scan		
Pregnancy evaluation	Ultrasound (transvaginal detects sooner than transabdominal)		First do HCG test
Fracture	X-ray		
Osteomyelitis	X-ray	Bone scan	
Arthritis	X-ray		
Pyloric stenosis	Ultrasound		
Meckel's diverticulum	Meckel's scan (nuclear medicine scan)		

HIDA = hepato-iminodiacetic acid, ERCP = endoscopic retrograde cholangiopancreatography, HCG = human chorionic gonadotropin.

CHAPTER 31

Laboratory Medicine

Important points:

1. Hyperkalemia may be caused by a hemolyzed blood sample or rhabdomyolysis (due to high intracellular potassium concentration).
2. Hyponatremia may be caused by hyperglycemia, hyperproteinemia, or hyperlipidemia; these forms of secondary hyponatremia will correct with correction of the glucose, lipid, or protein levels.
3. Correcting hyponatremia aggressively (especially with hypertonic saline [3%]) may cause brainstem damage (central pontine myelinolysis).
4. Alkalosis may cause hypokalemia and symptoms of hypocalcemia (perioral numbness, tetany) due to cellular shift; acidosis may cause hyperkalemia by the same mechanism.
5. High levels of amylase and lipase may be due to sources other than the pancreas (salivary glands, GI tract, renal failure, ruptured tubal pregnancy), but elevation of both in the same patient usually is due to pancreatitis.
6. Alkaline phosphatase can be elevated by biliary disease, bone disease, or pregnancy. If the elevation is due to biliary disease, gamma-glutamyltranspeptidase (GGT) and/or 5-nucleotidase (5-NT) also should be elevated.
7. Hypothyroidism can cause elevated cholesterol.
8. Elevated creatine kinase (CK) may be due to muscle injury (striated or myocardial), drugs (HMG-CoA reductase inhibitors) or burns (CK-MB is more specific for cardiac muscle).
9. Hypokalemia and/or hypocalcemia may be due to hypomagnesemia. You cannot correct the hypokalemia until you correct the hypomagnesemia.
10. Watch for hypophosphatemia in diabetic ketoacidosis.
11. Blood urea nitrogen:creatinine ratio > 15 usually implies dehydration.
12. Positive results on the rapid plasma reagin or Venereal Disease Research Laboratory test for syphilis may be due to systemic lupus erythematosus.
13. In patients with isosthenuria and hyposthenuria—the inability to concentrate urine—think of diabetes insipidus or sickle cell disease/trait.
14. The erythrocyte sedimentation rate (ESR) is a worthless test in pregnancy; ESR is elevated by pregnancy itself. A high-normal blood urea nitrogen:creatinine ratio may mean renal disease in pregnancy.

CHAPTER 32
Ethics

Important points:

1. Do not force adult Jehovah's witness patients to accept blood products.
2. If a child has a life-threatening condition and the parents refuse a simple, curative treatment (antibiotics for meningitis), first try to persuade the parents to change their mind. If you cannot, your second option is to get a court order to give the treatment. But do not give the treatment until you talk to the courts if you can avoid it.
3. Let competent people die if they want to do so. *Never* force treatments on adults of sound mind. Respect wishes for passive euthanasia, but avoid active euthanasia.
4. Do not tell anyone how your patient is doing unless he or she is directly involved with care and needs to know or is an authorized family member. If a colleague asks about a friend who happens to be your patient, refuse to answer.
5. Break confidentiality only in the following situations:
   - The patient asks you to do so.
   - Child abuse is suspected.
   - The courts mandate you to tell.
   - You have a duty to protect life. (If the patient says that he or she is going to kill someone or him- or herself, you have to tell the intended victim, the authorities, or both.)
   - The patient has a reportable disease. You must report to authorities, let them deal with it.
   - The patient is a danger to others. If the patient is blind or has seizures, let the proper authorities know so that they can take away the patient's license to drive. If the patient is an airplane pilot and a paranoid, hallucinating schizophrenic, authorities need to know.
6. Informed consent involves giving the patient information about the *diagnosis* (his or her condition and what it means), the *prognosis* (the natural course of the condition without treatment), the *proposed treatment* (description of the procedure and what the patient will experience), the *risk/benefits* of the treatment, and the *alternative treatments*. The patient is then allowed to make his or her own choice. The documents seen on hospital wards that patients are made to sign are *neither required nor sufficient* for informed consent; they are used for medicolegal purposes (i.e., lawsuit paranoia).
7. When the patient is incompetent, a guardian (surrogate decision maker or health care power of attorney) should be appointed by the court.

8. Living wills and do-not-resuscitate orders should be respected and followed if done correctly. For example, if in a living will the patient says that a ventilator should not be used if he or she is unable to breathe independently, do not put the patient on a ventilator, even if the spouse, son, or daughter makes the request.
9. Depression always should be evaluated as a reason for the patient's "incompetence." Patients who are suicidal may refuse all treatment; this decision should not be respected until the depression is treated.
10. Patients can be hospitalized against their will in psychiatry (if they are a danger to self or others) for a limited time. After 1–3 days, patients usually get a hearing to determine whether they have to remain in custody. This practice is based on the principle of beneficence (a principle of doing good for the patient and avoiding harm).
11. Restraints can be used on an incompetent or violent patient (delirious, psychotic) if needed, but their use should be brief and reevaluated often.
12. Patients under 18 do not require parental consent in the following situations:
    - If they are emancipated (married, living on their own and financially independent, parents of children, serving in the armed forces)
    - If they have a sexually transmitted disease, want contraception, or are pregnant.
    - If they want drug treatment or counseling.

    Some states have exceptions to these rules, but for boards let such minors make their own decisions.
13. If a patient is comatose and no surrogate decision maker has been appointed, the wishes of the family generally should be respected. If there is a family disagreement or ulterior motives are evident, talk to your hospital ethics committee. Use courts as a last resort.
14. In a pediatric emergency when parents are not available, treat the patient as you see fit.
15. Do not hide a diagnosis from patients (including pediatric patients) if they want to know the diagnosis—even if the family asks you do so. Do not lie to any patient because the family asks you to do so. The flip side also applies: do not force patients to receive information against their will. If they don't want to know the diagnosis, don't tell them.
16. If a patient cannot communicate, give any required emergency care unless you know that the patient does not want it.
17. Withdrawing and withholding care are no different in a legal sense. Just because the patient is on a respirator does not mean that you cannot stop it.
18. In terminally ill patients, give enough medication to relieve pain. Opioids are commonly used.

CHAPTER 33
Photos

Although some questions with photos can be figured out without looking at the photo, this is not always the case. You should be able to recognize the entities listed below. The *Color Atlas and Text of Clinical Medicine* by Forbes and Jackson is a great source. For other good atlases, see your librarian.

Blood smears:

- Howell-Jolly bodies (asplenia/splenic dysfunction)
- Basophilic stippling (lead poisoning, thalassemia)
- Malaria
- Spherocytosis
- Target cells (thalassemia, severe liver disease)
- Heinz bodies/"bite cells" (G6PD deficiency)
- Schistocytes/helmet cells (disseminated intravascular coagulation, thrombotic thrombocytopenic purpura, microangiopathic hemolysis)
- Multiple myeloma
- Acute lymphoblastic leukemia, chronic lymphocytic leukemia
- Auer rods (acute myeloid leukemia)
- Chronic myelocytic leukemia
- Acanthocytes (abetalipoproteinemia)
- Teardrop cells (myelofibrosis, myelodysplasia)
- Iron deficiency anemia
- Sideroblastic anemia
- Folate/B_{12} anemia (macrocytic, hypersegmented neutrophils)
- Sickle cell disease
- Reticulocytes
- Aplastic anemia ("dry" bone marrow tap)
- Chediak-Higashi cell
- Reed-Sternberg cell (Hodgkin's lymphoma)
- Dohle bodies (toxic lymphocytes; for boards, think of Epstein-Barr virus)
- Hairy cell leukemia

Ophthalmology:

- Kayser-Fleischer ring (Wilson's disease)
- Bacterial conjunctivitis (especially in neonates)
- Glaucoma (closed-angle attack or acute)
- Graves' disease (exophthalmos)
- *Diabetic fundus*
- Hypertensive fundus
- Central retinal artery occlusion (fundus)
- Central retinal vein occlusion (fundus)
- Papilledema
- Retinoblastoma (white reflex instead of red)
- Xanthelasma
- Corneal arcus (in patients < 50, a marker for hypercholesterolemia)
- Roth spots (think of endocarditis)
- Herpes simplex keratitis (dendritic ulcer seen with fluorescein; avoid steroids)
- Cataracts (bad enough to notice with the naked eye)
- *Orbital cellulitis*

Dermatology/skin findings:

- Pityriasis rosea
- *Neisseria* sp. septicemia (severe purpura)
- Lyme disease (erythema chronicum migrans)
- Tinea capitis
- Scabies
- Psoriasis (*skin findings and nail pitting*)
- Cheilitis/stomatitis (think of B vitamin deficiencies)
- Toxic shock syndrome, scalded skin syndrome
- Abdominal striae (Cushing's syndrome)
- Erythema marginatum (rheumatic fever)
- Janeway and Osler lesions (endocarditis)
- Acanthosis nigricans (marker for visceral malignancy)
- Syphilis (chancre, condyloma lata, secondary syphilis rash)
- Herpes (I and II)
- Varicella zoster virus (chickenpox, shingles, trigeminal and ophthalmic involvement)
- Henoch-Schönlein purpura (rash)
- Erythema multiforme (target lesion)
- Malar rash (lupus)
- Heliotrope rash (dermatomyositis)
- Oral hairy leukoplakia (caused by Epstein-Barr virus; seen in HIV-positive patients)
- Basal cell cancer

- Squamous cell cancer
- Melanoma
- Actinic keratosis
- Stasis dermatitis/venous insufficiency (skin changes, ulcers)
- Arterial insufficiency (skin changes)
- Diabetic foot ulcers (similar in appearance to arterial insufficiency ulcers but usually *painless*)
- Vitiligo (associated with pernicious anemia and hypothyroidism)
- Impetigo
- Raynaud's phenomenon (finger autoamputation; often seen in scleroderma)
- Temporal arteritis (tortuous-looking temporal artery)
- Clubbing of the fingers
- Acne
- Adenoma sebaceum (tuberous sclerosis)
- Condyloma acuminata
- Molluscum contagiosum
- Bitot's spots (vitamin A deficiency)
- Café-au-lait patches (neurofibromatosis in patients with normal IQ, McCune-Albright syndrome with mental retardation)
- Varicose veins
- Cullen's sign
- Grey-Turner sign
- Erythema infectiosum (slapped cheek rash with fever resolution just before rash appears)
- Sturge-Weber syndrome (hemangioma; port-wine stain on one side of face)
- Cavernous hemangiomas (in children, most lesions resolve on their own)
- Hirsutism (know conditions associated with it)
- Rocky Mountain spotted fever rash
- Pyoderma gangrenosum (think of inflammatory bowel disease)
- Erythema nodosum (think of inflammatory bowel disease, infections [the classic example is *Coccidioides immitis* or tuberculosis], or sarcoidosis)
- Pretibial myxedema (Graves' disease)
- Neurofibromatosis (skin)
- Keloids (usually in blacks)
- Allergic contact dermatitis
- Tinea corporis and tinea cruris

Microscopic findings:

- Gram stain (gram-negative = red, gram-positive = blue) plus clustering tendencies
- Caseating granulomas (tuberculosis, fungi)
- Noncaseating granulomas (sarcoidosis)
- Goodpasture's disease (linear immunofluorescence in kidney)
- Gout (needle-shaped crystals from a joint with no birefringence)

- Pseudogout (needle-shaped crystals with positive birefringence)
- *Trichomonas* sp.
- Clue cells (*Gardnerella* sp. vaginitis)
- *Giardia* sp.
- Koilocytosis (think of human papillomavirus or cytomegalovirus)

Radiologic findings:

- Lobar pneumonia
- Sinusitis (maxillary or frontal sinus opacification)
- Sarcoidosis
- Osteoarthritis (osteophytes, interphalangeal joint changes)
- Multiple myeloma (punched-out skull x-rays)
- Osteosarcoma (sunray or sunburst pattern)
- Duodenal and jejunal atresia ("double-bubble" sign)
- Esophageal atresia (barium x-ray)
- *Pleural effusion*
- Congestive heart failure on chest x-ray
- Small bowel obstruction (air-fluid levels)
- Toxic megacolon (Hirschsprung's disease or inflammatory bowel disease, infection)
- Pneumothorax
- Grossly abnormal ventilation-perfusion scan
- Classic chest x-ray of tuberculosis
- Chest x-ray findings of asbestosis (plaques)
- Abdominal aortic aneurysm on angiogram
- Achalasia (esophagus on barium enema)
- Volvulus on barium enema (bird's beak)
- Epidural hematoma (CT)
- Subdural hematoma (CT)
- Appearance of a major cerebrovascular accident (stroke) on CT/MRI
- Berry aneurysms on angiogram
- Slipped capital femoral epiphysis (x-ray)
- Nephrolithiasis on abdominal x-ray (radiopaque)
- Coarctation of aorta (on angiogram)
- Multiple sclerosis (plaques on MRI)
- Pancoast tumor on chest x-ray (know associated Horner's syndrome)
- Lung abscess on chest x-ray (air-fluid level)
- Bossing of the skull on x-ray (think of hemolytic anemias, especially thalassemias and sickle cell disease, and in elderly patients Paget's disease)
- Colon cancer on barium enema (apple-core and napkin-ring lesions)
- Liver tumors on CT (metastasis 20 times more likely than primary tumor)

- Severe carotid artery stenosis on angiogram
- Shoulder separation on x-ray
- Lytic lesions of bone on x-ray (think of malignancy)

Other photos:

- Rheumatoid arthritis (swan-neck deformity, boutonnière deformity, ulnar deviation, rheumatoid nodules)
- Osteoarthritis (Heberden's and Bouchard's nodes)
- Gout (podagra, tophi)
- Dactylitis (sickle cell disease)
- Down syndrome (facies, simian crease)
- Turner's syndrome (body habitus, widely spaced nipples, webbed neck, cubitus valgus)
- Horner's syndrome (unilateral ptosis and miosis and history of hemianhydrosis)
- Bell's palsy (facial asymmetry)
- Cushing's syndrome (facies, striae)
- Graves' disease (exophthalmos)
- Acromegaly (facies)
- Peutz-Jeghers syndrome (freckling pattern on face)
- Achondroplasia (overall appearance; usually autosomal dominant)
- Candidal infection (vaginal, thrush)
- Gonorrhea (yellowish discharge)
- Erb's palsy (waiter's tip)
- Polycystic kidneys (gross appearance)
- Fetal alcohol syndrome (facies)
- Decubitus ulcers (best prevention is frequent turning of patient)
- Pseudohermaphrotidism (picture of ambiguous genitalia; look for 21-hydroxylase deficiency)
- Tanner stages (male and female)
- Congenital syphilis (Hutchinson's teeth, saddle nose deformity)
- Osteomyelitis extending to the skin (think of *Staphylococcus* or *Salmonella* sp. in sickle cell disease)
- Scleroderma (late-stage facies)
- Spina bifida (gross appearance; encephalocele, meningoceleocele, meningomyelocele, occulta/patch of hair)
- Strawberry tongue (scarlet fever and Kawasaki's disease)
- Acute tonsillitis (*Streptococcus* sp. or Epstein-Barr virus; rarely diphtheria in unimmunized patient)
- Acute pharyngitis (viral or streptococcal)
- Gynecomastia (normal finding in pubertal males)
- Tenosynovitis (think of gonorrhea if the patient is sexually active)
- Hypertrophy of the heart (gross specimen; severe disease)

- Dilated cardiomyopathy (gross specimen; severe disease)
- Karyotype showing Down (trisomy 21), Turner's (XO), or Klinefelter's (XXY) syndrome
- Fetal heart strips (normal, short-term, and long-term variability; early, variable, and late decelerations)

CHAPTER 34

Signs, Symptoms, and Syndromes

Babinski's sign: stroking the foot yields extension of the big toe and fanning of other toes in patients with upper motor neuron disease.

Beck's triad: jugular vein distention, muffled heart sounds, and hypotension in cardiac tamponade; do pericardiocentesis.

Brudzinski's sign: pain on neck flexion with meningeal irritation.

Charcot's triad: fever and chills, jaundice, and right upper quadrant pain in patients with cholangitis.

Courvoisier's sign: a painless, palpable gallbladder should make you think of pancreatic cancer.

Chvostek's sign: tapping on the facial nerve elicits tetany in hypocalcemia.

Cullen's sign: bluish discoloration of periumbilical area due to retroperitoneal hemorrhage (pancreatitis).

Cushing's reflex: hypertension, bradycardia, and irregular respirations with very high intracranial pressure.

Grey-Turner sign: bluish discoloration of flank from retroperitoneal hemorrhage (think of pancreatitis).

Homan's sign: calf pain on forced dorsiflexion of the foot in patients with deep vein thrombosis.

Kehr's sign: pain in the left shoulder with a ruptured spleen.

Leriche's syndrome: claudication and atrophy of the buttocks with impotence (seen with aortoiliac occlusive disease).

McBurney's sign: tenderness at McBurney's point with appendicitis.

Murphy's sign: arrest of inspiration when palpating right upper quadrant under the rib cage in patients with cholecystitis.

Ortolani's sign/test: a palpable or audible click with abduction of an infant's flexed hip means congenital hip dysplasia.

Prehn's sign: elevation of a painful testicle relieves pain in epididymitis (vs. torsion).

Rovsing's sign: pushing on the left lower quadrant produces pain at McBurney's point in patients with appendicitis.

Tinel's sign: tapping on the volar surface of the wrist elicits paresthesias in carpal tunnel syndrome.

Trousseau's sign: pumping up a blood pressure cuff causes carpopedal spasm (tetany) in hypocalcemia.

Virchow's triad: stasis, endothelial damage, and hypercoagulability (three broad categories of risk factors for deep vein thrombosis).

WORD ASSOCIATIONS

Word associations are not all 100% accurate, but they are useful in emergencies.

- Friction rub: pericarditis
- Kussmaul breathing: deep, rapid breathing seen in metabolic acidosis (think of diabetic ketoacidosis)
- Kayser-Fleischer ring: Wilson's disease
- Bitot's spots: vitamin A deficiency
- Dendritic corneal ulcers: herpes keratitis (seen best with fluorescein; avoid steroids)
- Amaurosis fugax: temporary, painless, monocular blindness seen in transient ischemic attack (watch out for temporal arteritis; if it is suspected, start steroids before biopsy confirmation to prevent blindness)
- Cherry-red spot on the macula: Tay-Sachs disease (no hepatosplenomegaly) or Niemann-Pick disease (hepatosplenomegaly)
- Bronze (skin) diabetes: hemochromatosis (look also for cardiac and liver dysfunction)
- Malar rash: lupus erythematosus
- Heliotrope rash: dermatomyositis
- Clue cells: *Gardnerella* sp. infection
- Meconium ileus: cystic fibrosis
- Rectal prolapse: cystic fibrosis
- Salty-tasting baby: cystic fibrosis
- Café-au-lait spots: neurofibromatosis (if mental retardation is present, think of McCune-Albright syndrome or tuberous sclerosis)
- Worst headache of patient's life: subarachnoid hemorrhage
- Abdominal striae: Cushing's syndrome (or possible pregnancy)
- Honey: infant botulism
- Left lower quadrant tenderness/rebound: diverticulitis
- Children who torture animals: conduct disorder (may be antisocial as adults)
- Currant jelly stools in children: intussusception
- Ambiguous genitalia and hypotension: 21-hydroxylase deficiency
- Cat-like cry in children: cri-du-chat syndrome
- >10 lb. baby: maternal diabetes
- Anaphylaxis from immunoglobulin therapy: IgA deficiency
- Postpartum fever unresponsive to broad-spectrum antibiotics: septic pelvic thrombophlebitis (give heparin for an easy cure and retrospective diagnosis)

- Increased A2 hemoglobin and anemia: thalassemia
- Heavy young woman with papilledema and negative radiology: pseudotumor cerebri
- Low-grade fever in first 24 hours after surgery: atelectasis
- Vietnam veteran: posttraumatic stress disorder
- Bilateral hilar adenopathy in a black patient: sarcoidosis
- Sudden death in a young athlete: hypertrophic obstructive cardiomyopathy
- Fractures or bruises in different stages of healing (children): child abuse
- Decreased breath sounds in a trauma patient: pneumothorax
- Shopping sprees: mania
- Constant clearing of throat (children): Tourette's syndrome
- Intermittent bursts of swearing: Tourette's syndrome
- Koilocytosis: human papillomavirus or cytomegalovirus
- Rash after ampicillin or amoxicillin for a sore throat: Epstein-Barr virus infection
- Daytime sleepiness and occasional falling down (cataplexy): narcolepsy

CHAPTER 35

Abbreviations

AAA	abdominal aortic aneurysm
Ab	antibody
abx, Abx	antibiotics
ABC, ABCD, ABCDE	**a**irway, **b**reathing, **c**irculation, **d**isability, **e**xposure (trauma protocol)
abd	abdominal
ABG	arterial blood gas
ABO	blood types (A, B, AB or O)
AC	abdominal circumference
ACE	angiotensin-converting enzyme
ACE-I	angiotensin-converting enzyme inhibitor
ACL	anterior cruciate ligament
ACTH	adrenocorticotropic hormone
ADH	antidiuretic hormone
ADHD	attention-deficit hyperactivity disorder
AF	amniotic fluid
AFI	amniotic fluid index
afib	atrial fibrillation
AFP	alpha-fetoprotein
AIDS	acquired immunodeficiency syndrome
ALL	acute lymphoblastic leukemia
ALT	alanine aminotransferase
AML	acute myeloid leukemia
ANA	antinuclear antibody
ANCA	antineutrophil cytoplasmic antibody
ANOVA	analysis of variance
ANS	autonomic nervous system
AP	anteroposterior
ARDS	adult respiratory distress syndrome

ARF	acute renal failure
ASA	acetylsalicylic acid (aspirin)
ASAP	as soon as possible
ASD	atrial septal defect
ASO	antistreptolysin O (in streptococcal infection)
AST	aspartate aminotransferase
ATG	antithymocyte globulin
Aut	autosomal
AV	arteriovenous or atrioventricular
AVM	arteriovenous malformation
AXR	abdominal x-ray
AZT	azidothymidine (zidovudine)
B, β	beta
BAL	dimercaprol
BE	barium enema
BM	bone marrow
BMR	basic metabolic rate
BP	blood pressure
BPD	biparietal diameter
BPH	benign prostatic hyperplasia/hypertrophy
BPM	beats per minute
BPP	biophysical profile
BSO	bilateral salpingo-oophorectomy
BT	bleeding time
BUN	blood urea nitrogen
Bx, bx	biopsy
C	centigrade (e.g., 37° C) or complement (e.g., C1, C3, C4)
C&S	culture and sensitivity
c-section	cesarean section
c-spine	cervical spine
Ca	calcium
CA	cancer
CAD	coronary artery disease
CBC	complete blood count
cc	cubic centimeter
CCU	coronary/cardiac care unit
CD	cluster of differentiation (e.g., CD4, CD8)
CEA	carcinoembryonic antigen
cGy	centigray

CHD coronary heart disease or congenital hip dysplasia
Chem chemistry
chemo chemotherapy
CHF congestive heart failure
CK creatine kinase
Cl chloride
CLL chronic lymphocytic leukemia
cm centimeter
CML chronic myelocytic (or myelogenous) leukemia
CMV cytomegalovirus
CN cranial nerve
CNS central nervous system
CO carbon monoxide or cardiac output
CO_2 carbon dioxide
COPD chronic obstructive pulmonary disease
CPD cephalopelvic disproportion
CPK creatine phosphokinase
Cr creatinine
CRF chronic renal failure
CRP c-reactive protein
CSF cerebrospinal fluid
CST contraction stress test
CT computed tomography scan
CV cardiovascular
CVA cerebrovascular accident (stroke)
CVP central venous pressure
CVS chorionic villus sampling
Cx culture
CXR chest x-ray
D&C dilation and curettage
DDI dideoxyinosine (HIV medication)
Derm, derm dermatology
DES diethylstilbestrol
DI diabetes insipidus
DIC disseminated intravascular coagulation
diff differential or difficile (e.g., *Clostridium diff* or *C. diff*)
Dig digoxin
DIP distal interphalangeal (joint)
DKA diabetic ketoacidosis

dl	deciliter
DM	diabetes *mellitus*
DMSA	2,3-dimercaptosuccinic acid, succimer
DNA	deoxyribonucleic acid
DNR	do not resuscitate
DPL	diagnostic peritoneal lavage
DUB	dysfunctional uterine bleeding
DVT	deep venous thrombosis
Dx, dx	diagnosis
EBL	estimated blood loss
EBNA	Epstein-Barr nuclear antigen
EBV	Epstein-Barr virus
ECG	electrocardiogram
EDTA	edetate
EEG	electroencephalogram
EF	ejection fraction
EKG	electrocardiogram
ELISA	enzyme-linked immunosorbent assay
EMG	electromyogram
EPS	extrapyramidal system
ER	emergency room
ERCP	endoscopic retrograde cholangiopancreatography
ERT	estrogen replacement therapy
ESP	extrasensory perception
ESR	erythrocyte sedimentation rate
ESRD	end-stage renal disease
EtOH	alcohol (ethanol)
F	fluoride or female
FDP	fibrin degradation product
Fe	iron
FEP	free erythrocyte protoporphyrin
FEV	forced expiratory volume
FEV_1	forced expiratory volume in 1 second
FFP	fresh frozen plasma
FSH	follicle-stimulating hormone
FTA-ABS	fluorescent treponemal antibody-absorption test (for syphilis)
FTI	free thyroxine index
FVC	forced vital capacity
Fx, fx	fracture

g, gm gram

G-6-PD, G6PD glucose-6-phosphatase deficiency

GBS group B *Streptococcus*

GERD gastroesophageal reflux disease

GFR glomerular filtration rate

GGT gamma-glutamyltranspeptidase

GH growth hormone

GI gastrointestinal

GnRH gonadotropin-releasing hormone

GU genitourinary

GYN gynecology or gynecologic

H2 histamine type 2 receptor

H&H hemoglobin and hematocrit

H&P history and physical examination

HAV hepatitis A virus

HbA1c glycosylated hemoglobin

HBIG hepatitis B immune globulin

HBcAb/Ag hepatitis B core antibody/antigen

HBeAb/Ag hepatitis B "e" antibody/antigen

HBsAb/Ag hepatitis B surface antibody/antigen

HBV hepatitis B virus

HC head circumference

HCC hepatocellular carcinoma

HCG human chorionic gonadotropin

HCl hydrochloric acid

Hct hematocrit

HCV hepatitis C virus

HDL high-density lipoproteins

HDV hepatitis D virus

HELLP hemolysis, elevated liver enzymes, low platelets

Hep hepatitis

HEV hepatitis E virus

H. flu *Haemophilus influenzae*

Hgb hemoglobin

5-HIAA 5-hydroxyindoleacetic acid

Hib *Haemophilus influenzae* type b (vaccine)

HIV human immunodeficiency virus

HLA human leukocyte antigen

hMG human menopausal gonadotropin

HOCM	hypertrophic obstructive cardiomyopathy
HPV	human papilloma virus
hr	hour/hours
HRT	hormone replacement therapy
HSP	Henoch-Schönlein purpura
HSV	herpes simplex virus
HTN	hypertension
HUS	hemolytic uremic syndrome
HVA	homovanillic acid
Hx	history
I&D	incision and drainage
IBD	inflammatory bowel disease
IBS	irritable bowel syndrome
ICP	intracranial pressure
Ig, IG	immunoglobulin (e.g., IgA, IgM, IgG, IgE)
IM	intramuscular
IOP	intraocular pressure
IPV	inactivated poliovirus vaccine
IQ	intelligence quotient
IU	international units
IUD	intrauterine device
IUGR	intrauterine growth retardation
ITP	idiopathic thrombocytopenic purpura
IV	intravenous
IVC	inferior vena cava
IVDA	intravenous drug abuse
IVF	intravenous fluids
IVIG	intravenous immunoglobulins
IVP	intravenous pyelogram
JRA	juvenile rheumatoid arthritis
JVD	jugular venous distention
JVP	jugular venous pressure
K	potassium
KCl	potassium chloride
kg	kilogram
KOH	potassium hydroxide
L	liter
LA	left atrium
LAE	left atrial enlargement

lb	pound
LBW	low birth weight
LCP	Legg-Calvé-Perthes syndrome
LDH	lactate dehydrogenase
LDL	low-density lipoproteins
LES	lower esophageal sphincter
LFT(s)	liver function test(s)
LGI	lower gastrointestinal (below the ligament of Treitz)
LH	luteinizing hormone
LLQ	left lower quadrant
LMN	lower motor neuron
LMP	last menstrual period
LOC	loss of consciousness
LR	lactated Ringer's solution
L:S	lecithin:sphingomyelin ratio
LSD	lysergic acid diethylamide
LUQ	left upper quadrant
LV	left ventricle
LVF	left ventricular failure
LVH	left ventricular hypertrophy
M	male
MAI	*Mycobacterium avium-intracellulare* complex
MAO	monoamine oxidase
MAO-I	monoamine oxidase inhibitor
MAST	military antishock trousers
MBP	myelin basic protein
MCHC	mean corpuscular hemoglobin concentration
MCP	metacarpophalangeal (hand joint)
MCV	mean corpuscular volume
MEN	multiple endocrine neoplasia
met	metabolic (e.g., met. alkalosis)
mets	metastasis
MG	myasthenia gravis
MHA-TP	microhemagglutination assay for antibodies to *Treponema pallidum* (for syphilis)
MI	myocardial infarct
ml	milliliter
mm	millimeter
MMR	measles, mumps, rubella (vaccine)
mo	month/months

MR	mental retardation
MRA	magnetic resonance angiogram
MRI	magnetic resonance imaging scan
MRSA	methicillin-resistant *Staphylococcus aureus*
MS	multiple sclerosis
MVP	mitral valve prolapse
Na	sodium
NEC	necrotizing enterocolitis
NG	nasogastric
NGT	nasogastric tube
NH3	ammonia
NHL	non-Hodgkin's lymphoma
NPH	isophane insulin suspension
NPO	nothing by mouth
NPV	negative predictive value
NS	normal saline
NSAID	nonsteroidal anti-inflammatory drug
NST	nonstress test
N/V	nausea/vomiting
O_2	oxygen
OA	osteoarthritis
OCP	oral contraceptive pill
OD	overdose
OGT	orogastric tube
OGTT	oral glucose tolerance test
OM	otitis media
OPV	oral poliovirus vaccine
OR	operating room
PAC	premature atrial contraction
PAN	polyarteritis nodosa
Pap	Papanicolaou smear
PCL	posterior cruciate ligament
PCN	penicillin
PCOS	polycystic ovary syndrome
PCP	phencyclidine or *Pneumocystis carinii* pneumonia
PCWP	pulmonary capillary wedge pressure
PDA	patent ductus arteriosus
PE	pulmonary embolus
PEEP	positive end-expiratory pressure

PG prostaglandin (e.g., PGE2, PGF) or phosphatidylglycerol
PH pulmonary hypertension
PID pelvic inflammatory disease
PIH pregnancy-induced hypertension
PIP proximal interphalangeal (joint)
PKU phenylketonuria
PMN polymorphonuclear leukocyte
PMS premenstrual syndrome
PO_4 phosphate
PPD purified protein derivative (tuberculosis skin test)
PPROM preterm premature rupture of the membranes
PPV positive predictive value
prn as needed
PROM premature rupture of the membranes
PSA prostate-specific antigen
pt/pts patient/patients
PT prothrombin time
PTCA percutaneous transluminal coronary angioplasty
PTH parathyroid hormone
PTT partial thromboplastin time
PUD peptic ulcer disease
PVC premature ventricular contraction
PVD peripheral vascular disease
PZA pyrazinamide
RA right atrium or rheumatoid arthritis
RAE right atrial enlargement
RAI radioactive iodine
RBC red blood cells
RDW red blood cell distribution width
Rec recessive (e.g., autosomal rec.)
REM rapid eye movement (dream sleep)
RF rheumatic fever
Rh Rhesus blood-group antigen
RI reticulocyte index
RLQ right lower quadrant
RNA ribonucleic acid
RPR rapid plasma reagin test (for syphilis)
RSV respiratory syncytial virus
RUQ right upper quadrant

RV right ventricle
RVF right ventricular failure
RVH right ventricular hypertrophy
S1, S2, S3, S4 heart sounds 1–4
SBO small bowel obstruction
SCD sickle cell disease
SCFE slipped capital femoral epiphysis
SCID severe combined immunodeficiency disease
SD standard deviation
SES socioeconomic status
SIADH syndrome of inappropriate antidiuretic hormone secretion
SIDS sudden infant death syndrome
SLE systemic lupus erythematosus
SOB shortness of breath
S/P status post (after)
SSRI serotonin-selective reuptake inhibitors
Staph *Staphylococcus*
Stat immediately
STD sexually transmitted disease
Strep *Streptococcus*
SVC superior vena cava
SvO_2 systemic venous oxygen saturation
SVR systemic vascular resistance
Sx (Sxs) symptom (symptoms)
T_3 triiodothyronine
T_4 thyroxine
TAH total abdominal hysterectomy
TB, Tb tuberculosis
TBG thyroid binding globulin
TCA tricyclic antidepressant
TE tracheoesophageal
Tet tetralogy (of Fallot)
TFTs thyroid function tests (usually means TSH, T_4, free T_4 index, T_3 resin uptake)
TIA transient ischemic attack
TIBC total iron-binding capacity
TIPS transjugular intrahepatic portosystemic shunt
TM tympanic membrane
TMP/SMZ trimethoprim-sulfamethoxazole
TORCH toxoplasma, other, rubella, cytomegalovirus, herpes

tPA tissue plasminogen activator

TRH thyroid-releasing hormone

TSH thyroid-stimulating hormone

TTP thrombotic thrombocytopenic purpura

TURP transurethral resection of the prostate

Tx treatment or therapy

UA urinalysis

UC ulcerative colitis

UGI upper gastrointestinal (proximal to the ligament of Treitz)

UMN upper motor neuron

URI upper respiratory infection

US ultrasound

UTI urinary tract infection

UV ultraviolet

VACTERL vertebral, anal, cardiac, tracheoesophageal, renal, limb (malformations)

Vanco vancomycin

VCA viral capsid antigen (in Epstein-Barr virus)

VDRL Venereal Disease Research Laboratory test (for syphilis)

VFib or Vfib ventricular fibrillation

VIP vasoactive intestinal peptide

VIPoma pancreatic tumor that secretes vasoactive intestinal peptide

Vit vitamin

VMA vanillylmandelic acid

V/Q ventilation/perfusion (ratio)

vs. versus

VSD ventricular septal defect

VTach or Vtach ventricular tachycardia

VUR vesicoureteral reflux

vWF von Willebrand's factor

VZIG varicella zoster immunoglobulin

WBC white blood cells

WPW Wolff-Parkinson-White syndrome

yr year/years

ZES Zollinger-Ellison syndrome

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