INTERNAL MEDICINE

CORE CURRICULUM

Book 5

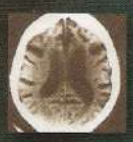
Eleventh Edition

HANNAMAN

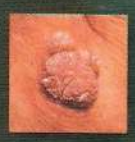
2005 / 2006

General Internal Medicine

Neurology



Dermatology



MedStudy

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11th Edition

Internal Medicine Review Core Curriculum

Book 5 of 5

Topics in this volume:

General Internal Medicine

Neurology

Dermatology

Authored by Robert A. Hannaman, MD

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Internal Medicine Review

Core Curriculum

General Internal Medicine

Authored by Robert A. Hannaman, MD

Many thanks to

Doug Paauw, MD
Professor of Medicine
Rathmann Family Foundation
Endowed Chair in Patient Centered Clinical Education
Head Section of GIM
Department of Medicine
University of Washington School of Medicine
Seattle, Washington

General Internal Medicine Advisor

General Internal Medicine

RADIOLOGY

CT/MRI/ULTRASOUND

CT—Advantages: quick, sensitive for acute hemorrhage and calcifications. Excellent boney definition. Can use CT in cases when MRI cannot be used (pacemaker, metal prostheses, metallic foreign objects). Roughly half the cost of an MRI.

CT—Disadvantages: insensitive compared to MRI in the posterior fossa (brainstem and cerebellum) and floor of the middle fossa. Also much less sensitive than MRI for many common CNS problems.

CT is used in the workup of:

- lung masses
- abdominal masses
- thoracic aneurysm
- severe headache
- chorea
- lymphoma
- staging of lung cancer
- bronchiectasis
- seizures
- restrictive cardiomyopathy
- pheochromocytoma
- adrenal masses.
- meningitis (before LP and if there is papilledema or focal neurologic signs)
- head injury (for bleeds and fractures)
- spinal nerve compression symptoms (or myelography prn)
- empty sella (usually initially found on x-ray)
- brain abscesses (toxoplasmosis = ring-enhancing lesions)

To determine bone density, quantitative CT may be done, but it is more expensive and gives a higher radiation dose than absorptiometry (see osteoporosis on pgs 10-3 and 10-8). CT is better than MRI for seeing CNS blood; it is usually the first test done in the Emergency Department for acute onset of central neurologic deficits or significant trauma to the head. The sensitivity for diagnosis of subarachnoid hemorrhage within the first 24 hours of symptoms is 96%!

Table 10-1: ABNORMAL Tissues—Weighted MRI vs. CT

	Acute Bleed	Infarct	Tumor (with enhancement)	MS Plaque
T1	Bright	Dark	Dark	Dark
T2	Bright	Bright	Bright	Bright
CT	Bright	Dark	Bright if well vascularized	Dark or Isodense

Table 10-2: NORMAL Tissues—Findings on Weighted MRI and on CT

	Air	Water	Fat	Bone	White Matter	Gray Matter
T1	Dark	Dark	Bright	Whitish	Lt gray	Med gray
T2	Dark	Bright	Bright	Very dark gray	Darker gray	Darker gray
CT	Dark	Dark	Dark	Bright	Gray	Gray

Helical CT is a newer method of CT scanning in which a table moves continuously through a gantry containing an always-on x-ray source. This provides faster, thinner slices. Organs (including the entire thorax) can be scanned during a single breath-holding episode. Conventional CT requires that the breath be held during each slice; it is much slower, as the x-ray source needs to be reset after each slice. The exact clinical role for helical CT is still being developed. Areas where it is being used diagnostically are:

Thorax—3-D visualization of the airways; assessing metastatic and solitary pulmonary nodules; diagnosing pulmonary emboli. Using helical CT for the diagnosis of PE has been the most widely studied and in many medical centers is the most common test used for the diagnosis of PE. The interobserver variability for reading helical CT scans for PE is much less than for reading ventilation/perfusion scans. The negative predictive value of a normal helical CT for ruling out PE is 98%.

Abdomen—Diagnosing cause of urinary colic (instead of using intravenous pyelograms [IVPs]); working up liver masses; diagnosing or excluding appendicitis or diverticulitis.

Vascular system—Besides pulmonary angiography, helical CT is being evaluated for use in diagnosing stenoses, aneurysms, and AV malformations in other areas of the body. Because of loss of resolution due to heart pulsations, helical CT is not good for visualizing coronary arteries.

MRI is based on computer analysis of the electromagnetic energy released by protons after they have been excited by radio frequency waves. Protons, when in a magnetic field, tend to wobble, the way a top can wobble, at a specific frequency dependent on the strength of the magnetic field being applied. Some of these wobbling protons can absorb energy supplied at the same frequency as that of the wobble—which is in the radio frequency (RF) range. When the RF pulse is stopped, the protons quickly release this energy and "decay" back to the pre-RF pulse state at an exponential rate. The electromagnetic energy being given off is read as a shift in the net magnification. The MRI machine sets up the magnetic field, applies the radio frequency, and then measures the duration of the return of the net magnetic field to normal. The half-life in the return-to-pre-pulse level of the parallel component of net magnetization is T1 (as in $e^{-k/T1}$). That of the perpendicular component is T2. In pure water, T1 = T2. With biological tissue, T2 is much shorter than T1.

What in the world does this mean?! Well, the outcome is that the sensors can be tuned to T1 or T2 (or proton-

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density, or spin-echo, or perfusion, or diffusion, etc.), resulting in the same tissues appearing different in the differently weighted images. Examples: In T1 images, the gray and white matter appear as stated (gray = gray and white = white), while in T2 images the gray matter still appears gray, but the white matter appears dark gray. CSF appears black in T1 and white in T2, etc. See Table 10-1 and Table 10-2 for more on the differences in T1-weighted vs. T2-weighted, as compared with CT images.

Advantages of MRI include:
- high soft-tissue contrast resolution
- sensitivity to iron buildup in tissues
- sensitivity to blood flow
- sensitivity to tissue edema (diffusion-weighted—infarct detection)
- the ability to reconstruct images in planes of any orientation
- no susceptibility to beam-hardening artifacts
- absence of ionizing radiation

MRI is preferred over CT for most CNS diseases because MRI has increased sensitivity to soft tissue variations (including white vs. gray matter), and can be reconstructed in different views (sagittal, coronal, and transverse). MRI is also preferred over CT in the workup of osteonecrosis (avascular/aseptic necrosis) of the hip and for spinal cord diseases/problems (MRI is not affected by bone).

More specifically, MRI is the procedure of choice for:

CNS disease:

Brain—best for:
- determining size, location, and extent of neoplasms, abscesses, and cysts.
- detecting demyelinating plaques.
- determining neurodegenerative problems such as atrophy, old infarcts, iron deposits, and white matter disease.

Spine—best for all myelopathy (spinal cord problems)—from intrinsic cord lesions to all causes of cord compression; e.g., best for working up suspected disk herniation and for spinal stenosis.

Non-CNS disease:

Bones—osteonecrosis of the hip.

Lung—for evaluating abnormalities at apex, near spine, and at the thoracoabdominal junction. Also useful for evaluating solid organs.

Disadvantages of MRI: It cannot be used on persons with pacemakers, ferromagnetic aneurysm clips, or metal prostheses.

Myelography using CT and iohexol (a non-ionizing iodine-based contrast agent) is not done much anymore but still may be done in a patient with spinal cord impingement if there is a contraindication to MRI or occasionally to clarify an ambiguous or negative MRI with highly suggestive impingement symptoms.

Ultrasonography is used in the workup of:
- cold thyroid nodules
- gallstones,
- heart vegetations,
- heart valve problems,
- pericardial effusion,
- in obstetrics
- kidney dysfunction after transplant
- aortic root disease (Marfan syndrome),
- cold thyroid nodules (solid vs. cystic),

Ultrasound has a very important use in diagnosing high-grade carotid stenosis as the cause of ischemic cerebrovascular disease; patients with high-grade stenosis do better with an endarterectomy + medical therapy than with medical therapy alone.

Doppler ultrasound is best for evaluating a septal rupture of the heart and severity of valve stenosis. It is also used to follow below-the-knee DVT (for migration above the knee). Remember that Doppler ultrasound (like impedance plethysmography) is better at finding above-the-knee DVTs than below-the-knee DVTs.

Ultrasound or CT can be done for workup of chronic pancreatitis and for evaluating/measuring abdominal and popliteal aneurysms. For thoracic aneurysms, transesophageal ultrasound is just as effective as CT (and ultrasound, of course, is less expensive than CT).

LUNG DISEASES

V/Q Scan

The ventilation scan is usually done with Xe^{133}; the perfusion scan is always done with Tc^{99m} microaggregates. You do the ventilation scan before the perfusion scan.

Pre-pneumonectomy: Do quantitative V/Q scans to evaluate lung function in borderline patients (i.e., $FEV_1 < 1.6$–2L). Compare the scans to the pre-op FEV_1 and consider surgery if the post-op FEV_1 is predicted to be > 800 cc.

COPD: The ventilation scan shows delayed Xe washout.

Pulmonary emboli: Risk of PE is high if there are segmental mismatched perfusion defects (i.e., no associated ventilation defect). Matched defects still have a 25% probability of PE! See the Pulmonary Medicine section for more. Besides acute PE, the DDx of a V/Q mismatch includes old embolism, A-V fistula, and a tumor compressing the vessels. The V/Q scan for the diagnosis of PE is not very helpful in patients with severe underlying lung disease (such as COPD). Pulmonary angiography is the gold standard to rule out PE. Contrast venogram is the gold standard test used to rule out possible associated DVT.

CARDIOVASCULAR DISEASES

Thallium stress test: This test is much more sensitive and specific than the exercise ECG stress test. Tl^{201} is distributed to the myocardial tissue in proportion to blood flow. Infarcted areas and scarred tissue show up as "cold spots." Ischemic sections show up as areas of decreased uptake. Increased heart rate increases the sensitivity of the test, so you usually use a treadmill. Decreased uptake while under stress, that then clears up over the next few hours, is a sign of ischemia

notes

Quick Quiz

1) Which imaging study is best for ruling out a bleed in the CNS?
2) Which imaging study is preferred for working up CNS *disease*?
3) Patients with high-grade carotid stenosis are best treated with which therapies?
4) If a bone scan is negative, what does that tell you about the probability of osteomyelitis?

in that area. Increased lung uptake just after exercise indicates stress-induced LVF.

Use dipyridamole, a strong coronary artery dilator, instead of exercise when the patient is unable to exercise.

Tc99m pyrophosphate concentrates in infarcted cardiac tissue. Uptake is maximum 2–3 days after injection. It is limited in its usefulness, so it is only occasionally used (if other tests are equivocal).

Radionuclide ventriculography (RNV) is especially good for checking ejection fraction (normal EF > 45%). EF increases with exercise in normal patients, but this effect is blunted in patients with ischemic heart disease. RNV also shows wall motion defects; they can be global (tamponade, constrictive pericarditis) or regional (MI, ventricular aneurysm). There are 3 techniques for RNV:

1) "First-pass RNV" is just a video of the bolus of Tc^{99m}-labeled RBCs passing through the heart.
2) "Gated pool scanning" is done after a bolus of Tc^{99m} has reached equilibrium. In this, there is made a composite image, formed by averaging many images taken at the same time in each cycle.
3) "Gated first pass," is a combination type of RNV, where several gated images are taken during first pass of the bolus.

For all practical purposes the RNVG has been replaced by estimated EF done by echocardiography. The one remaining niche for RNVG has been for use as a sensitive measure of EF pre- and post-cardiotoxic chemotherapy.

Peripheral scans: The Tc^{99m} radionuclide peripheral nuclide scan has less resolution than contrast arteriogram or venogram. Contrast venogram is the gold standard for DVT.

BONE DISEASE

Bone Scan

Bone scintigraphy (bone scan). The usual agent is technetium Tc 99m methylene diphosphonate, which binds to hydroxyapatite crystals present during osteoblastic activity—as occurs with new bone formation. This occurs with almost all bone injuries, especially trauma, osteomyelitis, and cancer. A negative scan will rule out osteomyelitis, but a positive scan is fairly nonspecific! A common cause of increased uptake is arthritis.

Bone scintigraphy is still very useful for the following:

1) Stress fractures. Specifically, finding stress fractures not seen by x-ray. Stress fractures are a crack in the cortical bone caused by repeated low-level impact. Plain-film radiography has a sensitivity as low as 15% for finding stress fractures(!)—but it is still the first test performed when a stress fracture is suspected. Delayed bone scan films typically show an intense spindle-shaped (fusiform) area of cortical uptake in the area of the stress fracture.
2) Acute fractures. Although MRI has pretty much supplanted the bone scan for finding occult fracture in trauma patients, bone scan is still used to detect suspected fracture in patients for whom the x-ray was negative or equivocal. Generally this is a followup procedure because best results are achieved > 72 hr after the acute event. Examples: wrist/elbow/rib fractures. It is also useful in osteoporotic patients in determining number and age of osteoporotic fractures.
3) Bone metastases. The bone scan is the best screening procedure for bone metastases. These typically show up as multiple asymmetric foci of intense tracer uptake. Note that symmetric increased uptake usually means nonmalignant disease. Remember bone metastases are common in lung, prostate, and breast cancer.
4) Paget disease. Bone scan is the most sensitive means for detecting Paget disease and should be the first test you do when this disease is suspected—most commonly because of an elevated alk phos is the initial finding.

Remember that there is bone lysis without a blastic response (so a negative bone scan) with multiple myeloma, eosinophilic granuloma, and a rapidly growing cancer involving the bone.

If you see decreased uptake in a hip, think of osteonecrosis (otherwise called aseptic or avascular necrosis—found with femoral neck fractures and in patients on high-dose glucocorticoids). MRI confirms the diagnosis.

Osteoporosis

Photon absorptiometry measures bone mass. Single photon absorptiometry is used in bones with little overlying tissue (usually the radius), but dual photon absorptiometry is required to determine bone mass in areas such as the spine and hips. Because the spine is the first area to have bone loss in osteoporosis, the dual absorptiometry is more sensitive than single for early osteoporosis. Another equally sensitive method is quantitative CT scan, but it is more expensive and gives a higher radiation dose. Remember: Bone loss can proceed at different rates in different bones, so assess each area of interest separately! (see osteoporosis on pg 10-8)

GI DISEASES

Abnormal GI anatomy is best seen with CT scan. For esophageal motility, gross disturbances are best studied with barium swallow and manometry, but you may detect subtle disturbances better with radionuclide studies. Evaluate gastric emptying with a Tc^{99m} test meal. A solid meal is better than

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liquid for finding mild emptying disorders. GI bleed: Radionuclide studies with (yes, you guessed it) Tc^{99m}-labeled RBCs or Tc^{99m}-labeled sulfur colloid are good only for determining GI bleed distal to the duodenum and proximal to the colon. GI bleeds occurring proximal to the jejunum and in the colon are usually best evaluated with endoscopy. In bile duct obstruction, the HIDA scan (hepatic Tc^{99m}-iminodiacetic acid scan) is the procedure of choice; a positive test is non-visualization of the gallbladder. All other obstructions and abnormalities are best detected by ultrasound, oral cholecystogram, and/or CT scan. Liver: CT scan is best for finding and initial evaluation of all focal liver abnormalities.

URINARY TRACT

You typically do IVP to evaluate obstructive problems. You use ultrasound, IVP, and CT to evaluate anatomic problems. In acute renal failure, do ultrasound first. Then, if tumors are detected, do CT/MRI. Use radionuclide imaging to determine renal function; e.g., after ultrasound and renal biopsy in the evaluation of renal dysfunction in a renal transplant patient.

There are 4 agents used for renal radionuclide scans.

1) Tc^{99m} Diethylenetriamine penta-acetic acid (DTPA) is an inulin analog that is excreted by glomerular filtration and so indicates GFR.
2) I^{131} orthoiodohippurate is excreted only by tubular secretion.
3&4) Tc^{99m} dimercaptosuccinic acid (DMSA) and Tc^{99m} glucoheptonate are used for checking the amount of functional renal cortex (not used much).

ENDOCRINE

Thyroid Scan

You cannot do radioactive iodine uptake if the patient has recently had iodinated products. $I^{123 \text{ or } 131}$ uptake is diffusely increased in Graves disease and decreased in thyroiditis and factitious hyperthyroidism (intentional over-replacement with thyroid hormone). You can determine thyroid nodule function also by amount of I^{123} uptake; nodules will be either "hot" or "cold." Cold nodes are always fine-needle aspirated. See thyroid function tests in the Endocrinology section.

One can usually safely give I^{131} treatment to hyperthyroid patients, but it is not safe to give it to either pregnant patients or patients with severe hyperthyroidism.

Pheo

I^{131}-metaiodobenzylguanidine (I^{131}-MIBG) will concentrate in pheochromocytomas in 1–2 days.

INFECTIONS

$Gallium^{67}$ concentrates in WBCs and lymphoma cells. $Indium^{111}$-tagged WBCs are attracted to inflammatory sites. You can use either of these studies to find occult abscesses, but the indium scan is usually preferred. Use a Gallium scan if a splenic abscess is suspected (indium normally localizes in the spleen, so is of no help) and to evaluate pulmonary infection (especially probable PCP in AIDS patients with normal chest x-ray—although not done much anymore). You should not do an indium scan within 1 month of a Gallium scan. Note: If the location of the abscess is suspected, first do a CT scan in this location.

PHARMACOLOGY

PHARMACOKINETICS

Absorption

First-pass effect: Oral drugs are absorbed via the GI tract and pass into the portal vein, which goes to the liver. Drugs metabolized by the liver will then undergo "first-pass" metabolism. These drugs require a much higher oral dose to be as effective as a parenteral dose of the same medicine. Common drugs that undergo first-pass effect are:

1) opiate related: meperidine, morphine, and naloxone
2) calcium antagonists: nifedipine, verapamil, and diltiazem
3) some beta-blockers: labetalol, metoprolol, and propranolol
4) tricyclic antidepressants
5) benzodiazepines
6) anticonvulsants: valproic acid and phenytoin
7) NSAIDs: ibuprofen, ketoprofen, naproxen, and indomethacin
8) other: cyclophosphamide, theophylline, warfarin, and metronidazole

Some drugs require an acid environment for absorption—especially itraconazole and ketoconazole. These drugs should not be used with H_2 blockers or proton pump inhibitors.

A very important interaction that interferes with absorption occurs when cations combine with thyroid hormone or quinolones. This is especially common with calcium, iron, and antacids containing magnesium and aluminum.

Distribution

Volume of distribution (V) [Know]: This is the effective volume for determining the total amount of drug in the body and for determining the loading dose. The total amount of drug in the body (D_T) is equal to the volume times concentration:

$$D_T = V\,(C_p)$$

so the volume of distribution is:

$$V = D_T/C_p$$

V = the volume of distribution. This is the apparent volume into which the drug is dispersed. C_p is the concentration of the drug in the plasma. If the tissues hold more drug than the plasma at equilibrium, "V" will be large. Rule of thumb: If the drug is dosed at each half-life, the total amount of drug (D_T) is double the maintenance dose.

Note that the loading dose does not depend on excretion capability! The loading dose in a patient with renal failure is the same as that in a healthy patient, but, if the drug is cleared by

notes

Quick Quiz

1) What will be the difference in radioactive iodine uptake in Graves vs. thyroiditis?
2) If you find a cold nodule on radioactive iodine uptake, what is your next diagnostic step?
3) If you suspect a splenic abscess, which test is indicated first—Gallium scan, indium scan, or CT scan?
4) Define 1st order kinetics.
5) How long should you wait before checking a blood level for a drug that follows 1st order kinetics?
6) What drugs does warfarin interact with most severely?

the kidney, the subsequent maintenance dose will be very different.

Excretion

Drugs mainly excreted by the liver include all of those mentioned above under high first-pass effect.

In a person with cirrhosis, the decreased first-pass effect increases the effective bioavailability of the above drugs. Clearance is also decreased, so the effective dose of a drug may be very small.

Meperidine is metabolized by the liver to normeperidine, which is an active metabolite causing CNS stimulation (including seizures). Normeperidine is cleared by the kidney. So carefully watch a patient with hepatic or renal dysfunction when on meperidine!

First-Order

First order kinetics: The rate at which a drug is cleared is independent of the drug concentration. After one half-life, the drug level in the body will be only half of the initial level. It is possible to determine the half-life by checking two blood levels at a certain interval (between doses).

As seen in Table 10-3, 5 half-lives after a patient is started on a first-order drug (without a loading dose) the drug level will be 97% of steady state. Also, if a first-order drug is stopped after 5 half-lives, the drug will be 97% gone. So, when starting patients on a medication (with no loading dose), usually wait 3 to 5 half-lives before rechecking the blood level to see if you need to adjust the dosage.

Table 10-3

# half-lives	% of steady state
1	50
2	75
3	87.5
4	93.75
5	96.875

Drug Interactions

Note

There are thousands of drug interactions, but several are so serious—and thus frequently on the Boards—that we will cover them here.

Warfarin interactions

The interaction between warfarin and trimethoprim-sulfa can markedly raise the INR. This interaction both displaces warfarin from protein binding sites and affects metabolism leading to marked elevations of the INR. Trimethoprim-sulfa has a short half-life, so this interaction occurs in the first few days of therapy. Table 10-4 outlines the most important warfarin interactions

Table 10-4

Warfarin Interactions	
Most Severe:	Possible:
TMP/Sulfa	Ciprofloxacin
Erythromycin	Omeprazole
Amiodarone	Clarithromycin
Propafenone	
Ketoconazole/fluconazole	
Itraconazole	
Metronidazole	

Drugs that cause hyperkalemia

Several drugs cause hyperkalemia and are crucial to know. ACE inhibitors, ARBs, spironolactone, and other potassium-sparing diuretics all can cause severe hyperkalemia. The risk is far greater when several of these drugs are combined (as seen in the treatment of heart failure). Trimethoprim can cause hyperkalemia by blocking amiloride-sensitive channels in the renal tubule. The risk is greatest in the elderly and with use of high-dose trimethoprim-sulfa.

Statin Interactions

The most life-threatening reaction to a statin is rhabdomyolysis. The risk is much greater when statins are combined with drugs that slow their metabolism. The drugs that affect statin metabolism are fibrates, erythromycin, cyclosporine, azole antifungals, protease inhibitors, verapamil, and diltiazem. Grapefruit juice will also markedly raise the blood levels of

notes

some statins by inhibiting initial metabolism. Lovastatin and simvastatin are most affected.

STATISTICS

SENSITIVITY AND SPECIFICITY

The Bayesian 4-Square

Note: T = true, F = false, P = positive, N = negative

KNOW statistics perfectly!

To make sense of the 4-square used in answering sensitivity and specificity questions, we will go over Figure 10-1. Let's assume we have a group of cattle being tested for a deadly disease. They go through the testing station on the left and are directed to either the upper corral if their test is positive or down if their test is negative. All cattle are then driven across the corral to the right, but this disease is so deadly, all the diseased cattle die before they get to the far right of the corral. So we are left with the four sets of cattle. This square is very useful in determining sensitivity, specificity, and positive and negative predictive value.

Sensitivity takes into account only those who have the disease. Sensitivity = true positives (# of patients with disease who test positive) divided by the total # of patients with disease (those who test positive plus the false negatives). Or ... sensitivity = TP/(TP + FN). (See Figure 10-1.)

Specificity takes into account only those who do not have the disease. Specificity = true negatives (# of patients without disease who test negative) divided by # of patients without the disease. Or ... specificity = TN/(TN + FP).

To help remember: Note that sensitivity takes into account only those who have the disease and specificity takes into account only those who do not have the disease. This means that each one is independent of the prevalence of the disease in the selected population! Prevalence of disease is just the percentage of the population with the disease.

The "positive predictive value" (PPV) of a diagnostic test is the probability of disease in a patient with a positive test—i.e., PPV = P(disease | positive test). To figure this, you take into account the numbers of both the true positives and the false positives. This combination does reflect prevalence. The formula is PPV = TP/(TP + FP). Makes sense; true positives divided by all those who test positive! If a disease is rare, even if the sensitivity and specificity are high, the false positives may greatly outnumber the true positives, making the chance of having the disease with a positive test (PPV) much less. This is one of the main factors used to determine whether a screening program is feasible.

The "negative predictive value" (NPV) of a diagnostic test is the probability of not having a disease if the test is negative—i.e., NPV = P(no disease | negative test). Using the 4-square, the formula is TN/(TN + FN).

The prevalence (or prior/pretest probability) is merely the fraction of the population who have the disease. This is (Total with disease)/Total, or (TP + FN)/((TP + FN) + (FP + TN)).

Not all the data may be given in a question asking you to find sensitivity, specificity, PPV, etc.; it is very useful to use Table 10-5 in its stripped-down form (Table 10-6). You insert the given values and then calculate for the blank spaces! The givens in the following example are filled in and solved in the following series. When all the spaces are filled in, the question is easily answered. Know this stuff!

Example: Incidence of cancer is 1/200 in a population. In a test under consideration, if sensitivity = 99% and the frequency of abnormal tests in the population is 1.3%, what is the ratio of false positives to true positives ... and is this a good screening test? To solve, first draw the Table 10-6 and fill in the given numbers. This gives us Table 10-7.

If the population is not given, assume 1 million. 1/200 incidence gives 5,000 total persons with cancer. 0.013 x 1 million gives 13,000 total abnormal tests. Then just subtract to find the number without cancer (995,000) and the number of normal tests (987,000). [Note that the 5,000 and 995,000 are the denominators in the sensitivity and specificity equations!]

Then we find the other blanks in the order shown 1, 2, 3, and 4. Blank (1) is the only one requiring thought:

Sensitivity = TP/(TP+FN) or .99 = TP/5,000
So: TP = 4,950.

The others are found by subtraction. See Table 10-8.

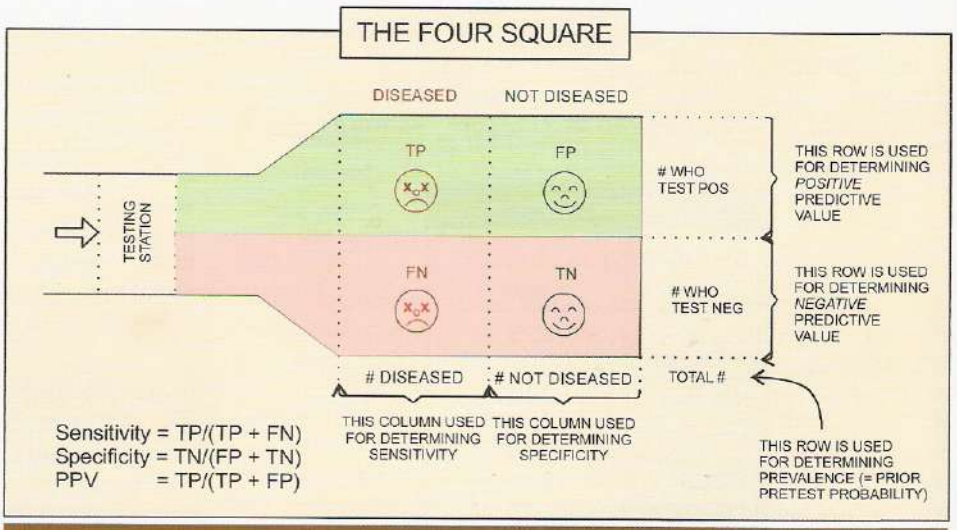


Figure 10-1

Notes

Quick Quiz

1) You have invented a test that is 90% sensitive and 95% specific for screening of breast cancer. If you tested 100 women with known breast cancer, how many would the test pick up?
2) On the test they tell you that a study shows a new treatment for lung cancer improves survival by 60% and the P-value for the study is 0.2. Based on this, would you recommend this treatment?
3) On the test they tell you that a study shows a newer treatment for lung cancer improves survival by 5%, and the 95% confidence interval for the study is 1.6 to 4.9. Assuming treatments have the same side effects, would it be worthwhile considering the new treatment?

Once you have the entire matrix filled in, you can solve any problem provided there is enough information. In this example, PPV = TP/(TP + FP) = 38%—*not* a good percentage for a screening test! If data given to solve the problem are insufficient, it will become apparent when you are unable to fill in all the blanks.

What happens if you change the threshold for normal in a test? If you increase the threshold for what is normal, you will get more negative tests—both true-negative and false-negative. This will decrease the sensitivity and increase the specificity.

Why is this? Assume we did this for the previous example. Because the numbers of people with and without the disease remain the same, the denominators in the sensitivity and specificity equations remain the same. In the sensitivity equation, the numerator decreases (decreased TP due to increased FN), so sensitivity decreases; i.e., fewer of those with the disease are found by the test.

In the specificity equation, the numerator increases, so specificity increases; i.e., those testing negative are less likely to have the disease.

As a quick trick, think of the threshold for normal of the test as being the line in the 4-square that divides the top from the bottom—as the threshold increases, the line rises, indicating decreasing numbers of TP and FP and increasing numbers of FN and TN. As the threshold decreases, the line goes lower, indicating increasing positives and decreasing negatives. Because the denominator stays the same, just see what happens to TP and TN. If TP increases, sensitivity increases. If TN increases, specificity increases.

You will also see that any time the test normals are redefined, sensitivity will increase at the expense of specificity and vice-versa.

As disease prevalence and incidence decrease, the number of false positives increases while the number of false negatives decreases—so the ratio of false positives to false negatives increases. This occurs because there is no change in the sensitivity or specificity of the diagnostic test.

Table 10-5

	Disease	No Disease	Total
Abn tests	TP	FP	TP+FP
NI tests	FN	TN	FN+TN
Total	TP+FN	FP+TN	

Table 10-6

I. Sketch this FIRST:

	with	without	Total
Abn tests			
NI tests			
Total			

Table 10-7

II. Based on the GIVEN:

	with	without	Total
Abn tests	1	3	13,000
NI tests	2	4	987,000
Total	5,000	995,000	1,000,000

Note that the 5,000 and 999,000 are the DENOMINATORS in the sensitivity and specificity equations!

Table 10-8

III.

	with	without	Total
Abn tests	4,950	8,050	13,000
NI tests	50	986,950	987,000
Total	5,000	995,000	1,000,000

notes

P-Value

The *P*-value is a way of expressing a study's statistical significance. Suppose a randomized trial compares 2 drugs and concludes that Drug A is better than Drug B. The smaller the *P*-value, the more confident we can be that drug A really is better than drug B and that this is not simply a chance occurrence. Thus, if a study has a *P*-value of .05, the likelihood that the results are due to chance is only 1 in 20 (= 5%; or $P = .05$). *P*-values of less than .05—such as .01 or .001—imply even greater statistical significance. For some arbitrary reason, a *P*-value less than or equal to .05 is considered statistically significant.

The above is probably ($P < .05$, ha!) all you need to know for most questions on *P*-values, but you should know more of the theory. *P*-value is the probability of the result in question occurring, assuming that the distribution of occurrences used for the calculations is correct. Let's do a rough "for instance": Say you normally see one case of giardiasis in your office per week. Then one week you see 4 cases and you wonder if an epidemic of giardiasis has started. How often should you see 4 cases a week, if you normally see only one case per week?

What you assume is chance variation results in a mean (average) incidence of giardiasis of one case per week and that the variation in occurrences is per a certain distribution. This is generally called the "null" or "chance" hypothesis. The distribution can be plotted from thousands of cases, or we can further assume it follows a standard distribution such as the Poisson distribution. Assuming this is correct, what is the probability of 4 cases occurring in one week? What you do is go to a table that displays various values of the distribution and read the *P*-value off the table. In this case, $P = .019$.

The way to read this is, "Assuming that the average incidence of giardiasis is 1 case per week and further assuming that the weekly incidences of giardiasis fit into a normal Poisson distribution, then the probability of 4 cases per week occurring by chance is 1.9%." This seems small, and it is, but it does mean that you can expect to see 4 cases per week about once per year (assuming the assumptions are correct!). Now, if you see 4 cases again the following week ... !

A recent addition to the literature (and Boards) has been the use of "95% confidence intervals." This essentially is the same as a $P < 0.05$, but they will give you values that vary. If the "95% confidence interval" does NOT cross 0, then it is considered significant. For example, if they tell you the 95% confidence interval is 0.5 to 1.9, then that would be a significant result. However, if they tell you the 95% confidence interval is -0.7 to 1.6, then that is a nonsignificant result! Know this!

Type 1 And Type 2 Errors

Type 1 and Type 2 errors:

Type 1 = concluding that there is a difference (reject null hypothesis) when there is no difference. This is typically expressed by the *P*-value. This reflects the willingness of the investigator to declare a benefit when there is none.

Type 2 = concluding that there is no difference (accept null hypothesis) when one exists. In other words, this is the likelihood that the trial will miss a true difference between the two test groups.

Meta-Analysis

Meta-analysis is the retrospective analysis of many studies concerned with the same topic. There are several methodological flaws and biases involved with this, as well as several severe statistical restraints. Compiling studies with differing type 1 and type 2 errors is difficult. Other areas of difficulty include ages of participants and assumptions of the magnitude of difference expected between the experimental groups.

Not only will you be asked about all of the above, but you will also see sensitivity, specificity, predictive values, and *P*-values repeatedly in your medical reading.

Number Needed to Treat

The number needed to treat (NNT) is the number of people who need to be treated for a period of time to prevent one event. NNT is calculated by taking the inverse of the absolute risk reduction between intervention and control groups.

$NNT = 1/RR$

Example: A new drug is studied to see if it can reduce heart failure mortality. Mortality in the treatment arm (active drug) was 10/100, while mortality in the placebo arm was 30/100 during a 4-year followup.

NNT= 1/(30/100–10/100)= 1/(.3 - .1) = 5

This means five patients must be treated for four years to prevent one death.

GERIATRICS

BONE

Osteoporosis is common in the elderly and is generally suspected by clinical presentation. There are many risk factors for primary osteoporosis:

- advanced age
- female gender
- Northern European ancestry
- postmenopausal
- positive family history
- prolonged inactivity
- thin build
- glucocorticoid use
- tobacco use
- alcohol use
- anticonvulsant use.

Secondary causes of osteoporosis that you rule out in a workup include

- Cushing syndrome
- hypogonadism
- hyperthyroidism
- hyperparathyroidism
- osteomalacia
- multiple myeloma.

The most significant x-ray findings are multiple vertebral compression fractures.

The 3 most accurate methods of diagnosis (by determining loss of bone mineral density) are:

- quantitative CT,
- dual photon absorptiometry (DPT), and
- dual energy x-ray absorptiometry (DEXA or DXA).

notes

Quick Quiz

1) What are the secondary causes of osteoporosis that you rule out in a workup?
2) What is the preferred method of screening in osteoporosis?
3) A patient on alendronate presents with difficulty swallowing. What is the likely etiology?
4) True or false: DVT can still occur in women with hip fractures while on DVT prophylaxis therapy.
5) Memorize the 4 stages of pressure sores.
6) If an elderly patient presents with weight loss and disinterest in activities, what diagnosis should be at the top of your list?

Quantitative CT scan gives a larger dose of radiation and is more expensive. CT scan and DPT take a lot of time. DEXA is the preferred method. It is the newest, the quickest (about 15 minutes), the least expensive, and the most accurate! Precision of DEXA is +/– 1–2% whereas precision of DPT is +/– 2–5%.

Bone mineral density (BMD) reports usually have two results—the T score and the Z score. The T score compares results with normal young healthy bone; a T score of –1.0 means the BMD is 1 standard deviation (SD) less than normal—about 10% low. A T score of –2.5 or lower is the definition of osteoporosis (about 25% below normal), whereas those between –1 and –2.5 suggest osteopenia. The Z score compares the BMD result to age- and sex-matched controls and is not used for treatment but rather to see if there is accelerated osteoporosis, which would suggest secondary factors such as drugs might be involved. The USPTF recommends screening all women age 65 or older with DEXA scans, and selectively screening women 60–64 based on the presence of osteoporosis risk factors.

Treatment and prevention of osteoporosis:

- Premenopausal (preventive): elemental calcium 1.0 gm q.d.
- Postmenopausal: elemental calcium 1.5 gm +/– estrogen replacement +/– bisphosphonate.
- Both: weight-bearing exercises, adequate vitamin D (800 IU/day needed for proper absorption of calcium).

FDA-approved drugs are:

1) hormone replacement therapy (HRT),
2) the bisphosphonates alendronate (Fosamax®) and risedronate (Actonel®),
3) calcitonin, and
4) raloxifene (Evista®).

HRT may prevent or reverse the development of osteoporosis, BUT its use in the peri- and postmenopausal woman is a two-edged sword. See HRT in Geriatric endocrinology, pg 10-11.

The bisphosphonates are analogues of pyrophosphate and, like estrogen, inhibit bone resorption. Bisphosphonates and HRT appear to have an additive effect.[1] They effectively act as antagonists of parathyroid hormone (which causes resorption—a release of calcium from the bone into the serum). Alendronate is indicated when HRT is not indicated (or else not wanted by the patient). Alendronate is both poorly absorbed and a notorious cause of severe esophagitis; the patient must carefully follow the recommendations to take it with a full glass of water on an empty stomach and not eat or lie down for 30 minutes after ingestion. Risedronate was FDA approved April 2000 for the prevention and treatment of postmenopausal osteoporosis. It has the same clinical effect as alendronate but may have fewer GI side effects. Even so, the same dosing precautions are taken as with alendronate.

Calcitonin-salmon nasal spray at 200 mg/d increases bone mineral density and therefore decreases risk of hip and vertebral fractures.[2,3]

Raloxifene. During the development of antiestrogens, it was discovered that some substances that block the effect of estrogen on some tissues actually mimic estrogen on others! These are called selective estrogen-receptor modulators (SERMs). Examples are tamoxifen and raloxifene. The effect of raloxifene on bone and lipid levels is similar to, but less than, estrogen—but! … it exerts estrogen-antagonistic effects on the breast and uterus and may be less likely to cause cancer than traditional HRT (1999 STAR trial ongoing—Study of Tamoxifen and Raloxifene). Raloxifene is FDA approved for both prevention and treatment of postmenopausal osteoporosis.

A note on parathyroid hormone: Parathyroid hormone initially promotes an increased rate of bone resorption. It also increases calcium absorption from the gut, and the net effect is increased serum calcium level and new bone formation. Because of this it is being evaluated as treatment for osteoporosis. This seems odd at first because the blocking of its resorptive effect is how the other drugs work—but it is the net effect that is being studied. I suspect that soon treatment will include calcium, vit D, PTH, and a resorption blocker.

Fractures are the most serious consequence of osteoporosis. There are 1.5 million fractures per year due to osteoporosis, with 300,000 of those due to hip fracture. Mortality due to hip fractures is about 20% the first year! Femoral neck and intratrochanteric fractures account for 97% of hip fractures.

Wearing hip protectors can reduce hip fracture risk by 50–66%.

Femoral neck fractures are intracapsular and occur below the femoral head but above the trochanters. Displaced femoral neck fractures often disrupt the blood supply to the femoral head and result in osteonecrosis and/or nonunion; therefore, the treatment of choice is either femoral head replacement or total hip arthroplasty. Undisplaced femoral neck fractures have a low incidence of osteonecrosis and nonunion, so these are usually treated with internal fixation with pins or screws.

Intertrochanteric fractures are extracapsular and are usually treated with internal fixation with a "sliding hip screw."

In both types of fracture, the main goal is achieving mobility and function as soon as possible, thereby avoiding the morbidity and spiraling complications due to poor mobility:

DVT occurs in 48% of hip fracture patients without anticoagulants. With anticoagulation, DVT occurs in 24% and 27% respectively for those on Coumadin or subQ low-molecular-weight heparin.

notes

MOBILITY and GAIT

Falling

Age is associated with increased instability and falls. 25% of patients age 70 and 50% of patients age 80 fall each year! The elderly have a stiffer, less agile gait with decreased position reflexes. The falls result in fractures and, if the patient cannot get up, possibly hypothermia and dehydration. Treat by assessing gait and checking medications for possible etiology. Check vision. It may be necessary to restrict certain activities, improve lighting at home, decrease hazards, and place extra supports (bars in the shower, etc.) at home. There is an increased incidence of post-prandial falls in the elderly. This is due to a decrease in blood pressure (systolic and diastolic), which is thought to be due to the carbohydrates in the meal.

Risk factors for falls are:

- age
- female gender
- past history of falls
- cognitive impairment
- lower extremity weakness
- balance problems
- arthritis
- psychotropic drug use

The drugs most commonly implicated are benzodiazepines antidepressants, and anti-seizure drugs.

There are 4 quick office tests that can be done to assess the risk for fall in the elderly[4]:

- gait speed (slower = ↑ risk)
- tandem (heel-to-toe) walk
- visual acuity
- calf circumference (smaller = ↑ risk)

The major predictor for fracture from a fall is osteoporosis. Because some neuromuscular dysfunctioning and many visual acuity problems are amenable to treatment, always do a full workup on a patient with a history of falling.

Always check for syncope as a cause of the fall and do a syncope workup if the patient does not remember the fall or if the history is suggestive. Syncope occurs more often in patients with coronary heart disease, orthostatic symptoms, cerebral vascular disease, aortic stenosis, and decreased functional states.

Immobility

Patients adapt to bedrest, and the longer a patient is immobilized, the harder it is to ambulate again. Immobilization causes decreased ADH secretion → diuresis → decreased blood volume → orthostatic symptoms. Also, immobilization causes muscle atrophy. The heart continually deconditions after 2 days of bedrest. The elderly are more affected by bedrest because they have less reserve than young people. Treat with rehabilitation.

Pressure Sores

Pressure sores. There is about a 5–10% incidence in hospitals, 20% in nursing homes. Sustained pressure is the main etiologic factor. Other factors include shear, infection, moisture, and friction. There are 4 stages of pressure sore formation. Stage I is non-blanching erythema. At this stage there are reddish macules. Stage II is partial-thickness skin loss seen as a small superficial ulcer. Stage III is full-thickness skin loss. Stage IV is loss of tissue down to the muscle, tendon, or bone. Most common places that pressure ulcers occur are the heels, trochanter, sacrum, and iliac crest.

To prevent a soft tissue ulcer, rotate an immobilized patient side to side (30-degree angle) every 2 hours. This prevents contact against the major pressure points mentioned above. If an ulcer already exists, there should be absolutely no pressure allowed against the area, and ensure adequate nutrition with additional vitamin C (one gm/d). Remove necrotic tissue (wet-to-dry dressings, Water Pik, surgical). Use an antibiotic solution (dilute sodium hypochlorite or very dilute iodine solution). Dilute the povidone-iodine solution to less than 1% solution (normal is 10%); otherwise it decreases wound healing capability. Cover the wound with a saline dressing. If it is an earlier-stage wound (stages I–III), one of the easier-to-use dressings can be applied. DuoDerm® is a hydrocolloid dressing. Hydrocolloid dressings do not allow oxygen to penetrate, so do not use these if there is infection. Thin films (OpSite®) allow oxygen to penetrate. As far as the specialized beds, the air bed (e.g., Clinitron®) is very expensive and not proven superior. Animal studies with pulsed DC current across the wound are promising.

IMMUNE FUNCTION

Decreased immunity is age related. Total T and B cell numbers stay the same, but the number of CD4 T cells increases with age, while the number of CD8 T cells decreases with age. Also only half of the T cells remain competent! This is why the patients can get herpes zoster, reactivation of tuberculosis, and possibly the polio virus.

ENDOCRINE

Diabetes

Aging is associated with decreased carbohydrate tolerance, shown as a slight increase in fasting glucose. Elderly patients also have an increased incidence of hypoglycemia after being started on hypoglycemics for DM. Worst are the first generation agents such as chlorpropamide (29%). Surprisingly, glyburide, which is the most popular oral hypoglycemic drug, has about twice the incidence of hypoglycemia in the elderly compared to glipizide (27% vs. 14%!).[5] Be cautious with metformin use in the elderly because of the high prevalence of renal insufficiency in this population. Measure CrCl prior to use of metformin in patients > age 80, and do not give the drug to patients with a CrCl less than 60.

Hyperthyroidism

Most older persons with new-onset hyperthyroidism present with some symptoms suggestive of hypothyroidism, so be sure to check for both! Most of the classic symptoms of hy-

notes

Quick Quiz

1) What are the risk factors for falls in the elderly?
2) Name the 4 office tests done to assess the risk of falling in the elderly.
3) What are the risks and benefits of HRT in elderly women?
4) How does dementia differ from delirium?

perthyroidism, such as hyperreflexia, heat intolerance, tremor, nervousness, polydipsia, and increased appetite are usually absent in elderly persons with hyperthyroidism. Suspect hyperthyroidism in elderly patients with fatigue, anorexia/weight loss, and tachycardia (this complex often termed "apathetic hyperthyroidism"). With hypothyroidism, atrial fibrillation and anorexia occur more frequently in older than in younger persons.[6]

Hormone Replacement Therapy

The risks and benefits of hormone replacement therapy in postmenopausal women are not fully defined. There is no standard of care yet. HRT definitely alleviates vasomotor and other menopausal symptoms.

Estrogens with progestin are associated with an increased risk of cardiovascular events in the first year and shows no benefit at 7 years out (HERS trial). The use of HRT in women with known coronary artery disease is controversial at this point. Generally, if the woman is already on hormonal replacement, it may or may not be *continued*, but you would not *start* it after an AMI.

The HERS trial also showed increased risk of thromboembolism and biliary tract surgery in those on long-term HRT therapy.

One study suggests HRT may improve cognitive function and have some benefit re Alzheimer disease. HRT also appears to delay/prevent osteoporosis, but its long-term use is associated with the development of endometrial and breast cancer.[9]

Long-term unopposed estrogen use may increase the lifetime risk of endometrial cancer 10-fold, whereas short-term use increases the risk 3-fold. Cyclic therapy with a progestin added significantly reduces the risk of endometrial cancer, BUT it may actually increase the risk of breast cancer (over that with estrogen alone).

Because of the risk either way, it is strongly suggested that the decision to treat or not is determined after discussion between the doctor and the well-informed patient.

HRT frequently causes breast pain and vaginal bleeding—a common reason for discontinuing treatment … which reminds me (and you):

A woman should undergo endometrial assessment if she has postmenopausal bleeding[10]:

- in the absence of HRT therapy,
- after she has been on combined HRT continuously for 1 year without bleeding, or
- at an unexpected time during cyclic replacement.

Raloxifene is the SERM (selective estrogen-receptor modulator) also discussed in the Bone topic under Geriatrics (starts on pg 10-8). The effect of raloxifene on bone and lipid levels is similar to, but less than, estrogen—but! … it exerts estrogen-antagonistic effects on the breast and uterus and may be less likely to cause cancer than traditional HRT (1999 STAR trial ongoing—Study of Tamoxifen and Raloxifene). Raloxifene does not cause breast pain or vaginal bleeding but it unfortunately causes hot flashes—a common reason for discontinuation. It is approved for both prevention and treatment of postmenopausal osteoporosis.

MENTAL / NEUROLOGIC

Delirium

Delirium is confusion with altered consciousness. It is a common problem in the elderly. Main features are abnormal attention span (easily distracted), disorganized thinking (may have hallucinations), and altered consciousness (with increased or decreased mental activity). There are many precipitating causes of delirium, including an acute alteration of the patient's life; e.g., new surroundings, physical or mental stress, and decreased sleep (post-op is a common setting to have it). Many medications may induce delirium in the elderly, most commonly the anxiolytics, cardiac medications, and cimetidine. The quinolone antibiotics are a common cause of delirium. Acutely discontinuing sedatives, benzodiazepines, alcohol, and pain medications may cause withdrawal delirium.

Note that delirium occurs in up to 56% of elderly patients during acute care hospitalizations! Precipitating factors include drugs, infection, malnutrition, multimeds (> 3), use of a bladder catheter, and use of physical restraints.[11]

Treatment of delirium is supportive care and the removal of any underlying cause. Things such as signs, a night-light, newspaper, radio, etc., help orient the patient and prevent decompensation. It is also necessary to minimize daily stress. If needed, immediate pharmacologic treatment should be with a drug with little extrapyramidal effect (loxapine and perphenazine are the least expensive; olanzapine, clozapine, quetiapine, ondansetron are much more expensive). If the patient is having anticholinergic delirium, consider using agents with higher extrapyramidal potential (haloperidol).[12,13]

Dementia

Patients with dementia have an insidious onset with progressive deterioration of cognition, but no altered consciousness as in delirium. Demented patients have a decrease in recent memory, trouble with impulse control, and decreased simple problem-solving ability. About 2/3 are treatable. Of the rest,

notes

about 1/2 have Alzheimer disease, and 1/4 have multi-infarct dementia. Treatable causes of dementia are drugs, then depression, then normal pressure hydrocephalus. See the Neurology section for more on dementia, including Alzheimer disease. Briefly: Donepezil (Aricept®), an acetylcholinesterase inhibitor, is the most established treatment for Alzheimer disease although recent studies show only a transient effect; its role in vascular dementias is uncertain. Tacrine, a less specific acetylcholinesterase inhibitor, is not used anymore due to liver toxicity. Ginkgo biloba extract appears to slow the progression of dementia[14], and vitamins A and D are associated with improved cognition in elderly patients.[15]

Depression

Depression is the most common mental problem in the elderly, but it is also common in other age groups. Look for vegetative signs, weight loss, and dysphoria. Often it is a reactive depression 2° to a disease (CVA, Parkinsonism, etc.). A host of drugs can precipitate depression. These include the following:

- alcohol
- antineoplastics
- beta blockers
- corticosteroids
- hormones
- sedatives
- cardiac drugs
- antiparkinsonian drugs
- cimetidine
- cycloserine
- psychotropics
- stimulants

Also remember that there is a direct correlation between erectile dysfunction (ED) and depression.

Treatment is usually psychotherapy combined with antidepressants, and sometimes electroconvulsive therapy (ECT). Previously, tricyclic antidepressants and MAO inhibitors were the mainstay of treatment. Now, the selective serotonin reuptake inhibitors (SSRIs) are the 1st-line therapies. Newer drugs, which act on multiple receptors, are also being used. The most common reason for stopping these agents is sexual dysfunction! See Table 10-9.

With antidepressants in the elderly, always start with low dose and increase dosage slowly. Maintenance therapy with a combination of both psychotherapy and antidepressants is much better than either type of treatment alone.[16]

Sleep Disturbance

Sleep disturbance is a common problem in elderly persons. These disturbances include difficulty falling asleep, frequent wakings (up to 60%), and waking too early. Although benzodiazepines are often given for these symptoms, they may actually cause or worsen insomnia. In one study,[17] both depression and benzodiazepine use were independently highly associated with poor sleep initiation. Best therapy with long term effectiveness (in patients with uncomplicated insomnia) is behavioral—not pharmacologic.[18]

Table 10-9: Antidepressants. Selective Receptor Blockers

DRUG	T 1/2 (hrs)	BLOCKS	Notes	Drug of choice for...	Caution!...
Fluoxetine (Prozac®, Serafem®)	72	SSRI	*May cause anxiety and insomnia.		...with insomnia
Paroxetine (Paxil®, Pexeva)	20	SSRI	*Most anticholinergic of the SSRIs		...if anticholinergics are to be avoided. ...with insomnia
Sertraline (Zoloft®)	25	SSRI	*GI discomfort common		...with insomnia ...with irritable bowel
Fluvoxamine (Luvox®)	15	SSRI	*Most sedating of the SSRIs	...pts with agitation ...pts with insomnia ...pts with obsessive-compulsive disorder	...with irritable bowel
Citalopram (Celexa®)	35	SSRI	*		
Nefazodone (Serzone®)	3***	SSRI and 5-HT2 and has anti-alpha adrenergic activity	Maintains sleep architecture; sexual dysfunction unlikely	...pts with insomnia; ...to maintain sexual activity	Interacts with cytochrome P-450 system..caution with benzodiazepines and antihistamines**
Venlafaxin (Effexor®)	4	SSRI and norepinephrine reuptake and some dopamine reuptake			...with insomnia. Do not use if pt has hypertension.
Bupropion (Wellbutrin®)	15	Reuptake of dopamine and some norepinephrine	Sedation unlikely, sexual dysfunction unlikely		May increase blood pressure. Do not use if pt has insomnia.
Mirtazapine (Remeron®)	20	Presynaptic alpha2 receptor (increases seritonin and norepi release) AND 5-HT2 AND 5-HT3	Agitation unlikely, sexual dysfunction unlikely. Good for insomniacs.	...pts with insomnia; ...to maintain sexual activity	Most anticholinergic of all these. May increase blood pressure

*All the SSRIs have a tendency to cause agitation, sedation, and sexual dysfunction. Pure SSRIs are NOT likely to increase blood pressure.
**May use loratadine (Claritin®) or lorazepam (Ativan®) with nefazodone ***T 1/2 is higher in elderly, esp women
Note: Buspirone is a 5-HT1A agonist which can be combined with the SSRIs to decrease the dose or improve efficacy.

notes

Quick Quiz

1) What drugs commonly pricipitate depression in the elderly?
2) Know Table 10-9!
3) What is the best therapy for insomnia in the elderly?
4) What should you do for an elderly woman who is on chronic low-dose benzodiazepines for "nerves"?
5) What is the most frequent reason for hospitalization in the elderly?
6) Should isolated systolic hypertension be treated in the elderly?
7) What is a common reason for anti-depressants to be discontinued by patients? This is why these agents are sometimes prescribed for men with premature ejaculation.
8) Urinary incontinence is common in geriatric women. Is it a normal consequence of aging?

Dizziness

Dizziness is common in the elderly but is not a normal consequence of aging. It is often a multifactorial problem associated with disorders of multiple organ systems.[19] There is a similar multifactorial association with falls, functional dependence, and urinary incontinence in the elderly.[20] Any such findings suggest the need for a careful workup to determine which of the problems are treatable. Note that about 30% of geriatric patients with severe dizziness have a cardiovascular etiology—reliably suggested by a history of lightheadedness or syncope, pallor, need to sit or lie down, and symptoms being precipitated by long standing.[21]

DRUG DEPENDENCE

Many elderly patients are dependent on low-dose benzodiazepines (BDZ) or narcotics. For these patients, you should attempt a slow withdrawal of these medications.[22] These have often been mis-prescribed or mismanaged as treatment for anxiety, insomnia, depression, transient pain, drug withdrawal, etc. Use a slow taper to withdraw. General principles: Taper BDZs over 3–6 months after switching to an equivalent dosage of a water-soluble BDZ, such as oxazepam (slower onset, less addictive potential). With narcotic dependence, first determine the cause of pain (if any) and treat it with a non-narcotic drug (NSAID, acetaminophen). Avoid long half-life narcotics in treating geriatric pain.

CARDIOVASCULAR

Walking more than 4 hours per week is associated with a dramatic decrease in cardiovascular-related hospitalizations of persons > 65.[23]

As long as hypertension is treated, it does not matter what type of antihypertensive agent is used (newer or older type drug).[24]

The 6-month mortality rate after an MI increases with age—from 4% around age 66 to 12% when older than 80 (first MI, with thrombolytics, discharged from hospital). Only about 75% of eligible patients are receiving aspirin on discharge from the hospital. Be sure to prescribe an antiplatelet drug to these patients![25]

The incidence of congestive heart failure (CHF) in the elderly is increasing dramatically and is now the number 1 cause of hospitalizations in the elderly (number 2 is pneumonia—see below!). Early control of isolated systolic hypertension has been shown to decrease the incidence of heart failure and therefore decrease hospitalizations and improve the quality of life.[26] Previously, isolated systolic hypertension was often ignored, with the apparently incorrect thinking that it was a functional response to aging vessels. So treat isolated systolic hypertension in the elderly!

Treat CHF itself primarily with diet, diuretics, and ACE inhibitors. Digoxin is indicated only for more severe heart failure. Isosorbide dinitrate and beta-blockers have an important secondary role. Use of NSAIDs is an important precipitant of CHF in elderly patients with risk factors for CHF.

LUNG

Pneumonia is the number 2 cause of hospital admissions in the elderly (after CHF). Initiating antibiotic therapy as soon as possible results in a dramatic decrease in mortality rate.[27] Initiate antibiotic therapy on a clinical basis, even without chest x-ray if that would delay the treatment.

UROLOGY

Incontinence

Urinary incontinence

Normal micturition is dependent on an intact neurologic pathway from the brainstem to the bladder, which causes relaxation of the sphincter muscle's tonic contractile state just milliseconds before contraction of the detrusor (bladder muscle). Additionally, voluntary control of micturition requires communication between the cerebral cortex and the brainstem.

Urinary incontinence, although a common geriatric problem (1/3 of elderly women!), is always considered a pathologic condition and is not a normal consequence of aging! Normal age-related changes to the urinary tract (decreased flow rate and bladder capacity, increased residual volume) may predispose to incontinence.

Urinary incontinence problems may be thought of as either a "storage problem" or an "outflow" problem. Storage problems are bladder (detrusor) over- and under-contractility, while the outflow problems are outlet obstruction or incompetence.

notes

There are 3 general symptom-based terms given to urinary incontinence:

1) Urge incontinence = Detrusor overactivity (cystitis, detrusor hyperreflexia)
2) Stress incontinence = Outlet incompetence (urethral hypermobility, sphincter problem)
3) Overflow incontinence = Outlet obstruction, anticholinergics, detrusor underactivity, psychogenic retention BPH

Let's discuss these.

1) Urge incontinence is the most common cause of geriatric incontinence. With urge incontinence, there is passage of small amounts of urine even with a non-distended bladder. This is caused by detrusor instability (overactivity), usually caused by CNS problems (termed detrusor hyperreflexia), but also sometimes a result of cystitis.

Detrusor hyperreflexia is due to progressive loss of communication between the frontal lobes and the micturition center in the brainstem. As the bladder loses the modulating influence from the brain, it tends to spasm more often (hyperreflexic). It is best treated with behavioral therapy (bladder training) in which the patient progressively delays voiding by 5–10 min per day until a goal of every 2–3 hours is attained. Bladder training is more effective than the more commonly prescribed therapy of antimuscarinic agents (oxybutynin, tolterodine, hyoscyamine, tricyclic antidepressants), which both relax the detrusor and have other anticholinergic side effects.[28] Even so, these antimuscarinic agents are helpful when used as an adjunct to bladder training—short-term, as needed.

2) Stress urinary incompetence (SUI) is second in frequency in geriatric women. With SUI, the urethra cannot maintain the pressure gradient required for urinary control when there is an increase in intraabdominal pressure (cough, jumping, etc.). It is usually due to a hypermobile urethra. This may be due to multiple vaginal deliveries, pelvic surgery, or postmenopausal hormonal changes (low estrogen → atrophic relaxation of the vaginal wall → lack of support for the urethra). Stress incompetence is initially best treated with Kegel exercises (perineal muscle contractions) and nightly application of conjugated steroid cream to the external urinary meatus. Use of estrogen cream is controversial if the patient has a history of breast cancer. Only 10% of cases are caused by an actual sphincter muscle problem. Note that elderly women with urinary incontinence often have a mixture of SUI and urge incontinence.

3) Overflow incontinence (usually prostate hypertrophy causing outlet obstruction) is second in frequency in geriatric men (after urge incontinence) and rare in women. Outlet obstruction causes a distended bladder and high-volume *post-void retention*. Anticholinergic drugs are the most common causes of drug-induced overflow incontinence. Most types of overflow incontinence do indeed cause urgency and may be seen as a type of urge incontinence.

↑PVR

Detrusor underactivity is usually due to a neurologic problem (termed detrusor areflexia). Think of diabetic neuropathy, MS, and trauma/lesion to the sacral cord or pelvic nerves.

Psychogenic retention leads to overflow incontinence.

Benign prostatic hyperplasia (BPH) increases in incidence from about 10% at age 30 to 90% at age 85 (!)—with about 15% of those causing problems urinating. Previously, transurethral resection of the prostate (TURP) was the only treatment for BPH, but this procedure has significant morbidity and about 20% of patients have no relief with the procedure. Now pharmacologic therapy has surpassed TURP for the initial treatment of BPH. Agents used are alpha-blocking agents (terazosin, doxazosin, tamsulosin—an $alpha_{1A}$ blocker) and blockers of 5-alpha-reductase (finasteride).

In one study,[29] comparing the alpha-blocking agent terazosin (Hytrin®) with finasteride (Propecia®, Proscar®), terazosin provided by far the best symptomatic relief. This is especially true for smaller prostates and is thought to be due to relaxation induced in the muscular portion of the gland. The finasteride is not nearly as effective as terazosin for immediate symptom relief, but it may work better (albeit more slowly) on large prostates.

Note 1: Finasteride blocks the conversion of testosterone to dihydrotestosterone (DHT). DHT is a potent androgen on which both BPH and male-pattern baldness are dependent.

Note 2: Of the 3 postsynaptic alpha-blockers, tamsulosin is the most specific for the subtype receptor ($alpha_{1A}$) found in the prostate stroma. It is also the one with the least side effects such as postural hypotension.

Fecal Incontinence

Fecal incontinence (geriatric) is usually caused by fecal impaction and the secondary overflow incontinence. The impaction is usually caused by lax muscles and neuronal degeneration. Typical presentation is an elderly person with complaints of diarrhea, fecal incontinence, and abdominal discomfort, and the finding of hard stool in the rectal vault.

Impotence

Overview

Male sexual dysfunction is classified as follows: sexual aversion disorder, orgasmic disorder, premature ejaculation, hypoactive sexual desire disorder, and erectile dysfunction (ED). We will discuss ED.

ED review: ED is defined as the persistent (> 3 mo) inability to achieve or maintain an erection sufficient for satisfactory sexual performance.

The smooth muscle in the flaccid penis is in a state of tonus or *contraction due to alpha stimulation by norepinephrine*. cGMP is made along with cAMP (made by the norepinephrine and vasoactive intestinal peptide (VIP) pathways). This cGMP cause the relaxation of the smooth muscle in the penis, which increases the inflow through the helicine artery into the erectile tissue. The swelling of this tissue causes

notes

Quick Quiz

1) What is the best treatment for urge incontinence?
2) What is the best treatment for stress urinary incompetence?
3) What is the initial treatment for BPH?
4) Explain the common presentation for fecal incontinence in an elderly patient.
5) What is the most common cause of neurogenic impotence?
6) Which medications most commonly cause impotence?
7) If they present a young male to you on no medications with impotence, what is the most likely etiology? What if he is on beta-blockers?
8) What is the mechanism of action for sildenafil?

compression of the outflow venules resulting in a sustained erection.

ED can be caused by organic or psychological problems, or as a side effect of medications. Most causes of ED are at least partially organic. The organic causes are neurogenic, vascular, hormonal, and normal aging.

Classic Presentations and Causes of ED

Organic causes: Usually slow onset. Loss of nocturnal and morning erections.

- Neurogenic: Usual cause is diabetes. Other causes are surgical procedures, MS, ALS, Parkinson, other causes of peripheral neuropathy.
- Vascular: Usual cause is diabetes and/or cardiovascular disease. Other causes are surgical procedures, inflammatory conditions, pelvic fracture.
- Hormonal: Often a loss of libido. Symptoms may include gradual onset of frontal headaches or visual disturbances (space-occupying tumor); hot flashes and decreased need for shaving (decreased androgens); fatigue + weight gain + dry skin + constipation (hypothyroidism from low TSH).
- Normal aging: Sexual potency does decrease with age.

Medications: Especially beta blockers, methyldopa, and thiazide diuretics. Also inotropic agents, hormones, lipid-lowering drugs, and even NSAIDs. Antidepressants meds may cause a loss of libido without affecting erectile function.

Psychogenic: Usually acute onset. This is the usual cause for impotence in younger patients. They continue to have nocturnal and morning erections. ED is directly correlated with depression. Unfortunately, the serotonin reuptake receptor inhibitors (SSRIs) are associated with a very high incidence of sexual dysfunction.[30]

In elderly men, ED is caused by vascular compromise in 50% (indicated by a low penile brachial pressure index [PBPI]). ED due to vascular compromise indicates increased risk of present and future major vascular disease. Medications cause about 25% (usually beta blockers, methyldopa, and thiazide diuretics).

Treatment Options for ED

First-line:

Sildenafil citrate (Viagra®) inhibits phosphodiesterase type V (PDE5), an enzyme that inactivates cGMP. It works very well—about 70% across the board, 43% in those with radical perineal prostatectomy, 50–60% in diabetic ED, 90% in those with psychogenic origin and spinal cord injury. Side effects are due to its vasodilatory properties—headaches, flushing, dyspepsia (due to PDE5 blockage in the lower esophageal sphincter), bluish hue (due to transient blockage of PDE6 in the retina). Contraindications are any concurrent nitrates. Relative contraindications are CHF, hypotension, unstable angina, HCM, and severe aortic stenosis.

Vardenafil (Levitra®) is similar in mechanism, effectiveness, and side effects to sildenafil.

Tadalafil (Cialis®) has the same mechanism of action as sildenafil and tadalafil but a longer half-life. Erectile function may be improved for up to 36 hours.

Vacuum devices work well but are clumsy to use. They are indicated only when oral therapy is contraindicated or the patient prefers them to oral therapy.

Yohimbine is a naturally occurring alpha-blocker. It has minimal effect but, because it is inexpensive and has minimal side effects, it is often tried on patients with a mostly psychogenic etiology. Better than placebo but much less effective than sildenafil.

Trazodone is occasionally used (antidepressant, serotonin uptake inhibitor). Not very effective.

Second-line:

Alprostadil (prostaglandin E1) injected into the corpora cavernosa of the penis works well. It is especially useful in patients with ED due to neurologic dysfunction.

Third-line:

Penile implants. Various types—hydraulic, semirigid and flexible rods. Usually used only for those who have failed all other therapy. May have devastating complications.

HEARING

Decreased hearing is age related. About 1/3 of patients > 65 have a hearing loss. Most common cause is presbycusis, which is just age-related decreased function of the inner ear. Be sure to check for cerumen impaction. See other causes of decreased hearing on pg 10-35.

IATROGENIC

There is a 20% chance of a hospitalized elderly person getting a serious iatrogenic problem (which prolongs the hospital stay). Antibiotics are the most common medications causing

notes

complications in hospitalized patients. The most common serious adverse effect of these antibiotics is pseudomembranous colitis, which is caused by *C. difficile*.

ETHICS

Read the ACP's "Ethics Manual."[31] This is also available online at "www.acponline.org/ethics/ethicman.htm"

The physician's duty to the patient is based on:

A) Beneficence—the duty to act in the best interests and welfare of the patient and the health of society, and

B) Nonmaleficence—the duty to do no harm to the patient, and

C) Respect for the patient's autonomy—helping the patient make free uncoerced choices.

These 3 principles are the basis for all ethical physician-patient interaction.

Let's look at specifics.

The patient's right to accept or refuse health care is based on 3 principles:

1) the philosophical concept of personal autonomy—a value held close to the heart in our culture,

2) personal liberty interest under the Constitution, and

3) common law right of self-determination.

Patients should be able to choose and follow their own ideas and plans for their life. Constraint of a person's free choices is permissible only when these choices infringe on another person's rights and welfare. Paternalism, the practice of overriding or ignoring preferences of patients in order to benefit them, used to be the standard of interaction between the physician and patient. Today, except for certain cases (mental illness, some emergencies), this is considered ethically improper. Patients should be an active part of the decision-making process. Patients require informed consent, which is defined as the willing acceptance of medical intervention after adequate disclosure by the physician of the nature of the intervention and all of its risks and benefits.

The physician's patients are entitled to disclosure of the following:

1) The patient's current medical status with the probable course, whether medical intervention is used or not.

2) The medical interventions that may help and the risks associated with them.

3) The physician's opinion about other alternatives.

4) The physician's own recommendations based on best clinical judgment.

The advance directive is the means patients have for stating which treatments they would accept or decline if they lost decision-making capacity. The advance directive may also specify general goals for medical care, and the patient's choice of a surrogate—a person with durable power of attorney for the patient's health care.

A living will is a more focused form of advanced directiv which the patient refuses life support when in a term condition. A lawyer is not needed to make a living will.

PATIENT'S COMPETENCY OR DECISION-MAKI CAPACITY. The decision-making capacity refers to the a ity to comprehend, evaluate, and choose among realistic tions. The decision-making capacity of the patient can be ficult to determine. There are many transitory or reversi conditions that can interfere with this capacity. Examples anxiety, depression, drug-induced confusion, and abnor metabolic states. The waxing and waning associated w certain conditions, such as organic brain syndrome, i manifestation of pathology, and the patient should be cons ered to have impaired capacity.

SURROGATE. A "surrogate" or "proxy" is a person who authorized to make decisions on behalf of an incapacita person. Traditionally the next of kin has been considered natural surrogate. In some states there is a well-defined list the order of next of kin with priority as natural surrogates e.g., spouse, then parents, then children, then siblings. A other option is for the subject to give someone durable pow of attorney. This means giving decision-making authorizati to a person who supersedes family members. Remember, t "contract for health care," if you will, is between the phy cian and the patient, not the patient's family.

The surrogate's decisions must promote the patient's wish and welfare. If the patient has expressed certain wishes or topic regarding medical intervention in the past, the surroga must use that knowledge in the decision-making process. the surrogate has no knowledge of the patient's wishes, th the surrogate must make decisions based on the patient welfare. Welfare should include consideration of sufferin preservation of life, restoration of function, and quality life, and should be considered as what a reasonable perso would want in similar circumstances.

EMERGENCY SITUATIONS. For patients unable to expre their preferences, the physician may perform life-sustainin emergency procedures under the presumption that the alte native would be death or severe disability. All states hav statutes allowing the physician to hold patients with certai psychiatric conditions against their will for medical and/o psychiatric treatment. This is often called a "medical hold."

QUALITY OF LIFE AND PAIN RELIEF IN PALLIATIV CARE. The quality of life in terminally ill patients in pain i considerably improved by proper pain relief. Terminal pa tients in pain are in a special situation, and their requests fo pain meds generally should be honored. The downside o pain medications is that they can cause confusion and a de creased ability to communicate. You have to strike a balanc between maximum pain relief with minimal decrease in con sciousness. The assistance of hospice workers in this situa tion can be very helpful.

notes

Quick Quiz

1) 6 months ago Mr. Jones, a man with terminal cancer, decided to invoke a living will that said he refuses all life support in case of cardiopulmonary arrest. Today he presents to the ER in severe distress and says he wants everything done, including intubation. His family doesn't want anything done, and you have the signed living will at the bedside. What should you do now that his personal preference has changed in the face of a signed living will and family wishes for nothing to be done?
2) You see a colleague in his car drinking beer on the way to work for a 12-hour shift in the ER. Are you obligated to inform anyone?
3) Know ALL of the scenarios in the ethics section!

PHYSICIAN-ASSISTED SUICIDE. The latest guidelines by the ACP and the AMA prohibit euthanasia (where the physician directly kills the patient). While the AMA denounces any form of physician-assisted suicide, the ACP is still formulating its position.

CPR and DNR. Cardiopulmonary resuscitation (CPR) is usually a standing order in a hospital—i.e., it is to be carried out, without specific order, on any patient who suffers cardiac or respiratory arrest. The only time CPR is not done is when there is an order stating such—a "do not resuscitate" (DNR) or "do not attempt resuscitation" (DNAR) or "No Code" order. The decision about non-resuscitation has three considerations that must be assessed:

1) Whether or not CPR would be futile—i.e., that the resuscitation would be unlikely to succeed or, if it did, another cardiac or respiratory arrest would soon follow.
2) The preferences of the patient.
3) Expected quality of life of the patient if resuscitation succeeds. It is the responsibility of the physician to initiate discussions with patients (or, if the patient is incompetent, with family members or a surrogate) who are terminally ill or have incurable diseases with an estimated 50% survival of less than three years. The attending physician should clearly write the "do not resuscitate" order on the order sheet in the patient's chart. The progress notes should detail the facts and opinions leading to that decision.

SUICIDE ATTEMPTS should always be treated despite the wishes of the patient. These patients are often "crying for help." They are also often in a pathological mental state that may be transitory or treatable. This situation is different from the patient who refuses life-sustaining treatment. The difference is that with refusal of care, the patients are not killing themselves—rather, they're refusing help that would keep them alive (uh, ... okay).

CULTURAL DIFFERENCES. A patient from another country/culture can present some ethical dilemmas. If the family of your elderly patient states they wish their grandmother not be told about a terminal illness such as cancer, you can explain to your patient that she is very sick and ask whether she wishes to make these decisions or prefers to have them made by another. If it is the custom, the patient often will want others to make the decisions. This can then be considered an authorized delegation of decision-making authority. If the patient says she wants to know everything and make her own decisions, you must side with the patient.

CONFIDENTIALITY AND PUBLIC WELFARE. The personal and medical information that a physician obtains from a patient is (ethically and legally) confidential. BUT! ... in general, if the conditions or disease of a patient can endanger other persons, the physician is legally and ethically obligated to report the situation to the appropriate parties. Many are straightforward and are written as legal statutes. Common examples are sexually transmitted diseases and conditions that could affect the operator of a motor vehicle, such as seizures and severe cardiac arrhythmias. Others are more difficult. A patient with a highly infectious serious disease (TB, meningococcemia) should not be allowed to infect others. These patients can be held against their will if their behavior is considered a threat to others. Less infectious diseases may necessitate informing the patient's employer (health care worker, food worker, etc.).

BRAIN DEATH. Physicians may stop treatment if a person is "brain dead" (loss of entire brain function, including brain stem). An EEG is not required for diagnosis. Organs can then be donated without patient's prior consent if the next of kin (surrogate) gives permission, knowing that the patient would want that.

PHYSICIAN-PHYSICIAN vs. PUBLIC WELFARE OBLIGATIONS [Know!]. The physician should not allow any incompetent or unethical conduct by other physicians. If you know of such conduct, the evidence should be presented to the appropriate entity. This may be the division chief or ethics committee of the hospital. Most state and many county medical societies now have confidential treatment of impaired physicians. Physicians who strongly suspect another physician is chemically impaired are obligated to urge the physician to seek treatment. If this impairment may affect medical competence, the obligation is to report the "credible evidence" to the local medical society. Note that the physician cannot act only on hearsay, but must have credible evidence before reporting it.

DRUG RESEARCH. It is unethical to use socioeconomic differences in choosing patients for a drug study unless the socioeconomic status is considered a variable. For example, you cannot ethically test a drug only on those who can pay for it. Conversely, you cannot ethically offer a free drug for research only to those in a lower socioeconomic status.

notes

Some scenarios:

1) A patient enters the hospital unconscious and near death with a terminal disease. What should the physician do if:
   a) the patient has a properly executed living will that states no intubation, CPR, etc.
   b) the patient has no living will, but family members say they strongly prefer the patient be allowed to die with dignity and without heroics.
   c) same as "a" but family members (many of whom are lawyers) say they want all possible heroic measures be done—and threaten dire consequences if their wishes are not followed!
2) A patient comes to the ER with an extensive acute MI, is mentally competent, and refuses to be admitted despite being fully informed of the possible consequences. What do you do?
3) A respirator-dependent patient requests in writing to be extubated. What do you do?
4) A female health care worker who is found to have hepatitis B antigen positivity requests that you not tell her supervisor at the hospital where she works.
5) A man is diagnosed with inoperable metastatic cancer. He states to his physician that he does not want his wife to know.
6) A newly married man just finds out that he has an autosomal dominant serious genetic disease such as Huntington disease. He requests that the physician not tell his wife.
7) A man finds out he is HIV positive and requests that you not tell his spouse.
8) A woman with suspected meningococcal meningitis refuses to be admitted and wants to go back to work.

Answers:

1) a) Follow instructions in the living will.
   b) In this situation the physician needs more information; needs to know the wishes of the patient, not the family!
   c) Follow instructions in the living will; the contract is between you and the patient. Besides, so far, all living wills have held up in court.
2) You must show caring for the patient's situation, yet attempt to dissuade the patient from leaving. If the patient still leaves, it is prudent to have the patient sign out "AMA"—against medical advice (the patient is not legally required to do this). You cannot stop patients from leaving unless you think they are mentally incompetent or a danger to others (e.g., they want to drive home).
3) You need more information (mentally competent, fully informed, etc.). This is a problem with probable far-reaching consequences, not just for you, but for the patient's other doctors, the hospital, and the patient's family. First step is to contact the hospital's ethics committee. You may also need assistance from the patient's other doctors, family, psychiatry, and social services.
4) This health care worker has a direct obligation not to cause harm to the patients with whom she interacts. If she refuses to inform the hospital infection control team, then you are obligated to do so.
5) Although the physician can strongly encourage the man o his wife's moral right to know the situation, communicatin this to the spouse is ultimately the patient's obligation an not the physician's.
6) In this case, the physician should first strongly encourag the man to tell his wife. If that fails, the last resort is for th physician to tell the wife because of the risk of harm to fu ture children.
7) In all HIV cases, the physician must make sure that any body at-risk (e.g., through sexual contact or IV drugs) is no tified. Whenever patients say they are going to do the noti fication, the physician must ensure it is done. Usually this obligation is taken care of by the state health department.
8) This patient may be held against her will for the good o public welfare.

PREOPERATIVE EVALUATION

Preoperative evaluation of a patient to determine the risks of having a cardiac event in the perioperative period is a topic that has been stressed strongly lately—in the literature and on the Boards. There have been several guidelines produced by different medical societies. We will go over the AHA/ACC "Guidelines for Perioperative Cardiovascular Evaluation for Noncardiac Surgery" and the ACP "Guidelines for Assessing and Management of Perioperative Risk from Coronary Artery Disease Associated with Major Noncardiac Surgery." These two guidelines have some significant differences and significant similarities. It is the similar areas on which you are likely to be tested.

Study Figure 10-2. Note that on this diagram and the following ACP diagram, any younger patient with no risk history may proceed directly to minor surgery without being evaluated per the flowchart. The chart diagrams the 3 assessments that the AHA & ACC want you to do.

1) The 1st assessment is determining the clinical risk profile for that patient. This is done with a history and physical exam and an ECG for men older than 40 years and women older than 55 years, and in any patient with suspected heart disease.

2) The 2nd is determining functional capacity. This is expressed in metabolic equivalent levels or METs, that correlate with oxygen consumption. Functional capacity is considered excellent if > 7 METs, moderate if 4–7 METs, and poor if < 4 METs. (A symptom that relates to level 3–4 METs is angina with walking one or two blocks or climbing one flight of stairs. Angina with walking more than two blocks or more than one flight of stairs is in the 5–6 MET area. Using a history of symptoms, you can determine the patient's functional capacity.

Note: From the chart, you can see that the functional capacity, in this protocol, basically adds one more risk category. Rather than the original low risk, moderate risk, and major risk, there is now a new low-to-moderate risk category that

notes

Quick Quiz

1) Know Figure 10-2 and Figure 10-3!!! Make up a bunch of scenarios for yourself. Example: An 80-year-old man without significant medical problems who jogs 5 miles a day and needs prostate surgery—what workup, if any, does he require?
2) (The Boards may not simulate real life.) You are seeing a 38-year-old man who smokes 2 packs a day of cigarettes with chief complaint of "cold ." You have 20 patients in the waiting room who are waiting to be seen. Besides his smoking, what 11 other things should you counsel him about?
3) What is the 5th vital sign?

includes both low-risk patients with poor functional capacity and moderate-risk patients with good functional capacity.

3) The 3rd consideration is the risk of the surgery in the assessment (Table 10-10). The AHA/ACC recommends a stress test for all moderate-risk patients with poor functional capacity and for moderate-risk patients with good functional capacity if they are having a high-risk surgery. As noted on the chart, this latter group is in the same category as the low-risk group with poor functional capacity—i.e., they too would require a stress test for any high-risk surgery. The stress test in the AHA/ACC protocol can be an exercise stress test, dipyridamole thallium imaging (DTI), or dobutamine stress echocardiography (DSE). The major-risk patients go into a similar stratification protocol as that shown in the ACP preoperative risk assessment diagram (Figure 10-3).

The ACP has come up with its own set of guidelines for evaluating preoperative cardiac risk (See Figure 10-3 and Table 10-11). As with the AHA/ACC guidelines, younger patients with no risk history may proceed directly to minor surgery without being evaluated per the flowchart. Study the ACP chart. You'll notice that all patients with a low-to-moderate risk index can proceed directly to surgery except for those moderate-risk patients who are having vascular surgery. These patients have a dipyridamole thallium imaging (DTI) or dobutamine stress echocardiography (DSE)—not an exercise stress test. The major-risk patients from each protocol are treated similarly. Basically you determine what is the cause of their risk and if it is modifiable. If this patient has ischemic heart disease, determine if the patient is a candidate for revascularization per the AHA protocol. For patients with CHF, valvular heart disease, or significant arrhythmias, optimize their medical therapy if time allows. Once medical therapy is optimized and the patient is more stable, then re-evaluate using the same protocol. If the patient has non-modifiable factors, such as old age, cancel the surgery or modify it to make it less risky to the patient.

DIFFERENCES BETWEEN THE TWO PROTOCOLS:

The ACP protocol is more of an "evidence-based" protocol. This results in a leaner, easier-to-remember protocol.

1. The ACP does not use functional capacity in its protocol. They state that this assessment has not been shown to add to the clinical risk index evaluation in this setting.
2. Whereas the AHA uses exercise stress testing in addition to the DTI and DSE, the ACP has found that the standard exercise stress testing shows poor predictive value in patients having surgery. Additionally, the only stress testing that has shown to have good predictive value, especially strong negative predictive value, are the DTI and DSE in intermediate-risk patients having vascular surgery. It is not proven of use in those patients having non-vascular surgery.

SIMILARITIES BETWEEN THE TWO PROTOCOLS:

The following similarities between the protocols are what you are most likely to be tested on. Note that in both protocols, young patients with no systemic disease undergoing minor surgery need not go into the flow chart at all and may proceed directly to surgery.

1. Both protocols inherently agree that non-invasive testing should not be used routinely and that all stratification strategy should include assessment for known operative risk factors.
2. They are in agreement that low-risk patients with good functional capacity can proceed directly to surgery with no other tests.
3. Major-risk patients in each protocol go through a similar workup.

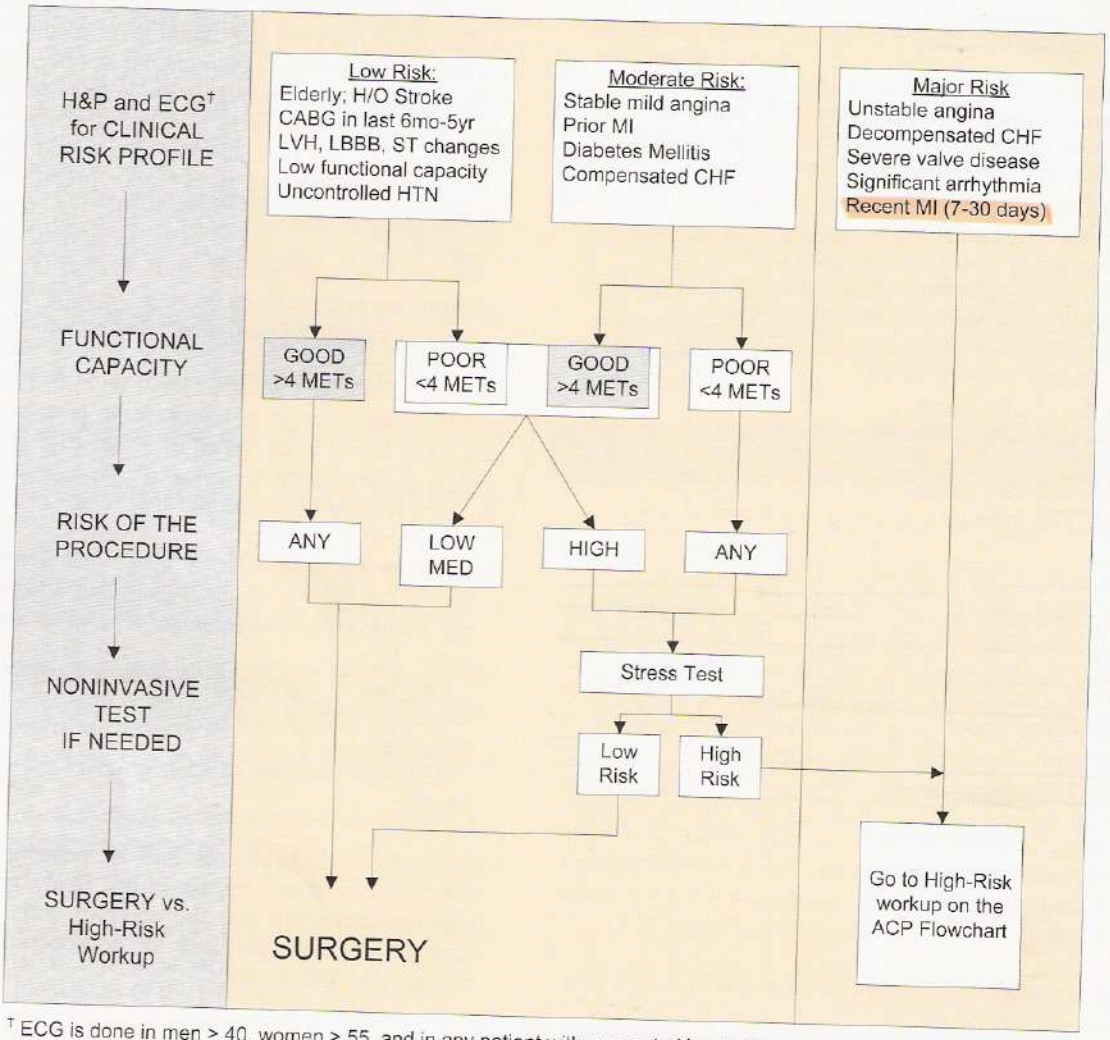
Additionally both guidelines and all other guidelines concur that coronary artery bypass is not likely to improve short-term outcomes and that the coronary artery bypass indications are the same as those for non-operative patients (i.e., use the AHA guidelines).

Scenarios on the IM Boards you are likely to encounter are:

1. a low-risk patient who can proceed directly to surgery of any type without non-invasive testing,
2. a moderate-risk patient with good functional capacity who can go directly to a non-vascular surgery,
3. a major-risk patient who needs further workup as defined in the charts prior to going to surgery.

The areas of the protocol not likely to be questioned are those that are controversial. This especially includes the area for moderate-risk patients receiving high-risk non-vascular surgery. While the AHA/ACC suggests an exercise stress test is equivalent to DTI and DSE, the ACP recommends using only the DTI or DSE and not the exercise stress test.

notes



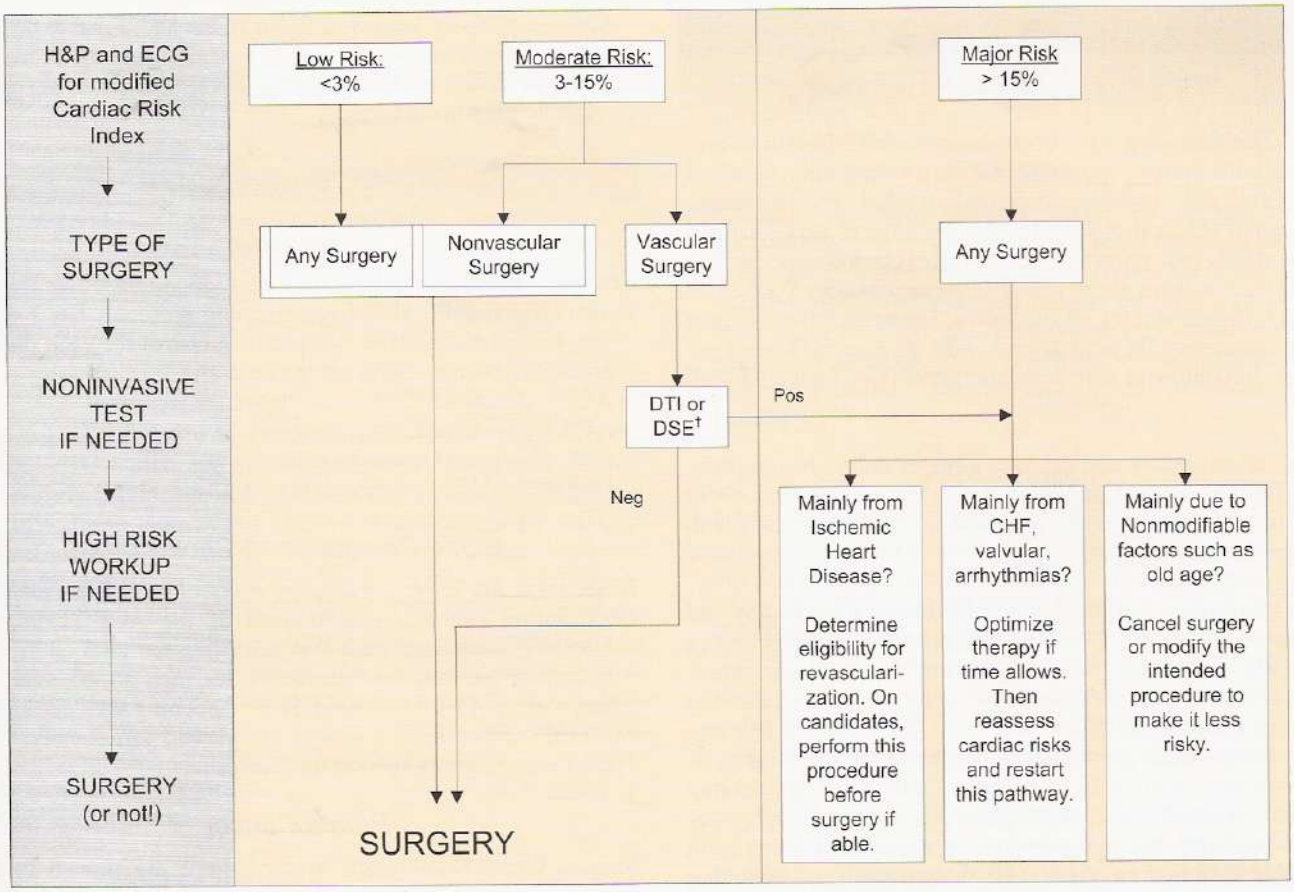
† ECG is done in men > 40, women > 55, and in any patient with suspected heart disease.
This flowchart is based on the American Heart Association and the American College of Cardiology statement article: "Guidelines for Perioperative Cardiovascular Evaluation for Noncardiac Surgery" Circulation 1996;93:1278-1317.

Figure 10-2: The AHA/ACC Preoperative Cardiac Risk Assessment

Table 10-10

"RISK OF PROCEDURE" (used in AHA/ACC diagram above)	
LOW Risk	Endoscopies, local biopsies, breast biopsies, vasectomy, cataract surgery.
MEDIUM Risk	Surgeries: Carotid endarterectomy, intraperitoneal, intrathoracic, orthopedic, prostate, Head and Neck.
HIGH Risk	Surgeries: Aortic and major vascular, cardiothoracic, emergent major surgery, long procedures with large blood loss and/or fluid shifts.

notes



† DTI = dipyridamole thallium imaging; DSE = dobutamine stress echocardiography.
This flowchart is based on the American College of Physicians position paper titled "Guidelines for Assessing and Managing the Perioperative Risk from Coronary Artery Disease Associated with Major Noncardiac Surgery". *Ann Intern Med.* 1997;127:309-312.

Figure 10-3: ACP Preoperative Cardiac Risk Assessment

Table 10-11

Modified Cardiac Risk Index		
Finding	Grouping	Points
Myocardial infarction within 6 months	Coronary artery disease	10
Myocardial infarction more than 6 months ago	Coronary artery disease	5
Class III Canadian Cardiovascular Society angina	Coronary artery disease	10
Class IV Canadian Cardiovascular Society angina	Coronary artery disease	20
Unstable angina within 6 months	Coronary artery disease	10
Alveolar pulmonary edema within 1 week	Alveolar pulmonary edema	10
Alveolar pulmonary edema, ever	Alveolar pulmonary edema	5
Suspected critical aortic stenosis	Valvular disease	20
Rhythm other than sinus or sinus plus atrial premature beats on last preoperative ECG	Arrhythmias	5
More than 5 premature ventricular contractions at any time prior to surgery	Arrhythmias	5
Poor general medical status *		5
Age over 70		5
Emergency operation		10
TOTAL: Add up the points. 0-15 = Low risk (Class I); 16-30 = moderate risk (Class II); and > 30 = high risk (Class III). Then use this modified risk index in the first step of the ACP Preoperative Cardiac Risk Assessment diagram.		
* (pO_2 < 60 mm Hg, pCO_2 > 50 mm Hg, K < 3.0 mEq/L, HCO_3 < 20 mEq/L, BUN > 50 mg/dL, creatinine > 3 mg/dL, abnormal SGOT, signs of chronic liver disease, bedridden for non-cardiac causes)		

How these 2 work…

From Table 10-11, add up the points:

- 0-15 = low risk (Class 1)
- 16-30 = moderate risk (Class II)
- > 30 = high risk (Class III)

Then use this modified risk index in the first step of the flowchart in Figure 10-3.

PREVENTIVE MEDICINE

PATIENT EDUCATION

[Know] The following have been shown to have improved outcomes with patient education, so review and counsel about the following: tobacco, firearms, alcohol and substance abuse, and physical activity level. Check the elderly for functional status, gait abnormalities, and for osteoporosis risk factors. Teach women about breast self-examination. Teach men about self-examination of the testes. Teach all patients about self-examination for skin disease, gum disease, STD, and nutrition. Recommend seat belts and good fluid intake. Got all that?

Firearm-related injury and death is a major public health problem. The physician's ethical role is to counsel patients about firearm safety and become involved in community efforts to prevent firearm injuries.[32–34]

Smoking cessation. Per the Agency for Health Care Policy and Research (AHCPR) Smoking Cessation Clinical Practice Guideline[35]: At each patient visit, ask about tobacco products. The AHCPR guideline even recommends that tobacco usage be added as the fifth "vital sign." If the patient smokes, give strong, clear, personalized antismoking counseling. If the patient is willing to quit, set a "quit date" (preferably within 2 weeks), recommend pharmacologic therapy (nicotine/bupropion), provide personal or group counseling, and schedule a followup visit. Tell discouraged smokers that most previous smokers required many (> 5) attempts to quit.

Pharmacologic antismoking therapy has a long way to go.[36,37] Right now we have only nicotine products and bupropion. Both nicotine products (including the over-the-counter nicotine products) and bupropion appear equally effective.

Note that cigar smoking increases the risk of coronary heart disease (relative risk = 1.27), COPD (1.45), and cancers of the mouth and throat (2.02).[38]

Bladder cancer is inversely associated with fluid intake. Incidence in the high fluid-intake group is half that in the low fluid-intake group.[39]

Folate supplementation decreases the risk of colon cancer. With long-term use, relative risk decreases 25%![40]

See Geriatrics section, starting on page 10-8, for a discussion of osteoporosis prevention.

There is no consensus regarding antithrombotic prophylaxis for stroke even though its usage does decrease the stroke incidence. This lack of consensus reflects the facts that anticoagulant therapy is the best choice for preventing stroke caused by emboli from the heart, whereas carotid endarterectomy is the best treatment for symptomatic moderate-to-severe carotid artery stenosis. Briefly, stroke risk reduction: aspirin, 22%; dipyridamole, 16%; aspirin + dipyridamole, 37%; ticlopidine, 33%.[41,42] Although ticlopidine alone is more effective than aspirin alone, it is much more expensive—especially when you factor in the additional expense of semiweekly blood tests the first 3 months and the more serious side effect profile (diarrhea 20%, rash 14%, severe reversible neutropenia 1%).[42]

SCREENING EXAMS

Overview

Screening protocols: Table 10-12 provides a rough summary.

Every official entity detailing screening protocols has a different, but usually similar, suggested protocol for each disease. In the following, abbreviations used are:

ACP = American College of Physicians
ACS = American Cancer Society
NCI = National Cancer Institute
USPSTF = U.S. Preventive Services Task Force

Blood Pressure and Cholesterol

Blood pressure: Every 2 years and every clinical encounter.

Cholesterol: The recommendations of the ACP (1996) and USPSTF guidelines state that screening for total cholesterol is appropriate but not mandatory for men 35–65 years old and women 45–65 years old. If the screening total cholesterol is near the threshold, it should be repeated periodically.[43] See the Endocrinology section for treatment.

Breast Cancer

Manual breast exams with mammograms are proven to help only when done on patients > 50 years old, and all groups

Table 10-12: Screening Exam Recommendations

SCREENING EXAMS	
Counseling re smoking	Each visit
Counseling, other	Initial visit and then periodically*
Blood Pressure	Each visit; at least every 2 years
Cholesterol	Every 5 years is appropriate
Manual Breast Exams	Yearly after age 40
Mammograms	Yearly after age 50*
Digital Rectal Exam	Yearly after age 40
FOBT	Yearly after age 50
Sigmoidoscopy	Every 3-5 years after age 50
Pap Smear	Every 3 years*
PSA	Inconclusive*

* See text for more information

notes

Ticlopidine
Side effect → neutropenia

Quick Quiz

1) Memorize Table 10-12!
2) In a 75 y/o man should you do a PSA for screening?
3) When should PAP smears be initiated?
4) What are the live-virus vaccines?
5) Who should not receive a live-virus vaccine?
6) What patient groups should get the pneumococcal vaccine.

recommend a yearly breast exam after age 40 and a yearly mammogram after age 50 (mammography with breast exams is slightly better than mammography alone). Before 50, there is still strong controversy, but most physicians are starting mammograms q 1–2 years at age 40. Examples: Between ages 40 and 50, ACS = yearly; ACP = based on risk factors; NCI Advisory Board = q 1–2 years; USPTF = q 1–2 years. There is a high incidence of false positive mammograms in patients between the ages of 40 and 50 (as high as 30–50% if patients have a yearly mammogram from age 40 to 50). Discuss this with patients before their mammogram. Studies of self-examination of the breast have had inconclusive results, but most groups recommend it. This is in addition to yearly office breast exams.

Prostate Cancer

Prostate Specific Antigen (PSA) testing has contributed to the increased finding and treatment of early prostate cancer. Although no trials have been concluded indicating its effectiveness as a screening test, consumer demand is making it a common one. The American Urological Association recommends PSA and digital rectal exam yearly for men > 50 years old. The ACP and ACS recommend that a PSA be done between the ages of 50 and 69—with frequency the result of discussion of pluses and minuses with the patient. No PSA screening is recommended for > 70 years.

Colorectal Cancer

Digital rectal exam (DRE) is effective only for detecting late prostate lesions and has a very low sensitivity for detecting colon cancer (< 5%). The general recommendation is yearly as part of the annual exam in patients > 40 years. Regarding only colorectal cancer screening, DRE is done along with endoscopy (every 5–10 years).[44–46]

Fecal occult blood testing (FOBT) has proven its utility even though the sensitivity is low (studies vary wildly: 35–80%) . Hemoccult: Take 6 samples from 3 consecutive stools. Current recommendations are yearly after age 50.[13–15]

Sigmoidoscopy: Many groups do not recommend this because of its low sensitivity (it misses all the more proximal colon lesions). The ACS and the ACP recommend it every 3–5 years, starting at age 50. Surveillance colonoscopy, with intervals determined by the initial study, is recommended for all those at high risk for colon cancer.[13–15] More in the Gastroenterology section.

Pap Smear

Pap smears have been proven effective, but the recommended interval between these tests varies. Most recommend starting at age 18 or when sexually active. When there have been 3 negative results with annual exams, continue every 3 years until 60 to 65 years old. If previous Pap smears have been negative, patients > 70 years old do not need further smears. See the Oncology section for workup of abnormal PAP smears.

Vaccinations

Adult Vaccinations.[47,48] [Know!]

Vaccines: The attenuated live virus vaccines are mumps-measles-rubella (MMR), oral polio, nasal influenza, and yellow fever. The attenuated live bacteria vaccines are typhoid and BCG (bacille Calmette Guerin). In immunosuppressed patients, these attenuated vaccines may cause the disease they vaccinate against. The dead virus vaccines are injectable polio, rabies, and influenza. Dead bacteria vaccines are cholera, *H. influenza*, pneumococcal, meningococcal, typhoid (two types).

Note: Hep A & B are now recombinant vaccines, not dead!

All except the attenuated live vaccines can be given in pregnancy. So do not give MMR, oral polio (not used anymore in the U.S.), yellow fever, typhoid, nasal influenza, or BCG vaccines to pregnant patients or to patients with a congenital immunodeficiency.

The following vaccines are given to AIDS patients: yearly influenza, hepatitis B, pneumococcal, HiB, and any childhood vaccines not yet received, such as MMR and Td, following the standard revaccination protocols. Even though MMR contains attenuated viruses, it can still be given to AIDS patients. Do not give HIV patients nasal influenza, oral polio, or smallpox vaccines.

BCG (bacille Calmette-Guérin) vaccine is an anti-TB vaccine used in many countries but not much in the U.S. This is for 2 reasons:

1) Effectiveness is questionable since 5 major studies show effectiveness of 0–76% (!) and
2) BCG immunization may cause a positive tuberculin skin test, complicating later evaluation for therapy.

However, previous BCG should not deter workup of positive PPD. Do not give BCG to pregnant patients or immunocompromised patients.

Streptococcus pneumoniae: The vaccine against 23 serotypes is recommended for persons older than age 2 years with asplenia, SS, or any debilitating disease or those in poor living conditions. Also for anyone older than age 65 years. Repeat once in 5–6 years. Some of these recommendations seem a

notes

asplenic pts
Sickle cell dz
>65 yo

little odd because the vaccine requires a well-functioning immune system and is most effective in persons < 55 years old and in good health! There is a new conjugated pneumococcal vaccine approved only for children so far.

Influenza vaccine is *inactivated* and includes 2 type A strains and 1 type B strain. It is generally effective within 2 weeks. It is given every year after the age of 50 and also yearly to high-risk patients and their household contacts. Also recommended for all health care and community workers. Consider it for any adult. It takes 2 weeks for the vaccine to provide a protective immune response.

Measles vaccine (Attenuvax®; although usually given as part of MMR vaccine) is a *live* vaccine recommended for all susceptible people older than 12 months. Persons born before 1956 are considered immune.

Varicella Virus vaccine (*live*) (Varivax®) is recommended for all individuals older than 12 months who are not immune. Note that a history of chicken pox by the patient is sufficient for assuming immunity. If the adult patient doesn't know or believes he/she has had no previous infection, check immune status by lab (as up to 91% are immune) before giving the vaccine.

Hepatitis A vaccine (*inactivated*) (Havrix®, VAQTA®). Unless otherwise contraindicated, inactivated hepatitis A vaccine is indicated in persons 2 years of age or older who are at increased risk of infection by HAV, including those with chronic liver disease and travelers outside of the U.S. (except for Northern and Western Europe, New Zealand, Australia, Canada, and Japan).

Hepatitis B Vaccine is recommended for all those who are at or may be at increased risk and ALL ADOLESCENTS. Booster doses can be given q 7 years—but not currently recommended. If the antibody level is > 10 IU/ml, booster dose is not needed. If a patient has been exposed to hepatitis B and has had the complete vaccination series but the antibody level is unknown, give HBIG and a booster dose.

Tetanus and diphtheria (Td). Tetanus booster is recommended once every 10 years after the primary series. The booster may be given at 5 years for "dirty" wound management.

Lyme vaccine is no longer available.

Meningococcal polysaccharide vaccine is a quadrivalent vaccine (serotypes A, C, Y, W-135). It is not recommended for the general public; it has a short duration of efficacy, is not effective in children < 2 years old (who are at highest risk for endemic disease), and is not effective against serotype B—the serotype that causes most problems. It is recommended for persons with effective asplenia, military recruits, travelers to endemic areas, and for controlling outbreaks due to serotypes covered by the vaccine. This vaccine is now recommended by some authorities for college freshmen who will be staying in dormitories.

Rabies. Preexposure vaccination is recommended for those at occupational risk and travelers (and especially their children) planning extended stays in areas where dog rabies is enzootic.

MMR. It is recommended that persons born after 1956 receive two doses of live measles vaccine. These should be given not less than 1 month apart, but can be given years apart. Most persons have received only the first one as a child. The present recommendations are one dose at 15 months (12 months in endemic areas) and the second dose at age 4–6 years (previously was 12 years). All young adults (since they would have been born after 1956) who have had only one live measles vaccine should receive another.

Typhoid vaccine is recommended for travelers (> 2 years old) who go outside of the usual tourist areas within Latin America, Asia, and Africa. The parenteral dose is not recommended any more. A newer oral attenuated live vaccine is recommended for those > 2. It has a protection rate of 70–90%.

Yellow fever vaccine is recommended for travel in equatorial Africa and much of tropical South America. Don't forget it is a LIVE virus vaccine!

Cholera vaccine is not very effective and is rarely required.

Polio vaccine is not routinely recommended to persons > 18 years old. Polio vaccine is recommended for previously unimmunized travelers to endemic areas. A booster is indicated for travelers who have had only the primary vaccination who travel to areas where exposure to the wild-type virus is likely. Only the inactivated vaccine is recommended in the U.S.

Japanese Encephalitis vaccine (JE-Vax) is recommended for travelers who will stay a long time in rural Asia.

Smallpox vaccine is available on demand. Military personnel and selected physicians have been vaccinated. Contraindications to vaccination are: eczema or household contacts with exfoliative skin conditions; immunosuppression, including from HIV and doses of corticosteroids > 20 mg/day; radiation therapy; and pregnancy.

PROPHYLAXIS

Malaria

Malaria prophylaxis. Physicians should check with the CDC which type of prophylaxis is required. Mefloquine (Lariam®) 250 mg once per week is recommended for travelers to most areas with chloroquine-resistant malaria. Mefloquine causes neuropsychological side effects in 0.2–0.5%.

notes

Quick Quiz

1) Is history of chicken pox sufficient to assume immunity and therefore no need for the vaccine?
2) Who should get hepatitis A vaccine?
3) A nurse has a needle-stick injury from a patient with known chronic hepatitis B. Her antibody to hepatitis B surface antigen is 20IU/ml. What treatment if any is indicated for hepatitis B in this scenario?
4) True or False: All health-care workers exposed to a patient who died from meningococcemia should be prophylaxed within 48 hours.
5) What are the treatment options for travelers' diarrhea?
6) What is the most effective way to prevent the spread of disease in a hospital?

Chloroquine (300 mg base) once per week is recommended for most other places. Other drugs: doxycycline 100 mg qd (84–100% effective); primaquine (85–95%); and azithromycin (83%).

Meningococcemia

Meningococcemia chemoprophylaxis may be done with rifampin, ciprofloxacin, or ceftriaxone. Each is 90–95% effective in reducing nasopharyngeal carriage of *N. meningitidis*. Remember that ciprofloxacin is not routinely given to children or pregnant women (possible cartilage damage). Ceftriaxone is usually reserved for pregnant women. Note: Healthcare workers do not receive chemoprophylaxis unless they had recent "intimate" oral contact with the case patient … er, like with intubation!

Travelers' Diarrhea

Travelers' diarrhea (TD)[49,50]: 2 approaches—empiric self-treatment or prevention.

For prevention and treatment, fluoroquinolones, trimethoprim/sulfamethoxazole (but much resistance) and azithromycin are used.

For prevention of TD:

Daily dosages (mg) for prevention (use < 1 mo)

- norfloxacin 400
- ciprofloxacin 500
- levofloxacin 500
- ofloxacin 300
- azithromycin 250–500

For self-treatment, have the patient determine the severity of diarrhea and treat accordingly:

- 1–2 stools/24hr: None; loperamide.
- 3 stools/24hr: Add single dose antibiotic.
- 6 stools/24hr and fever or blood: Continue antibiotic x 3 d ± loperamide.

Dosages (mg) for self-treatment (single dose/multiple dose):

- norfloxacin (800/400 b.i.d.)
- ciprofloxacin (750/500 b.i.d.)
- levofloxacin (500/500 q.d.) ofloxacin (400/200 b.i.d.)
- azithromycin (1000/500 q.d.)

IATROGENIC INFECTIONS

Controlling the spread of infections and antimicrobial resistance in hospitals:

1) Prevention: Vaccinate patients and healthcare workers according to protocols and remove any type of catheter and any ET tube ASAP.
2) Eradication: Get cultures immediately, treat effectively, and monitor response.
3) Use antimicrobials with the narrowest effective spectrum ASAP (when C&S is back). Use vancomycin only when indicated.
4) Prevent transmission: Isolate the patient with uncontained infectious body fluids. Use standard infection control precautions. Wash your hands! (Really! Why are some so-called doctors still not doing this? Remember, "Do No Harm.")

A recent study (Ann Intern Med. 2004;141:1-8) reviews proper hand hygiene among physicians. Internists rated the highest at 87% (congratulations!...but could be better) and surgeons and anesthesiologists rated the lowest at 36% and 23% respectively!! Does that make you feel as queasy as it does me? Please push for ways to encourage proper hand hygiene at your hospital. Physicians tend to wash hands more if they see themselves as role models for the rest of the hospital staff.

POISONING

GAPS

Anion gap acidosis may be caused by lactic acid (cyanide, etc.), salicylates, ethylene glycol, or methanol.

Osmolal gap = (measured osmolality) − (calculated osmolality). Calculated osmolality = $2(Na^+)$ + glucose/18 + BUN/2.8. When the calculated osmolality is lower than the measured osmolality, it implies the presence of a significant amount of a low molecular weight substance in the serum (only low molecular weight substances are osmotically active). The concentration of one of these substances in the serum = osmolar gap x molecular weight.

Exogenous cases of increased OSMOLAR GAP (note that ALL end in "-ol" and MW = molecular weight):

1) Mannitol, sorbitol, and glycerol.
2) Ethylene glycol (MW = 62)
3) Alcohols (most common): methanol (MW = 37), ethanol (MW = 46), and isopropyl alcohol (MW = 60).

If a comatose patient has an osmolar gap and an anion gap, it is probably due to either ethylene glycol or methanol (in a question, only one of the two will be given as a possible an-

notes

swer). This is a rather academic exercise because ethylene glycol and methanol are toxic at such low levels the patients often have a normal osmolal gap!

Note: If a patient is more intoxicated-appearing than is consistent with the calculated blood level of ethanol, strongly consider ethylene glycol. It has nearly the same molecular weight as ethanol, but is toxic at much lower doses!

Note: Hyperlipidemia also causes an increased osmolal gap, so check for lipemic appearance of the serum also!

OVERDOSE MANAGEMENT

General management of a probable overdose patient who presents obtunded or comatose is cardiac monitoring. Give IV naloxone for possible narcotics; benzodiazepines and alcohol may also help. Check fingerstick glucose, and then give IV D_{50} prn. Pulse ox with supplemental oxygen prn. Give thiamine 100 mg IM or IV. Do chest x-ray (aspiration pneumonia or pulmonary edema) and ECG (acute MI, prolonged QT, signs of hyper/hypokalemia, arrhythmias etc.).

Lab should include ABGs with carboxyhemoglobin level, electrolyte panel, CBC, and comprehensive drug screen.

Physical exam should include a search for trauma and needle sticks/tracks. Repeat the neurologic exam periodically to check for deterioration.

Supportive care: Put such patients on their side. If a patient is obtunded, place an oral airway and suction. If there is respiratory depression, intubate the patient. After the patient is stabilized, do a gastric lavage with a large bore orogastric tube; this may be effective even hours after ingestion if the drug was ASA, anticholinergics, or narcotics (these cause decreased gastric motility). Lavage with only small amounts of tap water (100 cc) to prevent forcing the stomach contents into the duodenum. Follow with activated charcoal with sorbitol. If the activated charcoal is not mixed with sorbitol, follow it with Mg-citrate. Know that activated charcoal is not effective when the overdose is with the metals lithium and iron.

Note that there is a strong trend toward not lavaging patients with most overdoses. The thought is that lavage is, in most cases, ineffective, and using activated charcoal with cathartics is at least as effective if not more effective.

Shock is treated with CVP monitoring, IV fluids, +/− dopamine.

Continued dosing with oral charcoal is effective in decreasing the levels of a few drugs by gut dialysis (absorption via the enteric recirculation)—especially digoxin, phenobarbital, theophylline, tricyclics, and salicylates.

Alkalinization and acidification of the serum (and hence, the urine) are based on the principle that compounds in their ionized form are less tissue-permeable and more easily eliminated by the kidneys. Weakly acidic substances ionize in an alkaline environment while weakly alkaline substances ionize in an acidic environment. Alkalinization of the urine to a pH of > 7 increases excretion of ASA, tricyclics, and phenobarbital. Acidification of the urine with ammonium chloride increases excretion of amphetamine and phencyclidine (PCP). Mix 2.75 mEq/kg in 60 cc NS and give through the gastric tube. Clamp for 1 hour. Repeat q 6 hours until urine pH < 5.0.

Important: Hemodialysis may be necessary in patients with severe overdose or renal failure. It is effective in removing drugs with low molecular weights that are not lipid soluble, protein bound, or tissue bound—i.e., drugs with a small volume of distribution. These include lithium, chloral hydrate, salicylates, and alcohols (methanol, ethylene glycol, and ethanol). Note that the last 3 also cause an anion gap acidosis. Dialysis is not effective in removing benzodiazepines, opiates, or tricyclics.

Also: Charcoal hemoperfusion (blood pumped through a charcoal filter), in contrast to dialysis, removes drugs that are lipid soluble and protein bound! It can also remove some of the same drugs as dialysis. Also like dialysis, it is most effective in removing drugs with a low volume of distribution (V). Especially good for digoxin, theophylline, and salicylate overdoses.

SPECIFIC TOXINS

[Know this section!] Also refer to Table 10-13.

Isopropyl alcohol ("rubbing alcohol") is a common solvent and disinfectant. Like ethanol, it has CNS depressant effects. It is second to ethanol in the causes of alcohol overdose. The main metabolite is acetone, which causes a prolonged CNS effect. The acetone causes ketonuria, and the sweet odor of acetone is evident on the patient's breath. CNS depression is the major effect, although there may also be cardiac depression. Abdominal pain and vomiting are usually present. An osmolal gap increase of 8–9 mOsm is seen with the toxic level of isopropanol (50 mg/dL) and an increase of > 35 mOsm is seen with severe toxicity (> 200 mg/dL). Treatment: You may lavage the patient if < 2 hours has passed since ingestion. Make early use of hemo/peritoneal dialysis in severe cases.

Methanol (wood alcohol) toxicity is usually due to contaminated moonshine. It is only mildly inebriating, and many signs of toxicity are delayed > 24 hours—especially visual impairment, from blurring to blindness. The toxic metabolites are formaldehyde and formic acid. Serum analysis shows an increased anion gap and sometimes an increased osmolal gap. Treat with alcohol infusion, folic acid, and immediate dialysis. Give folic acid to increase metabolism of the formic acid.

Ethylene glycol: Alcohol dehydrogenase breaks down ethylene glycol to its very toxic metabolites, especially oxalate. Presence of oxalate is indicated by calcium oxalate crystals in the urine and hypocalcemia (oxalate chelates calcium). Suspect if a patient is intoxicated-appearing without an alcohol smell, but with an anion gap acidosis +/- osmolal gap. Treat with alcohol infusion (has 100x stronger affinity for alcohol dehydrogenase), bicarbonate for the acidosis, calcium prn, and immediate dialysis.

notes

Quick Quiz

1) If a comatose patient presents with BOTH an osmolar gap and an anion gap, what are the 2 possible agents that she may have ingested?
2) With which 2 poisonings with metals is activated charcoal not helpful?
3) For tricyclic overdose, what should you do to the urine?
4) Methanol causes what neurologic deficit?
5) Does ethanol cause an increased osmolal gap, anion gap, or both?
6) What is the common acid-base disorder presented on the Boards when a patient presents with ASA overdose?
7) A patient has a history of chronic intake of large amounts of acetaminophen. Will the Rumack-Matthew nomogram used for determining severity of ingestion be helpful?
8) Memorize Table 10-13.

Note that methanol and ethylene glycol are so toxic they may cause signs of toxicity at normal osmolality levels (i.e., normal osmolal gap).

Note that ethanol causes an increased osmolal gap but not an increased anion gap.

Salicylates are metabolized in the liver by conjugation with glycine or glucuronide. These pathways are quickly saturated in a person who has overdosed, resulting in acidemia. The increased ASA level initially causes hyperventilation through a central effect. This has a protective effect as the ASA crosses the blood-brain barrier (i.e., is more tissue permeable) when the system is acidemic. The high anion gap acidosis due to ASA can worsen with overlying lactic acidosis if patient gets pulmonary edema. If the patient stops hyperventilating, it is probably due to respiratory muscle fatigue. Questions about ASA poisoning may present a patient with a history of taking "over-the-counter pain *medicine*" who now shows an increased anion gap and a pH of 7.4. This is just the central respiratory *alkalosis balancing out the* metabolic acidosis.

Treatment of salicylate overdose: Lavage, activated charcoal with cathartic, and serum/urine alkalinization. Both hemodialysis and charcoal hemoperfusion have been used in severe cases (> 100–120 mg/dL). The charcoal hemoperfusion removes the salicylates better than hemodialysis but does not correct any fluid/electrolyte imbalance (patients are often hypokalemic).

Table 10-13

TOXIN	ANTIDOTE(S)
Acetaminophen	N-acetylcysteine
Digoxin	Ag binding fragment
Narcotics	Naloxone
Benzodiazepines	Flumazenil (Mazicon)
Nitrates	Methylene blue
Iron	Deferoxamine
Carbon monoxide	Oxygen
Ethylene glycol	*ETOH*
Methanol	ETOH
Organophosphates	Atropine, pralidoxime
Cyanide	Nitrates, Na-thiosulfate

Acetaminophen: 90% is metabolized in the liver, by glucuronidation or sulfation, to inactive metabolites. 5% is excreted unchanged through the kidneys. The last 5% is metabolized by way of the hepatic cytochrome P-450 system to active metabolites. One of the active metabolites is N-acetyl-*p*-benzoquinoneimine (NAPQI), which is highly hepatotoxic. Normally, the small amount of NAPQI is quickly detoxified by reacting with the sulfhydryl group of glutathione, forming nontoxic mercapturic acid. A large overdose results in depletion of the glutathione and subsequent increase in these metabolites. A severe overdose is often followed by mild N/V/D. It is only after 24–48 hours that liver toxicity ensues.

Alcohol-acetaminophen syndrome. Chronic moderate-to-heavy use of alcohol has a two-fold effect: The cytochrome P-450 system is cranked up (so that more NAPQI is produced) and the amount of glutathione is decreased (so less is available for detoxifying the NAPQI). Therefore, long-time users of moderate to heavy amounts of alcohol who take acetaminophen in normal or higher doses are at-risk for severe hepatic toxicity or liver failure.

Treatment of acetaminophen overdose: Gastric emptying if it is within 2 hours of being taken. Activated charcoal is beneficial and does not hinder use of NAC. Although there is great variability in the hepatic response to the overdose, a 4-hour post-ingestion acetaminophen level of > 250 µg/ml indicates a high probability of hepatotoxicity—if untreated. N-acetylcysteine (NAC, Mucomyst®, Mucosal®) is an effective antidote that works by increasing the availability of hepatic glutathione. Loading dose = 140 mg/kg followed by q 4 hour doses at 70 mg/kg for 17 doses. NAC is effective when given within 8 to 16 hours after the acetaminophen overdose. Treatment is based on the Rumack-Matthew nomogram.[51] Note that this nomogram is accurate only when the patient has no hepatic risk factors and took a single *dose at a known time.*

Theophylline: Lavage, activated charcoal, cathartic. Treat seizures with diazepam. Charcoal hemoperfusion may be indicated if the serum level is *> 50 µg/ml.*

Lithium toxicity: Mental status changes are the most common *manifestation—affecting > 90%.* Other *CNS changes include* seizures and symptoms due to encephalopathy (poor memory, incoherence, disorientation). Patients may also get Parkinsonian symptoms and movement disorders. Treatment: Activated charcoal

notes

Methanol + Ethylene glycol → can cause tox. ↑ nml osm.

Ethanol → causes ↑ osm gap but no anion gap

is not effective. Do gastric lavage, restore fluid and electrolyte balance, and use hemodialysis in severe lithium overdose cases. Consider severe intoxication when there are any symptoms characteristic of lithium poisoning, when the lithium levels are > 3.5 to 4 mmol/L, or when the serum level does not decrease appropriately.

Tricyclic antidepressants are lipophilic and are protein bound, so they have a very large volume of distribution and cannot be removed by dialysis. Give supportive treatment and watch for cardiotoxic side-effects. Tricyclics cause tachycardia and PR, QT, and QRS prolongation. The QRS prolongation is the ECG change that correlates most closely with the degree of intoxication! Ventricular tachycardia and fibrillation are also common. The cardiac problems often respond to maintaining an alkalemic state—either by hyperventilation if the patient is intubated or with IV bicarbonate. Keep serum pH 7.5 to 7.55 ("alkalinizing the urine"). Give lidocaine (first choice) or phenytoin as needed for arrhythmias.

Cocaine: Cardiotoxicity can occur no matter what the route of use. It causes rhythm disturbances (including V fib/tach) and MI. Suspect this in a young patient presenting with MI.

Phencyclidine (PCP) can cause acute psychotic agitation, seizures, dystonia (including laryngospasm), and hypertensive crisis. Severe dystonia can cause rhabdomyolysis. Treat with a calm environment and by acidifying the urine with ammonium chloride. Treat hypertension with diazoxide prn.

Anticholinergics cause dilated pupils, warm dry skin, tachycardia, hypertension, increased temperature, decreased bowel sounds, urinary retention, agitation, and hallucinations. Mydriasis = dilated pupils (big word, big pupils).

Stimulants cause dilated pupils, warm wet skin, tachycardia, hypertension, increased temperature, agitation, and psychosis. Note: The above two are very similar in physical presentation except that the stimulants cause sweaty skin.

Cholinergics cause small pupils, increased bowel sounds, diarrhea, increased salivation, muscle weakness, agitation, seizures. If poisoning is severe, the pupils can dilate. Miosis = constricted pupils (small word, small pupils).

Carbon monoxide:. Carbon monoxide quickly binds with hemoglobin—with an affinity about 250x greater than O_2. This carboxyhemoglobin (COHb) decreases arterial oxygen content, which leads to tissue hypoxia.

Especially suspect this if the patient has been working around cars or gas/oil heating units. Typical presentations are: 1) Sometime during the winter during a particularly bad flu season (red herring), a patient calls you from home, says her family is bedridden with a bad case of the flu with headache and lightheadedness. The patient may sound slow to respond. What should you do? 2) Patient calls in the winter and complains of headache and lightheadedness, which improves when he goes outside. Answer to both questions: Tell patient to get self and family out of the house immediately; send an EMS unit there immediately.

The brain and heart are especially sensitive to CO. Poisoning often causes long-term-to-permanent CNS impairment with cognitive (i.e., memory and learning), personality, and movement disorders.

Fetal hemoglobin has especially high affinity for CO, so treat pregnant patients aggressively.

If you suspect carbon monoxide poisoning, get a carboxyhemoglobin level. A hand-held breath analyser can quickly rule out CO poisoning, but ethanol causes false positives. Mild to moderate CO toxicity occurs at 15–30%; moderate to severe toxicity occurs if > 30%; > 50% is often fatal. "Cherry red" coloration is rare.

Treat with 100% O_2—this decreases the half-life of COHb from about 5 hr to 1 hr. Hyperbaric O_2 further decreases the half-life to 30 min, but its main benefit is that it decreases the CO-induced ischemic reperfusion injury to the brain.[52,53] One study[54] suggests that hyperbaric treatment of patients with even moderate poisoning (i.e., symptomatic but no loss of consciousness) results in a dramatic decrease in neurologic sequelae. Although definitive studies are pending, hyperbaric oxygen is generally given for moderate to severe CO poisoning. Many centers routinely use it in all patients with a COHb level of 25% or greater and in pregnant women with a level of 15% or more. Use it for all patients presenting with:

- syncope
- coma
- seizures
- any new focal neurologic defect
- any neurologic symptoms persisting after 2–4 hours of 100% O_2 therapy

Smoke inhalation: Respiratory impairment results from the noxious chemicals in the lungs or laryngeal/airway edema. Suspect laryngeal involvement if face or airways are burned (e.g., singed nasal hairs).

Cyanide poisoning clues: Patient's breath has an almond odor, and the patient has bright red venous blood. Cyanide immediately binds to the ferric molecule in the mitochondrial cytochrome oxidase complexes, thereby blocking cellular aerobic metabolism. These patients very quickly develop headache, tachycardia, and tachypnea. This may quickly progress to coma and various cardiac arrhythmias.

Treatment is the 3-step cyanide antidote package.

- Step 1 is amyl nitrate held under the patient's nose for 30 sec.
- Step 2 is to administer 3% sodium nitrite IV. The nitrites convert hemoglobin to methemoglobin (the ferric form of hemoglobin), which more effectively competes with the cytochrome oxidases for the cyanide. Amyl nitrate inhalation causes a 3–5% methemoglobinemia while the sodium nitrate causes 20% methemoglobinemia.
- Step 3 is sodium thiosulfate IV, which acts as a substrate for the enzyme rhodanese. This enzyme converts the cyanide released from hemoglobin to inactive thiocyanate, which is excreted renally.

notes

Quick Quiz

1) What ECG finding correlates most closely with the degree of intoxication of a tricyclic antidepressant?
2) A 30-year-old man presents with acute MI. What drug should you suspect?
3) What finding on an ECG correlates best with degree of tricyclic antidepressant ingestion?
4) Know carbon monoxide poisoning!
5) What are the 3 drugs used for cyanide poisoning?
6) How do you check for ongoing lead exposure? What if for exposure 2 years ago? What if 10 years ago?
7) What is the treatment for organophosphate poisoning?

Inorganic lead: For ongoing exposure, check whole blood lead level. After exposure has occurred, RBC protoporphyrin and zinc protoporphyrin levels will remain elevated for several months. For evaluating the effect of exposure from years before, the best test is to measure urine lead 24 hours after giving 1 gm of EDTA. Organic lead is lipid soluble and rapidly excreted, and previous exposure is not detectable! Know all this lead stuff!

Insecticide: Organophosphate and carbamate poisonings present identically. Symptoms include increased salivation, miosis (small pupils), N/V/D, and abdominal cramps. Affected patients also complain of chest tightness and generalized weakness. Organophosphates are more toxic than carbamates; they bind irreversibly to acetylcholinesterase, whereas the carbamate binding is reversible. This is reflected by a decrease in the level of RBC (not plasma!) acetylcholinesterase for several months after organophosphate poisoning, while it returns to normal within hours after carbamate poisoning. Treatment: The route into the body is dermal absorption (especially organophosphates), so decontaminate by removing clothes and showering with soap. For moderate to severe symptoms, give atropine (1–2 mg IV, repeat q 5 min prn). Additionally, for organophosphates only (not carbamate), give 2-protopam (2-PAM) IV.

OPHTHALMOLOGY

OVERVIEW

Aqueous humor is produced by the ciliary body, flows through the pupil into the anterior chamber, and then goes through the trabecular network and into Schlemm's canal. The greater the resistance to this flow in the trabecular network and Schlemm's canal, the greater is the intraocular pressure. Normal pressure is < 21 mm Hg. See Figure 10-4.

GLAUCOMA

Glaucoma is an insidious disease in which a prolonged elevated intraocular pressure causes progressive visual field loss due to optic nerve damage. It is the 3rd major cause of blindness in the U.S. and the leading cause in the world. Treatment is aimed at decreasing intraocular pressure.[55] There are three broad classifications: open angle, closed angle, and congenital. They are further divided into primary and secondary.

Primary open angle glaucoma is the most common type. It is called "open angle" because the orb has elevated pressure with no closure of the inlet of the trabecular network.

These patients suffer unnoticed gradual loss of peripheral vision that can progress to legal blindness before it is detected. The disease is diagnosed by 1) progressive loss of peripheral vision, 2) high intraocular pressure, and 3) abnormal cup-to-disc ratio (> 50% in either eye or any asymmetry between eyes). All patients above age 50 should have eye exams every 2 years to check for glaucoma; patients over age 65 should have annual exams.

The most common treatment consists of:

Beta blockers (topical): These dramatically decrease intraocular pressure—probably by decreasing production of aqueous humor. It is thought aqueous humor production is mediated by tonic sympathetic (beta) stimulation.
- Nonselective (timolol, carteolol, levobunolol, metipranolol—which may have systemic side effects such as lethargy, bradycardia, exacerbation of COPD);
- Beta$_1$-selective (betaxolol)

Other medications that may be used include:

Adrenergic agonists: Early on, these decrease production of aqueous humor by constricting the vessels of the ciliary body and decreasing ultrafiltration. Later they increase aqueous humor outflow.
- Nonselective (epinephrine)
- Alpha$_2$-selective (apraclonidine, brimonidine)

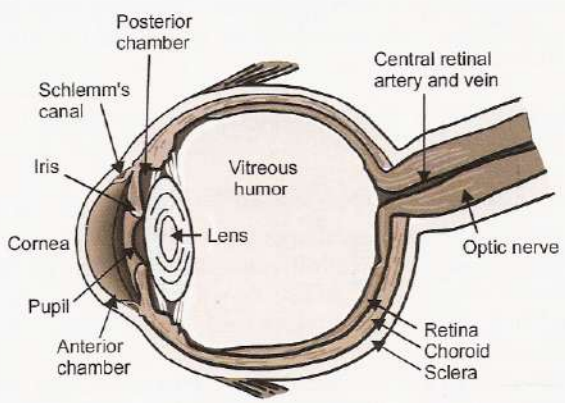


Figure 10-4: Structures of the Eye

notes

LEAD:
Ongoing Exposure – whole blood lead level.
After exposure – RBC protoporphyrin, Zinc protoporphyrin] for months.
Years later – 24° urine lead. c EDTA
Organic lead – lipid soluble & excreted
previous exposure is not detectable

Cholinergic agonists: These stimulate parasympathetic receptors at the neuromuscular junctions → retracting the longitudinal muscle of the ciliary body → opening the trabecular network. These cause pupil constriction.
- Direct-acting cholinergic agonist (carbachol, pilocarpine)
- Cholinesterase inhibitor (demecarium, echothiophate, physostigmine)

Carbonic anhydrase inhibitors: Carbonic anhydrase converts CO_2 to bicarbonate. In the eye, the formation of bicarbonate → sodium into the eye → sodium is followed by water → which increases intraocular pressure
- Oral (acetazolamide, which rarely causes idiosyncratic aplastic anemia)
- Topical (brinzolamide, dorzolamide—these are equally effective)

Primary closed angle (angle closure) glaucoma, the most severe form of narrow angle glaucoma, is an ocular emergency—know it well. It is common among Asians. The elevated intraocular pressure is caused by mechanical obstruction of aqueous outflow through the trabecular network, due to an anomalous iris configuration (inherited or caused by lens swelling) or iris neovascularization (secondary to diabetes, inflammation, or carotid occlusion). The resulting rapid increase in intraocular pressure causes severe eye pain, nausea, and halos around lights.

Physical exam shows decreased vision, increased intraocular pressure, a narrow anterior chamber (difficult to assess), corneal edema, conjunctival hyperemia, and a fixed, mid-dilated pupil. The diagnosis can be missed if nausea is severe and eye pain is mistaken for headache.

Immediate treatment objectives are: pupil constriction (topical pilocarpine), pressure lowering (oral sorbitol or IV mannitol plus topical beta blockers), and relief of obstruction (prompt laser iridectomy). If an ophthalmologist is immediately available, transfer care. If not, give the patient:
- topical pilocarpine 2% every 5 min x 3,
- topical timolol 0.5% x 1, and
- oral or IV acetazolamide 500 mg x 1, then refer for laser iridectomy.

Over-the-counter medications often include admonitions to "avoid use in patients with glaucoma." These warnings apply only to patients with narrow angle glaucoma not already treated with iridotomy.

THE RETINA

Retinal Detachment

Retinal detachment may occur spontaneously. It often presents as flashes or streaks of light (photopsias), showers of black dots (hemorrhage), or a "shade coming down" or "waving curtain" in a portion of the visual field. Visual acuity may be normal initially.

Presumptive diagnosis is based mainly on history, but occasionally a portion of the retina appears elevated or folded on ophthalmoscopic exam.

Treatment: This condition requires an emergent referral because untreated partial detachment can progress over hours to total retinal detachment with permanent blindness. Small retinal detachments are treated with laser surgery to tack down the area. Larger detachments require scleral buckling (a band around the sclera to restore contact of retina with the wall of the eye), trans-scleral drainage of fluid, vitrectomy (removal of vitreous), or injection of gas or other fluid into the eye (to tamponade the retina).

Retinal Vascular Occlusion

Retinal artery occlusion. Occlusion of the central retinal artery—usually embolic—causes sudden, painless, unilateral blindness. This is a true ocular emergency where every minute counts. Retinal edema (sparing the relatively thin fovea) creates pallor and the appearance of a "cherry red spot" in the macula.

Treatment is directed toward dislodging the embolus, and includes ocular massage, paracentesis of the anterior chamber (to lower pressure), and carbogen (O_2+CO_2) inhalation to dilate retinal vessels. While waiting for the ophthalmologist, have the patient get into the Trendelenburg position and breathe into a paper sack. You may massage the affected globe with the your index fingers (5 sec pressure, 5 sec no pressure, repeat). Unfortunately, all these temporary measures are rarely effective. Patients subsequently require a thorough systemic evaluation for embolic and carotid disease.

Retinal vein occlusion causes sudden, painless, near-total loss of vision. Causes include hypertension, polycythemia vera, and Waldenstrom macroglobulinemia. Retinal edema is accompanied by hemorrhage—not a cherry red spot.

Diagnosis is made with an ophthalmoscopic exam showing a "blood and thunder" fundus with multiple hemorrhages.

Unlike retinal artery occlusion, there is no effective acute treatment, and it is not considered an emergency.

Age-related macular degeneration is the leading cause of irreversible acquired legal blindness in developed countries. There are 2 types: atrophic (or "dry") and neovascular (or "wet"). Atrophic is by far the more common.

Background: The fovea is responsible for fine (20/20) visual acuity. The fovea and surrounding retina is called the macular area. Although the macula comprises only 2% of the visual field, 25% of the cone photoreceptors are here, and it correlates with half of the primary visual area of the brain!

Atrophic age-related macular degeneration causes a gradual loss of central acuity down to 20/400 (peripheral vision is spared).

Neovascular age-related macular degeneration is somewhat amenable to treatment with laser photocoagulation and photodynamic therapy.

Risk factors for both types include smoking and low levels of zinc and antioxidants in the diet. There is an ongoing trial assessing the effect of taking antioxidant and zinc supplements on the development of age-related macular degeneration.[56]

notes

Quick Quiz

1) Differentiate between open-angle and closed-angle glaucoma. Which is a medical emergency?
2) What is the treatment for open-angle glaucoma? For closed-angle glaucoma?
3) Describe the findings with retinal detachment.
4) What is the treatment for retinal detachment?
5) How do retinal artery occlusion and retinal vein occlusion differ?
6) What is the leading cause of acquired legal blindness in the U.S.?
7) Optic neuritis may signal the development of what neurologic disorder?
8) What is vitreous hemorrhage?
9) Does most trauma resulting in an abnormal finding to the eye require ophthalmologic consult?

OPTIC NERVE

Optic neuritis is an inflammation of the optic nerve. Many patients eventually develop multiple sclerosis (MS). Affected persons virtually always slowly regain vision. If they don't, the incorrect diagnosis was probably made.

The majority have ocular pain—especially with eye movement. The optic disc is usually normal initially ("the doctor sees nothing, the patient sees nothing") and only later develops a pallor. The patient should be referred to an ophthalmologist. Treatment with oral glucocorticoids is not indicated, and even IV glucocorticoids are controversial because the long-term outcome is the same.[57] This is not an emergency. Typically an MRI is done, looking for signs of MS.

Optic nerve infarction is the ophthalmologic danger with giant-cell (temporal) arteritis. Other signs and symptoms: malaise, fever, weight-loss, muscle aches, jaw claudication, elevated ESR (erythrocyte sedimentation rate). Corticosteroids are started as presumptive treatment even before the diagnostic temporal artery biopsy is done.

VITREOUS HUMOR

Vitreous degeneration occurs in all elderly persons. They tend to get bothersome floaters, brief unilateral flashing lights (from the vitreous traction on the retina), and vitreous detachment (with a sudden shower of floaters and flashing lights). Vitreous detachment is not dangerous unless it damages the retina.

Vitreous hemorrhage is a cause of sudden, painless, loss of vision. It is caused by either a vitreous detachment tearing a retinal vessel or as a result of breakage of the fragile blood vessels in diabetics with the neovascularization (proliferative diabetic retinopathy).

Any patient with vitreous detachment should be referred to an ophthalmologist, who will look for retinal detachment and defects that, when repaired, may forestall retinal detachment. The eye with vitreous hemorrhage must be examined by ultrasound to check for retinal detachment.

CATARACTS

The crystalline lens of the eye is a clear biconvex structure behind the iris and supported by the zonules. The lens is initially pliable and reactive to accommodation. As the lens ages it gets less pliable and may get less clear. Any lens opacity is called a cataract. Cataracts cause a very gradual, painless, progressive loss of vision. Treatment is cataract surgery with replacement of the lens.

CRANIAL NERVE DYSFUNCTION

Cranial nerve involvement is suspected in a patient presenting with sudden onset of painless double vision. See Figure 10-5.

6th CN (abducens) supplies the lateral rectus. Paralysis: Cannot move the eye laterally.

4th CN (trochlear) paralysis: Eye is deviated upward and the head tilted toward the uninvolved side (Bielschowsky sign).

3rd CN (oculomotor). Motor: Two branches, superior and inferior. The superior branch supplies the superior rectus and the levator palpebrae superioris (eyelid muscle). The inferior branch innervates the inferior rectus, inferior oblique, and the medial rectus. There is also a parasympathetic component of CN III, which is yet another branch. It results in tonic constriction of the pupil. Complete paralysis of CN III results in an eye that is deviated "down and out" (due to unopposed activity of the superior oblique [CN IV] and lateral rectus [CN VI]), a ptotic eyelid, and a dilated pupil. If the eye is not di-

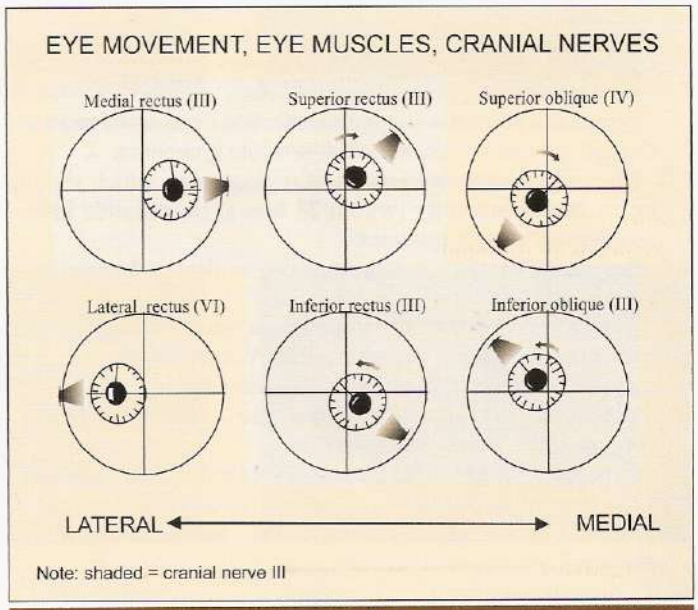


Figure 10-5

notes

lated, the patient probably has diabetic vascular disease affecting only the somatic branches.

EYE INJURY

Trauma

Trauma. Check acuity; inspect anterior chamber for layered blood (hyphema), corneal laceration, subconjunctival hemorrhage, puncture wound, or pupil distortion; ophthalmoscopy to confirm clear view of retina and lack of hemorrhage. If there is pain, instill fluorescein to check for corneal abrasion and evert, inspect, and swab the upper lid, looking for a foreign body. Any abnormal finding, except perhaps a small corneal abrasion, requires consultation .

Alkali Injury

Alkali injury is a special form of trauma where a treatment delay of minutes can devastate the eye. Alkali rapidly penetrates the cornea and enters the anterior chamber, where it wreaks havoc. Treatment is immediate, consisting of profuse irrigation, with lid eversion to remove any alkali-containing particles. Check pH of tears to confirm that it is normal before discontinuing irrigation. Vessels may be blanched by alkali solution in severe injury, paradoxically creating the appearance of a "white and quiet" eye.

RED EYE

The most common cause of a red eye is conjunctivitis. Conjunctivitis may be bacterial, viral, or allergic. By far the most common cause of acute red eye is viral—usually adenovirus. A red eye may also indicate more urgent conditions. Workup should include evaluation of certain key differentiating features—acuity, pain, and photophobia (light sensitivity). Other features to assess are pre-auricular adenopathy, amount and type of discharge, and the location and amount of redness.

1. If visual acuity is decreased, this may indicate a serious problem requiring prompt consultation.
2. Pain is not common in typical infectious causes of red eye. Consider iridocyclitis, keratitis, or acute glaucoma.
3. Photophobia is a key feature of iridocyclitis, which should be evaluated promptly (within 24 hours) for possible intensive topical steroid treatment.
4. Pre-auricular adenopathy (may be tender) is highly suggestive of adenoviral conjunctivitis.
5. Discharge, if purulent, suggests bacterial etiology. Clear exudate more likely suggests viral. White, stringy exudate may be allergic, especially if associated with pruritus. If there is no pruritus, it is more likely dry eye (keratoconjunctivitis sicca—see below).
6. Type of redness. Bright confluent blood red is seen with subconjunctival hemorrhage. Ciliary flush (red near corneal limbus only) suggests iridocyclitis, keratitis, or angle closure. Diffuse conjunctival hyperemia is nonspecific.

Iridocyclitis (iritis, anterior uveitis) is an autoimmune inflammation involving the anterior structures of the eye. It occu as a solitary problem but is also seen with many disease You can make a presumptive diagnosis by the findings ocular pain, photophobia, and a ciliary flush, with a norm cornea and normal intraocular pressure. Slit lamp exam r veals inflammatory cells floating in the aqueous humor deposited on the corneal epithelium. This presentation r quires emergent referral! Treatment: steroids (reduce i flammation and scarring) and cycloplegics (to preve synechiae).

Keratoconjunctivitis sicca (keratitis) is most common in th elderly and in middle-aged women. It may be an early sign systemic inflammatory disease, including Graves disease rheumatoid arthritis, and sarcoidosis. Treat most cases wit artificial tears (electrolyte solutions, methylcellulose, or othe formulations).

Viral conjunctivitis is by far the most common cause of re eye. Patients have diffuse conjunctival hyperemia and pro fuse watery discharge. No specific treatment, just practic strict hygiene. It should resolve in 5-7 days.

Bacterial conjunctivitis may be caused by staph, strep, *H. influenza*, *Pseudomonas*, or *Moraxella*. Most cases of bacteria conjunctivitis will resolve in 5 days even without treatment!—BUT—we DO treat and follow closely because, if i does become complicated, the patient can have vision loss Red eye with profuse purulent discharge is the typical presentation. Treat uncomplicated cases with 10% sulfacetamide Reserve aminoglycosides for the more serious cases. If complicated, obtain cultures (swab conjunctiva), initiate treatment with an aminoglycoside or quinolone, and refer to an ophthalmologist.

Neisseria conjunctivitis (can be gonococcal or meningococcal) is a "hyperacute" (severe conjunctival discharge and redness) conjunctivitis that requires early recognition and aggressive topical treatment to prevent progression to corneal perforation. Systemic therapy is also indicated. In contrast, chlamydial conjunctivitis is chronic, insidious, and requires systemic therapy alone.

Contact lens wearers have impaired ability to fight conjunctivitis and are at high risk for developing vision-threatening complications. Pseudomonas conjunctivitis can progress to corneal perforation overnight in these patients. Any contact lens wearer with conjunctivitis should immediately discontinue use of the lenses. Start them on a topical agent that includes good *Pseudomonas* coverage and refer to an ophthalmologist. *Acanthamoeba* has become a common organism on Board exams, especially if the patient uses tap water for lens cleaning. Usually it progresses rapidly to keratitis!

OTHER EYE INFECTIONS

Endophthalmitis (infection inside the eye) can have an ocular or systemic source. Patients present with decreased visual acuity, hazy cornea, pain, and hypopyon (layering of white cells visible in the anterior chamber.) Refer immediately. Treat-

notes

Quick Quiz

1) What virus is responsible for many cases of conjunctivitis?
2) You have diagnosed iridocyclitis; what should you do next?
3) A contact lens wearer presents with severe keratitis and says she uses tap water frequently for lens care. What organism should you consider?
4) A patient presents with a penetrating wound to the orbit. What unusual organism should you be concerned about—remember this is very serious!
5) Define the terms chalazion and stye.

ment is systemic and intraocular antibiotics. Remember, if trauma to the orbit is involved, suspect *Bacillus cereus*!

Periorbital cellulitis usually is a rapidly progressive cellulitis of the periorbital area, which may become orbital if not treated. Patients present with warmth, redness, and swelling around the eye. Key physical exam finding is normal extraocular muscle movement without diplopia, or pain with eye movement.

If the patient has disconjugate gaze, diplopia, or pain with eye movement, it is probable that the infection has moved into the orbital space. This warrants a periorbital CT or MRI, and IV antibiotics with staph and strep coverage.

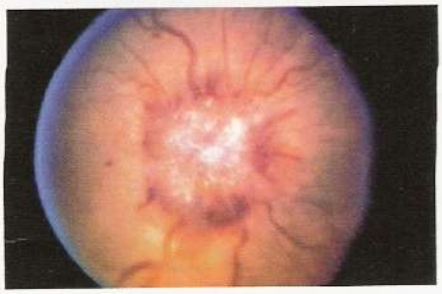
Chalazion is caused by obstruction of one of the tarsal (meibomian) glands forming a small nodule found in the tarsus under the eyelid. Not a problem unless secondary infection occurs. Such infections often require ophthalmologic surgery.

Stye is an abscess at the base of an eyelid. Treat it with warm compresses and a topical ophthalmologic antibiotic. Occasionally, it will require drainage.

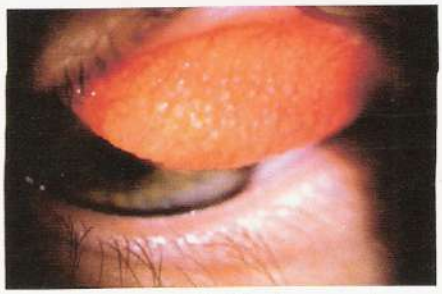
EYE EMERGENCIES – In BRIEF

Briefly, here is how to approach ophthalmologic emergencies.

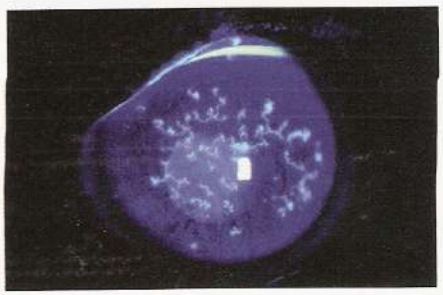
1) Treat emergently and immediately refer:
   alkali burn, trauma, orbital cellulitis, central retinal artery occlusion, angle closure glaucoma, optic nerve infarction in giant-cell arteritis.
2) Refer immediately without on-site treatment:
   penetrating ocular injury, endophthalmitis, retinal detachment, keratitis/keratoconjunctivitis.
3) Refer to be seen within 1-2 days:
   central retinal vein occlusion, optic neuritis, and vitreous detachment/hemorrhage.



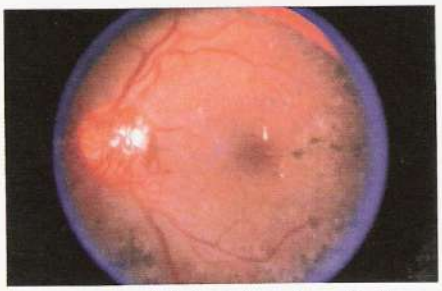
Papilledema: seen with increased intracranial pressure. Think of tumor and pseudotumor cerebri. Mimics optic neuritis/papillitis except papilledema is bilateral.



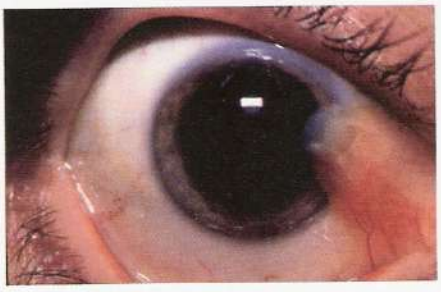
Allergic Conjunctivitis. Usually seasonal



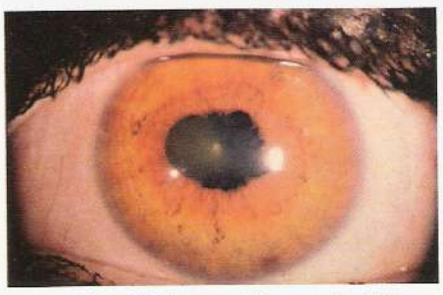
Herpes Keratitis of the cornea. Frequently recurrent.



Proliferative Diabetic Retinopathy: with disc neoplasia.

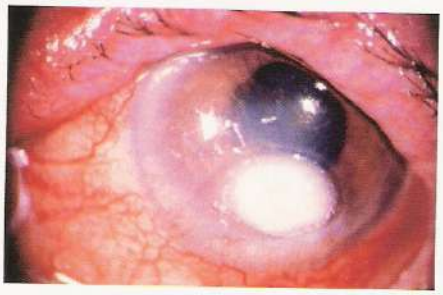


Pterygium: associated with exposure to ultraviolet light and dry wind. Seen in farmers, professional golfers, etc.

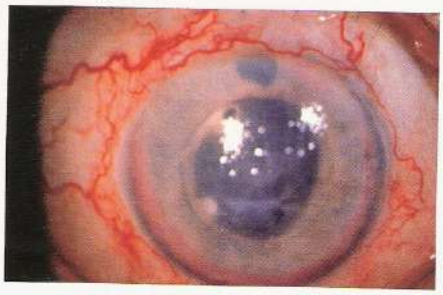


Synechiae. This is a possible sequela of iritis (iridocyclitis). 90% of iritis is idiopathic but it is seen in inflammatory diseases such as viral infections and CT diseases.

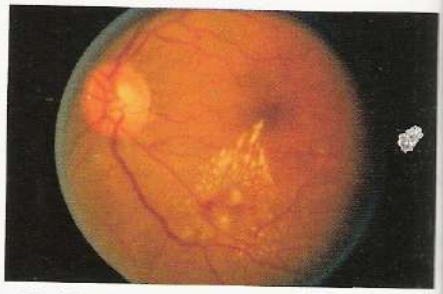
notes



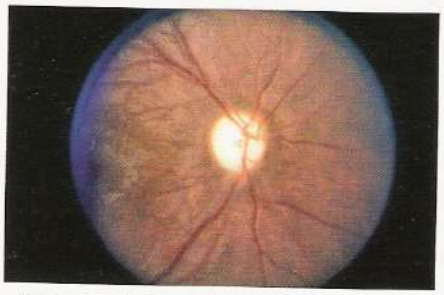
Corneal Ulcer. Usually caused by improper use of contact lenses. It is especially seen with the extended wear contact lenses.



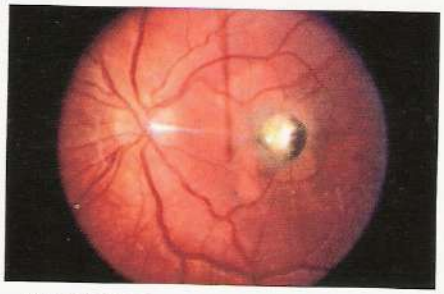
Proliferative Diabetic Retinopathy: Rubeosis. Blood vessels grow onto the iris. This may cause intractable glaucoma. Also caused by central retinal vein occlusion.



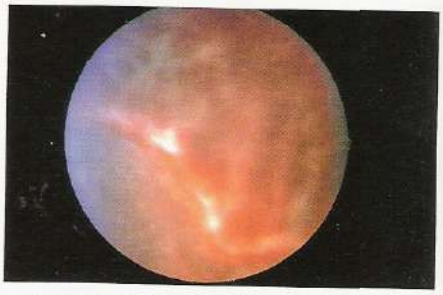
Hard Exudate as seen in NON-diabetic retinopathy. This is caused by leakage of protein and lipids from capillaries. Treatment is photocoagulation of the leaking capillaries.



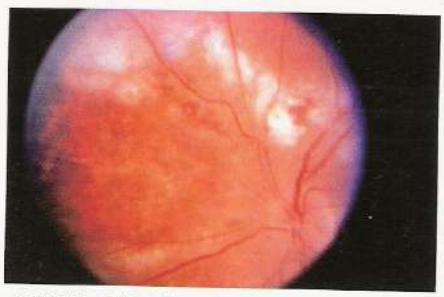
Optic Atrophy has various causes including proliferative diabetic retinopathy and central retinal artery occlusion. In older patients also consider ischemic optic neuropathy.



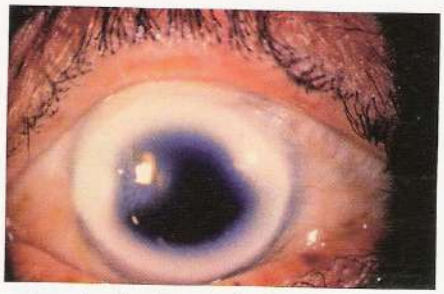
Toxoplasmosis



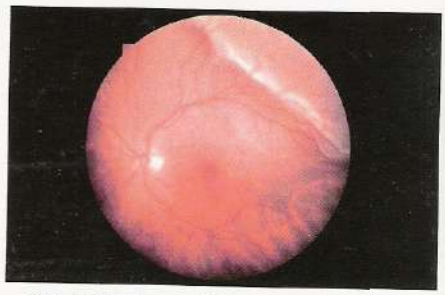
Proliferative Diabetic Retinopathy: Vitreous Hemorrhage.



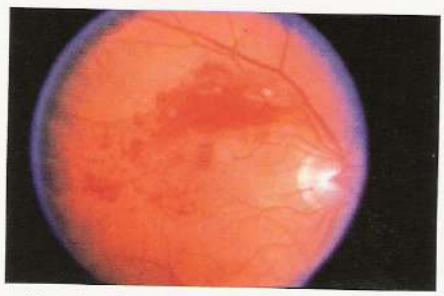
CMV Retinitis. Especially seen in people with AIDS.



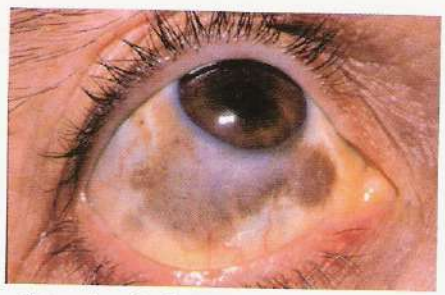
Arcus Senilis. Common in older patients. In patients < 40 yrs, it may be a sign of a lipid disorder.



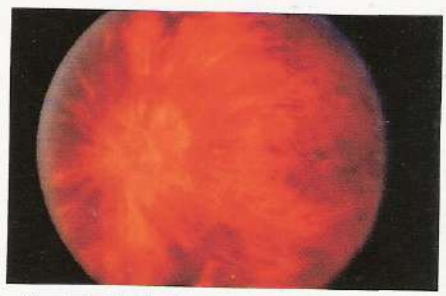
Retinal Detachment. This usually occurs in very myopic people. It often occurs after a vitreous hemorrhage.



Branch retinal vein occlusion (BRVO): main cause is hypertension but also seen with diabetes and with hyperviscosity syndromes. Think of this as exaggerated AV nicking with the artery pinching off the vein.



Heterochromia, Ocular Melanosis. This is a normal finding in darkly pigmented persons. Rarely caused by Fuch's iridocyclitis.



Central retinal vein occlusion (CRVO): Same causes as BRVO.

notes

Quick Quiz

1) A Rinne test is done. The patient can hear louder with the tuning fork on the bone. What does this mean?
2) A Weber test is done on the same patient. He can hear louder on the left side. What does this mean?
3) What is the best way to diagnose an acoustic neuroma?
4) KNOW Table 10-14!

EAR, NOSE, THROAT

HEARING LOSS

Hearing loss. Do the Rinne and Weber tests as explained below to differentiate between conductive and sensorineural hearing loss (Know these tests!). Conductive hearing loss occurs in middle ear infection, eustachian tube blockage, otosclerosis, TM perforation, and ceruminosis or any other impaction of the external canal. Sensorineural hearing loss is caused by either cochlear damage or nerve damage. *Sensory* loss may be caused by viral infections, ototoxic drugs, meningitis, cochlear otosclerosis, Ménière disease, and aging. *Neural* hearing loss is usually due to cerebellar angle tumors such as acoustic neuromas.

Presbycusis is the effect of aging on the auditory system. It usually causes bilateral symmetrical neurosensory hearing loss in the frequencies > 2000 Hz. One third of persons older than 65 years have some form of hearing loss, and this is the most common cause.

Otosclerosis is an autosomal dominant trait with poor penetrance. It is much commoner in white persons than in black persons. 10% of white persons develop otosclerosis; 1% become symptomatic.

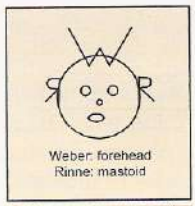


Figure 10-6

The Rinne test (See Figure 10-6 and Table 10-14) is based on the observation that air-conducted sound is normally louder than bone conducted. The base of the vibrating 256 Hz (best) tuning fork is placed over the mastoid, and the sound of this bone-conducted hearing is compared to the air-conducted sound the patient hears when the tuning fork is placed next to the ear on the same side. With no hearing loss, the air-conducted sound is loudest. With conductive hearing loss, the bone conduction is louder. With sensorineural hearing loss, both air and bone conduction are decreased, but the air conduction is perceived as being louder.

The Weber test consists of placing the base of a 256 or 512 Hz tuning fork on the middle of the forehead. The patient tells you whether the sound lateralizes to one side or stays in the middle. If the sound is perceived as being in the middle, the patient either has normal hearing or the hearing loss is symmetrical. If the sound lateralizes, there is either a conductive hearing loss in the ipsilateral ear or sensorineural loss in the opposite ear.

You can simulate the Weber test by humming and sticking your finger in one ear (causing a conductive hearing loss). If your hearing is normal, the sound lateralizes to the plugged-up ear.

Ménière disease is uncommon. Affected patients have recurrent, severe attacks of vertigo that persist for several hours and often are associated with vomiting and prostration. Patients have tinnitus, fullness in the ear, and progressive hearing loss (which is frequently one-sided) until deaf, at which time symptoms stop!

Acoustic neuromas (vestibular schwannomas) are benign, very slow-growing tumors of the eighth cranial nerve. Patients usually present with tinnitus, unilateral hearing loss, and gait imbalance. MRI is the diagnostic test of choice. Treatment is radiosurgery or surgical resection.

Table 10-14: Diagnosing Conductive vs. Sensorineural Hearing Loss with the Weber and Rinne Tests

FINDINGS ON RINNE AND WEBER TESTS		
TYPE OF HEARING LOSS (examples)	RINNE Position A = Air (i.e., fork held next to ear); Position B = Bone (i.e., base on mastoid)	WEBER Tuning fork base held at middle of forehead
None	Sound A > B	Sound does not lateralize
Sensorineural loss (in left ear)	Left ear: Both A & B decreased equally so still: Sound A > B	Lateralizes to the right ear
Conductive loss (in left ear)	Left ear: B > A	Lateralizes to the left ear

notes

OTITIS

Otitis externa is also called swimmer's ear. You can easily treat this with antibiotic ear drops. Malignant (necrotizing) otitis externa involves not only the canal, but also the subcutaneous tissues and sometimes the bone. It is usually due to either a *Pseudomonas* or *Proteus* infection. Suspect this in diabetics or the immunocompromised. If caught early enough, ciprofloxacin is usually sufficient treatment. If too late, long courses of parenteral antibiotics are required.

SINUSITIS

Sinusitis is inflammation in the paranasal sinuses. Acute sinusitis is defined as persisting up to 4 weeks. Chronic sinusitis is defined as persisting more than 4 (some say 8) weeks. Recurrent sinusitis is 3 or more separate episodes of acute sinusitis per year.[58]

The two most important factors in the development of sinusitis are patency of the ostia (blocked with thickened sinus secretions, sinus congestion, nasal polyps, trauma) and ciliary movement (immotile cilia syndrome).

In both, the most common causative organisms are *S. pneumoniae*, *H. influenzae*, and *Moraxella catarrhalis*. Chronic sinusitis may also be caused by *S. aureus*, group A strep, *P. aeruginosa* (esp. cystic fibrosis), and anaerobes such as *Fusobacterium* and *Bacteroides*.

Fungal sinusitis is seen in patients with diabetes (especially *Mucor*) and cancer, and in those receiving corticosteroid therapy.

Acute bacterial sinusitis patients have paranasal pain and pressure exacerbated by leaning forward. Purulent nasal discharge with tenderness over the affected sinuses is common. They may have fever and malaise. Note that patients with similar headache and pressure along with rhinorrhea and sneezing usually have allergic or viral rhinitis—not sinusitis.

Chronic sinusitis patients present differently, often with signs/symptoms such as chronic refractory sinus congestion, bad breath, postnasal drip, cough, or headache.

Nasal smears are most useful for differentiating allergic from bacterial sinusitis. High eosinophils are seen with both allergic rhinitis and nonallergic rhinitis with eosinophils syndrome (NARES). Bacterial sinusitis shows large numbers of neutrophils and bacteria.

Do not do sinus cultures except in refractory cases; these are usually an invasive procedure. A needle is introduced via the antral nose or under the lip into the maxillary sinus; fluid is injected and then aspirated. Do a sweat chloride on anyone with *Pseudomonas* growing from a sinus culture.

Radiography: X-rays showing opacification, air-fluid level (Waters view of the frontal and maxillary sinuses), and thickening indicate sinusitis. CT scan is the gold standard. In addition to the frontal and maxillary areas, it shows the ethmoid and osteomeatal complex. It also shows subtle thickening. The T2-weighted MRI is useful for differentiating inflammatory process (high-intensity bright) from a tumor (intermediate-intensity bright).

Treatment:

Current recommendations are to wait 7–10 days before treatment of acute sinus symptoms with antibiotics, because the vast majority of acute sinus symptoms are not due to bacterial infection.

Treat acute sinusitis with a 10–14 day course of amoxicillin or TMP/SMX. For beta-lactamase producing strains (40% of *H. influenzae* and most of *M. catarrhalis*) or if anaerobes are suspected, use amoxicillin with clavulanic acid. Other potentially useful antibiotics are quinolones, azithromycin, and 2nd generation cephalosporins.

Treat chronic sinusitis for a week more after symptoms resolve—and at least 3–4 weeks total. Same meds can be used. Choice is often dependent on picking something different from previously used ineffective agents.

Use endoscopic sinus surgery when medical therapy fails.

Allergic sinusitis is often treated effectively with immunotherapy with lasting benefit.[59]

WOMEN'S HEALTH

OFFICE OBSTETRICS

PREGNANCY. THE FOLLOWING IS A COMPILATION OF EVERYTHING WRITTEN ON PREGNANCY IN THESE CORE CURRICULUM BOOKS—PLUS MORE! THIS IS A FREQUENTLY QUESTIONED AREA ON THE BOARDS, AND THIS COMPILATION MAKES IT EASIER TO REVIEW PREGNANCY AS A SPECIFIC TOPIC.

◆ Gastroenterology:

Question: What conditions can cause abdominal pain with an elevated amylase? Answer: Acute pancreatitis, acute cholecystitis, intestinal infarction, diabetic ketoacidosis, perforated ulcer, salpingitis, and ectopic pregnancy!

Fatty liver: The fat globules are microvesicular in acute fatty liver of pregnancy and in Reye syndrome.

Hepatitis E: There is a very high risk of fulminant hepatitis in the third trimester of pregnancy—with a 20% fatality rate!

Hepatitis B: The HBV vaccine is safe to give to pregnant patients.

Inflammatory bowel disease: Both sulfasalazine and prednisone are safe in pregnancy.

◆ Pulmonary:

Pregnant women are more susceptible to DVT and pulmonary embolus. OK to do impedance plethysmography, ultrasound, and V/Q scan.

Do not give warfarin to pregnant patients (deformities are common especially if it is given in the 1st trimester). Use adjusted dose heparin instead.

◆ Cardiology:

Rubella during pregnancy is a common cause of supravalvular aortic stenosis, pulmonic stenosis, and other congenital cardiac defects.

notes

Quick Quiz

1) A diabetic patient is presented with a black eschar in the nares and severe sinus pain. What is the likely organism?
2) A pregnant woman has a DVT. What can you use for treatment?
3) Is elective cardioversion possible during pregnancy?
4) What is the problem with rubella being acquired in the first trimester?

Often mitral stenosis is first diagnosed when a pregnant patient presents with atrial fibrillation and pulmonary edema. The increased blood volume in pregnancy can cause a precipitous exacerbation of mitral stenosis—so consider treating all pregnant MS patients with digoxin. If severe mitral stenosis is found before pregnancy, valvulotomy should be performed.

Elective electrical cardioversion, procainamide, digoxin, and verapamil are all OK during pregnancy.

Porcine valves are less durable (especially in patients on hemodialysis) but do not require anticoagulation. They are indicated in patients > 65 years old and in patients with contraindications to anticoagulation (ulcers, etc.), and they are often given to women of childbearing age to preclude the use of anticoagulants during pregnancy.

Cardiac contraindications to pregnancy: Pulmonary hypertension of any type, Eisenmenger syndrome, Marfan syndrome with dilated aortic root, and chronic dilated cardiomyopathy with heart failure.

Relative contraindications: Closely watch pregnant patients with secundum ASD, aortic stenosis, or dilated cardiomyopathy. In the latter two, patients are usually kept at bedrest. Secundum ASD patients are usually not at risk for cardiac decompensation unless they develop atrial fibrillation.

Both mitral valve prolapse and hypertrophic cardiomyopathy are well tolerated in pregnancy.

◆ Infectious Disease:

Bacterial Infections:

UTIs: *Strep agalactiae* and *E. coli*. Treat with ampicillin, cephalexin, or nitrofurantoin. Ciprofloxacin is not given to pregnant women.

Listeria monocytogenes infections are associated with decreased cellular immunity syndromes like AIDS, lymphoma, and leukemia, but they are also seen in neonates, the elderly, and pregnant women. Suspect this in a pregnant woman with a UTI and negative urine culture.

Strep agalactiae (Group B) is also a cause of postpartum endometritis and bacteremia. So suspect this in any woman who develops a postpartum fever !

Approximately 5% of pregnant women have *Chlamydia trachomatis* in their genital tracts; antibiotic ointment in infants' eyes at birth does not prevent this conjunctivitis (it is for GC only).

Gonorrhea is more likely to disseminate in pregnant women. The newborn will be at risk for GC conjunctivitis.

Asymptomatic bacteriuria should be treated in pregnant women (1/3 go on to pyelo- nephritis!!), neutropenic patients, diabetics, and transplant patients.

Syphilis is often asymptomatic in pregnant women.

Parasitic Diseases:

Toxoplasma gondii is serious in the immunocompetent only if acquired during pregnancy when it can cause congenital toxoplasmosis (resulting in mental retardation and chorioretinitis). The fetus is more likely to have a congenital infection if the disease is acquired later in pregnancy (15% 1st trimester; 70% last trimester).

Viral Infections:

Viruses with the greatest teratogenic potential are CMV, varicella zoster, herpes simplex, and rubella. This is especially true if acquired in the first trimester.

CMV is ubiquitous and the most common cause of congenital viral infection. 1–2% of all newborns have the infection in utero, but only a few have any abnormalities. These abnormalities, which range from mild neurologic problems to microcephaly, usually occur in mothers with a primary CMV infection.

Rubella is German measles (ss RNA virus). If it is acquired by a pregnant patient in the first trimester, there is an 80% chance that the baby will have congenital defects—usually severe. Defects include cataracts, heart problems, mental retardation, and fetal death. It is diagnosed in the mother by the hemagglutination inhibition test. If this test is negative in a newly exposed pregnant patient, repeat it in 3 weeks (after incubation period) before making any decisions. If it is then positive, a therapeutic abortion is considered. You can diagnose rubella prenatally by finding rubella IgM antibody in fetal blood. Immune globulin will not prevent the infection, but it may give some fetal protection in the patient who declines therapeutic abortion.

Varicella-zoster infection has a slight risk of causing congenital defects. The pregnant woman with chicken pox has a 10% chance of developing severe pneumonia.

HIV: There is a mother-to-fetus transmission risk of 30%.

◆ Nephrology:

During pregnancy, there is increased calcium absorption and excretion because the 1,25-$(OH)_2$D3 is > 2 x normal. Even so, frequency of renal stones is the same as in the non-pregnant patient. The urinary tract of the pregnant patient is dilated and, if stones do develop, most pass easily!

There are two types of hypertension that can occur during pregnancy: Chronic essential hypertension in pregnancy and pregnancy-induced hypertension. Pregnancy-induced hypertension (PIH—previously called preeclampsia), when present, usually occurs in the third trimester, and stops after delivery. Patients have hypertension, peripheral edema, and edema of the kidney with proteinuria. The serum chemistry is significant only for an elevated uric acid. There are risk factors for pregnancy-induced hypertension/preeclampsia. These

notes

Table 10-15

Most asked-about DRUGS in PREGNANCY	
Dangerous	Relatively safe drugs
1. Valproic acid, Trimethadione	1. Prednisone
2. ACE inhibitors, ARBs	2. Heparin
3. Ciprofloxacin	3. Sulfasalazine (B)
4. Podophyllin – condoloma (anogenital warts)	4. Digoxin (C), verapamil (C), procainamide (C), cardioversion
5. Methimazole	5. Clonidine (C), labetolol (C), calcium channel blockers in trials
6. I^{131}	6. PTU
7. Most antihistamines	7. Chlorpheniramine (C)
8. Warfarin	8. Gentamicin (C)
9. Nitroprusside	9. Betalactams (all are B except moxalactam is C)
10. Most aminoglycosides (D)	10. Amphotericin B (B)
11. Doxycycline, TCN	
12. Metronidazole in 1st trimester	

include a serum creatinine > 1.2, BP > 160/100, increased liver enzymes, retinal hemorrhage, platelet count < 100,000, or microangiopathic hemolytic anemia. Treatment of PIH is hospitalization, bedrest, and treatment of the hypertension. Medications used are the tried-and-true hydralazine, methyldopa, and diazoxide. Labetalol, clonidine, and calcium channel blockers are undergoing trials. ACE inhibitors (teratogenic) and nitroprusside (cyanide poisoning) should not be used for PIH! If the hypertension occurs before the third trimester, it is probably latent essential hypertension being "brought out" by the pregnancy.

PIH is suggested in a pregnant patient with new onset hypertension, proteinuria, and rapid weight gain with edema in the third trimester. Patients have diffuse vasospasm, a low-grade DIC with associated decreased platelets, and a decreased antithrombin III (good diagnostic test).

SLE with lupus nephritis: If the disease has been in remission, there is a 90% chance of a successful pregnancy. If it flares up during pregnancy, however, 25% of the fetuses die, usually from the lupus anticoagulant antibody causing thrombotic events.

Pregnancy and chronic renal failure. If the creatinine is < 2 and the patient with CRF is not hypertensive, there is not an increased risk of abortion or malformation, and there is no increase in the rate of progression of the renal disease. There is an increased risk of PIH.

As renal failure progresses, chance of pregnancy decreases. Dialysis patients rarely become pregnant. In stable renal transplant patients, the outcome of pregnancy is usually great!

◆ Endocrinology:

Prolactinomas: If the prolactin level is > 200 it is virtually always a prolactinoma, even in a nursing woman, although it may reach this high in pregnancy. If pregnancy is an issue, bromocriptine is recommended as it will restore menses in 80% of affected women and 90% of those become pregnant. By contrast, transsphenoidal surgery will restore menses in 70% of women, of whom only 70% become pregnant.

Thyroid tests: If the TBG is elevated, as in pregnancy, there will be more binding sites available so more T_4 will be bound. The body responds to the resultant decrease in free T_4 by making more. The result of increased TBG is that the total T_4 is increased, the T_3RU is decreased (i.e., TBG increased), and the free T_4 index is normal (Free T_4 level is normal).

Always treat pregnant hypothyroid patients and follow their TSH during pregnancy because their requirements may increase.

Treatment of Graves: PTU or methimazole for children through young adulthood. Treat pregnant patients with PTU as methimazole can cause aplasia cutis in the fetus.

Amenorrhea. Pregnancy is the most common cause, of course, so always order a beta-HCG as the first test in working up secondary (and primary, for that matter) amenorrhea.

Know that GnRH can be given via a pump in a pulsatile fashion. Women with secondary amenorrhea from a low GnRH have been able to use this means to successfully become pregnant and bear children.

The luteinizing hormone test is increased artifactually in germ cell cancer and pregnancy because the elevated HCG in each cross-reacts with the LH test.

Diabetes mellitus. In pregnancy, strict control, even before conception, is important (always maintain glucose < 110!). Before conception, control of blood sugar reduces fetal malformation and, during pregnancy, it reduces miscarriages, fetal anomalies/death, and newborn problems. It may (or may not) prevent macrosomia (birth weight > 9 lb.). With pregnancy, a diabetic patient requires about 50% more insulin (from increased resistance). This increased requirement is gone immediately after delivery, so observe patient carefully the day after delivery.

Strict diabetic control not only helps fetal status in pregnancy but it has been shown to help virtually all the other complica-

notes

Quick Quiz

1) Know Table 10-15!
2) Are ACE-inhibitors safe in pregnancy?
3) A pregnant woman has Graves disease. What can you use to treat her?
4) What is a common finding in pregnant women who have not had prenatal care?
5) Dysfunctional uterine bleeding usually does not require any workup. True or False?

tions of diabetes, including the nephropathy, retinopathy, and neuropathic symptoms.

◆ Hematology-Oncology:

Fe deficiency is commonly seen in pregnant women who have had no prenatal care.

Early menarche, late menopause, and late first pregnancy are associated with breast cancer.

◆ Neurology:

Seizures and pregnancy. The risk of teratogenesis is 2% of normal births. This increases to 5% in patients with an untreated seizure disorder. The risk in treated epileptics is 8%! Absolutely avoid valproic acid and trimethadione in pregnant patients.

◆ Rheumatology:

SLE: Prednisone should be continued in SLE patients wishing to become pregnant if there is a history of a recent exacerbation.

If an SLE patient becomes pregnant, usually all anti-SLE drugs including prednisone are stopped and the patient is watched. There is often a spontaneous remission in pregnancy (as there can be with RA). There is a high risk of spontaneous abortion and, if the patient has anti-Ro antibody, there is an increased risk of neonatal lupus and congenital complete heart block. Anticardiolipin and lupus anticoagulant are associated with thrombosis and fetal loss. Low-dose ASA is often given in the pregnant SLE patient to decrease the chance of thrombosis (although it is not clear whether it is effective!).

Pregnancy is a predisposing factor for gonococcal arthritis.

◆ Dermatology:

In pregnant patients, avoid most antihistamines. The ones that are used are hydroxyzine, chlorpheniramine, and tripelennamine (PBZ®).

Condyloma acuminatum: Anogenital warts are generally treated with podophyllin 25% in a tincture of benzoin, but this is teratogenic, so do not give to pregnant patients.

◆ Miscellaneous:

One can usually safely give I^{131} treatment to hyperthyroid patients, but it is not safe to give it to either pregnant patients or patients with severe hyperthyroidism.

◆ Drugs in pregnancy: See Table 10-15.

FDA use-in-pregnancy ratings.

A: Controlled studies show no risk.
B: There is no evidence of risk in humans.
C: Risk cannot be ruled out. Most drugs. Human studies are usually lacking.
D: There is positive evidence of risk.
X: It is contraindicated in pregnancy.

OFFICE GYNECOLOGY

Office gynecology has been partially covered in previous sections. Especially review gynecologic infections in the Infectious Disease section. Pap smear, ovarian cancer, and breast cancer are covered in the Oncology section. Osteoporosis is discussed under Geriatrics in the General Internal Medicine section. Amenorrhea is discussed in the Endocrinology section.

Dysfunctional uterine bleeding (DUB) refers to excessive bleeding due to persistent anovulation in a reproductive age woman with ovaries capable of producing estrogen. The patient's period may be too frequent, too long, or with too heavy of a flow. DUB is a diagnosis of exclusion. There are many, many causes, including hypothyroidism, liver disease, renal disease, coagulopathies, pregnancy complications, anatomic lesions, and drugs, among others.

Treatment for young women with DUB is usually oral estrogen-progestin preparations. Oral contraceptives containing 35–50 µg of ethinyl estradiol are often used. Four tablets a day are given initially; this increases bleeding for 1–2 days and generally stops the bleeding in 3–4 days. The patient is then given 2 pills per day for 20 more days. Withdrawal bleeding will then occur within 2 to 5 days of the stopping of treatment. This hormonal therapy is given for 2–3 more cycles, using one pill per day, and then stopped.

Premenstrual tension syndrome (PMS) is a group of symptoms, which most often start during the late luteal phase and are gone within 1–2 days of the onset of menses. The biochemistry of this dysfunction has not been established. No single treatment has been proven effective, but the cause may be multifactorial, and there are many avenues of treatment to explore with each patient. You can achieve ovulatory suppression with oral contraceptives. These patients may also respond well to the newer mini pill, which contains only progestin. Other similar options include Depo-Provera® and Norplant®. Oral natural progesterone has been used with varying success. Various dietary changes help some patients, such as avoiding caffeine, salt, sugar, alcohol, and/or chocolate. Vitamin supplements such as vitamin B_6 and vitamin E have also been tried and sometimes are effective. Magnesium 360 mg as magnesium pyrrolidone carboxylic acid orally

notes

t.i.d., given from day 15 to the first day of menses, may also help. Note that no one of the above treatments is effective for everyone.

OFFICE PSYCHIATRY

PSYCHOSOCIAL DISORDERS

Anorexia nervosa syndrome usually begins post-puberty and in early adulthood. It almost always occurs in white middle-to-upper-class women.

Diagnosis is clinical. Typically:

1) Weight loss has resulted in a weight at least 15% under ideal.
2) Patients have a preoccupation with food and have an intense fear of becoming fat.
3) There are disturbances in the way body weight and size are experienced. These patients have a distorted self image and, despite often extreme weight loss, they not only deny thinness but complain of feeling fat. This is a "soft" criterion because many young women have a similar self-perception, although without the weight loss.
4) Women have had absence of 3 or more consecutive menstrual cycles.

In advanced cases, patients become emaciated, bradycardic, and hypotensive. Lab studies show anemia, hypokalemia, and hypoalbuminemia. These patients are at risk for sudden death from ventricular tachyarrhythmias.

Treatment. It is important to establish a supportive advisor role with the patient. Patients are very resistant to psychotherapy, and outpatient supportive care often works just as well as inpatient therapy. Explain the dangers of starvation, such as sudden death, and set realistic short-term goals for weight gain. Acknowledge the patient's perception and continually reinforce that you will not let her get fat as she gains weight. Treatment is long-term with frequent failures and setbacks. Antidepressants may exacerbate severe anorexia because they are dietary depressants. Cyproheptadine, an appetite stimulant, may help a little. Outcome is very poor in 20–30%.

Bulimia is the term used for binge eating of large amounts of food followed by purging—either with vomiting or with laxatives. It may be a variant of anorexia nervosa, and many bulimia patients have a history of anorexia in their past. Even so, these patients are usually not < 85% of ideal weight.

Diagnosis is clinical. Typical symptoms:

1) Recurrent episodes of binge eating. At least 2 per week for at least 3 months.
2) Sense of lack of control over eating behavior.
3) Overly concerned with body weight and shape.
4) Regular use of self-induced vomiting, laxatives, dieting, fasting, and vigorous exercise to prevent weight gain.

The most common lab abnormalities are hypokalemia and metabolic alkalosis from vomiting and laxative use.

Treatment is again supportive, with the focus of slowly decreasing the amount of food eaten and decreasing the frequency of binge-eating episodes. Treatment, as with anorexia, is long-term, with frequent failures and setbacks. Desipramine and (probably) other antidepressants are often effective but need to be continued long-term.

Anxiety disorders are classified into generalized anxiety disorder, which is chronic and low grade, and panic disorder, with brief and dramatic panic attacks.

Panic disorder is diagnosed when four attacks have occurred within one month, or one or more attacks are followed by one month of intense fear of another attack. These patients often have phobic avoidances of places or situations associated with attacks. Secondary major depression is a common complication. Treatment of panic disorder is usually with **SSRIs** and anxiolytics such as benzodiazepines and buspirone HCl (BuSpar®). The optimal treatment is an SSRI, with only short-term use of benzodiazepine. Psychotherapy may have some benefit.

Bipolar disorder occurs when a patient has a manic or hypomanic (mild manic) episode, even if the patient has never had a depressive episode. Most manic patients are euphoric and have inflated self esteem, decreased need for sleep, and pressured speech. Hypersexuality is common, as is overspending. Some patients are just irritable, possibly paranoid also, and this is termed dysphoric mania. Psychotic symptoms are common during manic episodes. The depression is identical to common depression. Lithium is effective treatment in 75% of cases, but therapeutic response is very slow (4–6 weeks for full effect) so antipsychotics are often simultaneously started for acute manic episodes.

Depression is discussed briefly in the Geriatrics section (see pg 10-12). Of course, this does not mean it only occurs in the elderly, but the general population has the same treatment options as the elderly.

Neuroleptic malignant syndrome (NMS) is an idiosyncratic response to potent neuroleptics resulting in autonomic dysfunction, extrapyramidal symptoms, and high fever. The fever may reach 106°F. The neuroleptics most commonly involved are haloperidol, piperazine phenothiazines, and thiothixene. NMS is thought to be due to a depletion of dopamine. It persists for up to 10 days after the drug is stopped. Treatment is stopping the causative drug and cooling the patient. Give oral dopamine agonists also to counteract the depletion. Bromocriptine is the drug of choice, but you may also use amantadine and dantrolene.

GENETICS

Histocompatibility antigens are the antigens involved in graft rejection. Many of the histocompatibility genes are closely grouped on chromosome 6, and this area is called the Major Histocompatibility Complex (MHC). The human MHC is termed HLA. There are three classes of antigens found on cells that are associated with the HLA. Again, all the HLA genes are on chromosome 6.

notes

Quick Quiz

1) A young woman is brought in by her husband for weight loss and lack of menses for 6 months. What diagnosis should you consider?
2) How does anorexia nervosa differ from bulimia?
3) Describe a patient with neuroleptic malignant disorder. [You will be asked this on the test!]

Class I HLA antigens: All have the same molecular weight. These antigens are produced by the HLA-A, HLA-B, and HLA-C regions on chromosome 6. These antigens are on most body cells except RBCs.

Class II antigens are in the HLA-D region. Class III HLA antigens are formed in the HLA B-D region. They consist of three complement component structures.

General review of transcription and translation: The DNA has coding sequences called exons, separated by non-coding sequences called introns. The gene for one small protein may

Table 10-16

IMPORTANT CONGENITAL ABNORMALITIES (and asso section in the MedStudy Books)

System	Autosomal Dominant	Section	Autosomal Recessive	Section
GI	Gilbert	1	Alpha1-antitrypsin deficiency	1
	Familial polyposis syndromes including Familial p., Gardner synd., Peutz-Jeghers synd, and Juvenile p.	1	Hemochromatosis	1
			Wilson disease	1
Renal	Polycystic kidney disease	4		
Endocrine	F. combined hypercholesteremia	5	Dysbetalipoproteinemias	5
	F. hyperTRIGLYCERIDEmia	5	Vitamin D dependent rickets	7
	Multiple Endocrine Neoplasia	7		
	Benign F. Hypocalciuria	7		
Hematologic	von Willebrand disease	8	Sickle cell anemia	8
	C,S, and antithrombin III deficiency	8	Beta-thalassemia	8
	Hereditary spherocytosis	8	Factor deficiency (5,7,10,11,12,13)	8
	Dysfibrinogenemias	8	Glanzman thrombasthenia	8
			Bernard-Soulier	8
Neurologic	Charcot-Marie-Tooth I, some type II	11	Charcot-Marie-Tooth type II	11
	Huntington chorea	11		
	Myotonic dystrophy	11		
Other	Marfans	5	Cystic fibrosis	3
	HCM (IHSS)	5	Homocystinuria	
	Neurofibromatosis	9	Albinism	
	Hereditary Angioedema	9	Deafness	
	Mastocytosis	9		

notes

consist of 20 of each, with 95% of the space being introns. The full gene (introns + exons) is transcribed by DNA dependent RNA polymerase into RNA. The introns are then spliced out of the RNA before it leaves the nucleus, thereby forming the messenger RNA (mRNA). The mRNA is then translated into protein: Each three base sequences compose a codon, which determines which amino acid will be attached when it is translated.

Point mutations are a change to a single base. It can result in either a missense or a nonsense mutation. Missense mutation is when a point mutation causes a different amino acid to be produced, as in SS (valine is substituted for glutamic acid). Nonsense mutation produces a stop codon, which stops the translation.

Insertion and deletion mutations: These cause a "frame shift," which causes an abnormal protein from that point to the end.

Splicing mutations result from a point mutation at the area defining the junction between the intron and the exon. This results in dysfunctional proteins. Beta thalassemias often are caused by splicing mutations.

Acquired chromosomal abnormalities (See Table 10-16): A viral gene that can transform DNA is called a viral oncogene. The human chromosomes also contain genes that are associated with malignancy, called cellular oncogenes or proto-oncogenes. These proto-oncogenes probably have something to do with embryonal development and are otherwise silent, but, with certain chromosomal rearrangement, they become active. In both Philadelphia and Burkitt, the proto-oncogene becomes active by an acquired reciprocal translocation.

The Philadelphia (Ph1) chromosome t(9,22) was the first chromosomal abnormality found to be associated with malignancy (first found in CML). The switch causes the "c-abl" proto-oncogene to be moved from chromosome 9 to 22.

Burkitt lymphoma and its leukemic analog, ALL (FAB type 3), have a reciprocal translocation that switches the proto-oncogene "c-myc" on chromosome 8 to chromosome 14, 22, or 2: i.e., t(8-14), t(8-22), or t(2-8). Chromosome 14 has the heavy chain locus. The lambda light chain locus is on chromosome 22, and the kappa light chain locus is on chromosome 2.

Most leukemia and lymphoma patients have a chromosomal abnormality. Solid tumors rarely have abnormal chromosomes.

OTHER (lab)

ERYTHROCYTE SEDIMENTATION RATE

The erythrocyte sedimentation rate (ESR) is a measurement taken on a vertically hung tube of blood, indicating the number of millimeters RBCs settle over one hour. Besides the set factors determining the normal ESR (gravity vs. buoyant force), an increase in aggregation of the RBCs will increase the ESR. Erythrocytes have a net negative charge. Many plasma proteins have a positive charge that negates the charge on the RBCs, resulting in increased aggregation (and increased ESR). The large number of positively charged proteins in multiple myeloma (MM) not only increases the ESR but also causes rouleaux formation. Acute phase reactants increase aggregation in the inflammatory diseases. The Westergren ESR is recommended over the Wintrobe because it is more accurate—especially at increased sed rates.

Many diseases are associated with an elevated ESR, so this test is nonspecific. But it can be useful. The normal ESR is usually given as < 20, but it actually varies. Women normally have a higher ESR than men, and ESR increases with age. A rule of thumb for calculating normal ESR for patients between the ages of 20–65 years is: Men—divide age by 2. Women—divide (age + 10) by 2.

ESR is usually elevated in a patient with metastatic cancer, whereas it is often normal in cancer patients without metastases. ESR is elevated in inflammatory diseases, including infections. It is especially high (mean > 90 mm/hr) in temporal arteritis and polymyalgia rheumatica. It is of no value as a screening test in asymptomatic patients or patients with vague symptoms. Usually it only helps confirm the diagnosis in a patient with a probable infection or inflammatory condition, and even in these situations it has a low sensitivity and specificity.

Table 10-17

ELEVATIONS OF ALKALINE PHOSPHATASE

ISO-ENZYME	CAUSE	ETC...
Hepatic	Primary biliary cirrhosis Primary sclerosing cholangitis Acute cholecystitis	i.e., any cause of biliary obstruction. Alk phos is 3 to 10 x normal
	Liver -parenchymal disorders	e.g., hepatitis and cirrhosis. usually 1 to 2 x normal
	Reaction to medication	e.g., chlorpropamide
Bone	Late pregnancy	From the placenta
	Bone mets Osteomalacia Osteitis fibrosa cystica (hyperparathyroidism) Paget disease	

notes

Quick Quiz

1) On which chromosome are all of the HLA genes located?
2) Define the Philadelphia chromosome yet again.
3) What diagnosis should you be concerned about in an asymptomatic elderly patient with an isolated elevated alkaline phosphatase?
4) Name 3 disorders where you will have a LOW leukocyte alkaline phosphatase.

Table 10-18

LEUKOCYTE ALKALINE PHOSPHATASE	
ELEVATED IN:	PCV Myeloid metaplasia Some inflammatory diseases
DECREASED IN:	CML Wilson disease PNH Occasionally Hodgkin

PCV = Polycythemia vera; CML = chronic myelogenous leukemia; PNH = paroxysmal nocturnal hemoglobinuria.

ALKALINE PHOSPHATASE

Leukocyte alkaline phosphatase, serum alkaline phosphatase—a review:
Know Table 10-17 and Table 10-18.

PAGET DISEASE

Paget disease occurs in just less than 1% of people > 40 years old in the U.S. It is the usual cause of increased alkaline phosphatase in an asymptomatic elderly person. The disease results from greatly increased osteoclast activity and the associated increased reBuilding osteoBlast activity. Etiology: possibly a slow virus. Remember, the associated hypervascularity may cause high-output heart failure!

Treatment is not required in the majority of patients but may be needed if heart failure, bone pain, or nerve compression develops.

Drugs used: Bisphosphonates (etidronate, pamidronate, and alendronate) are newer drugs effective in the treatment of Paget disease. SC or IM calcitonin has also been shown effective. Glucocorticoids in high doses are sometimes used—especially when there is high-output heart failure.

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OPEN-ENDED QUESTIONS

1) What is the radiologic test of choice in the workup of spinal cord impingement?

[MRI.]

2) What type of ultrasound works as well as CT for diagnosing a thoracic aneurysm?

[Transesophageal ultrasound.]

3) What value must the predicted post-op FEV1 be before a pneumonectomy is performed?

[> 800 cc.]

4) Besides acute pulmonary embolism, what are some of the other causes of a V/Q mismatch?

[Old thromboembolic disease, A-V fistula, or a tumor compressing the blood vessels.]

5) In the thallium stress test and the pyrophosphate scan: Which chemical concentrates in infarcted areas ... and which chemical concentrates in proportion to blood flow? Which test will have cold spots ... which test will have hot spots?

[Infarcted areas: Tc99m pyrophosphate; hot spots. Blood flow: thallium; cold spots.]

6) In the thallium stress test, what problem is suggested if there is increased lung uptake of thallium just after exercise?

[Stress-induced left ventricular failure.]

7) How does the radionuclide venogram compare with the contrast venogram in the diagnosis of DVT?

[The contrast venogram has more resolution.]

8) Name 3 cases in which lytic bone processes may not show up on bone scan.

[Multiple myeloma, eosinophilic granuloma, and a rapidly growing cancer involving the bone.]

9) Is a bone scan better for ruling in or out osteomyelitis?

[A normal bone scan rules out osteomyelitis. There are many causes of a positive bone scan.]

10) What change in the bone scan will be seen with aseptic necrosis?

[There is decreased uptake.]

11) What is the most sensitive and least expensive method used to determine early osteoporosis of the spine?

[Dual photon absorptiometry.]

12) Which type of photon absorptiometry (single or dual) would be used for determining bone mass in the hips?

[Dual photon absorptiometry is used for determining bone density of the spine and hips.]

13) Tc^{99}-labeled RBCs are best used to locate a GI bleed in what area of the GI tract?

[Areas distal to the duodenum and proximal to the colon.]

14) In what single disorder is the HIDA scan the test of choice?

[Bile duct obstruction.]

15) When is radionuclide imaging of the kidney done? Which radionuclide scan is done to determine GFR? Which type of scan is done to determine tubular secretion?

[Radionuclide scan of the kidney is done to determine renal function. Tc99m Diethylenetriamine penta-acetic acid (DTPA) is an inulin analog which is excreted by glomerular filtration and so indicates GFR. I^{131} orthoiodohippurate is excreted only by tubular secretion.]

16) When is it not safe to give I^{131} thyroid treatment to hyperthyroid patients?

[It is not given to pregnant patients or patients with severe hyperthyroidism.]

17) What radionuclide is used to diagnose pheochromocytoma?

[I^{131}-metaiodobenzylguanidine (I^{131}-MIBG) will concentrate in pheochromocytomas in 1–2 days.]

18) When searching for an occult abscess, when would a gallium scan be used instead of an indium scan?

[Indium is usually preferred over a gallium scan. Because indium normally localizes in the spleen, a gallium scan is preferred if splenic abscess is suspected. Gallium scan is also preferred in the evaluation of pulmonary infection.]

19) If a patient with normal hepatic function is put on meperidine and soon develops seizures, what other organ function should be checked?

[Renal function. Normeperidine, the active metabolite of meperidine that causes CNS stimulation, is cleared by the kidneys.]

20) After starting a patient on a new drug with no loading dose, how many half-lives are usually allowed to pass before checking blood level or for prn dosage adjustment?

[3–5 half-lives.]

21) Regarding specificity and sensitivity, which is independent of the prevalence of the disease in a selected population?

[Both are independent of prevalence (= % of the population with disease). Sensitivity denotes only how effective a test is in diagnosing a disease in a patient who already has it. Its formula is (True positives)/(Total # with disease). Specificity is how good a negative test is at showing the patient does not have disease. The formula for specificity is (True negatives)/(Total # without disease).

22) In what case would the number of false positives be high despite a very high specificity and sensitivity?

[When the prevalence of the disease is very low, the positive predictive value (PPV) of a test is low despite a high specificity and sensitivity.]

23) How is the positive predictive value used in determining whether a screening program is feasible?

[PPV = TP/(TP + FP). If the PPV is low, screening is ineffective.]

Note: Study the tables and text in the Statistics area. Put in your own values. You will definitely be asked several questions about this.

24) In geriatrics, know what is and what is not age-related (i.e., a normal consequence of aging).

[Age-related: decreased immunity, decreased carbohydrate tolerance, decreased hearing, and increased frequency of falling. Not age-related: incontinence, dementia, and delirium.]

25) Which medications are associated with delirium in the elderly? Which with withdrawal delirium?

[Anxiolytics, cardiac medications, and cimetidine can cause delirium. Sedatives, benzodiazepines, ETOH, and pain medications can cause withdrawal delirium.]

26) How is dementia differentiated from delirium?

[Dementia has no associated altered consciousness as in delirium.]

27) What is the most common treatable cause of dementia in the elderly?

[Depression.]

28) Which of the antidepressant drugs are less sedating and which are more sedating?

[Less sedating antidepressants: nortriptyline and desipramine. More sedating: imipramine, doxepin.]

29) Which antidepressant would be used in an elderly person already on an anticholinergic drug?

[Trazodone.]

30) What is the most common cause of urinary incontinence in the elderly?

[Detrusor instability and overactivity. This is called "urge incontinence."]

31) What type of impotence is an indication of major vascular disease?

[Impotence associated with a low "brachial pressure index" is due to vascular compromise. This is the cause of impotence in 50% of elderly men. It is an indication of present or future major vascular disease.]

32) What drugs are most commonly associated with impotence?

→ [The most commonly associated drugs are beta-blockers, methyldopa, and thiazide diuretics.]

33) Why is there an increased incidence of post-prandial falls in the elderly?

[This is due to a decrease in blood pressure (systolic and diastolic), which is thought to be due to the carbohydrates in the meal.]

34) Is a patient more or less likely to have orthostatic symptoms after prolonged bedrest? Why?

[More likely. Immobilization causes decreased ADH secretion → diuresis → decreased blood volume → orthostatic symptoms. Also, immobilization causes muscle atrophy. The heart continually deconditions after 2 days of bedrest. The elderly are more affected by bedrest because they have less reserve than young people. Treat with rehabilitation.]

35) Of the following five factors, which is the main etiologic factor in pressure sores: infection, shear, pressure, friction, or moisture?

[Sustained pressure.]

36) What are the four stages of pressure sores? Where do they most commonly occur?

[Stage I is non-blanching erythema. Stage II is partial-thickness skin loss seen as a small superficial ulcer. Stage III is full-thickness skin loss. Stage IV is loss of tissue down to the muscle, tendon, or bone. Most common places: the heels, trochanter, sacrum, and iliac crest.]

37) What type of dressing should not be used on a pressure sore if there is an infection?

[Hydrocolloid dressings.]

38) What is the most common cause of decreased hearing in the elderly?

[Presbycusis.]

39) In treatment of an adult, mentally competent patient, when do the wishes of the physician prevail over that of the patient?

[Never.]

40) If a patient enters the hospital unconscious and near death with a terminal disease, what should the physician do if 1) the patient has a properly executed living will that states no intubation or CPR ... 2) the patient has no living will, but family members say they strongly prefer he be allowed to die with dignity and without heroics ... 3) same as #1, but family members (many of whom are lawyers) say they want all possible heroic measures done—and threaten dire consequences if their wishes are not followed.

[1) Follow instructions in the living will. 2) In this situation the physician needs more information; needs to know the wishes of the patient, not the family! 3) Follow instructions in the living will; the contract is between you and the patient. Besides, so far, all living wills have held up in court.]

41) If you strongly suspect another physician is chemically impaired, what should you do?

[Physicians who strongly suspect another physician is chemically impaired are obligated to urge that physician to seek treatment. If the physician's impairment may affect medical competence, the obligation is to report the "credible evidence" to the local medical society. Note that a reporting physician cannot act only on hearsay, but must have credible evidence before reporting it.]

42) What do you do if a patient tells you that a family member was sexually harassed by one of your partners?

[Tell the patient to encourage the family member to repeat the accusation to the county medical board. Offer your assistance in contacting the board, filling out forms. This does not say you believe or disbelieve any accusations. You are just helping your patient contact the proper bodies for such grievances where they can be best worked out.]

43) Is an EEG required for the diagnosis of brain death?

[No.]

44) What 4 conditions must be met before informed consent has been legally obtained?

[1) Patient must be competent to make the decision. If not, then a legal guardian can make the decision. If there is no legal guardian, family members can assist the decision process by relaying what they know of the patient's wishes. 2) Information must be given to the patient so the patient understands it. 3) The information must consist of what any reasonable person would want to know and must be consistent with the information given by other physicians. 4) The decision must not be coerced in any way.]

45) In what areas of preventative medicine has patient education proven to be of benefit?

[Tobacco, alcohol, and substance use, and increasing physical activity level.]

46) After what age are mammograms definitely of benefit as a screening test?

[After age 50.]

47) Are breast self-exams beneficial?

[Results have been inconclusive.]

48) What is the general age group for which pap smears are recommended?

[Every 1 to 3 years between the ages of 18 and 60 or 70 years. After the age of 70, previously negative patients definitely do not need Pap smears.]

49) Which are the live vaccines and which are the dead vaccines and what is their significance in a patient who is immunocompromised?

[Vaccines: The attenuated live virus vaccines are mumps-measles-rubella (MMR), oral polio, and yellow fever. The attenuated live bacteria vaccines are typhoid and BCG (bacille Calmette Guerin). These may cause the disease in immunosuppressed patients. The dead virus vaccines are: injectable polio, rabies, and influenza. Dead bacteria vaccines: cholera, H. influenza, pneumococcal, meningococcal, typhoid (two types). Note: Hep A & B are now recombinant vaccines, not dead!!]

50) What poisonings can cause a high anion gap acidosis?

[Lactic acid (cyanide), salicylates, ethylene glycol, and methanol.]

51) What are the exogenous causes of an increased osmolal gap?

[Three main groups cause an increased osmolal gap. Note that all of the causes end in "-ol." 1) Mannitol, sorbitol, and glycerol; 2) Ethylene glycol; 3) Alcohols are the most common cause: methanol, ethanol, and isopropyl alcohol.]

52) If a comatose patient has an elevated anion gap and an elevated osmolal gap, what are two likely causes?

[Ethylene glycol or methanol.]

Review and know the general treatment of a patient with an unknown drug overdose.

53) "Gut dialysis" with oral activated charcoal will assist in the elimination of what drugs?

[Digoxin, phenobarbital, theophylline, tricyclics, and salicylates.]

54) What drugs will be eliminated more quickly with alkalinization of the urine? With acidification of the urine?

[Alkalinization of the urine to a pH of > 7 increases excretion of acidic drugs (ASA, tricyclics, phenobarbital). Acidification of the urine with ammonium chloride increases excretion of basic drugs, e.g., amphetamine and phencyclidine (PCP).]

55) With what drug overdoses is dialysis useful? What do these drugs have in common?

[Dialysis removes drugs that are not lipid soluble, protein bound, or tissue bound (i.e., have a small volume of distribution). E.g., lithium, chloral hydrate, salicylates, and alcohols (methanol, ethylene glycol, and ethanol).]

56) With what drug overdoses is charcoal hemoperfusion useful? What do these drugs have in common?

[In contrast to dialysis, charcoal hemoperfusion removes drugs that are lipid soluble and protein bound. It can also remove some of the same drugs as dialysis. Also like dialysis, it works best in removing drugs with a low volume of distribution (V). Especially good for digoxin, theophylline, and salicylate overdoses.]

57) Why is folic acid given to a patient with a methanol overdose?

[Methanol overdose is treated with ethyl alcohol (ETOH) infusion and immediate dialysis. Folic acid is given to increase metabolism of formic acid (a toxic methanol metabolite).]

58) An overdose of which drug will produce calcium oxalate crystals in the urine? What is the treatment for this overdose?

[Ethylene glycol. Treat with ETOH infusion (100x the affinity for alcohol dehydrogenase), bicarbonate for the acidosis, calcium prn, and immediate dialysis.]

59) Which of the ECG abnormalities caused by tricyclic antidepressants correlates most closely with the degree of intoxication?

[QRS prolongation.]

60) Which type of drug abuse is most likely in the young patient who presents with an acute MI?

[Cocaine.]

61) If a patient with severe salicylate poisoning presents with a PCO_2 of 40, what is the probable cause?

[The patient has probably stopped hyperventilating due to severe respiratory muscle fatigue.]

62) What 4-hour post-ingestion acetaminophen level indicates a high probability of hepatotoxicity if not treated?

[> 250 µg/mL.]

63) What is the treatment for acetaminophen overdose?

[N-acetylcysteine (Mucomyst®)—loading dose = 140 mg/kg followed by q 4 hour doses at 70 mg/kg for 17 doses. Best when given 8–16 hours after ingestion.]

64) Overdoses of both anticholinergics and stimulants can cause dilated pupils, tachycardia, HTN, agitation, and fever. What physical finding can differentiate between them?

[Anticholinergics cause warm dry skin whereas stimulants cause warm clammy skin.]

65) In carbon monoxide poisoning, what carboxyhemoglobin levels indicate mild to moderate, moderate to severe, and usually fatal poisoning?

[Mild to moderate at 15–30%; moderate to severe if > 30%. > 50% is often fatal.]

66) In checking for inorganic lead poisoning, what different tests are done if the patient has ongoing exposure, had the exposure several months ago, or had the exposure several years ago?

[For ongoing exposure, check whole blood lead level. After exposure has occurred, RBC protoporphyrin and zinc protoporphyrin levels will remain elevated for several months. For evaluating the effect of exposure from years before, the best test is to measure urine lead 24 hours after giving 1 gm of EDTA.]

67) What type of lead is soluble and quickly excreted and therefore undetectable soon after exposure?

[Organic lead.]

68) There are two classes of insecticides that are anticholinesterases: organophosphates and carbamates. Poisoning with which one will cause an increase in RBC acetylcholinesterase for several months? Why? For which poisoning is 2-protopam given?

[Organophosphates are the more toxic. They bind irreversibly to acetylcholinesterase, whereas the carbamate binding is reversible. Organophosphates cause an increase in the level of RBC acetylcholinesterase for several months, while the level returns to normal within hours after carbamate poisoning. Treatment: Remove clothes and shower with soap. For moderate to severe symptoms, give atropine (1–2 mg IV, repeat q 5 min prn). For organophosphates, but not carbamate, give 2-protopam (2-PAM) IV.]

69) What do singed nasal hairs in a smoke inhalation victim suggest?

[That a laryngeal area burn should be ruled out.]

70) Review and know the antidotes for the following overdose poisonings (all discussed in this General Internal Medicine section): iron, ethylene glycol, cyanide, carbon monoxide, nitrates, acetaminophen, narcotics, methanol, digoxin, organophosphates, and benzodiazepines.

71) In what way does the ESR often vary in patients with cancer?

[The ESR is usually normal in patients with non-metastatic cancer and elevated when there are metastases.]

72) What is the usual type of glaucoma? How does the fundus cup-to-disk ratio change in glaucoma? Does glaucoma affect both eyes equally?

[The usual form of glaucoma is "open-angle," in which the anterior chamber remains open and the trabecula visible. If this type is caught early enough, blindness can be prevented. The fundus exam shows a higher than normal cup-to-disc ratio (> 50%). Because glaucoma is usually asymmetrical, any asymmetry (between left and right eyes) in the cup-to-disc ratios is glaucoma until proven different.]

73) What causes closed-angle glaucoma?

[It is due to mechanical obstruction of aqueous flow through the trabecular network. This can be due to anomalous iris configuration (inherited or due to lens swelling) or iris neovascularization (from diabetes, inflammation, or carotid occlusion).]

74) What are causes of a cloudy cornea?

[Trauma, acute glaucoma, infection.]

75) What causes a ciliary flush? Conjunctival hyperemia?

[Ciliary flush is redness near the conjunctival limbus only. It is seen in closed-angle glaucoma, iridocyclitis, and corneal inflammation (keratitis). Conjunctival hyperemia is nonspecific — it is usually caused by allergy and viral or bacterial infections.]

76) What do the following eye discharges suggest? Clear? Purulent? White & stringy?

[Clear: viral infection. Purulent: bacterial conjunctivitis. White and stringy: allergy or keratoconjunctivitis sicca.]

77) What are the causes of conductive hearing loss? Of sensorineural?

[Conductive: middle ear infection, eustachian tube blockage, otosclerosis, TM perforation, and ceruminosis or any other impaction of the external canal. Sensorineural: damage to the cochlea or nerve.]

78) What does the "lateralizing to the left ear" mean in the Weber test?

[The Weber test consists of placing the base of the tuning fork on the middle of the forehead. If the sound lateralizes, there is either a conductive hearing loss in that ear or sensorineural loss in the opposite ear. If the sound does not lateralize, the patient either has normal hearing or the hearing loss is symmetrical.]

79) Using the Rinne test, in which cases is bone-conducted sound louder than air-conducted sound: sensorineural loss, conductive loss, normal?

[Bone-conducted sound is only loudest in conductive hearing loss. Air-conducted sound is loudest in normal ears and when there is some degree of nerve loss.]

80) Review and know all of the pregnancy-related issues summarized at the end of the GIM section.

81) On which chromosome are the HLA genes found?

[Chromosome 6.]

82) On which cells are HLA I antigens not found?

[HLA I antigens are not found on erythrocytes. They are found on most other cells.]

83) In gene transcription and translation: What is a codon? An exon? An intron?

[In mRNA, each 3 base sequences compose a codon, which determines which amino acid is attached when it is translated. DNA has coding sequences called exons, separated by non-coding sequences called introns.]

84) Of the 4 types of mutation (point, insertion, deletion, splicing), which types cause the following problems: frameshift? missense mutation? nonsense mutation? dysfunctional protein?

[Frameshift mutations are caused by either insertion or deletion mutations which result in an abnormal protein from that point to the end. A missense mutation occurs when a point mutation (change to a single base) causes a different amino acid to be produced — as in SS disease, in which valine is substituted for glutamic acid. A nonsense mutation occurs when a point mutation produces a stop codon, which stops the translation. Dysfunctional proteins are often caused by splicing mutations which result from a point mutation at the area defining the junction between the intron and the exon.]

MedStudy

11th Edition

Internal Medicine Review

Core Curriculum

Neurology

Authored by Robert A. Hannaman, MD

Many thanks to

Steve Karceski, MD
Assistant Clinical Professor of Neurology
Columbia Presbyterian Medical Center
Associate Director of the Columbia Epilepsy Center
New York, New York

Neurology Advisor

Neurology

COMA

Consciousness depends on the degree of a person's alertness and attention. Both the reticular activating system (RAS) *and* the cerebral cortex must be working in order to sustain normal consciousness. *Lethargy, stupor, obtundation*, and *coma* are terms that are applied to diminishing levels of consciousness. Establishing the diagnosis of coma depends on the neurological exam: It is the absence of all responses to the external environment. Components of the neurological examination must include observations about respiration (and respiratory patterns), pupils, and motor responses (or a lack thereof). Motor responses such as *decerebrate* and *decorticate* posturing may help to localize the site of injury.

Coma is caused by either a decrease in the activity of the reticular activating system *or* a process that involves the cerebral cortex of *both* hemispheres. The RAS resides within the brainstem. Injury to the brainstem, such as a hemorrhage in the pons or midbrain, can cause coma. Drugs—prescribed, OTC, and illicit—also affect the RAS directly.

Plum and Posner classify the causes of coma as
1) supratentorial, 2) infratentorial,
3) metabolic, 4) diffuse, or 5) multifactorial.

Physical examination of the comatose patient:

Respirations: Cheyne-Stokes respiration describes a particular pattern of breathing where the patient has periods of hyperventilation alternating with apnea. This pattern occurs in bilateral cerebral disease, impending herniation, and brainstem lesions, and can be due to metabolic causes. Apneustic breathing consists of inspiratory pauses, and is due to a lesion of the pons. Ataxic breathing is very irregular, and usually indicates a lesion of the medulla.

Pupils: See Table 11-1. Remember that in the comatose patient, an asymmetry between the sizes of the pupils must be considered as pathologic.

Oculocephalic testing (doll's eyes) and ice water calorics (eyes look toward the cold) test the same vestibular-brainstem-ocular muscle pathway. Doll's eyes: If the patient is unconscious yet neurologically intact, and the head is turned, the eyes keep "looking" in the initial direction, and then slowly return to midline. If the comatose patient does NOT have doll's eyes nor has nonreactive ice water calorics, there is a problem in the midbrain or pons. Generally, doll's eyes are preserved in early metabolic coma. The exceptions are metabolic comas due to barbiturates and phenytoin.

Testing of doll's eyes, which requires moving the head, should be done only after C-spine injury has been ruled out.

Testing:

Of course, the first part of any evaluation is the history and physical examination. Obtain a CT or MRI of the brain very quickly in order to narrow the differential, especially when the cause is unclear. CBC, electrolytes, BUN, creatinine, glucose, ABG, and toxicology screen for illicit drugs may be needed. Other tests such as an EEG may be helpful to identify nonconvulsive status epilepticus, especially when there is a prior history of seizures. In one series of comatose patients in whom the cause was unknown, 8% were found by EEG to be in nonconvulsive status epilepticus. Finally, you may need to do cerebrospinal fluid examination (including the usual bacterial and viral tests) when you suspect infection.

Supratentorial coma is due to an injury of the hemisphere(s).
Lateral (uncal) herniation: An expanding mass lesion (tumor, stroke, hemorrhage) will force the uncus under the tentorium. This puts pressure on the brainstem and therefore the reticular activating system. Because of the course of the third cranial nerve, the herniating uncus compresses this nerve, causing an enlarged pupil *ipsilateral* to the side of herniation.
Central herniation: Injury to the thalamus (such as hemorrhage) results in diminished consciousness very early in its course. Later, the pupils become mid-position and fixed. As the herniation continues, the course begins to merge with that of uncal herniation. In other words, central and uncal herniation syndromes can be differentiated early on, but their later courses merge.

Infratentorial coma is due to an injury that causes destruction or compression of the brainstem. Problems that can do this include basilar artery occlusion with pontine infarction, cerebellar infarction or hemorrhage, and posterior fossa neoplasms. Expansion of the contents of the posterior fossa will force the contents of this compartment in one of two directions: up (upward herniation) or down (downward herniation). Upward herniation pushes the posterior fossa contents up under the tentorium, compressing the brainstem. Downward herniation forces the cerebellar tonsils down through the foramen magnum, compressing the medulla. Signs of in-

Table 11-1

PUPILS IN COMA				
SIZE		DESCRIPTION	CAUSE	Examples
●	•	One dilated unreactive pupil	Parasympathetic nerve problem	Oculomotor nerve compression from uncal herniation. Rupture of internal carotid artery aneurysm.
•	•	One pinpoint pupil (miosis)	Sympathetic nerve problem (Horner)	Lateral medullary syndrome; hypothalamus injury
•	•	Two midpoint nonreactive pupils	Parasympathetic and sympathetic nerve destruction	Midbrain disruption (can cause one or both pupils to become midpoint and nonreactive); Anoxia; Hypothermia; Anticholinergics; Severe barbiturate overdose.
●	●	Two dilated unreactive pupils		Anoxia; Hypothermia; Anticholinergics; Severe barbiturate overdose.
•	•	Two pinpoint reactive pupils		Opiates; Pontine destruction.

notes

fratentorial herniation include pinpoint pupils and irregular (ataxic) breathing patterns.

Metabolic coma. There are many, many causes of metabolic coma, including ischemia, hypoxia, hypoglycemia, organ disease (lung, liver, kidney), and drugs, among others. Patients have changes in respiratory pattern and mentation early in metabolic encephalopathy. The pupils are typically reactive unless the coma is due to anticholinergics or the patient has anoxic brain damage.

CONDITIONS THAT MIMIC COMA

Locked-in Syndrome: Locked-in syndrome is rare, and is due to a lesion that involves the lower brainstem. The RAS is spared, but almost all motor pathways from the cerebral cortex to the body are interrupted. The person will be awake and aware of the surrounding environment, but may have only the ability to control eye movements (the nuclei that control eye movements are above the lesion), and therefore may be able to communicate using these. Because the cerebral cortex is spared, an EEG will be normal.

Vegetative state: Severe, bilateral cerebral dysfunction (doll's eyes are normal) with an operating RAS. It is called persistent vegetative state if it has lasted > 1 month. These patients may sleep and wake normally, but have no cognitive function. It is often caused by anoxic brain damage (e.g., after MI).

Brain death: Document that the patient is unresponsive, has no pupillary function (midbrain), no doll's eyes (pontine), and is apneic (must be off ventilator long enough for $PaCO_2$ to rise to > 60). EEG is helpful if it establishes there is no activity in the cerebral cortex, but it is NOT required for diagnosis.

HEADACHE

OVERVIEW

The history and examination are crucial in diagnosing the type of headache. These include the *quality* of pain (dull, sharp, throbbing, constant), *location*, *duration*, and *exacerbating* or *ameliorating* factors.

MIGRAINE

Migraines are unilateral (up to 60% of the time), throbbing, and last several hours. Rarely, they may last up to three days. Triggers include certain foods (like aged cheese, caffeine, and nitrate preservatives). Loud noises or bright lights may make the headache worse. Sleep and darkness may help to lessen the pain. They are frequently associated with nausea and vomiting. Common migraine occurs without an aura. Classic migraine may be preceded by visual symptoms such as sparkling lights (*scintillating scotomata*) in as many as one-third of migraineurs. Basilar migraine affects the brainstem, and causes vertigo, dysarthria, diplopia, and possibly loss of consciousness.

Acute Treatment: This refers to any treatment that is given within the first hour of the headache. Acetaminophen, aspirin, and non-steroidal anti-inflammatory medications (NSAIDs) are effective in many patients. If you've tried these and they've failed, then try the "triptans": sumatriptan, rizatriptan, or naratriptan. Dihydroergotamine (DHE) may be effective in some patients. You may try narcotics, but their use should be restricted to 2 days per week. Increased use of these agents may lead to dependence, and can transform the headache into a chronic headache called *rebound headache*.

Prophylactic Treatment: These medications are taken daily. The goal of treatment is to lessen the pain and reduce the number of attacks. The frequency of attacks will determine whether prophylaxis is needed: Usually the cutoff is more than 2–3 headaches per month. There is usually a lag of 2–4 weeks between the start of prophylaxis and its effect. The major categories of these agents are as follows: beta-blockers (propranolol), tricyclic antidepressants (amitriptyline, nortriptyline), anticonvulsants (valproate), calcium channel blockers (verapamil).

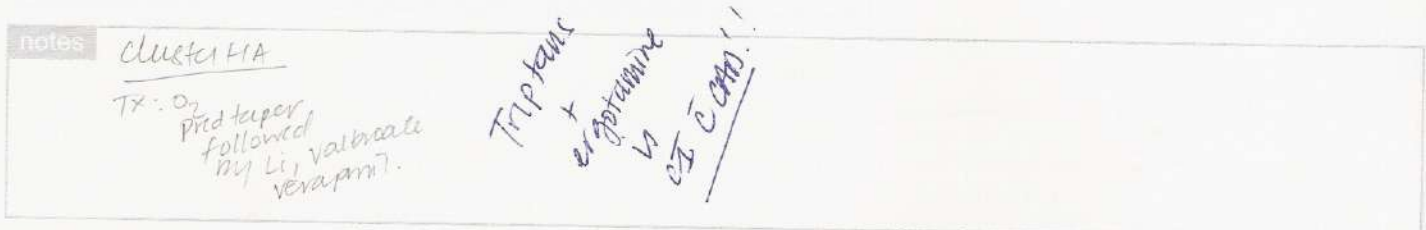
Acephalic migraine (migraine without headache) may present with abnormal transient neurologic dysfunction such as visual symptoms. For instance, it can cause "fortification scotomas" that constantly change in size and may be bilateral.

CLUSTER

Cluster headache is a distinct syndrome that frequently responds to treatment. The term cluster is derived from the periodicity of the headaches: They can occur up to several times per day for a few weeks before remitting. The daily attacks may occur at the same hour each day (in 50% of patients). Often, the pain is described as severe, and like an "ice-pick" or a "hot poker," and is peri-orbital or retro-orbital. The pain peaks quickly (in 5–10 minutes), and the headache resolves in 60–120 minutes. In about 50%, the headaches will predictably occur within 2 hours of falling asleep. 70% of patients find that alcohol triggers their headache. Men are affected much more than women (8:1 in one series).

Treatment: Acute treatment is usually ineffective, because by the time the medication is taken and absorbed, the headache is over. There is one exception: Oxygen (8–10 L/min) may abort the headache. Since acute treatment is usually ineffective, the mainstay of treatment is to prevent the clusters. Prednisone (40–60 mg/day for 10 days followed by a taper), lithium, verapamil, and valproate are effective.

notes



Quick Quiz

1) What could cause bilateral pinpoint reactive pupils?
2) Is an EEG required for diagnosis of brain death?
3) List prophylactic treatment agents for migraine.
4) Describe the common signs of a cluster headache. How do you treat it?
5) Describe the common signs of a tension headache. How do you treat it?
6) A coital headache normally lasts how long? If it lasts significantly longer, what disorder do you rule out?
7) What physical finding is almost always found in patients with pseudotumor cerebri?

TENSION

Tension headache is a term that is still used to describe a chronic, bilateral, constant, non-throbbing, "squeezing," type of pain. Once believed to be due to muscular contraction, many now believe that this is another type of migraine. The treatment of tension headache is the same as for migraine.

COITAL

Coital headache occurs more often in men than women (4:1 ratio). The headache begins during intercourse, usually close to orgasm. It has an abrupt onset and usually resolves after a few minutes. They are benign. If the headache does not resolve after two hours or is accompanied by vomiting, one should suspect subarachnoid hemorrhage.

POST-TRAUMATIC

Post-traumatic or post-concussion headache: This may occur even after a minor head injury. It may be vascular, like migraine, but some have proposed that the headache is due to abnormal neurotransmission within the brain. Symptomatic treatment is usually effective, and the syndrome spontaneously remits.

TEMPORAL ARTERITIS

Temporal arteritis usually occurs in patients > 55 years old. History is usually recent onset of headache. Physical exam is significant for temporal artery tenderness. Do not miss this diagnosis! Do an erythrocyte sedimentation rate followed by a temporal artery biopsy if indicated. More in the Rheumatology section.

PSEUDOTUMOR CEREBRI

Pseudotumor cerebri [Know!] (idiopathic intracranial hypertension) usually occurs in premenopausal (i.e., childbearing age) obese women. Obesity appears to have a strong causal association with pseudotumor cerebri, as 90% of patients with it are obese. It is more likely to occur during pregnancy. Drugs that are associated with pseudotumor cerebri are glucocorticoids, tetracycline, and vitamin A.

Symptoms include headache and horizontal diplopia. There is almost always a peripheral visual field loss, which is often asymptomatic. Severe, irreversible visual loss occurs in 10% of patients.

On exam, papilledema is a hallmark finding. CT/MRI and CSF pressure > 250 mmH_2O for diagnosis (normal CSF pressure is 50–180).

Treat patients with mild symptoms with acetazolamide (drug of choice) or furosemide. Treat more severe cases with prednisone—initially 60 mg/d. Lumboperitoneal shunts (and the like) are reserved for cases refractory to medications.

THALAMIC

Thalamic pain: Severe, debilitating, refractory pain (head and elsewhere) following weeks to years after a thalamic infarct (which often has total hemianesthesia).

DEMENTIA

Dementia is a progressive deterioration of cognitive function in the patient with a normal level of consciousness (encephalopathy, on the other hand, causes altered states of consciousness—from delirium to stupor).

Demented patients have deterioration in memory, judgment, and abstract thinking.

In the initial workup, first rule out drugs as the cause. Other causes of possibly treatable dementias that must be excluded are B_{12} deficiency (which can also cause a polyneuropathy and myelopathy with a spastic ataxia), Wilson disease (can also cause cerebellar ataxia and psychiatric symptoms), heavy metal poisoning (arsenic, mercury, and lead), hypothyroidism, chronic subdural hematoma, and normal pressure hydrocephalus. Also consider infection and inflammation: syphilis, sarcoidosis, chronic meningitis, lupus cerebritis, Whipple disease, and vasculitis.

Hypothyroidism can cause dementia and psychiatric, vestibular, and auditory changes.

You should especially suspect chronic subdural hematoma in alcoholics and in patients on anticoagulants.

Normal Pressure Hydrocephalus (NPH) is a potentially treatable cause of dementia. It often occurs after head trauma, meningitis, or subarachnoid hemorrhage. One thought about how this develops is that there is obstruction of the outflow

notes

of cerebrospinal fluid. However, the intracranial pressure is normal, there is no papilledema, and the person has no headache. NPH causes a gradually worsening dementia, gait ataxia, and urinary incontinence. Often, the gait problems and incontinence *precede* the dementia. You confirm diagnosis by LP (normal pressure, normal CSF components). The LP may also result in transient improvement in some of the neurological symptoms. The treatment is lumboperitoneal shunt, and certain tests may help to identify patients who are most likely to respond to shunting. These include improvement after LP, isotope cysternography, and dynamic MRI, which measures the direction of CSF flow. None of these is universally helpful, and there is no agreement as to which test is most helpful in selecting patients for a shunting procedure.

Alzheimer disease is the most common cause of dementia after age 60. 1st-degree relatives have a 4 x normal increased risk of developing it. Initial signs: Poor recent/short-term memory, poor naming, and imprecise speech. Then, usually after several years, frontal lobe signs develop: Apathy, sloppiness, and decreased spontaneity. And only after these symptoms develop do the patients develop gait disturbances. Alzheimer patients have a normal LP.

Image 11-1 shows a CT scan with typical findings of dilation of sulci and fissures, ventricular enlargement, and reduction in brain size.

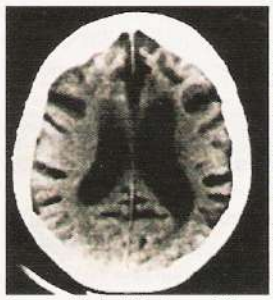


Image 11-1: Alzheimer CT

The anticholinesterase drugs—tacrine (Cognex®) and donepezil (Aricept®)—are reported to improve memory but only temporarily. Not of much benefit. Many other drugs are undergoing trials.

It is important to evaluate all patients with dementia in order to rule out a reversible (i.e., treatable) cause.

Multi-infarct dementias usually have prominent motor, reflex, visual, and gait abnormalities, but they typically do not have the difficulty in naming associated with Alzheimer disease. In an elderly patient presenting with dementia and no motor symptoms, the major differential is Alzheimer disease vs. multi-infarct dementia. Besides naming difficulty, another big difference is the onset of symptoms. Multi-infarct dementia typically has abrupt stepwise deterioration of mental function amidst which the patient may improve somewhat. On the other hand, Alzheimer disease has a slow, steady progression.

Pick disease is similar in presentation and course to Alzheimer disease. These patients have severe atrophy of the frontal lobes and partial atrophy of the temporal lobes. A CT or MRI showing this atrophy suggests Pick disease but does not confirm it because Alzheimer disease may present with the same atrophy. The only sure way to differentiate between the two is histologic diagnosis—usually during autopsy. The treatment is identical to Alzheimer.

Creutzfeldt-Jakob Disease is one of the prion diseases (more detail in ID section). It develops as a rapidly progressive dementia (weeks as opposed to years as in Alzheimer). One characteristic clinical feature is startle myoclonus (response to loud noises or startle). The disease involves the cerebral cortex, basal ganglia, and spinal cord. It is rare: One person in one million is affected. It mainly affects middle-aged and elderly patients (average age of onset is 60). Diagnosis is confirmed by the characteristic pattern on EEG (.5 to 2 Hz sharp waves on a diffusely slowed background). It is fatal in less than 1 year in > 90%. The diagnosis can be definitively made only by brain biopsy.

Parkinson disease (PD) is caused by a loss of dopaminergic neurons in the substantia nigra. 30% of patients will develop cognitive and behavioral changes, i.e., dementia (see the later discussion under Movement Disorders on pg 11-16).

Progressive supranuclear palsy is similar to Parkinson disease (discussed on pg 11-17).

Huntington Disease causes both a dementia and a movement disorder (see also Movement Disorders). It is inherited (chromosome 4). It causes mental deterioration, characteristic chorea-athetoid movements, and personality changes (progressing to psychosis) all of which typically begin in persons in their late 30s. Those affected are aware of these problems, and may develop depression. You may see atrophy of the caudate nuclei on CT or MRI ("boxcar" ventricles). Although you can minimize some of the symptoms with antipsychotics and neuroleptics, there is no known treatment for the disease itself.

AIDS is the most common cause of dementia in younger patients. Dementia affects half of all AIDS patients.

Many symptoms in a patient with depression are the same as those in a patient with dementia, except patients with depression will not have the grasp/suck reflexes. Also, immediate recall is usually poor in depression, but good in dementia.

Depression can be reactive or endogenous. Symptoms are the same for both. In endogenous depression, patients may have an abnormal response to the dexamethasone suppression test; the initial suppression of cortisol is normal, but it is not suppressed as long as normal (normal is > 24 hours).

DIZZINESS

When the term "dizziness" is used, one should try to differentiate among the following:

Vertigo = a sense of spinning or swaying.

Lightheadedness = presyncope. "I feel like I'm going to pass out."

Imbalance = unsteadiness.

notes CJD
Dx EEG — sharp waves on a diffusely slow background
Brainbx

Quick Quiz

1) How does normal pressure hydrocephalus present? How can you diagnose it?
2) How does multiple-infarct dementia present?
3) How does Alzheimer dementia present?
4) What chromosome is associated with Huntington?
5) Dementia in a young person should make you suspect what infectious disease?
6) How can you differentiate dementia from depression?
7) In vestibular neuritis, is hearing usually affected?
8) What is the characteristic triad of Ménière disease?
9) Name and explain the 4 types of seizure.
10) What is the difference between a complex and a partial seizure?

Vague = not one of the three above. It may be hard for the affected person to describe. Some believe that this symptom may indicate an underlying psychiatric condition, but this is a "soft" call.

Nystagmus is an involuntary oscillation of the eyes. The movements may be pendular (like a pendulum) or jerk. Jerk nystagmus has two components: fast and slow. The eyes "drift" (= slow component), and try to quickly recover (= fast component). The type of nystagmus may indicate its cause. For instance, drugs (like antiepileptic medications) cause horizontal *and* vertical gaze-evoked nystagmus (it occurs when the person looks right, left, or up)—in other words, it is present "in all directions." Isolated vertical gaze-evoked nystagmus usually indicates disease in the posterior fossa.

Jerk nystagmus is most common in vestibular disorders, but does not indicate whether the lesion is within the central nervous system or whether it involves the cranial nerve itself. Upbeating jerk nystagmus usually indicates a lesion in the pons, but can be seen in lesions of the medulla or cerebellum. Downbeating jerk nystagmus indicates a lesion at the cervicomedullary junction.

Benign positional vertigo (BPV) describes recurrent brief episodes of vertigo that are brought on by changing head position. It may be caused by head trauma, labyrinthitis, or aging. Many patients have been found to have otoconia in the semicircular canal. (Otoconia are crystals that reside in the saccule and utricle. When they escape this region, they cause symptoms of vertigo). Most BPV resolves spontaneously or with the Epley maneuver which moves the otoconia to a position of the inner ear less likely to induce vertigo. Symptomatic treatment is meclizine or diazepam.

Vestibular neuritis (vestibular neuronitis, acute peripheral vestibulopathy) causes a sudden onset of non-positional vertigo that is self-limited, but lasts weeks to months and occasionally can recur. Vestibular neuritis is caused by an inflammatory process affecting the vestibular portion of the eighth cranial nerve. It usually does not have associated tinnitus. Hearing is not affected. Treatment is symptomatic only (such as with meclizine).

Acute labyrinthitis is similar in that it presents with non-positional vertigo, but it does have an associated hearing loss. There is usually a history of a viral infection.

Aminoglycoside toxicity can cause some initial hearing loss and, later, intermittent mild vertigo.

Ménière Disease begins in the 3rd and 4th decade of life. The characteristic triad is episodic vertigo (often associated with nausea and vomiting), tinnitus (ringing in the ears), and hearing loss. It usually begins unilaterally, but can become bilateral in 20–30% of patients. One possible cause is an increase in the endolymphatic fluid pressure, which is in part related to salt intake (salt restriction may help to minimize the symptoms). Diuretics also help. If needed, a shunting procedure can alleviate the symptoms by relieving the pressure.

Vertebrobasilar TIAs (transient ischemic attacks) may cause intermittent, recurrent vertigo. A TIA is usually easy to diagnose because it also causes other symptoms of vertebrobasilar insufficiency such as bilateral visual loss, dysarthria, diplopia, ataxia, and bilateral extremity motor or sensory dysfunction. Do an MRI/MRA. It may be necessary to obtain trans-cranial Dopplers or an angiogram.

Know the causes of tinnitus mentioned above. Other causes include aspirin overdosage and high noise levels.

SEIZURES

Seizures arise from the cerebral cortex.

Postictal altered mental status is very common after loss of consciousness due to a seizure—this is the main symptom used to differentiate between seizure and syncope.

All seizures can be conceptualized as either partial or generalized. The terms are used to describe the onset of the seizure. Partial (or focal) seizures are those whose onset is limited to a section of one hemisphere, whereas generalized seizures involve the entire brain from the onset. Partial seizures are further divided into simple partial (consciousness is maintained) and complex partial (loss of consciousness). A simple partial seizure may evolve into a complex partial, and either type of partial seizure may evolve into a generalized seizure. The critical differentiation is that many partial seizures are due to a focal brain lesion, while the etiology of many generalized seizures is genetic—although this is a generalization and there are many exceptions to this rule!

notes

Tinnitis
- ASA
- ↑noise
- acute labyrinthitis
Ménière

Table 11-2

MAIN ADVANTAGES and DISADVANTAGES of ANTICONVULSANTS		
Drug	Used to Treat	Advantages/Disadvantages
Phenytoin	Partial (1) Generalized tonic-clonic (alt)	GOOD: Long half-life so dose 1-2x/d BAD: Gum hyperplasia, hirsutism, coarsening of features, lymphadenopathy, osteomalacia. Saturation kinetics so toxicity may present at near-normal doses.
Carbamazepine	Partial (1) Generalized tonic-clonic (alt)	GOOD: First-order kinetics with toxicity level significantly above therapeutic range. BAD: Hyponatremia, leukopenia, thrombocytopenic, aplastic anemia, and hepatotoxicity
Valproic acid	Generalized tonic-clonic (1) Absence (alt) Partial (alt-esp if it generalizes)	BAD: GI side effects (less with Depakote formulation). May rarely cause bone marrow suppression and hepatotoxicity/liver failure.
Ethosuxamide	Absence (1) only	BAD: Rarely causes bone marrow suppression
Lamotrigine	Partial (adjunctive use)	BAD: May cause severe rash and Stevens-Johnson syndrome
Gabapentin	Partial (adjunctive use)	GOOD: The only one with NO significant drug interactions. Renal clearance so it is useful in those with liver disease. BAD: Ataxia, amnesia.
Clonazepam	Absence (short-term adjunctive use only)	BAD: Loses efficacy
Phenobarbitol	Partial (last choice)	BAD: Sedation in adults, hyperactivity in children among other cognitive changes.
Note: (1) = primary drug.; Note: any of the above can cause ataxia, dizziness, and somnolence		

The discussion here addresses four general types of seizure:

1) A generalized tonic-clonic seizure is also known as a grand mal in older epilepsy literature. Another commonly used term to describe this type of seizure is convulsion.
2) Absence seizures used to be called petit mal. These are generalized seizures with no aura or postictal symptoms. They can be induced by hyperventilating. Absences have a characteristic 3-per-second spike and wave pattern on EEG. 2/3 of affected children outgrow it.
3) Simple partial seizures are focal seizures that affect a small volume of cortex. Consciousness is preserved. The symptoms of a simple partial seizure depend on the region of cortex from which the event is generated. For instance, a partial seizure arising in the occipital lobe (visual cortex) may be manifest by complex visual hallucinations (e.g., spinning colorful spheres). Jacksonian seizures are simple partial seizures that involve the motor strip.
4) Complex partial seizures involve a large enough volume of cortex to cause a disruption in cognition or awareness. They often originate in the temporal or frontal lobes. Pure temporal lobe seizures have no clonic motor component; patients present only with abnormal behavior or mental function.

Alcohol decreases the seizure threshold. Cocaine can "kindle" seizures.

Workup of an initial seizure.

- When obtaining the history, check for alcohol or drug use, head injury, sleep deprivation, diabetic history, and thyroid or parathyroid surgery.
- Lab tests should include glucose, sodium, calcium, LFT, and BUN. If there are any meningeal symptoms, do a lumbar puncture and include a VDRL of the spinal fluid.
- Do either an MRI or a CT after the first seizure to rule out a structural abnormality; MRI is almost always the best neuroimaging test. Neuroimaging is normal in classic childhood absence seizures and certain genetic epilepsy syndromes.
- An EEG showing epileptiform spikes (+/- a following slow wave) will confirm the diagnosis of seizure and may localize the origin of the seizures. A normal EEG never excludes the diagnosis of epilepsy.
- After an initial seizure, the risk of recurrence is increased when there is an abnormal EEG, when there is a history of a prior neurologic injury, when there is a family history of seizures, when the first seizure is a partial seizure, and/or when the MRI reveals an abnormality.

notes

Quick Quiz

1) What imaging study is done after a new-onset seizure?
2) What factors contribute to the risk of recurrence after an initial seizure?
3) Know Table 11-2. Especially the primary therapies.
4) A patient presents with papilledema and signs of meningitis. What should you do before you do the LP?

Acute treatment of seizures: Intravenous benzodiazepines (lorazepam or diazepam) are the usual treatment of choice. Benzodiazepines are the drug of choice because although a full loading dose of phenytoin also is effective, it takes longer to infuse.

Alcohol withdrawal seizures are usually treated acutely with IV benzodiazepines or phenytoin (again, benzodiazepines first). The only way to keep alcohol withdrawal seizures from occurring is to stop drinking! uh ... completely!

Status epilepticus is defined as a seizure lasting > 30 minutes or a series of 2 or more seizures without regaining consciousness in between. It is considered a medical emergency. A cause can be determined about 2/3 of the time. Usual causes in adults include stroke, alcohol or other drugs, stopping or changing seizure medications, hypoxia, CNS infection, metabolic causes, tumor, and trauma.

Typical treatment of status epilepticus in the adult: Give thiamine and then D_{50} 50 ml if the rapid glucose test is low; then benzodiazepine (lorazepam 0.1 mg/kg or diazepam 0.2 mg/kg). This is often followed by a loading dose of phenytoin. If the patient is still seizing, maximize the phenytoin dose, then proceed to a barbiturate (phenobarbital or pentobarbital).

Chronic treatment of seizures (See Table 11-2):

Treatment of epilepsy: Antiepileptic medications are the mainstay of treatment. However, it is increasingly recognized that epilepsy surgery, designed to remove the area that causes the seizures, is very effective. In addition, the vagus nerve stimulator (VNS) is an effective treatment for most seizure types. It is a pacemaker-like device that sends intermittent electrical stimuli to the vagus nerve. These impulses are transmitted to various regions of the brain, and disrupt epileptic seizures.

Partial seizures: Almost all available antiepileptic medications (AEDs) are effective in the treatment of partial seizures. The notable exception is ethosuximide, an agent that is used only to treat absence seizures. With few exceptions, the AEDs are considered roughly equally effective. The main differences are that the older AEDs are generally cheaper; however, the newer ones are generally better tolerated (i.e., fewer side effects).

Generalized seizures: The list of effective agents for generalized seizures is shorter, and includes valproate, lamotrigine, topiramate, levetiracetam, and felbamate.

When can you stop the medication? This must be individualized. Risk factors include a seizure within the last 2 years, epileptiform spikes on the EEG, abnormal MRI, and a late age of onset of the seizures.

Seizures and pregnancy: The background risk for birth defects is 2–3%. In women with epilepsy on one medication, the risk is 4–6%. If the woman is on more than one medication, the risk is 8%. In other words, you should maintain a pregnant woman on monotherapy and at the lowest dose of medication possible. The goal of treatment during pregnancy is to control the seizures—uncontrolled seizures can cause placental abruption and early labor and premature delivery. When the risk of teratogenicity is compared to the problems that seizures cause during pregnancy, the risks of uncontrolled seizures is greater!

INFECTIONS

BACTERIAL

Acute meningitis: Diagnose with analysis of the CSF. If there are focal neurologic signs or papilledema, do a CT before the lumbar puncture. CSF latex agglutination tests are not recommended anymore in the initial evaluation of meningitis; they test for *H. flu*, *Strep pneumoniae*, *Staph aureus*, *Neisseria meningitides*, and *Strep agalactiae* (group B beta-hemolytic). With suspected meningitis, start antibiotics immediately after the LP and blood cultures; do not wait for any LP results. Also, if the LP is going to be delayed more that 30–60 min, start antibiotics immediately! Treatment is covered in the Infectious Disease section.

Neurosyphilis is discussed in the Infectious Disease section.

Brain abscess: The classic triad of symptoms is headache, fever, and focal neurological deficit(s). Most abscesses arise from intracranial extension of cranial infections (sinuses, teeth, etc.) or after skull fracture or neurosurgical procedures. Much less often they are due to seeding (as in bacterial endocarditis). In adults, the most common organisms are *staph* and *strep* species. (*S. epidermitis* after a penetrating head injury.) In infants, gram negative bacteria are more common. In the immunocompromised, one must consider *toxoplasmosis*.

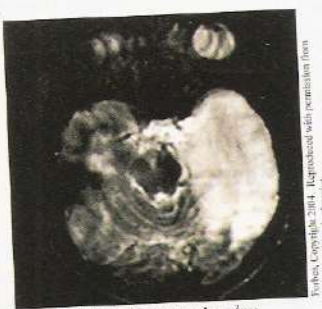


Image 11-2: Herpes simplex encephalitis-MRI.

VIRAL

Viral encephalitis: CSF will have increased lymphocytes, normal-to-slightly-increased protein, and normal glucose. EEG is almost always abnormal with diffuse slowing or focal temporal changes. The MRI is more sensitive than CT and may show focal changes early-on.

notes

Herpes simplex encephalitis is the most common type of non-epidemic viral encephalitis. In adults, it is usually due to a reactivation of the HSV-1 virus, although 25% are due to primary HSV-1 infection. HSV-2 is sexually transmitted and causes aseptic meningitis only. Treat HSV encephalitis with IV acyclovir.

If mosquitoes are around, look for arboviruses, particularly West Nile, and the equine viruses!

Diagnosis of viral encephalitis: Specific CSF antibody studies and polymerase chain reaction (PCR) DNA amplification of the herpes virus now allow for an easy, rapid, and accurate diagnosis of herpes simplex viral encephalitis in many cases.

Myelitis: viral infection of the spinal cord; classic one is poliomyelitis!

Slow viruses:

1) Subacute sclerosing panencephalitis (SSPE) is caused by the measles virus; most cases occur around age 10, many years after the initial infection.
2) Progressive multifocal leukoencephalopathy (PML): Look under demyelinating diseases on pg 11-16.

Prion: Creutzfeldt-Jakob disease (CJD): See under Dementias, which starts on pg 11-3.

Infection with HIV can result in dysfunction of any part of the nervous system. Patients get subacute encephalitis, peripheral neuropathies, vacuolar myelopathy, and aseptic meningitis. We will discuss these in the order just listed.

HIV encephalopathy is the most common neurologic defect in AIDS patients. It results in clinical dementia (AIDS dementia complex or AIDS encephalopathy) in half of AIDS patients and is evident in 90% of postmortem AIDS brain biopsies! These patients usually have apathy, forgetfulness, and poor concentration. They have decreased motor skills early in the disease—first seen as deterioration in their penmanship. Know that the differential diagnosis includes progressive multifocal leukoencephalopathy (below), toxoplasmosis (below), and lymphomas.

Myopathy in AIDS is uncommon and usually due to zidovudine (ZDV, AZT). Patients present with a generalized (proximal > distal) weakness and an elevated CPK. Treatment is to stop the AZT. Poliomyelitis is more likely to occur in AIDS patients. Differentiation between AZT myopathy and poliomyelitis may require muscle biopsy.

Peripheral AIDS neuropathy has two forms:

1) In chronic inflammatory demyelinating polyneuropathy there is progressive weakness of the legs and loss of deep tendon reflexes. There is a high protein level and a high cell count in the patient's CSF.
2) Distal symmetric polyneuropathy is common in AIDS patients (1/3 get it). They get paresthesias of the feet and distal weakness in the legs. These are usually treated with tricyclic antidepressants or gabapentin (Neurontin®).

Progressive multifocal leukoencephalopathy (affects white matter only) is usually seen in AIDS patients. It is caused by the papovavirus (= JC virus), resulting in a progressive demyelination of the CNS white matter. Symptoms are varied and usually start with abnormal mentation and then slurred speech. Diagnose with brain biopsy.

Vacuolar myelopathy causes progressive weakness, incontinence, hyperreflexia, and ataxia. In this, there is vacuolation and deterioration of the dorsal and lateral spinal columns. It is uncommon. This must be differentiated from spinal cord compression due to some other cause (lymphoma, etc.).

FUNGAL and PARASITIC

Brain abscess and AIDS: If you see multiple ring-enhancing lesions, think toxoplasmosis (CNS lymphoma is less likely). As this is a flare-up of an old infection, patients have IgG, but not IgM antibody to *T. gondii*! Treat with sulfadiazine, pyrimethamine, and leucovorin. Do a brain biopsy if there is only one lesion, if there is no improvement after treatment, or if there is a mass effect. Relapses occur often.

Neurocysticercosis is the most common worldwide parasitic CNS infection. It is caused by ingesting food or water contaminated with *Taenia solium* (a tapeworm). It will form cysts in the brain, which initially cause no symptoms; but when the cyst walls break down several years later, it causes cerebral edema, usually with seizures as the first symptom. Early on, CT shows multiple, one centimeter, cystic lesions. Later, they calcify and are half that size. Although you treat intestinal tapeworm with niclosamide, you treat CNS infection due to tapeworm with albendazole (first choice) or praziquantel with a corticosteroid.

Cryptococcal meningitis: CSF may appear normal, so always check cryptococcal antigen titers. Treat with amphotericin-B and flucytosine. And again, relapses occur.

STROKE

OVERVIEW

The definition of a stroke is based on duration and cause. Typically a stroke must

1) have a sudden onset,
2) persist at least 24 hours, and
3) have a neurologic deficit that fits a vascular area of the brain.

Symptoms lasting less than 24 hours are called a transient ischemic attack, or TIA. Sudden onset of symptoms also occurs with migraine, trauma, and epilepsy. Symptoms from brain abscesses and neoplasms tend to evolve over weeks.

ISCHEMIC STROKES

1) Thrombotic strokes. Atherosclerotic occlusion is most common in the internal carotid, middle cerebral, vertebral, and basilar arteries. The initial neurologic symptoms often occur in a slow, stepwise progression (i.e., *stroke in evolution*). If the patient has a history of TIAs in the same distribution as the presenting symptoms, the stroke is probably thrombotic.

notes
AZT/ZDV – myopathy
TX Crypto meningitis
• ampho.
• flucytosine
TX toxo
sulfadiazine
pyrimethamine
leucovorin
TX CNS cysticercosis
Albendazole
or praziquantel
+ steroids
TX intestinal tenea
niclosamide

Quick Quiz

1) It is summertime. A patient in Louisiana presents with headache and signs of encephalitis. Which is more likely: herpes or an arbovirus?
2) An AIDS patient presents with multiple ring enhancing lesions. What is the diagnosis?
3) A Mexican immigrant presents with seizures and lesions on MRI. What is the likely organism?
4) What is different for the onset of strokes in thrombotic vs. embolic etiologies?
5) How will MCA strokes present?
6) What finding might you see in a patient with a stroke involving the corpus callosum?
7) How will a posterior cerebral artery stroke present?
8) What is Wallenberg syndrome?

If the patient has not had TIAs, a clear differentiation between thrombotic and embolic may be difficult. Other, rarer, causes of thrombotic occlusion are lupus anticoagulant, polycythemia, meningovascular syphilis, dissecting aortic aneurysm, and thrombocytosis.

2) Embolic strokes: Neuro deficit is usually worst at onset. Embolic strokes are usually not preceded by a TIA, whereas thrombotic strokes usually are. Emboli from the heart usually go to the middle > posterior > anterior cerebral arteries. With cerebral emboli, the weakness is greater in the distal extremity. This is because more of the other hemisphere is involved in the proximal limb.

Middle cerebral artery (MCA) stroke: These result in contralateral weakness (hemiplegia), sensory loss (hemianesthesia), and a homonymous hemianopsia. If the dominant hemisphere is involved (the *left* side in most people, even left-handed individuals), these patients will experience aphasia. If the nondominant hemisphere is involved, they may experience changes in spatial perception, and may develop *hemineglect* syndrome. In addition, the patients may have impaired gaze (aka a *gaze preference)*—they look toward the side of the lesion for 1–2 days after the stroke. If the infraction is in the upper division and spares the diencephalon, the weakness and sensory loss will be most prominent in the face and arm.

Anterior cerebral artery (ACA) stroke: When this artery is affected, the weakness and sensory loss affect the contralateral leg more than the contralateral arm. Urinary incontinence and gait abnormalities may also be present. If the corpus callosum is affected, patients may have a tactile anomia (they cannot name an object by touch, but can name it on sight).

Posterior cerebral artery (PCA) stroke usually causes contralateral homonymous hemianopsia (usually an upper quadrantanopsia). There may be *mild* contralateral weakness and sensory loss, color anomia, and/or memory loss. If the patient has anomia for colors, the posterior aspect of the corpus callosum may have been affected. If disruption of blood flow occurs bilaterally, the memory loss is severe and persistent.

Single hemisphere strokes usually do not affect paraspinal muscles or muscles of the pharynx, jaw, and forehead. If these muscles are affected, think bilateral hemispheric involvement or brainstem stroke (below).

Vertebral and/or basilar artery occlusion is the usual cause of brainstem strokes. That the problem involves brainstem (posterior fossa) structures is suggested by

- bilateral extremity motor and sensory dysfunction (quadriplegia in severe cases),
- "crossed" motor and sensory findings (e.g., right face, left arm),
- Horner syndrome,
- cerebellar signs,
- stupor and coma, and
- cranial nerve dysfunction not usually affected by single hemisphere strokes, such as pharyngeal weakness, jaw weakness, and deafness.

A vertebral stroke may cause lateral medullary syndrome (also called Wallenberg syndrome), which has a mixed bag of symptoms: nausea, vomiting, nystagmus (vestibular nuclei), ipsilateral Horner syndrome, ipsilateral palate and vocal cord weakness, and "crossed" sensory loss (ipsilateral face and contralateral body).

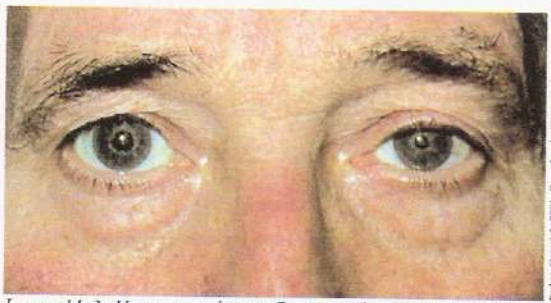


Image 11-3: Horner syndrome. Ptosis and miosis of left eye.

There are various other brainstem infarction syndromes, which will not be covered here and are unlikely to be seen on the Boards. Except for lateral medullary syndrome, which was just discussed, they are more associated with cancer. Examples of these are medial/lateral medullary, m/l inferior pons, and m/l superior pons syndromes.

Small artery disease, usually due to chronic hypertension, can lead to occlusion of very small arterioles with resultant small areas of brain necrosis. Over time, resorption of these necrotic regions causes small cysts or "lacunae" to develop. Although most are silent, hallmarks of symptomatic lacunar infarcts are: pure hemiplegia (with no sensory dysfunction) or pure hemisensory stroke (with no motor dysfunction). Multiple bilateral frontal lobe lacunae can result in pseudobulbar palsy.

Remember, there are other causes of intracranial hemorrhage, including anticoagulants, bleeding diatheses, trauma, and bleeding into a tumor mass.

Notes

Treatment of ischemic stroke: If the stroke occurred less than 3 hours ago, the CT is negative, and the patient's laboratory studies (hematocrit, platelets, and PT/PTT/INR) are normal, tissue plasminogen activator (t-PA) has been shown to be effective in reversing the neurological deficits.

If greater than 3 hours has elapsed, the management is conservative. The patient's blood pressure will be elevated after a stroke—do not lower the blood pressure precipitously, as this may worsen the neurological deficits.

If the stroke occurs in the posterior fossa, the patient should be admitted immediately under close observation—remember, expansion of the contents of the posterior fossa can cause either upward or downward herniation. These patients are at great risk for sudden deterioration after their stroke.

HEMORRHAGIC STROKE

Hemorrhagic stroke is usually due to bleeding from the small arteries of the parenchyma. The two most common causes are hypertension and amyloid angiopathy. Because the bleeding is due to the small arteries, the symptoms usually evolve gradually but continuously.

Hemorrhagic stroke occurs in the following areas of the brain (from the most common site to the least common):

1) Putamen and adjacent internal capsule (50%). If the hematoma involves the internal capsule, there is contralateral hemiparesis and usually sensory loss and hemianopsia. This type of hemorrhage is virtually indistinguishable from a middle cerebral artery infarct.
2) Thalamus: contralateral hemiplegia and hemianesthesia. The sensory signs are often greater than the motor signs.
3) Pons: usually causes coma, pinpoint pupils, and complete paralysis. There may be decerebrate posturing bilaterally.
4) Cerebellum: onset with acute dizziness, ataxia, and vomiting with no change in mentation and no loss of consciousness.

Amyloid angiopathy is a common cause of hemorrhagic stroke after the 5th decade of life. The hemorrhage tends to be lobar and subcortical. It rarely involves the deep structures (as does a hypertensive bleed). Hemorrhages may recur within months or years. Dementia occurs in 30%. There is no known treatment.

Subarachnoid hemorrhage (SAH) usually results from bleeding from a saccular ("berry") aneurysm. Aneurysms are most common at the bifurcation of vessels in the Circle of Willis or its major branches. The age where this most likely occurs is between 40 and 60, and women are affected more than men. The majority occur in the anterior circulation: 40% of aneurysms affect the internal carotid artery, 35% involve the anterior cerebral artery, and 20% the middle cerebral artery. Subarachnoid hemorrhage can also occur after a parenchymal bleed when there is rupture into the ventricular system.

The characteristic symptoms of SAH are the acute "thunderclap" "worst headache of my life" sensation in combination with neck stiffness. Common associated symptoms include loss of consciousness, nausea/vomiting, and photophobia. More than 1/3 give a history of suspicious symptoms days or weeks earlier—the "sentinel bleed." The most important determinant of outcome is the neurological condition of the patient upon arrival at the hospital. If comatose, the prognosis is poor.

Diagnosis: Do a CT first. If this is negative and the CT shows no contraindications, then do a lumbar puncture. The CT misses 10% of subarachnoid bleeds. The CSF is bloody with xanthochromic supernatant. However, even clear CSF does not preclude the diagnosis because it may take hours after onset of the bleed before you find RBCs in the CSF. Cerebral arteriography is the procedure of choice for finding aneurysms.

Complications of SAH: After a sentinel bleed, rebleeding is common. The risk is highest in the first 24 hours, but the risk remains high for at least one month. Vasospasm may occur in up to 70% of patients, and begins 3–5 days after the hemorrhage. It reaches a peak at 5–14 days, and resolves in 2–4 weeks. The third major complication is hydrocephalus, which occurs in 15–20% of patients after SAH. The likelihood of hydrocephalus depends on the volume of intraventricular and subarachnoid blood. Seizures may occur in 5–10%. 2/3 of seizures begin within the 1st month after the hemorrhage, while the remaining occur within the 1st year.

The initial treatment is to prevent the aneurysm from bleeding again, by surgical clipping. Once this is done, the remaining treatment focuses on preventing the complications. If surgery is not possible, you may treat the aneurysm using interventional neuroradiological techniques such as the introduction of platinum coils.

Other aneurysms: Mycotic aneurysms are caused by septic emboli—usually from bacterial endocarditis. They are usually small and occur in the distal vasculature. This is in contrast to saccular aneurysms that occur more proximally, at the branch points of the arteries (e.g., at the point where the Middle Cerebral Artery branches off of the Internal Carotid Artery).

Subdural hematoma is not always due to direct trauma, as deceleration forces can also cause it. Subdural bleeds are usually of venous origin. Symptoms may be fluctuating. If the hematoma has been there over a week, the blood may be isodense and not seen on CT or MRI. Still, MRI is the best means of diagnosis.

Epidural hematomas, because of their arterial origin, evolve more rapidly than subdural hematomas. These are usually caused by temporal trauma that damages the middle meningeal artery. It occurs in association with temporal bone fractures. Diagnosis is made by CT, which will identify both the hematoma and the skull fracture. Symptoms are mainly due to compression of the underlying hemisphere and may be relieved if you evacuate the clot and relieve the pressure.

Transient global amnesia is transient short term memory loss. Patients recover completely within several hours. It is considered benign. It is listed here because most neurologists consider the cause to be embolic; however, the exact cause is unknown.

notes

Quick Quiz

1) When is t-PA effective for strokes?
2) What sensory and motor losses are seen with stroke that affects the putamen?
3) How will an internal capsule stroke present?
4) How does a thalamic stroke present?
5) How does a pons stroke present?
6) How does a cerebellar stroke present?
7) Describe the symptoms of a subarachnoid hemorrhage.
8) After an SAH, when is the patient most likely to rebleed?
9) Which is arterial in origin: subdural or epidural hematomas?
10) What is Wernicke syndrome? How is it treated?
11) Describe the findings in subacute combined degeneration due to B_{12} deficiency.

NEOPLASMS

CNS metastases typically cause slow onset of symptoms, although they can cause an abrupt onset of symptoms if there is hemorrhage into the tumor. Parenchymal brain metastases occur most commonly with lung, renal, and breast cancer and with melanoma and lymphoma. Dural metastases occur with breast and prostate cancer.

Epidural metastases at the level of the spinal cord cause back pain; usually worse when lying down. New onset of bladder or bowel dysfunction, i.e., incontinence, urgency, etc. are very important symptoms that should alert you to consider spinal epidural metastases ... especially in the setting of new onset back pain.

In a patient with a history of cancer and new onset cord compression symptoms, metastases must be ruled out! Meningeal malignancy is most frequent in lymphomas, carcinoma of the breast, and melanoma.

Treat metastases with whole brain irradiation and chemotherapy, and give steroids for widespread metastases, an unapproachable single metastasis, or herniation. All treatments are only palliative. For an approachable single metastasis, do surgery, then irradiation.

METABOLIC AND TOXIC DISORDERS

Wernicke syndrome is characterized by global confusion that worsens over days to weeks. Abnormal eye movements are typical, and include horizontal nystagmus, and a disordered conjugate gaze that progresses to ophthalmoplegia (usually a 6th cranial neuropathy). The pupils may become sluggishly reactive to light. The person may have trouble standing or walking due to truncal ataxia. Wernicke encephalopathy is due to thiamine (B_1) deficiency.

Korsakoff syndrome merges with Wernicke. Korsakoff syndrome may emerge as the symptoms of Wernicke are treated. The amnesia that occurs with Korsakoff can be both retrograde and anterograde. Attention and mentation appear normal. Patients will often *confabulate* because of the memory problems.

Immediate treatment with thiamine resolves the problem of Wernicke and prevents Korsakoff syndrome. Once Korsakoff syndrome develops, thiamine has only partial effect on 50% *of these patients. Treatment for Wernicke encephalopathy is* thiamine 50 mg IVPB and 50 mg IM. This is followed by 50 mg IM q.d. until a normal diet resumes, at which time the patient gets oral thiamine supplements.

In the Nephrology section we discuss how IV glucose given to a chronic alcoholic causes a decrease in the already depleted stores of phosphate and can cause hypophosphatemia. A similar sequence can occur with the thiamine stores, and IV glucose can precipitate Wernicke encephalopathy in a thiamine-deficient person (e.g., an alcoholic).

Drug toxicity: Lithium—low serum Na^+ causes increased lithium resorption from the kidney. Toxic lithium levels cause seizures and coma; treat with hemodialysis. Anticholinergics: "mad as a hatter." Dilated pupils, flushed, febrile, with secondary urinary retention.

DISEASES OF MUSCLE AND NERVE

MYELOPATHIES

Myelopathy is spinal cord disease. Remember, "myelo-" means bone marrow or, in this case, spinal cord—not muscle ("myo"). Typical manifestations are gait ataxia, spasticity, and hyperreflexia.

Subacute combined degeneration of the spinal cord is due to B_{12} deficiency, causing segmental loss of myelin (especially in the dorsal and lateral columns). Initial symptoms are a "*pins and needles*" *feeling, followed by stocking/glove* decreased reaction to pinprick, weakness, spasticity, clonus, and extensor plantar reflexes. Mental changes include confusion, apathy, delusions, paranoia, and mental deterioration.

AIDS patients get a vacuolar myelopathy with vacuolation and deterioration of the dorsal and lateral spinal columns. When AIDS patients present with myelopathy, you must rule out other causes such as spinal cord compression.

Besides tumor/lymphoma/myeloma, know the following compression-induced myelopathies:

Cervical spondylotic myelopathy begins with changes in the intervertebral discs. These changes occur gradually, and accumulate with age. Neck pain is common. If the disc herniates, it will compress a nerve root, causing a radiculopathy at that level. This presents as numbness, weakness, and hypore-

notes

flexia in the corresponding region that is supplied by the nerve root. When the spondylosis becomes more severe, it may begin to compress the spinal cord, causing spasticity, hyperreflexia, and gait abnormalities (the same signs as spinal cord compression).

If a rheumatoid arthritis patient presents with a post-op focal neuro deficit, suspect C1-2 spinal cord trauma induced by intubation. This is likely if the patient has chronic asymptomatic C1-2 subluxation. Anesthesiologists are generally well aware of this susceptibility. Of course, other mechanisms can cause similar injury in these patients.

Thoracic sensory levels are: T4 at nipple line and T10 at umbilicus. Thoracic spondylosis is unusual; therefore, if a patient develops thoracic disease, it is almost always due to another cause such as a tumor.

Lumbosacral: The spinal cord itself is not affected by L-S problems, but the cauda equina and nerve roots can be damaged in this area of the spine—usually the L4, L5, or S1. These result in a radiculopathy (from Latin, *radix* = root). Affected dermatomes are:

- L5 = great toe (L5 = Large toe) and
- S1 = lateral side of foot by the small toe (S1 = Side of foot near Small toe).

Affected myotomes:

- L5 = weakness of the great toe extensor and ankle dorsiflexion (standing on the heel), presents as foot drop;
- S1 = weakness of ankle plantar flexion (standing on the toes).

See Table 11-3 through Table 11-5.

Lumbar spinal stenosis [Know!; see Table 11-3] is a congenital narrowing of the spinal canal. These patients are more susceptible to impingement of the cauda equina—secondary to disc disease, ligamentous degeneration, and arthritis.

This compression is worsened by upright posture extending the spine; patients complain of a deep progressive ache in the legs after standing or walking for a few minutes. These symptoms are relieved by sitting or squatting (flexing hips/spine).

Differential diagnosis includes claudication, which also causes symptoms when walking (i.e., worsens with exercise of the leg muscles) but not when standing upright. See Table 11-3. Confirm the diagnosis of lumbar spinal stenosis impingement with an MRI.

Syringomyelia is a progressive myelopathy caused by cavitation of the central spinal cord. It can be idiopathic, developmental, or acquired. About 2/3 of cases are associated with Arnold-Chiari malformation—a congenital malformation in which there is a downward shift of the cerebellum and medulla through the foramen magnum into the cervical area of the spine, sometimes with syrinx (cyst) formation.

Symptoms of syringomyelia typically occur across the shoulders ("cape-like") and upper limbs; the patient initially has relatively normal sense of light touch and vibration, but no sense of pain or temperature. When the anterior horn is affected, weakness and atrophy of the upper limbs occur—starting in the hands and moving proximally to include the arms and then shoulder muscles. Occipital and nuchal headaches are also very common.

Spinal epidural abscess (a medical emergency) is often misdiagnosed initially. Predisposing problems include bacteremia (pneumonia or IV drug use), furunculosis, and back injury. It may start as a spinal osteomyelitis and progresses to an abscess, causing cord compression.

Initial symptoms include a few days to 2 weeks of fever and backache with localized tenderness. Then radicular pain, then effective transection of the cord.

It is best diagnosed with MRI, although CT is also used. Perform myelography if the abscess is not clearly seen by MRI (or CT, if that was the only option). Treatment is immediate decompression with laminectomy and drainage and then appropriate antibiotics. Suspect this in anyone who has been bacteremic from any cause and presents with back pain and fever. Remember the main symptom of epidural abscess is back pain.

Anterior horn cell problems [Know!] cause motor defects only. Amyotrophic lateral sclerosis (ALS), or Lou Gehrig disease, is the most common cause of anterior horn cell disease. ALS is almost unique in that it causes both upper motor neuron and lower motor neuron signs—this is the hallmark of ALS. A patient with ALS has diffuse hyperreflexia and spasticity (upper motor neuron) along with fasciculations, weakness, and atrophy (lower motor neuron). Polio used to be the most common cause of anterior horn cell disease, so now post-polio syndrome must also be considered. Post-polio syndrome causes areflexia and progressive weakness. "Spinal muscle atrophy" is a set of hereditary disorders of the anterior horn lower motor neurons.

Table 11-3: Lumbar Spinal Stenosis vs. Claudication

	Are symptoms better or worse with:		
	WALKING	STANDING	SITTING
Lumbar Spinal Stenosis	Worse	Worse	Better
Claudication	Worse	Better	Better

NEUROPATHIES

Overview

Neuropathies can be divided into several categories. If the process involves only one nerve, it is called mononeuropathy. Mononeuropathies are generally due to entrapment (as with carpal tunnel syndrome). If two or more nerves are affected, the term mononeuropathy multiplex is used. Mononeuropathy multiplex results from systemic disorders like diabetes or vasculitis.

notes

Quick Quiz

1) What is lumbar spinal stenosis?
2) How is lumbar spinal stenosis diagnosed?
3) What is syringomyelia?
4) What should you suspect in a patient with back pain and bacteremia?
5) What disease presents with BOTH upper motor neuron as well as lower motor neuron deficits?
6) Nocturnal awakening with hand pain is frequently due to what?
7) How do you distinguish between peroneal nerve compression and L5 radiculopathy in a patient?
8) A hiker from Connecticut presents with new onset of foot drop. What infection should you consider?

Those that symmetrically involve the peripheral nerves in a diffuse manner are called peripheral neuropathies. There are many causes of peripheral neuropathy (see below).

The workup for any neuropathy includes glucose, ESR, creatinine, T4, CBC, and a chest x-ray. Serum protein electrophoresis, immunoglobulin electrophoresis, and quantitative immunoglobulin assays are also done if the patient is > 40 years old. Along with inflammatory neuropathy, hereditary neuropathies are the most frequently missed cause of polyneuropathy. Therefore your evaluation of peripheral neuropathies should include a careful family history!

Focal Compressive/Mononeuropathy

Focal mononeuropathies are caused by localized peripheral nerve damage—usually from a compression injury. The main sites of compression are the ulnar nerve at the elbow, the median nerve at the wrist, and the peroneal nerve at the knee (discussed below). Because radiculopathies and mononeuropathy multiplex can have presentations identical to focal compressive neuropathies, they must also be considered in the workup of patients presenting with the focal neuropathic symptoms. [Know the following!]

Acute wrist drop (radial neuropathy) is usually from nerve compression but is occasionally seen as a result of diabetic nephropathy (discussed below). It has been called "Saturday night palsy" because it often is caused by drunks passing out with an arm compressed beneath them. This usually resolves slowly over several weeks or months.

Lower brachial plexus injury (2° surgery/tumor) causes a claw-hand deformity.

Carpal tunnel syndrome is median nerve entrapment typically causing paresthesias and weakness to the first 3 digits of the hand, but patients can have pain anywhere in the arm or shoulder! Median nerve entrapment at the wrist is almost invariably associated with nocturnal awakening with hand pain or paresthesia. It is usually due to repetitive stress. Initial treatment is neutral-alignment wrist splints and modifying the repetitive stress. If this is ineffective, steroid injection may help. Next step is median nerve release.

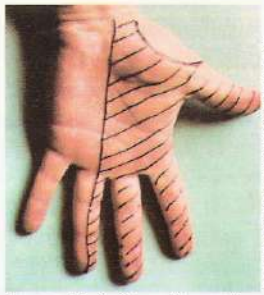


Image 11-4: Carpal tunnel syndrome-palmar L hand

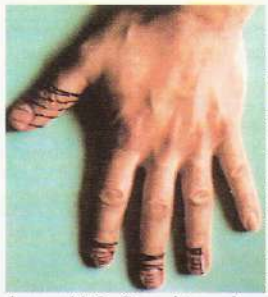


Image 11-5: Carpal tunnel syndrome-dorsal L hand

Ulnar neuropathy causes paresthesias in the little finger and a decreased ability to abduct the index and little finger. It is usually due to lesions at the elbow but also occurs at the entrance of the ulnar nerve to the cubital tunnel and at the wrist. Rarely, trauma to the heel of the hand can result in an ulnar injury.

Sciatic nerve compression can, like S1 radiculopathy, cause difficulty standing on toes. Unlike S1, it does not cause a decreased ankle jerk when compared to the opposite ankle. Know Table 11-4.

Table 11-4: S1 Radiculopathy vs. Sciatica

	Able to Tiptoe?	Decreased Ankle Jerk?
S1 Radiculopathy	NO	YES
Sciatica	NO	NO

Peroneal nerve compression [Know—see Table 11-5]. Compression usually occurs at the proximal head of the fibula, causing foot drop. L5 radiculopathy also causes foot drop. To distinguish between the two: Patients with peroneal nerve compression cannot evert the foot well but can still invert it, while L5 radiculopathy prevents or hinders both eversion and inversion. Also it is useful to test proximal L-5 innervated muscles such as the hamstrings and thigh abductors, which will not be affected with peroneal nerve compression. Know

Table 11-5: L5 Radiculopathy vs. Peroneal nerve Injury

	Foot Drop?	Able to Invert Foot?	Able to Evert Foot?
L5 Radiculopathy	YES	NO	NO
Peroneal nerve Injury	YES	YES	NO

notes

that Charcot-Marie-Tooth disease can cause symptoms similar to peroneal nerve compression.

Mononeuropathy Multiplex

Note that mononeuropathy multiplex can present identically to the compressive focal neuropathies above.

Consider all of the following as possible causes of mononeuropathy +/- multiplex: rheumatoid arthritis, DM (see next), connective tissue diseases, vasculitis, polyarteritis, and Lyme disease (think of this in a hiker with new onset footdrop).

When the cause is inflammatory, it is usually called mononeuritis multiplex.

With suspected Lyme neuropathy, do an LP. This typically shows high lymphocytes, high protein, normal glucose (the other spirochetal disease, syphilis, can cause the same CSF findings, so do a VDRL also [the treponemal antibody tests, FTA-ABS or MHA-TP, can be positive in Lyme disease!]).

A brachial neuritis may follow a vaccination and causes extreme tenderness, pain, some muscle weakness/atrophy, and occasional loss of biceps reflex; it improves in one or more years.

Bell's palsy is caused by dysfunction of the external 7th cranial nerve. It affects one side of the face, including the forehead. It is usually idiopathic. It causes ipsilateral facial muscle paralysis, and occasionally results in no taste on anterior 2/3 of tongue, loss of lacrimation, and hyperacusis. Pre-geniculate lesions are associated with the loss of taste, salivation, and lacrimation, while more distal lesions spare these functions. Differentiating from cortical lesions is easy if the weakness is pronounced. Cortical lesions spare the muscles of the forehead and upper eyelid. 80% recover completely. Prednisone x 10 days (5d at 60 mg, 5d tapering) is often given for Bell's palsy and appears to shorten the course.

Multiple sclerosis (MS): Although 10% of patients with MS can present with an inflammatory radiculitis, MS is only rarely a cause of an isolated mononeuropathy or polyradiculopathy.

Note: If a patient has intermittent symptoms of a mononeuropathy in an extremity, always ask about symptoms elsewhere in the body at the same time. For example, if a patient has intermittent carpal tunnel symptoms but also has facial symptoms at the same time, this is more indicative of TIAs and not an actual mononeuropathy.

Polyneuropathies

Inflammatory polyneuropathies: Guillain-Barré is the most common inflammatory polyneuropathy. Symptoms include an ascending paralysis (including pulmonary muscles) and areflexia caused by a segmental demyelination of the peripheral nerves. CSF examination typically shows an elevated protein and occasionally a slightly increased cell count. Nerve conduction studies show slowed conduction. Plasmapheresis is very useful but only if it is started within the first 2 weeks of the disease. Low- and moderate-dose steroids are contraindicated, although high-dose methylprednisolone (1–2 gm/day) may help—especially if the patient is in a great deal of pain (this topic is undergoing much debate). Complete recovery is the norm, but 10% of patients have significant residual weakness.

Charcot-Marie-Tooth (CMT) disease is also called hereditary motor and sensory neuropathy and formerly was also called peroneal muscular atrophy. CMT is by far (90%) the most common inherited peripheral polyneuropathy; there are over 10 types.

There are two main types of CMT. Type I is demyelinative (slows nerve conduction velocity) and autosomal dominant, whereas type II is axonal (conduction velocity is only slightly slowed) and may be autosomal recessive or autosomal dominant. CMT usually is of very slow onset (contrary to the other neuropathies) and typically does not get severe. CMT may present as a foot drop/weakness or sensory loss in a stocking distribution.

Diabetic neuropathy [Know] is a peripheral neuropathy which mainly causes sensory changes. Treatment: Amitriptyline +/- perphenazine is most effective for chronic, burning pain, or carbamazepine for shooting pains. The affected nerves that cause motor changes include the third and sixth cranial nerves, the peroneal nerve (foot drop), and the radial nerve (wrist drop). Exam questions have the patient presenting with diplopia and (pick one) chronic sensory dysfunction, wrist drop, or foot drop.

Alcoholic neuropathy is the second-most common neuropathy after diabetic neuropathy. It is mostly due to the associated nutritional deficiencies—because well-nourished alcoholics rarely, if ever, develop neuropathy. Alcohol is directly toxic to muscle tissue. Symptoms of alcoholic neuropathy start with pain and numbness in the feet in a stocking distribution. Patients slowly recover with multivitamin therapy and abstinence from alcohol.

Also consider "chronic inflammatory demyelinating polyneuropathy." This has a progressive weakness—usually distal but sometimes proximal and distal—and decreased sensation similar to what Guillain-Barré has. It may follow a chronic progressive or chronic relapsing course. As with Guillain-Barré, LP and EMG are helpful in making a diagnosis. Unlike with Guillain-Barré, glucocorticoids frequently hasten recovery and prevent relapse. Plasmapheresis may help.

Diphtheria toxin can cause a painless polyneuropathy.

About 1/3 of patients with AIDS get a symmetric distal polyneuropathy that is sensory or sensorimotor (see AIDS under Viral Infections on pg 11-7).

Toxic polyneuropathy is usually sensory (paresthesias, pain, etc.) B_6 overdosage and arsenic should be ruled out. If the patient has acute onset of motor changes due to a toxin, consider organophosphates as the cause.

notes

Quick Quiz

1) Describe a patient's neurologic progression with Guillain Barré syndrome.
2) Diabetic neuropathy usually is sensory; however, what motor nerves are also occasionally affected?
3) What are the symptoms of alcoholic neuropathy?
4) Weakness that occurs with repetitive muscle movements suggests what disease?
5) When is the edrophonium test useful in myasthenia gravis?
6) What are the symptoms of Lambert-Eaton Syndrome?
7) What laboratory value would you expect to be elevated in muscular dystrophy-type diseases?

Thiamine deficiency often presents with a polyneuropathy; 80% of patients with Wernicke encephalopathy have a variable degree of polyneuropathy; often with 6th cranial nerve ocular palsy and ataxia in addition to the mental disturbance.

Porphyric polyneuropathy usually causes symmetrical proximal muscle weakness.

Plasmacytomas: MM, etc. can cause a demyelinating peripheral polyneuropathy.

Denervated muscle results in hypo/atonia and rapid, extreme muscle atrophy and fibrillation (not fasciculation, which is more due to nerve irritation).

Differentiating between the polyneuropathies is aided by the time of onset. Short time of onset (days) suggests porphyric, Guillain-Barré, and certain toxic polyneuropathies. A very long onset (over several years) is seen with the hereditary disorders such as Charcot-Marie-Tooth or chronic inflammatory demyelinating polyneuropathy. Subacute onset (several weeks to 2 years) occurs in the majority: toxicity (lead and glue-sniffing cause motor effects while INH and vincristine cause sensorimotor effects); nutritional deficiencies (especially B_1, B_6, and B_{12}); paraneoplastic (see Lambert-Eaton below); and rheumatologic disorders.

NEUROMUSCULAR JUNCTION

Myasthenia gravis [Know] is an autoimmune phenomenon. Patients have autoantibodies to the postsynaptic acetylcholine receptor. It is associated with thymomas about 10% of the time. Thymomas usually occur in older patients and indicate a worse prognosis (higher mortality). Patients generally present with intermittent symptoms, which are usually worse at the end of the day. Diplopia and ptosis are common. Weakening with repetitive muscle stimulation during the physical exam suggests the diagnosis—so weakness while brushing hair suggests the diagnosis.

Diagnosis of myasthenia gravis is best confirmed by means of quantitative acetylcholine receptor antibodies. This test is positive in 80–90% of patients with generalized myasthenia. The edrophonium test is of use only while the patient has a quantifiable sign such as ptosis. Routine electrodiagnostic studies, including repetitive nerve stimulation studies as well as single-fiber EMG, are useful in confirming the diagnosis. Do thyroid function studies because 30% of these patients with myasthenia gravis have thyroid disease. Do CT of the chest in all confirmed diagnoses to rule out thymoma.

Treatment may consist of anticholinesterase agents, thymectomy, and/or steroids. Of the anticholinesterase agents, pyridostigmine has the fewest side effects. Thymectomy used to have a bad name, but it is now recommended for most patients with generalized myasthenia, since 90% of myasthenic patients without thymomas will have very good results. Results for patients with thymomas are worse. Cyclosporine may also be effective. Prednisone is frequently used for ocular myasthenia, and prednisone or plasmapheresis is used to get the patient ready for thymectomy.

Treat myasthenic crisis with plasma exchange or intravenous immune globulin. Myasthenic crisis is, by definition, when a patient needs to be put on a ventilator.

Lambert-Eaton syndrome is associated with oat cell carcinoma (2/3) and autoimmune diseases. It is itself an autoimmune disease in which antibodies are produced that are specific for calcium channels in presynaptic peripheral nerve terminals—causing decreased release of acetylcholine from the nerve terminals. Typical symptoms are proximal muscle weakness, aching thighs, dry mouth (autonomic dysfunction), and hyporeflexia, especially in the lower extremities. Lambert-Eaton syndrome rarely involves the ocular muscles. It looks like myasthenia gravis except that repetitive exercise may improve the weakness. EMG can help distinguish between the two.

MYOPATHIES

Inflammatory: Dermatomyositis, polymyositis, and inclusion body myositis. Both dermatomyositis and polymyositis cause proximal muscle weakness, and both respond to glucocorticoids. Inclusion body myositis is a less common type of myositis in which patients do not respond to glucocorticoids. Muscle biopsy in inclusion body myositis shows vacuolar inclusions. More in Dermatology section on dermato/polymyositis.

Metabolic: In all types, there are mitochondrial collections in muscle fibers, causing ragged-red fibers.

Duchenne muscular dystrophy is an X-linked disorder that causes progressive muscle weakness starting at about 2 years of age and progressing to death as a young adult. The weakness is more proximal than distal. Look for an elevated CPK.

notes

Mysthema Gravis — 30% have thymoma ✓ CT chest
— ✓ TSH to R/O thyroid dz

Myotonic dystrophy is a common inherited neuromuscular disorder. It is autosomal dominant with extreme variability in expression. Some patients' family members will have a suggestive EMG but will not have symptoms. Main signs and symptoms are weakness, sleep apnea, cardiac conduction defects, mitral valve prolapse, and testicular atrophy.

Charcot-Marie-Tooth disease is a myopathy already discussed under polyneuropathies.

NEUROMA

Morton neuroma (or Morton metatarsalgia) is a fairly common disease of the foot in which the patient has metatarsal pain. Generally it is diagnosed with MRI or ultrasound that shows a small intrametatarsal ovoid mass. Differential diagnosis includes a metatarsal stress fracture. Treatment is surgical excision.

DEMYELINATING DISEASES

Multiple sclerosis (MS) is a disease that usually begins between the ages of 20 and 30. Women are affected more often than men (about 2:1). The incidence is higher in higher latitudes of both the northern and southern hemispheres. An infectious agent has been proposed as a cause; however, this is unproved. It is clear, however, that the demyelination that occurs is due to an autoimmune process. IgG immunoglobulins to myelin can be found in the cerebrospinal fluid (when these globulins are examined using electrophoresis, a few "bands" appear, thus the term *oligoclonal bands*).

MRI shows the characteristic pattern of myelin loss; however, MRI is not diagnostic. The diagnosis must be made by the history and examination, and is supported by the results of medical testing.

Image 11-7 shows an MRI with characteristic findings of "high signal" regions in the white matter of both hemispheres.

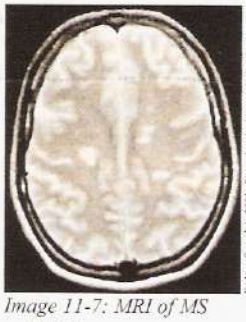


Image 11-7: MRI of MS patient

The neurological symptoms depend on the region of brain that is affected. There are two types of MS: *relapsing-remitting* and *gradually progressive*. The relapsing-remitting type can transform into the progressive type.

There is no cure for MS. For acute attacks, especially those that cause severe symptoms (such as visual loss), the treatment is high-dose corticosteroids. Methylprednisolone, 1 gm/day for seven days, can be followed by a rapid prednisone taper. Beta-interferons (Avonex®, Betaseron®) are effective in limiting the number and severity of relapses, and can slow the progression of disease in the chronic progressive form. Another therapy is copolymer I (Copaxone®), a mixture of four amino acids.

The MRI is the diagnostic test of choice. In patients with MS, the MRI shows white matter disease, which is very characteristic for MS. White matter disease due to ischemic disease (elderly) and vasculitis both have a very different pattern of distribution from that seen with MS. Evoked action potentials can establish the diagnosis of MS by identifying a clinically silent second lesion. 90% of MS patients have increased IgG and oligoclonal IgG bands in the CSF (virtually all cases of subacute sclerosing panencephalitis also have increased IgG). So the workup includes an MRI, an LP, and evoked potentials. Treat acute attacks with steroids. ACTH, which stimulates the release of endogenous steroids, is not used much now.

Progressive multifocal leukoencephalopathy (affects white matter only) is a progressive demyelination that is usually seen in patients with AIDS. It is associated with the papovavirus. Visual defects are common—usually a homonymous hemianopia. Other symptoms include mental changes such as personality change, confusion, and dementia. Motor weakness occurs late in the disease. Diagnose with brain biopsy.

Central pontine myelinolysis (osmotic demyelination syndrome) occurs in a patient with severe hyponatremia that is corrected too quickly. It may occur whether the onset of hyponatremia is acute or subacute, but is more likely the longer the patient has been hyponatremic. These patients may present with quadriparesis, mutism, pseudobulbar palsy, swallowing dysfunction, and/or locked-in syndrome. See the Nephrology section under hyponatremia for more.

MOVEMENT DISORDERS

PARKINSON DISEASE

Parkinson disease (PD) is a clinical diagnosis.

Parkinson disease is caused by a dropout of dopamine-producing cells in the substantia nigra of the midbrain. In a normally functioning brain, the nigrostriatal neurons produce dopamine. This dopamine is released in the basal ganglia, where it has a complex effect on the motor system. When there is a decrease in dopamine from deterioration of the substantia nigra, slowness and stiffness result.

Note that many drugs can cause secondary parkinsonism. The usual culprits are dopamine-depleting drugs such as reserpine or dopamine antagonists such as phenothiazines or butyrophenones. You must exclude these causes before the diagnosis of PD can be made.

Signs and symptoms of PD: Four major characteristics: Resting tremor, Rigidity and flexed posture, Retarded movement, and loss of postural Reflexes (4 R's).

- Resting tremors at a rate of 4–5 Hz (cycles per second) occur in the distal extremities. Tremor is usually the first symptom noticed.
- Parkinson patients have diffuse increased muscle tone, which, combined with the tremor, causes the "cogwheeling"

notes

Quick Quiz

1) What findings in CSF are helpful for the diagnosis of MS? What other tests are done for the workup of MS?
2) What causes Parkinson disease?
3) Name the 4 Rs of Parkinson disease.
4) Is dementia common in Parkinson?
5) What are the common side effects of L-dopa?
6) What is the classic eye finding with progressive supranuclear palsy?
7) What is the treatment for progressive supranuclear palsy?
8) What is the rate for a normal physiologic tremor?
9) What is the rate for essential tremor?

seen with passive range of motion of the limbs. The flexed posture includes the entire body. The spine, elbows, hips, and knees are flexed. Classic hand position is flexed MCP joints with straight IP joints.

- Hypokinesia and bradykinesia are the most common findings. With hypokinesia, the patient has decreased amplitude of intentional motions—especially with repetitive tasks. Bradykinesia is difficulty initiating movement, slowness of movement, and decrease or loss of spontaneous movement (masked facies, tendency to sit motionless, decreased blinking, etc.).
- Loss of postural reflexes eventually causes falls and then inability to stand without assistance. The festinating gait is due to impaired postural reflexes. It occurs as the patient walks faster and faster to keep under the forward center of gravity caused by the forward-curved body.

Note that 30–50% of affected patients develop dementia.

Treatment of PD: Maintaining activity levels and exercising are important goals that keep patients independent as long as possible. There are two approaches for treatment: increasing the dopamine and decreasing the acetylcholine. The dopaminergic approach is the mainstay of therapy. Agents used in the treatment of parkinsonism: levodopa plus carbidopa (Sinemet®), amantadine, bromocriptine, and deprenyl. Treatment decreases the symptoms and may slow progression of the disease, but will not reverse the disease process.

Mild symptoms may respond to anticholinergics such as amantadine, Cogentin®, and Artane®. Anticholinergics can cause altered mental status, including psychosis, especially in patients > 70. Antihistamines and tricyclics, which have some anticholinergic properties, may be used in older patients for initial therapy.

The mainstay of treatment for moderate symptoms is L-dopa, which is combined with carbidopa in the preparation called Sinemet®. L-dopa acts as a precursor for dopamine synthesis in the basal ganglia. The carbidopa decreases the peripheral effects of L-dopa, such as postural hypotension and cardiac arrhythmias. It does not help with the central side effects of L-dopa. A high protein diet can block the absorption of L-dopa. Drug holidays are ineffective with L-dopa.

Although L-dopa is the most effective drug for PD, because it has so many long-term complications its use is delayed as long as possible—especially in younger patients. Selegiline (deprenyl) delays the need for L-dopa for 6–12 months.

L-dopa side effects are significant and frequent. The worst side effect is involuntary movement disorder, which may present as facial-lingual dystonia, chorea, and athetosis. Also, psychiatric symptoms develop in 30% of patients. These range from agitation, confusion, and depression to hallucinations.

On-off phenomenon in PD is the alternating hyperkinesia and hypokinesia that develops in about 20% of patients. It usually occurs after several years on L-dopa and is thought to be due to decreased response to L-dopa.

To reduce the overall daily dose of L-dopa or to even-out the serum levels of this drug, other medications such as bromocriptine (dopamine receptor agonist) or deprenyl (Eldepryl®; selegiline) are added. Deprenyl is an MAO inhibitor (which blocks the catabolism of dopamine). It is the only drug that may (not proven) slow the progression of the disease. Both allow a decrease in the dosage of Sinemet. Either one can be used as monotherapy for PD, but has a weaker benefit than L-dopa.

Neural tissue transplant and vitamins C and E are being evaluated.

PROGRESSIVE SUPRANUCLEAR PALSY

Progressive supranuclear palsy (PSP) is similar to Parkinson disease in that patients have similar bradykinesia, abnormal gait, increased muscle tone, and tend to develop mild dementia. These patients tend to have an erect posture with hyperextension of the neck—especially later in the course of the disease. They usually do not have a tremor. Within 2 years the patients develop the classic symptom of a vertical ophthalmoplegia in which the patient cannot voluntarily look up or down. At this time the patients have trouble reading, eating, and walking down stairs. Within another 2–3 years, the patients may be unable to walk. There is no specific treatment, but tricyclic antidepressants may help some of the symptoms.

TREMORS

Action tremors occur with intentional movement and disappear at rest. They have two main causes:

- exaggerated physiologic tremor
- essential tremor

The rate of the normal physiologic tremor is 9 Hz. It is aggravated by anxiety, hyperthyroidism, and certain drugs (theophylline, beta-agonists, etc.) Essential (familial) tremor has a rate of 7 Hz. It is autosomal dominant and benign. The essential tremor is decreased by ingesting a little alcohol. Propranolol is effective in half of patients; primidone may help the others.

notes

TARDIVE DYSKINESIA

Tardive dyskinesia is usually a result of long-term antipsychotic drug use. It consists of chorea of the lips, tongue, face, and neck. Occasionally, it affects the limbs. Exchanging the dopamine antagonist antipsychotic with reserpine may help, but reserpine also may cause tardive dyskinesia because it is a dopamine-depleting agent.

OTHER MOVEMENT DISORDERS

Neuroleptic malignant syndrome is an unusual response to antipsychotics, resulting in fever, rigidity, and altered mental status.

Hemifacial spasm is a motor analogue to trigeminal neuralgias (tic douloureux). 80% of patients have a tortuous, dilated basilar artery that irritates the facial nerve! Treat with surgery or carbamazepine.

Gilles de la Tourette is treated with haloperidol.

Torticollis is treated with botulinum toxin.

Blepharospasm is bilateral eye closure, which may be accompanied by Meige syndrome (which has grimacing, smacking lips, and twisting of the neck). Botulinum toxin provides temporary relief.

MISCELLANEOUS SIGNS, SYMPTOMS, AND DISORDERS

ACUTE ONSET UNILATERAL BLINDNESS

In older patients, this blindness is usually due to either ischemic optic neuropathy (secondary to giant cell arteritis or idiopathic) or retinal artery occlusion (secondary to emboli from the carotid artery or heart). In the younger patient, think optic neuritis, but sometimes it can be from migraine. Migraine-induced blindness usually resolves rapidly, whereas blindness due to any of the other mentioned causes is prolonged or permanent. See Table 11-6.

There are two common ocular manifestations after an episode of optic neuritis: These are dimming of vision after exercise or with a fever, and a persistent, intermittent Marcus Gunn pupil ("afferent pupillary defect"). With Marcus Gunn pupil, the affected pupil will constrict when light is directed at the other eye but not when the light is shone directly at it. There is impaired direct light reflex but normal consensual response. When a bright light is shifted from eye to eye, it appears that the affected pupil dilates (although it is actually only recovering from the consensual response).

Ischemic optic neuropathy, optic neuritis, and papilledema all can present with swollen discs with fundal splinter hemorrhages. Remember that temporal (giant cell) arteritis also causes diplopia and jaw claudication.

Although most cases of optic neuritis rapidly resolve, about 70% of persons with optic neuritis eventually are diagnosed with multiple sclerosis, although it may take many years.

Malingering as a cause of blindness (mono/bi) can be ruled out with evoked action potentials.

DIPLOPIA

Pseudotumor cerebri produces headache and horizontal diplopia and usually occurs in premenopausal (childbearing age) obese women. There is also an increased incidence during pregnancy. Drugs that may cause it are glucocorticoids, tetracycline, and vitamin A. Severe, irreversible visual loss occurs in 10% of patients. CSF pressure > 250 for diagnosis. CT and MRI are usually normal except for small ventricles. Usual treatment is with diuretics or frequent lumbar punctures.

SCOTOMAS

Scotomas are not associated with blindness. Do a complete ophthalmologic exam on any patient with any type of scotoma.

Acephalic migraine (migraine without headache) can cause "fortification scotomas" that constantly change in size and may be bilateral.

Moore's lightning streaks occur in older patients upon entering a darkened area. They are caused by the vitreous pulling on the retina; they are benign.

Retinal detachment causes flashes followed by decreased vision (from blood) or increased floaters.

VISUAL FIELD DEFECTS

Bitemporal hemianopsia is not caused only by pituitary adenomas. Other possible causes are: craniopharyngioma, meningioma, aneurysm of the circle of Willis, and, rarely, sarcoidosis and metastatic carcinoma.

DM and MS can cause oculomotor palsies without pupillary changes.

Table 11-6: Causes of Acute Onset Unilateral Blindness

Age	Disease	Etiology
Older (> 50)	Anterior ischemic optic neuropathy OR	Giant cell arteritis or Idiopathic
	Central retinal vein occlusion	HTN; amaurosis fugax if transient
Younger (< 40)	Optic neuritis	Think MS! Common 1st presentation

notes

Quick Quiz

1) What is a Marcus Gunn pupil?
2) What is acephalic migraine?
3) What are flashes followed by decreased vision suggestive of?
4) What is the quartet of symptoms that can occur with narcolepsy?

Reflex sympathetic dystrophy causes pain, swelling, dysesthesias, and vasomotor instability in an extremity after a traumatic injury.

INCONTINENCE

Incontinence has many causes: Dementia and stupor, frontal lobe lesions, pyramidal tract dysfunction, dysautonomias (Shy-Drager, Parkinson), spinal cord/nerve root lesions, peripheral polyneuropathy, bladder/rectal problems. Stress incontinence (incontinence with sneeze or cough) is common in women who have had children delivered vaginally.

IMPOTENCE

Impotence: Sympathetic innervation is responsible for ejaculation and erection in response to mental stimuli and during REM sleep. The parasympathetic reflex arc causes erection to tactile stimulus, so patients with sympathetic denervation can still have sex. They work independently of each other. "Point and Shoot" "Parasympathetic and Sympathetic."

NARCOLEPSY

Narcolepsy is associated with HLA-DR2. Narcolepsy quartet:

1) narcolepsy
2) cataplexy (3/4 of patients! With excitement, limbs become flaccid.)
3) hypnagogic hallucinations (occur as patient falls asleep)
4) sleep paralysis (on waking). Treat with methamphetamine or methylphenidate. Treat the cataplexy with tricyclics.

OTHER

Sarcoidosis: Neurosarcoidosis is uncommon and presents as aseptic meningitis or just about any neuropathy or myopathy. Patients usually have the commoner signs of sarcoidosis. All types, including intracranial masses, are treated with prednisone.

Collagen vascular diseases: Sjögren syndrome—25% get neurologic complications.

notes

OPEN-ENDED QUESTIONS

1) Name the 3 factors that define a stroke.

[Sudden onset, symptoms persist > 24 hours, and the neurological deficit fits a vascular area of the brain. Subarachnoid bleed is an exception to the last criterion.]

2) What are the 3 most common sources of a subarachnoid bleed?

[Cerebral saccular (berry) aneurysms, hypertensive intracerebral hemorrhage with ventricular rupture, and A-V malformations.]

3) Which type of cerebral hemorrhage will usually not have focal neurologic signs?

[Subarachnoid bleed.]

4) Where do half of all intracerebral bleeds originate? What are the signs and symptoms of a hemorrhage in this area?

[The putamen and adjacent internal capsule. If it involves the internal capsule, there is contralateral hemiparesis and usually sensory loss and hemianopsia.]

5) In which type of hemorrhage is there a "thunderclap" headache and in what type is there a dull headache?

[Thunderclap: subarachnoid; dull: intracerebral.]

6) What are the sequelae of amyloid angiopathy?

[Amyloid angiopathy is a cause of multi-infarct dementia and is also found in patients with Alzheimer disease. It causes recurrent intracerebral bleeds.]

7) Which type of stroke is suggested by a recent history of TIAs?

[Thrombotic stroke. Embolic strokes are usually not preceded by TIAs.]

8) How do you differentiate middle, posterior, and anterior cerebral artery emboli from the patient's symptoms?

[With middle artery embolus, the hemiparesis is worst in the face and arm; whereas, with an anterior artery embolus, the patient is most affected in the leg, with the arm less affected and the face unaffected. Posterior emboli usually cause only homonymous hemianopsia.]

9) In what way does the onset of symptoms differ in thrombotic and embolic strokes?

[Thrombotic: slow, stepwise progression. Embolic: abrupt; neuro deficit is worst at onset.]

10) What is the lateral medullary syndrome and what type of stroke causes it?

[Also called Wallenberg syndrome, it is caused by a vertebral stroke. It results in a mixed bag of symptoms (nausea, vomiting, nystagmus, ipsilateral Horner syndrome, ipsilateral palate and vocal cord weakness, and "crossed" sensory loss [ipsilateral face and contralateral body]).]

11) What cardiovascular disorder is associated with lacunar infarcts? How do the symptoms of lacunar infarcts differ from other cerebral infarcts?

[Small artery disease, usually due to chronic hypertension. Lacunar infarcts are the only cerebral infarcts that present with pure hemiplegia or pure hemisensory stroke.]

12) If a patient from an MVA gets a CT that shows a lenticular blood clot adjacent to the left temporal skull, what type of hematoma is this?

[Epidural hematoma.]

13) What is the two-step approach to treating a patient with a single approachable brain metastasis?

[First surgery, then irradiation.]

14) What areas of the brain must be damaged/impaired to cause a coma?

[Either the reticular activating system or both hemispheres of the brain.]

15) What triad of symptoms is seen in Wernicke encephalopathy?

[Wernicke encephalopathy (due to a B_1 deficiency) presents with at least the first 2 components of the triad of ocular nerve palsy, gait ataxia, and mental disturbance.]

16) What is the difference between Wernicke encephalopathy and Korsakoff syndrome?

[Korsakoff syndrome (or psychosis) is the residual amnesic state that stays after the Wernicke encephalopathy has resolved. Patients with Korsakoff syndrome have a decreased ability to learn despite normal level of alertness and normal immediate recall. Treatment of Wernicke encephalopathy with thiamine will prevent Korsakoff syndrome.]

17) What is the most common cause of coma?

[Drugs.]

18) For the following scenarios name the most probable cause of coma: a) A comatose patient arrives to the ER breathing shallowly. Pupils are pinpoint and doll's eyes are negative. b) Same presentation except pupils are 4 mm and nonreactive.

[a) Narcotic overdose. b) Barbiturate overdose.]

19) In which way does the onset of symptoms differ between uncal vs. central herniation?

[Central herniation results in early decreased consciousness and little effect on pupils whereas uncal herniation compresses the oculomotor nerve, causing an ipsilateral dilated pupil and oculomotor paralysis except for upward and lateral gaze.]

20) What is the difference between locked-in syndrome and vegetative state?

[Locked-in syndrome: Lesion spares the RAS, but affects the lower brainstem, causing paralysis and mutism. The EEG is normal! Vegetative state: severe, bilateral cerebral dysfunction (doll's eyes are normal) with an operating RAS. These patients sleep and wake normally, but have no cognitive function. It is often caused by anoxic brain damage].

21) Is the EEG required for the diagnosis of brain death?

[No. Just document that the patient is unresponsive, has no pupillary function, no doll's eyes, and is apneic. EEG is helpful, but not required.]

22) What is the most common myelopathy affecting only motor function? What are the classic physical findings seen with this disorder?

[Amyotrophic lateral sclerosis (ALS, Lou Gehrig disease). Polio was once the most common cause of anterior horn disease. Classic findings in ALS include diffuse hyperreflexia and spasticity (= upper motor neuron = myelopathy), along with fasciculations, weakness, and atrophy (lower motor neuron).]

23) What are the signs of post-polio syndrome?

[Areflexia and progressive weakness in a patient with a history of polio.]

24) What effect can B_{12} deficiency have on the spinal cord?

[It causes a syndrome known as "subacute combined degeneration of the spinal cord," which presents as a generalized myelopathy.]

25) If an AIDS patient presents with gait ataxia, spasticity, and hyperreflexia, what are two of the most probable causes?

[Spinal cord compression must be ruled out. Another cause that is occasionally clinically significant is vacuolar myelopathy.]

26) What is the probable diagnosis if a patient has lower extremity pain and weakness that occurs when walking down hills or standing upright, and resolves when sitting or bending forward?

[Lumbar spinal stenosis.]

27) What is the Arnold-Chiari malformation and what disorder might it cause?

[Downward shift of the cerebellum and medulla through the foramen magnum. It is the most common craniovertebral cause of syringomyelia.]

28) In what way does a radiculopathy differ from a myelopathy?

[Radiculopathy is a lower motor/sensory neuron problem, and these patients have loss of function along a nerve pathway. Myelopathy is an upper motor neuron problem in which there is spasticity and hyperreflexia below a certain nerve level.]

29) What is the preferred initial test in diagnosing a supposed spondylitic myelopathy?

[MRI. If then needed, a myelogram with metrizamide.]

30) What are the similarities and differences between sciatica and S1 radiculopathy?

[Although both cause difficulty standing on tiptoe, S1 radiculopathy also causes decreased ankle reflex.]

31) How is peroneal nerve compression differentiated from L5 radiculopathy?

[Although both cause foot drop and trouble everting the foot, with L5 radiculopathy the patient is also unable to invert the foot.]

32) What are the usual causes of mononeuritis multiplex?

[Rheumatoid arthritis, DM, connective tissue diseases, vasculitis, polyarteritis, and Lyme disease.]

33) How does diabetic neuropathy present? How are the dysesthesias treated?

[Diabetic mononeuritis +/- multiplex usually causes sensory changes. Treat the dysesthesias with amitriptyline +/- perphenazine, which works best for chronic, burning pain or with carbamazepine for shooting pains. The motor neuropathies include cranial nerves III and VI, the peroneal nerve (foot drop), and the radial nerve (wrist drop).]

34) What is the most common inflammatory polyneuropathy, how does it present, and how is it treated?

[Guillain-Barré. Ascending paralysis and areflexia. Treat with plasmapheresis if within 2 weeks of onset. High-dose steroids are controversial.]

35) What are the classic MRI findings in patients with multiple sclerosis?

[The MRI shows white matter disease very characteristic for MS. The white matter disease due to ischemic disease and vasculitis has a different pattern of distribution.]

36) In what patient group is progressive multifocal leukoencephalopathy seen; what is its etiology?

[AIDS patients. It is a progressive demyelination associated with the Papovavirus.]

37) Why should thyroid function tests always be done for patients with myasthenia gravis?

[Because TFTs are abnormal in 30% of these patients.]

38) How does Eaton-Lambert syndrome differ from myasthenia gravis?

[Eaton-Lambert syndrome is associated with oat cell carcinoma and autoimmune diseases. It causes a diffuse neuropathy like myasthenia, but spares the ocular muscles.]

39) What are the 4 major clinical characteristics of Parkinson disease?

[The 4 R's: Rigidity, Resting tremor, Retarded movement, and loss of postural Reflexes.]

40) What mechanism allows both anticholinergic and dopaminergic drugs to be used in the treatment of Parkinson disease?

[Parkinson disease is thought to be caused by an overactivity of cholinergic neurons in the basal ganglia, which is due to a decreased inhibitory effect of the dopamine-producing neurons in the substantia nigra of the midbrain.]

41) Which type of tremor is decreased by ingestion of a little ETOH?

[Essential tremor.]

42) What motor disorders respond to botulinum toxin?

[Torticollis and blepharospasm (as in Meige syndrome).]

43) An AIDS patient with multiple ring-enhancing lesions seen on CT of the head is probably infected with what organism?

[*Toxoplasma gondii*.]

44) What is the usual cause of non-epidemic viral encephalitis? How is this diagnosed and treated?

[Herpes simplex. Diagnosis is made by PCR test of the CSF for herpes virus. Treat with acyclovir.]

45) Name 3 types of encephalitis caused by slow viruses.

[1) Subacute sclerosing panencephalitis (SSPE), 2) Progressive multifocal leukoencephalopathy (PML), and 3) Jakob-Creutzfeldt disease (JCD).]

46) What is the most common worldwide parasitic CNS infection? How is it transmitted? How is it treated?

[Neurocysticercosis, which is caused by the tapeworm Taenia solium, which is transmitted by ingesting contaminated food or water. Treat with albendazole (first choice) or praziquantel. Note: Niclosamide is also used to treat tapeworm, but it works only on those in the intestine.]

47) What is the first sign on physical exam seen in a patient with early HIV encephalopathy?

[Decreased motor skills, seen as deterioration of penmanship.]

48) If a patient being treated for AIDS presents with generalized muscle weakness and an elevated CPK, what is the probable cause?

[Zidovudine (ZDV, AZT).]

49) What is/are the usual cause/s of acute onset of unilateral blindness in a 30-year-old patient? In a 60-year-old patient?

[30-year-old: optic neuritis. 60-year-old: either ischemic optic neuropathy or retinal vein occlusion.]

50) If a 60-year-old patient with acute onset of unilateral blindness also complains of jaw claudication, would the diagnosis be retinal vein occlusion or ischemic optic neuropathy?

[Ischemic optic neuropathy. Jaw claudication is caused only by giant cell (temporal) arteritis.]

51) If a 30-year-old patient complains of dimming of vision after exercise, what is the suspected etiology and what specific test should be done on physical exam to further clarify the diagnosis?

[Optic neuritis. Check for an afferent pupil defect (Marcus Gunn pupil). In this, the pupil constricts when light is directed at the other eye but not when the light is shone directly at it.]

52) If a 65-year-old patient complains of bright flashes of light when going into a darkened area, what would be the probable cause? What prognosis does this have?

[Moore's lightning streaks. Benign.]

53) How does dementia differ from encephalopathy?

[Dementia is a progressive deterioration of cognitive function in a patient with a normal level of consciousness. Encephalopathy, on the other hand, causes altered level of consciousness—from delirium to stupor. Demented patients have deterioration in memory, judgment, and abstract thinking.]

54) What are the treatable dementias that must be excluded in a dementia workup?

[Drugs, B_{12} deficiency (which can also cause a polyneuropathy and myelopathy with a spastic ataxia), Wilson disease (can also cause cerebellar ataxia and psychiatric symptoms), heavy metal poisoning (arsenic, mercury, and lead), hypothyroidism, chronic subdural hematoma, and normal pressure hydrocephalus. Also consider infection and inflammation: syphilis, sarcoidosis, chronic meningitis, lupus cerebritis, Whipple disease, and vasculitis.]

55) What type of dementia is suggested when the dementia had an acute onset (over weeks) and the patient has an exaggerated startle reaction?

[Jakob-Creutzfeldt disease.]

56) What cause would you suspect in a 52-year-old patient presenting with urinary incontinence, a wide-based gait, concrete thinking, and fairly poor memory? What do you see on CT with this problem?

[Normal-pressure hydrocephalus. The CT/MRI shows enlarged ventricles without correspondingly enlarged sulci (i.e., not atrophied).]

57) How does the Shy-Drager syndrome differ from Parkinson disease?

[Shy-Drager syndrome is the combination of Parkinson symptoms with autonomic insufficiency.]

58) What is the classic physical finding in progressive supranuclear palsy that differentiates it from Parkinson disease?

[These patients have findings similar to those seen in Parkinson disease but, in addition, patients with supranuclear palsy cannot voluntarily look down or up. They usually do not have a tremor.]

59) How are the mental changes seen in depression different from those seen in dementia?

[Immediate recall is usually good in dementia and poor in depression. Many other symptoms are similar except patients with depression do not have grasp and suck reflexes.]

60) Why is ergotamine not used for more than one treatment regimen every 3–4 days?

[It can cause rebound headaches.]

61) How does the pain in a cluster headache differ from that in a classic migraine headache?

[Migraine headaches are usually unilateral, intermittent, throbbing headaches lasting from 4 hours to 3 days. Cluster headaches occur daily for several weeks and then stop occurring for a long period of time. They often wake the patient in the AM or soon after falling asleep in the evening (they often start in REM sleep). Symptoms usually consist of an "ice pick–like" or "hot poker–like" sharp periorbital pain. The pain peaks early (5–10 min) and is short-lived (up to 2 hours, but usually 30–45 min).]

62) Which type of headache is associated with an ipsilateral Horner syndrome, tearing, and rhinorrhea?

[Cluster headache.]

63) What is the treatment of choice for an acute cluster headache?

[Oxygen, 8–10 L/min, is the treatment of choice in an acute cluster headache. Other drugs that may work are 4% lidocaine nose drops (only occasionally effective), fast-acting ergotamine, and sumatriptan (a serotonin agonist).]

64) In what ways does a tension headache differ from a migraine headache?

[Tension headaches are typically chronic, bilateral, constant, several hour, daily, with the feeling of a tight band around the head (non-throbbing). Migraine headaches are usually unilateral, intermittent, throbbing headaches lasting from 4 hours to 3 days.]

65) How is acute labyrinthitis differentiated from vestibular neuritis as a cause of vertigo?

[Acute labyrinthitis is similar to vestibular neuritis in that it presents with non-positional vertigo, but acute labyrinthitis has an associated hearing loss.]

66) Which causes of vertigo are associated with hearing loss?

[Acute labyrinthitis, aminoglycoside toxicity, and Ménière disease.]

67) Which anticonvulsant drugs are associated with: Ataxia? Liver failure? Gum hyperplasia and hirsutism? Leukopenia and thrombocytopenia?

[Ataxia can be caused by any of the seizure medications. Liver failure can be caused by valproic acid. Both gum hyperplasia and hirsutism may occur in patients on phenytoin. Leukopenia and thrombocytopenia: carbamazepine.]

68) How do the medical treatments for the 3 classes of seizures differ?

[1) Petit mal/absence seizures are treated with valproic acid or ethosuximide. 2) Grand mal seizures are treated with phenytoin, carbamazepine, valproic acid, and sometimes phenobarbital. 3) Focal and complex partial seizures are treated with phenytoin or carbamazepine (primidone and phenobarbital are alternatives). For especially refractory seizures, surgical ablation of the epileptic focus may be done.]

69) What are the 4 classic findings in a patient with narcolepsy (the narcolepsy quartet)?

[Narcolepsy quartet = 1) narcolepsy 2) cataplexy (with excitement, limbs become flaccid.) 3) hypnagogic hallucinations (occur as patient falls asleep) 4) sleep paralysis (on waking).]

MedStudy

11th Edition

Internal Medicine Review

Core Curriculum

Dermatology

Authored by Robert A. Hannaman, MD

Many thanks to

Margery A. Scott, MD
Professor of Dermatology
Department of Dermatology
Eastern Virginia Medical School
Norfolk, Virginia

Dermatology Advisor

Dermatology

COMMON SKIN PROBLEMS

ATOPIC DERMATITIS

Atopic dermatitis (AD) has three stages: infant, childhood, and adult (least common). Each stage may be a continuation of the previous stage or may be a new finding. It is multifactorial, occasionally with increased IgE. Usually there is a family history of asthma and/or rhinitis. Patients have a decreased itching threshold and dry skin. They develop pruritic skin rashes: initially erythematous, edematous, papular patches found on the head and neck. Extensor surfaces tend to be involved in infants; in children and adults, involvement is more often flexural. These may become scabbed and weepy, at least partly from scratching.

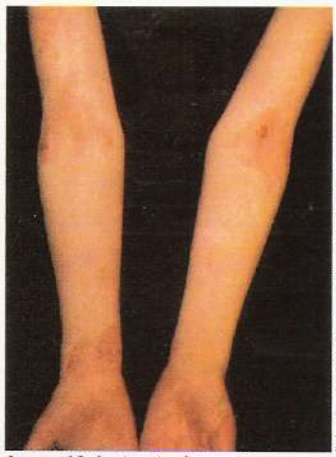


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Image 12-1: Atopic dermatitis

Hydration, water-trapping agents, and occasional moderate-strength topical glucocorticoids are the mainstay of treatment for AD.

Tacrolimus (Prograf®) and pimecrolimus (Elidel®) are new topical immunosuppressants that are effective alternatives to topical corticosteroids. Since these don't cause skin atrophy, they are especially good for facial lesions.

Oral cyclosporine is used for severe AD.

Antigens such as *S. aureus*, dust mites, and *Malassezia furfur* (causes tinea versicolor) can exacerbate AD. Because of decreased skin defenses, AD patients tend to get chronic bacterial and fungal skin colonization and infections. Occasionally, oral antibiotics are given to decrease colonization of *S. aureus* and thus improve atopic dermatitis.

SEBORRHEA

Seborrheic dermatitis manifests as erythema and has a greasy scale. It especially involves the scalp (dandruff), eyebrows, paranasal area, and external auditory canal. There is a strong causal association with *Malassezia furfur*, but we don't know if this is a cause or result of the dermatitis.

Seborrheic dermatitis is common in HIV patients.

Treatment: frequent washing and an antiproliferative shampoo for the dandruff. The active ingredients in antiproliferative shampoos are selenium sulfide, zinc pyrithione, and tar.

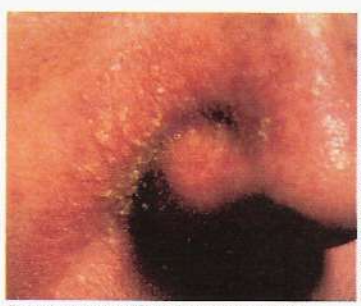

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Image 12-2: Seborrheic dermatitis

Ketoconazole and metronidazole are also effective agents for skin and scalp.

INTERTRIGO

Intertrigo is an irritant dermatitis caused by maceration and friction and is usually found in the skin folds of obese patients.

CONTACT DERMATITIS

Contact dermatitis can be caused by a chemical irritant or be of allergic origin. The allergic type is due to a delayed hypersensitivity reaction in the skin. Patients first become sensitized to the antigen with one or many exposures. After sensitization and upon re-exposure, the skin will develop a pruritic lesion in 1/2 to 2 days. Most common allergens are nickel, chromium, neomycin, and oleoresin (poison oak, poison ivy, and poison sumac). Treatment is cool compresses (Burow's solution = aluminum acetate 1:20) and topical glucocorticoids. If severe, give systemic glucocorticoids.

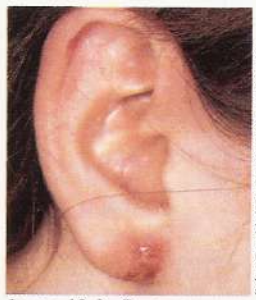

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Image 12-3: Contact dermatitis from earring

ACNE

Acne vulgaris. The clinical manifestations of acne vulgaris are open and closed comedones and inflammatory papules and pustules on the face, chest, and back.

Comedonal acne is a noninflammatory acne, which develops in early teenage years.

Inflammatory acne is due to *Propionibacterium acnes* within the follicle.

Note that acne is a common manifestation of increased androgens; it is often an external manifestation of polycystic ovary syndrome in women. PCOS occurs in 5–10% of women, and about 1/3 of women with acne have PCOS.

Treatment of acne vulgaris:

Comedonal (noninflammatory) acne:

Topical retinoids are drug of choice for comedonal acne. These include adapalene, tretinoin, and tazarotene.

Effectiveness: tazarotene > adapalene > tretinoin.

Side effects: tazarotene > tretinoin > adapalene.

Side effects are mainly skin irritation and photosensitivity.

Mild inflammatory acne:

Benzoyl peroxide in combination with topical erythromycin or clindamycin is used to treat the *P. acnes* of inflammatory acne. The com-

notes

bination therapy decreases development of resistance.

Moderate to severe inflammatory acne:

This usually requires oral antibiotics or oral isotretinoin in addition to the above topical therapy. The oral antibiotics used are tetracycline, doxycycline, minocycline, and erythromycin. TMP/SMX is occasionally used. Isotretinoin (Accutane®; 1.0 mg/kg/d) is highly effective in resistant cases but is also a powerful teratogen.

Acne rosacea: (mostly middle-aged patients) acne-like lesions, erythema, and telangiectasias on the central face. Even before the lesions, the patients may have a flushing reaction to various stimuli (alcohol, stress, etc.). Once the rosacea manifests, the flush may become permanent. Rhinophyma (big nose) also occurs. Treatment is usually tetracycline, topical metronidazole, or sulfacetamide preparations.

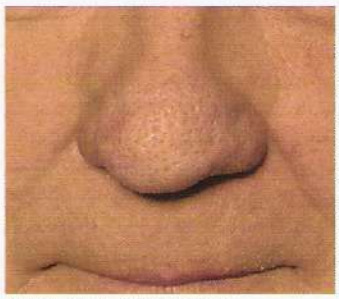

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Image 12-4: Acne rosacea

HIDRADENITIS

Hidradenitis Suppurativa is a chronic inflammatory scarring process involving apocrine gland-bearing areas. The problem starts with occlusion of the hair follicles, with subsequent inflammation of adjacent apocrine glands (sweat glands in the axilla and groin areas). This disease occurs in both sexes—women tend to have more axillary and vulvar involvement while perianal involvement is more frequent in men.

The disease process can range from mild to severe (induration, scarring, pitting, and draining abscesses).

No good treatment. Give tetracycline or erythromycin, then a topical antibiotic for prophylaxis. This often is ineffective. Surgical excision is the only definitive therapy for severe cases.

MOUTH FINDINGS

KNOW ALL OF THESE!

Hyperpigmented gingiva is seen in Addison disease.

Koplik's spots are small white vesicles on an erythematous base, which are found on the palate in patients with measles. These usually precede the skin lesions by several days.

Hairy leukoplakia most commonly occurs in AIDS patients. It appears as areas of ribbed whiteness along the sides of the tongue. This is due to Epstein-Barr virus in the superficial layers of the tongue's squamous epithelium.

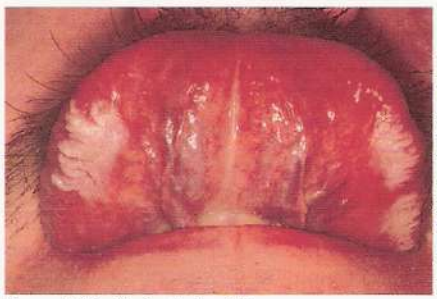

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Image 12-5: Hairy leuloplakia

Peutz-Jeghers syndrome (multiple intestinal hamartomatous polyps) should be ruled out in patients with melanotic pigmentation (freckles) on the lips and buccal mucosa.

Beefy red tongue and angular cheilitis are associated with glucagonomas—discussed under Skin Findings on pg 12-8.

Macroglossia (big tongue) is associated with multiple myeloma, primary amyloidosis, lymphoma, hemangioma, acromegaly, and Down syndrome.

White lesions: candidiasis, hairy leukoplakia (AIDS), lichen planus. Lichen planus also causes ulceration.

"Geographic tongue" has the appearance of migratory denuded red patches. It is asymptomatic and benign.

"Strawberry" tongue is associated with scarlet fever and Kawasaki disease (mucocutaneous lymph node syndrome; children only).

"Bald tongue" is an atrophy of the tongue associated with pellagra, iron deficiency anemia, pernicious anemia, and xerostomia (salivary gland problems as seen in Sjögren syndrome, lymphoma, mumps, and sarcoidosis; occasionally idiopathic).

CUTANEOUS DRUG REACTIONS

The most frequent drug-associated skin changes include:

PCN:

1) immediate hypersensitivity reaction; anaphylaxis (IgE)
2) delayed hypersensitivity reaction; immune complex reaction such as vasculitis, or morbilliform eruption.

Tetracycline: photosensitivity.

NSAIDs: cause urticaria/angioedema in 1%, asthma in 0.5%, and may cause photosensitivity or toxic epidermal necrolysis.

Phenytoin:

1) hypersensitivity syndrome: purpura, facial edema, lymphadenopathy, and hepatitis.
2) various skin reactions including erythema multiforme.
3) hypertrophied gums.

Glucocorticoids: skin changes including striae, atrophy, and acne-like lesions.

Coumadin necrosis: necrotic patches of skin appearing 3–10 days after starting warfarin.

Radiocontrast dye can cause urticaria/erythema (1/15), and anaphylaxis (1/1000). There is a 30% repeat reaction incidence in someone with a previous reaction to contrast dye. The repeat reaction can be very serious. Prophylaxis with diphenhydramine and glucocorticoids (start 1–2 days prior) will decrease this reaction 10-fold.

notes

Quick Quiz

1) What is seborrhea?
2) What is intertrigo?
3) Contact dermatitis is an example of what type of hypersensitivity reaction?
4) Know the quick correlates listed under "MOUTH FINDINGS."
5) Nail pitting with onycholysis is a fairly specific finding in what dermatologic disorder?

INFLAMMATORY SKIN DISEASES

PSORIASIS

Psoriasis is a response triggered by T-lymphocytes in the skin. There are quite a few manifestations of psoriasis:

Plaque psoriasis is the most common form. It presents in young adults with well defined, stable, slow-growing, non-pruritic, erythematous skin lesions with distinctive mica-like (silvery) scales. It is usually symmetrical and occurs on extensor surfaces of the knees and elbows, the sacral area, and the scalp. Koebner phenomenon (outbreak in the area of an abrasion) is common. See Rheumatology section for psoriatic arthritis.

Guttate (eruptive) psoriasis is an abrupt eruption of multiple small lesions, which usually occurs on the trunk of children or young adults with no previous history of psoriasis. There is a strong association with group A Beta hemolytic strep.

Flexural (inverse) psoriasis affects skinfold areas. Called inverse because it is not on the extensor surfaces.

There are two severe cutaneous types:
1) erythrodermic psoriasis
2) pustular psoriasis

Erythrodermic psoriasis is an exfoliative reaction in which the entire surface of the skin becomes red, warm, and scaly, and the patients are unable to control body temperature (hypo/hyperthermia is common). Dehydration, hypoalbuminemia, and anemia of chronic disease are common sequelae. The erythroderma and psoriasis of any type are often precipitated/exacerbated by sunburn, infection (virus, strep pharyngitis), and drugs (especially antimalarials, gold, lithium, and beta blockers). Alcohol and cancer do not exacerbate psoriasis. Treatment usually includes acitretin (Soriatane®) and sometimes methotrexate.

Pustular psoriasis has many small pustules, often coalescing to form "psoriatic lakes of pus." Two forms:
1) The *localized* form affects only the palms and soles. It is associated with DIP joint arthritis.
2) The rare *generalized* form (von Zumbusch) is the most severe form of psoriasis and may occur with the erythrodermic type, and treatment is most often acitretin (Soriatane®).

Nail changes: The most specific nail finding is an "oil slick" (glycoprotein) deposition in nails. "Ice pick" pitting of the nails is common. These pits will usually be in small groups on the nail. Thickened nails and onycholysis (separation of distal nail from the nail bed) are also common in psoriasis. Having pitted nails in association with onycholysis is fairly specific for psoriasis.

Clinical course is usually of lifelong duration but often with variable severity. The most common drugs that exacerbate psoriasis are beta blockers, lithium, and antimalarial drugs.

Diagnose by physical exam and sometimes a skin biopsy.

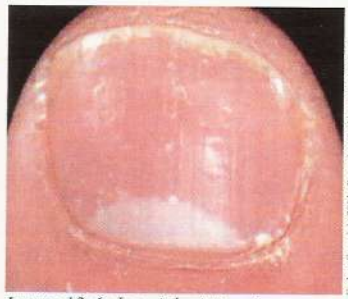

Image 12-6: Ice pick pitting in Psoriasis

First we will go over the drugs and processes used in treatment:

Corticosteroids: Plaques are usually treated with topical corticosteroids.

Tar is time-honored and still used often in a compounded preparation with a corticosteroid. Tar preparations stain clothes but are well tolerated.

Retinoids (vitamin A derivatives):
- Tazarotene gel (Tazorac®, a retinoid) compares well with topical steroids
- Acitretin, a second-generation retinoid, is used for the severe forms of all types.

Vitamin D_3 analog:
- Calcipotriene (Dovonex®, a synthetic vitamin D_3 analog) compares well with topical steroids.

Immunosuppressants:
- methotrexate
- cyclosporine

Biologic immunomodulators:
These are new effective treatments for psoriasis!
- T-cell memory effector inhibitor: alefacept (Amevive®)
- Antibody to CD11A: efalizumab (Raptiva®)
- TNF-alpha inhibitors: etanercept (Enbrel®), infliximab (Remicade®), adalimumab (Humira®)

Ultraviolet light may be added to the above treatments. UVB (290–320 nm) therapy is often used. Narrow band UVB (311 nm) is looking to be (few good studies) more effective but more expensive.

"PUVA" (oral psoralen + UVA light [320–400 nm]) is also very effective and you usually give it to those who fail UVB. UVA penetrates more deeply than UVB and is less likely to burn (hence the photosensitizing psoralen), but is associated with increased likelihood of skin cancer.

Methotrexate is commonly used for widespread psoriasis, especially with arthritis. Remember to not give methotrexate to patients with liver/renal disease or a history of alcohol abuse or HIV disease.

notes

Note that several drugs used to treat RA also treat psoriatic arthritis and psoriasis. E.g., cyclosporine, methotrexate, and etanercept (Enbrel®; a TNF receptor blocker).

Now we will go over how to treat psoriasis:

Mild plaque psoriasis: Treat with hydration and water trapping agents. Use topical low-potency corticosteroids, calcipotriene, or topical retinoids (tazarotene) for mild plaques.

Guttate psoriasis: Treat with UVB plus or minus topical steroids. Treat any streptococcal infection!

Flexural psoriasis: Treat with low-potency corticosteroids.

Moderate psoriasis: Treat with high-potency topical corticosteroids, calcipotriene, topical retinoids (tazarotene), or UVB therapy.

If widespread or severe, use a combination of UVB or PUVA, oral retinoids (acitretin), biologic immune-modulators, and immunosuppressants.

CUTANEOUS LUPUS

Systemic lupus erythematosus (SLE):

Malar (butterfly) rash occurs in about half of SLE patients. This rash is erythematous and either flat or slightly edematous and often occurs after sunlight exposure on sun-exposed areas (photosensitive). No scarring.

Patchy alopecia is common.

More on SLE in the Rheumatology section.

Discoid lupus erythematosus (DLE):

Discoid lesions which are erythematous and raised with a slight tight scale. They cause atrophic scarring. They usually occur on the face, scalp, and neck. Only 5–10% of DLE patients develop SLE.

SCLERODERMA

Scleroderma has no satisfactory treatment.

Morphea is a localized scleroderma characterized by plaques that become sclerotic with a hypopigmented center and erythematous border. It usually occurs in children or young adults. It can be just a few lesions (localized morphea) or widespread with some confluence (generalized morphea).

Regular scleroderma (systemic sclerosis) usually starts with recurrent nonpitting edema of the face and distal extremities. Sclerosis of the skin begins at the distal digits and moves proximally. Patients may develop tight unwrinkled skin over the face, and the fingers may become tight and sausage-shaped. No nail changes.

Limited scleroderma (previously CREST) is a grouping of syndromes that includes a milder systemic sclerosis. These patients present with calcinosis cutis (small tender nodules on the fingers), Raynaud syndrome, esophageal dysmotility, sclerosis of the fingers, and telangiectasias.

SARCOIDOSIS

Overview

Sarcoidosis is an immune-related noncaseating granulomatous disease that often affects the lungs, lymph nodes, eyes, and skin. Skin involvement is seen in about 20% of cases. Lesions are:

- Erythema nodosum (EN, see next). Sarcoidosis is one of the most common causes of EN. Unlike the other skin findings, this is associated with a good prognosis.
- Maculopapular rash mainly around face.
- Scar sarcoidosis presents as granulomatous changes in a healing skin wound (laceration, tattoo, etc.).
- Plaque-like lesions.

Sarcoidosis is one of the most common causes of erythema nodosum (see below).

Sarcoidosis is the second-greatest mimic of other diseases (first is syphilis); it can mimic any dermatologic disease but a vesicular eruption.

Lupus pernio is a type of sarcoidosis that has skin changes ranging from violaceous lesions on the tip of the nose and earlobes to large purple nodules/tumors on the face and fingers. It has a slow onset and almost never resolves!

The best prognosis of the sarcoid skin changes is with E. nodosum or the small papules. Treat cutaneous sarcoid with intralesional/topical steroids, occasionally antimalarials, and methotrexate. Dapsone is ineffective.

ERYTHEMA NODOSUM

Erythema nodosum consists of red, very painful, warm nodules that usually appear on the shins. Although sarcoidosis is one of the most common causes of erythema nodosum, other causes include inflammatory bowel disease, infection (TB, streptococcal, fungal), and drugs (esp. oral contraceptives, sulfas, and penicillins). Know these!

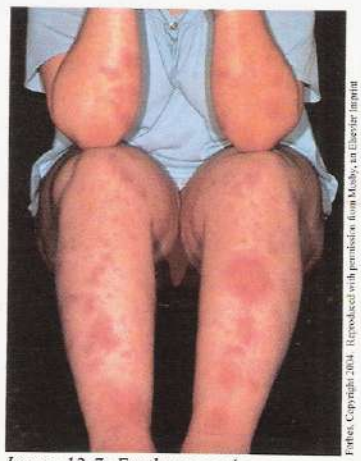

Image 12-7: Erythema nodosum

DERMATOMYOSITIS

Dermatomyositis (see Rheumatology section): Buzzwords: periorbital heliotropic rash (+/- periorbital edema). This is a violaceous, sometimes scaly rash in a photosensitive distribution, which looks very much like a localized allergic reaction.

Gottron papules are also seen in dermatomyositis. These are flat-topped, reddish to violet, sometimes scaling papules; sometimes it just looks like "cigarette paper" crinkling of the skin over the knuckles (MCP, PIP, and/or DIP). Gottron papules are the most specific finding with dermatomyositis. In Board

notes

→ cigarette paper on knuckles.

Gottron papules
Heliotrope rash → periorbital
] Dermatomyositis

Quick Quiz

1) What systemic lung disease is one of the common causes of erythema nodosum? Know the other causes too!
2) If you see the words "periorbital heliotropic rash," think of this!
3) How does zinc deficiency manifest?
4) What 2 organisms can cause impetigo?

questions, these are often described only as a "rash" or "eruption" over the knuckles.

Treatment: For glucocorticoids, add immunosuppressives if needed for skin changes. Remember, in older patients, dermatomyositis may indicate cancer (usually GI). Livedo reticularis is pretty nonspecific; it is seen in dermatomyositis but also in cutaneous polyarteritis nodosa, SLE, cholesterol embolism (atheroembolism), and there is a fairly common benign idiopathic type.

REITER SYNDROME

Reiter syndrome causes pustular scaly lesions on the palms and soles (keratodermia blennorrhagica) and circinate balanitis on the penis. See Rheumatology section.

VASCULITIS

See Rheumatology section for complete coverage of vasculitis. The main cutaneous reaction with vasculitis is palpable purpura. If a child presents with arthralgias, abdominal pain, and palpable purpura, think Henoch-Schönlein purpura.

PYODERMA GANGRENOSUM

Pyoderma gangrenosum is an inflammatory ulcer usually occurring on the legs. It is often associated with inflammatory bowel disease. It can also occur with rheumatoid arthritis, leukemia, IgA gammopathy, and chronic active hepatitis. Although a skin biopsy is not diagnostic, it serves to exclude other causes for ulceration. Treating the colonized bacteria usually does not help. Treatment is prednisone.

VITAMIN DEFICIENCIES

Deficiency of B_{12}, folate, or niacin may cause diffuse hyperpigmentation.

Zinc deficiency causes an irritant eczematoid red rash, which usually involves the nasolabial folds, extensor surfaces, and perineum/scrotum.

SKIN INFECTIONS

BACTERIAL

Much of the following is also covered in the Infectious Disease section.

Erythrasma is a well-defined, reddish lesion with some slight scaling. It is usually found in the axilla, groin, and toe webs. In obese women, it is seen under the breasts. Although gram-positive *Corynebacterium minutissimum* is frequently isolated from the lesion (especially after it has become scaly or macerated); it appears to be polymicrobial in origin. DDx: Fungal infection and intertrigo (an irritant dermatitis found in the skin folds of obese patients). Diagnosis: It fluoresces bright red with the Wood's lamp. Treat with oral or topical erythromycin +/- an "-azole" antifungal cream.

Streptococcus pyogenes (group A strep)

Group A strep is an occasional cause of impetigo—a skin infection confined to the epidermis. Most is due to *S. aureus*.

Ecthyma starts as an impetigo and then becomes deeper, causing shallow ulcerations.

Erysipelas is an explosive superficial cellulitis (caused by group A strep), usually confined to the dermis, and spread quickly through skin lymphatics. There is a clear demarcation line of swelling and redness indicating the extent of infection. It usually starts from a superficial abrasion, typically around the central face, with erythema and swelling.

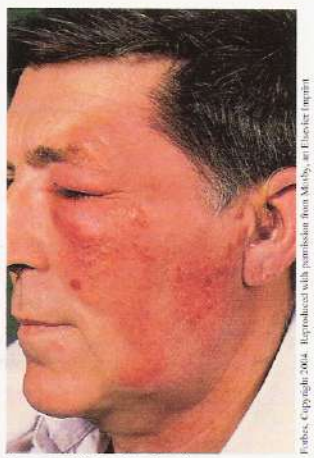

Image 12-8: Erysipelas

Necrotizing fasciitis (streptococcal gangrene) has been making press lately. It is a deep cellulitis involving the subcutaneous fat and fascia. Unlike erysipelas, it does not have a distinct border and can be difficult to diagnose early. Also the infection can be polymicrobial (e.g., group A strep + anaerobes). There is high mortality even with appropriate medical and surgical intervention.

Scarlet fever causes "scarlatina"—a fine red sandpaper-like rash with desquamation of the skin, commonly occurring during healing.

Streptococcal toxic shock syndrome has been appearing lately. It causes symptoms similar to staphylococcal TSS described next. Even with high-dose IV PCN, the mortality rate is about 30%!

Penicillin is far and away the best treatment for a known group A strep infection. Give oral PCN (x 10 days) or IM benzathine PCN. Erythromycin for PCN-allergic. Clindamycin is often added to PCN when there is serious infection such as necrotizing fasciitis or toxic shock.

notes

PCN – best treatment for. Strep infection.

S. aureus is responsible for several skin syndromes.

- It is by far the most common cause of impetigo—this starts as an erythematous, vesicular lesion, which quickly becomes pustular and crusty ("honey-colored crust").
- Bullous impetigo usually occurs in young children and presents with the acute onset of large, loose bullae.
- Patients with staphylococcal scalded skin syndrome (SSSS) present with tender, red, peeling skin—due to circulating toxins from localized staph infection or colonization, usually occurring at a non-skin site (sinuses; umbilicus in infants). Skin changes are similar to those seen in toxic epidermal necrolysis (which is noninfectious, rather a side effect of drugs), so consider it during the workup. The skin in SSSS separates much more superficially than in toxic epidermal necrolysis—through the granular layer of the epidermis; therefore, SSSS is a much less serious disorder.
- *S. aureus* is the main culprit in toxic shock syndrome (TSS). TSS presents with abrupt development of hypotension and shock. Patients have a diffuse scarlatiniform rash followed by desquamation of the palms and soles.
- Staphylococcal scarlet fever can mimic streptococcal scarlet fever.
- Staph is also a common cause of furuncles and folliculitis.

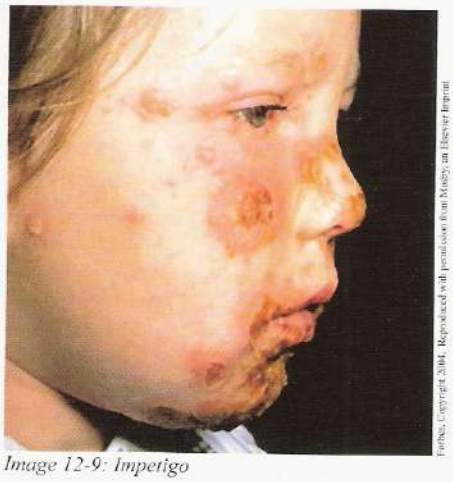

Image 12-9: Impetigo

Toxic epidermal necrolysis is not a result of infection, but is similar to SSSS above, so I will mention it here. It also results in a peeling or exfoliating of large areas of skin, but it occurs at a deeper level than SSSS. In contrast to SSSS, patients with toxic epidermal necrolysis do poorly (mortality about 40%). It is considered a variant of Stevens-Johnson syndrome. It is usually caused by a hypersensitivity reaction to a drug.

Disseminated gonococcal infection causes a few (usually < 12) papular petechial lesions, which become pustular—usually around the joints. Culture of exudate is usually negative. Culture is usually positive when taken from the site of infection (usually genital area).

Meningococcemic skin signs start as macular or petechial lesions and evolve to large purpura.

Pseudomonas causes a variety of skin infections. It is the cause of "hot tub folliculitis." Normal chlorine levels will prevent the growth and possibility of infection with this organism. The pustules from hot tub folliculitis resolve without treatment in 1 week. Pseudomonal septicemia causes small dark-centered (necrotic) papules. In a very ill, neutropenic patient this papule can evolve to ecthyma gangrenosum—a necrotic ulcer with an erythematous rim.

Animal bites: *Pasteurella multocida* often causes infection from dog and cat bites. Human bite infections are caused by multiple bacteria. Treatment: Clean and lavage well and give AM/CL (amoxicillin clavulanate) as prophylaxis.

RICKETTSIAL

Rocky mountain spotted fever is usually heralded by several days of fever. Then the patient gets small lesions, which progress in distribution from peripheral to central and in type from macular to petechial to purpuric.

SPIROCHETAL

Lyme disease is often heralded by erythema chronicum migrans. This typically is a slowly (over about one week) enlarging annular erythematous rash with a clear center. Occasionally the center will not be clear. See Infectious Disease section.

A chancre indicates primary syphilis. Diffuse scaling papules on the palms and soles, trunk, penis, and mucosal surfaces suggest secondary syphilis. Gummas occur in tertiary syphilis.

VIRAL

Warts (verrucae) are caused by any one of more than 60 types of human papillomaviruses (HPV).

- Verruca vulgaris is the common wart; you can treat it with liquid nitrogen, topical acids, CO_2 laser, etc.
- Verruca plana is the flat wart.
- Verruca plantaris is the plantar wart. It is usually caused by HPV 1, 2, or 5. Treatment may consist of a strong acid (trichloroacetic acid), concentrated (40%) salicylic acid plaster, liquid nitrogen, or laser.
- Condyloma acuminata are the anogenital warts. They are often caused by HPV 6 and 11. They are sometimes caused by HPV 16, 18, and 31—the HPVs associated with cancer of the cervix. You may treat them with podophyllin 25% in a tincture of benzoin, trichloroacetic acid, liquid nitrogen, or CO_2 laser. Podophyllin is teratogenic, so do not give it to pregnant patients. A newer treatment is topical imiquimod (Aldara).

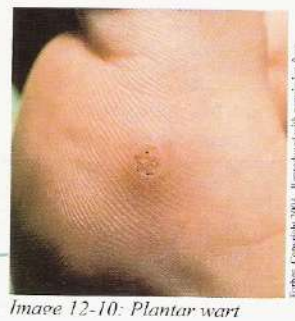

Image 12-10: Plantar wart

notes

HPV
16
18
31
Cancer

Quick Quiz

1) How does SSSS differ from toxic epidermal necrolysis?
2) What do the lesions of disseminated gonococcal infection look like?
3) Be able to recognize ecthyma gangrenosum and know what organism is responsible. Usually will see it in a febrile neutropenic patient!
4) What agent is used to treat a cat bite?
5) Molluscum contagiosum if seen in an adult should raise your suspicion for what immunodeficiency?
6) Recognize tinea versicolor.

Molluscum contagiosum is caused by a Pox virus. It consists of smooth, umbilicated pearly papules. It usually occurs in children, but you may also see it in the pelvic area of sexually active young adults, and it is common in AIDS patients. It can be sexually transmitted in adults. Know all the above facts!

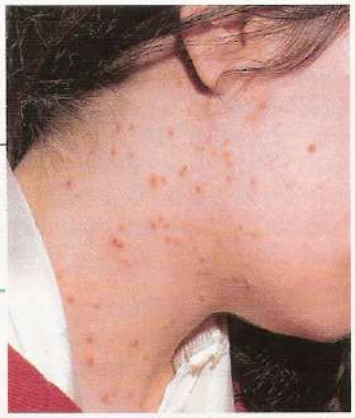

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Image 12-13: Molluscum contagiosum

Measles (rubeola) has several stages. The prodromal stage lasts 3–4 days with fever, malaise, sinus discharge, and a hacking cough. Koplik's spots often appear on the palate 1–2 days before the onset of rash. The red maculopapular rash starts on the forehead and quickly spreads downward with the densest concentration of lesions from the forehead to the shoulders.

Rubella (German measles, 3-day measles) is benign except when it occurs in pregnant women. Congenital rubella results in a variety of serious birth defects: heart malformations, ocular defects, microcephaly, mental retardation, deafness, TTP, and bone problems.

Varicella-zoster virus (VZV) causes two diseases: chicken pox and herpes zoster (shingles). Herpes zoster is reactivation of VZV in a person who has had chickenpox.

Chicken pox: Only 10% of persons > age 15 are susceptible to infection. Rash is initially maculopapular and rapidly progresses to vesicles and then to scabbed lesions. These tend to come in "crops" over 2–4 days.

The herpes zoster skin manifestation is grouped vesicles along a dermatome. Topical acyclovir is not effective although oral/IV acyclovir does help. Oral famciclovir and valacyclovir are also effective.

In the immunocompromised, you should treat both chicken pox and herpes zoster with intravenous acyclovir.

FUNGAL

Tinea capitis (scalp ringworm), tinea corporis (common ringworm), tinea cruris (jock itch—differential diagnosis includes moniliasis, which has satellite lesions), tinea pedis (athlete's foot), and tinea unguium (nails).

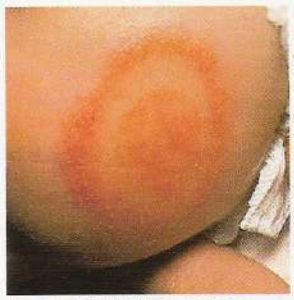

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Image 12-11: Tinea corporis

Candidiasis of the mouth (thrush) causes white semi-adherent plaques on the tongue and mucosa. Vaginal candidiasis has similar plaques with cheesy discharge.

Most fungal skin infections are controlled by topical antifungal creams. Miconazole, clotrimazole, and topical terbinafine (Lamisil®) are usually used. Tinea capitis requires oral therapy.

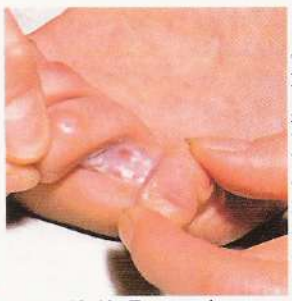

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Image 12-12: Tinea pedis

Tinea versicolor is caused by *Pityrosporum orbiculare* (also termed *Malassezia furfur*). Skin infection results in hypopigmented to reddish-brown spreading macules usually on the upper torso and upper arms. Lesions do not fluoresce red with Wood's lamp as erythrasma does (pg 12-5), although they may sometimes have a yellowish fluorescence. KOH skin scraping: spaghetti and meatballs. Treatment: imidazole creams, selenium sulfide shampoo, and/or oral ketoconazole.

PARASITIC

Lice (*Pediculus humanus capitis/corporis*): head or body louse. *Phthirus pubis* is the pubic louse ("crabs"). Treatment:

Body lice: 1% lindane cream or lotion.

Head lice: Preferred treatment is over-the-counter permethrin cream 1% (Nix cream rinse®) because it kills both lice and eggs. It is approved for head lice only. The more toxic drugs, 1% lindane shampoo, and pyrethrin + piperonyl butoxide (RID, etc.), do not kill the eggs and require another treatment a week later. In the US, resistance is growing against all preparations.

Body lice live in clothes and are on the body only when feeding. Treatment is bathing and topical pyrethrin + piperonyl butoxide and clean clothes.

Pubic lice: lindane shampoo or pyrethrin + piperonyl butoxide.

notes Molluscum → Pox
Children
Sexually transmitted in adults
Common in AIDS

Scabies is caused by a mite (*Sarcoptes scabiei*) which tunnels into the skin to lay eggs. It is spread by skin to skin contact (will not live > 48 hours without a host!).

Treat with 5% permethrin (better) or lindane. Apply lindane 1% cream or lotion over the entire body except the face and scalp. Leave it on 6 hours before rinsing off; 6 hours is just as effective as 12 or 24 hours. Lindane has CNS toxicity, so you should not use it in infants and young children. Alternative: 5% permethrin, which is safe for infants and in pregnancy. Another option in infants and pregnant patients is sulfur ointment (10%) X 3; first at diagnosis, then 24 hours later, and one week later.

SKIN CANCER and SKIN FINDINGS

Basal cell carcinoma (BCC)—Arises from epidermal basal cells and is the most common form of skin cancer. The usual type of BCC is characterized by translucent pearly papules, often with telangiectatic vessels. It spreads by local extension and, when large enough, gets a "rodent eaten" appearance. BCC is due to ultraviolet (UV) radiation; it is therefore associated with sun exposure, and you will usually find it on the head and neck, but you may see it elsewhere. UVA (320–400 nm) is the weakest and is the type used in sun-tanning parlors, but it still can cause cancer. UVB (290–320 nm) is the cause of sunburn and is 1000x more erythemogenic than A. Know that the metastatic potential of BCC is < 0.1%.

Squamous cell carcinoma (SCC)—From keratinizing epidermal cells, this occurs especially in fair-skinned persons and on exposed areas like dorsum of hands, forearms, ears, and lower lip. It has several associated precancerous lesions—especially actinic keratosis. In contrast to the low metastatic potential of BCC, SCC has a 0.3–3.7% metastatic potential—and even higher on the ear (11%) and lower lip (13%)! Metastatic rate of recurring tumors is 30%.

Melanoma is also common in fair-skinned people, especially those who have had severe sunburn in childhood. There has been a 300% increase in the past 40 years—probably due to an increase in sun exposure among youths. Other risk factors are dysplastic nevus (below), family history of melanoma, a high number of ordinary melanotic nevi, a congenital melanotic nevus, and immunosuppression. Heavily pigmented people have rates 3-5% as high as the rate for fair-skinned people. It is almost always completely curable if caught early enough.

Age of the patient, location of the lesion, and (most importantly) DEPTH of the lesion are prognostic factors. Age < 50 and location on the trunk are better prognostic factors. Lesions < 0.76 mm in depth have a 99% 5-year survival. Lesions > 3.6 mm have a < 50% 5-year survival. If the lesion is < 0.76 mm, you may safely excise the melanoma with a 1 cm tumor-free margin (previously a 5 cm margin was recommended).

Dysplastic nevi are markers for propensity to develop malignant melanoma. Most melanomas arise de novo. Removing all the moles does not prevent melanoma development. Standard of care is close follow-up and monitoring utilizing photographic documentation. If a patient with a dysplastic nevus has two relatives with malignant melanoma, the patient has a 300 x N chance of getting malignant melanoma!

Sézary syndrome and mycosis fungoides are the main forms of cutaneous T-cell lymphoma. Sézary syndrome has peripheral blood involvement and poorer prognosis.

Paget disease of the breast is something you should consider anytime there is a persistent (despite treatment), unilateral, oozing, eczematous plaque in the area of the areola. It is virtually always due to underlying breast cancer. By far the most common cause of an acute eczema-type rash on an areola is just a contact dermatitis or skin irritation. Consider Paget disease only if there is no response to treatment.

Peutz-Jeghers syndrome consists of multiple hamartomatous polyps plus melanotic pigmentation (freckles) on the lips and buccal mucosa. Even though these polyps are hamartomas, there is still some risk of cancer because an occasional adenoma will occur. Note that normal darkly pigmented people and people with Addison disease may have similar intraoral dark spots.

Sweet syndrome is also called febrile neutrophilic dermatosis. Patients have high fever and painful red plaques, about 1 inch in diameter. A skin biopsy shows a dense neutrophilic infiltrate. 10% or less are associated with leukemia (AML and myelomonocytic leukemia are the most common). Corticosteroids are usually quickly effective.

Glucagonomas (secreting pancreatic alpha cell tumors) can cause a beefy red tongue (think GLucagonoma = GLossitis), angular cheilitis, and a necrolytic migratory erythematous rash.

The 4 cancers that most commonly have cutaneous metastases are lung cancer, GI cancer, and melanoma, and breast cancer in women.

Macroglossia associated with pinch purpura (purpura that develop from pinching or stroking the skin) strongly suggests multiple myeloma and/or cutaneous amyloidosis.

BLISTERING LESIONS

Porphyria cutanea tarda (PCT) is the most common type of porphyria. It causes hyperpigmentation and tense blisters in sun-exposed areas, milia, skin fragility, and increased facial hair. This most common type of porphyria is caused by a congenital or acquired decreased activity of uroporphyrinogen decarboxylase, which allows a buildup of phototoxic porphyrins in the skin. Symptoms can be induced by inges-

notes

Quick Quiz

1) What is the metastatic potential for basal cell carcinoma?
2) Squamous cell carcinoma has a high risk of metastatic transformation on which body parts?
3) For melanoma, what is most important in prognosis?
4) What are the main forms of cutaneous T-cell lymphoma?
5) What will induce porphyria?
6) What is PCT?
7) What is the pathognomonic lesion for erythema multiforme?
8) Which virus particularly can be responsible for erythema multiforme?

tion of estrogen or alcohol! Many patients have associated hepatitis C. Lab results usually show an increased serum Fe, Hct, ALT, and AST. To screen, check for increased urinary coproporphyrins and uroporphyrins. Patients may have dark or pink urine. Treatment is the same as for hemochromatosis: regular phlebotomies. Antimalarials may also help.

Porphyria variegata (variegate porphyria) is also known as South African porphyria. Patients may get blisters on sun-exposed areas and have mechanical fragility of the skin. These patients may also have abdominal pain, polyneuropathies, and mental disturbances. Treatment of acute attacks is the same as for acute intermittent porphyria (AIP): glucose and hematin. Differential diagnosis: Note that AIP presents similarly to variegate porphyria except without the skin changes. PCT (above) presents with the skin changes and without the neuro/mental changes!

Epidermolysis bullosa: Patients have blistering after minor skin trauma, caused by congenital structural defects of the skin. There are many different classifications. It is genetically transmitted.

Epidermolysis bullosa acquisita, like bullous pemphigoid, is also caused by antibodies directed against the basement membrane. The target antigen is Type VII collagen.

Bullous pemphigoid causes recurrent crops of tense blisters. It has an autoimmune etiology. There are anti-basement membrane antibodies, although it is unclear what the specific target antigen is. Treatment is primarily glucocorticoids.

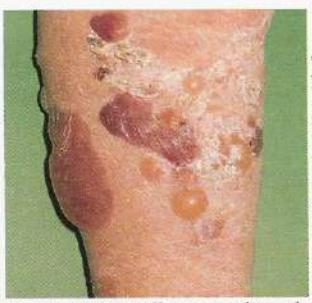

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Image 12-14: Bullous pemphigoid

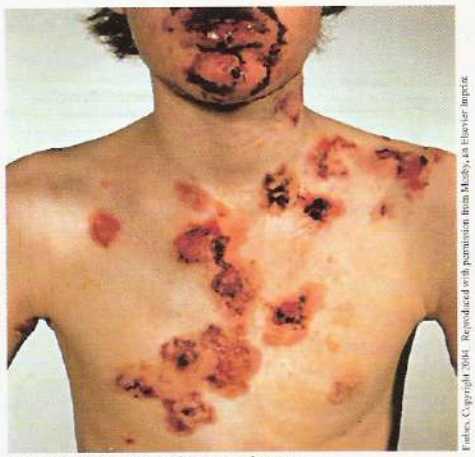

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Image 12-15: Pemphigus vulgaris

Pemphigus vulgaris probably has a multifactorial etiology with a common autoimmune result. There is an antibody against the desmosomal proteins. This causes acantholysis (the separation of epidermal cells from each other due to decreased cohesion), which results in the formation of large, loose bullae that will peel off and leave denuded skin. Oral mucosal involvement is common, and any cutaneous area can be affected.

Treat pemphigus vulgaris with high dose glucocorticoids +/- cyclosporine/ azathioprine / cyclophosphamide.

Nikolsky sign is epidermal sliding with digital pressure on the skin and indicates the acantholysis that causes the symptoms (Nikolsky sign is also seen in toxic epidermal necrolysis and staphylococcal scalded skin syndrome (SSSS)).

Erythema multiforme consists of well-defined lesions varying from annular to target shape. Palms and soles are frequently involved and mucous membranes may be affected. The target- or iris-shaped lesions are pathognomonic for erythema multiforme. The lesions may also be edematous or bullous. It is caused by many infectious and noninfectious diseases and drugs. Infectious causes may be bacterial, viral (especially *Herpes simplex*), or mycoplasmal. Noninfectious causes are primarily drug-induced.

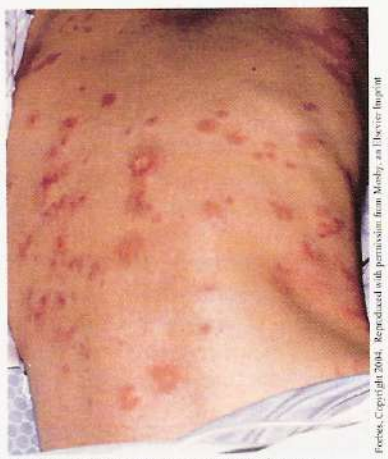

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Image 12-16: Erythema multiforme

Know that the most common causes of photosensitive reaction are side effects of medication such as thiazides, tetracycline, phenothiazine, sulfonamides, quinolones, and piroxicam (Feldene®). Rule these out first.

notes

Dermatitis herpetiformis is a skin disease where there are very pruritic vesicular lesions, usually on the extensor surfaces and mid to lower back, caused by IgA deposition. It is often associated with Celiac disease (gluten-sensitive enteropathy).

ROUND LESIONS

Stevens-Johnson syndrome is a severe form of erythema multiforme. Glucocorticoids are controversial and, if you use them, it should be for only a very short time.

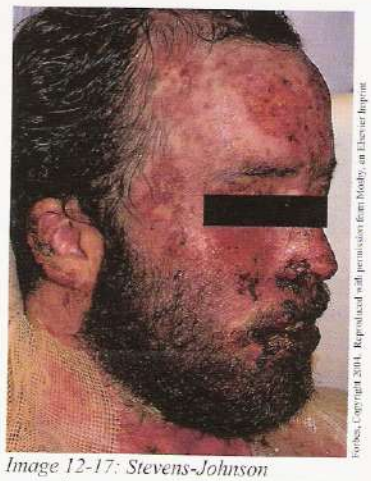

Image 12-17: Stevens-Johnson syndrome

Granuloma annulare is an annular, ringworm-like lesion without scaling, which usually appears on the distal portion of the extremities. It often occurs in children and young women. It usually is self-limited, disappearing in months to a few years.

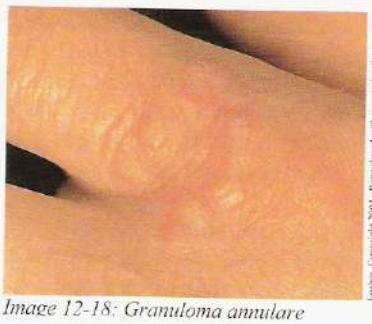

Image 12-18: Granuloma annulare

Nummular eczema consists of small circular (nummular = coin-shaped) lesions that are more common on the lower legs and are often associated with dry skin. They are very common in the elderly and have no pathologic significance. Rule out fungal infection.

Pityriasis rosea is something you see especially in children and young adults. It develops into pruritic small papulosquamous oval lesions with the long axis parallel to skin folds and rib lines in a "Christmas tree" pattern. A herald patch precedes subsequent lesions by 1–2 weeks. It probably has a viral etiology (possibly picornavirus). The disease is self-limited, usually lasting 4–8 weeks. Treatment is symptomatic. Note that Tinea versicolor (= Pityriasis versicolor) has no relationship with Pityriasis rosea.

PIGMENT CHANGES

Vitiligo is spreading macular depigmentation. It usually occurs in healthy persons, but rarely it may also be part of the autosomal recessive polyglandular deficiency. In this, there may be any of the following: DM, Graves disease, Addison disease/adrenal insufficiency, hyper- or hypothyroidism, hypoparathyroidism, pernicious anemia, and vitiligo. Anytime you see a patient with vitiligo, think of this!

Tuberous sclerosis is uncommon and autosomal dominant. It is associated with seizures, mental retardation, periungual fibromas, and hypopigmented (ash-leaf) macules. You will see these macules best with a Wood's lamp. Adenoma sebaceum manifests in these patients as numerous mid-facial papules, which are actually angiofibromas.

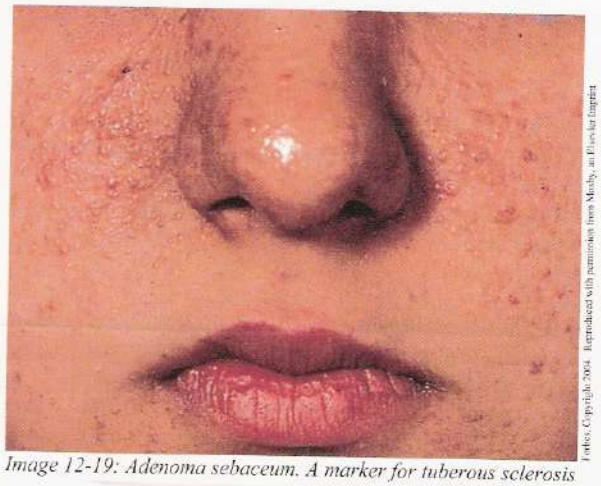

Image 12-19: Adenoma sebaceum. A marker for tuberous sclerosis

Café au lait spots are brown macules that occur in association with neurofibromatosis (von Recklinghausen disease), Albright disease, but also, to a lesser degree, in people with no disease (1–2 spots are normal and common). In neurofibromatosis, 78% of patients have > 6 spots, and 95% have at least one spot > 1.5 cm. In Albright disease, the spots have a more irregular outline.

Acanthosis nigricans is hyperpigmented skin with a thickened, velvety appearance, most noticed in the skin folds. Involvement of the axilla is usually shown as an example. It rarely is familial. Although you will usually see this in obese patients, it is also associated with GI cancer, many endocrinopathies, and several autoimmune problems. The malignant acanthosis nigricans is severe and progressive and is usually associated with gastric adenocarcinoma. Associated endocrinopathies include Cushing disease, hyper- and hypothyroidism, acromegaly, and insulin-resistant DM. Overuse of niacin may also cause acanthosis nigricans!

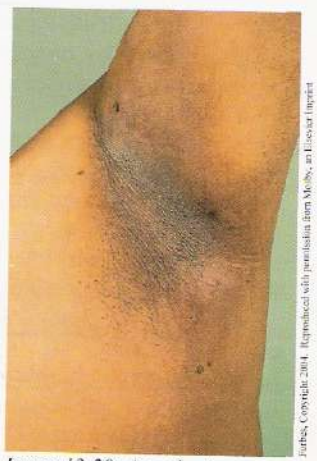

Image 12-20: Acanthosis nigricans

Diffuse hyperpigmentation may occur in biliary sclerosis, scleroderma, Addison disease, hemochromatosis (a gray-

notes

Vitiligo
DM
Graves
↑ or ↓ thyroid
hypo para thyr.
pernicious anemia

Quick Quiz

1) What skin finding might you see in an autosomal recessive polyglandular deficiency?
2) What is characterized by a "Christmas tree" pattern and a herald patch?
3) Hyperpigmented areas of the axilla are usually due to what?
4) What causes oral hairy leukoplakia in AIDS patients?

ish/bronze coloration), and with the use of busulfan. Other causes include primary biliary cirrhosis, porphyria cutanea tarda, malabsorption and/or Whipple syndrome, pellagra (niacin deficiency), B_{12} deficiency, and folate deficiency. Check for metastatic melanoma in "slate-blue" patients!

Hyperpigmentation in sun-exposed areas: amiodarone, porphyria cutanea tarda, phenothiazines. Hyperpigmentation is diffuse but darker in sun-exposed areas in pellagra, biliary sclerosis, and scleroderma. Methotrexate can cause a reactivation of sunburn.

Black lesions: See Table 12-1.

Table 12-1

BLACK LESIONS
1. Rhinocerebral mucormycosis
2. Anthrax
3. Ecthyma gangrenosum
4. Emboli into distal extremities
5. Melanoma/lentigo
6. Coumadin skin necrosis
7. Glucagonomas cause necrolytic dermatitis

PRURITUS

The most common cause of itching in elderly patients is dry skin. Other causes seen across the age spectrum include:

1) hyper- or hypothyroidism
2) malignancy: think lymphoma—especially Hodgkin, but also breast cancer
3) Fe deficiency (even if patient not anemic)
4) chronic (but not acute) renal failure, commonly treated with ultraviolet B phototherapy or activated charcoal.

AIDS-RELATED SKIN LESIONS

AIDS-related lesions include the following: xerosis (dry skin), seborrheic dermatitis (in virtually all patients!), telangiectasias, herpes simplex, herpes zoster, folliculitis, Kaposi sarcoma (KS), and oral candidiasis. AIDS patients also often get condyloma acuminata, molluscum contagiosum, and bacillary angiomatosis. Bacillary angiomatosis resembles KS, but is caused by a gram negative bacillus similar to the one that causes cat scratch fever.

Treat the seborrheic dermatitis with topical hydrocortisone +/– an antifungal shampoo.

The folliculitis is usually due to a yeast, *Pityrosporum orbiculare*. This yeast is often part of the normal skin flora. This yeast also causes tinea versicolor. Treat with systemic ketoconazole.

Oral "hairy" leukoplakia is a corrugated tongue with white lesions along the side. You see it virtually only in patients with HIV infection. Epstein-Barr virus is the cause.

Kaposi sarcoma is usually seen as < 0.5 cm purple/red/violet macular/papular lesions. They are usually oval with a long axis along skin folds (like Pityriasis rosea) and occur anywhere on the body.

Herpes zoster is often refractory to treatment in these patients. Treat with acyclovir or famciclovir. Do not give valacyclovir to immunocompromised patients.

Cryptococcus infection may imitate molluscum contagiosum.

DIABETIC SKIN LESIONS

Diabetes-associated skin lesions include eruptive xanthomas due to hypertriglyceridemia. Eruptive xanthomas are usually an indication that the diabetes is out of control; they will resolve when the diabetes is again under control.

Necrobiosis lipoidica diabeticorum, as the name suggests, is associated with diabetes in 75% of cases. It is a thin, atrophic, vascular plaque that appears on the shins. It is subject to trauma and ulceration.

Diabetic skin spots (diabetic dermopathy) are dark macules; they are common and often appear on the shins. They have no clinical significance.

notes

OPEN-ENDED QUESTIONS

1) In what patient group is intertrigo usually found?

[Intertrigo is an irritant dermatitis usually found in the skin folds of obese patients.]

2) Is contact dermatitis an early or delayed hypersensitivity reaction?

[Delayed.]

3) What are the most common allergens that cause contact dermatitis?

[Nickel, chromium, neomycin, and oleoresin (poison oak, poison ivy, and poison sumac).]

4) How does acne vulgaris differ from acne rosacea?

[Acne vulgaris: open and closed comedones and inflammatory papules on the face, chest, and back. Acne rosacea (mostly middle-aged patients): acne-like lesions, erythema, and telangiectasias on the central face.]

5) How can you decrease the reaction to radiocontrast dye?

[Prophylaxis with diphenhydramine and glucocorticoids (start 1–2 days prior) will decrease this reaction 10-fold.]

6) What is the Koebner phenomenon?

[Outbreak of psoriasis in an area of an abrasion or other injury. Koebner phenomenon also occurs in lichen planus.]

7) Which of the following changes are specific for psoriasis: thickened nails, onycholysis, pitted nail?

[Pitted nails, in association with onycholysis, are fairly specific for psoriasis.]

8) What are the differences between the two types of cutaneous psoriasis: erythrodermic psoriasis and pustular psoriasis? Which one of these is associated with DIP joint arthritis?

[Erythrodermic psoriasis: exfoliative reaction in which the entire surface of the skin becomes red, warm, and scaly and the patients are unable to control body temperature (hypo- and hyperthermia are common). Pustular psoriasis: many small pustules, often coalescing to form "lakes of pus"—usually confined to the palms and soles but rarely generalized. The latter is associated with DIP joint involvement.]

9) How will serology (ANA, anti–ds DNA, anti-Sm, DIF) differ in subacute cutaneous lupus, SLE, and discoid lupus?

[Subacute cutaneous lupus: + Ro/La (SS-A/SS-B) antigen (in 60%) which causes a positive speckled ANA. It often has a negative anti-ds-DNA and negative anti-Sm. Active SLE: usually peripheral ANA pattern. Discoid lupus: usually have a negative ANA, negative anti–ds DNA, and negative anti-Sm, but a positive lesional DIF (95% !)]

10) Which type of lupus is associated with congenital heart block?

[Subacute cutaneous lupus.]

11) What is the usual outcome of lupus pernio?

[Lupus pernio is a cutaneous type of sarcoidosis. It has a slow onset, and it virtually never resolves.]

12) Name 6 causes of erythema nodosum.

[Any 6 of the following: Sarcoidosis, inflammatory bowel disease, TB, streptococcal, fungal infections, oral contraceptives, sulfa drugs, and penicillins.]

13) What is the more specific finding in dermatomyositis: the periorbital heliotrope rash or Gottron papules?

[Gottron papules are the most specific finding in dermatomyositis.]

14) With what disease is pyoderma gangrenosum most often associated?

[Inflammatory bowel disease.]

15) If an obese patient presents with a rash in the inguinal area, and the rash fluoresces bright red with the Wood's lamp, what is the disorder and how is it treated?

[Erythrasma (caused by *Corynebacterium*). Erythromycin.]

16) What is the difference between impetigo, ecthyma, and erysipelas?

[Impetigo: starts as an erythematous, vesicular lesion that quickly becomes pustular and crusty ("honey-colored crust"). Ecthyma: starts as an impetigo which then becomes deeper, causing shallow ulcerations. Erysipelas: superficial cellulitis, usually of the central face, with erythema and swelling. Ecthyma and erysipelas are usually caused by Group A streptococcus; whereas, impetigo is usually caused by *S. aureus*.]

17) How does staphylococcal scalded skin syndrome (SSSS) differ in etiology and outcome from toxic epidermal necrolysis?

[Staph scalded skin syndrome (SSSS): Patients present with tender, red, peeling skin, usually due to circulating toxins from localized staph infection or colonization. Toxic epidermal necrolysis is not a result of infection. It is also a sloughing away of skin, but it occurs at a slightly deeper level than SSSS. In contrast to SSSS, patients with toxic epidermal necrolysis do poorly (mortality about 40%). It is almost always caused by a hypersensitivity reaction to a drug.]

18) What is the organism that commonly causes infection in dog and cat bites?

[*Pasteurella multocida*.]

19) What is the treatment of choice for dog, cat, and human bites?

[Debridement with copious lavage. Then prophylaxis is oral AM/CL (amoxicillin clavulanate).]

20) Which papilloma viruses are associated with condyloma acuminata and with cancer of the cervix?

[HPV 16, 18, and 31 are associated with cancer of the cervix. HPV 6 and 11 are the more common causes of condyloma acuminata and are not associated with cancer of the cervix.]

21) For what 2 skin parasites is 1% lindane used?

[1) Lice –all types. 2) Scabies (*Sarcoptes scabiei*).]

22) In which patient group is lindane contraindicated? Why?

[Infants and very young children. CNS toxicity.]

23) Which skin cancer is associated with severe sunburn in childhood?

[Malignant melanoma.]

24) Which type of ultraviolet light is used in suntanning parlors? Will it cause cancer?

[UVA. Although weaker than UVB, UVA can still cause cancer.]

25) What are the two treatment options for dysplastic nevi? In which patient group would you always remove the nevus?

[Close follow-up and monitoring using photographic documentation. If the patient has one or more relatives who have had malignant melanoma, the dysplastic nevus is just removed.]

26) If a female patient presents with a pruritic eczematous plaque on the areola and nipple and treatment for a contact dermatitis is unsuccessful, what disease is likely?

[Paget disease of the breast.]

27) What 4 cancers are the most common cause of cutaneous metastases?

[Lung cancer, GI cancer, malignant melanoma, and breast cancer in women.]

28) What is Sweet syndrome?

[Also called acute neutrophilic dermatosis. Patients have high fever and painful red plaques, about 1 inch in diameter, due to a dense neutrophilic infiltrate. 10% or less are associated with leukemia. Corticosteroids are usually quickly effective.]

29) What skin manifestations are seen with glucagonomas?

[Beefy red tongue, angular cheilitis, and a necrolytic migratory erythematous rash.]

30) With what diseases is macroglossia associated?

[This is associated with pinch purpura (purpura that develop from pinching or stroking the skin) and is highly suggestive of multiple myeloma or cutaneous amyloidosis.]

31) What is Nikolsky sign and with what two diseases is it associated?

[Nikolsky sign is epidermal sliding with digital pressure on the skin and is an indication of the acantholysis. Acantholysis is seen in pemphigus vulgaris and toxic epidermal necrolysis.]

32) Which bullous skin disorder is associated with an anti–basement membrane antibody?

[Bullous pemphigoid.]

33) What is the etiology of porphyria cutanea tarda and what are some of the precipitating substances?

[It is caused by a congenital or acquired decrease in activity of uroporphyrinogen decarboxylase, which allows a buildup of phototoxic porphyrins in the skin. Estrogen or ETOH may precipitate the symptoms.]

34) What urinary tests are done to screen for porphyria cutanea tarda?

[Check for increased urinary coproporphyrins and uroporphyrins. Urine may be dark or pink.]

35) With which GI disease is dermatitis herpetiformis associated?

[Celiac sprue (gluten sensitive enteropathy).]

36) What type of lesion is pathognomonic for erythema multiforme?

[Target lesion.]

37) What viral infection is especially associated with erythema multiforme?

[Herpes simplex.]

38) What is Stevens-Johnson syndrome?

[Stevens-Johnson syndrome is a severe form of E. multiforme.]

39) What is the treatment for granuloma annulare?

[Granuloma annulare is a ringworm-like lesion seen in children and young women. It is self-limited.]

40) In what patient group is nummular eczema usually found?

[This occurs very commonly on the shins of the elderly. No treatment is indicated.]

41) What disorder should be ruled out in a patient with vitiligo?

[Polyglandular deficiency.]

42) What cancer should be ruled out in a 60-year-old patient with acanthosis nigricans?

[GI cancer (especially gastric adenocarcinoma).]

43) What endocrinopathies are associated with acanthosis nigricans?

[Cushing, hyper- and hypothyroidism, acromegaly, and insulin-resistant DM, but usually not adrenal insufficiency.]

44) Which drug can actually cause a reactivation of a previous sunburn?

[Methotrexate.]

45) What is the difference in occurrence and number of café au lait spots seen in: neurofibromatosis, Albright disease, and healthy persons?

[In neurofibromatosis, 78% of patients have > 6 spots and 95% have at least one spot > 1.5 cm. In McCune-Albright disease, the spots are more irregular. Note that 1–2 spots are common in healthy persons.]

46) What disease entity has hypopigmented macules that are easiest to see under the Wood's lamp?

[Tuberous sclerosis.]

47) What is the most common cause of pruritus in elderly patients? What other causes should be ruled out?

[Dry skin is the most common cause of pruritus in the elderly. Other causes include hyperthyroidism, hypothyroidism, malignancy (especially lymphoma and breast cancer), Fe deficiency, and chronic renal failure.]

48) What is the cause of oral hairy leukoplakia, how does it present, and in what patient group is it found?

[Oral hairy leukoplakia is a disease caused by Epstein-Barr virus and seen virtually only in AIDS patients. The disease presents with a corrugated tongue with white lesions along the side.]

49) Which type of skin cancer is usually oval with the long axis parallel to the skin folds?

[Kaposi sarcoma.]

50) Name 3 skin lesions seen in diabetics. What is their significance?

[Eruptive xanthomas indicate diabetes is out of control. They resolve when the diabetes is once again under control. Necrobiosis lipoidica diabeticorum is a thin, atrophic, vascular plaque that appears on the shins. It is subject to trauma and ulceration. No other clinical significance. Diabetic skin spots (diabetic dermopathy) are dark macules that are common and often appear on the shins—no clinical significance.]

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P.O. Box 38148
Colorado Springs, CO 80937-8148
(800) 841-0547