Med Surg

QUICK NOTES

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1 Cardiology I Exam Notes

1.1 Cardiology Terms & Introduction

- **Preload**: the 20% of blood remaining in the atria at end of diastole
- 80% of ventricular filling occurs before atrial kick
- increase preload by inspiration or valsalva
- **Afterload**: the volume of blood in the ventricles after atrial contraction
- **Cardiac output**: volume of blood ejected from ventricles in one minute; normally 5 L
- increased by increasing HR, contractility, or blood volume (or decreasing resistance)
- **Stroke volume**: volume of blood ejected with each heartbeat
- **Myocardial contractility**: ability of cardiac muscle to shorten with a given load
- **ejection fraction**: a quantification of contractility; EF = SV/EDV
- **Starling’s law**: stroke volume increases as end diastolic volume increases due to greater stretch put on walls of ventricles
- **Stenosis**: narrowing to forward flow
- **Regurgitation (insufficiency)**: backward leakage while valve should be closed
- **Collaterals**: normally nonfunctioning small vessels that interconnect coronary arteries
- function when blockage creates upstream pressure, forcing the collaterals open
- Heart sounds review
  - S3 in CHF
  - S4 in HTN
- Coronary vessel dominance: we want to identify which artery perfuses the posterior 1/3 of the interventricular septum: is it the right coronary artery or the left circumflex (or both)?
- SA node typically supplied by the right coronary artery, but can also be left circumflex
- AV node supplied by whichever is dominant
- **Coronary artery disease (CAD) (aka coronary heart disease CHD)**: narrowing of vessels supplying the heart caused by atherosclerosis and/or hardening of the arteries

![Diagram of the heart](image)

1.2 Pharmacology: Lipid Lowering Drugs

- **Statins**: act as analogues for liver cholesterol synthesis to inhibit the actions of HMG-CoA reductase → liver upregulates LDL-R to try and draw cholesterol out of circulation
- First line medication for lower LDL!
- Can decrease LDL by 20-60%, decrease TG by 7-30%, and increase HDL by 5-15%
- doubling the does results in an additional lowering of LDL by ~6%, with HDL increase of ~10-15%
• Proven to decrease risk of major cardiovascular events and total mortality, including CAD, MI, stroke, and peripheral vascular disease
• Administered at bedtime, when cholesterol synthesis peaks
• Kinds:
  • atorvastatin: CYP3A4 metabolism
  • lovastatin: CYP3A4 metabolism
  • pravastatin: less interactions = good choice for someone on many meds, urinary excretion
  • rosuvastatin: less interactions = good choice for someone on many meds, biliary excretion
  • simvastatin: CYP3A4 metabolism
• Contraindications: pregnancy or potential pregnancy, active or chronic liver disease, concomitant use of CYP3A4 inhibitors
• Interactions: amiodarone, cyclosporine, macrolides, protease inhibitors, large amounts of grapefruit juice
• Side effects: elevated LFTs, myalgia (no change in CK), myopathy (CK increase), rhabdomyolysis (high CK with organ damage)
• Monitor: LFTs (stop statin if increase to 3-5x upper limit of normal)

1.2.1 Drugs to Increase Lipoprotein Lipase Activity
• Fibric acid derivatives: stimulate PPARα, a transcription factor that promotes lipid metabolism → increased oxidation of fatty acids and increased metabolism of fatty acids
• can reduce LDL by 5-10%, reduce TG by 20-50%, and increase HDL by 10-20%
• trials show decrease in major coronary events
• kinds:
  • gemfibrozil:
  • fenofibrate:
• contraindications: severe renal disease, severe hepatic disease
• side effects: dyspepsia, gallstones, myopathy
• Bile Acid Sequestrants: inhibit bile salt recycling → liver breaks down more cholesterol to make new bile
• Add to the LDL-lowering effects of statins
• reduces LDL by 15-30%, no effect on TG, mildly helps increase HDL
• Cons: requires several doses per day, concomitant drugs must be taken at a different time
• Good for persons needing only moderate LDL lowering or women considering pregnancy
• Kinds:
  • cholestyramine:
• Contraindications: TG > 400 (could increase chance of pancreatitis)
• relative: TG > 200
• Side effects: constipation, GI upset, decreased absorption of other drugs

1.2.2 Drugs to Inhibit Cholesterol Absorption
Nicotinic acid (niacin): blocks the breakdown of fats needed for VLDL synthesis → shift in LDL composition from small and dense to larger and more buoyant (less likely to deposit in arteries)
• typically used in combination with other lipid-lowering drugs
• lowers LDL by 5-25%, lowers TG by 20-50%, and increases HDL by 15-35%
• contraindications: chronic liver disease, gout
• relative: DM, hyperuricemia, PUD
• side effects: flushing (prevent with aspirin before), hyperglycemia, hyperuricemia, GI distresses, hepatotoxicity

Ezetimibe: inhibits cholesterol absorption at the brush border of the small intestine
• can be used alone to increase LDL by 15-20%, TG decrease by 5-10%, minimal increase of HDL = similar to bile acid sequestrant, but better tolerated
• frequently used in combination with statins
• contraindications: active liver disease

Fish Oil: used to lower TG by 20-50%, with a minor increase in LDL and HDL
• side effects: increased risk of bleeding, diarrhea
• prescription brand name is Lovaza

1.3 **Clinical Medicine: Lipids**

1.3.1 **Dyslipidemia**

- **Lipoproteins:** cholesterol, triglyceride, and insoluble fat blood transporters
- **Dyslipidemia:** an elevation of plasma cholesterol, triglycerides, or both
- primary dyslipidemia: genetic causes
  - most people with LDL > 190 have some genetic component such as:
    - monogenic familial hypercholesterolemia:
    - familial defective apolipoprotein B:
    - polygenic hypercholesterolemia:
  - detection of these disorders needs to be done in young adulthood to prevent CAD
  - usually requires a statin + a bile acid sequestrant to achieve therapeutic goals
- secondary dyslipidemia: any non-genetic cause of dyslipidemia
  - diabetes
  - hypothyroidism
  - obstructive liver disease
  - chronic renal failure
  - drugs that increase LDL and decrease HDL
  - diet
  - sedentary lifestyle
  - treat these causes first if present, then re-check LDL and establish goal based on risk category
    - switch to diet low in saturated fat and cholesterol
    - ingest soluble fiber and plant stanols & sterols
    - lose weight
    - increase activity: reduces VLDL & LDL, raises HDL
    - even as secondary prevention, exercise can reduce total mortality by 20% but won’t reduce chance of having another nonfatal MI
  - dyslipidemia promotes atherosclerosis, with greatest risk on carotid and coronary vasculature

1.3.2 **Metabolic Syndrome:**

It is a group of risk factors that occur together and increase the risk for coronary artery disease, stroke, and type 2 diabetes.
- Characteristics: abdominal obesity, atherogenic dyslipidemia, raised blood pressure, insulin resistance, pro-thrombotic state (impaired fibrinolysis and endothelial dysfunction), inflammation, elevated apolipoprotein b
- Considered to be the secondary target of overall CAD risk reduction
- Clinically identified by presence of 3+ of these factors:
  - abdominal obesity (waist > 40 in for men, 35 in for women)
  - triglycerides > 150
  - low HDL (men < 40, women < 50)
  - BP > 130/85
  - fasting glucose > 110
- Treatment: weight management, increased activity, treat HTN, therapeutic aspirin, treat elevated triglycerides or low HDL

1.3.3 **Diagnostic Methods for Dyslipidemia**

- Inflammatory markers and lipid levels important for risk factor identification and modification
- Labs
• **homocysteine**: blood amino acid associated with cardiac disease, stroke, and peripheral vascular blockages
  - lowered by folic acid
  - can be genetic

• **lipoprotein A (Lpa)**: inhibits thrombolysis and enhances LDL retention in arterial walls
  - elevation may or may not risk factor for cardiac disease

• **apolipoprotein B**: LDL component

• **lipid profile**: includes total cholesterol, HDL, LDL, triglycerides
  - total cholesterol and HDL can be measured even if patient was not fasting
  - if TG are > 400, you need to adjust results of LDL level to be accurate: \[ \text{corrected LDL} = \frac{\text{total cholesterol} - \text{HDL} - \frac{\text{TG}}{5}}{1} \]

• **direct LDL (dLDL)**: a measure of LDL for nonfasting patients or when TG are > 400 or when chylomicrons are present

### 1.3.4 Screening for Dyslipidemia

- Red flag clinical presentations: corneal arcus (cholesterol deposit in cornea) in patient under 40, xanthomas (thickening of tendons due to cholesterol accumulation), xanthelasmas

- **Lab tests**
  - in patients 20-35 with risk factors (DM, FH, or other cardiovascular risks), get a fasting lipid profile every 5 years
    - if test is non-fasting, total cholesterol and HDL values are still valid
  - in patients with no known risk factors, begin screening in men at age 35 and women at age 45
    - if lipids are good, continue screening every 5 years
  - in pediatric patients with high cardiovascular risk (obesity, HTN, FH), get a lipid profile between 2-10 years of age, and every 3-5 years thereafter
  - For patients without known CAD or CAD equivalents, calculate 10-year risk of developing CHD using Framingham scoring
    - high risk is known CAD or having a CAD risk equivalent □ 20% chance of developing CAD
      - when you would want to set LDL goal < 100
    - moderate risk is having 2+ CAD risk factors □ 10-20% chance of developing CAD
      - when you would want to set LDL goal < 130
    - lower risk is having no or one risk factor
      - when you would want to set LDL goal < 190

### 1.3.5 Treatment of Dyslipidemia

**ATP III guidelines**

- Total cholesterol
  - optimal is < 200
  - 200-239 is borderline high
  - greater than 240 is very high
- Triglycerides
  - less than 150 normal
  - 150-199 borderline high
  - 200-499 high
  - greater than 500 very high
- LDL: the primary target for CAD risk reduction
  - otherwise healthy individuals:
    - less than 100 is optimal
    - 100-129 is near optimal
    - 130-159 is borderline high
    - 160-189 is high
    - greater than 190 is very high
  - HDL should be > 40

Determining a treatment plan for patients
1. get a fasting lipid profile
   a. determine patient history of CAD (or risk equivalents) and other high risks for CAD
      • known CAD puts pt at a 20x greater risk for MI: includes patients with angina, history of cardiovascular procedures
      • CAD equivalents:
        o diabetes
          ▪ if female diabetic, want to increase HDL to > 50
        o symptomatic carotid artery disease
        o peripheral arterial disease
        o abdominal aortic aneurysm
      • major risk factors:
        o smoking
        o hypertension
        o low HDL (< 40)
          ▪ low HDL alone is a strong predictor for CAD
          ▪ low HDL associated with insulin resistance and related risks: high triglycerides, obesity, inactivity
          ▪ other causes of low HDL: smoking, high carb intake, drugs such as β blockers, anabolic steroids, and progesterone
        o family history of premature CAD (means there is a genetic component)
        o age (men > 55, women > 65)
      • consider other major risk factors for CAD for which targeting will not help the end outcome, although they will modify clinical judgment (???)
      • obesity: distribution more important than BMI
        o inactivity: better to be fat and fit than thin and sedentary!
        o impaired fasting glucose
        o elevated inflammatory markers
        o homocysteine
        o thrombotic abnormalities
        o endothelial dysfunction
        o elevated triglycerides alone are a risk factor for CAD
          ▪ contributing factors: obesity, inactivity, smoking, high alcohol, high carbs, disease such as DM, chronic renal failure, and nephrotic syndrome, certain drugs including β blockers and estrogens, and genetic disorders
   b. tailor the treatment plan for each patient:
      • if lipid panel is optimal, encourage them to continue making good choices
      • for patients without CAD or CAD risk equivalent, but abnormal lipids:
        o usually, first you will set LDL goal to reach and aim for that
          ▪ (unless TG are > 500, then you want to address that first to prevent pancreatitis)
            • (extremely low fat diet, weight management, activity, fibric acid derivative or nicotinic acid)
            • (once this is under control, then address LDL)
          ▪ if 2+ CAD risks, want to keep LDL under 130
          ▪ if 0-1 CAD risks, want to keep LDL under 160
        o begin with therapeutic lifestyle changes, such as low fat diet, weight management, and increased activity (this includes patients with suspected metabolic syndrome)
          ▪ try this for 3-6 months
        o if LDL goal is not met at follow-up with just lifestyle changes, consider meds (statin, bile acid sequestrant, or nicotinic acid)
          ▪ if 2+ CAD risks with 10-20% calculated risk, start meds with LDL > 130
          ▪ if 2+ CAD risks with < 10% calculated risk, start meds with LDL > 160
          ▪ if 0-1 CAD risks, definitely start meds with LDL > 190, and maybe sooner
          ▪ if patient is pediatric, drug therapy should begin if child is at least 8 years old
            • statins are often first line therapy in peds (adjusted dosing)
        o follow-up post meds:
• if LDL goal is not met, add higher dose statin or another med (bile acid sequestrant, nicotinic acid)
• if LDL goal is met but triglycerides are still elevated, set another goal for all non-HDL cholesterol (should be LDL goal + 30)
  • add or intensify meds to lower LDL, or add nicotinic acid or fibrate to lower VLDL
• for CAD or CAD equivalent patients: start lifestyle changes and meds right away
• LDL goal is < 100 or < 70 if very high risk
• for isolated low HDL in CAD or CAD equivalent patients, add nicotinic acid or fibrate
• for elderly patients:
  o know that cholesterol elevates progressively with age
  o studies show that treating known CAD up to age 75 results in significant reductions in cardiac morbidity and mortality
  o treating elderly patients without known CAD (primary prevention) does not have much data

1.4 Pharmacology: Antihypertensives

1.4.1 Choosing Pharmacotherapy
• Think about the strength of evidence for use of a particular medication
• Consider comorbid conditions and compelling indications for more aggressive therapy
• Cross-check with current meds being taken
• Consider patient insurance and cost of copay

Diuretics: increase urine flow by inhibiting ion transport in the kidney

**Thiazides:** inhibit Na and Cl reabsorption in the distal convoluted tubule → increased urine volume, decreased blood volume
• drugs of choice in the treatment of primary HTN
• more effective than loop diuretics unless CrCl < 30 (loop diuretics act earlier in the nephron = more time for them to work with reduced nephron functioning)
• are Ca sparing = can use in osteoporotic patients
• formulations:
  • chlorthalidone: twice as potent as HCTZ, most evidence
  • indapamide:
  • hydrochlorothiazide (HCTZ)
  • metolazone:
  • chlorothiazide:
• contraindications: anuria, CrCl < 30, careful in gout
• side effects: hypokalemia, hyperuricemia, hyponatremia, hypercalcemia, hyperglycemia
• monitor: electrolytes, BP

**Loop diuretics:** block Na/K/Cl cotransporter in ascending loop of Henle → decreased reabsorption of Na and Cl → increased urinary excretion, decreased blood volume
• more potent Cl reabsorption than thiazides
• commonly used to reduce pulmonary edema in CHF
• kinds:
  • furosemide:
  • bumetanide:
  • torsemide:
  • ethacrynic acid:
• contraindications: anuria, volume depletion
• side effects: hypokalemia, dehydration, orthostatic hypotension, photosensitivity
• monitor: electrolytes, BP, volume status

**Potassium-sparing diuretics:** most enhance Na excretion and retain K at the distal convoluted tubule
• not very potent alone
- kinds:
  - spironolactone: inhibits aldosterone R at the distal convoluted tubule
    - side effects: gynecomastia or hirsutism because it binds nonspecifically to other steroid receptors, hyperkalemia
  - eplerenone:
    - side effects: hyperkalemia
  - monitor: BP, electrolytes, endocrine

### 1.4.2 Drugs That Interfere with the Renin-Angiotensin System

**Angiotensin converting enzyme (ACE) inhibitors:** prevent conversion of angiotensin I to angiotensin II → Na excretion and K retention (by decreasing aldosterone production), decreased vasoconstriction
- used in treatment of HTN and CHF
- don't affect glucose levels
- ok to use in renal pts that have no renal function left (can't hurt them any more)
- kinds:
  - benazepril:
  - enalapril:
  - lisinopril:
  - contraindications: ARF, angioedema, hyperkalemia, pregnancy, bilateral renal artery stenosis
  - side effects: hyperkalemia, renal failure (so stop if serum Cr increases by 30% or more), hypotension, cough (switch to ARB)
  - monitor: BP, electrolytes, renal function

**Angiotensin II receptor blockers (ARBs):** interfere with binding of angiotensin to its receptor → effects similar to ACE inhibitors
- ok to use in renal pts that have no renal function left (can’t hurt them any more)
- kinds:
  - irbesartan:
  - losartan:
  - olmesartan:
  - valsartan:
  - contraindications: same as ACE inhibitor
  - fewer side effects: hyperkalemia, increased SCR, increased BUN, hypotension, syncope
  - monitor: BP, electrolytes, renal function

**Aldosterone antagonists:** act on tubules to promote Na/Cl excretion and K retention
- eplerenone:

**Direct renin inhibitors (DRIs):** blocks conversion of angiotensinogen to angiotensin I
- contraindications: renal failure, hyperkalemia
- monitor: K, serum Cr

### 1.4.3 Drugs That Decrease Peripheral Vascular Resistance or Cardiac Output

**Direct vasodilators**
- calcium channel blockers (CCBs): inhibit entry of Ca into cells → dilation of arteries, decrease in HR → decrease in afterload
- particularly useful in elderly pts
  - dihydropyridine CCBs: work at the peripheral vasculature
    - nifedipine: HTN and angina
    - amlodipine: HTN and angina
    - side effects: edema, flushing, headache, reflex tachycardia
  - non-dihydropyridine CCBs: work at the heart vasculature and act as a negative chronotrope (decrease HR) and negative inotrope (weaken force of contraction) = useful in a-fib
    - verapamil: HTN, supraventricular tachycardias, unstable angina, chronic angina, vasospastic angina
    - diltiazem: same as verapamil but no unstable angina
• side effects: constipation, conduction problems
  o contraindications: heart failure
• other direct vasodilators
  o hydralazine and minoxidil directly relax arterioles
  o hydralazine + isosorbide used in CHF for ACE/ARB intolerance
• mechanism unclear

Sympathetic nervous system depressants
• α and β blockers: can’t acutely discontinue because this could result in acute tachycardia (downregulation of the system)
  o α-1 blockers: dilate arteries and veins
  o central α-2 agonists: used specifically during substance withdrawal or pregnancy
    ▪ clonidine: an α-2 agonist that reduces central sympathetic outflow, but is associated with increased incidence of falls = only use for refractory HTN
    ▪ methyldopa: drug of choice for HTN in pregnancy (ACEI/ARB not safe) but requires multiple doses per day
      • cautious use with known CAD
      • side effects: CNS, orthostasis, peripheral edema
      • monitor: HR
• β blockers: prevent sympathetic stimulation of the heart (decrease HR, decreased contractility, decreased cardiac output, and decrease renin)
  ▪ questionable role in treatment of essential HTN unless pts have heart failure or recent MI
  ▪ strict β-1 blockers: use for asthma or COPD pts (don’t want to block bronchial relaxation!)
    • atenolol:
    • metoprolol:
  ▪ block at multiple receptors
    • propranolol: β-1 and β-2
    • labetalol: β-1, β-2, α-1 blocker
  ▪ contraindications: 2nd or 3rd degree heart block, cardiogenic shock
    • relative contraindications: bradycardia
  ▪ side effects: weakness, dizziness, bradycardia, sexual dysfunction, dyslipidemia, reduced cardiac output, impotence, exercise intolerance, bronchospasm
    • can mask signs of hypoglycemia (won’t sweat)!
  ▪ monitor: BP, HR, glucose
1.5 Clinical Medicine: Hypertension

1.5.1 Hypertension Background

- leading cause of death worldwide
- 75% of diabetics have HTN
- an treatable risk factor for stroke, CHF, peripheral vascular disease, aortic dissection, a-fib, kidney failure, dementia, MI
- hypertension has greatest impact on cerebral and renal vasculature!
- pulse pressures is the difference between systolic and diastolic
- diastolic pressures rise natural until age 50 and then decreases progressively, while systolic BP rises throughout life □ increase in pulse pressure
- fatality of HTN is correlated to the pulse pressure
- the larger the difference, the greater the risk for fatal MI or stroke
- HTN developed before age 50 typically involves systolic and diastolic BPs
- HTN developed after age 50 is isolated systolic HTN, due to unavoidable hardening of the large arteries
- systolic BP > 140 is considered to be a greater cardiovascular risk in this age group than high diastolic BP

Resistant hypertension: persistence of BP > 140/90 despite treatment (and patient compliance) with full doses or 3 or more different classes of meds (including a diuretic)

- could be pseudoresistant hypertension (white coat syndrome): chronic HTN is well controlled outside of the office
- inadequate medical regimen for patient: not using appropriate diuretic, renal impairment, inadequate dosing
- patient nonadherence or faulty diet: high salt, alcohol, tobacco
- exacerbating drugs: cocaine, methamphetamine, NSAIDs, other stimulants, oral contraceptives, EPO, natural licorice, cyclosporine, tacrolimus, herbal products
- consider causes of secondary hypertension

Primary (essential) hypertension: idiopathic but with known risk factors; 95% of all cases

- risk factors affect extracellular fluid volume, heart contractility, or vascular tone:
- can have genetic defect for impaired sodium excretion
- stress, obesity, drug or substance abuse
- variable renin activity
- variable sympathetic response
- insulin resistance, diabetes
- inadequate dietary potassium and calcium
- resistant vessels

Secondary hypertension: has an identifiable, treatable cause; 5% of all cases, a result of:

- chronic renal disease: causes expanded plasma volume with peripheral vasoconstriction
- most frequent cause of secondary HTN
  - and HTN can also cause CKD
- 85% of CKD pts will develop secondary HTN
- would see proteinuria and elevated creatinine
- renovascular stenosis: occurs when ill-perfused kidneys (due to atherosclerosis or fibromuscular dysplasia) release a lot of renin □ vasoconstriction
- stenosis due to fibromuscular dysplasia will have a knobby appearance on cardiac cath
- a frequent cause of HNT refractory to treatment
- coarctation of the aorta: congenital abnormality causing narrowing of the aorta □ increased resistance
- often accompanies bicuspid aortic valve or Turner’s syndrome
- hyperaldosteronism: usually caused by aldosterone-producing tumor or hyperplasia of the adrenals □ too much Na/K reabsorption □ water retention

Cushing’s syndrome: pituitary adenoma that produces ACTH □ lots of cortisol □ HTN
• **Pheochromocytoma**: adrenal tumor producing catecholamine
  • typically 35-45 years old, no risk factors for HTN, may feel hot, flushed, anxious, or have a headache
  • huge problem when undiagnosed because outpouring of catecholamines during a surgical or radiologic procedure can lead to severe hypertensive crisis and death

**Obstructive sleep apnea**: tissues sensing intermittent hypoxia summon renin-angiotensin system to increase BP

**Hypertensive urgency**: severe elevation of blood pressure with no evidence of progressive target organ damage or dysfunction
  • no raised intracranial pressure
  • occurs when pts have known HTN but have been noncompliant with meds or diet, or regimen was inadequate
  • clinical presentation: BPs usually > 220/110, with severe headache, SOB, evidence of stable or no target organ damage
  • need to lower BP slowly over several hours: laβlol, clonidine, captopril
  • lowering too much too fast could cause dramatic drop in pressures ☐ cerebral hypoperfusion and infarct

**Hypertensive emergency**: acute, severe elevation of BP with evidence of rapidly progressing target organ damage
  • clinical presentation: BPs usually > 220/140, SOB, chest pain, altered mental status, weakness, dysarthria
  • target organ damage presenting as MI, acute CHF with pulmonary edema, renal failure, encephalopathy, intracranial hemorrhage, eclampsia (with pregnancy), aortic dissection
  • if seeing papilledema on funduscopic exam, think **malignant hypertension**
    • most common in young adults with prior renal disease, black males, pregnancy, or collagen vascular disease
  • treatment requires immediate and gradual reduction of BP but not to normal parameters, only to < 160/110
  • 10% decrease in 1st hour followed by 15% decrease in next 3-12 hours
  • requires use of IV meds:
    • for vasodilation: sodium nitroprusside, nicardipine, fenoldopam, nitroglycerin, enalaprilat, clevidipine, furosemide
    • adrenergic blockers: laβlol, esmolol, phentolamine

### 1.5.2 Screening for HTN

USPSTF strongly recommends screening for all adults, at a minimum of every 2 years

### 1.5.3 Diagnosing HTN

JNC7 HTN guidelines:
  • Normal BP: <120/<80
  • Pre-HTN: 120/80 - 139/89
  • HTN stage I: 140/90 - 159/99
  • HTN stage II: >160/>100

HTN = repeatedly elevated pressures >140/90
  • should be based on 2+ readings that are at least 1 week apart
  • may want to treat high risk individuals at a lower threshold (130/80)
  • ex. diabetics, CKD, cardiovascular disease, cerebrovascular disease, LVHs
  • cautiously treat isolated systolic HTN in the elderly
  • indapamide +/- perindopril a good route to go
  • in pregnancy can only use certain meds: methyldopa, laβlol, hydralazine, nifedipine

Assess target organ damage: neurologic, ophthalmic, cardiovascular, renal, vascular
  • labs: UA for proteinuria, blood chemistry (creatinine, glucose, K, Na), lipid profile, EKG to look for VH
- Assess cardiovascular risk
- Black patients have greater risk of complications from untreated HTN
- Detect rarer, secondary causes of HTN

1.5.4 Management of HTN

**Lifestyle modification:** weight loss and DASH diet has the greatest effect

**Meds:** most single meds will only lower BP by 10-20 points, so pt will probably need multiple
- otherwise healthy individuals
- Prehypertension □ should start with lifestyle changes
- Stage I HTN □ usually start with a thiazide diuretic
- Stage II HTN □ 2 drug regimen with one being a thiazide
- High cardiovascular disease risk groups require tighter control (BP goal < 130/80), and intervention with drugs begins at the prehypertensive stage: CHF, CAD, CKD, DM, post MI, post stroke
- Classes of anti-HTN meds with additive effect against comorbid diseases
  - CHF: diuretic, β blocker, ACE inhibitor, ARB, aldosterone antagonist
  - CAD: β blocker, ACE inhibitor, Ca channel blocker, diuretic
  - MI: β blocker, ACE inhibitor, aldosterone antagonist
  - Diabetics: β blocker, ACE inhibitor, diuretic, ARB
  - CKD: ACE inhibitor, ARB
  - Stroke: ACE inhibitor, diuretic

1.6 Pharmacology: Ischemic Heart Disease

1.6.1 CAD

Pharmacologic goal is to reduce the myocardial oxygen demand/
- β blockers reduce HR and contractility
- Ca channel blockers reduce systemic vascular resistance and decrease contractility
- Nitrates cause venous dilation □ decrease preload □ decrease oxygen demand
- Antithrombotics like aspirin prevent clots in the coronary arteries

1.6.2 Antiplatelet Drugs

**ADP-R antagonists:**

Kinds:
- Aspirin:
- Clopidogrel:
  - Ticagrelor:
- Side effects: dyspnea, bradyarrhythmias
- Preasugrel:

**Glycoprotein IIb/IIIa-R antagonists:** prevent platelet aggregation by blocking the binding of fibrinogen and vWF to the glycoprotein-R on platelet surfaces

Kinds:
- Abciximab: only if PCI planned
- Side effects: bleeding, thrombocytopenia, allergic reaction, hypotension
- Eptifibatide: renal dosing available
- Side effects: bleeding, hypotension
- Tirofiban: renal dosing available, may be less effective than abciximab during PCI

Thrombolytic Drugs: activate plasminogen □ fibrinolysis

Kinds:
- Alteplase
• reteplase:
• tenecteplase:

Nitrates: dilate blood vessels to reduce cardiac preload and reduce vessel resistance, decreased end diastolic volume, decreased stress on myocardial walls, decreased oxygen demand by the myocardium

Kinds:
• isosorbide dinitrate: oral long-acting
• isosorbide mononitrate: oral ong-acting
• nitroglycerin: PRN or chronic, spray, ointment, patch, paste, or oral
• drug of choice for relieving acute coronary spasm causing angina

Side effects: headaches, postural hypotension, flushing, dizziness, reflex tachycardia.

1.7 Clinical Medicine: Ischemic Heart Disease

1.7.1 Diagnostic Methods Background for Ischemia

Procedures: myocardial ischemia workup
1. first, do a resting EKG
   a. after that:
   • normal resting EKG consider doing a stress test (exercise tolerance test): EKG on a treadmill
     o keep in mind contraindications for any exercise testing
       ▪ absolute: acute MI in last 48 hours, refractory unstable angina, arrhythmias causing hemodynamic issues, symptomatic/severe aortic stenosis, uncontrolled/symptomatic CHF, acute PE, acute myocarditis or pericarditis, acute aortic dissection
       ▪ relative: LCA stenosis, moderate stenotic valvular disease, severe HTN, electrolyte abnormalities, hypertrophic cardiomyopathy, tachy/brady arrhythmias, 2nd or 3rd degree AV block
     o if patient can’t exercise, consider doing a pharmacologic stress test: agent injected to simulate exercise
       ▪ dobutamine will stimulate increased cardiac contractility and systemic vasoconstriction
         • contraindications: BP > 180/120, history of v-tach or a-fib, MI in last 3 days, aortic stenosis, recent β blocker
       ▪ adenosine and persantine: increase flow in non-diseased coronary arteries = can better visualize blocked areas when using contrast
         • adenosine contraindications: COPD, asthma, emphysema, recent β blocker, recent theophylline, recent caffeine
         • persantine contraindications: asthma, emphysema, severe COPD, resting systolic BP < 100, LCA disease, unstable angina, acute MI, recent β blocker, recent theophylline, recent caffeine
     o hold the β blockers before the test! want to be able to achieve HR
       • other drugs that can blunt BP or HR: digoxin, β-adrenergic blocking agents, vasodilators
       • interpretation of stress test:
         • ST changes without angina 70% chance of significant CAD
         • ST changes with angina 90% chance of significant CAD
         • bottom line: the greater the ST changes, the greater the chance of CAD
         • a systolic BP drop > 10 points BAD NEWS BEARS, indicative of severe disease that can’t be compensated for by raising BP
         • ***remember that false positives are common on stress tests
o if resting EKG is abnormal do an exercise echo (real exercise or pharmacologically induced) or nuclear stress test or cardiac stress MRI
  • stress echocardiography: evaluates cardiac blood flow indirectly by assessing effect of exercise on myocardial wall motion
    • movement interpretation depends on the reader performing the echo
    • sensitivity and specificity affected by presence of baseline wall movement abnormality, poor imaging windows, adequacy of exercise, and presence of bundle branch blocks
    • highly specific
  • nuclear stress test: imaging using radioactive tracers used to look for ischemia and infarcts
    • highly sensitive
  • cardiac stress MRI: radiofrequency waves and magnetic fields used to generate detailed images of the heart
    • adenosine is the only agent used for cardiac MRI
    • excellent choice for valvular disease, ischemia, aortic abnormalities, congenital abnormalities
    • costly!
    • contraindications: gunshot wound, shrapnel, metal prosthesis, or other source of metal, obesity, claustrophobia
b. if needed cardiac catheterization: gold standard for imaging, utilizes radiation and contrast
  • can put in stent during same procedure
  • left heart route goes in through femoral or radial artery
    • allows for assessment of LV function: EF, left ventricular end diastolic pressure
    • assessment of aortic & mitral valves
    • assess for wall movement abnormality or LVH
    • assessment of coronary anatomy
    • can allow for imaging of abdominal aorta, renal arteries, iliac arteries
  • right heart route goes through femoral vein into vena cava
    • can assess RV pressures & pulmonary HTN
    • assess for shunts or congenital abnormalities
    • assess for valvular abnormalities
    • assess for constrictive or restrictive pericarditis

Procedures: STEMI or NSTEMI
1. EKG
   a. plain-style echocardiography (obviously no exercise with it) or other imaging
   b. primary percutaneous coronary intervention (aka PCI or angioplasty): mechanically widening obstructed arteries using a stent
   • can be done during cardiac catheterization
     c. coronary artery bypass grafting (CABG): arteries or veins harvested from elsewhere in the patient are grafted to areas of blockage to allow blood flow to circumvent the obstructed area

Lab monitoring for ACS drug treatment
• monitor UFH with PTT
• monitor LMWH therapy with anti-factor Xa test
• can’t monitor fondaparinux
• if using warfarin, monitor INR

Cardiac labs:
• creatinine phospokinase (CK): found in skeletal muscle throughout the body
• shows up in 1-6 hours, peaks in12, lasts up to 1.5 days
• takes time to do the complete assay
• includes components of muscle, cardiac, and brain tissue
  • CK-MM: skeletal muscle specific creatinine kinase, elevated in trauma or crush injury
  - will also be elevated after running a marathon or lifting weights
  • CK-MB: cardiac specific creatinine kinase, elevated in MI
  - can now test directly for
  - helpful to know because EKG will not always detect MI when cardiac enzymes will show elevation
  • CK-BB: brain specific creatinine kinase, elevated in stroke
  - shows up in 3-12 hours, peaks at 1 day, lasts 2-3 days
• troponin T (TnT): cardiac specific damage marker
  - will include all cardiac damage, including damage from defibrillation, arrhythmias, cardiac procedures, CHF, myocarditis, vasospasms, cardiomyopathies
  - elevation begins within an hour of the infarct occurring (first marker to show)
  - drawn serially to see progression of MI
  - remains elevated for 5-14 days after MI = helpful for pts who waited to get treatment or had minimal symptoms
  - problem: it is falsely elevated in renal disease due to decreased clearance
• aspartate aminotransferase (AST): nonspecific liver enzyme
• lactate dehydrogenase (LDH): found in all cell injury states = nonspecific
  - shows up in 10 hours, peaks at 1-2 days, lasts 10-14 days
• myoglobin: nonspecific marker of muscle necrosis
  - shows up in 1-4 hours, peaks at 6-7, lasts up to 1 day
  - now is typically replaced by troponin tests
• brain natriuretic peptide (BNP): secreted from ventricles stressed by CHF
  - levels can vary individually = use it as a gauge, not a specific or sensitive test
  - falsely elevated in renal failure
  - levels rise with age
• C reactive protein (CRP): a nonspecific acute phase inflammatory protein
  - elevated a few days PRIOR to MI
  - can be elevated chronically with inflammation-prone individuals (hormone therapy, tobacco)
  - levels are artificially lowered by statins, niacin, fibrates, moderate alcohol, aspirin, exercise, weight loss
  - a more specific and sensitive version of the test is hsCRP

1.7.2 Coronary Artery Disease

Pathophysiology
• affects large and medium arteries
• characterized by endothelial dysfunction, vascular inflammation, lipid/cholesterol/Ca/cellular debris buildup in vessel wall
• can also cause electrical problems
• begins in childhood with lipid deposition and inflammation
• inflammatory events: LDL oxidation, infection, toxins (nicotine), hyperglycemia, increased homocysteine
  - oxidized LDL impairs vasodilation □ continual vasoconstriction
• inflamed vessel wall attracts sticky LDL as well as macrophages
• progression of plaques influenced by risk factors
• can become calcified
• risks promoting atherosclerosis: age, gender (women protected by estrogen), FH, sedentary lifestyle, tobacco, HTN, diabetes or insulin resistance (causes greater atherosclerosis), hyperlipidemia
  - smoking has greatest effect on carotid and peripheral vasculature
  - diabetics are considered to be at the risk of CAD that a normal person who has already had one MI is at
    ▪ diabetics have accelerated atherosclerosis with many small plaques scattered throughout vs a non-diabetic who has a few, large, isolated blockages
- diabetes has greatest effect on coronary vasculature
- diabetics are at greater risk of CHF or death after having an MI, bypass, or stent
- acute MI is from a plaque deposit that has suddenly burst
- activation of body clotting system
- MI can also happen from progressive narrowing of vessels
  - slow process
  - formation of collaterals
  - progressive angina

Classification of CAD to normalize between providers:
- class I: no limitations or symptoms with normal activity
- class II: slight limitations and normal activity results in symptoms
- class III: marked limitation and minimal activity results in symptoms
- class IV: symptoms present with minimal activity and at rest

Causes of Chest Pain: must determine true cardiac chest pain vs non-cardiac chest pain
- stable angina: chest pain with activity or stress
- unstable angina: chest pain at rest

Pain with determined cardiac origin = must be some kind of coronary ischemia
- atherosclerosis, occlusion caused by vasospasm (cocaine, methamphetamines, stimulants), coronary artery dissection from blunt trauma, congenital abnormalities, aortic stenosis, hypertrophic cardiomyopathy, coronary thrombus or embolus (missed warfarin dose?), acute aortic dissection

Pain with non-cardiac origin
- costochondritis is reproducible on palpation
- intercostal shingles
- cervical or thoracic spine disease, including thoracic outlet syndrome
- GI: peptic ulcer disease, GERD, chronic cholecystitis
- pulm: PE, pneumonia, pneumothorax

1.7.3 CAD Presentations

Angina pectoris: stable angina; deep pressure-like pain in substernal region that may radiate to neck or jaw following physical exertion or emotional stress
- transient, 2-30 minutes only
- remits with rest or sublingual nitroglycerin
- usually as a result of chronic coronary atherosclerosis
- clinical presentation: SOB, elevated BP, S4+, arterial bruits, abnormal funduscopic exam (papilledema, AV nicking, cotton wool, corneal arcus (bluish rim around iris)), xanthelasma or xanthelomas, CHF from transient LV dysfunction, murmurs (during ischemic event only from transient papillary muscle dysfunction)
- “typical” pain symptoms more common in middle-aged men, and may be absent in women, elderly, and diabetics
  - elderly: weakness, SOB, alt ment
  - women: anxiety
  - diabetics: SOB

investigation:
- EKG between angina might be normal or may show Qs from prior MI, LBBB, RBBB, fascicular blocks
- EKG during angina may show ST depression (from the angina) or elevation (from injury incurred), or T wave inversion (from the ischemia)
- labs:
  - CK, CKMB, troponin should be negative
  - elevated cholesterol, high glucose
- CXR: may be normal or show evidence of CHF or arterial calcifications
- stress test:
  - development of typical angina + ST changes is highly indicative of CAD
    - no ST changes = 70% chance
    - BP drop during exercise means severe blockage
no angina? ST segment changes might still be significant for CAD

- treatment
- work on risk factors
- meds: daily aspirin, clopidogrel, β blocker, ACE inhibitor, nitrates PRN, statins
- stent or bypass if necessary

**Acute coronary syndrome:** includes STEMI, NSTEMI, or unstable angina

- typically from acute plaque rupture followed by thrombus
- can also have MI from cocaine overdose (causes vasoconstriction or makes myocardium hypermetabolic), or chronic cocaine use (causes cardiac arrhythmias) - in this case, give a β blocker

**Clinical presentation:**
- acute MI: new, sudden chest pain, jaw, neck, throat, scapular, or arm pain, dyspnea on exertion, nausea, vomiting, fatigue, hypotensive HTN, tachy or bradycardia, S3+ and/or S4+, signs of CHF, systolic murmurs (may hear ventricular septal defect murmur from heart blown due to high pressure)
  - will also hear a friction rub on day 2-3

- unstable angina: chest pain is now with greater frequency, severity, with less activity, or at rest
  - pain is refractory to nitroglycerin

**Investigation**
- EKG likely to show inverted T waves (ischemia) and ST depression or elevation
- labs: cardiac enzymes will tell you if it is unstable angina vs NSTEMI
  - MI will cause myocyte death positive labs

**Initial treatment for suspected STEMI or NSTEMI**

1. antiplatelet therapy: give aspirin and clopidogrel
   - prasugrel can be used in place of clopidogrel if PCI is planned (may have better outcome) but avoid in active bleeding, planned CABG, over age 75, prior stroke or TIA
   - ticagrelor can be used in place of clopidogrel with or without PCI (may have better outcome) but avoid in active bleeding or history of ICH
     a. initiate anticoagulant therapy
        - no PCI needed or expected: UF heparin or enoxaparin (LMWH) best
          - fondaparinux (factor Xa inhibitor) good for patients with increased bleeding risk
          - warfarin only used for certain indications (mechanical valve, pulmonary embolism, atrial fibrillation) due to increased bleeding risk
          - continue for duration of hospital stay
        - planned PCI: UF heparin or enoxaparin best
          - bivalirudin can also be used with heparin allergy
            - but can’t give bivalirudin if any lytics were given!
            - stop after PCI procedure
     b. when to give glycoprotein IIb/IIIa antiplatelet drugs: abciximab, eptifibatide, or tirofiban
        - STEMI: yes if PCI planned
          - then stop after PCI procedure
        - NSTEMI: yes if PCI or other diagnostic catheterization planned
     c. regain perfusion
        - best choice is PCI if available, but must be done within 3 hours of chest pain onset
        - PCI unavailable (and for STEMI only) initiate fibrinolytic therapy: streptokinase, alteplase, reteplase, or tenecteplase
          - estimate risk of intracranial hemorrhage before giving
          - lytic contraindications: prior hemorrhagic CVA, ischemic CVA in last 3 months, active internal bleeding, known intracranial neoplasm, suspected aortic dissection, most recent chest pain > 12 hours ago, cerebral arteriovenous malformation
            - relative: BP > 180/110, lumbar or other noncompressible puncture, CPR > 10 min, pregnancy, menstruation, trauma in last 2-4 weeks, major surgery in last 3 weeks
        d. determine bypass vs angioplasty during PCI imaging
bypass or angioplasty:
- if only 2 vessels have blockage but proximal LAD is involved

bypass only:
- if LCA blockage > 50-75%
- if 3 vessels have blockage and EF is < 50%
  - if EF is > 50%, still consider doing bypass if the angina was severe, with prior MI, or with resting EKG changes
- if only 1-2 vessels have blockage but EF is < 50% with ischemia occurring at low exercise

angioplasty has a questionable outcome for 3 vessel blockage
- other interventions: give oxygen, monitor serial EKGs and cardiac enzymes

half of STEMI deaths occur within 1 hour of event from ventricular fibrillation

meds to continue at home after ACS event (STEMI/NSTEMI or unstable angina)
- clopidogrel 2-4 weeks to 1 year
  - 1 year if stent was placed
- daily aspirin
- statins
- ACE inhibitor (or ARB if ACEI intolerant)
- β-blocker (slowly titrate off if patient has LV failure),
- try Ca channel blocker if unsuccessful
- nitrates PRN or continuously (but no mortality benefit)
- prognosis
- complications: arrhythmias, CHF, right ventricle infarction, ventricular ruptures, mural thrombi (thrombi adhered to vessel walls), stroke, pericarditis, angina

Sudden cardiac death: unexpected and nontraumatic death in stable patients who die within 1 hour after onset of symptoms
- cause: ventricular tachycardia, acute ischemia or infarction
- rarely, congenital deformities, pulmonary HTN, neoplasm, sarcoid/amyloid, vasculitides, LVH, conduction disorder

Prinzmetal’s angina (variant angina or vasospastic angina): angina at rest caused by vasospasms of coronary arteries, with no correlation to stress or exertion
- sites of spasm (typically RCA) frequently adjacent to plaques
- EKG shows ST elevations
- only affects women less than 50!
- may be associated with migraines, Reynaud’s
- treatment: pt must refrain from all stimulants and certain medications that can aggravate the spasms
- give certain prescriptions to alleviate: nitrates, Ca channel blockers, β blockers
- possible complications: acute MI, v-tach, v-fib, sudden cardiac death

1.8 Pharmacology & Clinical Medicine: Heart Failure

1.8.1 Congestive Heart Failure Background

Congestive heart failure: impairment of the ventricle to fill with or eject blood
- as inadequate cardiac output occurs, all organ systems are affected by reduced nutrients and oxygen
- body tries to compensate
  - increase ventricular filling during diastole □ increased stroke volume
  - norepinephrine release □ increased cardiac contractility
  - myocardial remodeling (slow): after acute event causing dead tissue there is dilation of L ventricle and scar formation over damaged area
    - gets body through the acute event but eventually □ stiff area of scar tissue with improper ventricular relaxation during diastole
    - ***results in an eventual DECLINE in heart function
      - reverse cardiac remodeling with ACE inhibitors
can have low or high cardiac output CHF
• most CHF is of the low output variety, due to:
  o pumping against high vascular resistance
• impaired filling of stiff ventricles
• rarely CHF can result in high cardiac output
• but each stroke volume will be low
• chronic activation of sympathetics and renin-angiotensin-aldosterone system leads to decreased response (and vasodilation)???
• cardiac remodeling occurs
• patients are chronically volume overloaded
• high metabolic demands can result in CHF of the high output variety!
  o ex. hyperthyroidism, anemia, AV fistulas, vitamin B1 deficiency, liver disease, multiple myeloma, Paget’s disease, polycythemia vera, sickle cell, tachycardia, morbid obesity, carcinoid, acromegaly, severe psoriasis = treat underlying cause to treat the CHF!

Common causes:
• ischemic cardiomyopathy: when blockage in artery causes hypoxic tissue that will eventually impact the pumping of the heart
• valvular cardiomyopathy: dysfunctional valves, including regurgitation or stenosis
• hypertensive cardiomyopathy: stiffened walls as a result of hypertension
• frequently results in diastolic congestive heart failure:

Less common causes of CHF:
• myocardial disease:
• dilated cardiomyopathy:
• hypertrophic cardiomyopathy:
• restrictive cardiomyopathy: when scarring of the pericardium restricts heart movement
• myocarditis: infectious, toxic, or idiopathic
• pericardial disease:
  o typically due to viral infection
  o results in stabbing chest pain that is better with leaning forward
• pericarditis:
• pericardial effusion/tamponade:
• pericardial constriction:

Classification
Stages of CHF:
• stage A: at high risk but no known disease yet = treat early to prevent symptoms
  -use an ACE inhibitor
  - HTN, CAD, DM, FH of cardiomyopathy
  -work in quitting smoking, increasing activity, limiting alcohol
• stage B: asymptomatic disease
  - add a β-blocker to the treatment regimen
  - previous MI, LV systolic dysfunction, asymptomatic valvular disease
• stage C: prior or current symptoms = symptomatic heart failure
  - add a diuretic or digoxin or device
  - reduce salt intake
  - known structural heart disease, SOB, fatigue, reduced exercise tolerance
• stage D: advanced symptoms or refractory to treatment = end stage with marked symptoms at rest
  - stage where people get placed on heart transplant list
  - add positive inotrope or device to regimen

Functional classification of CHF (similar to CAD):
• class I: no symptoms
• class II: symptoms with moderate exertion
• class III: symptoms with minimal activity or ADLs
• class IV: symptoms at rest

Risk factors for development of CHF: age, HTN, tobacco, DM, obesity
• -substance abuse is a risk due to constant stimulation of heart from amphetamines
• -alcoholism because associated cirrhosis may cause R sided heart failure
• -common CHF precipitators: CAD, MI, valvular disease, congenital heart disease, HTN (diastolic dysfunction), viral infection, pregnancy, idiopathic

CHF symptoms: dyspnea on exertion or at rest, paroxysmal nocturnal dyspnea, orthopnea, lower extremity, abdominal, or sacral edema (3rd spacing of extra fluid around heart), palpitations, weakness, anorexia
• comorbid symptoms: chest pain, palpitations, fatigue, syncope
• presenting symptoms are often only with exertion
• exercise results in inadequate cardiac output is not perfusing tissues, so resps are increased to compensate
• exercise increases heart rate, so ventricles have less time to fill

1.8.2 CHF Diagnostic Methods

Echocardiography: ultrasound used to provide information about structure, anatomy, and physiology of the heart
• no ionizing radiation generated
• inexpensive
• quality of the image depends on the operator’s skill, patient’s body type, presence of barrel chesting and other chest wall anatomy
• diagnostic utility:
  • assessing cardiac structure size and function
    - LVH
    - LV dysfunction: ischemia
    - valves: morphology and mobility
    - pericardium
    - wall motion abnormalities: regional vs global
    - contractilities
    - congenital abnormalities
  • estimate ejection fraction
    - very important post-MI
• assessing cardiac masses
• measuring RV and pulmonary pressures
• collapse of vena cava is normal and indicates normal central venous pressure
  - won’t collapse if pressures are high
• assessing murmurs: diastolic and cardiac
• evaluating syncope
• pre-op screening for clots before ablation of irritable foci causing arrhythmias
• assessing cardiac sources of emboli: looking for patent foramen ovale or atrial septal defect
  - biggest risk in having a communication between sides of the heart is that you lose the filtering property of having all blood flow through the lungs, so that emboli are able to move from the right side of the heart to the left
  - can use saline contrast to do a bubble study: + if bubbles seen in both sides of the heart
• assessing pericardial effusion, pulmonary embolism, pulmonary hypertension
• transthoracic echocardiography: standard echo, done over chest wall
• transesophageal echocardiography: more helpful in viewing posterior structures of the heart but more invasive
• quality not compromised by obesity or pulmonary disease
• helpful in assessing for suspected endocarditis and subsequent valvular damage
• improved visualization of vegetations, thrombi, masses, or left atrial appendage clot (most likely source of CVA/TIA)
EKG
- many CHF patients will have LVH
- end stage CHF results in low voltage due to electricity going through greater muscle mass?
- evidence of ischemia or prior infarction (Q waves)

Cardiac biomarkers if suspecting ischemic etiology
- CK/MB
- Troponin

Cardiac cath in acute CHF with unstable angina or MI
- do left ventriculogram to evaluate LV function, calculate EF, assess wall motion, and to look for mitral regurgitation
- do an arch shot to assess for aortic regurgitation or aortic defects
- do coronary angiography to assess for blockages

Chest X-ray with PA and lateral views
- look at size and shape of cardiac silhouette for cardiomegaly
- Kerley B lines: sharp, linear densities from interlobular interstitial edema
  - pathognomonic for CHF!
- look for pleural effusions
- commonly caused by left sided CHF
  - effusions will be transudative, small-med sized, and free-flowing

BNP levels

1.8.3 Developing a CHF Treatment Plan
1. History and physical exam for presenting symptoms □ assess risk category
- Vitals: O2, weight loss, BP, HR
- Inspection: pallor, cyanosis, cool or moist skin, use of accessory muscles
- Lungs
  - if L sided failure □ crackles, rales, possible wheezes, dullness at base of lungs, frothy or pink sputum
  - if R sided failure □ mostly clear lungs with dullness at the bases
- CV/PV
  - diminished or bounding pulses
  - JVP reflects right atrial pressure elevations
    - hepatojugular reflux (press on liver to watch excess fluid increase JVP)
  - if L sided failure □ S3 or S4, mitral regurgitation
  - if R sided failure □ right sided S3 or S4, tricuspid regurgitation,
    - S2 sound (made of A2 and P2) is normally dominated by closure of the aortic valve (A2), but because pressures are high on the R side you will also hear a loud pulmonic valve closure (P2)
- Abdomen
  - hepatomegaly
  - pulsatile, tender liver
  - ascites
- Extremities
  - edema

a. Investigation
- EKG & labs to assess etiology
- Echo to assess EF
- Cardiac cath to rule out ischemia and assess valves and pressures
  b. Pharmacologic treatment - -Start appropriate drug therapy for acute vs chronic disease (red = proven mortality benefit)
o treatment goal is to decrease cardiac workload, control excess fluid, and increase contractility
- reduce cardiac workload
  - ACE inhibitors or ARBs (-pril or -sartan): vasodilate reduced peripheral resistance & reduced BP reduced afterload and preload
    - won't change HR or cardiac output
    - will aid in diuresis
  - hydralazine + isosorbide dinitrate: found to be most beneficial to black men as an add-on therapy to those already on β-blockers and ACE inhibitors that are still symptomatic
    - decreased mortality, increased EF, improved exercise tolerance
    - requires frequent dosing
    - side effects: GI, headache
- β blockers reduce sympathetic stimulation
  - warning: can reduce cardiac output, cause bradycardia
  - dihydropyridine Ca channel blockers
  - for hyponatremic patients, you can use a vasopressin antagonist (tolvaptan), because it does not interfere with electrolyte balance, but it costs lots of $$$
- control excess fluid
  - diuretics (thiazide, loop, or K sparing): should not be used alone
    - if renal function is impaired, use a loop diuretic
    - if one dose isn't working, up it or add a second, or try IV infusion
      - idea of sequential nephron block: start with a loop diuretic then work sequentially down the nephron to target more distal parts
  - aldosterone antagonists (spironolactone, eplerenone)
- increase contractility
  - digitalis: improves contractility and cardiac output by inhibiting Na/K ATPase and enhancing release of Ca from SR
    - reduces plasma norepinephrine, renin, and aldosterone
    - low therapeutic index due to toxicity= only add if pt is persistently symptomatic on other drugs
    - lots of drug interactions
    - won’t distribute into fat tissue = don’t increase dose for obese pts
  - inotropes are last-resort or short-term only (life-limiting)
    - for end stage CHF waiting for transplant
    - for exacerbation, nonperfusion, or hypotension
- statins?

***Pharmacist says: avoid in all CHF patients: antiarrhythmic drugs, non-dihydropyridine Ca channel blockers, NSAIDs
- but Sherrie says:
  - can consider antiarrhythmics (mismatch between size of R/L heart can lead to asynchronous beating)
  - anticoagulative therapy (controversial)
    - low EF - consider warfarin
    - ATP III recommends giving aspirin to reduce prothrombic state

C. Non-pharmacologic treatment:
- behavioral modification
  - avoidance of salt, alcohol, other CHF exacerbators
  - exercise to make body more efficient at a given workload, to lose weight, and to prepare for transplant
- devices
  - automatic implantable cardioverter defibrillators (AICD):
    - for those with EF < 35%
    - proven mortality benefit
  - intra-aortic balloon pump (IABP):
### 1.8.4 Specific CHF Presentations and Treatments

**Systolic heart failure:** problem with contraction, heart does not squeeze well, and cardiac output is insufficient

- **EF < 55%**
- **causes:**
  - most commonly ischemic heart disease and/or MI
  - long-standing HTN causes stiffening of heart wall (a diastolic problem) but will eventually wear out the pump of the heart = becomes a systolic problem
  - valvular heart disease: because greatest pressures are on left side of heart, valvular disease on left side is more symptomatic than on right side
  - idiopathic (viral infection?)
  - myocarditis
  - toxins: alcohol, cocaine, hyperthyroidism, lead
  - overwhelming illness or sepsis
  - DM
- **investigation:** Echo for LV & reduced EF & dilation, EKG for LVH signs, CXR for cardiomegaly and/or pulmonary edema, BNP levels

**Diastolic heart failure:** heart does not relax enough — elevated filling pressures — high pressure gradient which causes water portion of blood to diffuse across heart and into tissues — edema

- **EF > 55%**
- **preserved pumping ability, but heart will eventually wear out and EF will decline**
- **most common in older females with HTN**
- **causes:** HTN — L ventricular hypertrophy, acute ischemia, restrictive cardiomyopathy (amyloid, ESRD on dialysis, sarcoid), DM
- **diastolic dysfunction naturally increases with age**
- **investigation:** Echo for LVH, EKG for LVH signs, CXR for pulmonary edema, BNP levels
- **Systolic/diastolic heart failure can coexist!**
- ex. ischemic heart disease
  - MI causes dead tissue with loss of contracting myocardium = systolic component
  - scarring from MI cause reduced compliance of ventricle = diastolic component

**Right-sided CHF**

- **causes:**
  - most common cause is left sided heart failure: L side of heart is damaged so everything backs up into the lungs and right side of the heart
  - congenital heart lesion such as atrial septal defect
  - tricuspid or pulmonic valve disease
  - pulmonary disease such as COPD, interstitial lung disease, pulmonary emboli
  - pulmonary HTN means pressures feeding lungs are high — transfer of the pressure to the heart
  - always due to an underlying problem

**Acute (flash) pulmonary edema:** rapid fluid accumulation in the air spaces and parenchyma of the lungs

- **causes:** MI, acute valvular lesion, HTN, end stage valvular disease, severe systemic illness, pulmonary embolism
- **presentation:** tachypnea, tachycardia, HTN (or hypo if grave), hypoxia, crackles
• treatment: IV diuretics, nitrates, inotropes, pressors, ACE/ARB or hydralazine + nitrate, morphine, antiarrhythmics, oxygen
• DON’T give β blockers in acute phase

**Acute heart failure (overt)**
• causes: massive MI, tachyarrhythmias, infective endocarditis with valve rupture
• presentation: severe SOB, rales, hypoxia, cyanosis, pallor, chest pain, tachycardia or bradycardia, hyper or hypotensive (BAD if hypo), cool skin, diaphoresis, tachypnea, respiratory distress, poor mental status

**Decompensated heart failure**: decompensation of a chronic or acute heart failure; patient is clinically deteriorating and requires early and aggressive therapy
• symptoms: new or worsening of existing symptoms, dyspnea, fatigue, edema, new murmurs □ findings consistent with worsening LV function
• patients are “cold and wet” = cold due to hypoperfusion, wet due to pulmonary congestion and volume overload
• investigation: EKG, Echo, CXR
• loop diuretics
• oxygen
• morphine to depress respirations
• nitroglycerin or nitroprusside (if HTN) to vasodilate and reduce preload and afterload without reducing contractility
• inotropes
  □ pos inotrope to stimulate forceful heart contractions (dobutamine or milrinone) □ dobutamine for patients in shock with low BP
• synthetic BNP (brain natriuretic peptide) for vasodilation to decrease preload
  □ huge $$$ for similar results to nitroglycerine or furosemide
• ACE or ARB
• DON’T give β-blocker!
• mechanical interventions if necessary
• figure out and treat underlying cause! (ex. thyroid, anemia)

### 1.9 Pharmacology & Clinical Medicine: Arrhythmias

#### 1.9.1 Electrical Problems of the Heart
• Symptoms: palpitations, racing heart, dizziness, syncope
• Comorbid precipitators: CAD, MI, congenital malformations, CHF

#### 1.9.2 Antiarrhythmic Drugs
• Na channel blockers: block Na entry into cell during depolarization □ prolonged refractory period, and suppress automaticity of the Purkinje and His fibers
• class IA drugs useful for treatment of atrial and ventricular arrhythmias
• class IB drugs are used for ventricular arrhythmias
• B blockers slow conduction through SA and AV nodes and increase refractory period
• good for treating tachyarrhythmias from excess sympathetic activity
• K channel blockers prolong repolarization
• good for treating intractable ventricular arrhythmias
• Ca channel blockers slow conduction through AV node and increase AV refractory period
• stop arrhythmias requiring AV conduction
• Others: adenosine, digoxin

### 1.10 Clinical Medicine: Cardiovascular Disease Prevention

**Primary prevention**: treat risk factors to prevent development of disease
- 7 biggest risk factors
- can’t prevent age, family history, or gender
- can prevent modifiable risks: hyperlipidemia, hypertension, diabetes, smoking
  - often coexist with other big risk factors
  - Framingham risk is used to help decide whether or not to treat primary hyperlipidemia
    - ATP III recommends focus on lowering LDL
- other modifiable risk factors: obesity, inactivity, CKD, metabolic syndrome, high alcohol

**Secondary prevention**: treat established disease to prevent recurrence or debilitation
- known cardiovascular disease = treat cholesterol regardless of numbers
2 Cardiology II Exam Notes

2.1 Valvular Heart Disease, Infective Endocarditis, and Rheumatic Fever

2.1.1 Background

- Mitral valve is the only one with 2 leaflets!
- Today most valvular disease is due to degenerative calcific changes that occur naturally with aging
- probably same mechanism as atherosclerosis
- can lead to stenosis, regurgitation, or both
- Cardiac cath vs echo?
  - echo
    - estimates RV and pulmonary pressures
    - estimate ejection fraction
    - look at wall and valve morphology
  - cardiac cath
    - left heart route directly measure LV and diastolic pressures
    - right heart route directly measure RV and pulmonary pressures
    - do cardiac cath instead of echo when you want to assess CAD
- Rheumatic fever and valvular disease
- order of valves affected by rheumatic fever: mitral, aortic, tricuspid, pulmonic
- disease is a result of immune response to the infection vs infection itself
- can result in regurgitation and/or stenosis
- diagnose with Jones criteria: must have 2 major criteria or 1 major + 2 minor
  - major: carditis, polyarthritis, chorea, erythema marginatum, subq nodules
  - minor: arthralgia, fever, elevated acute phase proteins, prolonged PR interval, previous history of Group A strep or rheumatic fever
- treatment: bedrest if there is significant cardiac disease, salicylates and steroids, heart failure management, penicillin

Infective endocarditis: bacterial infection of the endocardium and/or a valve

- can be spurred by transient bacteremias caused by IVs or operations
- agent is usually viridans strep or staph
- organism determines acute vs subacute presentation
at risk: those with mitral valve prolapse, bicuspid aortic valve, IVDU, prosthetic valve recipients
presentation: fever (days to weeks), headache, myalgias, cough, arthralgias, weight loss, cardiac issues, petechiae of the palate or conjunctiva, embolic phenomena, new murmur
subungual "splinter" hemorrhages
painful purple lesions on the extremities (Osler nodes)
painless erythematous lesions on the palms & soles (Janeway lesions)
exudative lesions of the retina (Roth spots)
investigation:
blood cultures, CBC □ anemia, leukocytosis, elevated sed rate, UA □ hematuria, proteinuria, + rheumatoid factor antibody
TEE (better than regular echo) □ oscillating vegetations, abscesses, valve perforation or dehiscence, new regurgitation
Duke diagnostic criteria (2 major, 1 major + 3 minor, or 5 minor)
o major: + blood culture, evidence of endocardial involvement
o minor: predisposition, fever, vascular/immune phenomena, microbial involvement, echo findings?
treatment: IV antibiotics 4-6 weeks, may need surgical valve replacement
anticoagulation contraindicated
prophylaxis before procedures? new guidelines say it isn’t necessary unless your patient is highest risk group (prosthetic valve, previous endocarditis, cardiac transplant with valvular disease, congenital malformations)
not recommended for those with prior CABG, pacemaker, ICD, mitral prolapse or regurg, atrial-septal defect, prior rheumatic fever

Stenosis: narrowing or obstruction to forward flow □ generation of high pressure that heart must pump against
slow progression, chronic disease
symptoms will precede LV dysfunction
usually intervene just for symptoms
compensatory mechanism for increased pressure is hypertrophy: enlargement of heart wall
a result of concentric hypertrophy: new sarcomeres added in parallel to existing sarcomeres □ wall increases in thickness
normal LV wall thickness is <12cm

Aortic valve stenosis: obstruction □ increased pressure in LV □ LVH □ eventual heart failure □ systolic dysfunction □ progression of heart failure & irreversible LV injury
from calcification:
associated with 50% increase in risk of cardiovascular death and MI
a result of inflammation, lipid accumulation, upreg of ACE, infiltration of tissue with macrophages and T-cells
development has same risk factors as for CAD: HTN, hyperlipidemia, DM, smoking, metabolic syndrome
senile aortic stenosis: age-related calcific build-up on a normal tricuspid valve
occurs by age 60-80
bicuspid aortic stenosis: congenital abnormality that accelerates calcific build-up = stenosis occurs 10 years sooner than normal age-related stenosis
treatment: statins
rheumatic fever-related aortic stenosis: causes adhesion and fusion of cusps
can also cause aortic regurgitation and mitral valve disease
classification:
• normal valve is 3-4 cm²
• mild stenosis is < 1.5 cm² with pressure < 25 mm Hg
• moderate stenosis is 1-1.5 cm² with pressure 25-40 mm Hg
• severe stenosis is < 1 cm² with pressure > 40 mm Hg
presentation:
• if early, may be asymptomatic with murmur
• systolic ejection: harsh, heard at aortic with potential radiation to neck
• S4 from the HTN
• late: DOE, SOB, angina (end-stage), syncope, CHF, paroxysmal nocturnal dyspnea, orthopnea, presyncope
• exam: pulsus parvus et tardus (pulse is slow in relation to contraction, and weak), hyperdynamic displaced apical impulse
• investigation: EKG for LVH, CXR for cardiomegaly, echo for valvular morphology/gradient/LV function (or cardiac cath to assess for all this plus concomitant CAD)
• treatment:
  • no proven benefit with drugs other than statins
  • valve replacement if severe
  • aortic balloon valvotomy as bridge to surgery or palliative

**Mitral valve stenosis:** elevated LA pressure • LA hypertrophy • transmission of high pressures to pulmonary vasculature • pulmonary edema

• background:
  • most commonly due to rheumatic heart disease (occurs 10-20 years after fever)
  • rarely due to congenital malformation or connective tissue disease
• mostly in women
• cardiac output is reduced
• can progress to right-sided heart failure
• hypertrophy of tissue makes it unhappy and prone to electrical problems like afib
• worsens with pregnancy because there is more demand for cardiac output • increased HR
• valve size is usually < 1.5 cm²
• presentation: fatigue, dyspnea, orthopnea, hemoptysis, peripheral edema, palpitations, afib (or associated embolic events)
• S1 will be loud and palpable
• opening snap of mitral stenosis after S2
• low pitched diastolic rumble at apex (best heard in LLD or accentuate with exercise)
• accentuated P2
• RV heave if it has progressed to pulmonary HTN
• investigation
  • use echo to classify stage
    • normal if valve is 4-6 cm² with pressure gradient of 0 mm Hg
    • mild if valve is 2-4 cm² with pressure < 8 mm Hg
    • moderate if valve is 1-2 cm² with pressure of 8-12 mm Hg
    • severe if valve is < 1 cm² with pressure > 12 mm Hg
• treatment
  • if asymptomatic, may only need prophylaxis for endocarditis
  • initially try:
    • HTN management: diuretics & salt restriction to reduce blood volume, nitrates
    • afib management: anticoagulation for high embolic risk
    • beta-blockers: control HR to prevent pulmonary edema (greater HR = greater disparity between what is pumped out and what the lungs are returning)
  • if patient remains symptomatic after meds or has episodes of pulmonary edema, decline in exercise capacity, or evidence of pulmonary HTN:
    • mitral valve replacement
    • balloon valvuloplasty

**Tricuspid stenosis:** causes diastolic pressure gradient between RA and RV

• background:
  • uncommon in adults
  • affects more females
  • most frequently a result of rheumatic disease
  • rarely an isolated disease = other mitral/aortic defects usually coexist
• presentation: symptoms related to elevated RA pressures such as edema, hepatosplenomegaly, ascites, fatigue, weakness
• diastolic murmur is soft, high-pitched, and brief at left sternal border
  o increases with inspiration
• JVD with giant venous A waves (whatever that means)
  o palpate liver to accentuate
• treatment: if symptomatic with mean valve gradient is $> 5$ mm Hg balloon valvuloplasty or valve replacement

**Pulmonic valve stenosis:**

- background:
  - most commonly congenital, presenting in adulthood
  - can also be acquired as a result of rheumatic fever or a complication of arrhythmia ablation procedures
- presentation: DOE, fatigue, presyncope, cyanosis
- JVP with a-waves
- split S2 with soft P2
- ejection click followed by crescendo-decrescendo (“diamond”) systolic murmur at left sternal border
- common to hear S4 as well
- investigation: echo RV, pulmonic valve pulls up a bit (“doming”) during systole due to the narrowed orifice, transpulmonic gradient

**Regurgitation (Insufficiency):** backward leakage while valve should be closed increased volume in chamber springing the leak

- mitral or tricuspid
- can be acute or chronic
- LV dysfunction can precede symptoms
- need to monitor LV function
- intervention is both for symptom management and preservation of cardiac function
- compensatory mechanism for increased volume is dilation: enlargement of heart chambers
- a result of eccentric hypertrophy: new sarcomeres are added in series to existing sarcomeres sarcomeres lengthen rather than thicken but ventricles dilate to the same extent = no change in proportion

**Aortic valve regurgitation:** causes increased end-diastolic vol in LV dilation of LV to accommodate increased end-diastolic pressure in LV backup into pulmonary circulation

- from aortic cusp or valve disease
- congenital: bicuspid or unicuspid
- infectious: rheumatic fever, infective endocarditis
- inflammatory: SLE, RA
- anorexic drugs
- from disease of aortic root: unhealthy tissue of cusp, annulus, or valve
- ex. Marfan syndrome, syphilis, ankylosing spondylitis, cystic medial necrosis, aortic dissection, trauma
- presentation
- if acute bacterial endocarditis, prosthetic valve dysfunction, aortic dissection
  o since there is no time for LV compensation, there will be flash pulmonary edema
  o classic physical findings will be absent
  o treatment: nitroprusside and surgery
- if chronic:
  o symptoms of left-sided heart failure
  o increased pulse pressure
  o diastolic murmur: soft, blowing decrescendo at 1st and 2nd pulmonic due to regurgitant spray hitting the bicuspid -can cause premature closure of the bicuspid
  o S3 gallop: high pitched at 1st and 2nd pulmonic from changed ventricular compliance
  o Austin Flint murmur: mid-diastolic, low frequency murmur at the apex from regurgitant flow competing with inflow from the left atrium = functional mitral stenosis
  o DeMusset sign: head bob with each heartbeat
water hammer (Corrigan pulse): radial and carotid pulses are abrupt/distensive with fast collapse
Traube sign (pistol shot femoral): booming systolic and diastolic sounds heart over femoral artery
Muller sign: systolic pulsations of the uvula
Duroziez sign: systolic murmur heard over the femoral artery when compressed proximally, diastolic murmur heard when compressed distally
Quincke sign: capillary pulsations seen in fingernails or lips
Hill sign: when the SBP in the popliteal space is > 20 mm Hg higher than brachial SBP

- investigation: same as for aortic stenosis
- treatment:
  - med: vasodilators (ACE or ARB or hydralazine + nitrates) reduce afterload, endocarditis prophylaxis in certain patients
  - aortic valve replacement if having symptoms of CHF, if acute with hemodynamic compromise, or if ejection fraction is < 55%

Mitral regurgitation: causes increased end-diastolic vol in LA dilation of LA to accommodate increased end-diastolic pressure in LA backup into pulmonary circulation

- background:
  - most commonly due to pathological weakening of connective tissue or mitral valve prolapse
  - other causes: ischemic LV dysfunction post MI, dilated cardiomyopathy, rheumatic fever, ventricular dilation, papillary muscle dysfunction, mitral annulus calcification, congenital abnormality, bacterial endocarditis, anorexic drugs
- presentation:
  - acute: flash pulmonary edema, cardiogenic shock, new murmur
    - from bacterial endocarditis or other infection, papillary muscle rupture, chordae rupture, necrosis
  - chronic: asymptomatic for years, then progressive L heart failure, afib
    - holosystolic murmur at apex with radiation to axilla
      - severity of leakage correlated with duration of murmur rather than intensity
      - exaggerate with valsalva
      - decrease with squatting
  - soft S1
  - S3 often present
  - JVD
  - laterally displaced apical impulse
  - investigation: EKG for LVH, echo, cath to grade severity
  - treatment:
    - ACEI to reduce afterload
    - diuretics
    - digoxin
    - endocarditis prophylaxis
    - if acute surgery for repair (vs replacement)

Tricuspid regurgitation: failure of the tricuspid valve to close properly during systole leakage into the right atrium

- background
- can be present in small degrees and be normal
- causes of mod-severe regurg: Ebstein's anomaly (displacement of valve towards apex), rheumatic disease, carcinoid, endocarditis, trauma from previous surgery
- presentation: symptoms of RV failure
- anasarca (woody looking edema)
- JVD with c-waves & hepatojugular reflux
- pulsatile liver
- holosystolic murmur at left sternal border
  - increases with inspiration
- afib
- treatment: only if severe
- diuretics for R-sided heart failure, digoxin for arrythmias, treatment for pulmonary HTN
- surgery: repair is better than replacement
- prognosis: not good if pulmonary HTN is present

**Pulmonic valve regurgitation:** the backward flow of blood into the right ventricle during diastole

- background:
  - most commonly from dilation of annulus from pulmonary HTN or dilation of pulmonary artery (connective tissue disorder)
  - also can be from infective endocarditis or complication from prior surgery
  - rarely from congenital malformations, carcinoid, syphilis, or rheumatic fever
- presentation
- can be tolerated asymptptomatically for many years if it the only defect
- palpable RV heave
- low-pitched diamond shaped diastolic murmur in 1st and 2nd pulmonic spaces
- if there is pulmonary HTN □ RV failure symptoms
- investigation: echo □ RV-PA pressure gradient > 50 mm Hg
- treatment: balloon valvotomy

**Mitral Valve Prolapse:** displacement of an abnormally thickened mitral valve leaflet into the left atrium during systole □ elongated chordae tendinae

- Background:
  - more common in women
  - associated with collagen vascular diseases such as lupus, RA, ankylosing spondylitis, Ehler-Danlos, or Marfan’s
  - usually presents in young adulthood
- Presentation: most patients are asymptomatic, otherwise fatigue, atypical chest pain, palpitations, anxiety disorders, postural orthostasis, and sympathetic hyperreactivity are common
- others: chest wall deformities, embolic event, bacterial endocarditis, arrythmias
- rarely progresses to mod-severe mitral regurgitation
- mid-systolic click +/- mitral regurgitation
- Treatment: endocarditis prophylaxis, beta-blockers for palpitations, aspirin for clot risk
- surgery if severe (similar criteria to mitral regurgitation, but lower threshold)

### 2.2 Vascular Disease

**Aortic Aneurysm:** a collection of blood between the vessel layers that causes the area to dilate 1.5+ times greater than normal

- aneurysm could be abdominal, thoracic, at the root, or in the arch
- most commonly below the kidney
- can also have thoracoabdominal aortic aneurysm

**Abdominal aortic aneurysm**

- background
- normally the aorta is ~ 2cm, it becomes aneurysmal when > 3 cm
- more common in men
- more commonly rupture in COPD patients
- vs pseudoaneurysm: a collection of blood and connective tissue located outside of the vessel wall
- caused by atherosclerosis and inflammation, with genetic/environmental influence
- categorized based on morphology: saccular, fusiform (most common)
- causes disruption of blood flow □ prothrombotic state
- rupture of the aneurysm most commonly occurs into the retroperitoneal space but is more deadly when it occurs in the peritoneal space
  - 80% mortality with rupture
- risk factors for development: tobacco use, age, HTN, hyperlipidemia, atherosclerosis, male, familial predisposition
- diabetes is protective!
- risk factors for rupture: rapid progression, female, FH, uncontrolled HTN, smoking, COPD
- prevention:
  - USPSTF recommends an US screen in all men age 65-75 who have ever smoked
  - Vascular Consensus Statement: screen all men 60-85, all women 60-85 if they have a cardio risk factor, and both sexes > 50 years old with FH of AAA
- presentation: usually discovered on accident during physical exam, otherwise may have pain in abdomen or back
  - if ruptured: severe pain, palpable abdominal mass, hypotension
- investigation
- abdominal US
- CT if US is not informative or pre-op
- treatment
- endovascular repair
  - stent is placed
  - considered elective in males at 5.5 cm and females at 4.5 cm
  - consider doing earlier if there is rapid expansion
  - indicated for higher risk patients with conducive anatomy (when stent can make it through the groin)
  - unfavorable anatomy may require open surgical repair
- open surgical repair: aneurysm replaced with graft
  - if not big, keep watching it and reimage, work on risk factor modification
  - don’t want to surgically intervene too early because the surgery has significant morbidity/mortality

**Thoracic aneurysm**: further classified as ascending, descending, or arch
- background
  - much less common than AAA
  - could be ascending or descending thoracic aorta, or arch
  - most to least common: aortic root or ascending aorta, descending aorta, arch
  - spontaneous rupture less common than AAA
  - symptomatic patients have greater chance of rupture
- **ascending thoracic aortic aneurysm**: usually due to cystic medial necrosis (elastin degeneration) weakening of aortic wall formation of fusiform aneurysm
  - often involves aortic root as well aortic valve insufficiency?
  - cystic medial necrosis may be a normal result of aging but is accelerated by HTN, connective tissue disorders, RA, and bicuspid aortic valve
  - causes other than cystic medial necrosis: vasculitis, syphilis, atherosclerosis
- **aortic arch aneurysm**: can be an extension of ascending or descending aneurysm
  - seen with history of trauma or deceleration injury (MVA, hockey, etc)
- **descending thoracic aorta aneurysm**: primarily caused by atherosclerosis
- presentation: most patients asymptomatic at diagnosis
  - potential vascular symptoms: aortic insufficiency, CHF, thromboembolic event
  - potential mass effect symptoms: SVC syndrome (compression from enlargement of aorta), tracheal deviation, cough, hemoptysis, dysphagia, hoarseness
  - steady, deep, severe substernal/back/neck pain
  - excruciating pain if ruptured
  - hematemesis if ruptured into the esophagus
- investigation:
- CXR widened mediastinum, enlarged aortic knob, tracheal displacement
- MRI or CT if negative
- echo
- treatment: surgeries are much more complicated than for AAA with greater risks, rarely done
- weigh risk of rupture (increased for Marfan’s or bicuspid aortic valve)
• when surgery is indicated (gender is not considered in these kinds of aneurysms):
  o ascending aortic aneurysm ≥ 5.5 cm
    ▪ aortic root replacement: Bentall or David procedure (David more common)
  o Marfan’s or bicuspid valve ≥ 5 cm
  o aortic valve replacement ≥ 4 cm
  o descending aortic aneurysm ≥ 6 cm

Aortic Dissection: a tear in the inner wall of the aorta causes blood to flow between the layers of the wall of the aorta, tearing the layers apart and creating a false lumen

• Background
  • can be acute or chronic
  • predisposition to tearing with connective tissue disorder, bicuspid aortic valve, or coarctation of the aorta
  • more common in men 60-70 years old
    ▪ but for females there is an increased risk in pregnancy in last trimester
  • often preceded by medial wall degeneration or cystic medial necrosis
  • tear usually goes in direction of blood flow but can go backwards
  • most occur in the ascending or descending aorta, just past aortic valve or at ligamentum arteriosum
  • usually a result of poorly controlled HTN

• Presentation
  • acute: sudden, excruciating, “ripping” pain in chest, hyper or normotensive, shock, pulse discrepancy, syncope, acute aortic regurg, focal neuro deficits or CVA due to nonperfusion of brain

• Investigation
  • CXR: widened mediastinum, left sided pleural effusion, or could look normal
  • EKG for LVH or signs looking like inferior MI (cusps associated with dissections are in the same region)
  • TEE
    • acute: do CT
    • follow up with serial MRA or MRIs

• Treatment
  • all pts need aggressive BP control
  • may be based on classification
    • Debakey classification: takes into account origin of dissection
      ▪ Debakey I = ascending aorta with extension to the arch and maybe beyond that
      ▪ Debakey II = ascending aorta only
      ▪ Debakey III = descending aorta only
    • Stanford classification: more commonly used, doesn’t care about the origin
      ▪ Stanford A = any involvement of ascending aorta
        • go directly to surgery
      ▪ Stanford B = not involving ascending aorta
        ▪ may be medically managed unless there are symptoms of rupture, ischemia, ongoing pain, uncontrolled HTN, or aortic regurg
        ▪ higher mortality procedure
  • chronic or asymptomatic: drugs + yearly re-imaging

Acute Arterial Insufficiency: Critical Limb Ischemia
• Signs of acute arterial occlusion, the 6 P’s: pain, pulselessness, pallor, paresthesia, paralysis, poikilothermia
• Causes:
  • traveling embolism from the heart, aorta, or large arteries
    ▪ common in those with afib
    ▪ also from valvular disease, prosthetic valve, ischemic disease
    ▪ rarely from a DVT
  • thrombus in situ (clot is formed where it came from): atherosclerotic plaque, trauma, or a result of hypercoagulable disorders
• Treatment: revascularization via IV heparin, thrombolitics, surgical thromboembolectomy, or surgical bypass

Peripheral Arterial Disease: systemic atherosclerosis distal to the aortic arch
At risk: smokers, diabetics, those with HTN, hyperlipidemia, or those with obesity

Presentation:
- intermittent claudication (cramps induced by exercise and relieved by rest) that is reproducible
  - in buttock, hip, thigh, upper or lower calf, or foot, depending on which artery is affected
- diminished peripheral pulses
- femoral bruits
- cool skin or abnormal skin color
- poor hair growth (look for those shiny hairless toes!)
- pain at rest, especially at night, due to ischemia
- ulceration or tissue necrosis

Investigation: must rule out Baker cyst, compartment syndrome, arthritis, nerve root compression, spinal stenosis, and venous claudication

compare arm BP to ankle BP (ankle/brachial index): take BP measurements all along legs to determine if there is variation in pressures
  - normally ankle SBP should be 10-15 mm Hg higher than arm SBP
  - if ratio is <0.9  peripheral vascular disease
  - if ratio is <0.7  intermittent claudication
  - if ratio is <0.4  patient will have pain at rest
  - if ratio is <0.1  impending tissue necrosis

CT to look for vessel narrowing

Treatment
- risk factor modification, smoking cessation, walking program
- antiplatelet therapy to prevent thrombi from the sluggish blood flow
- revascularization if necessary via open surgery or stent

Thrombophlebitis: sluggish blood flow causes local thrombosis
- At risk: those with varicose veins, pregnant or postpartum women, pts with blunt trauma, IVs, DVTs, or hypercoagulable states
- Presentation: inflammation, induration, erythema, and tenderness along a superficial vein (usually the saphenous)
- must be linear vs circular (commonly seen at IV sites, suggests cellulitis)
- fever and chills  septic phlebitis from IV line
- Treatment: local heat and elevation, bed rest, NSAIDs, anticoagulation of extension into deep veins
- symptoms resolve in 7-10 days

Chronic Venous Insufficiency: Varicose Veins
- From incompetent valves in the saphenous veins and branches due to damage or venous dilation
- Presentation: asymptomatic or dull/aching pain in legs that is worse after standing, pruritis
- may have history of DVT
- may also see brownish thinning of the skin above the ankles or mild edema
- Investigation: must look for causes such as retroperitoneal venous obstruction, AV fistula, congenital venous malformation
- rule out CHF, chronic renal disease, decompensated liver disease, lymphedema, autoimmune disorders, or arterial insufficiency from PAD
- Treatment: compression stockings, leg elevation, endovenous ablation, sclerotherapy, rarely greater saphenous vein stripping
- Complications: thrombophlebitis
- rarely ascends

Deep Venous Thrombosis: thromboembolism involving the deep veins of the lower extremities or pelvis
- Most frequently in deep veins of the calf
- At risk: those on prolonged bed rest, immobilized pts, airplane travelers, pts with malignancy or nephrotic syndrome or hypercoagulable state
- Prevention: DVT prophylaxis in surgical patients
- Presentation: could be asymptomatic, otherwise aching/dull calf pain that is worse with walking, edema, palpable cord, low grade fever, tachycardia
Homan’s sign is + half the time
Investigation: D-dimer, lower extremity US, VQ if PE suspected, hypercoagulable workup labs
diagnose using Wells criteria: score of less than 2 indicates DVT unlikely, > 6 highly likely
- clinical evidence or PE is #1 suspicion 3 points
- HR >100, immobilization or surgery in past 4 weeks, previous DVT or PE 1.5 points
- cancer or hemoptysis 1 point
Treatment: heparin + warfarin, thrombolytics, embolectomy, IVC filter if pt can’t be on warfarin or has recurrent clots
Complications: PE, ischemic limb, varicose vein formation, chronic venous insufficiency

Giant Cell Arteritis (Temporal Arteritis): systemic panarteritis affecting medium and large vessels
- Affected patients are > age 50
- Presentation: polymyalgia rheumatica, headache, scalp tenderness, visual symptoms, jaw claudication, throat pain, blindness
- Investigation:
  - sed rates, C-reactive protein, IL-6 elevated
  - CBC mild normocytic anemia with thrombocytosis
  - temporal artery biopsy
  - prednisone to prevent blindness
  - watch for thoracic aortic aneurysms (at greater risk from the arteritis)

Reynaud’s Disease: syndrome of paroxysmal digital ischemia caused by exaggerated digital arteriole response to cold or emotional stress
- Primarily affects young women
- First pallor then rubor
- May be primary or secondary to other disease states
- Presentation: fingers, toes, ears, nose
- Treatment: Ca channel blockers or nitrate therapy for chronic vasodilation, treat underlying condition

2.3 Myocardial and Pericardial Disease

2.3.1 Cardiomyopathy

Dilated cardiomyopathy: enlargement of the ventricles
- background
- most common kind of cardiomyopathy
- causes early cardiac dysfunction with gradual development of symptoms
- wide variety of causes with a final common pathway
  - from alcoholism (10+ years) direct myocyte toxicity
- presentation: patients are often asymptomatic incidental finding on routine physical exam
- LV dysfunction exercise intolerance, fatigue, weakness, dyspnea, systemic and pulmonary congestion
- symptoms of R-sided failure are a late finding with poor prognosis
- chest pain from ischemia or decreased coronary reserve
- cardiomegaly displaced apex with enlarged PMI
- normal or low BP with decreased pulse pressure
- may hear S3
- systolic murmur because dilated heart chambers pull on valves and don’t allow them to close all the way
- secondary mitral or tricuspid regurg
- investigation:
  - electrolytes, thyroid function tests, sed rates, antinuclear antibody, ferritin, HIV test
  - CXR
  - EKG for sinus tachycardia, interventricular conduction delays, Q waves
  - echo: ejection fraction, wall motion abnormalities/ischemia, underlying valvular disease
    - use findings to rule out pericardial disease
  - cardiac cath: to do coronary angiogram, assess pressures, maybe do a biopsy
- cardiac MRI: good information about infiltrative processes
- treatment: identify and treat the correctable cause of the cardiomyopathy
- alcoholic toxicities can be reversible
- heart failure symptoms: salt and fluid restriction, vasodilators, beta blockers, diuretics
- arrhythmia management: ICDs
- eval for transplant

**Hypertrophic cardiomyopathy**: a result of inappropriate hypertrophy of the septum with disorganized muscle bundles → hypercontractility of LV with reduced ventricular volume, fibrosis of tissue
- background:
  - hypertrophy unrelated to valvular disease or HTN
  - can be asymmetric or global enlargement of the septum (or apex if Japanese)
  - abnormal thickness and arrangement of wall muscle puts pt at risk for electrical dysfunction
  - in many HCM patients there is obstruction to outflow of blood from LV (dynamic outflow obstruction)
    - usually due to abnormal changing of pressure gradient during systole due to systolic anterior motion of the mitral valve (SAM, a kind of backwards mitral prolapse) □ LV must build up more pressure to overcome the regurg
      - increased O2 demand with increased filling pressures
  - most commonly in men ages 30-50
- can be familial
- risk of sudden death is higher in <30-35 year olds due to arrhythmias
- can progress to dilated cardiomyopathy
- presentation: clinical deterioration is slow, most are asymptomatic or only mildly symptomatic
- dyspnea, angina, fatigue, syncope, afib
- patients without gradient will have minimal findings: LV lift, S4
- patients with established outflow obstruction: forceful/displaced apical impulse from thickened muscle, systolic thrill, S4, harsh crescendo systolic murmur +/- mitral regurg murmur
- investigation:
  - must distinguish from aortic stenosis!
    - valsalva will increase the murmur of HCM while it will decrease the murmur of AS
    - carotid pulses will be brisk with mid-systolic decline in HCM while they are always sluggish in AS (parvus et tardus)
- labs:
  - EKG □ LVH, ST/T changes, giant T wave inversion (Japanese apical), Q waves
  - echo □ LVH, asymmetric septal hypertrophy, outflow obstruction with SAM/dynamic pressure gradient
  - cardiac cath to evaluate gradient
- treatment: manage symptoms
  - beta blockers for angina, dyspnea, pre-syncope
    - reduce outflow obstruction during exercise
    - reduce O2 demand
  - Ca channel blockers to reduce contractility, decrease outflow gradient, improve diastolic relaxation, and increase exercise capacity
  - treat tachyarrhythmias: pacemaker or AICD
  - surgical strategies: myectomy or mitral valve surgery, percutaneous ethanol ablation (inject alcohol into thickened septum to kill it)
  - transplant for those with LV dilation

**Restrictive cardiomyopathy**: abnormal diastolic function □ normal contractility but rigid and stiff ventricular walls
- background:
  - a result of an infiltrative process such as amyloid (deposition of abnormal heart proteins), hemochromatosis, sarcoidosis, eosinophilic disease, or glycogen storage disease
  - infectious cause: HIV poor prognosis
  - presentation: signs of R-sided heart failure predominate
• diastolic resistance to filling - pulmonary pressures must increase to deliver blood - pulmonary HTN -
wearing out of right atrium

Myocarditis: inflammatory process of the heart
• Background:
• most commonly due to infection
• can also be from allergic reactions, drugs, inflammatory illness, toxins (cocaine)
• mechanisms: straight-up invasion of the myocardium, deposition of toxins, or autoimmune attack
• can be a cause of idiopathic cardiomyopathy
• Presentation: anywhere from asymptomatic to fulminant heart failure
• chest pain, pericarditis, displaced PMI
• tachycardia out of proportion to fever
• Investigation:
• EKG - ST/T wave abnormalities
• echo - LV dysfunction
• labs: viral serologies, viral culture of stool/throat/pericardial fluid
• endocardial MRI to confirm myocarditis

2.3.2 Pericardial Diseases

Acute pericarditis: acute inflammation of the pericardium
• background:
• idiopathic or viral
• can be caused by MI, any kind of heart surgery, TB, neoplasm, or trauma
• tissue has increased vascularity with fibrous adhesions and exudate
• presentation:
• chest pain: pleuritic, hard to distinguish from ischemia, aggravated by laying down
• pericardial friction rub: pre-systolic, ventricular systolic, and early diastolic
• dyspnea from chest pain
• symptoms of underlying illness
• investigation:
• serial EKGs - diffuse ST elevation with inverted T waves, then return of ST to baseline with flat T waves, then T wave inversion, then normal T waves
  o may also have PR depression
• labs: inflammatory markers, myocardial markers
• echo for effusion
• pericardiocentesis for patients with tamponade
• biopsy?
• treatment: treat underlying cause
• watch for development of tamponade
• pain relief: bed rest, NSAIDs, aspirin, corticosteroids, colchicine
• antibiotics +/- drainage
• IV anticoagulants
• prognosis: usually self-limiting, some can have recurrent symptoms (give chronic colchicine therapy) B.)

Hemorrhagic pericarditis: usually caused by TB
• cause: spread via blood or endocarditis, post-op infection

Purulent pericarditis: usually caused by *Staph aureus* or *Strep pneumoniae*
• cause: spread via blood or endocarditis, post-op infection

Post-infarction pericarditis: from local inflammation
• causes pain for 1-6 weeks
• may hear friction rub even without pericarditis
• discontinue anticoagulation therapy if effusion develops
• treat with high dose aspirin (avoid NSAIDs and corticosteroids)
• symptoms can often blend with Dressler's syndrome: malaise, fever, pericardial discomfort, effusion, leukocytosis post-MI
• unknown cause, maybe autoimmune
• same treatment as post-MI pericarditis

Neoplastic pericarditis: frequently from lung cancer, breast cancer, leukemia, or lymphoma
• nodular tumor deposits in pericardium from hematogenous or lymphatic spread
• often asymptomatic

Cardiac tamponade: increase in intrapericardial pressure secondary to fluid buildup
• background:
  • causes diminished distension of chambers in diastole = decreased stroke volume
  • initial circulatory compensation with progressive decline
  • can be caused by any kind of pericarditis or effusion but most common in malignancy
• presentation:
  • Beck’s triad: hypotension (heart not filling properly), elevated venous pressure (increased pericardial pressure transferring to neck veins), muffled heart sounds due to increased fluid
  • also dyspnea, weakness, stupor, chest pain
  • elevated JVP, tachypnea, tachycardia, friction rub, pульсус paradoxus (BP variation)
• investigation:
  • CXR = heart may look large but otherwise no characteristic changes
  • EKG findings associated with acute pericarditis or effusion
    o electrical alternans: QRS keeps changing axis because there is so much fluid sloshing around
• cardiac cath treatment: volume resuscitation, pericardiocentesis, pericardial window

Constrictive pericarditis: thick, fibrotic pericardium restricts diastolic filling
• background:
  • constriction is symmetric = equalization of pressures throughout chambers = rapid early diastolic filling with limited late diastolic filling = no kick = reduced stroke volume
  • can be caused by progression of acute pericarditis to fibrous scarring
  • otherwise idiopathic, connective tissue disease, post-op, ESRD, post-radiation
• presentation:
  • Kussmaul’s sign: normal variance in pressures during breathing don’t occur because the heart is so encased = steady or rise in JVP
    o also occurs in restrictive cardiomyopathy but not in tamponade
• systemic congestion = hepatosplenomegaly, ascites, edema, pulmonary congestion
• may hear pericardial knock in early diastole
• no palpable apical impulse
• no S3
• may have pульсус paradoxus
• investigation
  • CXR
  • EKG = may be low voltage
  • echo = effusion
• treatment: pericardial stripping (pericardium peeled away from the heart)

2.4 Arrhythmias

2.4.1 Atrial Fibrillation
• Investigation
• 12 lead EKG
• CXR
• echo
• thyroid panel
• Holter monitor or stress test
• Treatment
• hemodynamically unstable □ cardiovert
• borderline stable □ gentle rate control with IVF support
• stable:
  o rate control: target this vs rhythm for less mortality
    ▪ not always tolerated in patients with cardiomyopathy or diastolic dysfunction (lose atrial kick)
    ▪ goal is < 110 during normal activity
    ▪ 1st choice is beta blocker
    ▪ 2nd choice is Ca channel blocker
    ▪ digoxin only works at rest
  o anticoagulation: weigh risk of stroke vs bleeding with CHADS2 score
  o cardioversion: electrical vs chemical
    ▪ only considered for symptomatic patients that can’t tolerate it, or those with first or sporadic episodes
    ▪ with onset < 48 hours can go right to cardioversion
    ▪ if ? onset or > 48 hours □ TEE before any cardioversion attempt
    ▪ warfarin for 4 weeks post cardioversion
    ▪ drugs post cardioversion to maintain sinus rhythm

2.4.2 Atrial Flutter
• Does not respond as well to rate or rhythm control drugs
• Stroke risk not as high as with afib
• First line treatment in symptomatic patients is ablation

2.4.3 Supraventricular Tachycardia
If not sinus, then it is
• AV nodal reentry tachycardia: most common kind, round-and-round circle
• P’s buried in QRS
• brief episodes
• long-term control with beta blockers or Ca channel blockers
• ablation of slow pathway is treatment of choice
• AV reentry tachycardia: retrograde conduction via accessory pathway
• P’s after QRS
• commonly occurs with Wolf-Parkinson-White
  ▪ DO NOT GIVE typical rate control meds as they preferentially slow the AV node and may promote aberrant rhythms to be conducted down the accessory pathway! = give procainamide until pathway is ablated
• junctional tachycardia
3  Dermatology Exam Notes

3.1  Introduction to Dermatology

3.1.1  Structure of the Skin

1. Epidermis: outermost
   - layers:
     - stratum corneum: flat dead cells that are 8-15 layers thick
     - stratum granulosum: transitional layer
     - stratum spinosum: differentiating tissue
     - stratum basale: mitotic tissue
   - cells:
     - most are keratinocytes that produce keratin and have immune function role
     - melanocytes: also found in hair follicles, brain, and eyes
       - same number in all races
     - Langerhans cells: APCs

   a. Dermis

   - layers:
     - papillary dermis:
     - reticular dermis: contains blood vessels, hair follicles, sebaceous glands, muscle, sweat glands
       - eccrine glands for thermoregulation
       - apocrine glands for scent
   - cells: fibroblasts for collagen synthesis, mast cells, macrophages

   b. Subcutaneous fat

3.1.2  Lesions

<table>
<thead>
<tr>
<th>Primary lesion type</th>
<th>Info</th>
<th>Example</th>
<th>Picture</th>
</tr>
</thead>
<tbody>
<tr>
<td>Macule</td>
<td>Flat, nonpalpable, &lt; 1 cm</td>
<td>vitiligo</td>
<td><img src="example.jpg" alt="Macule Example" /></td>
</tr>
<tr>
<td>Patch</td>
<td>Macule &gt; 1 cm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Papule</td>
<td>Raised, palpable, &lt; 1 cm</td>
<td>BCC, psoriasis, seborrheic keratosis</td>
<td><img src="example.jpg" alt="Papule Example" /></td>
</tr>
<tr>
<td>Plaque</td>
<td>Papule &gt; 1 cm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vesicle</td>
<td>Raised, contains clear liquid, &lt; 1cm</td>
<td>Chicken pox</td>
<td></td>
</tr>
<tr>
<td>--------------------</td>
<td>--------------------------------------</td>
<td>-------------</td>
<td></td>
</tr>
<tr>
<td>Bulla</td>
<td>Vesicle &gt; 1cm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pustule</td>
<td>Raised, contains inflammatory cells and fluid, variable size</td>
<td>acne</td>
<td></td>
</tr>
<tr>
<td>Nodule</td>
<td>Raised, solid, deeper than a papule, &lt; 1cm</td>
<td>Metastatic melanoma</td>
<td></td>
</tr>
<tr>
<td>Tumor</td>
<td>Nodule &gt; 1 cm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wheal</td>
<td>Firm, edematous papule or plaque that contains bound fluid, flat-topped elevations, transient</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Secondary lesion type**

<table>
<thead>
<tr>
<th>Scale</th>
<th>Info</th>
<th>Example</th>
<th>Picture</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crust</td>
<td>Collection of serum, blood, or pus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Erosion</td>
<td>Focal loss of epidermis that heals without scarring</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ulcer</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fissure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atrophy</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Special skin lesions**

<table>
<thead>
<tr>
<th>Excoriation</th>
<th>Info</th>
<th>Example</th>
<th>Picture</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comedone</td>
<td>Blackheads and whiteheads pathognomonic for acne;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Condition</td>
<td>Description</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-----------</td>
<td>-------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Milia</td>
<td>Small, superficial keratin cyst from sun damage from sun damage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cyst</td>
<td>Has a visible opening</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Burrow</td>
<td>Narrow, elevated tunnel from a parasite</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lichenification</td>
<td>Thickening of the skin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Telangectasia</td>
<td>Dilated superficial skin vessels</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Petechiae</td>
<td>Nonblanchable blood deposit &lt;1 cm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Purpura</td>
<td>Petechiae &gt; 1 cm</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### 3.1.3 Diagnostic Procedures
- Magnification
- **Diascopy**: vascular lesions
- Special preps
- mineral oil: good for scabies
- KOH: good for fungus & yeast, always scrape border of lesion
- **Tzanck smear**: helpful for virus detection in vesicle fluid, looks for multinucleated giant cells
- Gram stain
• Biopsy
• Patch testing: for suspected contact allergies (type IV delayed-onset hypersensitivity)
• Wood’s lamp: UV light with nickel oxide filter detects certain porphyrin-producing organisms
• some tinea capitis agents fluoresce green
• erythrasmas (Corynebacterium minutissimum) fluoresce coral red
• vitiligo fluoresces white
• porphyria cutanea tarda fluoresces pink or orange
• Acetowhiteness: vinegar turns dead skin white

3.2 Common Bacterial Skin Infections

3.2.1 CA-MRSA
• Infections by his are on the rise
• Clinically and microbiologically different from hospital MRSA
• presentation is dermatologic
• more commonly in pediatric and non-white patients (Native Americans, blacks), homeless, populations in close quarters, daycare kids, competitive athletes
• Investigation:
• lesions may look more purplery
• must culture and do sensitivities
• Treatment: I&D, +/- antibiotics for large lesions, pedes, pts with systemic symptoms (Septra, clinda, linezolid)

3.2.2 Common Bacterial Skin Infections
Superficial infections:
• impetigo: scabbing eruption with lesions that can be bullous (clear or turbid fluid) or non-bullous (honey-crusted erosions with erythema)
• agents: caused by Strep pyogenes or Staph aureus
• subtypes:
  o ecthyma: a deep type of impetigo that extends into the dermis; ulcerative with a thick, tender yellow-gray crust
• agents: Strep, Pseudomonas, Staph
• children and elderly at risk
risk factors: trauma, underlying dermatosis (atopic dermatitis or herpes), poor hygiene, previous antibiotics, warm temps, high humidity
new lesions by auto-inoculation
treatment: topical mupirocin (MRSA) or Altabax (MSSA), systemic cephalosporins or dicloxacillin
intertrigo: nonspecific infection of rubbing skin surfaces

agents:
- bacterial: Strep pyogenes, Strep agalactiae, Pseudomonas
  - borders are more defined, no satellite lesions
  - neck folds in babies = Strep
  - if caused by Strep it will really stink!
- erythrasma: a type of bacterial intertrigo caused by Corynebacterium minutissimum

- common in the groin, also in feet webs, axillae
- brownish color
- diabetics at increased risk
- bright red with Wood’s lamp
- treatment: topical benzoyl peroxide, mupirocin, +/-imidazoles, systemic doxycycline, macrolides
- yeast: highly inflammatory
  - confused with psoriasis, seborrheic dermatitis, atopic dermatitis
  - treatment: topical antibiotics, steroids?

Pyodermas
- types:
  - abscess: localized, wall-off pus collection that progresses from firm to fluctuant
    - can develop at any cutaneous site
  - furuncle: deep-seated erythematous nodule with a rim of fine scale that develops a central necrotic plug
    - aka epidermal inclusion cyst (technically NOT a sebaceous cyst)
    - can develop in hairy areas or areas of friction
  - carbuncle: large area of coalescing abscesses or furuncles
  - risk factors: trauma, chronic Staph carrier, diabetes, obesity, poor hygiene, minor immunologic deficits
• prevention: antibacterial soaps daily, monthly Betadine or Hibiclens showers, control of predisposing conditions
• treatment: I&D with removal of loculations (may need to wait and do compresses until it is soft), +/- systemic antibiotics (shouldn’t need them)

**Soft tissue infections**

• types:
  • *cellulitis*: infection of deep dermal and subcutaneous layers with indistinct borders
  • agents: *Strep pyogenes*, *Staph aureus*
  • affects any cutaneous site
  • *erysipelas*: a more superficial type of cellulitis characterized by sharp, raised borders with clear demarcation from uninvolved skin
    • caused almost exclusively by *Strep pyogenes*
    • LE and face most affected
• risk factors: trauma, surgery, mucosal infection, underlying dermatoses, immunodeficiency
• presentation: acute, diffuse skin inflammation with warmth and tenderness, may have systemic symptoms
• treatment: therapy must be systemic!
• penicillinase-resistant synthetic pencillins (cloxacillin, dicloxacillin) or macrolide if allergic
• supportive: rest, elevation, warm compresses

**Infectious folliculitis**: infection of upper portion of hair follicle

• subtypes:
  • *pseudofolliculitis barbae*: aka barber’s itch, a result of foreign body reaction to ingrown hairs
  • keloidal folliculitis: found at nape of neck, often coalesces into furuncles over months to years
  • more common in blacks
  • treat with cyclic antibiotics
• hot tub folliculitis: caused by *Pseudomonas*, short incubation of 1-5 days

• lesions clear spontaneously
• agents can be fungal, viral, or bacterial
• bacterial: most commonly *Staph aureus*, also gram negatives, *Pseudomonas*
  - evolves into pyodermas
• risk factors: shaving, friction, immunosuppression, topical steroids
• prevent with antibiotic soaps
• presentation: single, scattered papules or pustules that are not tender or pruritic
• predilection for the face, scalp, neck, legs, trunk, and buttocks
• treatment: usually a 7-10 day course of oral antibiotics that cover *Staph* = 1st gen cephalosporin or macrolide if allergic

3.2.3 Less Common Bacterial Skin Infections

**Erysipeloid**: single plaque with sharp borders usually seen on the hand
• caused by *Erysipelothrix rhusiopathiae* and usually seen in poultry/fish/animal carcass handlers

**Necrotizing soft tissue infections**: continuum of disease that begins with soft tissue infection and progresses to multi-organ failure
• agents: usually polymicrobial, can be *Strep pyogenes*, *Staph aureus*, *Clostridium*, *Bacteroides*, *Peptostreptococcus*, *Enterobacter*, *Proteus*, *Pseudomonas*
• types:
  - **Ecthyma gangrenosum**: caused by *Pseudomonas*
  - **Fournier’s gangrene**: perineum, caused by *E. coli*, *Klebsiella*, *Proteus*, or *Bacteroides*
    - male predominance
• infection initiated by an insect bite or surgical wound, then spreads hematogenously
• common sites: perineum, extremities, trunk
• risk factors: PVD, impaired cellular immunity (DM), IVDU, smoking, alcohol, HTN, CAD, chronic steroids, lymphedema, varicella lesions, genital trauma or infection
• presentation: pain out of proportion to physical findings

**Acute lymphangitis**: infection of subcutaneous lymphatic channels usually from trauma → erythematous linear streaks extending from the wound to site of skin break

• agent: usually *Strep pyogenes*, less commonly *Staph aureus*, rarely *Pasteurella multocida*, *mycobacteria*, *Sporothrix*
• treat with antibiotics to cover *Strep* and *Staph*

**Cutaneous anthrax**
• acquired from infected animals or their products, contaminated feed, soil
• begins as papulovesicular lesion → necrosis → eschar-covered ulcer
• treat with cipro or doxycycline

**Cutaneous mycobacterial infections**

• single nodule that ulcerates or crusts, joined to other nodules by satellite lesions
• lesions usually clear spontaneously but excision may help
• anti-TB drugs not helpful, these are different species

**Vibrio infections**

• macular area develops into bullous lesions that are often symmetric → necrotic ulcers
• initial cellulitis doesn’t look any different from regular cellulitis
• skin disease can develop secondary to enteric infection
• at risk: immunocompromised, high serum Fe, occupational exposure to fish, seafood, brackish water

3.3 **Fungal and Viral Infections of the Skin**

3.3.1 **Superficial Fungal Infections**

**Dermatophytoses:** infections of the hair/nails by keratin-loving fungi

• **dermatophytes:** Microsporum, Trichophyton, Epidermophyton
• the most common skin fungal infections
• risk factors: atopy, steroid use, dry skin, occlusion, high humidity
• transmission: person-to-person, fomites, animal-to-human, environmental
• infections are known clinically as “ringworm” or “tinea + ____”
• **tinea pedis:** foot infection characterized by erythema, scaling, vesicles, maceration in web spaces

•

•

• risk factors: increased sweating, shoes, contaminated public floors
• more common in males
• multiple presentations:
  • can have involvement of toenails or bacterial 2° infection
  • interdigital
  • “moccasin” with involvement of heels, soles, lateral foot
  • inflammatory/bullous with erupting vesicles
• treatment:
  • topical: 2-4 weeks of imidazoles or allylamines
  • oral: for severe or refractory cases; 2-6 weeks of same agents
  • exposure to air
• **tinea cruris:** aka jock itch, subacute or chronic infection of the groin and medial thighs with erythematous, scaling, well-demarcated plaques
- o risk factors: obesity, tight clothing
  o supar
  o investigation: differentiate from candidiasis and erythrasma
  o treat topically
- **tinea corporis**: subacute infection of the neck, trunk, or extremities with sharp-bordered plaques of varying sizes possibly with smaller pustules or vesicles within the border
  o lesions enlarge peripherally and may have an area of central clearing
  o treat topically
- **tinea capitus**: scalp infection; ecto/endothrix depending on penetration of hair shaft, can see broken-off hairs resembling black dots or **kerion** (swollen, painful nodule)
  o most common in kids 6-10 steroids and 6-12 weeks of antifungals (DOC terbinafine-dermatophytes only, not **Candida**) if kerion is present
  o can add topical ketoconazole or selenium sulfide to reduce transmission

**Candidiases**
- **cutaneous/intertriginous**
- infections involve sites where maceration and occlusion create a warm, moist environment
  o breasts, abdominal folds, axillae, groin, web spaces, angular cheilitis, diapers
- risk factors: obesity, diabetes, hyperhidrosis, steroids
- treatment: nystatin (**Candida** only), imidazoles, steroids sparingly
- mucocutaneous
- nail
- systemic

**Tinea (pityriasis) versicolor**: opportunistic infection caused by Malassezia furfur □ multiple well-demarcated, hyper- or hypopigmented macules with fine scaling
- white, pink, shades of brown
- upper trunk, axillae, groin, thighs, face, neck scalp
- stimulated by oils, greasy cosmetics
- investigation: characteristic “spaghetti and meatballs” under microscope
- treatment: topical selenium sulfide, imidazoles, oral ketoconazole (single dose sweaty workout style)
- lesions may persist for some time even after treatment

3.3.2 Invasive/Subcutaneous Fungal Infections

**Background:**
- usually transmitted via traumatic implantation
- agents are saprophytes living in soil and vegetation in warm climates
- Sporothrix, Exophila, Fonsecaea, Madurella, Pseudallescheria
- infections progress slowly
- suspect in patients with outdoorsy habits with persistent lesions unresponsive to antibiotics

3.3.3 Viral Infections of the Skin and Mucous Membranes

**Viral exanthems:** skin eruptions secondary to systemic infection
- agents: rubella (German measles), varicella, roseola (sixth disease), erythema infectiosum (fifth disease)
- similar manifestations can also be seen in *Strep pyogenes*, *Staph aureus*, and meningococcal infections
- common in kids and adolescents, whereas adults have immunity to many of these infections
- presentation:
  - rash may be preceded by a prodrome of fever, malaise, sore throat, nausea, vomiting, abdominal pain
  - may be accompanied by oral lesions (“enanthems”)

**Hand-foot-mouth disease:** common systemic viral illness characterized by oral lesions and a vesicular exanthem limited to the distal extremities

- agent: Coxsackie virus and some other enteroviruses
- epidemics every 3 years

**Non-genital herpes simplex**
- herpes labialis: aka cold sores, fever blisters; grouped vesicles on an erythematous base
- usually HSV-1 but can be HSV-2
- usually perioral but can be anywhere on the face and auto-inoculate to other areas
- -treatment: penciclovir, acyclovir, valacyclovir
- herpetic whitlow: herpes on the fingertip
- herpes gladiatorum: herpes anywhere else on the external body
• complications: systemic symptoms, conjunctival autoinoculation, Bell's palsy, erythema multiforme, 
  *eczema herpeticum*, severe infection in immunocompromised

**Varicella-zoster virus**

- prevention: Zostavax vaccine
- single dose indicated for patients over 60
- primary infection is varicella, secondary is zoster (shingles)
- treatment: high dose acyclovir within 72 hours of onset
- prednisone if over age 50
- analgesics
- complications: post-herpetic neuralgia, pain at site of shingles for years, ophthalmic complications, 
  hemiplegia

**Molluscum contagiosum**: distinct flesh colored or pearly white papules with umbilicated centers

- agent is a poxvirus
- common in children and sexually active adults
- transmission is skin to skin
- treatment: lesions usually resolve spontaneously but can take a year, otherwise cryotherapy

**HPV warts**: see warts lecture

### 3.4 Contact Dermatitis

#### 3.4.1 Background

- An eczematous dermatitis caused by exposure to environmental substances
- substances are either irritants (not immunologically mediated) or allergens (type IV hypersensitivity)
  - irritants: organic solvents, soaps
    - high concentration required for response
    - onset is gradual
    - rash borders are indistinct (unless acute?)
  - allergens: low molecular weight haptens
    - low concentration
    - onset is rapid with sensitization
    - defined borders
- May require sunlight acting on substance to cause the dermatitis
- Presentation:
  - inflammation is acute, subacute, or chronic
  - occurs in characteristic distribution
- Investigation:
  - distinguish irritant from allergic dermatitis by provocation tests
    - apply substance to antecubital fossa twice daily for a week
      - contact urticaria 15-30 min after application suggests allergic etiology
  - patch testing
    - indicated when dermatitis is chronic, recurrent, or deters work or life activities
    - test site should be free of dermatitis
    - patch stays on for 48 hours and is read at 72-120 hours:
      - +? = doubtful reaction: mild redness only.
      - + = weak, positive reaction: red and slightly thickened skin.
      - ++ = strong positive reaction: red, swollen skin with individual small water blisters.
+++ = extreme positive reaction: intense redness and swelling with coalesced large blisters or spreading reaction.

IR = irritant reaction. Red skin improves once patch is removed. NT = not tested.

- these test for type IV hypersensitivities rather than type I (which scratch skin tests check for)
- complicated by people with “angry back syndrome” (skin hypersensitivity nonreproducible testing results)
- re-test with serial dilutions
- dilution of irritants will reduce reaction while dilution of allergens will not

- histology is not helpful
- Treatment:
  - allergen avoidance
  - topical or systemic steroids
  - emollients or other barriers
  - oral antihistamines
  - UVB and PUVA to help response subsite

3.4.2 Irritant Contact Dermatitis
- Accounts for 80% of cases of dermatitis
- Common irritants: water, soaps, detergents, wet work, solvents, greases, acids, alkalies, fiberglass, dusts, humidity, chrome, trauma (chronic lip licking)
- Acute: occurs within minutes to hours of exposure, accompanied by pain, burning, stinging, or discomfort exceeding itching
- acids, alkalies
- involves tissue destruction
- presentation: bullae and erythema with sharp borders
- Chronic: onset within 2 weeks of exposure, with many people in the same environment similarly affected
- low-level irritants
- presentation: poorly-demarcated erythema, scale, pruritus
- Presentation:
  - dry, fissured, thickened skin, usually palmar
  - macular erythema, hyperkeratosis, or fissuring predominating over vesicular change
  - glazed, parched, or scalded-appearing epidermis
  - not likely to spread
  - vesicles juxtapositioned closely to patches of erythema, erosions, bullae, or other changes
- Investigation:
  - differential: dermatophytosis, psoriasis, pustular psoriasis, dyshidrosis-pompholyx, atopic dermatitis, pustular bacterid, keratoderma climactericum
  - negative patch test
  - healing process proceeds without plateau upon removing of the offending agent

Atopic Dermatitis: an inflammatory, chronically relapsing, non-contagious and pruritic skin disorder
- Cause uncertain, could be a variety of factors
- Seen in patients with a history of environmental allergies, asthma, eczema
- Investigation:
  - patch test to look for pustular reactions

3.4.3 Allergic Contact Dermatitis
- Common allergens:
  - metallic salts
  - plants
  - allergens from Compositae plant family: parthenolide, tansy, feverfew, pyrethrum
  - can also be airborne
  - fragrances: balsam of Peru, fragrance mix, benzyl alcohol, benzaldehyde
nickel has cross-reactivity with chocolate, tea, and whole wheat

cross-reactivity between similar antigens: poison ivy ~ mango ~ poison oak ~ lacquer tree ~ cashew shell ~ Indian marking nut ~ black varnish tree

preservatives: methylchloroisothiazolinone, quaterium-15, bronophol, imidazolidinyl urea, diazolidinyl urea, DMDM hydantoin

formaldehyde in wrinkle-free clothing, especially cotton and rayon

propylene glycol: also in brownie mix

oxybenzone: in moisturizers, cosmetics, shampoos, nail polish, lip sticks

bacitracin and neomycin (and possibly gentamycin and other -mycins)

thiuram: in rubber gloves, insoles, box toes, lining, adhesives, disinfectants, germicides, insecticides, soaps, shampoos

mercaptobenzothiazole: in rubber shoes, cutting oil, antifreeze, greases, cements, detergents, flea and tick sprays

bleached rubber: plain rubber is ok, but once it gets bleached you better watch out!

chrome: leather tanning agents

sorbic acid (food preservative)

Causes a T-cell mediated response to kill cells

Accounts for 20% of cases of contact dermatitis

Presentation:

acute: macules, papules, vesicles, bullae

chronic: lichenified, scaling, fissured lesions

uncommon on scalp, palms, soles, or other thick-skinned areas that allergens can’t get through

uncommon to have mucous membrane involvement

systemic with an oral or IV agent on top of previous topical sensitization

painful, dry, fissured, hyperkeratotic eczema beginning at nail margin

  o associated with tuliposide A allergen from Alstroemeria (Peruvian lily)

nickel can penetrate rubber gloves

parabens can be used on unaffected body parts without producing a dermatitis reaction on affected body parts

sorbic acid allergy will not improve with topical steroids because the acid is present in the steroid cream

Investigation:

nickel allergy: dimethylglyoxime test using sweat, pressure, and friction with a nickel-plated object

parabens can have a false negative on patch test

bleached rubber allergy will have a negative patch test to plain rubber

Contact Urticaria

Strongest inciting agents: benzoic acid, sorbic acid, cinnamic acid or aldehyde, foods (chicken, fish, veggies), topical meds

Can lead to contact dermatitis with repeat exposures

Latex Hypersensitivity

Not a contact dermatitis because it is a type I (immediate onset) hypersensitivity, with symptoms within 1 hour of exposure

Risk factors: atopy (previous sensitization), frequent glove use, hand eczema, childhood surgeries

Presentation: skin as well as respiratory and mucosal symptoms

3.5 Common Inflammatory Dermatoses

3.5.1 Papulosquamous Diseases
Psoriasis: a systemic, immunologic, genetic disease manifesting in the skin +/- joints
- a hyperproliferation of the epidermis with altered differentiation inflammation of the epidermis and dermis with accumulation of T-cells and cytokines
- flared by streptococcal infections, injury, trauma, drugs (Li, beta-blockers, antimalarials, systemic steroids), low humidity, emotional stress, overtreatment
- presentation:
  - lesions are most commonly on the scalp, elbows, legs, knees, arms, trunk, lower body, palms and soles
    - occur at sites of trauma
  - red scaling papules coalesce into round-oval plaques with a silvery white adherent scale
  - pustules may border lesions
  - variable pruritus
- extracutaneous manifestations: nails (onycholysis, yellowing, pitting), geographic tongue, joints
  - arthritis: destructive polyarthritis, ankylosing spondylitis, DIP arthritis
  - asymmetric or symmetric
- associated with cardiovascular disease, depression, lymphoma
- types of psoriasis:
  - chronic plaques: sharply defined erythematous scaling plaques in ~symmetric dist
    - most common type
    - lasts months to years
    - can have nail involvement
  - erythrodermic psoriasis: generalized erythema with scaling and exfoliation
    - accounts for 10% of cases
    - can occur at any age
    - presentation: patients are very sick, with hypo- or hyperthermia, protein loss, dehydration, renal and cardiac failure
    - investigation: may need to do a punch biopsy to differentiate from contact dermatitis
  - pustular psoriasis: individual or coalescing sterile pustules 1-10 mm that are generalized or localized

- guttate psoriasis: small papules of short duration
  - usually in kids and young adults
  - associated with recent streptococcal infection
  - can also see the “typical” plaque lesions on the knees and elbows

- intertriginous
- treatment: strategy is to control disease, decrease area involved, decrease erythema, scaling, and lesion thickness, maintain remission, avoid adverse effects, and improve QOL
- topical therapies:
  - anthralin
  - steroids
  - tars
  - vit D analogs: very expensive
  - retinoids such as tazarotene
  - Taclonex ointment
- phototherapy: UVB (vs tanning beds that are mostly UVA)
- systemic therapies:
retinoids: acitretin
- anti-cytokines: methotrexate
- immunomodulators:
  - cyclosporine
  - biologics: adalimumab, alefacept, etanercept, infliximab, ustekinamab
- treating depression can help the psoriasis

**Seborrheic dermatitis:** a chronic inflammatory papulosquamous dermatosis with genetic and environmental causes

- possible agent: Pityrosporum ovale
- types:
  - infants: cradle cap
    - treatment: remove scale, treat infection, reduce inflammation
  - young children: tinea amiantacea and blepharitis
  - adolescents and adults: classic seborrheic dermatitis
- causes: inflammation, bedridden, chronic illness, neurologic disease
- presentations:
  - fine, dry, white scalp scaling
  - involvement of eyebrows, nasolabial folds, external ear canals, postauricular fold, presternal area
  - less common: involvement of the axillae, groin, umbilicus
- investigation:
  - persistent or resistant cases should be cultured for dermatophytes
  - AIDS-associated seborrheic dermatitis
    - may precede AIDS symptoms
    - severity often parallels clinical deterioration
- treatment:
  - frequent washing of all involved areas
    - use anti-dandruff shampoos
  - topical steroids
  - maintenance therapy may be needed

**Pityriasis rosea:** a common, benign, usually asymptomatic self-limited dermatosis

- may have viral origin (HSV-7 or 8)
- most patients are between 10 and 35
- presentation:
  - may have recent history of infection with fatigue, headache, sore throat, lymphad
  - initially just one 2-10 cm herald lesion that is raised with a fine scale
  - 7-14 days later diffuse eruptions show up on trunk dermatomes that are salmon pink in white patients and hyperpigmented in black patients
    - fine ring of scale known as collarette scale
• can mimic rash of secondary syphilis although rash is in a different location
• lesions are asymptomatic or pruritic at night or with heat
• treatment: most beneficial within first week
• oral antihistamines and topical steroids
• oral prednisone
• UVB phototherapy
• prognosis: eruption clears in 1-3 months

**Lichen planus:** inflammatory, pruritic, planar, polyclanar purple papules
• possible causes:
  • exposure to gold, chloroquine, methyldopa, penicillamine
  • exposure to film processing chemicals
  • secondary syphilis
  • graft vs. host disease s/p bone marrow transplant
• usually occurs in 40s
• risk factor: liver disease
• presentation: varies from a few chronic plaques to generalized eruption
  • various patterns: actinic, annular, atrophic, follicular, guttate, hypertrophic, linear, localized, vesiculobullous = may need to do histology because there are so many presentation forms
  • primary lesion is 2-10 mm flat-topped papule with an irregular angulated border
• surface of lesions have lacy-reticulated pattern of white lines (*Wickham's stria*) correlating to areas of epidermal thickening
• most commonly on wrist flexors, forearms, legs above the ankles
• variable pruritus
• treatment:
  • topical steroids
  • intralesional steroids
  • systemic steroids
  • cyclosporine
  • retinoids
  • methotrexate
  • PUVA
  • antihistamines
• prognosis: eruption can clear in one year but may recur; unpredictable course E.) Tinea corporis

Syphilis

Drug reaction

### 3.6 Cutaneous Manifestations of Systemic Diseases

#### 3.6.1 Autoimmune Disorders

**SLE:** > 85% of patients will have skin findings, and some only have skin findings
• acute cutaneous SLE: localized or generalized rash of the face, scalp, upper extremities
• malar or “butterfly” rash
• papules, papular urticaria
• scaly plaques (more subacute)
• discoid lesions (more chronic)
• bullae
• palmar erythema
• subacute cutaneous SLE: lesions of the shoulders, forearms, neck, upper trunk
• usually no facial lesions
• not strictly associated with SLE; can be other diseases
• lesions are annular or papular (psoriaform)
  • begin as small erythematous papules with scale
  • can also uncommonly resemble erythema multiforme
• chronic cutaneous SLE (discoid lupus): face, neck, and scalp
• localized or generalized
• lesions are classically discoid
  o begin as well-defined scaling plaques that extend into hair follicles
  o expand slowly and heal with scarring, dyspigmentation, or atrophy
  • can resemble nummular eczema, psoriasis
• other manifestations: alopecia, oral ulcers, photosensitivity, lupus profundus (panniculitis; subcutaneous nodules), vasculitic lesions, livedo reticularis (lacey purple), urticaria

**Dermatomyositis:** one of the idiopathic inflammatory myopathies
• classic lesion is heliotrope: erythematous or violaceous macular rash of eyelids and periorbital area, often accompanied by edema
  • other lesions:

  • Gottron's papules: slightly raised pink, dusky red, or violaceous papules over the dorsal MCP/PIP or DIP joints, or over the wrists, elbows, or knees
  • Gottron's sign: macular rash over same areas as papules
  • V sign: macular photosensitivity over anterior neck, face, or scalp
  • shawl sign: macular rash over posterior shoulders and neck
  • poikiloderma: mottled red-brown discoloration from previous dermatomyositis lesions
  • calcifications on the elbows, trochanteric, and iliac areas
  • linear erythema over the extensor surfaces of the hands
  • nail changes: periungual erythema, telangiectasias, cuticle overgrowth

**Scleroderma**

• localized lesions: rarely progress to systemic
• morphea: localized plaques in a band-like distribution
• linear scleroderma: line of thickened skin that can affect muscle and bone underneath
  • most common up through 20s
- **systemic:** *sclerodactyly* (tight hands), Raynaud’s, sclerosis of face, scalp, and trunk, periungual telangiectasia, pigmentation abnormalities, *calcinosus cutis* (subdermal calcifications)

**Vasculitides**
- Dermal manifestations are usually a result of disease secondary to infection (*Strep pyogenes*, Hep B, Hep C), drugs (sulfonamides, penicillins), connective tissue disease
- Hallmark is palpable purpura
- Primarily on the Les
- Can progress to ulceration and necrosis

### 3.6.2 Endocrine Disorders

**Diabetes**
- Cutaneous manifestations:
  - **acanthosis nigricans:** thickened, hyperpigmented, velvety plaques on neck, axillae, or body folds that are associated with obesity and insulin resistance
  - **diabetic dermopathy:** atrophic, < 1 cm brown lesions on lower extremities
    - A result of microangiography
    - Most common cutaneous manifestation of DM
    - Lesions are asymptomatic and resolve after 18-24 months
  - **diabetic bullae:** appear spontaneously, usually on the hands and feet
    - May be associated with peripheral neuropathy or longstanding DM2
    - Three types: sterile (heal without scarring), hemorrhagic (scar), and non-scarring (triggered by sun exposure)
  - **necrobiosis lipoidica diabeticorum:** flesh-colored or red-brown papules that evolve into waxy plaques
    - Center of lesion becomes yellow and atrophic +/- telangiectasias
    - From degeneration of collagen
    - Usually on shins
  - Treatment: topical or intralesional steroids
  - Infections
  - Lesions secondary to peripheral neuropathy or PVD
  - Diabetic ulcers
    - Can lead to osteomyelitis
  - **granuloma annulare:** uncommon benign skin disorder of papules and plaques in an annular distribution
    - Hands, feet, knees, and elbows
    - Localized, generalized, or perforating
    - More common in women

### 3.6.3 Immune Disorders

**Dermatitis herpetiformis:** chronic skin disorder associated with Celiac disease; erythematous papules or plaques studded with vesicles
- Due to IgA deposition in the skin in response to gluten
- classically located on the elbows, knees, buttocks, scapular areas, scalp
- symmetric and intensely pruritic
- treatment: gluten-free diet, dapsone, sulfapyridine

**Urticaria & angioedema:** localized swelling of skin or mucous membranes
- immunologic and non-immunologic causes
- more common in females
- characteristic lesion is a transient, pruritic wheal that is warm
- not cellulitis because it doesn’t hurt!
- urticaria:
  - mediated by IgE, cytotoxic/immune complex deposition, physical factors (heat, cold, pressure, light), direct mast cell release, malignancy, infection, or emotional stress
- classification:
  - **acute urticaria:** occurs once and lasts days up to 6 weeks
    - triggers: foods, drugs, infection, stress, latex, environmental agents
  - **chronic urticaria:** recurrent or constant urticaria of 6 weeks or greater
    - usually due to autoimmunity or chronic disease

- investigation:
  - labs: CBC, liver panel, thyroid panel, renal panel, ESR or CRP
  - biopsy if vasculitis is present
- patients can have systemic symptoms such as fever
- angioedema is urticaria that extends into the subcutaneous tissue
- most commonly involves the face but other sites can be affected
- treatment:
  - H-1 or H-2 blockers
  - doxepin
  - glucocorticoids if acute (not if chronic!)
  - epinephrine
  - around-the-clock antihistamines if chronic

**Sarcoidosis:** chronic multisystem granulomatous disease
- skin involvement in 25% of patients
- lesions can be diverse and non-specific, but some are specific
- usually asymptomatic
- predilection for scarred/tattooed areas
- macules, papules: brown, yellow, or purple on face or extremities
- nodules: brown or purple on face, trunk, and extremities
- plaques: annular or serpiginous +/- scales, on butt, trunk, extremities
- classic lesion is **lupus pernio:** infiltrating violaceous plaque on the nose, cheeks, ears, or lips

### 3.6.4 Metabolic Disorders

**Xanthelasma:** soft yellow plaques occurring near medial canthus of eyelid
- more prominent on upper lid
- relatively rare
- more common in women in 40s-50s
- half of cases are associated with elevated lipid levels
- treatment: reduction of serum lipids, surgical excision

### 3.6.5 Venous Insufficiency

- Multiple skin manifestations secondary to decreased or absent return of venous blood and increased capillary pressure
- Presentation:
- pitting edema
- varicose veins
- stasis dermatitis: appears eczematous +/- papules, excoriations, pruritus
  - on LEs and ankles
  - often mistaken for cellulitis
  - can be concomitant with irritant contact dermatitis or bacterial superinfection
  - treatment: compression, oral antibiotics, topical steroids
- hyperpigmentation: mottled blue and purple
- skin fibrosis (lipodermatosclerosis)
- venous ulcers: usually above the medial malleolus
  - bacterial superinfection is always present
- atrophie blanche

### 3.6.6 Misc. Disorders

**Erythema nodosum**: a cutaneous reaction to antigenic stimuli (infection, drugs like OCPs, IBD, maligna
- erythematous nodules limited to extensor surfaces of LEs
- very painful
- other symptoms: fever, arthralgias

**Erythema multiforme**: cutaneous immunologic response to varied antigens such as drugs, infection, systemic illness
- macule □ papule with vesicle or bulla in the center (iris lesion or target lesion)
- occurs on hands, forearms, feet, face
- usually symmetric
- can be painful or pruritic
- ranges from mild to severe
- patients present very ill, with fever and high white counts
- treat with steroids

**Stevens-Johnson syndrome** and **toxic epidermal necrolysis**: widespread bullae on trunk and face with mucous membrane involvement
- can have epidermal detachment
- treatment: systemic steroids with monitoring of fluids and electrolytes

**Infective endocarditis**: Osler nodes, Janeway lesions, subungual hemorrhages

**Meningococcemia**: petechiae, purpura, necrosis

**Disseminated gonococcal infection**: hemorrhagic pustules

**Lyme disease**: erythema migrans, lymphocytoma cutis, acrodermatitis chronica atrophicans

### 3.7 Acne

#### 3.7.1 Background

- Acne vulgaris is an inflammatory disease of the hair follicles and sebaceous glands of the skin
- open comedones: blackheads
- closed comedones: whiteheads
- inflammatory papules, pustules, and cysts
- Pathogenesis is multifactorial, involving hormones, keratin, sebum, and bacteria
- begins as comedones in the hair follicles
- androgens stimulate sebaceous glands to produce more sebum
- *P. acnes* proliferates in this atmosphere □ further plugging and inflammation □ foreign body reaction
- rupture
- can lead to cysts, scarring, keloids, or pyogenic granulomas
- Affects face, neck, upper trunk, and arms
• Most common in teens 15-18, with no gender preference
• Usually ends by age 25
• Can be flared (but not caused) by sweating, chocolate, cell phones, hands on face, cosmetics
• Form of acne:
  • comedonal acne: blackheads and whiteheads predominate
  • inflammatory acne:
  • cystic acne (acne conglobata): characterized by cysts, fissures, abscess formation, deep scarring
    o more common in men
    o associated with oily skin
    o begins in puberty and worsens with time
    o more on trunk, less on face

3.7.2  Acne Treatments

Behavioral modification
• no picking or exfoliation
• only mild, gentle cleansing twice a day
• consider avoiding milk
• use oil free, non-comedogenic products

Topical comedolytics
• retinoids: increase cell turnover, prevent new comedones, chemically exfoliate
  • use a pea-sized amount all over skin once a day- not for spot treatments!
  • gels more effective than cream but more drying = best use with oily skin
  • allow 4-6 weeks for full effect; acne will get worse before it gets better
  • side effects: dry skin, irritation, sun sensitivity
• contraindicated in pregnancy!
• forms:
  o tretinoin:
  o adapalene:
  o tazarotene:
• azelaic acid: antikeratinic, antibacterial, anti-inflammatory
• better option for patients who want to get pregnant
• glycolic acid & salicylic acid preparations: chemically exfoliate and enhance penetration of other topicals by reducing pH
• caution: sun sensitivity

Topical antibacterials
• benzoyl peroxide: the workhorse against acne
• no drug resistance
• concentrations from 2.5 to 10%
• clindamycin
• with or without benzoyl peroxide (with decreases resistance)
• contraindicated in patients with h/o UC, pseudomembranous colitis
• erythromycin
• with or without benzoyl peroxide
• high P. acnes resistance
• sulfur-containing preparations
• metronidazole
• more for treating rosacea
• dapsone: for treatment of inflammatory acne
• usually paired with a retinoid

Oral therapies
• oral antibiotics: allow 2-4 weeks to work
• minocycline: anti-inflammatory as well as antibacterial
• more expensive
• side effects: vertigo, bluish-gray discoloration of skin, mucosa, teeth, and nails, lupuslike syndrome (long-term), serum sickness, hepatitis, pseudotumor cerebri
• contraindications: pregnancy, peds
• doxycycline:
  • side effects: photosensitivity, GI upset, vaginitis
  • contraindications: pregnancy, peds
• tetracycline:
  • side effects: photosensitivity, GI upset, staining of teeth, photo-onycholysis, hepatitis, pseudotumor cerebri
  • contraindications: pregnancy, peds
• erythromycin: used less frequently due to emerging resistance
  • good option for pregnancy and peds
• side effects: GI upset, vaginitis
• others: clindamycin, ampicillin, cephalosporins, Septra (2nd line due to side effects)
• oral isotretinoin: for severe, nodular, cystic, inflammatory, recalcitrant acne
  • tightly regulated by FDA via iPledge system due to strong teratogenicity
  • requires monthly visits with a registered provider
  • usually one 5 month course is sufficient
  • some patients may need additional course after a 2 month rest period
  • used alone without any other acne treatments
  • side effects: dry skin, cheilitis, headaches, myalgias, arthralgias, bone pain, osteopenia, mood changes or depression, elevated glucose, elevated TG, hepatotoxicity, decreased night vision, hearing changes
  • oral hormonal treatments: for patients with adult acne, hirsutism, PCOS, premenstrual flares
  • oral estrogens (OCPs): suppress sebaceous gland uptake of testosterone and peripheral metabolism of testosterone
  • all of them will work
  • side effects: HTN, hypercoagulability, hyperkalemia
• spironolactone: for poor OCP candidates
  • acts as androgen receptor blocker
  • decreased serum testosterone
  • side effects: menstrual irregularities, hyperkalemia, breast tenderness
  • contraindications: pregnancy (category X)

Additional therapies
• intrallesional steroids: risk of causing permanent divet
• comedo extraction
• photodynamic therapy
• laser therapy
• CO2 lasering for icepick scarring
• chemical peel
• Algorithm:
  • mild, comedonal acne: start with a topical retinoid
  • add benzoyl peroxide or topical antibiotics if needed
  • moderate acne with papules and pustules: start with a topical retinoid + benzoyl peroxide (or benzoyl peroxide + topical antibiotic)
  • add oral antibiotic if needed
  • severe nodular acne: start with topical retinoid + benzoyl peroxide (or benzoyl peroxide + topical antibiotic) + oral antibiotics
  • refractory severe acne: oral isotretinoin

3.7.3 Acne Vulgaris Lookalikes
• Hydradenitis suppurativa (acne inversa): plugged sweat duct, inflammation and bacterial growth, rupture, ulceration and fibrosis, sinus tract formation
• a chronic and relapsing condition
- seen in the axillae, inguinal folds, perianal area
  - rarely on the scalp
- hallmark is double comedone
- treatment: oral antibiotics, topical antibiotics and washes, intralesional triamcinolone as needed, oral prednisone course, surgical I&D or excision
- Steroid acne
- Drug acne: Li, tetracyclines (paradoxically), phenytoin, OCPs, isoniazid D.) Cutting oils and other occlusives
- Infectious folliculitis
- Rosacea: etiology not well understood
- triggers: hot or spicy foods, alcohol, exercise, sun
- resembles acne but also has flushing, telangiectasia, and lingering erythema on the forehead, chin +/- eyes
  - no comedones!
- late manifestation is rhinophyma (large bulb-shaped nose)
- treatment:
  - topical metronidazole, sulfacetamide + sulfur, azelaic acid
  - time-released oral doxycycline for anti-inflammatory effects
  - laser therapy
- Perioral dermatitis: etiology not understood
- grouped 1-2 mm papules on an erythematous base that goes on for weeks or months
  - no comedones
- can also be perinasal or periorbital
- treatment:
  - avoid cinnamon, tartar control toothpaste, whitening agents, heavy facial moisturizers, topical steroids
  - topical antibiotics

3.8 Warts

3.8.1 Background
- Caused by HPV infections of skin keratinocytes (cutaneous warts) or mucous membranes (condyloma acuminatum)
- occur in areas of skin trauma
- 100 serotypes = multiple infections
- Regression is dependent on cell-mediated immunity = occur more often in immunosuppressed patients
- Don’t have “roots” as they are confined to the epidermis
- Cause necrosis of capillaries (may only be seen after paring of lesion with surgical blade)
- Differentiate from callous by interruption of normal skin lines
- Oncogenic potential

3.8.2 Clinical Subtypes of Cutaneous Warts
- Verruca vulgaris: the common wart
  - common in ages 5-20
  - presentation: verrucous surface, thrombosed capillaries, loss of dermatoglyphics
    - can have fingerlike projections in kids
    - periungual are hard to treat without damaging nail matrix
- Verruca plana: flat wart
  - common in ages 5-20
  - commonly spread by shaving
  - presentation: flat-topped pink to brown papules, usually in linear formation
    - predilection for the face, dorsal hands, wrists, knees
- Verruca plantaris: plantar wart
  - presentation: verrucous surface, thrombosed capillaries, often coalesce into a “mosaic”
• prefers pressure points on the feet

3.8.3 Mucous Membrane Warts: Condyloma Acuminata

• Background:
  • often on the genitals, most common STD
    o cervix, vulvovaginal skin, anus, penis, perianal area
  • highest risk for oncogenesis with subtypes 16 and 18
  • Presentation: lobulated surface that is cauliflower-like, gray or pink
  • high-risk lesions are often hyperpigmented
  • Investigation:
    • can be misdiagnosed as moles or skin tags
  • cervical exam to look for dysplasia
  • Treatment:
    • cutaneous symptoms can spontaneously resolve
    • therapy to stimulate immune response
  • Prognosis: often recur following treatment, as tissue is killed rather than the HPV itself

3.8.4 Wart Treatments

• Physical destruction:
  • Cryotherapy: liquid nitrogen application, preferably twice
    o repeat every 2-4 weeks as needed
    o can cause hypopigmentation
  • Laser
  • Cautery
  • Duct tape occlusion
  • Excision
  • Cantharadrin (beetle juice): causes blistering □ risk of scar = not for face
    o done in office
  • Podophyllin gel: applied at home
  • Retinoids +/- occlusion
  • Salicylic acid
  • 5-fluorouracil
  • Immunomodulation:
    • imiquimod
    • cimetidine
    • squaric acid

3.9 Hair and Nails

3.9.1 Background

• Total number of hair follicles is present at birth
• Hair anatomy and physiology:
  • lanugo is the fine, soft nonpigmented hair in utero that is shed before birth
  • vellus hair is soft, nonpigmented, and short
    o lacks a medulla
  • terminal hairs are pigmented with variable length
    o androgens trigger vellus ↔ terminal hair switch
• hair follicle:
  o segment from skin opening to sebaceous gland opening is the infundibulum
  o from the sebaceous gland to the bulge is the isthmus
  o bulge formed by insertion of erector pili muscle into the follicle
  o transient portion that goes through stages of telogen, anagen, and catagen is the lower follicle
    □ anagen: growth phase that 85% of hairs will be in
- average duration of 3 years for the scalp
- max hair length determined by anagen duration
  - **catagen**: involution phase between growth and resting where all cell division stops
    - 3% of hairs are in this at any given time
    - lasts 10-15 days
  - **telogen**: the resting phase where club hair is produced
    - 12% of hairs
    - lasts 3 months as the old hair is pushed out
      - bulb at bottom of follicle contains stem cells
      - plucking hairs leads to breakage above this level
- color determined by eumelanin (brunettes, blondes, and grays) or pheomelanin (redheads)

3.9.2 Alopecia

Normal daily hair loss is 75-150 hairs

Causes:
- **alopecia areata**: increased lymphocytes around bulb  □ patchy, nonscarring alopecia
- associated with thyroid disease, stress, vitiligo, autoimmune disease, DM, atopic dermatitis
- a common cause of hair loss
- in men, women, and children
- presentation: see “exclamation point hairs” or associated nail pitting
  - can involve entire scalp
- treatment:
  - small patches will grow back on their own
  - topical and intralesional steroids speed up regrowth
- prognosis: worse with acute onset, extensive hair loss, or hair loss beginning over the ears
- androgenetic alopecia: inherited
- the most common form of hair loss
- presentation:
  - men: recession of frontal hairline, decreased length and thickness of hair shaft
  - women: later onset and less progressive than males
    - advanced loss associated with hirsutism
- treatment:
  - minoxidil (vasodilator), finasteride (5-alpha reductase inhibitor)
    - can’t stop or hair will fall out!
  - hair transplant
- **anagen effluvium**: loss of hair due to chemotherapy or radiation
- because anagen is most metabolically active it is targeted
- **telogen effluvium**: diffuse shedding of hair as more follicles are shifted from anagen to telogen
- occurs after stressful events, childbirth, massive blood loss, high fever, surgery, drugs, thyroid disease, crash dieting, car accident, stopping OCPs
  - more hairs are retained anagen phase during pregnancy
- loss can occur up to 3 months after event!
- almost always temporary with normal regrowth
- **trichotillomania**: pleasure or relief from pulling hair out
- investigation:
  - see pigment casts and **achordion** (stretching of epithelium) on biopsy
- **traction alopecia**: caused by constant pulling on hair follicles from wearing tight cornrows and braids
  - most commonly on the frontotemporal scalp
  - initially nonscarring but can progress to scarring
- Investigation:
  - history: meds, family h/o hair loss, recent fever, severe illness, general anesthesia, hyperandrogenic signs
    - hair pull test: anagen:telogen ratio should be 10:1
    - scalp biopsy: one vertical section and one for horizontal

### 3.9.3 Nail Diseases

<table>
<thead>
<tr>
<th>Condition</th>
<th>Info</th>
<th>Picture</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psoriasis</td>
<td>Oil spots, pitting</td>
<td><img src="image" alt="Psoriasis" /></td>
</tr>
<tr>
<td>Nail mechanical trauma</td>
<td></td>
<td><img src="image" alt="Nail Damage" /></td>
</tr>
<tr>
<td>Muercke's lines</td>
<td>Alternating white/pink lines, blanchable, associated with decreased protein synthesis (cirrhosis or nephrotic syndrome)</td>
<td><img src="image" alt="Muercke's Lines" /></td>
</tr>
<tr>
<td>Paronychia</td>
<td>Inflammation of nail fold, common in diabetics, wait staff, bartenders. Acute is Staph and chronic is Candida.</td>
<td><img src="image" alt="Paronychia" /></td>
</tr>
<tr>
<td>Beau's lines</td>
<td>Horizontal grooves in nail plate as a result of growth arrest s/p severe illness, fever, pregnancy al grooves in nail</td>
<td><img src="image" alt="Beau's Lines" /></td>
</tr>
<tr>
<td>Half &amp; halfails (Lindsey's nails)</td>
<td>Seen in chronic renal disease.</td>
<td><img src="image" alt="Half &amp; Halfails" /></td>
</tr>
<tr>
<td>Blue nails</td>
<td>Caused by Wilson's disease, argyria, ochronosis</td>
<td><img src="image" alt="Blue Nails" /></td>
</tr>
</tbody>
</table>
3.9.4 Nail Tumors

<table>
<thead>
<tr>
<th>Tumor</th>
<th>Info</th>
<th>Picture</th>
</tr>
</thead>
<tbody>
<tr>
<td>Digital mucous cyst (myxoid cyst)</td>
<td>Translucent papule at proximal nail fold.</td>
<td></td>
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<tr>
<td></td>
<td>Communicates with DIP and contains clear jelly. Can cause longitudinal ridge or indentation in nail plate distal to growth.</td>
<td></td>
</tr>
<tr>
<td>Melanoma</td>
<td>Dark pigmentation at the proximal nail fold (Hutchinson’s sign) or pigmented longitudinal nail streaks. Normal in blacks but can be true melanoma in whites!</td>
<td></td>
</tr>
<tr>
<td>Squamous cell carcinoma</td>
<td>Can mimic a nail fold wart.</td>
<td></td>
</tr>
</tbody>
</table>

3.10 Human Ectoparasites

3.10.1 Background
Clinically relevant arthropods are those that suck blood and transmit disease, those that bite/sting causing lesions, those that inject venom or allergens.

3.10.2 CRABS: Cutaneous Reactions to Arthropod Bites
- Allergic or inflammatory
- Cause a variety of lesions: transient erythema, bullae, hemorrhagic ulcers, necrosis
- papular urticaria: hallmark arthropod bite lesion; 2-8 mm erythematous, papulovesicular lesions usually in clusters
  - common culprits are fleas, mosquitoes, bedbugs
  - kids with pre-existing atopic dermatitis will have increased sensitivity to bites

3.10.3 Spider Bites
Most clinically important:
- black widow:
  - likes dark, dry places like basements, crawl spaces
  - bite is from defensive female
  - venom is a potent neurotoxin
  - only 25% of bites evoke a serious reaction: muscle cramping, HTN, tachycardia
    - treat these rxns with antivenom
  - brown recluse: like dark, quiet places like shoes and clothing
  - bites are defensive
• toxic protein in venom stimulates platelet aggregation and neutrophil infiltration □ necrosis and systemic effects
• bite lesion has a black center with minimal peripheral erythema
• no antivenom available

Generalized treatment:
• RICE
• tetanus booster
• analgesics
• antibiotics if there is a secondary infection

3.10.4 Mites

Scabies:
• spread by skin to skin or sex
• can live for 48 hours on clothing, bedding, and furniture
• highly contagious
• make burrows and lay eggs and poop in them □ intensely pruritic papules and pustular rash that is worse at bedtime
• predilection for the fiber webs, wrist flexors, elbows, axillae, penis, external genitalia, feet, ankles
  o babies < 1 year can get scabies from the neck up
• immediate and delayed hypersensitivity rxns
• normal incubation for first infection is 21 days
  o sequential infections have immediate rxn due to memory response
• “Norwegian” scabies make severe crusting and have a heavy infestation
• infected patients usually have underlying immunodeficiency
• variable pruritus
• investigation: scraping under oil immersion for mite, feces, eggs
• treatment: permethrin cream, lindane lotion (known neurotoxin, banned in Ca)
• apply at night and wash off in morning
• usually only single application needed
• can also do single dose ivermectin but it’s hard to find
• treat all family members!
• wash all bedding and clothing in hot water

Chiggers: aka redbugs, jiggers
• larval form injects digestive fluid into host to form a feeding tube
• feeds for 3-4 days then drops off
• presentation:
• causes papules or hives at suck site
  o predilection for the ankles, backs of knees, groin, axillae
• severe itching within 1 day
• treatment: immediate bath in hot soapy water, topical antihistamines, topical steroids, nail polish to starve it off?

Dust mites:
• feed on human scale
• associated with asthma, maybe atopic dermatitis

3.10.5 Ticks

Lesions:
• papule at site of bite from antigenic tick saliva
• local reaction of swelling, erythema
• classic lesion of erythema migrans 4 days to 3 weeks after bite
• only occurs half the time and is not diagnostic of Lyme
• can also get vesicles, malar rash, urticaria, nodules
• hardens after a few days  pruritus, tenderness

Uncommon lesions:
• rare granulomatous reaction
• lymphocytoma cutis: bluish nodule at site of bite or in remote location such as earlobe, areola, neck
• acrodermatitis chronica atrophicans: bluish erythema + edema

3.10.6 Lice

Body and head louse are *Pediculosis*

• lesions:
  • causes small erythematous papules on the axillae, neck, shoulders
  • hemorrhagic puncta and linear excoriations
  • vesicles
  • blueish brown macules at bite site called *maculae ceruleae* from heme breakdown
  • vectors for epidemic typhus, trench fever
  • hair of black children is rarely infested
  • presentation: scalp pruritus, excoriations, cervical adenopathy
  • treatment: permethrin cream, malathion
  • must re-treat in one week to treat eggs that hatch

Pubic louse is *Phthirus*

• can also infest eyelashes
• public lymphadenopathy
• treatment: lindane or permethrin

3.10.7 Bedbugs

• Painless bite  papular urticaria or vesicular, eczematous rash
• tend to be in linear clusters

3.10.8 Moths, Butterflies, Caterpillars, Bees and other Vespids, Fire Ants

• Caterpillars can cause dermatitis as well as systemic illness with urticaria and airway hypersensitivity
• the asp caterpillar is the most dangerous in the US
  • sting produces intense pain with a train-track pattern
• Gypsy moths can cause pruritic rash
• Bees
• treatment: remove stinger, 1st gen antihistamine?, oral steroids for severe local reactions
• Fire ant stings produce papular eruptions that cause a systemic response in 16% of the population
4 Emergency Medicine Exam Notes

4.1 Chest Pain Presentations & Cardiac Emergencies

4.1.1 Approach to Chest Pain Patient
- Evaluate if hemodynamically stable or unstable
- Potential etiologies: CV, pulm, GI, msk, psychogenic
- Typical symptoms may not always be present
- Assume worst until proven otherwise!
- Patients with acute MI may appear seriously ill or completely well

4.1.2 Initial Diagnostic Studies
- EKG within 10 minutes: could look normal, repeat as needed
- CXR
- Labs:
  - Cardiac biomarkers: myoglobin (old, not cardiac specific), CK (+ early), CK-MB, LDH (older test), troponin (+ for 10-14 days)
  - CBC: possible infection/cholecystitis
  - CMP
  - D-dimer
  - PT/PTT: in case someone needs to go emergently to the OR
  - Liver panel
  - Echo: LV and valve function, wall motion abnormalities, pericardial effusion, septal defects
  - V/Q scan or spiral CT to rule out PE

4.1.3 Chest Pain Observation Unit
- A unit for low-probability patients to be ruled out for MI
- No ongoing chest pain or ischemic EKG changes
- Serial EKGs, cardiac biomarkers, telemetry
- Provision of rapid treatment and resuscitation if needed while not sending someone home too early

<table>
<thead>
<tr>
<th>Non-CV CP: Pulmonary Origin -CV CP</th>
<th>Presentation &amp; PE</th>
<th>Investigation</th>
<th>Treatment</th>
<th>Special</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary embolism</td>
<td>Pleuritic chest pain</td>
<td>Dyspnea, non-pleuritic chest pain possible, anxiety, cough, syncope - Hypotension, shock, distended neck veins</td>
<td></td>
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<tr>
<td>Pneumothorax</td>
<td>Tracheal deviation, hyperresonance with breath sounds unilaterally.</td>
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<tr>
<td></td>
<td>Tension pneumo: hypotension, shock, distended neck veins.</td>
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<tr>
<td>Pneumonia</td>
<td>SOB, cough, fever, sputum production, rales, dullness</td>
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<tr>
<td>Asthma, COPD, Pulmonary edema</td>
<td>See Resp Emergencies lecture</td>
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<tr>
<td>Pleurisy</td>
<td>Inflammation of pleurae, friction rub, low grade fever</td>
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<tr>
<td>Pulmonary HTN</td>
<td>Loud P2 Ventricular lift</td>
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<thead>
<tr>
<th>Non-CV CP: GI Origin</th>
<th>Presentation</th>
<th>Investigation</th>
<th>Treatment</th>
<th>Special</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heartburn</td>
<td>Squeezing or pressure pain on exertion or rest,</td>
<td>May have relief with antacids or NG</td>
<td>Innervation of heart, esophagus, and stomach are similar - similar symptoms</td>
<td></td>
</tr>
<tr>
<td>Esophageal perforation</td>
<td>Acute, severe, unrelenting, diffuse pain in neck, chest, or abdomen</td>
<td>Radiation to back or shoulders</td>
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<tr>
<td></td>
<td></td>
<td>Exacerbation on swallow</td>
<td></td>
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<tr>
<td>Mallory-Weiss tear</td>
<td>See GIB lecture</td>
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<tr>
<td>PUD</td>
<td>Burning epigastric pain, postprandial symptoms or relief with food, n/v, weight loss, anorexia bleeding</td>
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<td></td>
</tr>
<tr>
<td>Cholecystitis</td>
<td>Epigastric/RUQ visceral pain, fever, chills, n/v, anorexia, pain radiation to back or scapula</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pancreatitis</td>
<td>Midepigastric, piercing pain that is constant, radiates to back, low-grade fever, chills, N/V, abdominal distension w/ exacerbation when supine, tachycardia, hypotension</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Non-CV CP:Other Origin</th>
<th>Presentation</th>
<th>Investigation</th>
<th>Treatment</th>
<th>Special</th>
</tr>
</thead>
<tbody>
<tr>
<td>Musculoskeletal</td>
<td>Sharp pain worse with movement or palpation</td>
<td>Responds to NSAIDs</td>
<td>Due to inflammation of chest wall structures Caution: some MI pts also have reproducible chest wall tenderness</td>
<td></td>
</tr>
<tr>
<td>Psychogenic: anxiety or pain disorder</td>
<td>Fleeting chest pain w/ variable onset or duration, reproducible symptoms on palpation but not with exertion</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Acute Coronary Syndrome</th>
<th>Presentation &amp; PE</th>
<th>Investigation</th>
<th>Treatment</th>
<th>Special</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unstable angina</td>
<td>May be new, sudden onset chest pain with SOB, nausea, diaphoresis May now be at greater frequency or severity or with less activity Chest pain at rest or nocturnally Pain now refractory to nitrates</td>
<td>EKG showing ST depression or T wave inversion Cardiac enzymes negative</td>
<td>Admission Morphine, O2, aspirin, NG Serial EKGs and enzymes β-blocker, ACEI, anticoagulation, statins Cardiac cath Clopidogrel after cath</td>
<td></td>
</tr>
</tbody>
</table>
| Myocardial infarction | Sudden onset chest pain, nausea, diaphoresis, SOB  
Chest pain > 30 min not responsive to NG  
Hypovolemia  
HTN or hypotension  
Tachy or bradycardia  
Signs of CHF  
Systolic murmurs  
Friction rub by day 2 | EKG showing early peaked T waves, ST elevation, Q waves, J point elevation | 33% are fatal  
1st EKG is negative in 40% of patients having MI  
Complications: arrhythmias, CHF, RV infarction, ventricular rupture, mural embolus, stroke, pericarditis, postinfarction angina |

| Sudden cardiac death | | | Usually ventricular tachycardia secondary to CAD, cardiomyopathy, or other disorder  
Usually occurs in early morning hours |

<table>
<thead>
<tr>
<th>Other Cardiac Problem</th>
<th>Presentation &amp; PE</th>
<th>Investigation</th>
<th>Treatment</th>
<th>Special</th>
</tr>
</thead>
</table>
| Stable angina pectoris | Deep, substernal pressure-like pain, radiates, SOB, transient (2-30 min)  
Ppt by emotional stress or physical exertion  
HTN, S4, bruits, AV nicking, papilledema, cotton wool spots, corneal arcus, xanthelasma, xanthomas, CHF, S3, murmurs  
Responds to rest or SL NG  
Distended neck veins with myocardial ischemia | Cardiac enzymes negative  
↑cholesterol and glucose  
CXR may show CHF or arterial calcifications | Risk factor modification  
Aspirin, β-blocker, ACEI, nitrates, statins  
Stent or CABG |
## Aortic dissection

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Treatment</th>
<th>Increased Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute or chronic Sudden onset retrosternal and back pain, HTN, hypovolemia, syncope, shock, pulse discrepancies, tamponade</td>
<td>EKG may show infarct pattern, LVH CXR showing widened mediastinum, L pleural effusion Bedside echo is highly sensitive and specific CT 1.) Achieve hypotension and bradycardia with β-blocker and nitroprusside 2.) Surgical repair for Stanford type A or medical therapy for Stanford type B (unless there is rupture, ischemia, or connective tissue disorder)</td>
<td>Increased Risk in pregnancy, connective tissue disease, bicuspid aortic valve or aortic coarctation Usually in ascending aorta Debakey and Stanford classifications</td>
</tr>
</tbody>
</table>

## AAA

<table>
<thead>
<tr>
<th>AAA (unruptured, see acute abdomen for rupture)</th>
<th>EKG may show infarct pattern, LVH CXR showing widened mediastinum, L pleural effusion Bedside echo is highly sensitive and specific CT</th>
<th>Abdominal US</th>
<th>Close monitoring Surgical repair depending on degree of aneurysm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Usually asymptomatic Prominent aortic pulsation Epigastric fullness or low back/hypogastric pain Pain is gnawing, hours to days in duration, nonpositional</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

## Thoracic aortic aneurysm

<table>
<thead>
<tr>
<th>Thoracic aortic aneurysm</th>
<th>CXR may show Need CT or MRI to be diagnostic Coronary angiography Close monitoring</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Can be asymptomatic Subternal, back, or neck pain CHF, ischemia, thromboembolism Mass effects: SVC syndrome, tracheal deviation, cough, hemoptysis, dysphagia, hoarseness</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Condition</td>
<td>Symptoms</td>
<td>Tests</td>
<td>Treatment</td>
</tr>
<tr>
<td>--------------------</td>
<td>---------------------------------------------------------------------------</td>
<td>-----------------------------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Pericarditis</td>
<td>Pleuritic, sharp, stabbing chest pain, radiation to shoulders, back, or neck</td>
<td>EKG showing diffuse ST elevation, CXR usually normal, CBC, BUN/Cr to rule out uremia</td>
<td>Outpatient if stable, treatment of underlying cause, patient if myocarditis, uremic pericarditis, enlarged cardiac silhouette or unstable</td>
</tr>
<tr>
<td></td>
<td>Pain is worse on inspiration or movement, worse supine, relieved by sitting up and leaning forward</td>
<td>Infection serologies, Thyroid panel, Echo Pericardiocentesis usually not needed until tamponade</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Low grade fever, dyspnea, friction rub, palpations or dysphagia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac tamponade</td>
<td>Beck’s triad: hypotension, elevated systemic venous pressures, small quiet heart, shock, distended neck veins, pulsus paradoxus, SOB, weakness, tachycardia</td>
<td>EKG shows low voltage</td>
<td>True emergency! Volume resuscitation, Pericardiocentesis, Consider pericardial window</td>
</tr>
<tr>
<td></td>
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</tr>
<tr>
<td>Hypertensive urgency</td>
<td>Severe headache, SOB Stable/no new end-organ damage or none at all BP usually &gt; 220/120</td>
<td>Observation with short-term labetalol, clonidine, captopril with 24 hour f/u</td>
<td>Due to patient nonadherence or inadequate regimen</td>
</tr>
<tr>
<td>Hypertensive emergency</td>
<td>Evidence of rapid progression to target end organ damage MI, acute CHF, ICH, pulmonary edema, stroke, renal failure, AMS, aortic dissection, eclampsia BP usually &gt; 220/140 Papilledema = malignant HTN</td>
<td></td>
<td>Admit Immediate, gradual reduction of BP not to normal range but to ≥ 160/110 to avoid cerebral, renal, or cardiac ischemia</td>
</tr>
</tbody>
</table>
### Pulmonary edema CHF
- See resp emergencies lecture

### Arrhythmias
- Hypotension, shock, distended neck veins

### Valvular abnormalities
- Mitral prolapse: mid-systolic click, inverted T waves
- Aortic stenosis: systolic ejection murmur transmitted to carotids, LVH
- Aortic regurgitation: diastolic murmur transmitted to carotids, wide pulse pressure, LVH

## 4.2 Infectious Disease Emergencies

<table>
<thead>
<tr>
<th>Misc. ID</th>
<th>Presentation &amp; PE</th>
<th>Investigation</th>
<th>Treatment</th>
<th>Special</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sepsis</td>
<td>Infection + SIRS (temp &gt; 38 or &lt; 36, HR &gt; 90, RR &gt; 20 or PaCO2 &lt; 32, WBC &gt; 12,000 or &lt; 4,000 or &gt; 10% bands) - Weakness, lethargy, AMS, hypotension</td>
<td>CBC - LFTs, bicarb, Cr, glu - PT/PTT - Lactate (marker of tissue hypoxia) - Blood cultures - UA &amp; culture - Sputum culture - CXR</td>
<td>1.) Respiratory stabilization 2.) Circulation: insert central venous catheter, IVF, pressors 3.) Empiric AB - 3rd gen cephalosporin - β-lactam + inhibitor - carbapenem + vanco</td>
<td>- Mortality 40-50% - E. coli, Strep pneumo, Staph aureus, GAS, anaerobes, MDR gram negs  - Fungi</td>
</tr>
<tr>
<td>Severe sepsis</td>
<td>Sepsis + 1+ related organ dysfunction (coagulopathy, thrombocytopenia, ileus, acute pulmonary injury, AMS, acute oliguria, Cr &gt; 0.5, ↑bili)</td>
<td>Sterile body fluid culture if suspected infection source</td>
<td>4.) Adjuncts: steroids, nutritional</td>
<td></td>
</tr>
<tr>
<td>Septic shock</td>
<td>-Sepsis + hypotension unresponsive to fluid resuscitation + tissue hypoperfusion</td>
<td>support, euglycemia</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Meningitis | -Headache, photophobia, seizures  
-Classic triad: fever, nuchal rigidity, AMS  
-Skin: purpura+Brudzinski’s: lifting head  
-Kernig’s: bicycle leg, pain on extension | -LP for CSF  
-1st tube: appearance, cell count, 2nd tube glu & protein  
-Bacterial = WBC > 1000 w/ > 80% PMNs, ↓glu, ↑protein  
-Viral = WBC < 1000 w/ > 50% PMNS, norm glu & protein  
-3rd tube stain & culture, PCR for Strep pneumonia, agglutination  
-4th tube repeat cell count  
-Blood cultures x2  
-CBC | 1.) Immediate empiric AB  
-2 hour window for LP  
-ceftriaxone or cefotaxime + vanco  
-add ampicillin if < 3 mo or > 55  
-add acyclovir if HSV suspect  
-immunocomp: vanco + amp + cefipime or meropenem  
-inpatient: vanco + ceftazidime or cefepime, or meropenem  
-contacts: cipro  
-2.) Dexamethasone for 4 days  
-3.) Adjunct: hydration, pain meds, anticonvulsants, antiemetics, ↓ICP | -Viral in summer  
-High mortality if bacterial (Strep pneumonia, N. meningitidis, GBS, H.flu, Listeria, uncommonly syphilis, Chlamydia, TB, Rickettsia)  
-neonates: GBS, E. coli, Listeria  
-0-5 & 14-21: usually Neisseria meningitidis  
-also consider Strep pneumonia if < 5 years old  
-ages 1 mo-50 overall most common is Strep pneumonia  
-ages > 50: Strep pneumonia is also #1 cause but consider Listeria as well  
-Fungi: Cryptococcus, Coccidioides, Histoplasmosis |
<table>
<thead>
<tr>
<th>Disease</th>
<th>Description</th>
<th>Admission</th>
<th>Treatment</th>
<th>Associated with</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meningococcemia</td>
<td>Bacteremia 2° to <em>Neisseria</em> meningitis</td>
<td>1.) Admit</td>
<td>1.) Ceftriaxone or cefotaxime (or pen G or chloramphenicol)</td>
<td>Associated with epidemic outbreaks</td>
</tr>
<tr>
<td></td>
<td>Typical meningitis sx and petechial rash, hypotension, shock or sepsis</td>
<td>2.) AB:</td>
<td></td>
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<tr>
<td></td>
<td>May have no clinical evidence of meningitis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HSV encephalitis</td>
<td>Headache, fever, AMS, seizures, speech difficulty, hemiparesis</td>
<td>CSF PCR,</td>
<td>IV acyclovir for 14-21 d</td>
<td>From primary infection, HSV recurrence, latent HSV</td>
</tr>
<tr>
<td></td>
<td></td>
<td>viral culture, antigen testing and brain biopsy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pneumonia</td>
<td>Fever, rigors, malaise, productive cough, pleuritic chest pain, SOB, AMS, myalgias, arthralgias, GI sx</td>
<td>CXR for infiltrates: consider aspiration if in right middle or upper lobe</td>
<td>Admit for RR &gt; 30, HR &gt; 125, SBP &lt; 90, comorbidities (PORT or CURB-65 scores)</td>
<td>Typically bacterial but can be viral in extremes of age</td>
</tr>
<tr>
<td>Increased or decreased fremitus, dullness, rales</td>
<td>CBC</td>
<td>Initiate treatment within 6-8 hours of arrival to ED</td>
<td>CAP: Strep pneumo, H.flu, M. cat, Klebsiella, Pseudomonas</td>
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<td></td>
</tr>
<tr>
<td>Inpatient: sputum stain and culture, blood culture</td>
<td>Inpatient: sputum stain and culture, blood culture</td>
<td>Outpatient: azithro, doxy, or respiratory FQ</td>
<td>Atypicals: Mycoplasma, Chlamydophila, Legionella</td>
<td></td>
</tr>
<tr>
<td>Urine for strep or Legionella</td>
<td>Urine for strep or Legionella</td>
<td>hi dose moxifloxacin (or 3rd gen ceph) + azithro</td>
<td>-Rarely Staph aureus</td>
<td></td>
</tr>
<tr>
<td>PCR</td>
<td>PCR</td>
<td>amox + clavulanate</td>
<td>-TB: need admission for workup and PPDs for all contacts</td>
<td></td>
</tr>
<tr>
<td>Serologies</td>
<td>Serologies</td>
<td>Inpatient: ceftriaxone + azithro</td>
<td>-Aspiration etiology likely in nursing home pts, alcoholics, sedated or narcotic-using pts, GERD</td>
<td></td>
</tr>
<tr>
<td>Rapid influenza test</td>
<td>Rapid influenza test</td>
<td>respiratory FQ</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>UTI &amp; Pyelonephritis</td>
<td>Mild to severe - Sepsis in infants, elderly, and immunocompromised - Cystitis: dysuria, frequency, urgency, suprapubic pain, +/- hematuria, midline suprapubic tenderness, rectal pain - Pyelonephritis: plus fever &gt; 100.4, flank pain, CVA tenderness, n/v, rigors - Elderly may have AMS only</td>
<td>UA with dipstick for blood, leukocyte esterase, nitrate - Urine microscopy for RBC, WBC, casts, bacteria, yeast, Trichomonas - Urine culture in select pts - Blood culture for suspect urosepsis - Imaging to rule out renal stone or abscess</td>
<td>3-5 days if simple cystitis in a female - 7-14 days if pyelonephritis, pregnant, complicated, frequent UTIs or prior treatment failure - UTI options: Septra, nitrofurantoin, quinolones, cephalaxin - UTI adjuncts: phenazopyridine, yeast prophylaxis - Pyelo options: cipro, levofloxacin, amoxicillin+ clavulanate, cephalaxin - Pyelo: admit for vomiting, uncontrolled fever, elderly, DM, renal failure or stone, immunocompromised pregnant, failed outpatient therapy</td>
<td>Differential: vaginitis, foreign body, HSV, cervicitis or PID, cervicitis, epididymitis, urethritis, musculoskeletal back pain - Usually E. coli, also Proteus, Klebsiella, Pseudomonas, Staph saprophyticus - Uncomplicated = healthy young nonpregnant female - Complicated = anything else</td>
</tr>
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</tr>
<tr>
<td><strong>STI</strong></td>
<td><strong>Presentation &amp; PE</strong></td>
<td><strong>Investigation</strong></td>
<td><strong>Treatment</strong></td>
<td><strong>Special</strong></td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>HSV</th>
<th>Pain, dysuria, pruritus, fever, headache, malaise, myalgias, inguinal lymphadenopathy</th>
<th>Viral culture or immunoassay to confirm</th>
<th>Valacyclovir or acyclovir</th>
</tr>
</thead>
<tbody>
<tr>
<td>Syphilis</td>
<td>Primary: painless chancre, Secondary: rash, Neurosyphilis</td>
<td>RPR, VDRL, or FTA-ABS</td>
<td>Penicillin G: single or multiple doses depending on stage</td>
</tr>
<tr>
<td>Chancroid</td>
<td>Painful ulcer(s), regional adenopathy</td>
<td>Single dose ceftriaxone or azithromycin</td>
<td></td>
</tr>
<tr>
<td>Genital warts</td>
<td></td>
<td>Refer for treatment or imiquimod</td>
<td></td>
</tr>
<tr>
<td>Skin &amp; Soft Tissue</td>
<td>Presentation &amp; PE</td>
<td>Investigation</td>
<td>Treatment</td>
</tr>
<tr>
<td>Impetigo</td>
<td>Bullous vs nonbullous (honey-crusted)</td>
<td>Cephalexin, dicloxacillin, Septra if MRSA suspected</td>
<td>GAS or Staph aureus</td>
</tr>
<tr>
<td>Pyoderma: abscess, furuncle, carbuncle</td>
<td>Throbbing pain and tenderness, erythema</td>
<td>Gram stain and culture drainage</td>
<td>I&amp;D</td>
</tr>
</tbody>
</table>

- GAS or Staph aureus
<p>| | | | | |</p>
<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Cellulitis</td>
<td>Edematous, erythematous inflammation of dermis and subcutaneous tissue</td>
<td>- CBC-CRP</td>
<td>- Outpatient: cephalexin, dicloxacillin, Augmentin, doxycycline, minocycline, Septra or clinda if MRSA</td>
<td>- GAS, Staph aureus Gram negs &amp; anaerobes in DM, PVD, bites</td>
</tr>
<tr>
<td></td>
<td>- Tenderness to palpation, fever, chills, malaise</td>
<td>- Wound culture and Gram stain</td>
<td>- Inpatient (rapid, unreliable, face, hand, systemic sx): clinda, vanco ± cefazolin</td>
<td>- Mycobacteria</td>
</tr>
<tr>
<td>Erysipelas</td>
<td>Painful, red, hot, shiny plaques with well demarcated borders</td>
<td>- Outpatient: amoxicillin + clavulanate, dicloxacillin, cephalaxin</td>
<td>- Inpatient: penicillin G, nafcillin, or ceftriaxone</td>
<td>- A more superficial cellulitis</td>
</tr>
<tr>
<td></td>
<td>- Fever, chills, malaise, nausea</td>
<td>- Gram stain and culture</td>
<td>- Vanco + clinda + piperacillin/tazobactam</td>
<td>- Usually GAS</td>
</tr>
<tr>
<td>Necrotizing soft tissue infection</td>
<td>Incubation period &lt; 3 days</td>
<td>- X-ray for gas</td>
<td>- Etiologies vary with anatomic site, usually polymicrobial with anaerobes</td>
<td>- GAS, Clostridium perfringens, MRSA</td>
</tr>
<tr>
<td></td>
<td>- Pain out of proportion to PE findings</td>
<td>- CBC, CMP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Misc. ID</td>
<td>Presentation &amp; PE</td>
<td>Investigation</td>
<td>Treatment</td>
<td>Special</td>
</tr>
<tr>
<td>---------</td>
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</tr>
<tr>
<td>Bites</td>
<td></td>
<td>-Test animal for rabies&lt;br&gt;-X-ray&lt;br&gt;-CBC, blood and wound cultures if febrile</td>
<td>-Bite &lt; 24 hours: exploration, irrigation, prophylax with Augmentin, moxifloxacin, or clinda + cipro&lt;br&gt;-Bite &gt; 24 hours: same ABs with 24 h f/u&lt;br&gt;-Mod-severe: admit for IV ampicillin/sulbactam, or moxifloxacin, OR</td>
<td></td>
</tr>
<tr>
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<td></td>
</tr>
<tr>
<td>Rabies</td>
<td></td>
<td></td>
<td>-Prophylaxis not indicated for vaccinated animal or healthy, domesticated animal&lt;br&gt;-Prophylaxis indicated for any bat exposure, wild or escaped domesticated animal bite</td>
<td></td>
</tr>
<tr>
<td>Condition</td>
<td>Symptoms</td>
<td>Diagnostics</td>
<td>Treatment</td>
<td>Notes</td>
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<td>------------------------------------------------</td>
</tr>
<tr>
<td>Septic arthritis</td>
<td>Pain, erythema, swelling, warmth, loss of function, fever, chills, n/v</td>
<td>CBC, ESR or CRP, Blood cultures, X-rays, Joint fluid analysis: septic if WBCs &gt; 50-60k and &gt; 50% neutrophils, gonorrhea culture of cervix or urethra</td>
<td>Admit for IV ceftriaxone + nafcillin, vanco if suspect MRSA</td>
<td>Usually hematogenous spread vs direct inoculation, Staph aureus, N. gonorrhoeae, GAS, GBS, enterobacteria, mycobacteria, syphilis</td>
</tr>
<tr>
<td>Osteomyelitis</td>
<td>Insidious or chronic onset, Pain, swelling, tenderness, overlying cellulitis, fever, chills, n/v</td>
<td>X-ray, CT or MRI, Bone scan</td>
<td>IV antibiotics for 4-6 weeks: nafcillin, vanco, ceftazidime, ceftriaxone, cipro</td>
<td>Surgical draining and debridement, Staph aureus, GAS, GBS, Polymicrobial in IVDU, Direct trauma: Staph or Pseudomonas</td>
</tr>
<tr>
<td>Environmental exposure: RMSF, lyme, ehrlichiosis, anaplasmosis, WNV, tularemia, babesiosis, CO tick fever</td>
<td>Fever, chills, rash, myalgias, Bite usually unrecognized</td>
<td></td>
<td>Doxycycline covers most</td>
<td></td>
</tr>
<tr>
<td>Infection in neutropenic patient</td>
<td>Fever recurrently &gt; 38° or one time &gt; 38.3° with ANC &lt; 500, Infection of catheter, skin, URT, lungs, abdomen, CNS</td>
<td>Culture skin and line sites, urine, sputum, stool, CBC, CMP, coag, UA, LP</td>
<td></td>
<td>CMV, HSV, VZV, Staph, Strep, enterobacteria, Pseudomonas, H. lu, Candida, Aspergillus</td>
</tr>
<tr>
<td>Infection in transplant patient</td>
<td></td>
<td></td>
<td>Aspergillus, Legionella, Cryptococcus</td>
<td></td>
</tr>
<tr>
<td>--------------------------------</td>
<td></td>
<td></td>
<td>-6 mo post tx: Cryptococcus</td>
<td></td>
</tr>
<tr>
<td>-Liver tx: enterobacteria, Candida</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>-Cardiac tx: pneumonia from Legionella, Aspergillus, or Toxoplasma CNS infection</td>
<td></td>
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</tr>
<tr>
<td>-Lung tx: <em>Pseudomonas, Aspergillus, atypicals</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infection in returning traveler</td>
<td>-if &lt; 2 weeks: malaria, Chik fever, rickettsial disease, influenza, yellow fever</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-2-6 weeks: malaria, hep A, hep E, leishmaniasis</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>-if &gt; 6 weeks: malaria, TB, hep B, hep E, rabies, typhoid fever</td>
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</tbody>
</table>

### 4.3 Respiratory Emergencies & Airway Management

#### 4.3.1 Background

Physiology of oxygenation:
- hypoxia is arbitrarily defined as PaO2 < 60 mm Hg = O2 of 90%

When is it respiratory distress?
- dyspnea (monitor) ☑ respiratory distress (intervene now) ☑ respiratory failure

Presentation of respiratory distress: tachypnea, tachycardia, stridor, hemoptysis, accessory muscle use, inability to speak in sentences, agitation, paradoxical movement of chest wall
How to intervene:

- updated BLS: circulation, airway, then breathing
- check for responsiveness
  - c. activate emergency response and get an AED
  - d. check carotid pulse and start CPR if no pulse felt within 10 seconds
  - e. defibrillation if indicated
- immediate airway control if needed
- establish initial airway: head tilt, chin lift, oro- or nasopharyngeal airway, or bag-valve-mask ventilation
  - o oropharyngeal: prevents blockage of glottis by tongue
    - measure from ear to corner of mouth
    - indications: deeply unconscious patient, absent gag reflex
    - contraindications: presence of gag reflex
    - does not prevent aspiration
    - still may require a head tilt
    - risk of inducing gagging, retching, or pharyngeal or dental trauma
  - o nasopharyngeal:
    - measure from earlobe to nose
    - indications: unconscious or AMS with suppressed gag reflex
    - contraindications: patient intolerance, nasal fx, marked septal deviation, coagulopathy
    - can be suctioned through
    - better tolerated in patients with intact gag reflex
    - can place safely without direct visualization
    - doesn’t prevent aspiration
    - poor technique can cause severe nosebleed
  - o problems with basic airway management:
    - can cause gastric distension and vomiting
    - no protection from aspiration
    - laryngospasm can occur
    - requires use of both hands
    - can only be used short-term
- anticipate need to intubate: orotracheal, LMA, glide scope, crico, nasotracheal intubation
  - o endotracheal intubation:
    - indications: surgical anesthesia, coma, no gag reflex, unable to handle
    - secretions, decreased PaO2 or increased Pa CO2 despite supplementation, respiratory burns, severe facial trauma, epiglottitis, large facial or neck abscesses, need to remove secretions
    - thyro-mental distance gives insight into ease of intubation
      - less than 6 cm will be difficult
greater than 7 cm will be easier
- “3-3-2” rule: if 3 fingers fit in the mouth, mentum to hyoid is 3 finger widths, and hyoid to thyroid is 2 fingers, this predicts successful intubation
- Mallampati score: grades oropharyngeal anatomy to assess difficulty in intubation
- check for obstruction make sure you can move the neck safely limit attempts to 15 seconds each, in between oxygenation
- Sellick maneuver: cricoid cartilage pressure to reduce aspiration risk
- BURP maneuver: backward, upward, rightward, pressure on thyroid cartilage to aid in visualization
- verify tube placement: visualization through vocal cords, symmetric breath sounds, no air
- heard over stomach, symmetric chest movement, colormetric CO2 detector, CXR
  - laryngeal mask airway: provides oval seal around laryngeal inlet at the esophageal junction
  - difficult airway may need retrograde intubation: inserting needle through cricothyroid membrane and advancing wire guide up through airway, then following wire with ET tube cricothyrotomy:
    - indicated for failed advanced airway, massive face trauma, cervical fx, upper airway obstruction
    - faster and safer than tracheostomy
  - rapid sequence induction and intubation (RSI): simultaneous administration of sedation and rapidly acting neuromuscular blocking agent
    - for planned intubations
    - induction agents include propofol, etomidate, ketamine, midazolam
    - paralytic agents include succinylcholine, vecuronium, mivacurium, atracurium, pancuronium, rocuronium
- get information from nurse and family
- ensure oxygen, heart monitoring, and IV access
- do a rapid assessment of patient’s status
- oropharynx: appearance of uvula, foreign body
- neck: tracheal deviation, distended neck veins, stridor
- cardiac: rate and rhythm
- chest: equal rise, trauma
- pulm: abnormal lung sounds
- skin: color, temp, diaphoresis

<table>
<thead>
<tr>
<th>Chest Wall Defects</th>
<th>Presentation &amp; PE</th>
<th>Investigation</th>
<th>Treatment</th>
<th>Special</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flail chest</td>
<td>Paradoxical respirations</td>
<td>CXR, Pulse ox, ABG</td>
<td>Mild/mod pain relief, intercostal nerve block, chest physiotherapy, judicious use of IVF, intubation analgesia</td>
<td>Seen in crush injuries or direct chest blow, can progress to hypoxia or respiratory failure</td>
</tr>
<tr>
<td>Pulmonary Collapse</td>
<td></td>
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</tr>
</tbody>
</table>
### Pneumothorax
- Chest pain, dyspnea, respiratory distress, hypotension, tracheal deviation, subcutaneous emphysema, unilateral breath sounds, tachycardia, JVD, cyanosis
- CXR
- Relief pressure with needle if tension
- Chest tube: water seal vs suction
- Closed = leak closes off
- Open = communication remains between lungs and pleural space
- Tension = communication open only during inspiration; increasing vol in pleural space and compression of adjacent lung

### Loss of Functional Lung Parenchyma
#### Pulmonary edema
- Rales, wheezing, pink & frothy sputum, peripheral edema, tachycardia, S3 gallop, HTN, JVD, cardiac arrhythmia, cool or diaphoretic skin
- CXR
- Pulse ox
- ABG, BNP, chem7, tox screen, cardiac enzymes
- EKG
- 100% O2 mask
- CPAP, BiPAP, or intubation to stent lungs open
- Nitroglycerin
- Morphine
- Hi dose diuretics & foley
- Treat underlying cause
- Cardiogenic: h/o CHF or ESRD, new arrhythmia, med nonadherence, dietary indiscretion
- Non-cardiogenic: heroin or narcotic overdose, sepsis, pulmonary contusion

#### Aspiration
- Rales, wheezing, pink & frothy sputum, peripheral edema, tachycardia, S3 gallop, HTN, JVD, cardiac arrhythmia, cool or diaphoretic skin
- CXR
- Pulse ox
- ABG, BNP, chem7, tox screen, cardiac enzymes
- EKG
- 100% O2 mask
- CPAP, BiPAP, or intubation to stent lungs open
- Nitroglycerin
- Morphine
- Hi dose diuretics & foley
- Treat underlying cause
- Cardiogenic: h/o CHF or ESRD, new arrhythmia, med nonadherence, dietary indiscretion
- Non-cardiogenic: heroin or narcotic overdose, sepsis, pulmonary contusion

### Airway Disease
- Presentation & PE
- Investigation
- Treatment
- Special
| Asthma | - Chest tightness, dyspnea, cough, wheezing  
- Desaturation  
- Pulsus paradoxus  
- Quiet chest, agitation, or confusion = warning signs of respiratory failure | - CXR  
- ABG | - Antibiotics if fever, productive cough, immunosuppression, or extremes of age  
- Supplemental oxygen  
- Albuterol to relax smooth muscle  
- Anticholinergics to decrease mucous  
- Epinephrine if impending respiratory failure  
- Steroids to prevent rebound | - Acute bronchoconstriction followed by subacute airway inflammation and mucous plugging |
| COPD | - Acute exacerbation: wheezing, fever, cough, ↓O2, pursed lip breathing, ↓breath sounds throughout | - CXR  
- CBC  
- ABG  
- Chem7 | - Steroids  
- CPAP or BiPAP  
- Supplemental oxygen: beware of CO2 retaining, goal PaO2 of ≥ 60  
- Broad spectrum AB | - Chronic bronchitis vs emphysema |
| Pulmonary Vascular | | | | |
| Pulmonary embolism | - Pleuritic chest pain, dyspnea, cough, hemoptysis, anxiety, tachypnea, tachycardia, fever, hypotension, signs of DVT | - ABG, CBC, chem7, PT/PTT, d-dimer  
- EKG  
- CXR  
- Doppler US of LE  
- V/Q scan  
- CT can miss small peripheral PE  
- Pulm angiography is gold standard | - Anticoagulants  
- Thrombolytics  
- Surgical embolectomy rarely used  
- IVC filter for patients with recurrent problems or can’t use anticoagulants | - Increased risk in malignancy, pregnancy, postpartum, estrogen use, genetic mutations, surgery or trauma, venous stasis |
## Miscellaneous Pulm Emergencies

<table>
<thead>
<tr>
<th>Presentation &amp; PE</th>
<th>Investigation</th>
<th>Treatment</th>
<th>Special</th>
</tr>
</thead>
<tbody>
<tr>
<td>Toxic ingestion</td>
<td></td>
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<tr>
<td>Electrolyte disturbances</td>
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<tr>
<td>Thyrotoxicosis</td>
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</tbody>
</table>

### 4.4 Genitourinary Emergencies

<table>
<thead>
<tr>
<th>Disease</th>
<th>Presentation &amp; PE</th>
<th>Investigation</th>
<th>Treatment</th>
<th>Special</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prerenal acute renal failure</td>
<td>- Oliguria or anuria&lt;br&gt;- Palpate pelvis for distended bladder or prostate enlargement</td>
<td>- Check vitals&lt;br&gt;- Check vol status&lt;br&gt;- Labs: BMP, BUN, electrolytes, Cr □ BUN:Cr ratio&lt;br&gt;- normal is 10:1&lt;br&gt;- prerenal is &gt; 20:1&lt;br&gt;- UA for RBCs and casts&lt;br&gt;- Renal &amp; bladder US&lt;br&gt;- CT</td>
<td>- Volume replacement&lt;br&gt;- Maximize cardiac output</td>
<td>- Usually from hypovolemia or other hypoperfusion of kidneys: sepsis, anaphylaxis, 3\textsuperscript{rd} spacing, decreased cardiac output</td>
</tr>
<tr>
<td>Renal ARF</td>
<td></td>
<td></td>
<td>- Low-dose dopamine&lt;br&gt;- Mannitol&lt;br&gt;- Dialysis</td>
<td>- Causes: acute interstitial nephritis, tubular necrosis, glomerulonephritis, SLE, vasculitis, Henoch-Schonlein purpura, thrombosis, NSAIDs, HTN, HUS</td>
</tr>
<tr>
<td>Postrenal ARF</td>
<td></td>
<td></td>
<td>- Relieve obstruction: Foley, stent, nephrostomy</td>
<td>- Causes: ureteral or bladder obstruction, urethral obstruction</td>
</tr>
<tr>
<td>End stage renal failure</td>
<td>- Multi-organ presentation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Condition</td>
<td>Symptoms</td>
<td>Investigations/Management</td>
<td>Differential Diagnosis</td>
<td></td>
</tr>
<tr>
<td>----------------------</td>
<td>---------------------------------------------------------------------------</td>
<td>-------------------------------------------------------------------------------------------</td>
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<td></td>
</tr>
</tbody>
</table>
| Dysuria              | Females: cystitis or pyelonephritis  
Young adult males: STD causing urethritis  
Older males: prostatitis | - Non-contrast CT  
-KUB: 90% of stones are radiopaque  
-US to look for hydronephrosis, may see stones | - Females: cystitis or pyelonephritis  
-Young adult males: STD causing urethritis  
-Older males: prostatitis |
| Urolithiasis         | Flank pain that is abrupt, severe, colicky, may radiate to scrotum or groin, n/v, previous episodes  
-CVA tenderness, LQ abdominal pain on palpation | - Non-contrast CT  
-KUB: 90% of stones are radiopaque  
-US to look for hydronephrosis, may see stones | - Inpatient: (needed if septic, complete obstruction, n/tractable n/v, solitary kidney, large or proximal stones)  
IVF, aggressive pain mgmt.  
-Outpatient: oral fluids, pain control, Flomax with urine straining, PCP f/u  
-Differential: AAA, appendicitis, tuboovarian abscess, ectopic pregnancy  
-Commonly Ca oxalate or phosphate  
- Struvite stones can be secondary to recurrent infection  
-Uric acid stones with h/o gout |
| Testicular torsion   | Abrupt onset of pain after sleeping or exertion in abdomen, inguinal canal, or scrotum  
Pain is non-positional  
-N/V  
Horizontal lie of testicle, absent cremasteric reflex | - Confirm torsion with scrotal US  
-Can attempt manual detorsion | - Urologic emergency, refer for repair within 4-6 hours  
-Pain control |
| Epididymo-orchitis   | Gradual onset of unilateral pain and swelling, fever, dysuria, local pain and swelling of epididymis + Prehn’s sign (relief with elevation of testicle) | - Analgesics  
-Testicular support  
-Stool softeners  
-Antibiotics: ceftriaxone or doxycycline if < 35, quinolones if > 35 | - Usually d/t gonorrhea if > 35  
-If under 35 consider E. coli, Enterobacter, Pseudomonas |
<table>
<thead>
<tr>
<th>Scrotal Masses</th>
<th>Presentation &amp; PE</th>
<th>Investigation</th>
<th>Treatment</th>
<th>Special</th>
</tr>
</thead>
<tbody>
<tr>
<td>Varicocele</td>
<td>Asymptomatic</td>
<td>US</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Feels like bag of spaghetti that increases with valsalva</td>
<td>Aspiration</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hydrocele</td>
<td>Gradually enlarging</td>
<td>US</td>
<td>Aspiration</td>
<td>Clear fluid</td>
</tr>
<tr>
<td></td>
<td>Painless</td>
<td>Aspiration</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Transilluminates</td>
<td>US</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spermatocele</td>
<td>Asymptomatic</td>
<td>US</td>
<td>Aspiration</td>
<td>Cloudy white fluid</td>
</tr>
<tr>
<td></td>
<td>Mass is separate from and above the testicle</td>
<td>Aspiration</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incarcerated inguinal hernia</td>
<td>Bowel sounds heard in scrotum</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Strangulated inguinal hernia</td>
<td>Loss of blood supply</td>
<td></td>
<td>Surgical emergency</td>
<td></td>
</tr>
<tr>
<td>Testicular tumor</td>
<td>Asymptomatic enlargement</td>
<td>US</td>
<td>Aspiration</td>
<td>Surgical exploration</td>
</tr>
<tr>
<td></td>
<td>Firm, nontender mass that does not transilluminate</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other Male Genital</th>
<th>Presentation &amp; PE</th>
<th>Investigation</th>
<th>Treatment</th>
<th>Special</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scrotal trauma</td>
<td>History of injury, scrotal hematoma, blood at urethral meatus</td>
<td>US</td>
<td>Urology consult</td>
<td></td>
</tr>
<tr>
<td>Fournier gangrene</td>
<td>Pain out of proportion to physical findings</td>
<td>Urology consult</td>
<td>Ampicillin, clinda</td>
<td>Debridement</td>
</tr>
<tr>
<td></td>
<td>Underlying diabetes or immuncomp</td>
<td></td>
<td></td>
<td>Shock or sepsis mgmt</td>
</tr>
<tr>
<td></td>
<td>Erythema, fever</td>
<td></td>
<td></td>
<td>Etiology is polymicrobial</td>
</tr>
<tr>
<td>Condition</td>
<td>Presentation &amp; PE</td>
<td>Investigation</td>
<td>Treatment</td>
<td>Special</td>
</tr>
<tr>
<td>--------------------</td>
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</tr>
</tbody>
</table>
| Urethritis         |                   |               | -Gonorrhea  - Ceftriaxone  
                    |                   |               | -Chlamydia  - Azithromycin or Doxycycline  
                    |                   |               | -Trichomonas  - Metronidazole  
                    |                   |               | -HSV  - Acyclovir  
                    |                   |               | -Treat sex partners |
| Priapism           |                   |               | -Urologic emergency  
                    |                   |               | -Subcutaneous terbutaline or Phenylephrine  
                    |                   |               | -Surgery |
| Phimosis           | -Inability to retract foreskin or void |               | -Emergent dorsal slit of foreskin |
| Paraphimosis       | -Inability to reduce retracted foreskin back over glans |               | -Emergent reduction  
                    |                   |               | -Dorsal slit if unsuccessful  
                    |                   |               | -Cure is circumcision |
| Acute prostatitis  | -Irritative voiding sx, malaise, fever, chills, back or rectal pain  
                    |                   | -Ceftriaxone, quinolone, azithromycin, Doxycycline, Septra  
                    |                   |               | -If < 35, likely gonorrhea or Chlamydia  
                    |                   |               | -If > 35, likely E. coli, Klebsiella, Enterobacter, or Proteus |
| Female Genital     | Presentation & PE | Investigation | Treatment | Special |
### Nonpregnant Vaginal Bleeding
- Check hemodynamic stability
- bHCG
- R/o coagulopathy
- Treat underlying cause
- IVF resuscitation (caution for hemodilution)
- If anovulatory, low down bleeding with estrogens and progesterones, go home with hi-dose OCPs with taper if bleeding is significant
- Dysfunctional vs ovulatory

### Chronic Pelvic Pain
- Usually not an emergency, just need to r/o emergency and provide f/u with PCP

### Acute Pelvic Pain
- R/o pregnancy
- US
- CBC
- Wet prep
- ESR or CRP
- Differential: PID, endometriosis, leiomyoma, ovarian cyst, ovarian torsion, ovarian abscess, UTI, msk cause, IBD, astroenteritis, ischemic mesentery, diverticulitis, appendicitis

### PID and Tubo-Ovarian Abscess
- Pain, fever, discharge, n/v, cervical motion and adnexal tenderness, d/c
- Ceftriaxone + azithro
- Doxycycline + metronidazole
- Neisseria gonorrhoeae, Chlamydia, polymicrobial with anaerobes

### Vulvovaginitis
- Discharge, odor, bleeding
- Wet prep
- Bacterial, Candida, Trichomonas
4.5 Acute Abdomen

4.5.1 Background

Pain:
- visceral pain is a result of distension, contraction, traction, compression, or torsions
- a sign of early ischemia or inflammation
- pain is crampy, dull, or achy, and poorly localized
- associated with pallor, diaphoresis, or vomiting
- patient is restless and can't stop moving
- midline pain is GI due to bilateral innervation
- unilateral pain could be kidney, ureter, ovary, gallbladder, ascending or descending colon, due to unilateral innervation
- parietal pain is a result of peritoneal surface making contact with the source of irritation
- rigidity and rebound tenderness
- patient will not want to move
- referred pain is aching, causes increased muscle tone and skin hyperalgesia

Acute abdomen: abrupt onset of nontraumatic abdominal pain less than 1 week in duration
- triage is critical
- consider EKG with CAD risk factors
- narrow differential by age, surgical history, toxic appearance
- age:
  - peds: appendicitis, intussusception, gastroenteritis, colic
  - adults: extensive differential
  - elderly: AAA, obstruction, neoplastic disease
- pain location:
  - RUQ: biliary colic, cholangitis, cholecystitis, hepatitis, PUD, atypical MI
  - LUQ: gastric ulcer, gastritis, pancreatitis, splenic rupture
  - RLQ: aortic aneurysm, appendicitis, Crohn’s, diverticulitis, ectopic pregnancy, endometriosis, hernia, colitis, ovary, PID, testicle, renal stone
  - LLQ: aortic aneurysm, diverticulitis, ectopic pregnancy, hernia, colitis, ovary, PID, testicle, renal stone
- PE:
  - abdomen: distension, obvious mass, scars, trauma, signs of liver disease, bowel sounds, dullness to percussion, liver size, fluid wave
    - decreased bowel sounds with ileus, mesenteric infarct, narcotic use, obesity
- increased bowel sounds with SBO, distension
- always palpate bad area last
- guarding:
  - voluntary guarding: muscle contraction in anticipation of exam
  - involuntary guarding: rigidity regardless of pressing on abdomen
    - a sign of peritonitis
- rectal exam
- pelvic exam
- testicular exam
- labs: H/H, CBC, amylase, lipase, ALT, AST, bili, alk phos, bHCG, lactate
- UA, blood cultures
- imaging:
- plain films for free air or obstruction
- US: cholelithiasis, choledritis, choledocholithiasis, biliary tract obstruction, pancreatic mass, biliary tract disease, renal, ovarian mass, hydroureter, ectopic pregnancy, AAA, free intraperitoneal air or fluid
- CT: appendicitis, pancreatitis, urolithiasis
  - a negative CT does not rule out serious disease
- red flags: extremes of age, severe pain with rapid onset, abnormal vitals, dehydration
- get a surgical consult for any acute abdomen without a clear diagnosis
- treatment:
- may be nonsurgical
- don’t withhold analgesics
  - opioids will not mask an exam
- antiemetics
- antibiotics to target specific gut flora if suspected infection or sepsis
  - GI: quinolone or metronidazole
  - gyn: doxycycline, cephalosporin, metronidazole

<table>
<thead>
<tr>
<th>Abdominal Problems</th>
<th>Presentation</th>
<th>Investigation</th>
<th>Treatment</th>
<th>Special</th>
</tr>
</thead>
</table>
| Appendicitis       | - Dull periumbilical pain that progresses to focal, sharp pain w/ RLQ radiation  
                    - Anorexia, n/v after pain begins  
                    - McBurney’s tenderness + Obturator sign + Psoas sign | - May have ↑WBCs  
                    - CT preferred in adults and nonpregnant women | - Surgical consult | - Most common in adolescents and young adults |
<table>
<thead>
<tr>
<th>Condition</th>
<th>Signs and Symptoms</th>
<th>Diagnostic Tests</th>
<th>Treatment</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intestinal obstruction</strong></td>
<td>Recent surgery or narcotic use, Diffuse, cramping, colicky pain, Vomiting, constipation, Pain localized to location of obstruction, Abdominal distension</td>
<td>Necrosis, ↑lactate, X-ray or CT (more sensitive)</td>
<td>Surgical vs medical, NPO w/ NG decompression, IVF, Bowel resection?</td>
<td></td>
</tr>
<tr>
<td><strong>Diverticulitis</strong></td>
<td>LLQ pain &gt; 1 day, n/v, fever, LLQ mass, abdominal distension</td>
<td>CBC, leukocytosis, May have + fecal occult, CT with contrast</td>
<td>IVF, pain management, antiemetics, Antibiotics: quinolone + metronidazole</td>
<td></td>
</tr>
<tr>
<td><strong>Cholecystitis and cholelithiasis</strong></td>
<td>Severe R sided abd pain, R shoulder pain, sharp and constant, occurs postprandial, peaks @ 9pm-4am, Female, fat, forty, fertile</td>
<td>↑WBCs, LFTs, bili, US, HIDA or ERCP is outpatient</td>
<td>IVF, pain management, Surgical, Antibiotics with advanced cases or perf</td>
<td></td>
</tr>
<tr>
<td><strong>Acute pancreatitis</strong></td>
<td>Alcohol use or cholelithiasis, Severe mid-epigastric pain radiating band-like to the back, Pain relief with bending forward, Restlessness, N/v, fever</td>
<td>Lipase &gt; 2x ULN, Amylase &gt; 3x ULN, ↑WBCs and LFTs, CT</td>
<td>Usually medical, IVF, pain management, NPO, antiemetics, bowel rest, Monitoring for complications: hemorrhage, sepsis</td>
<td></td>
</tr>
</tbody>
</table>
Ruptured AAA
- Older male smoker with underlying CV disease
- Sharp, severe, stabbing mid-abd pain radiating to the back
- Pulsatile mass
- Bedside US
- CT angiogram for stable aneurysm
- Immediate surgical management

Peritonitis
- Severe, nonfocal pain out of proportion to exam
- Fever, n/v, recent surgical procedure
- Nonspecific labs
- Lactate ↑ if ischemia
- Imaging not helpful
- Surgical vs nonsurgical

Ectopic pregnancy
- Any female of childbearing age with abd pain
- If rupture: severe lower abd pain, fever, vaginal bleeding
- + bHCG
- CBC
- T&S
- Transvaginal US
- 2 large bore IVs
- Immediate surgical management vs serial HCGs and US

4.6 GI Bleed

4.6.1 Background
- Overall GIB morality is 10-14%
- Most bleeds are upper
- History
  - get timeline: bleeding over minutes, hours or days
  - volume of blood lost
  - has it happened before (usually a second bleed will be from the same source)
  - precipitating factors
    - meds: gut-irritating aspirin and other NSAIDs, steroids, anticoagulants
      - iron or bismuth use can turn tongue black
    - alcohol use: if binge more likely to be variceal bleed, if chronic more likely to be ulceration
    - age
    - pain
  - PMH: aortic grafting puts pt at risk for aortic-enteric fistula, liver disease puts at risk for esophageal varices bleeding
  - Estimate location and amount of bleeding based on appearance of blood
    - hematemesis: blood emesis; a sign of upper GIB
    - coffee ground emesis: dark, old blood from stomach; upper GIB
    - hematochezia: red or maroon blood in stool
    - melena: dark, tarry stools
- associated with at least 50 mL of blood loss

- **PE:**
  - hypotension and tachycardia
- VS:
  - orthostatic hypotension with blood loss ≥ 15%
  - supine hypotension with blood loss ≥ 40%

- **skin:**
  - spider angiomata, palmar erythema, jaundice, gynecomastia → liver disease
  - petechiae or purpura → coagulopathy

- **look for ENT causes of bleeding:** dry nose, larynx, etc.
- **rectal exam:**
  - brown stool = not a massive bleed
  - maroon or BRB = current bleed

- **Investigation:**
  - labs: CBC every 2-8 hours, MCV, electrolytes, glucose, BUN:Cr (> 20:1 in upper GIB), PT/PTT, liver panel, T&S
  - serial EKG and cardiac enzymes if there are risk factors for heart disease (risk of cardiac ischemia in setting of hypovolemia)
  - EGD
  - abdominal x-ray series is not as helpful
  - angiography not ordered in ED setting
  - colonoscopy is diagnostic, therapeutic, and more accurate than scans or angiography

- **Treatment:**
  - NGT placement
  - stabilization and resuscitation
    - large-bore IVs with fluid replacement: crystalloid or pRBCs
  - oxygen
  - PPI
  - endoscopy
  - octreotide and ceftriaxone if suspecting varices

<table>
<thead>
<tr>
<th>Causes of Upper GIB</th>
<th>Presentation</th>
<th>Investigation</th>
<th>Treatment</th>
<th>Special</th>
</tr>
</thead>
<tbody>
<tr>
<td>Esophageal ulcer</td>
<td>Odynophagia, GERD, dysphagia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Erosive gastritis, esophagitis, or duodenitis</td>
<td>Jaundice, weakness, fatigue, anorexia, abdominal distension</td>
<td></td>
<td>From alcohol, NSAIDs, or aspirin</td>
<td></td>
</tr>
<tr>
<td>Esophageal or gastric varices</td>
<td></td>
<td></td>
<td>From portal HTN</td>
<td></td>
</tr>
<tr>
<td>Mallory-Weiss tear</td>
<td>Hematemesis ± previous vomiting episode</td>
<td></td>
<td>Most stop spontaneously</td>
<td>Supportive care</td>
</tr>
<tr>
<td>AVM</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Malignancy</td>
<td>Dysphagia, early satiety, involuntary weight loss, cachexia</td>
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<td>------------</td>
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</tr>
</tbody>
</table>
| Peptic ulcer disease | Epigastric pain or burning  
Gastric if shortly after eating  
Duodenal if 2-3 hours after eating with night awakening, relieved by eating |
| Definitive dx with EGD  
H. pylori serology, urea breath test, or stool Ag |
| Stop offending meds  
Bland diets DON’T help  
Antacids or acid suppression: H2 antagonists, PPIs, sulcralfate  
Prevention of NSAID ulcers: misoprostol  
Bismuth compounds  
H. pylori triple or quad regimen |
| #1 cause of upper GIB  
 Mostly caused by H.pylori, also NSAIDS, ZE syndrome, cigarettes  
Increased incidence in blacks  
Complications: GIB, perforation - peritonitis, gastric outlet obstruction |
| Gastric perforation | Anterior - sudden abd pain with guarding and rebound  
Posterior - back pain |
| X-ray: anterior = free air, posterior = no free air  
Normal or slight ↑lipase |
<p>| IVF, electrolyte correction, NGT, broad spec AB, surgery |
| Gastric outlet obstruction | Vomiting, dehydration, metabolic alkalosis, upper abd pain, early satiety, weight loss |
| X-ray showing dilated stomach shadow w/ large air-fluid level |
| IVF, electrolyte correction, NGT, surgery |
| Causes of Lower GIB | Presentation | Investigation | Treatment | Special |
| Hemorrhoids | | | | Most common cause of lower GIB |
| Diverticulosis AVM | | | | Commonly with ortic stenosis and HTN |</p>
<table>
<thead>
<tr>
<th>Cancer or polyps</th>
<th>Infectious gastroenteritis</th>
<th>Meckel diverticulum</th>
<th>Esophageal Conditions</th>
<th>Dysphagia</th>
<th>GERD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>`-Depends on severity</td>
<td></td>
<td></td>
<td>`-Barium swallow</td>
<td>`-Chronic heartburn, regurgitation, nausea, epigastric pain</td>
</tr>
<tr>
<td></td>
<td>`-CBC, BMP, bHCG</td>
<td></td>
<td></td>
<td>`-Endoscopy</td>
<td>`-Lifestyle &amp; dietary modification</td>
</tr>
<tr>
<td></td>
<td>`-UA</td>
<td></td>
<td></td>
<td>`-Esophageal manometry</td>
<td>`-Antacids or acid suppression</td>
</tr>
<tr>
<td></td>
<td>`-EKG</td>
<td></td>
<td></td>
<td>`-Biopsies</td>
<td>`-Surgical restructure of sphincter</td>
</tr>
<tr>
<td></td>
<td>`-Rectal exam</td>
<td></td>
<td></td>
<td>`-Fecal WBCs, culture, ova/parasites, C. diff</td>
<td>`-Acute vs chronic</td>
</tr>
<tr>
<td></td>
<td>`-Antidiarrheals: Imodium, Lomotil</td>
<td>`-Supportive care</td>
<td>`-Cipro or Septra if recent travel</td>
<td>`-Increased ICP, hyperemesis gravidarum, preeclampsia, DKA, med toxicity, abdominal obstruction or abscess</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>`-Antidiarrheals:</td>
<td>`-An alarm symptom</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>`-Antidiarrheals:</td>
<td>`-Oropharyngeal or esophageal</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>`-Antidiarrheals:</td>
<td>`-Associated with high fat food, nicotine, alcohol, caffeine, meds, pregnancy</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>`-Antidiarrheals:</td>
<td>`-Surgical restructure of sphincter</td>
</tr>
</tbody>
</table>

**Presentation**

**Investigation**

**Treatment**

**Special**
### Esophageal Perforation

- Severe vomiting followed by acute, severe chest pain or epigastric pain
  - Less common: sx after childbirth, weight lifting, fits of laughter, seizure, or forceful swallowing
- Tachycardia, tachypnea, hypotension
- Mackler’s triad: vomiting, chest pain, subcutaneous emphysema

### Esophageal Bleeding

- Endoscopy
- Endoscopic US
- Portal vein angiography
- Barium studies
- Capsule endoscopy

### Management

- Varies with severity, 60% self-resolve
- Broad-spectrum AB
- NPO
- NGT
- Emergent airway if needed
- Surgical stenting or repair
- Gastric lavage
- Electrocoagulation

### Ocular Emergencies

#### Background

Approach to patient with eye injuries:

- **History:** Type of injury and occurrence, if vision was normal prior to trauma, h/o eye surgery, symptoms other than decreased vision (pain, diplopia)
- **PE:** Vision, external exam, pupils, motility exam, anterior segment, ophthalmoscopy, intraocular pressure, peripheral vision
- Check each eye independently
- Always check vision
- Fluorescein stain
- If ruptured globe is suspected, protect eye with shield and keep NPO
<table>
<thead>
<tr>
<th>Eye Problem</th>
<th>Presentation</th>
<th>Investigation</th>
<th>Treatment</th>
<th>Special</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemical burn</td>
<td>- True ocular emergency</td>
<td></td>
<td>- Irrigate immediately before coming to ER with plain water, don’t add anything</td>
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<tr>
<td></td>
<td>- Continue irrigation at ER for 30 min, instill with anesthetic drops</td>
<td></td>
<td>- If pH remains abnormal, keep irrigating</td>
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<tr>
<td></td>
<td>- Instill cycloplegic drops to paralyze pupil and topical antibiotics</td>
<td></td>
<td>- Additional treatment depends on severity of injury</td>
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<td></td>
<td>- May need corneal transplant</td>
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<tr>
<td>Ruptured globe &amp; intraocular foreign body</td>
<td>- Hemorrhagic chimosis</td>
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<td>- Head CT</td>
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<td></td>
<td>- Hyphema</td>
<td></td>
<td></td>
<td>- US</td>
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<tr>
<td></td>
<td>- Pain, decreased vision</td>
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<td></td>
<td>- 360° of subconjunctival hemorrhage, corneal or scleral laceration, lowered IOP, intraocular contents outside globe</td>
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<tr>
<td>Hyphema</td>
<td>- Pain, blurred vision, h/o blunt trauma</td>
<td></td>
<td>- R/o open globe, hemorrhage with CT or US</td>
<td></td>
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<tr>
<td></td>
<td>- Blood in anterior chamber</td>
<td></td>
<td>- Serum protein electrophoresis in patients at risk for sickle cell (greater risk of damage to optic nerve)</td>
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<td></td>
<td></td>
<td></td>
<td>- Assume open globe</td>
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<td></td>
<td></td>
<td></td>
<td>- Consider admission</td>
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<td></td>
<td>- Avoid rebleeding</td>
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<td></td>
<td>- Eye shield</td>
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<td></td>
<td>- Minimal activity</td>
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<td>- HOB 30° to drain blood</td>
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<td></td>
<td></td>
<td></td>
<td>- Topical atropine</td>
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<td></td>
<td></td>
<td></td>
<td>- No aspirin or NSAIDs</td>
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<td></td>
<td></td>
<td></td>
<td>- Topical steroid</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>- Monitor IOP</td>
<td></td>
</tr>
<tr>
<td>Eyelid laceration</td>
<td>-Mechanism of injury</td>
<td>-CT to r/o foreign body or open globe</td>
<td>-Surgical repair</td>
<td>-Tetanus prophylaxis</td>
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<tr>
<td></td>
<td>-Sharp pain, foreign body sensation, photophobia, tearing, decreased vision, conjunctival injection, swollen lid</td>
<td>-Fluorescein stain with slit lamp exam -Full eye exam with lid eversion to look for foreign body</td>
<td>-Depends on size of abrasion and mechanism of injury, contact use -No contacts - erythromycin or polytrim ointment or drops -Contacts - tobramycin or fluoroquinolone drops to cover <em>Pseudomonas</em> -Cycloplegic agent -Consider patch or bandage -Refer if not getting better, contact lens wearer, white infiltrate</td>
<td>-Differential: dry eye or recurrent erosion syndrome, infectious keratitis</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Corneal abrasion</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>-Hypopyon</td>
<td>-Check IOP</td>
<td>-Broad-spectrum antibiotics until cultures come back</td>
<td>-Deeper than corneal abrasion</td>
</tr>
<tr>
<td></td>
<td>-H/o contact use overnight or when swimming, eyelid structure abnormality, chronic epithelial disease, immunosuppression -Classic ring appearance with <em>Acanthamoeba</em></td>
<td>-Slit lamp exam -Workup infectious cause</td>
<td>-Daily f/u</td>
<td>-Usually an infectious keratitis or noninfectious (autoimmune)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Corneal ulcer d/t keratitis</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>-Hypopyon</td>
<td>-Check IOP</td>
<td>-Broad-spectrum antibiotics until cultures come back</td>
<td>-Deeper than corneal abrasion</td>
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<tr>
<td></td>
<td>-H/o contact use overnight or when swimming, eyelid structure abnormality, chronic epithelial disease, immunosuppression -Classic ring appearance with <em>Acanthamoeba</em></td>
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<td>-Daily f/u</td>
<td>-Usually an infectious keratitis or noninfectious (autoimmune)</td>
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<tr>
<td>Condition</td>
<td>Symptoms</td>
<td>Diagnosis/Management</td>
<td></td>
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<td>--------------------------------</td>
<td>---------------------------------------------------------------------------</td>
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<tr>
<td>Central retinal artery occlusion</td>
<td>Cherry red spot, plaque may be seen inside blood vessel</td>
<td>R/o temporal arteritis: ESR</td>
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<tr>
<td></td>
<td>Sudden painless loss of vision</td>
<td>No proven treatment</td>
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<tr>
<td></td>
<td></td>
<td>-Lower IOP: topicals, Diamox, anterior chamber paracentesis</td>
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<td></td>
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<tr>
<td>Acute narrow angle closure glaucoma</td>
<td>High IOP</td>
<td>Slit lamp exam</td>
<td></td>
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<tr>
<td></td>
<td>Occurs after being in dark place or after anticholinergic use</td>
<td>Lower IOP: drops, orals, IV mannitol</td>
<td></td>
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<tr>
<td></td>
<td>Prior episode of blurry vision</td>
<td>Hold pilocarpine until seen by ophthalmmo</td>
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<td></td>
<td>Halos around lights</td>
<td>Laser peripheral iridotomy</td>
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<tr>
<td></td>
<td>Recent uveitis or eye surgery</td>
<td>At risk: women, farsighted patients, Asians</td>
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<td></td>
<td>Severe pain causing n/v, abdominal pain may disguise true location of pain</td>
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<tr>
<td>Endophthalmitis</td>
<td>H/o eye surgery</td>
<td>Injection of intravitreal antibiotics ASAP</td>
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</tr>
<tr>
<td></td>
<td>Hypopyon</td>
<td>Staph aureus, Staph epidermidis</td>
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<tr>
<td></td>
<td>Red eye</td>
<td>After glaucoma surgery: Strep, H.flu (can be years later)</td>
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<tr>
<td>Condition</td>
<td>Signs and Symptoms</td>
<td>Diagnosis/Management</td>
<td>Differential Diagnosis/Notes</td>
<td></td>
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<tr>
<td>------------------------</td>
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<tr>
<td>Conjunctivitis</td>
<td>- Extremely purulent discharge if gonococcal&lt;br&gt;- H/o contact lens use&lt;br&gt;- Other cold symptoms if viral</td>
<td>- Culture if very purulent&lt;br&gt;- Adults are usually viral supportive, throw out lenses, wash sheets and hands, avoid contacts until better&lt;br&gt;- Infants treat as bacterial, cover GC/Chlamydia, systemic therapy</td>
<td>- Allergic or infectious&lt;br&gt;- Contagious for 2 weeks</td>
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<tr>
<td>Stye</td>
<td></td>
<td>- Warm compresses&lt;br&gt;- Erythromycin ointment&lt;br&gt;- I&amp;D&lt;br&gt;- Steroids if recurrent</td>
<td>- From clogging of oil glands&lt;br&gt;- Hordeolum is acute&lt;br&gt;- Chalazion is chronic</td>
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<tr>
<td>Blepharitis</td>
<td>- Burning or gritty eyes&lt;br&gt;- Mattering in the morning</td>
<td>- Warm compresses&lt;br&gt;- Scrub eyelids with baby shampoo&lt;br&gt;- Doxycycline ointment helps with inflammation</td>
<td>- Differential: Meibomian gland cancer if ulceration is present</td>
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<tr>
<td>Retinal detachment</td>
<td>- Painless vision loss like a curtain covering eye, seeing flashes or floaters&lt;br&gt;- Vision may be 20/20&lt;br&gt;- Defect in confrontational visual fields&lt;br&gt;- Lower IOP&lt;br&gt;- H/o myopia, trauma, FH, cataract surgery</td>
<td>- Surgical repair</td>
<td></td>
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</tbody>
</table>
4.8 Introduction to Point of Care Ultrasound

4.8.1 Background

History of US
- US training for emergency medicine providers began in 1987
- real-time pictures, no waiting for the computer
- radiologists not always present
- many medical schools today are implementing US from day 1
- useful when there are limited resources or long transit times
- military, NASA, EMS are also using US

Benefits of US:
- no radiation
• noninvasive
• repeatable
• portable
• reliable
• greater patient satisfaction
• teaching opportunity
• decreased length of stay
• faster diagnosis
• fast tailoring of differential

US applications:
• diagnostic: abdominal aorta, echo, biliary, vascular, renal, ocular (globe rupture, hemorrhage, lens dislocation, retinal detachment), msk, FAST, pelvic, pulmonary
• procedural: aiding or pre-procedure
• arthrocentesis, thoracentesis, pericardiocentesis (make sure there is fluid first), abdominal line, PIV, abscess, tendon

4.8.2 US Technology
• Types of probes:
  • curved
  • linear paracentesis, regional nerve block (visualize before sticking), central fenestration
• IV procedure: first do a scout US to find the vessel, then insert IV using US guidance
• good for placing IVs
• phased
• Indicator helps you position
• Wavelength: varies for penetration vs detail
• Terms:
  • focal zone: middle of image where it is visualized best
  • depth: penetration of waves
  • gain: brightness of the screen or contrast
  • color flow:

4.8.3 US and DVT
• Risk factors for DVT: trauma, hypercoagulable state, IV drugs, age > 40, BCP, type A blood, obesity, surgery, smoking, immobilization
• Diagnosis of DVT using US:
  • deep vessel affected
  • vessel is noncompressible
  • poor augmentation
  • hyperechoic if older
  • hypoechoic if fresh

4.8.4 Focused Assessment with Sonography in Trauma Exam
• Positive FAST → straight to OR
• should take less than a minute
• less invasive than deep peritoneal lavage
• Where to start scanning?
• depends on presentation, mechanism of trauma, etc.
• Uses:
  • detection if internal bleeding: see hypoechoic areas
  • pericardial effusion

4.8.5 US and Skin
What can be visualized on US: cellulitis, abscess, foreign body, necrotizing fasciitis, fracture
- cellulitis: no definitive separation of skin layers, all gray
- cobblestoning and edema in subcutaneous tissue if severe
- abscess: circular collection of hypoechoic fluid, will squish down with US probe
- can also use US to guide drainage, although I&D is preferred
- necrotizing fasciitis: can visualize eroded bone, hyperechoic “starry night” pattern of gas
- help visualize suspected foreign body
- tendons exhibit anisotropy: brightness when it is perfectly perpendicular to the US probe
- helps differentiate from nerve
5 Emergency Medicine Exam II Notes

5.1 Burns

5.1.1 Background

- ABLS = advanced burn life support
- Majority of burns are small and are treated outpatient
- Overall 10% mortality rate
- House fires account for 70% of mortality and are mostly due to smoke inhalation
- Adult burns are usually from flame contact or ignition of clothing
- Pediatric burns are usually from scalding
- Skin provides protection from infection, injury, and fluid loss, and regulates body temperature
- Loss of skin means a loss of these functions

5.1.2 Zones of Injury

- Zone of hyperemia: area peripheral to and below the zone of stasis
- Characterized by minimal cell injury but with vasodilatation due to neighboring inflammation-induced mediators
- Completed recovery of this tissue is expected unless there is an additional severe insult such as an invasive infection or profound tissue inflammation
- Zone of stasis: Deep and peripheral to the zone of coagulation, there is a sizable area of tissue injury where cells are viable but can easily be further damaged
- Zone of coagulation: comprised of the surface tissue necrosis of the initial burn eschar
- Damage here causes irreversible injury

5.1.3 Burn Depth Classification

- First degree: superficial burns only involving the epidermis
- Ex. Sun burns, “flash” burns
- No blisters or edema, skin is pink or red, dry
- Will heal on their own in 3-6 days
- Are not included in burn calculations
- **Second degree**: partial thickness burn that involves the dermis
  - superficial partial = small amount of dermis involved
    - caused by flame, scalding, or chemicals
    - moist, pink/red, edema, blistering, extremely sensitive to touch as nerve
    - minimal damage to skin appendages
    - heals in 10-21 days
  - deep partial = significant amount of dermis involved, more than 50%
    - caused by grease, flame, or chemicals
    - fewer capillaries left = appears white, dry, moderate edema, decreased sensation & circulation = minimal pain
    - may scar
    - may convert to full thickness burn
    - healing takes > 21 days
  - tell these apart by degree of pain and pressure sensation

- **Third degree**: full thickness burn, entire epidermis and dermis is gone, extends to subcutaneous fat
  - a result of prolonged exposure to any heat source
  - extensive edema, dry, leathery, charred skin, no sensation or circulation
  - will not heal spontaneously, requires skin grafting
  - Fourth degree: penetration to the bone
  - usually requires amputation

5.1.4 **Calculation of Burn Area**

**Rule of nines**: you can estimate the body surface area on an adult that has been burned by using multiples of 9

- head = 9%
- chest (front) = 9%
- abdomen (front) = 9%
- upper/mid/lower back and buttocks = 18%
- each arm = 9% (front = 4.5%, back = 4.5%)
- groin = 1%
- each leg = 18% total (front = 9%, back = 9%)
- estimate 1% by using patient’s hand = must modify for kids!

5.1.5 **Management of Burns**

**Pre-hospital**:
- stop the burning process by removing clothing, irrigation to remove chemicals, etc.
- cool burn surface with saline
- don’t use ice water, it causes vasoconstriction
- cover or protect wound to prevent heat loss and keep it clean

**Emergency department**:
- airway: assess patency, smoke inhalation injury
- soot anywhere in the mouth indicates inhalation injury
- constantly reassess as upper airway edema can develop with fluid resuscitation within minutes
- breathing: assess for spontaneous respiration and bilateral air flow
- circulation: peripheral pulses, IV access immediately for resuscitation
- edema is a result of SIRS = decreased cardiac output = increased PVR, hypovolemic shock, acute renal failure
- fluid to use:
  - LR is the top choice as it is isotonic
  - hypertonic solutions will draw water out
  - even NS will leak sodium into extravascular tissue and cause dehydration
    - Parkland formula: for estimation of total fluid resuscitation volume needed for burn patients for first 24 hours (2-4 mL LR) x (wt in kg) x (% BSA burned) = divide by two, do first half in first 8 hours, next half in next 16 hours
lower resuscitation volume if urine output is too high

- myoglobinuria or hemoglobinuria can be seen following electrical injury or mechanical trauma

- assess disability
- remove all clothing
- keep room warm and protect patient against heat loss with blanket
- analgesics: IV morphine
- NG decompression
- Foley to monitor resuscitation efforts: very important, all decisions will be based off of this
- HPI: mechanism, use of alcohol or drugs
- PMH, allergies, meds, immunization status
- vitals: O2 sats, calculate weight
- baseline labs: ABG, CBC, electrolytes, glucose, UA, CO
- tetanus booster or Ig
- escharotomy is rarely indicated prior to transfer to a burn center
- incision extended down to the subcutaneous fat
- must avoid all major vessels, nerves, and tendons
- needed when dead skin is causing a tourniquet-like effect
  - indications: cyanosis of distal unburned skin on limb, unrelenting deep tissue pain, progressive numbness, progressive decrease or absence of pulses
- chest escharotomy indicated to relieve respiratory distress due to restricted chest wall expansion from edema

**Surgical:**

- wound excision down to viable tissue
- skin grafting (done in stages) for 3rd degree and deep 2nd degree burns

**Inpatient:**

- biological dressings for temporary coverage
- human allografts last 2-3 weeks
- porcine xenografts last 1-2 weeks
- synthetic Integra lasts 2-3 weeks
- daily cleansing and debridement for blisters > 2 cm
- topical antibiotics: common pathogens are *Staph aureus* and *Pseudomonas*
- silver nitrate: won’t penetrate eschar
- silver sulfadiazine: limited eschar penetration
- mafenide acetate: penetrate eschar but is extremely painful
- systemic antibiotics indicated with suspected infection (discoloration of wound, erythema, induration, fever, + blood cultures or wound cultures)
- vaseline gauze dressing after exudative phase

**Indications for referral to burn center:**

- 2nd degree burns > 10% total body surface area
- burns to the face, hands, feet, genitalia, perineum, or major joints
- 3rd degree burns
- electric injury
- chemical burns
- inhalation injuries
- burns accompanied by trauma

**5.1.6 Special Considerations**

**Smoke inhalation injury**

- smoke particles and toxins cause damage to airways □ inflammation, mucosal ulceration, necrosis of epithelium □ pulmonary edema, bronchospasm, pneumonia (most common cause of morbidity here), ARDS
• presentation: burn occurring in enclosed space, facial burn, singed nasal or facial hair, carbonaceous deposits in oropharynx
• investigation: fiberoptic bronchoscopy if injury is below glottis
• treatment:
  • injury above glottis consider preemptive intubation as laryngeal edema can occur within 24 hours of the injury
  • support with humidified oxygen, pulmonary physiotherapy, mucolytic agents and bronchodilators
• prognosis: should heal within 2-3 weeks

Carbon monoxide poisoning
• CO displaces oxygen from Hb
• presentation: depends on CO %
  • 5-10% mild headache and confusion
  • 11-20% severe headache, flushing, vision changes
  • 21-30% disorientation, nausea
  • 31-40% irritability, dizziness, vomiting
  • 41-50% tachypnea, tachycardia
  • greater than 50% coma, seizures, death
• investigation:
• warning: PaO2 will still look normal, must check CO level for correct diagnosis
• treatment: 100% O2, hyperbaric rarely needed

Electrical injury
• classified by voltage
  • high = ≥ 1000 volts
  • low = < 1000 volts
• extent of injury depends on type of current, pathway of flow, local tissue resistance, and duration of contact
  • AC is more dangerous, causes flexion contractures and inability to withdraw from electrical source — tetany, cardiac fibrillation, respiratory muscle paralysis
  • DC travels in one direction so that individual is thrown off of the electrical source, may see exit and entrance sites
  • current travels along bone to generate heat that damages adjacent muscle — can have deep muscle injury even when superficial muscle appears normal
• presentation: may look very minor but can be devastating internally
  • deep muscle injury can occur even when superficial muscle appears normal
  • may see myoglobinuria with severe muscle breakdown
• treatment:
  • cardiac monitoring to watch for fatal arrhythmias
  • fasciotomy to relieve compartment syndrome from extensive muscle damage
  • increase fluids for myoglobinuria and add NaCO2 to alkalinize urine and facilitate myoglobin clearance
  • -may need amputation

Lightning strike
• 30% mortality
  • 70% of survivors suffer serious complications: cardiac, neurologic
  • direct current, but not associated with deep burns

Circumferential burn: at risk for edema and subsequent loss of circulation

5.1.7 Chemical Burns

Chemicals involved:
• acids: cause coagulation necrosis and protein precipitation
  • ex. oxalic & HF acids, pool chemicals, drain cleaners
• bases: cause liquefaction necrosis = tissue damage worse than acids
• ex. hydroxides, carbonates, caustic sodas of Na, K, NH3, Li, Ba, ca, oven cleaners, drain cleaners, fertilizers, industrial cleaners, cements
• other organic compounds, such as petroleum products, cause cutaneous damage due to destruction of fat and cell membranes
• absorbed systemically — kidney and liver toxicity
• ex. phenols, creosote, gasoline, kerosene

HF burns
• presentation: severe pain for size of burn area, tissue necrosis, hypocalcemia as fluoride binds free serum Ca
• treatment:
  • flood wound with water
  • neutralize with topical Ca gel
  • cardiac monitoring as high concentrations of fluoride can be life-threatening
  • IV treatment of hypocalcemia
  • may need wound excision
  • burn center consult

Organic solvent burns:
• presentation: wounds may initially look superficial but develop to full thickness in 2-3 days
• treatment:
  • remove saturated clothing and brush off powder agents
  • continuous irrigation with water
  • don’t neutralize chemical as there is potential of heat generation

Ocular chemical burns:
• investigation:
  • pH paper if chemical is unknown
  • fluorescein stain exam of cornea
• treatment:
  • irrigate with saline until pH is neutral
  • topical anesthetic

5.2 Neurological Emergencies & Head and Spine Trauma

5.2.1 Background

Head injuries
• 80% are mild, 10% are moderate, and 10% severe
• causes: MVAs, falls, assaults, sports injuries, penetrating trauma
• Monro-Kellie Doctrine: total intracranial volume is fixed due to the inelastic nature of the skull
  • consists of brain, CSF, and blood volume
  • usually around 1500 mL in adults
• Cerebral perfusion pressure: net pressure of blood delivery to the brain \[ CPP = MAP - ICP \]
  • ischemia can occur when MAP is < 50 mm Hg
  • increased ICP can occur when MAP is > 150 mm Hg due to increased blood flow

Initial evaluation:
• ABC’s as with any emergency
• consider intubation for GCS < 8
• fingerstick blood glucose
• vitals:
• fever with infection or cerebral abscess
• HTN with…
- neuro exam: mental status, cerebral function (language and aphasia), cranial nerves, sensory examination (light touch, pinprick, vibration, dermatomes), motor examination (strength), reflexes, cerebellar (rapid alternating movements, finger to nose), gait (Romberg, heel to toe, walking backwards)
- pupils:
  - Adie pupil: tonically dilated pupil as a result of damage to the postganglionic fibers of the parasympathetic innervation of the eye, usually by a viral or bacterial infection
- pinpoint pupils with opiates or cholinergics
- dilated pupils with anticholinergics

**Important meds:**
- naloxone (Narcan)

### 5.2.2 Neuro, Head, and Spine Emergencies

<table>
<thead>
<tr>
<th>Altered Mental Status</th>
<th>Presentation &amp; PE</th>
<th>Investigation</th>
<th>Treatment</th>
<th>Special</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coma</td>
<td>Total or near total unresponsiveness, eyes closed, inability to arouse</td>
<td>Grade with GCS: eye opening, verbal, motor</td>
<td>Causes: metabolic (encephalopathy, toxins, drugs, environment, sepsis) or structural (trauma, stroke, tumors, seizures, infections)</td>
<td></td>
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<tr>
<td></td>
<td>CN3 dysfunction with uncal herniation</td>
<td>Differentiate systemic vs focal source</td>
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<tr>
<td></td>
<td>Decorticate posturing and biots with central herniation</td>
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<tr>
<td>Obtundation</td>
<td>-Lethargy, blunted cognition, awake but somnolent or slowed, arousable</td>
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<tr>
<td>Stupor</td>
<td>Asleep or semicomatose, only aroused when stimulated, revert back to sleep when stimulus is withdrawn</td>
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### Encephalopathies

<table>
<thead>
<tr>
<th>Encephalopathy</th>
<th>Presentation &amp; PE</th>
<th>Investigation</th>
<th>Treatment</th>
<th>Special</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypoxic encephalopathy</td>
<td>Hyperbaric oxygen therapy</td>
<td>Brain cell death within 5 minutes</td>
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<td></td>
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<tr>
<td>Hypoglycemic encephalopathy</td>
<td>-Initial confusion and delirium</td>
<td>-Thiamine followed by dextrose</td>
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<tr>
<td>Hyperglycemic encephalopathy</td>
<td>-Severe dehydration from osmotic shift of fluid (may be &gt; 10 L)</td>
<td></td>
<td>Most commonly seen with hyperosmolar nonketotic coma</td>
<td></td>
</tr>
<tr>
<td>Hepatic encephalopathy</td>
<td>-Associated cirrhosis</td>
<td>Lactulose to ↓ intestinal NH₃ production, titrated to 2-4 loose stools daily</td>
<td>Due to increased NH₃ and GABA</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Antibiotics to ↓ intestinal bacteria producing NH₃: metronidazole, neomycin, vanco</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Renal failure, loss of memory, impaired concentration, depression, delusions, lethargy, irritability, fatigue, insomnia, psychosis, stupor, catatonia, coma</td>
<td>Dialysis</td>
<td>Uremic encephalopathy</td>
<td></td>
</tr>
<tr>
<td>-----------------</td>
<td>--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>---------</td>
<td>-----------------------</td>
<td></td>
</tr>
<tr>
<td>Hypertensive encephalopathy</td>
<td>Transient migratory neurological symptoms, HTN emergency, malignant HTN, cerebral edema</td>
<td>Lower BP by no more than 25% initially with sodium nitroprusside, labetalol, trimethaphan, nicardipine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Toxic encephalopathy</td>
<td></td>
<td>Poisons: lead, cyanide, CO Drugs: opiates, benzos, paralytics, ecstasy, neuroleptics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neuroleptic malignant syndrome</td>
<td>Muscle rigidity, hyperthermia, altered mental status</td>
<td>-Benzos From adverse reaction to neuroleptic or antipsychotic</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>-Acute onset of confusion, visual</td>
<td>-Rapid cooling</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wernicke's encephalopathy</td>
<td>changes, ataxia</td>
<td>-Thiamine replacement -Usually in chronic</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>-Association with Korsakoff's</td>
<td>via IV banana bag or IM</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>psychosis</td>
<td>alcoholics</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>-Due to thiamine deficiency</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Seizures</td>
<td>Presentation &amp; PE</td>
<td>Investigation</td>
<td>Treatment</td>
<td>Special</td>
</tr>
<tr>
<td>Generalized: tonic clonic (grand mal)</td>
<td></td>
<td>Rule out psychogenic by checking CK and lactate (should be ↑ in true seizure) Differential: hyperventilation, chorea, myoclonic jerks, tic, narcolepsy, cataplexy Full workup for new onset, but may be outpt Existing à glucose, check drug levels, CT?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Generalized: absence (petit mal)</td>
<td>Loss of consciousness without loss of postural tone</td>
<td>Phenytoin or fosphenytoin for active seizing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Simple partial</td>
<td>-No change in consciousness</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complex partial</td>
<td>-Consciousness affected</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Status epilepticus</td>
<td></td>
<td>Stop seizure with benzos, phenytoin, or phenobarbital</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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### General anesthesia if refractory

<table>
<thead>
<tr>
<th>Traumatic Brain Injuries</th>
<th>Presentation &amp; PE</th>
<th>Investigation</th>
<th>Treatment</th>
<th>Special</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concussion</td>
<td>Headache, confusion, amnesia, ± loss of consciousness Nonfocal neuro exam</td>
<td>Can go home if low risk = no loss of consciousness, no posttraumatic amnesia, no moderate or high risk factors</td>
<td>Questionable d/c if any of above are + or with severe or increasing headache, persistent n/v, or intoxication</td>
<td>Widespread, microscopic damage</td>
</tr>
<tr>
<td>Intracerebral hemorrhage and contusions</td>
<td>Hard to distinguish from stroke</td>
<td>CT or MRI for grade II or III with symptoms persisting beyond 1 week</td>
<td>Keep out of play for 1 week if grade II occurs</td>
<td>Focal, macroscopic hemorrhage within the brain</td>
</tr>
<tr>
<td>Grade I = no loss of consciousness, transient confusion &lt; 15 min -Grade II = no loss of consciousness, transient confusion &gt; 15 min</td>
<td>Examine on sideline at 5 min intervals</td>
<td>Current reco say can return to play if better in 15 min for grade I, keep out of play for 1 week if 2nd grade I occurs</td>
<td>Contusion if ≤ 2/3 of tissue involved is blood and considered to be an ICH if more is involved</td>
<td></td>
</tr>
<tr>
<td>Grade III = loss of consciousness</td>
<td>Transport to facility for grade III</td>
<td>Brief grade III can return to play in 1 week, prolonged grade III can return after 1 month</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Intracerebral hemorrhage and contusions

- Grade I = no loss of consciousness, transient confusion < 15 min
- Grade II = no loss of consciousness, transient confusion > 15 min
- Grade III = loss of consciousness

### Cerebellar hemorrhage

- Sudden onset of dizziness, vomiting, truncal ataxia, inability to walk

#### Headache, confusion, amnesia, ± loss of consciousness

- Nonfocal neuro exam

#### Concussion

- Headache, confusion, amnesia, ± loss of consciousness
- Nonfocal neuro exam

#### Intracerebral hemorrhage and contusions

- Grade I = no loss of consciousness, transient confusion < 15 min
- Grade II = no loss of consciousness, transient confusion > 15 min
- Grade III = loss of consciousness

#### Cerebellar hemorrhage

- Sudden onset of dizziness, vomiting, truncal ataxia, inability to walk
<table>
<thead>
<tr>
<th>Neurologic Emergency</th>
<th>Presentation &amp; PE</th>
<th>Investigation</th>
<th>Treatment</th>
<th>Special</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Subarachnoid hemorrhage</strong></td>
<td>Can rapidly progress to herniation and coma</td>
<td>Head CT (neg won’t rule!)</td>
<td>Nimodipine to reduce cerebral vasospasm</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Focal deficits, severe constant headache, sentinel hemorrhage, vomiting, loss of consciousness, precipitating hypertensive event</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>“Worst headache of life”</td>
<td>LP for xanthochromia</td>
<td>Phenytoin seizure prophylaxis</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Neurosurgery consult</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Triple H therapy</td>
<td></td>
</tr>
<tr>
<td><strong>Subdural hematoma</strong></td>
<td>Head CT does not cross suture lines, brain parenchyma frequently compressed to the midline</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lucid interval following initial loss of consciousness</td>
<td>Noncontrast head CT showing crescent-shaped hematoma covering entire surface of a hemisphere, extends beyond suture lines</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Usually coexists with a skull fracture</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>May bleed quickly</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Epidural hematoma</strong></td>
<td>Due to tearing of middle meningeal artery</td>
<td>Due to tearing of bridging veins</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lucid interval following initial loss of consciousness</td>
<td>Due to tearing of bridging veins</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Usually coexists with a skull fracture</td>
<td>Due to tearing of bridging veins</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>May bleed quickly</td>
<td>Due to tearing of bridging veins</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Other Neurologic Emergencies

- **Presentation & PE**
- **Investigation**
- **Treatment**
- **Special**
<table>
<thead>
<tr>
<th>Syncope</th>
<th>Rapid, transient loss of consciousness à falls, followed by spontaneous and complete recovery</th>
<th>Must rule out other non-syncopal conditions leading to loss of consciousness, such as hypoglycemia, hypoxia, hyperventilation, epilepsy, intoxication, TIA, cataplexy, drop attacks, psychogenic syncope</th>
<th>A result of cerebral hypoperfusion</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>EKG</td>
<td>Causes: #1 is cardiac arrhythmia, orthostasis, valvular disease, acute MI, obstructive cardiomyopathy, atrial myxoma, acute aortic dissection, pericardial disease, PE, pulmonary HTN, cerebrovascular disease, neurally-mediated syncopal syndrome (vasovagal response, carotid sinus, situational)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Evaluate for blood loss: GI, pelvic, trauma</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>If incident was related to physical exertion à CBC, chem 7, glucose, imaging of chest and pelvis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stroke or TIA</td>
<td>Anterior cerebral artery à contralateral leg weakness &gt; arm weakness, mild cortical sensory deficits</td>
<td>Differential: thrombotic, embolic, or hemorrhagic stroke, transverse myelitis, Bell’s</td>
<td>Most are thrombotic, but can be embolic with a-fib</td>
</tr>
<tr>
<td></td>
<td>Try to localize using PE</td>
<td>Don’t Lower BP unless &gt;180/100</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TIA deficits should resolve within 30 min-24 hours</td>
<td>Airway protection</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lytic contraindications: minor symptoms, rapidly improving, prior ICH, glucose &lt; 50</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Thrombolytics if time of witnessed onset &lt; 3 hours</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Antiplatelets: aspirin, dipyridamole, clopidogrel</td>
<td></td>
</tr>
<tr>
<td>Transverse myelitis</td>
<td>Rapid onset of motor and sensory loss, sphincter problems, paresthesia, back and radic</td>
<td>-Supportive</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Vertebral tenderness to percussion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bell's palsy</td>
<td>Abrupt, isolated, unilateral peripheral facial paralysis</td>
<td>A diagnosis of exclusion</td>
<td>Prednisone?</td>
</tr>
<tr>
<td>--------------</td>
<td>------------------------------------------------------</td>
<td>-------------------------</td>
<td>------------</td>
</tr>
<tr>
<td></td>
<td>Entire face is affected (vs cortical stroke, where upper 1/3 of face is spared)</td>
<td>Head CT to r/o stroke or TIA</td>
<td>Acyclovir</td>
</tr>
<tr>
<td></td>
<td>Dry eyes, altered taste, mastoid pain, hyperacusis</td>
<td>Lyme titer</td>
<td>-Eye drops for lubrication</td>
</tr>
<tr>
<td>Guillain-Barre syndrome</td>
<td>Motor and sensory polyneuropathy, paresthesias, autonomic symptoms, areflexia</td>
<td>LP showing high protein and few monocytes</td>
<td>Supportive</td>
</tr>
<tr>
<td>Recent viral illness</td>
<td>EMG/NCS</td>
<td>Plasmapheresis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ascending weakness, from legs à trunk à arms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myasthenia gravis</td>
<td>Ptosis, diplopia, blurred vision, difficulty swallowing, dysarthria</td>
<td>Thymectomy</td>
<td>May be precipitated by infection or surgery</td>
</tr>
<tr>
<td>Muscle weakness with repetitive use</td>
<td>Neostigmine</td>
<td>Intubation if needed</td>
<td>Don’t use depolarizing or non-depolarizing agents during intubation</td>
</tr>
</tbody>
</table>

**Headaches**

<table>
<thead>
<tr>
<th>Presentation &amp; PE</th>
<th>Investigation</th>
<th>Treatment</th>
<th>Special</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meningitis until proven otherwise</td>
<td>Differential: subarachnoid hemorrhage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-CT</td>
<td>-LP</td>
<td>-MRI</td>
<td></td>
</tr>
<tr>
<td>Temporal arteritis</td>
<td>-Typically patient over 50</td>
<td>-ESR &gt; 50</td>
<td>Prednisone</td>
</tr>
<tr>
<td>-Temporal artery tenderness</td>
<td>New onset localized headache</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Migraine</td>
<td>Aura, n/v, unilateral pain that is pulsating, photophobia</td>
<td>Ask if migraine is typical</td>
<td>Ergotamine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>-Triptans</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>-DA antagonists</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>-Ketorolac</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>-Dexamethasone</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Opioids not recommended</td>
<td></td>
</tr>
<tr>
<td>Cluster headache</td>
<td>Excruciating unilateral lancinating pain that is periorbital, orbital, or temporal</td>
<td>-High flow oxygen</td>
<td></td>
</tr>
<tr>
<td>------------------</td>
<td>--------------------------------------------------------------------------------</td>
<td>------------------</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Conjunctival injection, lacrimation, congestion, rhinorrhea, facial swelling</td>
<td>-Ergotamine</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lasting 15 min to 3 hours</td>
<td>-Triptans</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Occurring daily for weeks</td>
<td>-NSAIDs for prevention</td>
<td></td>
</tr>
<tr>
<td>Tension headache</td>
<td>-Bilateral, non-pulsating</td>
<td>-Triptans if severe</td>
<td></td>
</tr>
<tr>
<td></td>
<td>-No nausea or vomiting</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Head and Spine Emergencies**

<table>
<thead>
<tr>
<th>Basilar skull fracture</th>
<th>Periorbital ecchymosis (raccoon eyes)</th>
<th>Investigation: Head CT</th>
<th>Treatment: Surgical repair with intracranial pressure management</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>-Battle’s sign</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>-Facial palsy or hearing loss from CN VII or VIII injury</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Scalp laceration</td>
<td></td>
<td>-R/o underlying skull fx</td>
<td>Wound care and repair with sutures or staples</td>
</tr>
</tbody>
</table>

**Spinal trauma**

<table>
<thead>
<tr>
<th>Neurologic deficits may or may not be present</th>
<th>Spinal immobilization with c-collar and longboard</th>
</tr>
</thead>
<tbody>
<tr>
<td>May have concomitant head injury</td>
<td>ABCs</td>
</tr>
</tbody>
</table>

**Central cord syndrome**

Disproportionately greater loss of motor power in the UEs than Les

<table>
<thead>
<tr>
<th>Varying degrees of sensory loss</th>
<th>A result of ligamentum flavum buckling à concussion or contusion to central cord</th>
</tr>
</thead>
<tbody>
<tr>
<td>Forced hyperextension injury</td>
<td></td>
</tr>
</tbody>
</table>

**Anterior cord syndrome**

Aplasia and dissociated sensory loss with loss of pain and temperature sensation

Caused by infarction of the cord in the region supplied by the anterior spinal artery, or disc herniation, bony fragment protrusion, or cord contusion from cervical hyperextension.
### Preservation of position sense, vibration, and deep pressure

**Brown-Sequard syndrome**
- Ipsilateral motor, vibration, pressure, and proprioception loss as well as contralateral loss of pinprick, pain, and temperature sensations?

<table>
<thead>
<tr>
<th>SCIWORA: spinal cord injury without radiographic abnormality</th>
<th>-A diagnosis of exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spinal cord injury</td>
<td></td>
</tr>
<tr>
<td>C3 or above à loss of diaphragmatic function</td>
<td></td>
</tr>
<tr>
<td>C4 à weak use of biceps and shoulders</td>
<td></td>
</tr>
<tr>
<td>C5 à use of shoulders and biceps</td>
<td></td>
</tr>
<tr>
<td>C6 à some wrist control but no hand function</td>
<td></td>
</tr>
<tr>
<td>C7 and T 1 à can straighten arms but poor dexterity of hand and fingers</td>
<td></td>
</tr>
</tbody>
</table>

### Worst prognosis

Caused by penetrating injury à hemisection of the cord

### 5.2.3 ENT Emergencies

<table>
<thead>
<tr>
<th>Auricular Emergencies</th>
<th>Presentation &amp; PE</th>
<th>Investigation</th>
<th>Treatment</th>
<th>Special</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hematoma</td>
<td></td>
<td>-I&amp;D with bolstering of both sides with dental rolls</td>
<td>-Failure to drain can result in cauliflower ear</td>
<td></td>
</tr>
<tr>
<td>Abscess</td>
<td></td>
<td>-I&amp;D -Empiric antibiotics -OR excision of cyst if</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Laceration</td>
<td></td>
<td>-Debridement and excision of protruding cartilage -Interrupted sutures -Antibiotics</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>External Auditory Canal</th>
<th>Presentation &amp; PE</th>
<th>Investigation</th>
<th>Treatment</th>
<th>Special</th>
</tr>
</thead>
<tbody>
<tr>
<td>Foreign body</td>
<td></td>
<td></td>
<td>-Attempt to remove if you think you can get it on the 1st try -ENT consult if complete</td>
<td></td>
</tr>
<tr>
<td>Insect</td>
<td>Acute otitis externa</td>
<td>Malignant otitis externa</td>
<td></td>
<td></td>
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<tr>
<td>--------</td>
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<td>------------------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Pain with manipulation of tragus</td>
<td>- May appear just like otitis externa</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Very itchy with spores if fungal</td>
<td>- Chronic otitis externa</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>- CT of temporal bone</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Admit for IV AB</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>- ENT consult</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>- May need mastoidectomy</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Consider especially in diabetics</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Agent: <em>Pseudomonas</em></td>
<td></td>
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</tr>
<tr>
<td>Middle Ear Emergencies</td>
<td>Presentation &amp; PE</td>
<td>Investigation</td>
<td>Treatment</td>
<td>Special</td>
</tr>
<tr>
<td>TM perforation</td>
<td>- Usually posterior tear due to curvature of ear canal</td>
<td>- Hearing test ASAP</td>
<td>- Quinolone ear drops</td>
<td>- Beware ototoxic ear drops</td>
</tr>
<tr>
<td></td>
<td>- Ragged, bloody hole in ear drum</td>
<td></td>
<td>- Recheck hearing in 1-2 months</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Decreased hearing</td>
<td></td>
<td>- May need surgical repair if chronic</td>
<td></td>
</tr>
<tr>
<td>Acute otitis media</td>
<td>- Hearing loss, ear pain, tinnitus, ear fullness, drainage with relief if perf</td>
<td></td>
<td>- If uncertain of infection, can wait a few days to see if it gets better</td>
<td>- Agents: <em>Strep pneumo, H. flu, M. cat</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- If ear is obviously infected, generally treat immediately with oral antibiotics for 10-14 days</td>
<td></td>
</tr>
<tr>
<td>Barotrauma</td>
<td>- Hi/o rapid pressure change like airplane or SCUBA diving</td>
<td>- Hearing test</td>
<td>- Nasal steroids</td>
<td></td>
</tr>
<tr>
<td>Acute mastoiditis</td>
<td>- Recent OM</td>
<td>- Clinical diagnosis</td>
<td>- Admit for IV AB</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Fever, otalgia, postauricular erythema, swelling, tenderness, protrusion of the ear</td>
<td>- CT scan if needing to delineate bony involvement</td>
<td>- ENT consult</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>- May need mastoidectomy</td>
<td></td>
</tr>
<tr>
<td>Bullous myringitis</td>
<td>- Extremely painful, bubbles on ear drum</td>
<td></td>
<td>- Macrolide like Biaxin</td>
<td>- Agents: <em>Mycoplasma, H. flu, Strep pneumo</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- Opiate pain meds</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Vertigo</th>
<th>Presentation &amp; PE</th>
<th>Investigation</th>
<th>Treatment</th>
<th>Special</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peripheral vs central?</td>
<td>- Peripheral: sudden, intense pain, paroxysmal or intermittent, worse with position change, nausea &amp; diaphoresis, rotary-vertical &amp; horizontal nystagmus, fatigue of symptoms, absent CNS symptoms</td>
<td>- Clinical diagnosis</td>
<td>- Admit for IV AB</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Central: sudden OR slow onset, less pain, constant, may or may not be worse with position change, may have nausea or diaphoresis, vertical nystagmus, no fatigue of symptoms, CNS symptoms</td>
<td>- CT scan if needing to delineate bony involvement</td>
<td>- ENT consult</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- May need mastoidectomy</td>
<td></td>
</tr>
</tbody>
</table>
### Benign Positional Vertigo (BPPV)
- Short-lived vertigo precipitated by head movements in which the ear goes down or back
- Lasts seconds to < 1 min
- Intermittent
- Better when holding head
- No hearing loss
- Must rule out stroke, MI + Dix-Hallpike maneuver
- Epley maneuver
- Caused by displaced otoliths in semicircular canals

### Meniere’s Disease
- Classic triad of episodic sensorineural hearing loss, vertigo for hours, and roaring tinnitus
- SNHL is low frequency and usually unilateral
- Ear fullness
- Diuretics
- Low sodium diet
- Anti-vertigo meds
- Surgical: endolymphatic sac decompression, gentamycin injection, selective vestibular nerve resection
- Due to increased endolymph pressure

### Vestibular Neuritis or Labyrinthitis
- Patients may think they are dying, severe vomiting, severe vertigo for 1-2 days, disabled
- Steroids
- PT
- Neuritis = only semicircular canals affected
- Labyrinthitis = vertigo + hearing loss
- Agent is probably viral
- Vertigo will last 24-48 hours, but patient will have several weeks of

### Inner Ear Emergencies
#### Unilateral Hearing Loss
- Must distinguish between outer, middle, inner ear causes
- External: cerumen impaction, infection, FB
- Middle: eustachian tube dysfunction
- Internal: sudden sensorineural hearing loss
- MRI with contrast of internal auditory canal
- When in doubt, always treat with high dose steroids and flu
- If untreated, hearing loss will be permanent in 4 weeks
- Causes: viral labyrinthitis, autoimmune, vascular compromise

### Otitis Media with Effusion
- Non-movable ear drum, opaque TM, air-fluid line, bubbles, amber discoloration
- Weber lateralizes to affected ear
- BC > AC in affected ear
- Must remove obstruction and retest hearing

### Sudden SNHL
- H/o SNHL occurring in last 72 hours, usually without warning
- Ho “pop” in ear before
- MRI with contrast of internal auditory canal
- When in doubt, always treat with high dose steroids and flu
- If untreated, hearing loss will be permanent in 4 weeks
- Causes: viral labyrinthitis, autoimmune, vascular compromise

### Nasal Emergencies
#### Foreign Body
- Nasal pain, pediatric sinus infections, nosebleeds, foul nasal odor, chronic nasal discharge, nasal
- AB: amoxicillin, cephalosporins
- Adjuncts: nasal saline lavage, nasal steroids, antihistamine, decongestant, mucolytic, Afrin
- Agents: Strep pneumo, H. flu, M. cat

#### Acute Sinusitis
- URI not clearing in 7-10 days, double sickening, localized facial pain, upper tooth pain, purulent nasal discharge, fever, cough, fatigue, facial pain upon percussion
- Bad-tasting, foul-smelling
- AB: amoxicillin, cephalosporins
- Adjuncts: nasal saline lavage, nasal steroids, antihistamine, decongestant, mucolytic, Afrin
- Agents: Strep pneumo, H. flu, M. cat
<table>
<thead>
<tr>
<th>Condition</th>
<th>Presentation &amp; PE</th>
<th>Investigation</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pharyngitis and tonsillitis</td>
<td>-Viral: diffusely pink throat, blisters, &lt; 5 days duration, cough, fever -Strep: brightly red, demarcated splotches, feverish, achy, rubbery lymphadenopathy -Tonsillar exudate (nonspecific for any agent)</td>
<td>-Rapid Strep with 24 hour culture</td>
<td>-AB if Strep pharyngitis: penicillin, amoxicillin, quinolones, erythromycin -Tonsillitis is generally treated but try to avoid penicillins to avoid mono reaction:</td>
</tr>
<tr>
<td>Peritonsillar abscess (aka quinsy)</td>
<td>-Hot potato voice, asymmetric soft palate, severe throat pain and dysphagia, inability to open jaw, copious salivation,</td>
<td>-Diagnosis is clinical</td>
<td>-I&amp;D with antibiotics: clindamycin, Unasyn</td>
</tr>
<tr>
<td>Epistaxis</td>
<td>-Get related history -Differentia: digital manipulation, septal deviation, inflammation, cold/dry air, FB, clotting disorder, HTN, leukemia, liver disease, anticoagulants, thrombocytopenia</td>
<td>-Try Afrin or Afrin-soaked sponge -Surgical: cauterization, embolization, arterial ligation -Manual compression - Packing with antibiotics for 3-5 days -Adjust warfarin therapy if needed</td>
<td></td>
</tr>
<tr>
<td>Dental Emergencies</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tooth fracture</td>
<td></td>
<td></td>
<td>-Application of topical sealant to fx -Referral to dentist</td>
</tr>
<tr>
<td>Tooth luxation</td>
<td></td>
<td></td>
<td>-Lateral or extrusive luxation - reposition manually and splint into place, f/u with dentist -Intrusive luxation</td>
</tr>
<tr>
<td>Dry socket</td>
<td>-Severe pain after tooth extraction</td>
<td>-X-ray to r/o retained</td>
<td>-Pain meds, f/u with</td>
</tr>
<tr>
<td>Acute necrotizing ulcerative gingivitis</td>
<td></td>
<td></td>
<td>-Chlorhexidine rinses, debridement by oral surgeon or ENT</td>
</tr>
<tr>
<td>Oral/Pharyngeal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Angioedema</td>
<td>-Marked swelling of oral soft tissue</td>
<td></td>
<td>-Stop ACEI if on -Benadryl, steroids, epinephrine if airway compromise or rapid</td>
</tr>
<tr>
<td><strong>Untreated sinusitis sequelae</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Parapharyngeal or retropharyngeal abscess
- Nuchal rigidity, stridor, sore throat, drooling
- CT scan
- Urgent ENT management with I&D
- Antibiotics: clindamycin, Unasyn
- Airway management
- Complications: mediastinal infection, airway obstruction, epidural abscess, necrotizing fasciitis, sepsis, erosion into carotid artery, jugular venous thrombosis

### Ludwig’s angina (cellulitis of oral floor)
- Coughing, unilateral wheezing, stridor, pneumonia, decreased breath sounds, bronchiectasis
- Drainage, IV AB
- Airway management
- Complications: mediastinal infection, airway obstruction, epidural abscess, necrotizing fasciitis, sepsis, erosion into carotid artery, jugular venous thrombosis

### Airway FB
- H/o s/p crush injury, swelling, subglottic stenosis
- Tracheostomy

### Cranial Maxillofacial Emergencies
<table>
<thead>
<tr>
<th>Presentation &amp; PE</th>
<th>Investigation</th>
<th>Treatment</th>
<th>Special</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mandible dislocation</td>
<td>Jaw pain, trismus, malocclusion</td>
<td>Evaluate ear canals and CNs</td>
<td>Analgesia and muscle relaxants followed</td>
</tr>
<tr>
<td>Mandible fx</td>
<td>H/o high energy blunt force trauma to skull</td>
<td>Tongue blade test, Imaging, Eval for malocclusion</td>
<td>Closed reduction ORIF with jaw wired</td>
</tr>
<tr>
<td>Facial fx</td>
<td>H/o blunt trauma to nose</td>
<td>Epistaxis, mucosal tear, septal deviation</td>
<td>Reduction if cosmetic deformity or loss of function, Emergent plastics consult, must be corrected within 3 days</td>
</tr>
<tr>
<td>Nasal fx</td>
<td>-CT of temporal bone</td>
<td>ENT consult</td>
<td>Complications: hearing loss, facial paralysis, CSF leak, vertigo, TM perf.</td>
</tr>
</tbody>
</table>

#### 5.3 Pediatric Emergencies

5.3.1 Background
- Pediatric vital signs:

<table>
<thead>
<tr>
<th>Abnormal vitals</th>
<th>&lt; 1 month</th>
<th>SBP &lt; 60</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-12 mo</td>
<td>SBP &lt; 70</td>
<td></td>
</tr>
<tr>
<td>1-10 years</td>
<td>SBP &lt; 70 + 2x age</td>
<td></td>
</tr>
<tr>
<td>&gt; 10 years</td>
<td>SBP &lt; 90</td>
<td></td>
</tr>
<tr>
<td>Any age</td>
<td>RR &gt; 60</td>
<td></td>
</tr>
<tr>
<td></td>
<td>HR &lt; 60</td>
<td></td>
</tr>
<tr>
<td></td>
<td>chest compressions indicated</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Rectal temp &gt; 100.4°</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Oral temp in AM &gt; 99.5°</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Oral temp in PM &gt; 100°</td>
<td></td>
</tr>
<tr>
<td>Infant</td>
<td>HR &gt; 200</td>
<td></td>
</tr>
<tr>
<td>1-8 years</td>
<td>HR &gt; 180</td>
<td></td>
</tr>
</tbody>
</table>
- Irritable infant differential: colic, reflux, dehydration, teething, constipation, corneal abrasion, sickle cell crisis, meds, obstruction, FB, hydrocephalus, fracture, infection
- Pediatric sedation:
  - sedation reduces awareness
    - minimal for non-painful procedures: Versed, Valium, Ativan
    - moderate aka conscious or procedural sedation
    - general anesthesia
  - analgesics reduce pain
  - dissociative anesthetics cause sedation as well as anesthesia
    - ex. ketamine
  - reversal agents:
    - naloxone for narcotics
    - flumazenil for benzos
- sedation protocol:
  - history, VS, PE
  - oxygen
  - suction
  - VS and cardiac monitoring

<table>
<thead>
<tr>
<th>Respiratory Emergency</th>
<th>Presentation &amp; PE</th>
<th>Investigation</th>
<th>Treatment</th>
<th>Special</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory distress</td>
<td>-Increased RR and effort, tachypnea, nasal flaring, use of accessory</td>
<td>-RR &gt; 60 needs rapid cardiopulmonary assessment</td>
<td>-Oxygen</td>
<td>-Frequently leads to cardiac arrest in kids</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>-Rapid sequence induction of intubation if needed</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>-IV access with fluids</td>
<td></td>
</tr>
<tr>
<td>Respiratory failure</td>
<td>-Abrupt onset of high fever, sore throat, stridor, dysphagia, drooling, trismus</td>
<td>-Avoid manipulation of epiglottis - investigate via nose instead</td>
<td>-Humidified O2, epi neb, Heliox</td>
<td>-Causes: upper or lower airway obstruction, parenchymal lung disease, abnormal ventilation</td>
</tr>
<tr>
<td></td>
<td>-Sitting child that won’t lie down, head leaning forward</td>
<td>-“Thumb sign” on lateral x-ray</td>
<td>-Intubation</td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>Croup (laryngotracheobronchitis)</td>
<td>-1-5 day prodrome of cough and coryza followed by 3-4 days of seal-bark cough, stridor</td>
<td>-X-ray showing steeple sign</td>
<td>-Humidified O2 for sats &lt; 90%</td>
<td>-Most common in 6 mo-3 years</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>-Dexamethasone</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>-Nebulized epinephrine</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>-Send home only if no stridor, well-appearing, good sats, reliable parents, 3 hours since last epi</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>-Agents: parainfluenza viruses</td>
</tr>
</tbody>
</table>
## 5.3.2 Pediatric Emergencies

### Bronchiolitis
- URI symptoms, wheezing, may have fever
- CXR showing hyperinflation, interstitial pneumonitis, infiltrates
- ELISA for RSV
- WBCs
- O2 sats
- Agents: RSV, parainfluenza, adenovirus, rhinovirus, Mycoplasma

### Asthma
- Cough, expiratory wheeze, SOB, tachypnea, retractions, nasal flaring
- Oxygen sats
- Peak flows
- CXR showing hyperinflation with flattened diaphragms
- Treat inflammation as well as constriction
- O2 if sats < 94%
- Nebulized or metered dose albuterol or levoalbuterol
- Ipratropium
- Inhaled steroids
- Subq epi (rare)
- Admit if unable to keep O2

### Pediatric Fever of Unknown Origin

<table>
<thead>
<tr>
<th>Presentation &amp; Investigation</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Septic workup for infants</td>
<td>- Admit infants &lt; 1 mo</td>
</tr>
<tr>
<td>&lt; 3 mo</td>
<td>- Empiric AB for infants &lt; 3 mo:</td>
</tr>
<tr>
<td>- Rochester criteria to ID</td>
<td>- Amoxicillin, gentamycin,</td>
</tr>
<tr>
<td>infants at low risk for</td>
<td>ceftriaxone, cefotaxime</td>
</tr>
<tr>
<td>bacterial infection</td>
<td>- Empiric AB for infants &gt; 3 mo:</td>
</tr>
<tr>
<td></td>
<td>- Ceftriaxone, cefotaxime</td>
</tr>
<tr>
<td></td>
<td>- Antipyretics: ibuprofen should</td>
</tr>
</tbody>
</table>

- IV access
- Meds: short-acting benzo ± opioid OR ketamine ± atropine ± benzo
- Rapid sequence intubation for peds:
  - Pre-oxygenate, pre-medicate, and sedate
  - Paralyze after sedation
  - Intubate
  - Confirmation of tube placement
  - Secure tube

### Febrile seizure
- Generalized motor seizure lasting less than 15 min, usually
- Evaluate for source of fever
  - LP, MRI, or EEG only if
  - Antipyretics
  - Benzo for status epilepticus
  - Genetic predisposition
<table>
<thead>
<tr>
<th>GI Emergencies</th>
<th>Presentation &amp; PE</th>
<th>Investigation</th>
<th>Treatment</th>
<th>Special</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bilious vomiting</td>
<td>-Differential: duodenal atresia, malrotation with volvulus, meconium ileus, necrotizing ileus, Hirschsprung’s</td>
<td>-NGT -IVF -Imaging -Surgery</td>
<td>-A sign of intestinal obstruction</td>
<td></td>
</tr>
<tr>
<td>Nonbilious vomiting</td>
<td>-Differential: appendicitis if over 5, intussusception, TE fistula, pyloric stenosis,</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Pyloric stenosis</td>
<td>-3-6 week old with projectile nonbilious vomiting, ravenous hunger, palpable pyloric olive -Poor weight gain -Visible peristaltic waves</td>
<td>-Distended, hypertrophic stomach on x-ray</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intussusception</td>
<td>-Periodic colicky abdominal pain, bloody currant jelly stools</td>
<td>-Plain films showing SBO</td>
<td>-Reduction or surgery</td>
<td>-Most common cause of intestinal obstruction in</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cardiovascular Emergencies &amp; Sudden Death</th>
<th>Presentation &amp; PE</th>
<th>Investigation</th>
<th>Treatment</th>
<th>Special</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac arrest</td>
<td>-CPR @ 30:2 with one rescuer or 15:2 with two rescuers</td>
<td></td>
<td></td>
<td>-Most commonly due to undetected cardiac disease: HCM, congenital coronary artery abnormality, Marfan’s, myocarditis -Reversible causes: hypoxemia, hypovolemia, hypothermia, hypo or hyperkalemia, tamponade, tension pneumothorax, toxins, poisons, drugs, thromboembolism -Traumatic causes: CNS or c-spine injury, CV injury, chest wall disruption, comorbid injury</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Chest pain</th>
<th>-Differential: rarely CV diseases (arrhythmias, IHSS, mitral prolapse, pericarditis, myocarditis), msk (strains, trauma, costochondritis), respiratory (asthma, pneumonia),</th>
</tr>
</thead>
</table>
5.4 Shock

5.4.1 Background

Occurs when there is inadequate oxygen delivery to meet the metabolic needs of the tissues = a state of metabolic failure → insufficient ATP → lactate accumulation, imbalanced ionic gradients, cellular swelling and rupture

- Early vs late shock?
- if it’s easy to detect, it’s late
  - severe altered mental status, hypotension, and death
- ANS is able to compensate for shock early on to maintain perfusion to the heart and brain
  - arteriolar vasoconstriction to shunt blood from skin to vital organs
  - venoconstriction to increase preload
  - increased HR and contractility
  - release of epi, NE, cortisol, ADH, stimulation of RAAS - clinical appearance of increased DBP, tachycardia, paleness, diaphoresis, decreased urine output
- You can have more than one kind of shock at the same time!

5.4.2 Shock in Trauma

- ATLS guidelines for shock assessment: designed for providers with no trauma background and limited clinical judgment for shock
- Shock in trauma is classified as hemorrhagic or non-hemorrhagic
- General shock management:

---

**SIDS**
- Sudden death of an infant under 1 year that remains unexplained
- A diagnosis of exclusion
- The most common cause of death in ages 1 mo to 1 year
- Theories: prolonged QT syndrome, hypoxia, apnea
- Prevention: breastfeeding, 

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<table>
<thead>
<tr>
<th>Other Pediatric</th>
<th>Presentation &amp; PE</th>
<th>Investigation</th>
<th>Treatment</th>
</tr>
</thead>
</table>
| Poisoning      | -Odor on breath  | -Tox screens | -Flush skin or eye exposure with water
-Oral gastric tube with activated charcoal for aspirin toxicity
-N-acetylcysteine for acetaminophen toxicity
-Deferoxamine IV for iron |
| Rash           | -Differential: meningococcemia, RMSF, ITP, viral exanthems, infestations, dermatitis | -Poison control center | -Orogastric tube with activated charcoal for aspirin toxicity |

---

5.4 Shock

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5.4.2 Shock in Trauma

- ATLS guidelines for shock assessment: designed for providers with no trauma background and limited clinical judgment for shock
- Shock in trauma is classified as hemorrhagic or non-hemorrhagic
- General shock management:
• recognize the shock: tachycardia, narrowed pulse pressure, cool, diaphoretic, delayed capillary refill, agitation any patient that is cool and tachycardic is in shock until proven otherwise
• determine shock etiology
  o usually evident from mechanism of injury
    ▪ trauma = likely hypovolemic or cardiogenic
    ▪ penetrating thoracic injury = obstructive shock
  o injury to spinal cord = neurogenic shock
  o delayed presentation = septic shock

5.4.3 Shock Without Trauma

General management:
• recognize the shock
• toxic appearance, altered mental status, HR > 100, RR > 22, PaCO2 < 32, urine output < 0.5 mL/hour, hypotension for longer than 20 min
• determine etiology
• hypovolemic:
  o sudden onset abdominal or low back pain with h/o HTN □ aortic dissection
  o abdominal distension with palpable abdominal mass □ ruptured AAA
• distributive:
  o fever or hypothermia □ sepsis
  o rigid abdomen □ peritonitis
  o unexplained bradycardia with hypotension □ negative inotropic drug ingestion, Addisonian crisis, or steroid withdrawal, hypothyroidism
• cardiogenic & obstructive: chest pain, SOB, persistent hypoxia, bradycardia

5.4.4 Hypovolemic Shock

Background:
• a result of inadequate circulating volume from blood loss or unreplaced fluid loss (vomiting, sweat, 3rd spacing) □ decreased venous return to the heard and decreased cardiac output
• types:
  o hemorrhagic:
    ▪ traumatic: hematoma, hemothorax, hemoperitoneum, placental abruption, etc.
    ▪ atraumatic: GIB, ruptured AAA, aortic dissection, ruptured ectopic pregnancy
  o dehydration: burns, DKA, adrenal crisis, vomiting, diarrhea, hyperosmolar state, pancreatitis, ascites

Presentation:
• mild hypovolemia (< 20% loss): □ decreased perfusion to skin, fat, muscle, bone
• normal arterial pH
• decreased pulse pressure, postural hypotension, cutaneous vasoconstriction, collapsed neck veins, concentrated urine, concentrated blood, pt feels cold
• mod hypovolemia (20-40% loss) □ decreased perfusion to liver, gut, kidneys
• metabolic acidosis
• thirst, tachycardia, moderate hypotension, oliguria, anuria
• severe hypovolemia (> 40% loss) □ decreased perfusion to heart and brain
• severe metabolic acidosis as well as respiratory acidosis
• mental status changes, arrhythmias, ischemic EKG changes, profound hypotension

Investigation:
• clear the chest, as a hemithorax can hold 2L of blood from aortic tears
• screen using CXR or chest CT if stable
  o widened mediastinum, depressed bronchus
• aortic angiography if stable
• clear the abdomen if CXR is normal (assume intra-abdominal or retroperitoneal hemorrhage)
• unstable pt □ FAST exam
- stable abdominal CT
- clear the pelvis/thighs as each thigh can hold 3-4 L of blood

**Treatment:**
- large-bore peripheral IVs with crystalloid bolus (2 L LR or NS), may need blood products
- different blood banks will stock different products but not whole blood, may need to order blood components to substitute for whole blood
- usually treat to a BP of 90-120
- for hemorrhagic shock:
  - stop the source of hemorrhage
    - hemotherax: large bore chest tube
    - pelvic hemorrhage: pelvic binder or MAST trousers
  - avoid pressors if hemorrhagic

### 5.4.5 Distributive Shock

**Background:**
- AKA warm shock
- a result of abnormal distribution of vascular volume ↓ vascular resistance and ↑ permeability
- same amount of fluid, but increased vascular compartment
- classic causes are sepsis, anaphylaxis, or neurogenic shock
- other causes: any other kind of shock that is prolonged enough that vasoconstriction can't be maintained, CO poisoning, cyanide poisoning

A.) **Septic shock:** usually due to overwhelming Gram neg infection systemic inflammatory response with arterial vasodilation and organ dysfunction
- -SIRS + infection + hemodynamic instability
- -presentation:
  - early signs: tachycardia, increased cardiac output, hypotension, fever, chills, bounding pulses, warm/flushed skin, hyperglycemia, confusion, hyperventilation, respiratory alkalosis
  - late signs: bradycardia, decreased cardiac output, hypothermia, coagulopathy, pulmonary failure, renal failure
- -investigation:
  - sepsis eval: temp > 38 or < 36, pulse > 90, RR > 20, PaCO2 < 32, WBCs > 12k or < 4k with > 10% bands
  - treatment: antibiotics, surgical debridement or resection, volume replacement, mechanical ventilation, vasopressors, inotropes

B.) **Anaphylactic shock:** when massive histamine release mucous membrane secretion, bronchoconstriction, vasodilation, urticaria
- presentation: apprehension, urticaria, cough, bronchospasm, hoarseness, stridor, hypotension, AMS, incontinence, death
- investigation:
- O2 and cardiac monitoring
- treatment:
- oxygen
- endotracheal tube or emergent cricothyrotomy
- early epinephrine and antihistamines (diphenhydramine, ranitidine)
- albuterol
- steroids for persistent or delayed reactions
- IV bolus if hypotensive
- send home with epi-pen

C.) **Neurogenic shock:** failure of the autonomic nervous system (spinal cord injury or regional anesthetics) loss of sympathetic tone and adrenergic stimulation (if above level of T4)
- will not occur with intracranial injury
- presentation: warm, flushed skin and bradycardia, venous pooling
• treatment: IVF, peripheral vasoconstrictors (phenylephrine, vasopressin), turn off epidural, methylprednisone for spinal cord injury

5.4.6 Cardiogenic Shock

Background:
• a result of failure of the heart muscle, arrhythmia, valvular or septal defects, or excessive afterload (systemic or pulmonary HTN)
  - ex. acute MI, CHF, cardiomyopathy, myocarditis, acute aortic insufficiency, myocardial contusion, prosthetic valve dysfunction, ruptured papillary muscle or septum, cardiac tamponade

Presentation:
• may have h/o blunt trauma or deceleration injury
• PE: JVD, rales, extra heart sounds, peripheral edema

Investigation:
• EKG
• CXR
• cardiac monitoring

Treatment:
• oxygen
• optimize volume status: balance fluid or diuretics
• reduce afterload: vasodilator
• optimize heart rate and rhythm: beta-blockers, anti-arrhythmics, pacemaker
• improve pump function: inotropes like epinephrine or intra-aortic balloon pump or ventricular assist device

5.4.7 Obstructive Shock

Background:
• AKA cardiac compressive shock
• occurs when extrinsic compression of the heart or great veins slowed blood return to the heart
• ex. pericardial tamponade, tension pneumothorax, diaphragmatic rupture, massive PE or other pulmonary obstruction, cardiac disease (subacute bacterial endocarditis, valve disease)

Presentation:
• PE: rales, Kussmaul’s sign, pulsus paradoxus, Beck’s triad (muffled heart sounds, JVD, hypotension)

Investigation:
• r/o PE with CT
• EKG to look for S1Q3T3

Treatment is to resuscitate with fluids and correct mechanical abnormality
• ex. pericardiocentesis, lytics

5.5 Orthopedic Emergencies

5.5.1 Basic Trauma Musculoskeletal Survey

• Primary survey: ABCs
• Secondary survey
• neuro: LOC, GCS, sensation
• head & neck: c-spine tenderness
• thorax and abdomen for deformity or tenderness
• pelvis: pubic tenderness, compress iliac crest
• spine: logroll patient to palpate entire spine
• palpate extremities for deformities, crepitus, tenderness
- passive range of motion in extremities
- Trauma x-ray series:
  - lateral c-spine: make sure you can see all the way down to C7
  - PA chest for pneumo or hemothorax
  - AP pelvis to look for pelvic fx
- Other imaging:
  - specific joint trauma views if needed
    - ex. shoulder: AP, scapular Y, axillary views
  - stress films can be particularly useful for the ankle
  - CT scans are frequently indicated

### 5.5.2 Orthopedic Emergencies

<table>
<thead>
<tr>
<th>True Emergency</th>
<th>Presentation &amp; PE</th>
<th>Investigation</th>
<th>Treatment</th>
<th>Special</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemodynamically unstable fracture</td>
<td>Pulsatile hemorrhage, expanding hematoma, audible bruit, pulseless limb</td>
<td>-AP view x-ray to look for = SI joint spaces, alignment of pubic symphysis, acetabulum -CT if fx identified or suspected</td>
<td>-Repair within 6 hours to restore circulation to extremity</td>
<td>-High energy pelvic fx associated with organ and vascular laceration -Femoral neck fx and hip dislocations are prone to avascular necrosis</td>
</tr>
<tr>
<td>Extremity arterial injury</td>
<td>Pain out of proportion to injury, pain with passive stretch, paresthesias, pulselessness</td>
<td>-Arteriogram for multilevel trauma</td>
<td>-If pressure &gt; 30 need OR for fasciotomy</td>
<td></td>
</tr>
<tr>
<td>Acute compartment syndrome</td>
<td>Vascular assessment -Decide limb salvage vs amputation</td>
<td>-Measure compartment pressures</td>
<td>-MESs score &gt; 7 needs OR for repair within 6 hours for warm ischemia or 12 for cold ischemia -Avoid tourniquet -Apply direct pressure to pressure points -Wrap amputation in LR or NS and keep on ice -Fracture Management</td>
<td>-Sharp cut has better prognosis over crush or tear</td>
</tr>
<tr>
<td>Mangled extremity or traumatic amputation</td>
<td>Fever, pain, leukocytosis, joint effusion</td>
<td>-Bone scan -MRI</td>
<td>-IV AB -I&amp;D -Hyperbaric oxygen</td>
<td>-Osteomyelitis agents: GAS, Staph -Joint agents: H. flu, GAS, E.coli, Neisseria gonorrhoeae</td>
</tr>
<tr>
<td>Threatened soft tissue or open fractures</td>
<td></td>
<td>-Reduction of displaced fractures and dislocations that are tenting or opening skin to relieve compromise -Open fx, wrap in saline dressings and take to OR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Septic joint or osteomyelitis</td>
<td></td>
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</tbody>
</table>
### Septic tenosynovitis
- Kanavel symptoms: diffuse or fusiform swelling of finger, pain along course of tendon, marked pain on passive extension, flexed finger at rest
- H/o puncture wound, bite, or punching someone else in the face
- IV AB
- I&D if progressing
- Tetanus and rabies prophylaxis
- Agent: Strep or Staph

### Other Ortho ED

#### Clavicle fx

- Posterior dislocations seen with h/o anterior force, seizure, electric shock
- X-ray: if anterior Bankart or Hill-Sachs lesions
- Reduction using maneuvers

#### Shoulder dislocation

- Nursemaid’s elbow

#### Humerus fx

#### Supracondylar fx

#### Olecranon fx

#### Radial head fx

#### Elbow dislocation

#### Subluxation of radial head

#### Forearm and wrist fx

#### Pelvic fx

#### Hip fx

- Most are posterior
- Leg stuck in hip flexion, adduction, and internal rotation
- Eval for neurovascular entrapment
- X-ray
- Reduce with Allis maneuver

#### Femoral shaft fx

- Closed reduction & nail

#### Tibial plateau fx

#### Tibial shaft fx

#### Fibular fx

### 5.5.3 Signs of Child Abuse
- Metaphyseal corner fx: a result of a ligament rupture from pulling or yanking mechanism
• Salter type fx are common injuries in ambulating children
• traction is an uncommon mechanism for non-accidental trauma and leads to corner fractures
• Long bone fx:
  • in older kids, are not by themselves indicative of abuse, it is more of a pattern
  • suggestive of abuse if seen in kids under 2
• Epiphyseal fx: a traction or rotation injury
• Vertebral compression fx are fairly specific for child abuse
• most are symptomatic and are identified on skeletal survey
• occur from violent hyperextension and hyperflexion
• Epiphyseal separations are moderately specific for abuse
  • a result of violent traction or rotation

5.6 Trauma Resuscitation

5.6.1 Background
• Triage of trauma based on mechanism of injury and appearance of severity
• red = unstable vitals, risk of losing airway, unresponsive, need immediate intervention
• yellow = less serious
• green = not at immediate risk of life or limb

EMS activates trauma levels to summon certain teams
• Trauma center designations
• ACS verification process
• Level I = specialty surgeons on call, MRIs can be done within an hour
• Level III and IV are more rural facilities that can stabilize a patient and then transfer for more definitive care
• Team approach to trauma:
  • attending and trauma surgeon stand back and monitor situation
  • residents are providing patient assessment
  • nurse on each side placing IVs
  • other nurses charting and drawing IVs
  • respiratory therapist
  • specialty surgeons

5.6.2 ATLS
1.) Primary survey: first and key part of trauma assessment, with identification of life-threatening injuries and simultaneous resuscitation
• A= airway maintenance with c-spine protection
  • intubate if GCS < 8, too agitated to allow PE, major head trauma, intoxication
  • c-spine immobilization while waiting for clearance
    • radiographic studies and/or clinical assessment
      • NEXUS study: ok to just clear clinically without imaging if there is no posterior midline tenderness, no evidence of intoxication, alert & oriented, no focal neuro deficits, no painful distracting injuries
• identify foreign bodies in airway
• goal is to prevent hypoventilation and hypoxia
• B = breathing and ventilation
• inspection, palpation, percussion, and auscultation of chest
• abdominal exam for potential bleed
• goal is to ID and manage the 6 life-threatening thoracic conditions: airway obstruction, tension pneumothorax, massive hemothorax, open pneumothorax (sucking chest wound), flail chest, and cardiac tamponade
• make sure there are = breath sounds bilaterally, midline trachea, = chest rise
• chest tube as needed
• pain control for flail chest
• check oxygen sats, ABG
• C = circulation with hemorrhage control
• identification of hypovolemic shock or blood loss
• IV access establishment with infusion of crystalloid
• check pulses, HR, BP
• D = disability & neuro eval
• basic: alert, verbal stimuli response, painful stimuli response, or unresponsive
• establish LOC: Glasgow coma scale
• pupils
• lateralizing signs
• rectal tone
• extremity movement
• spinal cord injury level
• Battle’s sign or raccoon eyes
• CSF or bleeding from ears
• E = exposure or environmental control
• completely undress patient and cover with warm blankets
• examine every part of body and every nook and cranny
• warm environment and warm IVF
• F = Foley and a finger or tube in every orifice, family, and friends
• controversial, every trauma patient may not need rectal exam
• find out everything you can from family & friends
• G = gastric decompression

2.) Secondary survey: after completion of primary survey and resuscitation efforts are underway
• complete H&P
• head-to-toe evaluation looking for injuries consistent with mechanism of trauma
• helps guide trauma imaging
• reassessment of all vitals
• portable x-ray of chest, c-spine, AP pelvis to look for things that need immediate intervention
• ex. open book pelvis, pneumothorax
• FAST US scan
• CT scan
• head CT indicated with evidence of significant skull fx, altered LOC, neurologic deficit,
• persistent vomiting, presence of scalp hematoma, abnormal behavior, coagulopathy, age > 65
• from Nexus II study
• arrange disposition: ICU, OR

5.6.3 Essential Skills and Procedures for Trauma

Needle thoracostomy
• Chest tube
• IV access
• Central venous access
• NG tube: may be needed with crash s/p chest stab, to check for GIB
• Foley catheter

5.6.4 Special Considerations
• Pediatrics:
• will look great and then rapidly lose vitals
  • will maintain BP until stage 4 shock
• a child who doesn’t want to play with you and have fun is really sick
  • “stat stuffed animal bedside” if child can be engaged, this is a better sign
• Elderly:
- a high-risk population as they don’t present until late
- minor injuries can lead to devastating consequences
- Penetrating trauma:
  - don’t pull it out!
  - can go downhill fast
6 Endocrinology Exam Notes

6.1 Introduction

6.1.1 Feedback Loops

A.) Hypothalamic-thyroid axis:
- TRH from hypothalamus → anterior pituitary secretes TSH → thyroid makes T4 and T3
- T3 and T4 feedback negatively on the hypothalamus and anterior pituitary

B.) Hypothalamic-pituitary-adrenal axis:
- CRH from hypothalamus → ant pit secretes ACTH → production of cortisol by adrenal glands
- cortisol feeds back negatively on the pituitary and hypothalamus
6.1.2 Endocrine Physiology Refresher

- Hypothalamus:
  - regulated by CNS, autonomic input, environment (light/temperature), and peripheral feedback
  - hormones stored in the hypothalamus: SS, DA, GnRH, GHRH, TRH, CRH
- Posterior pituitary:
  - releases hormones synthesized by the hypothalamus: oxytocin (induction of labor), ADH (prevention of free water loss)
- Anterior pituitary:
  - releases FSH (regulation of estrogen or spermatogenesis), LH (regulation of ovulation or testosterone), GH, TSH, prolactin, ACTH
- Adrenal glands sit on top of the kidneys and secrete: epinephrine, norepinephrine, dopamine, corticosteroids
- Thyroid secretes thyroxine
- Parathyroid secretes PTH
- Ovary secretes estrogen
- Testes secrete testosterone
- Pancreas secretes insulin and glucagon
- Liver secretes IGF-1

Primary disorders:
- 1° adrenal insufficiency involves the entire adrenal cortex: both aldosterone and cortisol affected
- 1° adrenal excess is usually caused by a benign adrenal tumor that produces only cortisol OR aldosterone, so the problem is confined to only one hormone

Secondary disorders:
- 2° adrenal disorder is due to ACTH excess or deficiency (a problem with the pituitary)
  - since ACTH only affects cortisol, only [cortisol] will be altered in a 2° disorder!
  - ACTH is formed from an intermediate compound (MSH), so if ACTH is in excess it will drive the reaction backwards to produce more MSH → dark pigmented skin

6.1.3 Adrenal Reminders

- Testing is not straightforward because:
  - serum cortisol levels fluctuate throughout the day (diurnal = highest in the morning, lowest in evening)
  - adrenals may recover slowly from suppression
  - Dynamic testing involving stimulation and suppression tests is required
  - -think about whether hormone levels are appropriate for the situation!

6.1.4 Tumors

- Adenoma: tumor of glandular origin, usually not malignant but can become so
• tend to hyperfunction ("inappropriate") in producing hormone but are not strictly under the normal regulatory control of feedback loops
• don’t cause problems when in a space with plenty of room
  o cause problems in small places like the pituitary
  o can press on the optic chiasm
• Carcinoma: a malignant tumor of epithelial or other similar origin
• Multiple endocrine neoplasias (MEN): rare genetic disorders that cause benign tumors in multiple glands
  • MEN 2a = medullary thyroid carcinoma, pheochromocytoma, parathyroid adenoma
  • MEN 2b = medullary thyroid carcinoma, pheochromocytoma, mucosal neuromas, marfanoid habitus

6.2 Diabetes Mellitus

6.2.1 Introduction

Diabetes: a group of metabolic diseases characterized by hyperglycemia as a result from defective insulin secretion or insulin action or both
• chronic hyperglycemia leads to nonenzymatic glycation of proteins → tissue damage
• types:
  • type 1 diabetes: deficiency or nonsecretion of insulin
    o autoimmunity against pancreatic islets
      ▪ serology can’t always diagnose as autoantibodies can wane with time
    o accounts for 5-10% of cases
  • type 2 diabetes: due to peripheral insulin resistance in muscle and fat as well as decreased pancreatic insulin secretion and increased hepatic glucose output
    o what insulin being produced is less than normal and it also doesn’t work as well as it should
    o accounts for 90-95% of cases
  • gestational diabetes: develops during pregnancy and resolves afterwards
    o may be caused by the pregnancy but also highly predisposes the woman to later developing DM2
• other causes:
  • latent autoimmune diabetes of adulthood (LADA): looks like DM1 but develops much later in life
  • maturity onset diabetes of the young (MODY): looks like DM2 but does not fit the typical picture of an obese child
    o cystic fibrosis, certain meds
  • Risk factors: FH, age > 45, certain ethnicities (Latino, Native American), habitual physical inactivity, medications (steroids for transplants, antipsychotics, antiretrovirals), obesity
  • fat cells produce hormones such as leptin, resistin, etc.
    o some are good and some are bad, causing pro-inflammatory states
• A progression from insulin resistance to full-blown diabetes
• insulin resistance → hyperlipidemia, HTN, obesity, IGT, PCOS → impaired glucose tolerance and increased post-prandial glucose → impaired fasting glucose → DM2
• issues surface as pancreas can’t keep up with increased insulin demands
• insulin resistance is an underlying characteristic of many other conditions: obesity, dyslipidemia, HTN, cardiovascular disease, stroke
• Epidemiology
• DM is the most common endocrine topic
• there are many people who go undiagnosed
  o more than 25% of those over age 65 have diabetes
6.2.2 Diabetes Presentation

- Fatigue, polyuria (osmotic diuresis from saturated glucose transporters) and polydipsia (increased serum osmolality), susceptibility to infection
- Blurred vision from alterations of osmotic content of lens and humors changes in refraction
- Weight loss from hypovolemia and increased protein catabolism, especially with DM1
- DM2-specific findings:
  - may be asymptomatic
  - PCOS hirsutism (abnormal hairiness)
  - acanthosis nigrans: skin hyperpigmentation in the neck folds, armpits, groin, knuckles, between the legs, at the elbow, under breasts, around umbilicus

6.2.3 Diabetes Prevention & Screening

- Prevention:
  - prediabetics must be counseled on the benefits of moderate weight loss and regular physical activity
    - study showed 58% reduction in risk with keeping food journals, visiting dietician regularly, and weight loss (better reduction than starting on metformin!)
- Screening:
  - USPSTF: screen all adults with sustained BP > 135/80
  - should be done regardless of age in all asymptomatic patients who are overweight, obese, or who have risk factors for diabetes
  - should be done for all other patients beginning at age 45, repeating every 3 years
  - pregnancy and gestational diabetes:
    - should be done at first prenatal visit in all pregnant women with risk factors
    - no risk factors = do at 24-48 weeks gestation using oral glucose tolerance test
    - women who develop gestational diabetes should be screened for persistent diabetes 6-12 weeks postpartum using a test other than A1C
    - women with history of gestational diabetes should have lifelong screening every 3 years

6.2.4 Complications of Diabetes

**Diabetic ketoacidosis:** a result of ketone buildup from fatty acid metabolism, resulting in acidosis
- hyperglycemia, nausea, vomiting, hyperventilation with fruity breath, lethargy, abdominal pain
- suspect in patients with persistent high blood sugars
- more common in DM1 but can happen in DM2
- represents a large chunk of diabetes healthcare costs
- labs: hyperglycemia > 250, glycosuria 4+, acidosis, low serum bicarb, serum ketones
- management: insulin drip, IVF, potassium, EKG monitoring

**Nonketotic hyperosmolar syndrome:** like DKA with high blood sugar, but without acidosis
- Stroke
- Eye issues: diabetes is the leading cause of blindness in adults
  - diabetic retinopathy: high glucose causes osmotic changes in the eye that damage the vasculature blockage of blood vessels and reduced oxygen supply to the retina neovascularization with weak vessels hemorrhage and exudates
    - -25x higher in diabetics
    - -can be treated with laser photocoagulation
- cataracts and glaucoma
- refer to ophthalmology for annual (or more frequent) eye exams
- Nephropathy and ESRD: occurs in 20-40% of diabetics
- leading cause of dialysis is diabetes
renal transplant is more promising than going on dialysis
Heart disease: a major cause of mortality for diabetics
DM2 is an independent risk factor for cardiovascular disease
treatment must be multifactorial because risks are related: control of cholesterol as well as blood pressure, etc.
even those who do not yet have diabetes but are at risk for it should begin reduction of CV disease risk factors
Foot and leg amputations
Neuropathy: distal symmetrical polyneuropathy with loss of motor and sensory function, especially of the long nerves
occurs in 60% of diabetics = the most common complication
hand and foot tingling and pain or numbness (usually bilateral vs a stroke which is unilateral)
  - hypersensitivity to light touch
  - can’t feel what you are stepping on
  - ulceration
  - infections
  - gangrene
can also have central autonomic neuropathy: cardiac denervation, painless MI, heat or exercise intolerance, orthostatic hypotension without increased HR to compensate, tachycardia, constipation or diarrhea, esophageal dysfunction, fecal incontinence, gastroparesis, cystopathy, ED, neurogenic bladder, unawareness of hypoglycemia, decreased diameter of dark-adapted pupil, sweating disturbances
hard to treat once it has occurred = diagnose and control diabetes as quickly as possible
Hypoglycemia
incidence is increased with acute illness, erratic food intake, poor coordination of insulin dosing with meals, vomiting, sepsis, worsening renal or liver function, too much insulin given, hypothyroidism, adrenal insufficiency, meds (acetaminophen, propranolol, anabolic steroids), alcohol
treat in alert patients with 15 g of rapidly available carbs
treat in an unconscious, severely symptomatic, or NPO patient with IV dextrose (D50)
Hyperglycemia
causes: insufficient insulin dosing, infection, dehydration, cardiac issue, increased counter-regulatory hormones (epinephrine), stress, surgery, hypoglycemia rebound, medications (diuretics, estrogens, β-blockers, corticosteroids)
Other factors affecting glucose tolerance: activity level, liver disease, hormonal tumors, pancreatic disorders, pregnancy

6.2.5 Diabetes Investigation & Diagnosis

Diagnosis: meet one of the criteria below, followed with confirmation of another criterion on another day

a.) fasting plasma glucose: no caloric intake for at least 8 hours
  - normal is 70-99
  - prediabetic if 100-125 mg/dL
  - diabetic if ≥ 126
b.) oral glucose tolerance test: timed blood draw after oral load of a specific amount of glucose
  - variations on 1, 2, or 3 hours; for 2 hours:
    - prediabetic if 140-199
    - diabetic if ≥ 200
c.) random glucose test: most common method of detection
  - diabetic if ≥ 200 with symptoms
Other tests:
  - hemoglobin A1C: measures a form of hemoglobin used to identify the average plasma glucose concentration over prolonged periods of time
  - can’t use POC measurements for diagnosis! must be laboratory A1C
  - life of RBC is ~ 120 days, so this test reflects average blood glucose during that timeframe
    - normally 3-6%
  - diabetic if HbA1C ≥ 6.5%
  - should normalize within 3 weeks of normoglycemic levels
• caveat: can’t use this test in patients with abnormal formation or turnover of RBCs
  o ex. chronic hemolysis, hemoglobinopathies, anemias, iron deficiency
• C-peptide: measures the “connecting peptide” created when proinsulin splits into insulin and C-peptide; used in most newly diagnosed diabetics
• decreased levels in DM1, normal or high levels in DM2
• can also be used to identify gastrinoma spread or malingering by insulin abuse
• fructosamine: also known as glycated albumin or glycated serum protein; reflects hyperglycemic period within the last few weeks to give information about short-term glycemic control
• useful in patients with chronic hemolytic anemias
• limited use in patients with low serum albumin, such as nephrotic states or hepatic disease
• urine microalbumin: checks for protein that should not be in the urine at amounts greater than 30 mg
• more sensitive than urine protein dipstick test
• correlates with nocturnal systolic blood pressure
• albumin to creatinine ratio from a random blood test can also be used

What kind of specimen to use?
• venous serum has no cells in it to use up the glucose and make it look falsely low
• capillary specimens are rapid and can be used for home monitoring
• urine specimens require BG > 160 to detect

6.2.6 Treatment & Diabetes Management
• Managing information between providers:
• fasting glucose of 126, OGTT of 200, and A1C of 7% are all equivalent to each other biologically
• Lifestyle modifications:
• insulin sensitivity improves with weight loss in patients with DM2
• Diabetic foot checks: test for neuropathy
• Labs:
• want A1C under 7%
  o reduces risk of cardiovascular disease, retinopathy, nephropathy, and neuropathy
  o lowering by any amount will improve health outcomes
  o essential for any patients who don’t check their own sugar
  o if patient has good control, check this 1-2 times a year, but if not check it q 3 months
• want random blood glucose ~140 (or 140-180 if critically ill)
  o promotes WBC functioning and facilitates wound healing
• check urine microalbumin
• ABCs
• aspirin, ACEI (and A1C control)
• β-blocker, blood pressure control
• cholesterol management
• diet, don’t smoke
• exercise
• Use of insulin:
  o type 1 diabetics:
    ▪ multiple dose insulin injections (basal and prandial)
    ▪ matching prandial insulin to CHO intake, pre-meal blood glucose, and anticipated activity
    ▪ use of insulin analogs
  o type 2 diabetics:
    ▪ may need larger doses relative to DM1 patients, and there is no maximum therapeutic effect of insulin
    ▪ can be used to decrease A1C
6.3 Diabetes Pharmacology: Oral Agents & Non-Insulin Injectables for Diabetes

***Oral agents will each only lower A1C by 1%

6.3.1 Contributors to DM2

- Impaired insulin secretion
- Insulin resistance
- Decreased glucagon suppression (liver constantly leaking sugar because glucagon is stimulating it)
- Glucagon is abnormally stimulated even through sugar levels are high
- Drugs can be designed to target these!

6.3.2 Insulin Secretagogues

A.) Sulfonylureas: increase insulin secretion by hugging the pancreas all day long
- Tend to burn out the pancreas after 3-5 years of use
- New patient: start on a 2nd gen agent at a low, single daily dose
- Educate about recognition and treatment of hypoglycemia
- Adjust dose as necessary every 3-4 weeks
- Consider a combination therapy when dose approaches max
- 1st generation:
  - Chlorpropamide: half-life is 72 hours = hypoglycemia is a problem
    - Other side effects: hyponatremia, SIADH, disulfiram-like reaction
  - Tolbutamide: shorter half-life, least potent, best for kidney disease
  - 2nd generation: don't work better than 1st gen but there are fewer side effects and fewer drug interactions
  - Glipizide: take on empty stomach, can be used with renal impairment
  - Glyburide:
  - Glimepiride:

B.) Meglitinides: hug pancreas with one quick squeeze
- Taken with a meal
- Squirts out just enough insulin to cover the meal
- Need to educate patient about hypoglycemia
- Repaglinide: a benzoic acid derivative that works better
- Nateglinide: a D-phenylalanine derivative

Contraindications: renal dysfunction, hepatic dysfunction, regimen?
Side effects: hypoglycemia, weight gain = now moving out of favor

Biguanides: decrease hepatic glucose output while increasing uptake by fat and muscles, also minimally decreases intestinal absorption of glucose

Metformin: every diabetic should be put on this at the time of diagnosis, tastes bad
- Contraindications or cautions: kidney disease, liver disease (site of lactate metab), elderly, heart failure, alcohol abuse or binge drinking, IV contrast
- Side effects: lactic acidosis, GI, weight loss, vit B12 depletion

Thiazolidinediones: Glitazones: increase glucose uptake in adipose and muscle and inhibit hepatic glucose output by the stimulation of PPAR-γ receptors
- Works opposite of metformin: first in the periphery and then in the liver
- DOCs if insulin resistant (abdominal obesity, PCOS, acanthosis nigricans)
- Kinds:
  - Pioglitazone: bladder cancer risk with increased duration or dose, once daily dosing
  - Rosiglitazone: cardiovascular side effects, fracture risk
  - Investigational studies are inconclusive regarding drug safety
Currently remains on the market with FDA restriction to access
- current users may continue but must be advised of side effects
- new users should only use if unable to achieve glycemic control on other meds
- patient eligibility must be documented by provider

- Contraindications and cautions: liver disease, heart failure, pregnancy or lactation
- Side effects: liver tox, fluid retention, weight gain (but can redistribute weight = pros outweigh cons), headache, fatigue, small ↓ in hemoglobin and crit, fracture risk

**α-Glucosidase Inhibitors:** decrease glucose absorption in the intestine
- Pharmacist says not to use because of the farts!
- Kinds:
  - acarbose:
  - miglitol:
- Contraindications: bowel disorders, liver or renal impairment

**Incretin Agonists:** help peptide hormones that are naturally released by the gut to normalize glucose profile; respond only when the blood sugar is high

**GLP-1 agonists:** aid native GLP-1 (secreted from jejunum and ileum after food ingestion) 
- insulin secretion with suppression of glucagon
- slowed gastric emptying
- reduced food intake and improved insulin sensitivity

- can’t use in DM1, they don’t have any insulin to secrete
- insulin secretion is linked to glucose, so they only work when blood sugar is high
- may increase β-cell mass and improve their functioning
- stimulates production of endogenous DPP-4 (an enzyme that breaks down endogenous GLP-1)
- diabetics will end up with no endogenous GLP-1 left because it will all get broken down by upregulation of DPP-4 by the agonist = why we need to use this drug with a DPP-4 inhibitor:
  - sitagliptin: renal dosing, can use in hepatic impairment
    - side effects: hypersensitivities, pancreatitis, URT infection, hypoglycemia when used in combination with sulfonylureas
  - saxagliptin: renal dosing, once daily but more interactions
    - side effects: headache, UTI, hypoglycemia when used in combination with sulfonylureas, URT infection, hypersensitivities
  - linagliptin: no renal adjustments needed
    - side effects: URT infection, hyperuricemia, hyperlipidemia, hypoglycemia when used in combination with sulfonylureas - contraindications or caution: pancreatitis or history of, DM1, renal disease
- kinds:
  - **exenatide:** SQ pen injection
    - increase dose after 30+ days if needed
    - decrease sulfonylurea dose in half to prevent hypoglycemia
    - patient education: doses must be 6 hours apart, can’t go in same site as insulin, only 1 time prime needed, take within 60 min of meal, skip meal = skip dose, refrigerate after opening
  - **long-acting exenatide:** 2 weekly SQ injections not correlated to meals
    - steady state achieved in 6 weeks, glycemic results in 2 weeks
    - add on to metformin, sulfonylurea, or glitazone
    - fasting blood glucose improvement more noticeable than post-prandial
      - but may see initial bump in fasting BG can continue short acting exenatide for a week past the long-acting initiation
    - patient education: requires reconstitution by patient, making up for a missed dose must be done at least 3 days prior to next dose
  - **liraglutide:** SQ pen injection once daily, independent of meals
    - initiate low and adjust up
    - decrease sulfonylurea dose in half to prevent hypoglycemia
    - not used with insulin because it will frequently cause hypoglycemia
    - more weight loss than exenatide
contraindications: pancreatitis, DM1, GI or gastroparesis, CrCl <30, thyroid cancer
• risk of thyroid tumors with long-acting exenatide and liraglutide, so counsel patients √ drug interactions:
  antibiotics, contraceptives, analgesics, sulfonylureas, insulin
  o administer all oral meds at least one hour prior
• side effects: nausea, vomiting, weight loss, injection site reaction

Amylin Agonists: aid amylin, a β cell hormone that is co-secreted with insulin √ suppression of glucagon secretion from pancreatic α cells, regulation of gastric emptying = enhancement of satiety
• DM2 have a moderate amount of amylin and DM1 have a tiny amount but are more sensitive to it = smaller dose for DM1

Pramlintide: a SQ pen injection used before meals
• decrease meal time insulin by half
• rarely used because it only serves to fine-tune blood sugar control while doubling the number of injections required per day
• patient education: meals must be 30g CHO or more, inject at different site than insulin
• contraindications: GI disorders
• drug interactions: antibiotics, contraceptives, analgesics
• side effects: nausea, anorexia, insulin-induced severe hypoglycemia in DM1

6.3.3 Nontraditional Agents
A.) Bile acid sequestrants: used as an adjunct treatment for DM2
• colesevelam: reduces A1C up to 0.5%
• really only used if patient needs lipid management and diabetes and can’t tolerate a statin
• patient education: must take other oral meds 1 hour before or 4 hours after
• contraindications: obstructive bowel disease, TG > 500
B.) Dopamine agonists: used as an adjunct treatment for DM2; may work by affecting circadian rhythms
• bromocriptine: modest decreases in A1C but significant GI effects
• contraindications: cardiovascular disease, PUD, psychosis, dementia

6.3.4 Glycemic Management of DM2
A.) Based on A1C:
• if 6.5-7.5% □ start on metformin unless contraindicated
  o alternatives:
    ▪ if post-prandial control is needed: GLP-1 agonist + DPP-4 inhibitor, α glucosidase inhibitor
    ▪ if there is metabolic syndrome or non-alcoholic fatty liver disease □ glitazone
• if 7.6-9% □ start on metformin + one of the following:
  o sulfonylurea
  o glitazone
  o GLP-1 agonist + DPP-4 inhibitor
  o meglitinide
• if > 9%:
  o if symptomatic □ insulin
  o if asymptomatic □ metformin + 1 or 2 oral agents
B.) Based on glycemic target:
• if fasting BG is high □ metformin, sulfonylurea, glitazone, long acting basal insulin
• if post-prandial BG is high □ meglitinide, GLP-1 agonist, rapid acting insulin, α glucosidase inhibitor
C.) When to initiate insulin:
• if 3+ oral agents are needed to control BG
• if A1C remains > 8.5% with dual therapy

6.3.5 Contraindications to Oral Agents
• Creatinine > 1.5 □ stop metformin
• Contrast dye or cardiac cath □ hold metformin
• Worsening hepatic function
• Advanced CHF

6.4 Insulin Dosing

6.4.1 Intro to Insulin

Formulations of insulin:
• rapid-acting: used as bolus insulin (meal coverage insulin or rescue insulin) peaks in 30 minutes to 1 hour, lasts 3-5 hours
• take 15 minutes before meal
• insulin aspart:
• insulin lispro:
• short-acting: also used as bolus insulin, peaks in 2 hours, lasts 3-6 hours
• take 15 minutes before meal
• regular insulin: may be purchased without a prescription
• intermediate-acting: onset in 2-4 hours, peaks in 6-10 hours, duration of 10-16 hours
• NPH insulin: also considered to be basal insulin; CLOUDY
  □ because it has longer peaks, you only do breakfast and supper
  □ may be purchased without a prescription
• long acting/basal:
  □ insulin detemir: onset in 2 hours, no peak, lasts 6-24 hours
    □ initiate as once a day, may need to go up to 2x daily
    □ longer duration because it is bound to albumin
  □ insulin glargine: onset in 5 hours, no peak, works for 20-24 hours
    □ long duration due to acidic pH
• insulin aspart protamine: e.) insulin mixes
  □ 70% NPH/30% regular: take 30 minutes before meals, more hypoglycemia risk
    □ regular insulin has a longer peak
    □ may be purchased without a prescription
  □ 75% insulin aspart protamine/30% rapid: take 15 minutes before meals

Factors affecting insulin absorption:
• strenuous exercise of injected limb within one hour
• rubbing injection site
• temperature: increased absorption with heat, decreased with cold
- site of injection: abdomen > arms > thighs
- lipohypertrophy delays absorption
- large doses (> 80 units) delay onset and duration
- hospitalization: depends on severity of illness, medications taken, diet

75 units of insulin = 0.75 mL, etc.

Syringes:
- U-100 syringe = 100 u of insulin per 1 mL
- short = 3/16 inch needle
- regular = ½ inch needle
- U-500 syringes were created for patients needing to take > 200 u of insulin a day
- they are 5x more concentrated than the U-100 syringes

Sliding scale insulin should never be used as monotherapy

6.4.2 Initiating Insulin in DM2
- Average-sized patient begin with 10 u basal insulin once daily
- Obese patient begin with 0.2 u/kg basal insulin once daily
- Mixed insulin begin with 0.6 u/kg/day
- 2/3 should be the morning dose
- 1/3 should be the evening dose (don’t want NPH to peak in the middle of the night so this dose is lower)

6.4.3 Initiating Insulin in DM1
1.) Establish insulin requirement (total daily dose):
- adult 0.5-0.7 u/kg/day
- prepubescent child 0.6-0.9 u/kg/day
- pubescent child up to 1.5 u/kg/day
- adolescent 0.6-1 u/kg/day
- insulin resistant if > 1 u/kg/day needed
2.) Calculate basal and bolus doses:
- individual injections of basal and bolus are best:
  - basal should be 50% of the total daily dose
  - remaining 50% is the bolus, which should be divided up into meal time doses
    - if using NPH as the basal, you must decrease the amount of bolus used by 20% and titrate up as needed
- if pt is unwilling to do multiple injections per day you can use a premixed insulin:
  - 2/3 of total daily dose should be the morning dose
  - 1/3 of total daily dose should be the evening dose

6.4.4 Switching NPH to Long Acting Insulin
- If NPH was once a day, a unit-to-unit change is ok
- If NPH was twice a day, calculate the total daily dose, decrease by 20%, and give it as a once day dose

6.4.5 Insulin Adjustment Algorithm

Rule of 1800: estimates the mg/dL BG that 1 unit of insulin will change your patient

\[\frac{1800}{TDD} = (x) \text{ mg/dL current BG} - \text{goal BG} \div (x) = \text{how many units to give to reach goal BG}\]
- tips:
  - a regular DM1 will usually change by 50 mg/dL for a 1 u bolus
  - an insulin resistant diabetic will usually change by 25-30 mg/dL for a 1 u bolus
  - an insulin sensitive diabetic could change as much as 70-100 mg/dL for a 1 u bolus

Rule of 500: estimates how many grams of carbs a unit of insulin will cover

\[\frac{500}{TDD} = (x) \text{ grams CHO covered by 1 u insulin}\]
• tips:
  • if frequent hypoglycemia, decrease dose by 0.5 u

Troubleshooting fasting hyperglycemia
• Somogyi (rebound) hyperglycemia: occurs anytime in response to a prior low BG
• low BG triggers glucagon and other counter-regulatory hormones
• fix: change insulin to prevent hypoglycemia
• dawn phenomenon: occurs between 3-5am when body sends out counter-regulatory hormones to
  increase blood sugar in response to waning insulin levels
• have pt get up and check BG at 3am to investigate a dietary cause
• fix: change insulin or move peak to a more physiologic time

6.5 Thyroid

6.5.1 Thyroid Physiology Review

• Thyroid hormone: T3 and T4 collectively
• production requires thyroid-synthesized thyroglobulin, which is stored in follicles until needed
• production also requires iodine and tyrosine
• TH control oxygen consumption, carbohydrate, fat, and protein metabolism, electrolyte mobilization, and
  vitamin A synthesis
• thyroxine (T4): thyroid has 50 day reserve supply
• T4-deiodinases in target cells-> T3
• triiodothyronine (T3): the major thyroid hormone, stimulates carbohydrate
  absorption from small intestine and increases fatty acid release from adipose
  o activates Na/K ATPases maintain high metabolic rate
  o upregulates β-adrenergic R in heart and nervous system
  ▪ overproduction of thyroid hormone racing heart, anxiety, nervousness
  o required for normal production of growth hormone
  ▪ cretinism: mental retardation due to low TH during fetal development; mother is low
    in iodine
• Thyroid hormone circulation:
• TH travels in plasma bound to thyroxine binding globulin, transthyretin, or albumin = inactive
“free” unbound TH accounts for very small percentages of T3 and T4 = active
  - this active TH bathes the hypothalamus and stimulates TRH if it gets too low
- severe illness or starvation decreases total and free T3, increase reverse T3, and doesn’t change free T4

6.5.2 Thyroid Examination

- Inspection and identification of landmarks
- Palpation
- Auscultation
- Lymph nodes: cervical and cervical chains

6.5.3 Thyroid Presentation and Investigation

- Approach: history, morphology of thyroid, other physical signs, chemical status, functional status, imaging, cytology
- general thyroid history: weight change, appetite, energy level, temperature preference, dysphasia, voice changes, bowel frequency, hair or skin changes, muscle cramps, muscle weakness, mood or temperament, tremor, palpitations, menstrual change, h/o neck irradiation, FH thyroid disease, h/o iodine, lithium, or certain meds
- PE: weight, HR, skin/hair, nails for onycholysis (atraumatic separation of nail from bed), exophthalmos or lid lag, thyroid size, contour, mobility, texture, or tenderness, thyroid bruits, cervical adenopathy, cardiac exam, DTR relaxation phase, pretibial edema
- Thyroid screening:
  - USPSTF concludes there is insufficient evidence
  - American Thyroid Assn recommends TSH screenings beginning at age 35 and then every 5 years
- When to be concerned about malignancy:
  - remember that only 5-15% of thyroid nodules are malignant
  - suspicious features: recent rapid growth, age < 20 or > 70, male, h/o head or neck irradiation, recent change in voice, breathing, or swallowing, firm nodule with irregular shape, nodule fixated to underlying tissue, regional adenopathy
- observe nodules that don’t meet criteria for biopsy
- Labs:
- thyroid profile: TSH + free T4
  - TSH (thyrotropin): used as a screen for thyroid disease
    - increased levels accelerate iodine metabolism and hormone production
    - elevated in primary hypothyroidism
      - f/u with free T4
    - depressed in primary hyperthyroidism and secondary hypothyroidism (pituitary failure)
      - f/u with free T4 & T3
    - pt must have normal hypothalamic-pituitary function and stable thyroid status for results to be applicable
- free T3: tested less often, usually to confirm a diagnosis of hyperthyroidism when T4 is low and T3 is an elevated isolation
  - thyroid releasing hormone (TRH):
- thyroxine binding globulin (TBG): amount will affect serum levels of T3 and T4
  - but physiologic thyroid status is determined by levels of free T3 and free T4
  - TBG is measured directly or by T3 uptake (aka thyroid hormone binding ratio): patient's serum is mixed with the labeled T3; then, resin is added to measure the amount of free labeled T3
    - if patient is truly hypothyroid, and TBG levels are normal, then there are many sites open for binding on the TBG (since the total TH level is low) labeled T3 binds mostly to the TBG, leaving little of it left for binding to the resin = low T3 uptake by the resin
    - if the patient is truly hyperthyroid, and TBG levels are normal, the patient's endogenous T4 will saturate the TBG binding sites more, leaving less room for the labeled hormone = greater binding to the resin (more left over) = high T3 uptake by the resin
  - TBG levels are increased by estrogen and pregnancy falsely low T3 uptake by the resin
TBG levels are decreased by androgens, nephrotic syndrome, or hepatic failure — falsely high T3 uptake by the resin

- **Free thyroxine index**: total T4 x TBG; a more reliable indicator of thyroid status in the presence of abnormalities in plasma protein binding because it takes into account both absolute hormone level and binding capacity of TBG
  - low in hypothyroidism
  - high in hyperthyroidism

- **TRH stimulation test**: administration of a small amount of TRH intravenously, following which levels of TSH will be measured at several subsequent time points
  - patients with normal function of the hypothalamic-pituitary axis respond by increasing the levels of TSH following TRH injection
  - patients with compromised HPA function may exhibit a delayed, blunted, or absent response to TRH administration

- **Anti-thyroid antibodies**: may occur in thyroiditis, diffuse hyperthyroidism, or Grave’s disease
  - caveat: can also occur in hypothyroidism or thyroid carcinoma
  - anti-TSH-R:
    - **Long-acting thyroid stimulator (LATS or TSI)**: IgG autoantibodies against TSH-R that either stimulate or sometimes inhibit release of TH
    - frequently positive in Grave’s, can follow titers for relapse
  - anti-thyroid peroxidase
  - anti-thyroglobulin and anti-microsomal antigen are high in lymphocytic thyroiditis/Hashimoto’s thyroiditis

- **Functional assessments**
  - **Radioactive iodine uptake**: a direct test of thyroid function
    - measured at 24 hours
    - normally 15-30%

- **Imaging**:
  - **Thyroid scan**: overactive areas will be dark/hot while less active areas are lighter or cold
    - of little value if TSH is normal!
  - **US**: imaging of choice for nodules, with predictors of malignancy being microcalcifications, blurred margins, size > 10 mm, hypoechoic, high vascularity
  - **CT**
  - **MRI or PET**: good for detecting thyroid cancers or lymphadenopathy
  - **Biopsy of a nodule**:
• FNA: should be done on all large hypoechoic nodules with other abnormal US findings
  o may be nondiagnostic up to 20% of the time
• open biopsy
• Interpretation of history, exam, labs, imaging:
  • what is the clinical impression and what do the labs say?
    o euthyroid
    o hyperthyroid
    o hypothyroid
• what did the exam tell you?
  o normal thyroid
  o goiter: symmetric or asymmetric
  o nodule: single or multiple
• put everything together:
  o euthyroid functioning with normal thyroid exam ⋆ look elsewhere for an explanation of symptoms
  o euthyroid functioning with goiter ⋆ US, consider trial of thyroxine for suppression
  o euthyroid functioning with solitary nodule ⋆ US, FNA
    ▪ concern is for malignancy
    ▪ don’t order a thyroid scan, it won’t help you because functioning is normal
  o hyperthyroid functioning with normal exam ⋆ thyroid scan
    ▪ Grave’s disease with low-lying thyroid (missed one exam), or maybe iatrogenic cause? referral
  o hyperthyroid functioning with goiter ⋆ treatment depends on diagnosis
    ▪ differential: Grave’s, toxic multinodular goiter, subacute thyroiditis, silent thyroiditis
  o hyperthyroid functioning with nodule(s) ⋆ thyroid scan
    ▪ HOT ⋆ ablation with radioactive iodine
    ▪ COLD ⋆ refer for FNA
  o hypothyroid functioning with normal exam ⋆ treatment depends on diagnosis
    ▪ differential: Hashimoto’s disease, iatrogenic cause, late thyroiditis
  o hypothyroid functioning with goiter ⋆ treatment depends on diagnosis
    ▪ differential: Hashimoto’s disease, multinodular goiter, late thyroiditis
  o hypothyroid functioning with nodule(s) ⋆ US, FNA
    ▪ concern for cancer if solitary

**Euthyroid Sick Syndrome:** a state of adaptation or dysregulation of thyrotropic feedback control where the levels of T3 and/or T4 are at unusual levels, but the thyroid gland does not appear to be dysfunctional.

This condition is often seen in starvation, critical illness or patients in intensive care unit

Investigation:
• labs:
  • low T3 and T4, low serum prealbumin (diminishes TH binding capability) ⋆ low FTI as well
  • normal TSH = euthyroid state
  • elevated reverse T3

**Hyperthyroidism:** excessive TH

Common causes:

a.) **Grave’s disease:** antibodies form to TSH-R that STIMULATE the R ⋆ hypertrophy of the thyroid and high [TH]
  • unresponsive to negative feedback
  • TH receptors are present in the nuclei of most cells = widespread effect of TH
  • PE: will have a symmetric, nontender goiter, ocular findings, and pretibial myxedema (boggy, nonpitting puffiness)
  • investigation:
    • TSH, free T3, free T4
thyroid uptake and scan □ uptake increased because thyroid is revved up and taking up more iodine

- treatment:
  - treatment of choice is radioactive iodine
    - results in later hypothyroidism 70% of the time
    - no increased cancer risk after 50 years of use
  - thionamides: drugs that block TH production
    - DOC is methimazole
    - if pregnant or not tolerating methimazole, can try propylthiouracil
    - these will take ~50 days to see effect due to body stores of TH
  - β-blockers to slow HR
  - surgery: subtotal thyroidectomy
    - may lead to hypothyroidism later
    - hyperthyroidism may recur
  - good signs for remission: small goiter, free T3 predominance, negative TSI (thyroid antibody) titer, decrease in goiter size with thionamide therapy

b.) toxic multinodular goiter: involves an enlarged thyroid gland that contains a small rounded nodules that produce too much thyroid hormone

- arises from a nontoxic multinodular goiter
- PE: enlarged, irregular thyroid +/- nodules (may not be able to feel through capsule)
- investigation:
  - TSH, free T3, free T4
  - thyroid uptake and scan: shows HOT toxic nodules
- treatment: radioactive iodine

c.) toxic nodule: single nodule with TSH-R mutation of its tissue produces excess TH

- usually in ages 30-40
- PE: enlarged, irregular, nodular thyroid, onycholysis of the ring finger
- investigation:
  - TSH, free T3, free T4
  - thyroid uptake and scan: shows HOT toxic nodule
- treatment: radioactive iodine

Rare causes:

a.) increased TSH production (trophoblastic disease)

b.) increased iodine intake (Jod-Basedow phenomenon)

c.) thyrotoxicosis factitia:

- Presentation: weight loss, hyperphagia, heat intolerance, increased sweating, frequent stools, oily hair or skin, exercise intolerance (due to heart changes), proximal muscle weakness, nervousness, irritability, sleep disturbances, tremor, palpitations or tachycardia, decreased menstrual flow, FH thyroid disease, onycholysis, exophthalmos, lid lag, thyroid enlargement, thyroid bruises, brisk DTR relaxation phase, pretibial myxedema
- Investigation:
  - labs:
    - depressed TSH
    - elevated free T4
    - elevated T3 resin uptake
    - elevated FTI
    - decreased cholesterol, triglycerides
    - hypercalcemia
    - increased LFTs: alk phos

**Thyroiditis:** several types; begins with onset of hyperthyroidism for 1-3 months, followed by 1-3 months of hypothyroidism, ending in euthyroidism
A.) de Quervain’s thyroiditis: subacute; due to TH leakage from destruction of thyroid gland secondary to a viral infection
- presentation: h/o pain in the thyroid gland, fever, enlarged, irregular, tender thyroid
- investigation:
  - TSH, free T4, free T3
  - sedimentation rate because this is an inflammatory process
  - thyroglobulin
  - thyroid uptake and scan: will be low because thyroid is shut down from attack
- treatment: aspirin or other NSAID, prednisone taper in severe cases

B.) Hashitoxicosis: silent or painless thyroiditis; a transient hyperthyroidism caused by inflammation associated with Hashimoto’s thyroiditis disturbing the thyroid follicles, resulting in excess release of TH
- presentation: h/o sudden hyperthyroidism, especially postpartum
- PE: enlarged, nodular thyroid seen only half the time
- investigation:
  - TSH, free T3, free T4
  - anti-thyroid antibodies
  - thyroid uptake and scan: will be low
  - treatment: β-blockers
- prognosis: self-limiting

Any thyrotoxicosis not adequately treated can progress to a thyrotoxic crisis (thyroid storm) that can be fatal!
- presentation: fever, profuse sweating, tachycardia, tremor, restlessness, delirium, psychosis, nausea, vomiting, stupor, coma, hypotension
- treatment: propylthiouracil, iodine, β-blocker
- support with IVF, glucose, correction of hypernatremia, acetaminophen, cooling blanket
- prognosis: mortality is 20%

Hypothyroidism: insufficient TH

Causes:
- primary hypothyroidism: loss of functioning thyroid tissue = not enough T4 • Hashimoto thyroiditis: destruction of thyroid tissue due to cytotoxic antibodies
- usually in ages > 50
- PE: enlarged, irregular, nodular thyroid, or may have nonpalpable thyroid
- labs:
  - TSH: high
  - free T4: low
  - positive anti-thyroglobulin
- treatment: TH replacement

- goiterous hypothyroidism: impairment of hormone biosynthesis with compensatory thyroid enlargement • nontoxic goiter: diffuse or nodular enlargement of the thyroid that is NOT due to an inflammatory or neoplastic process and is NOT associated with abnormal thyroid functioning
- endemic goiter: one that occurs in > 10% of a population due to lack of area iodine or impaired TH synthesis

- sporadic goiter: a result of environmental or inherited genetic factors but does not affect the general population
  - ex. multinodular goiter due to chromosome abnormality
  - treatment: suppress TSH with thyroxine to shrink the goiter □ can lead to thyrotoxicosis in a small minority
  - presentation: Li therapy, iodine deficiency or excess

- central hypothyroidism: due to lack of TSH from secondary (pituitary) or tertiary (hypothalamus) failure
much rarer than primary hypothyroidism
TSH will be low to normal, free T4 will be low
there will likely be other pituitary hormone deficiencies
can't follow TSH to adjust thyroid hormone replacement
Presentation: cold intolerance, fatigue, heavy menstrual bleeding, weight gain, dry skin, constipation, myxedema coma, bradycardia, delayed relaxation phase of DTRs, hoarseness, coarse hair, hair loss, myalgia, cognitive impairment, depression, decreased concentration, decreased hearing, FH thyroid disease, Li use, periorbital edema, goiter or no detectable thyroid tissue, myxedema
Investigation:
- all etiologies except for central will have high TSH
- depressed free T4
- depressed T3 resin uptake
- depressed FTI
- increased cholesterol, triglycerides, CPK, LDH, AST, prolactin, and carotene
- hyponatremia
- normochromic anemia
Treatment:
thyroid replacement therapy
- synthetic T4 = levothyroxine
  - half-life of 7 days, absorbed slowly, but equilibrates after 6 weeks
  - can make up dose if missed
  - dosing:
    - initiate full if young with no cardiac disease
    - start slow if old or with angina
    - should be constant except with pregnancy (↑), menopause, or aging (↓)
    - when withdrawing, start with every other day
  - monitor TSH after 6 weeks (equilibrium) and 6 months (euthyroid will increase clearance of T4), and then annually
    - TSH distribution is skewed to the left in replacement (?)
  - side effects: osteoporosis, increased cardiac contractility, increased risk of atrial fibrillation, allergy to tablet dyes
- synthetic T3 = liothyronine
  - rapidly absorbed in 2-6 hours
- can get mixed T3/T4
desiccated animal thyroid
  - caveat: higher ratio of T3/T4 than in humans, concentrations are variable

6.5.4 Thyroid Tumors
A.) Benign follicular cell tumors
- follicular cell adenoma:
- Hurthle cell adenoma:
B.) Malignant follicular cell tumors
- some are poorly differentiated or undifferentiated
- most are differentiated
  - most common being papillary
    - ages 30-50, more commonly in females
    - associated with ret oncogene
    - good survival rates
  - can also have differentiated follicular and Hurthle cell malignant tumors
    - follicular: age > 50, more commonly female, distant mets more common, 80% survival at 20 years
C.) Medullary thyroid carcinoma: arises from C-cells of the thyroid
- age > 40
- regional lymph node involvement
- mets to lung, bone, and liver
- associated with multiple endocrine neoplasia type 2

Malignancy treatment: aggressive surgery followed by radioactive iodine therapy to wipe out distant mets, thyroxine suppression (?)

### 6.6 Pituitary Disorders

#### 6.6.1 Anatomy Review

- Pituitary is housed in the sella turcica of the sphenoid bone
- Optic chiasm runs over the top of the pituitary while the cavernous sinus borders it laterally
- CT scan of the pituitary should show a posterior bright spot where ADH is stored
- pathological if not present!

#### 6.6.2 Causes of Pituitary Hormone Deficiencies: The 9 I's

- Invasion: pituitary tumor
  - may cause “mass effect” as they grow and compress the pituitary and surrounding structures symptoms of headache, peripheral vision loss, ophthalmoplegia and ptosis due to CN III and VI palsies, hypopituitarism
- Infarction
- Infiltration
- Injury/shearing force
- Immunologic cause
- Iatrogenic cause
- Infection
- Idiopathic
- Isolated
6.6.3 Categorization of Disorders

A.) Deficiencies of pituitary hormones: panhypopituitarism, diabetes insipidus, secondary hypothyroidism, secondary adrenal insufficiency, hypogonadotropic hypogonadism, growth hormone deficiency

B.) Excessive secretion of pituitary hormone: acromegaly/gigantism, hyperprolactinemia, Cushing’s, TSH secreting adenoma

C.) Primary deficits: primary hypothyroidism, primary adrenal insufficiency, primary hypogonadism

6.6.4 Hypogonadism

- Presentation: mood swings, decreased libido, osteoporosis
- women: amenorrhea, infertility
- men: erectile dysfunction, infertility
- Types:
  - primary hypogonadism: failure at the level of the testes or ovary
  - hypogonadotropic hypogonadism (secondary): pituitary does not secrete appropriate amounts of FSH or LH
    - congenital:
      - Kallman’s syndrome: a genetic disorder marked by anosmia (inability to perceive odors) and hypogonadism
      - can also see only one kidney or cleft lip
      - DAX-1 mutations: can lead to adrenal hypoplasia, adrenal insufficiency, or hypogonadism
    - acquired: malnutrition, severe illness or hospitalization, anorexia nervosa, prolonged exercise, exercise bulimia, obesity, DM2, high dose opioids or methadone, high dose glucocorticoids, pituitary adenoma, Rathke’s cleft cyst, apoplexy, metastatic cancer, aneurysm, craniopharyngioma, meningioma, germinoma, glioma, Langerhans cell histiocytosis, trauma, surgery, radiation, encephalitis, hemochromatosis
  - treatment: replace sex steroid unless contraindicated
    - estrogen for women until age 50
    - testosterone for men unless there is prostate disease
    - fertility needs: clomiphene for women, HCG injections for men

Investigation:
- history: is it congenital or acquired?
- MRI of the pituitary
  - exception: very low testosterone is more predictive of a central lesion
- labs: prolactin, iron/TIBC (hemochromatosis), other hormonal workup
- Treatment: hormone replacement
Growth Hormone Deficiency: lack of GH production by the pituitary

- Normal stimuli for GH: exercise, sleep, hypoglycemia, high protein diet, acute starvation
- Present in > 95% of patients with 3+ pituitary hormone deficiencies

- Has 3 causes:
  - pituitary tumor
  - pituitary damage
  - “pure” GH deficiency
- Presentation: low energy/fatigue, poor sense of well-being, decreased mentation, social isolation, more body fat and less lean muscle mass, poor exercise tolerance, dysregulated body temperature, weight gain, osteoporosis, hyperlipidemia
- Investigation:
  - stimulatory tests needed for definitive diagnosis (unless pt has 3+ other pituitary hormone disorders):
    - gold standard is insulin tolerance test: insulin infusion initiated to drop blood glucose to < 40
    - stress
      - normally should cause rise in growth hormone to > 5-10
      - can be dangerous, contraindicated in heart disease, elderly, seizures
    - can also do glucagon stimulation test
IGF-1 can be in normal range in half the patients with GH deficiency

- Treatment:
  - growth hormone replacement indicated for peds or symptomatic adults with 3+ pituitary deficiencies
    - controversial in symptomatic adults
    - younger patients and women on oral estrogens will require more
    - diabetics may need their meds adjusted
    - contraindicated with active malignancy
    - adverse effects: arthralgias, myalgias, joint stiffness, peripheral edema, paresthesias
    - d/c after 6 months if symptoms don’t improve

6.6.5 Acromegaly/Gigantism

- Acromegaly is due to GH secreting pituitary tumor in adulthood
- Gigantism is due to GH secreting tumor during puberty, before epiphyseal plate fusion
- Presentation: clinical features due to combined effects of increased GH and IGF-1
  - slow, insidious onset
  - most will have macroadenomas
  - enlarged soft tissue of the hands and feet, teeth splaying, diabetes, maxillofacial changes (prominent brow), hyperhidrosis, arthralgias, headaches, hypogonadal symptoms, visual deficit, fatigue, weight gain, galactorrhea
  - can also be subtle
  - cardiovascular disease: HTN, LVH, cardiomyopathy
  - increased malignancy risk: colon ca
  - visceral enlargement: thyroid, liver, kidneys, prostate
- Investigation:
  - labs: abnormal glucose, high phosphorus, prolactin
  - first screen with IGF-1(aka somatomedin C) test: unaffected by time, food intake, exercise, or sleep
    - higher in puberty and declines with age
    - if IGF-1 is normal, patient does not have acromegaly
    - low IGF-1 suggests GH deficiency
    - BUT normal IGF-1 can’t rule out GH deficiency!
  - most specific: GH after glucose tolerance test
    - positive if higher than normal GH
- pituitary MRI
- GHRH if MRI is negative
- Treatment
  - surgery
  - somatostatin analogs
  - GH receptor antagonists
  - dopamine agonists
  - radiation
• goals: normal life expectancy and reduce complications
  o lower IGF-1 to normal range
  o lower GH to < 1 ng/mL on glucose tolerance test
• treat symptoms and comorbidities
• bony abnormalities usually won’t regress

6.6.6 Diabetes Insipidus

• Types:
  • central diabetes insipidus: due to lack of ADH production in the hypothalamus insufficient release of ADH from the posterior pituitary
    o causes: idiopathic, familial, panhypopituitarism, infiltrative diseases (sarcoid, TB, Wegener’s), metastatic tumor, trauma, surgery, Wolfram syndrome (a genetic disorder causing DI, DM, deafness, and optic atrophy)
    o treatment:
      ▪ if transient use vasopressin, desmopressin
      ▪ for maintenance use desmopressin
  • nephrogenic diabetes insipidus: kidney is resistant to ADH
    o causes: amyloidosis, myeloma, Sjogren’s, sickle cell, hypercalcemia, recovery from ATN, lithium, foscarnet, methicillin, demeclocycline, colchicine
• Presentation: inability to concentrate urine, polyuria (5-10 L per day), polydipsia, hyponatremia, normal glucose
• Investigation:
  • inpatient differential diagnosis: mannitol, post-op diuresis, hyperglycemia, diuretics, zealous IVF, cured acromegalic
  • outpatient differential diagnosis: hyperglycemia, psychogenic polydipsia, osmotic load
  • direct serum ADH measurement is difficult (extremely low concentrations)
  • image pituitary
  • confirmatory diagnosis via water deprivation test: restrict water and follow Na, urine osmolality, urine output, weight, orthostatic BPs/HRs every 1-2 hours
    o positive if body weight decreases > 5%, serum Na > 145 mEq/L, or > 2 urine osmolalities differ by < 10%
    o then differentiate by administering desmopressin (synthetic ADH)
      ▪ central DI if urine volume decrease or there is > 50% increase in urine osmolality
      ▪ nephrogenic DI if there is < 50% change in urine osmolality
      ▪ psychogenic polydipsia if urine volume decreases and serum Na decreases

Syndrome of Inappropriate Antidiuretic Hormone (SIADH): excessive release of ADH from the posterior pituitary gland or another source ≠ hyponatremia and sometimes fluid overload
• Causes: tumors, pulmonary disease like TB, CNS disorders, radiation therapy
• Investigation:
  • labs: low serum osmolarity, low serum Na, high urine osmolality
  • get a water loading study: 1L water give, with hourly urine and serum osmolality collections for 5 hours
    o normal if urine osm < serum osm = diuresis of excess fluid
    o SIADH if urine osm > serum osm = retaining excess fluid

6.6.7 Panhypopituitarism

• Investigation: MRI of pituitary
• Treat underlying cause
• replace cortisol first
• thyroid hormone replacement
• sex steroid replacement

6.6.8 Hyperprolactinemia
- Prolactin is constantly produced unless suppressed by a specific inhibitory mechanism
- Prolactin suppresses GnRH → less LH and FSH → hypogonadism
- Causes:
  - usually due to prolactinoma
    - if > 1 cm = macroadenoma
    - if < 1 cm = microadenoma
    - accounts for 40-50% of all pituitary tumors
  - drugs: antipsychotics, Reglan, tricyclics, SSRIs, verapamil, alcohol (esp beer), heroin, cocaine
- Presentation:
  - women: galactorrhea, amenorrhea, infertility
  - men: erectile dysfunction, infertility, headache, mass effect, galactorrhea
- Investigation:
  - prolactin > 200 → pituitary adenoma, renal failure, pregnancy, prolactinoma
  - prolactin 20-50 → pituitary adenoma, renal failure, pregnancy, drugs, other pituitary tumor, hypothalamic tumor, chest wall stimulation
- Treatment for prolactinoma:
  - consider size, mass effect, androgen disruption, and patient desire for fertility
  - indications for therapy: macroadenoma or enlarging microadenoma, infertility, bothersome galactorrhea, gynecomastia, testosterone deficiency, oligo or amenorrhea, acne, hirsutism, bone loss
    - for macroadenoma, mass effect, visual field deficit, or fertility desired → start on dopaminergics
      - cabergoline is better tolerated and 90% effective
      - bromocriptine is cheaper but less tolerable and 67% effective
    - for microadenoma, no fertility desired, full visual field, no mass effect, or low androgen → start on hormone replacement
- surgery may be needed

### 6.6.9 TSH Secreting Pituitary Tumors

- Extremely rare
- Presentation: goiter, hyperthyroidism, and inappropriately elevated TSH (not being suppressed)
- tumor will also secrete GH, prolactin, and things with an alpha subunit (FSH, LH, TSH etc)
- Treatment:
  - surgery required
  - radiation and octreotide to control growth
  - may need I-131 ablation of thyroid tissue to control thyrotoxicosis

### 6.7 Adrenal Disorders

#### 6.7.1 Adrenal Gland Anatomy Review
Adrenal medulla: inner portion which secretes catecholamines (epi, norep, dopamine)

Adrenal cortex: outer portion which secretes corticosteroids (can refer to glucocorticoids or mineralocorticoids)

Has 3 layers:

1.) zona glomerulosa:
   - aldosterone: a major mineralocorticoid manufactured in the zona glomerulosa
   - stimulates renal reabsorption of Na with excretion of K = critical in prevention of hypovolemia and hyperkalemia
   - ACTH has NO effect on aldosterone!

2.) zona fasciculata:
   - cortisol: a major glucocorticoid manufactured in the zona fasciculata (and a little in the reticularis)
   - stress response □ very high [cortisol] □ inhibits DNA synthesis, stimulates protein catabolism, breaks down bone, and inhibits GH = counters effects of insulin
   - exhibits diurnal variation: highest in the morning with a nadir in the evening
   - also elevated during exercise or stress
   - prevents release of inflammatory substances in the body

3.) zona reticularis: manufactures androgens (and a little bit in the fasciculata)
   - testosterone:
   - corticosterone:
   - DHEA: produced in large amounts but no functional significance in adult life
   - androstenedione:

6.7.2 Adrenal Testing

1.) Cortisol
   - 24 hour urine free cortisol: evaluates overall cortisol production
   - the preferred screen for Cushing’s
   - salivary cortisol: obtained after rinsing the mouth, independent of salivary secretion rate

2.) ACTH:
   - blood ACTH: ordered as a baseline test to evaluate whether or not the pituitary is producing appropriate amounts of ACTH
   - high indicates primary adrenal insufficiency
   - low indicates secondary adrenal insufficiency
   - ACTH stimulation test: plasma cortisol is measured before and after injection of synthetic ACTH
   - used to diagnose adrenal insufficiency

3.) Dexamethasone suppression test: cortisol mimic is given to see if negative feedback on the hypothalamus/pituitary will occur □ suppression of further cortisol production
   - lower doses will not have a response in patients with Cushing’s but higher doses will
   - an ACTH-producing tumor will not respond to any dose

4.) CRH stimulation test: CRH is injected and cortisol and ACTH levels are measured at baseline, 30, and 60 min
   - normal: ACTH peak at 30 min, cortisol peak at 60 min
   - adrenal tumors or ectopic ACTH secreting tumors □ no response

5.) Aldosterone:

6.) Adrenal androgens: testosterone and androstenedione are the major ones

7.) 17-OCHS & 17-KS: glucocorticoid metabolites that are useful in determining cause of Cushing’s
   - urine 17-OCHS: indirect measure of excessive plasma glucocorticoids
   - limited use with certain drugs, estrogens, or urine glucose
6.7.3 Adrenal Insufficiency

Types:

a.) primary adrenal insufficiency (Addison’s disease): adrenal gland does not respond to ACTH or make adrenal hormones due to damage
   - includes entire adrenal cortex = mineralocorticoid (aldosterone) deficiency as well (usually)
   - presentation: skin hyperpigmentation, salt craving, hyponatremia, hyperkalemia, vitiligo, pallor, autoimmune thyroid disease, CNS symptoms in adrenomyeloneuropathy
     - onset will be abrupt if due to adrenal hemorrhage, necrosis, or thrombosis, meningococcal sepsis, Pseudomonas, coag disorders, metastatic cancer with bleed
     - onset will be slow if due to autoimmune adrenalitis, infectious adrenalitis, metastatic cancer, congenital adrenal hyperplasia, or adrenomyeloneuropathy
   - labs: frequently hypoglycemia and hyponatremia, hyperkalemia, low aldosterone, high renin due to increased renal sodium losses

b.) secondary adrenal insufficiency: failure of pituitary to secrete ACTH
   - causes: pituitary tumor, surgery, radiation, craniopharyngioma, isolated ACTH deficiency, Megace (drug used to stimulate appetite), long-term glucocorticoid therapy, sarcoidosis (inflammation reaches hypothalamus), hypothalamic tumor
   - presentation:
     - slow onset
     - no skin hyperpigmentation because ACTH is not in excess
     - intact RAAS □ hyperkalemia or hypotension is rare with this
     - insulin tolerance test
     - metyrapone test
   - treatment: steroids, with stress doses for trauma or surgery
     - no need for mineralocorticoid replacement because RAAS is intact

c.) tertiary adrenal insufficiency: failure of hypothalamus to secrete CRH
   - usually due to suppression of CRH and ACTH by exogenous cortisol use

d.) adrenal crisis: acute, life-threatening, low levels of cortisol
   - labs: low cortisol, low glucose, hyperkalemia, hyponatremia, elevated BUN
   - treatment: don’t wait for labs to come back before beginning treatment!
     - IVF (NS or D5+NS) for hypotension
     - IV dexamethasone (preferred because it won’t interfere with diagnostic testing) or hydrocortisone

- urine 17-KS: elevation indicates tumor or hyperplasia of adrenal cortex
- limited use with pregnancy, estrogens, penicillins, erythromycins, others

8.) Imaging
- x-rays used to look for calcifications of the adrenal cortex due to TB
- CT or MRI are used the most
- evaluate size and shape of the adrenals and pituitary
  - enlarged adrenals with infections and cancer
  - small or normal adrenals with autoimmune disease and secondary adrenal insufficiency
- US

9.) Renin:

10.) Urine catecholamines:
- interfered with by certain drugs
  - increased in caffeine, epinephrine, etoh, bananas, nitroglycerine, stress
  - reduced in clonidine, radiographic agents, renal failure

11.) Urine metanephrines:
- interfering drugs: peppers, codeine, acetaminophen
Presentation: chronic fatigue, joint pain, lack of appetite, unintentional weight loss, abdominal pain, nausea, diarrhea, cardiovascular instability and hypoglycemia (only when undergoing physical stress), hyponatremia, hypotension unresponsive to fluids or pressors

Investigation:
- tests:
  - morning cortisol levels (can’t use if pt is critically ill)
    - normally 6-24 µg/dL
    - levels > 18 are high enough to rule out adrenal insufficiency
    - low levels ≤ 3 rule in adrenal insufficiency levels between 3-18 need workup
  - synthetic ACTH (Cosyntropin) stimulation test
    - in a normal response to ACTH, baseline levels should more than double
      - pre or post-test cortisol > 18 rules out primary or secondary adrenal insufficiency
    - subnormal response is seen in primary adrenal insufficiency
      - can’t make enough cortisol out of the extra ACTH
    - explosive response is seen in secondary adrenal insufficiency
      - adrenal has been waiting for ACTH for so long that it makes a ton of cortisol
    - caveat: sensitivity and specificity of the test warrant further investigation
- once you have ruled in AI by either a low morning cortisol or subnormal ACTH response, THEN you check the plasma ACTH levels
  - high ACTH (>100) is consistent with primary AI
  - normal ACTH (5-45) rules out primary AI look for a secondary or tertiary cause!

Treatment:
- if chronic, glucocorticoid maintenance therapy is needed:
  - hydrocortisone
  - dexamethasone (small dose because it is the most potent of all the steroids)
  - prednisone
- chronic primary AI will also need mineralocorticoid replacement:
  - fludrocortisone is synthetic aldosterone
    - monitor adequacy with orthostatic vitals, serum K, plasma renin
    - dose may need increasing in the summer due to increased salt losses from sweating
    - dose may need to be lowered in pts with essential HTN, and don’t use K-sparing diuretics
- AI patients undergoing surgery need extra steroids to avoid hypovolemia and hypotension

**Cushing’s Syndrome**: general term for hypercortisolism at any level, including adrenal, ectopic, or pituitary source

**Causes:**
- exogenous: use of glucocorticoids
- endogenous: may be pituitary or adrenal
- pituitary hypercortisolism
  - excess ACTH production → excess cortisol
    - **Cushing’s disease**: refers specifically to an ACTH secreting pituitary adenoma resulting in high cortisol secretion
      - unresponsive to negative feedback by cortisol
- ectopic ACTH production: a non-pituitary tumor is secreting ACTH → excess cortisol
  - tumor unresponsive to negative feedback of high cortisol levels
  - seen in small cell lung ca, carcinoid tumors, pheochromocytoma, thymoma, pancreatic cell tumors, medullary carcinoma of the thyroid
- adrenal hypercortisolism: adrenal adenoma, adrenal carcinoma, micronodular hyperplasia, macronodular hyperplasia
  - excess cortisol released independently of ACTH stimulation
  - ACTH and CRH are suppressed (pituitary and hypothalamus are functioning normally)
Presentation: supraclavicular and dorsal fat pads (“buffalo hump”), central obesity, proximal muscle weakness, thinning of the skin, purple striae, spontaneous ecchymosis, osteopenia, HTN, early or delayed puberty, growth retardation, glucose intolerance, skin hyperpigmentation if ACTH dependent

- less specific: papular acne, vellus hypertrichosis of face, decreased libido, amenorrhea, infertility, fungal infections, poor wound healing, nephrolithiasis, polyuria, headaches, neuropsychiatric disorders, spinal epidural lipomatosis

Diagnosis is difficult!

- differential: always remember to check for exogenous glucocorticoid use
- always to labs first, before any imaging (to avoid incidental tumors and false negative scans)
- protocol:
  - 1.) establish presence of cortisol excess
    - 24 hour urine for free cortisol
    - low dose dexamethasone suppression test
    - elevated saliva cortisol test at night
  - 2.) establish ACTH dependence or independence
    - low plasma ACTH □
    - adrenal lesion?
      - do adrenal CT next
    - normal or high plasma ACTH □
      - ectopic production or Cushing’s disease
      - distinguish via:
        - CRH stimulation test
        - high-dose dexamethasone suppression test
        - petrosal sinus sampling
        - octreotide scintigraphy to localize ectopic source
        - MRI

Treatment:

- surgical resection is first line
- sometimes adrenalectomy is needed
- drugs to block adrenal response: somatostatin analogs, adrenal steroid synthesis inhibitors

6.7.4 Hirsutism and Virilization

virilization: when a female develops male secondary sex characteristics

Caused by androgen excess

- neoplasm, idiopathic or familial cause, PCOS, ovarian tumor, glucocorticoid resistance
- ACTH dependent causes:
  - congenital adrenal hyperplasia: inadequate cortisol +/- mineralocorticoid levels and usually an androgen excess that is caused by an enzymatic defect in the adrenal steroid hormone synthesis pathway
    - causes numerous clinical syndromes, including classic salt-wasting form and virilizing syndromes
    - non-classic presentations: hirsutism and menstrual irregularity in women, asymptomatic androgen excess in males
- ACTH-dependent Cushing’s syndrome
- androgen-secreting adrenal adenoma or carcinoma
  - adenoma rare, carcinoma more common
  - adenoma unresponsive to dexamethasone suppression
  - carcinoma unresponsive to high-dose dexamethasone suppression, with high DHEA concentration

Presentation:

- menstrual irregularities or amenorrhea
- defeminization: decreased breast size, frontal balding, deep voice
- female pseudohermaphroditism (with congenital adrenal hyperplasia)
- hirsutism with increased hair growth on the chin, upper lip, abdomen, chest
- acne from increased sebaceous gland activity
• PCOS
• LH:FSH ratio > 2
• but 1/3 of normal women may display this
• obesity and insulin resistance

Investigation:
• serum testosterone: free and total
• androstenedione: if > 1000 this implies ovarian or adrenal neoplasm
• DHEA-S: if > 700 this implies an adrenal source of androgen excess, get a CT
• increased plasma & urine 17-KS, increased plasma ACTH
• for amenorrhea:
• PCOS and ovarian failure workup
• LH & FSH, estradiol, testosterone & DHEA
• pelvic exam
• imaging:
• pelvic US
• abdominal CT with attention to the adrenal glands

Treatment:
• stop any offending meds
• give meds: oral contraceptives, metformin, anti-androgens (only if not pregnant)
• postmenopausal women can have a bilateral oophorectomy to catch any small tumors not seen on imaging

6.7.5 Primary Hyperaldosteronism

Presentation:
• HTN, muscle symptoms due to hypokalemia (cramping, weakness, periodic paralysis), or asymptomatic
• Conn’s syndrome: aldosterone-producing adenoma
• idiopathic hyperaldosteronism: due to bilateral hyperplasia of the zona glomerulosa
• primary adrenal hyperplasia
• adrenal carcinoma

Investigation:
• in order to effectively evaluate, patient must be off anti-aldosterone meds (spironolactone), preferably off ACEI and Ca channel blockers, and must be taking in at least 150 mEq of Na daily in order to suppress aldosterone production
• labs:
• chem 7 for hypokalemia and metabolic alkalosis
• low serum renin
• high serum aldosterone (ratio of aldosterone:renin > 20 is suspicious)
• elevated 24 hour urine aldosterone
• saline loading
• 18-OH cortisol level: indicative of aldosterone producing adenoma
• imaging: abdominal CT to look at adrenal glands
• adrenal vein catheterization to look for lateralization of elevated aldosterone level

Treatment:
• adenoma □ surgical resection
• idiopathic or poor surgical candidate □ medical therapy (mineralocorticoid receptor antagonist, spironolactone, Ca channel blocker, ACEI)

6.7.6 Disease of the Adrenal Medulla

A.) Pheochromocytoma: a neuroendocrine tumor of the adrenal medulla that secretes excessive amounts of catecholamines, usually norepinephrine and epinephrine
• the “rule of 10s” is that 10% of pheos will be extra-adrenal, bilateral, familial, malignant, or NOT associated with hypertension
• presentation: classic is the 5 P’s (pain-headaches, pallor-orthostatic hypotension, palpitations, pressure HTN, perspiration)
• investigation:
  • check what other medicines the patient takes that could account for symptoms
  • look for familial syndromes: MEN IIA, IIB, Von Hippel-Lindau, Von Recklinghausen
  • 24 hour urine for catecholamines and catecholamine metab (vanillylmandelic acid)
  • serum metanephrines or plasma catecholamines imaging
• treatment:
  o treatment of choice is surgical resection
    • watch for post-op complications of labile BP, hypotension or shock, hypoglycemia
  o meds: α-adrenergic blockade ALWAYS first, β-blockade next, Ca channel blockers

### 6.8 Disorders of Calcium Metabolism

#### 6.8.1 Skeletal System Physiology

• Roles of the skeletal system:
  • protect organs
  • locomotion
  • major part of metabolic control of mineral homeostasis of Ca and P
    • axial skeleton accounts for majority of metabolic activity
  • Parathyroid hormone is secreted from the 4 parathyroid glands
  • maintains adequate serum Ca levels
  • interacts with Mg to affect Ca metabolism in an unclear mechanism
  • can be directly measured in blood
  • Vitamin D
  • vit D metabolites are needed to absorb dietary Ca and P in the intestines, and they enhance the activity of PTH on mobilization of skeletal stores of Ca and P
• Bone remodeling
  • alkaline phosphatase is associated with bone deposition

• Calcium physiology
- when in balance, bone formation = resorption and GI absorption = renal excretion
- most is bound up in bone
- of Ca present in serum, half is free and not bound to anything
  - this is tightly regulated by PTH
- Phosphorus metabolism: not as tightly regulated as Ca

### 6.8.2 Disorders of Calcium Metabolism

A.) Hypercalcemia

1. **Measure intact PTH**
   - Elevated
   - Mid-upper normal
   - Low (<20 pg/mL)

2. **Evaluate for non-PTH mediated causes of hypercalcemia**
   - Low (<100 mg/24h, Ca/Cr < 0.01)
   - Normal (>100 but <200 mg/24/day)

3. **Consider guidelines for surgery**
   - Measure BMD
   - Refer for surgery or monitor

4. **Measure 25OHD**
   - Low (<20 ng/dL)
   - Normal

5. **Replete vitamin D and reassess urinary calcium excretion**
   - Likely primary HPTH
   - Likely FHH

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A.) Hypercalcemia
• causes:
  • if due only to accelerated bone resorption by osteoclasts:
    • think 1st hyperparathyroidism (problem with glands themselves) in outpatient settings
      ■ think malignancy in inpatient settings
      ■ together account for 95% of cases
      ■ other causes: familial hypocalciuric hypercalcemia, endocrine disease, immobilization, Li use
  • if due only to increased GI absorption □ milk-alkali syndrome (taking lots of Tums and milk together)
  • if due primarily to accelerated bone resorption but also to accelerated GI absorption of Ca □ granulomatous disease or lymphoma
  • other mechanisms: thiazides, aminophylline, estrogens, GH, recovery from AKI
  • presentation: altered mental status, nausea, vomiting, polyuria, polydipsia, stones, hypercalciuria
  • investigation: check PTH
  • treatment:
    • treat underlying cause
    • enhance calciuresis: PO and IVF, loop diuretics
    • meds:
      ■ bisphosphonates: inhibit osteoclast resorption
      ■ calcitriol
      ■ cinacalcet
      ■ last line: plicamycin, gallium nitrate
      ■ glucocorticoids: inhibit osteoclastic resorption and reduce intestinal absorption
    • surgical excision of tumor: monitor PTH intraoperatively to see when it goes down = tumor removed

B.) Hypocalcemia
• causes: inadequate PTH production (secondary hypopituitarism- a response to low Ca, surgery, autoimmune, radiation, infiltrative process), inadequate vit D production (deficiency, lack of sunlight, malabsorption, liver disease, kidney disease), PTH resistance, vit D resistance, certain drugs
• presentation:
  • acute: Chvostek’s sign (twitching of face and upper lip when tapped due to irritability of facial nerve), Trousseau’s sign (carpal spasm when BP cuff left on inflated), paresthesias, seizures, laryngospasm, bronchospasm, prolonged QT interval, hypotension, heart failure, arrhythmia, papilledema
  • chronic: ectopic calcification of the basal ganglia, extrapyramidal signs, Parkinsonism, dementia, subcapsular cataracts, abnormal dentition, dry skin
• treatment: calcium and vitamin D supplements

Osteomalacia: defective bone matrix mineralization due to inadequate Ca and P as well as deficient mineralization mechanisms

Causes:
• vit D disorders: deficiency, loss of vit D binding proteins (nephrotic syndrome), inadequate production of vit D or excessive catabolism, lack of end-organ response to vit D
• hypophosphatemia: inherited disorders, acquired disorders, longstanding hyperparathyroidism
• mineralization disorders: chronic renal failure, hypophosphatemia, meds
• in childhood = rickets

Presentation: diffuse bone pain (esp pelvis), waddling gait, muscle weakness, fractures and pseudofx of long bones, ribs, or pelvis

Treatment:
• vit D and Ca supplements
• P supplements if hypophosphatemic

Paget’s Disease: a localized disorder of bone remodeling with increased resorption and deposition of an irregularly woven bone matrix
Like a localized osteoporosis
Most commonly affects the pelvis, femur, spine, skull, and tibia
Presentation: pain, bowing, fx, headache, hearing loss
Investigation:
elevated alk phos is hallmark
elevated bone turnover markers
Treatment:
obisphosphonates to inhibit osteoclast resorption
calcitonin

6.9 Osteoporosis and Metabolic Bone Disease

Read: Cecil chapter 76, (osteoporosis)
7 ENT Exam Notes

7.1 Primary Care Otolaryngology

- Major nerves running through ear: vestibulocochlear, facial
- Can tell which ear you're looking at by direction of cone of light (always points forward)
- Tympanostomy tube is placed anteriorly because it creates less hearing loss

Auricular Hematoma: occurs when physical trauma to the auricle causes tissue shearing and swelling

Treatment: I&D with dental roll bolstering
- must be done stat because a coagulated hematoma will not break down but will eventually sclerose surrounding cartilage cauliflower ear

7.1.1 Cerumen Impaction

Otitis Externa: infection or inflammation of the external auditory canal
- Presentation: pain, hearing loss, otorrhea, fullness, itching
- Investigation
  - differential diagnosis: bacterial and fungal infections can look very similar
    - bacterial source accounts for 90% of all infections
      - most commonly Pseudomonas, also Strep and Staph
      - pain with manipulation of tragus and auricle
    - fungal source is most commonly Aspergillus, also Actinomyces and Candida
      - lots of itchiness
    - chronic cause is due to underlying skin condition such as eczema
    - malignant: osteomyelitis of the temporal bone (not cancerous) as a result of a chronic infection that is misdiagnosed or untreated in diabetics or the immunocompromised
      - causes auditory canal to swell shut
      - bony breakdown can progress through to cranial cavity
      - diagnose with gallium uptake scan
- Treatment
  - bacterial:
    - suction out purulent debris if qualified (not typically done in primary care)
    - insert wick for antibiotic drops if canal is narrowed
    - topical antibiotic drops:
      - neo/poly/HC is ototoxic and allergenic only use if TM is intact and only when not using a wick
      - fluoroquinolones such as ciprofloxacin and ofloxacin
  - fungal:
    - remove debris
    - use topical acetic acid/hydrocortisone drops, or clotrimazole drops, or CASH powder (good for fungal or bacterial treatment, contains chloramphenicol, amphotericin B, sulfamethoxazole, hydrocortisone), or violet dye
  - chronic
    - first treat the eczema (steroid cream)
    - then use water/vinegar washes and avoid Q-tips
  - malignant is usually caused by Pseudomonas but is an emergency and requires referral to ENT
    - mild or moderate cases may heal with a non-antibiotic topical agent with ear washes
    - if patient is diabetic, immunodeficient, has history of radiation to the ear, has a swollen shut ear canal, or has severe disease, consider systemic antibiotic therapy
- Follow-up: culture drainage for fungus if antibiotics fail

Myringosclerosis: scarring of the tympanic membrane
- Could be a result of tube placement or frequent infection
- Usually benign but can cause a conductive hearing loss if severe
- Treatment: if not symptomatic, don’t do anything about it!
7.1.2  Ear Drum Perforation
Presentation: perforation is usually posterior due to curvature of ear canal, with symptoms of hearing loss, tinnitus, otorrhea, bleeding
- acute perforation: edges are jagged with lots of redness
- ear pain is felt
- chronic perforation: no redness, edges are smooth with invagination of the membrane appearance of a rim
Treatment: watch and wait, treat if infected with topical drops, possibly tympanoplasty with paper patch (clinic) or graft (OR)

7.1.3  Eustachian Tube Dysfunction
- Occurs with blockage of the eustachian tube that allows air to exit middle ear but not come back in creation of negative pressure atmosphere in middle ear
- can lead to tympanic membrane retraction (visualized as depression above malleus)
- causes: nasal allergy, URI, nasopharyngeal mass, abnormal anatomy
- Presentation: ear pain, hearing loss, ear fullness
- Treatment:
  - if acute should be self-limiting and heals with time
    - treat allergy with nasal steroid spray
    - oral or topical decongestants
  - if chronic + hearing loss tube placement bilaterally
- Prognosis: risk of cholesteatoma if unhealed/untreated

Cholesteatoma: noncancerous skin cyst arising from retracted piece of TM or from skin cells seeding the middle ear after a perforation event
- Eventually the growth eats away at the bone and causes permanent conductive hearing loss
- Presentation: textbook is a pearly white mass behind the eardrum, but it typically just appears as a bulging mass with granulations inside retraction pocket
- Treatment: surgical excision to prevent from destroying tegmen and reaching cranial cavity

Otitis Media
A.) Chronic suppurative otitis media: middle ear infection with otorrhea coming out through hole
- occurs with TM perforation or tube
- treatment: 10 days of topical antibiotic drops (quinolones only d/t toxicity issues) such as cipro/hydrocortisone drops or ofloxacin
  - possibly surgery
  - consider chronic antibiotic suppression such as daily amoxicillin during winter and spring with monthly follow-up
B.) Otitis media with effusion (serous otitis media): when there is fluid behind the TM without presence of infection
- caused by chronic eustachian tube dysfunction, aftermath of acute otitis media, or barotrauma
- presentation: hearing loss, ear fullness, tinnitus
  - may have air-fluid line behind TM, bubbles, or retraction pocket
- investigation: need to rule out mass
- treatment: watch for 3-4 months, nasal steroids
  - tube placement if not better in 3-4 months
- prognosis: hearing loss can last for months
C.) Acute otitis media: inflammation of the middle ear due to anatomic or physiologic dysfunction of the eustachian tube allowing secretions to accumulate in middle ear
- offending agent is usually viral, bacterial (Strep pneumonia, H. flu, or Moraxella), or fungal
- frequently follows viral URI
- prevention: vaccines may offer some protection
- presentation: ear pain, hearing loss (hallmark! no loss = no infection), tinnitus, ear fullness
  - sharp pain with otorrhea if perforation
  - bulging red ear drum with whiteness behind
  - usually can’t distinguish viral from bacterial
- treatment: 10 days of oral antibiotics (DOC high dose amoxicillin), or observation with nonsevere illness
  - if pt had antibiotics in the last month: absolutely high dose amoxicillin +/- clavulanate, or
  - azithromycin is NOT used due to high levels of community Strep pneumo resistance
  - if PCN allergic:
    - immediate (type I) hypersensitivities: clarithromycin, clinda
    - other hypersensitivities: cephalosporins
  - no antihistamines or decongestants for kids
  - consider analgesics: acetaminophen, antipyrine/benzocaine if > 2 years, ibuprofen
- follow up:
  - fluid will persist in middle ear for months after infection has resolved
  - amoxicillin failure due to β-lactamase producing bacterial strains
    - switch to amox + clavulanate, macrolides, cephalosporins
    - no quinolones in kids due to risk of tendon rupture, abnormal bone development
    - if failure with recent antibiotic use, switch to clinda, ceftriaxone, or consider tympanocentesis
- prognosis: complications include labyrinthitis (inflammation of inner ear), meningitis, intracranial abscess, TM perforation, hearing loss, tympanosclerosis, facial nerve paralysis
  - mastoiditis: spread of infection to mastoid air cells
    - fever, otalgia, postauricular erythema, swollen/tender/protruded auricle
    - requires IV antibiotics, ENT consult, hospital admission, and frequently a mastoidectomy as it is close to critical structures

7.1.4 Tympanic Membrane Abnormalities

A.) Bullous myringitis: blistering and inflammation of the TM
- usually caused by Mycoplasma, H. flu, or Strep pneumo
- presentation: excruciating pain especially with coughing or sneezing
- treatment: oral antibiotics (macrolide) + topical antibiotic if vesicular rupture present, short term pain management with opioids
7.1.5 Ear Pain

Must distinguish true ear pain from referred pain

- otologic pain from: otitis externa or media, myringitis, eustachian tube dysfunction, ear canal abscess, ENT tumor, shingles flare or prodrome
- referred pain from: TMJ dysfunction, oral pain (pharyngitis, dental work, abscess), sinusitis, musculoskeletal neck pain, carotidynia, neck lymphadenopathy, parotitis, or trigeminal neuralgia

7.1.6 Hearing Loss

Presentations:

- **sudden sensorineural hearing loss**: sound gets in but you can’t process it; occurs suddenly within last 72 hours, usually without warning
  - sensory = problem with cochlea
  - neural = problem with brain
  - may be due to viral labyrinthitis, autoimmune issue, or vascular compromise
  - an otologic emergency! treatment must occur within 4 weeks of onset refer to ENT without delay
  - treatment is steroids with treatment of underlying cause
- **conductive hearing loss**: sound is blocked from getting in, could be one of a multitude of problems
  - problems with external auditory canal: cerumen impaction, foreign body, mass, exostosis, edema, otorrhea, congenital stenosis
  - problems with TM: sclerosis, perforation, retraction
  - problems with middle ear: OM + effusion, hemotympanum, acute OM, cholesteatoma
  - problems with the ossicles: discontinuity, sclerosis, malformation, fixation [treatment depends on identification and treatment of cause]

Investigation

- take a careful HPI: acute/gradual loss, fluctuating/progressive, uni/bilateral, time course, preceding illness, other associated symptoms
- medical history: use of ototoxic meds, ear surgery, trauma, TM perforation, or noise exposure
- FH of hearing loss?
- differential diagnosis: VINDICATE
  - vascular causes: HTN, CAD, DM, stroke, sickle cell
  - infectious cause: Lyme, syphilis, HIV, viral labyrinthitis, bacterial toxins, HSV, meningitis
  - neoplasm: acoustic neuroma, cancer mets to temporal bone
  - drugs: ototoxicity, general anesthesia
    - includes the aminoglycosides, vanco, erythromycin, chemotherapies (cisplatin, nitrogen mustard), furosemide, salicylates, quinine
  - idiopathic cause
  - congenital cause: absent CN8, intrauterine infection, teratogens, hypoxia, premature birth, low birth weight, hyperbilirubinemia
  - autoimmune cause: MS, autoimmune hearing loss, SLE, giant cell arteritis
  - trauma: noise, temporal bone fx, radiation
• endocrine/metabolic cause: hypothyroidism, Meniere’s, presbycusis, cochlear otosclerosis
• narrow down differential by ruling out conductive loss
• then further narrow down by unilateral or bilateral sensorineural loss
  • if unilateral: sudden SNHL, acute labyrinthitis, acoustic neuroma, Meniere’s disease, intracranial cause, noise induced trauma
  • if bilateral: HTN, DM, CAD, ototoxicity, hypothyroidism, presbycusis, Lyme, HIV, syphilis, autoimmune, noise induced trauma
• then narrow down based on when hearing loss occurred
• Treatment
  • identify and treat cause: medical therapy, office procedures, surgical correction, amplification (hearing aids)
• When to refer to ENT
  • tinnitus and hearing loss +/- vertigo
  • sudden hearing loss
  • chronic infection that is unresponsive to treatment
  • shingles of the ear
  • ear masses

7.1.7 Audiometry: Measuring Hearing Loss

A.) When to do?
• all newborns are screened with:
  • auditory brainstem response test: a brainwave recording of the infant’s reaction to sound in 8 waves
    • mnemonic “ECOLI”
      • 1 = E = 8th CN
      • 2 = C = cochlear nucleus
      • 3 = O = olivary nucleus
      • 4 = L = lateral lemniscus
      • 5 = I = inferior colliculus
      • 6/7 test the medial geniculate nucleus
  • otoacoustic emission test: measurement of the cochlear response to sounds using a microphone
• neonates with risk factors such as FH, in-utero infection, abnormal facial features, low birth weight, severe hyperbilirubinemia, ototoxic med exposure, bacterial meningitis, low Apgar scores, respiratory failure requiring > 5 days ventilation, known syndrome associated with hearing loss
• children with hearing/speech/language/developmental delay, infections associated with sensorineural loss, head trauma with loss of consciousness or skull fracture, known syndrome associated with hearing loss, use of ototoxic meds, serous otitis media for 3+ months
• adults with self-perceived hearing loss, physical exam abnormality, exposure to ototoxic meds or loud noise, severe head trauma, infection associated with hearing loss, FH of hearing loss, hypoxia, respiratory failure, tinnitus

B.) Primary care techniques
• basic audiometer tells you whether or not a person can hear a 25 dB tone
• Weber tuning fork test is good for testing unilateral hearing loss
  • midline hearing is either normal or there is an equal deficit in both ears
  • when sound is best heard in affected ear, it means there is conductive hearing loss in that ear
    • may be because the conduction problem of the incus/malleus/stapes/eustachian tube masks the ambient noise of the room, while the well-functioning cochlea picks the sound up via bone, causing it to be perceived as a louder sound than in the unaffected/normal ear
    • or may be because lower frequency sounds that are transferred through the bone to the ear canal escape from the canal, but if an occlusion is present, the sound cannot escape and appears louder on the ear with the conductive hearing loss
when sound is best heard in unaffected ear, it means there is a sensorineural hearing loss in the affected ear

- this situation is because the affected ear is less effective at picking up sound even if it is transmitted directly by conduction into the inner ear

- Rinne tuning fork test compares air conduction to bone conduction
  - here, a positive Rinne test indicates air conduction > bone conduction
    - could be normal or could be sensorineural loss in ear being tested
  - a negative Rinne means the tone is heard louder on the mastoid
    - indicates conductive hearing loss

C.) Pure tone audiometry: simultaneously tests air and bone conduction over a range of normal voice frequencies

- hearing level response is measured in dB (logarithmic)
  - normal hearing response @ 0-25 dB
  - mild hearing loss @ 25-45 dB for the tested frequency
  - moderate loss @ 45-65 dB
  - severe loss @ 65-85 dB
  - profound loss @ 85+ dB
  - deaf if you can’t hear at 120 dB

- measurement of air conduction
  - right ear response is marked by O’s, left ear response marked by X’s
  - can prevent cross-hearing (better ear compensating for ear with loss) by using a masking noise in the good ear
    - masked right ear now represented by Δ’s
    - masked left ear now represented by □’s

- measurement of bone conduction (headphones include a mastoid bone vibrator)
  - ***bone conduction lines are usually deleted by the tech for simplicity if they are = to air conduction!
  - right ear response is marked by <’s
  - left ear response is marked by >’s
  - can mask to prevent cross-hearing
    - masked right ear now represented by [‘s
    - masked left ear now represented by ]’s

- how to read the audiogram:
  1.) look at threshold of 25 dB
  2.) is hearing loss bilateral or asymmetric (R or L only)?
    - symmetric = lines for R and L ear match up fairly closely
    - asymmetric = hearing is different between ears
  3.) type of hearing loss: sensorineural, conductive, or mixed
    - if the air conduction thresholds show a hearing loss but the bone conduction thresholds are normal, then we call it a conductive hearing loss
    - if both the air conduction thresholds and the bone conduction thresholds show the same amount of hearing loss, we call it a sensorineural hearing loss
    - a mixed hearing loss is when the bone conducted thresholds show a hearing loss and the air conducted thresholds show an even greater hearing loss
  4.) severity
  5.) slope
    - flat when hearing loss is the same at all frequencies
      - common in diabetes
    - “ski slope” or descending when loss is greater at higher frequencies
      - usually due to presbycusis or chemotherapy if sensorineural
    - ascending slope when high frequencies are heard better than low frequencies
      - rare, this would be Meniere’s disease if sensorineural
    - even slope with a notch in it indicates loss at a specific frequency
      - usually due to loud noise exposure if sensorineural
    - U-shaped slope is rare and there is usually a genetic hearing loss

D.) Tympanometry: tests mobility of eardrum
• normally the middle ear and the rest of the world should have equal pressure corresponds to a tympanogram peak @ 0 = zero difference = “Type A”
  ▪ small area under curve means normal pressure but a more rigid TM
  ▪ large area under curve means normal pressure but a more floppy TM
• when there is a middle ear effusion or a hole in the TM, the ear drum does not respond to pressure changes = “Type B” corresponds to a flat tympanogram with no true peak
• when there is eustachian tube dysfunction the middle ear is under negative pressure = “Type C” corresponds to a negative tympanogram peak

E.) Ear canal volume
• too small (> 0.5) indicates obstruction or canal stenosis
• normal is 0.5-2.5
• too large (> 2.5) indicates perforated TM

F.) Speech audiometry: measures how well a patient recognizes speech
• speech threshold recognition: how quiet of speech a person can recognize, as measured in dB
• speech discrimination: how well a patient understands speech, normally > 88% of the words given

7.1.8 Otologic Surgeries
A.) Stapedectomy: performed when otosclerosis of the stapes fixation and loss of vibration
• prosthetic stapes put in
B.) Cochlear implant: indicated in profound bilateral deafness
• implanted electrode wraps around cochlea, while external magnet transmits signal to electrode
C.) Bone anchored hearing aid (BAHA): metal stud implanted in skull transmits vibrations via bone to bypass the ossicles
• helpful in someone who had to have their ossicles removed conductive hearing loss
• can also be used for unilateral sensorineural hearing loss, as the vibration will transmit through the skull to be received by the good ear
D.) Soundbridge: combination of cochlear implant and BAHA, where a wire carries external vibration to a floating mass transducer implanted in the middle ear
• for individuals that can’t use a traditional external hearing aid due to having a small canal, etc.

Tinnitus: abnormal perception of sound in the middle ear in the absence of a corresponding sound in the external environment
• Different kinds
  • subjective tinnitus: a sound only the patient can hear due to aberrant neurological signalling in the brain
    ▪ often a neurological response to hearing loss
    ▪ high freq loss hi freq tinnitus
    ▪ roaring/low freq loss low freq tinnitus
    ▪ can also be caused by meds like aspirin
  • objective tinnitus: when a clinician can perceive the abnormal sound emanating from the patient’s ear
    ▪ clicking with pharyngeal muscle spasm
    ▪ breathy with patulous (abnormally open) eustachian tube
    ▪ pulsatile/bruit with referred vascular sounds or tumor
• Can be high or low frequency
• Usually worse in quiet environments
• Investigation
• hearing test
• Treatment
• stop offending meds
• avoid caffeine and nicotine
• if due to sensorineural loss, there is no known surgical or pharmacological intervention
  ▪ use of background noise
  ▪ tinnitus retraining therapy
• if due to conductive hearing loss, resolving the underlying problem will resolve the tinnitus

**Vertigo:** a specific kind of dizziness that results in false impression of movement

Contrast to the catch-all term dizziness that refers to having no impression of movement, but imbalance or lightheadedness/presyncope/

• Different classes:
  - **Peripheral (otologic) vertigo:** caused by problems with the inner ear
    - **Benign paroxysmal positional vertigo:** occurs when otoliths dislodge into the semicircular canals
      - Intermittent vertigo lasting < 1 minute
      - Worse with head movements R/L when lying down
      - Better with head held still
      - Diagnose with Hallpike maneuver: positive if rotational nystagmus seen
      - Treat with Epley maneuver: repositioning the head over time to get the otoliths back in place
    - **Meniere’s disease:** a disorder of increased endolymphatic fluid
      - Episodic, sudden unilateral sensorineural hearing loss, roaring tinnitus, and vertigo for hours
      - Treatment: diuretics, low salt diet to lower ear pressure, anti-vertigo medication
        - Possible surgery for endolymphatic sac decompression, gentamycin injection, labyrinthectomy, or selective vestibular nerve resection
        - Acute labyrinthitis/vestibular neuritis: infection or inflammation of the inner ear, often due to latent viral infection
          - Severe, disabling vertigo for 24-48 hours followed by weeks of imbalance
          - Treatment: steroids and physical therapy
    - **Perilymphatic fistula:**
    - **Superior semicircular canal dehiscence:**
  - **Central (neurologic) vertigo:** a problem with the balance centers of the brain
    - **Multiple sclerosis**
    - **Migraines**
    - **Benign intracranial hypertension:**

**Investigation**

• Vast differential diagnosis: take a thorough history to narrow down
  - Cardiologic reasons: orthostatic HTN, arrhythmia, CAD
  - Neurologic causes: acoustic neuroma, TIA, stroke, Parkinson’s, neuropathy, migraine
  - Anemia
  - Psychologic causes (rarely): anxiety, panic
  - Metabolic: hyperthyroidism, menopause
  - Orthopedic: cervical disc disease, lower extremity arthritis
  - Geriatric: proprioception, off center of balance
  - Pharmacologic: polypharmacy or side effects

• **PE:** CN testing, Romberg, gait, nystagmus, ear exam, Dix-Hallpike test

• Special tests ordered if you’re still stumped
  - **Electro/video/nystagmogram:** measure reaction of nervous system to certain stimuli/stressors
  - Rotary chair
  - Fistula test
  - High-res CT of the temporal bone
  - MRI of the internal auditory canal

**Acoustic Neuroma:** a slow-growing noncancerous tumor of the Schwann cells surrounding CN 7/8

• Early presentation: asymmetric hearing loss, tinnitus, imbalance but not vertigo
• Late presentation due to brainstem compression
• Investigation: MRI with contrast of the internal auditory canals
• Treatment: observation or stereotactic radiation or surgery

7.1.9 Rhinology Background
Types of URI include colds, influenza, acute bronchitis, acute exacerbation of chronic bronchitis, croup, bronchiolitis, otitis media, acute pharyngitis, sinusitis, epiglottitis
- Having a tonsillectomy does not decrease incidence of colds
- Smokers have more severe colds with prolonged course
- No OTC cough and cold products available for children under 4
- especially avoid ephedrine, pseudoephedrine, phenylephrine, diphenhydramine, brompheniramine, chlorpheniramine
- Functions of the nose include nasal reflexes (may be linked to lower respiratory and vascular reflexes), and endocrine pheromone detection

7.1.10 Common Nose Issues
- Septal deviation: when septum is displaced from midline
- becomes a problem when crookedness is severe enough to impact breathing through nose
- Septal perforation: creates a hole going from one nostril to the other
- creates disrupted air flow/breathing, nasal crusting, and bleeding
- Nasal mucositis: irritation and infection of the nasal mucosa
- treatment: topical or oral antibiotic
  - clindamycin especially good at penetrating cartilage
  - need more rigorous course if infection spreads past vestibule into cartilage
- Epistaxis: nosebleed
  - anterior bleed occurs in Kiesselbach’s plexus (where you pick your nose)
  - posterior bleed occurs in Woodruff’s plexus
  - can be caused by picking, septal deviation, inflammation, cold or dry air, or a foreign body
  - systemic causes: clotting disorder, HTN, leukemia liver disease, anticoagulant therapy, thrombocytopenia
  - treatment: manual compression (hold soft part of nose and lean forward), oxymetazoline (Afrin; acts as vasoconstrictor to decrease blood flow), cauterization (one side at a time to avoid necrosis of septum), anterior or posterior packing (rarely done because it is painful), arterial ligation, surgical embolization (for patients with high BP and low platelets), “rapid rhino” inflation

7.1.11 Common Cold vs Influenza
- Colds
  - slow, insidious onset
  - fever only in kids
  - usually no headache or chills
  - sore throat, stuffy nose, sneezing
  - mild aches or weakness
- Influenza
  - rapid onset with symptoms worsening over 3-6 hours
  - fever > 100 for 3-4 days
  - usually no sore throat, stuffy nose, or sneezing
  - headache, chills, severe aches and weakness

Allergic Rhinitis: IgE-mediated reaction causing mast cells and basophils to release histamine, leukotrienes, serotonin, and prostaglandins — inflammation of the nasal mucosa
- Presentation: nasal congestion, rhinorrhea, sneezing, itching, watery eyes, allergic shiner (dilation of veins under eyes causes dark under eye circles), blue/hypertrophied turbinates (due to venous dilation), allergic salute (crease across top of nose from constantly rubbing)
- may also have nasal polyposis: excess tissue created as a result of inflammation that destroys normal nasal tissue and can disintegrate nasal septum and orbital wall without treatment
  - results in being more prone to infections
  - remove surgically if obstructing air flow
- Samter’s triad: syndrome of aspirin sensitivity, nasal polyposis, and asthma that is often seen with allergic rhinitis, frequently leading to severe pansinusitis
• Treatment: avoidance of allergens, nasal saline lavage, nasal steroid spray, antihistamines (oral, nasal, eye), leukotriene inhibitor, allergy shots
  o 2nd generation antihistamines indicated for allergic rhinitis:
    ▪ loratadine: for > 2 years old
    ▪ cetirizine: for > 6 months old
    ▪ fexofenadine: for > 6 years old
    ▪ desloratadine: for > 12 years old
    ▪ azelastine: nasal spray for > 12 years old
    ▪ olopatadine: nasal spray for > 12 years old
• intranasal glucocorticoids
  o generic available:
    ▪ fluticasone:
    ▪ flunisolide:
  o no generic:
    ▪ mometasone:
    ▪ budesonide:
    ▪ triamcinolone:
    ▪ beclomethasone:
    ▪ fluticasone furoate:
    ▪ ciclesonide:
• consider anticholinergic nasal sprays only if all other therapies fail

Vasomotor Rhinitis: non-allergy mediated inflammation of the nasal mucosa
• Causes: temperature, exercise, foreign body, fumes, food, medication
• Treatment: steroid or antihistamine sprays

Rhinitis Medicamentosa: rhinitis induced by overuse of topical decongestants — rebound congestion
• Treatment: stop using spray
  if needed, use nasal steroid taper, antihistamine spray, or Afrin taper

Viral Rhinitis: URI caused by adenovirus, parainfluenza, coronavirus, rhinovirus, etc.
• Presentation: symptoms should last < 7 days
  • sore throat, nasal congestion, clear rhinorrhea, fever, cough +/- phlegm, malaise, fatigue, sneezing, itching
• Treatment: supportive with OTC antihistamines, decongestants, mucolytics, fluids, ibuprofen/Tylenol, antitussives (codeine), expectorants, rest
  • best for runny nose: anticholinergics like ipratropium spray, cromolyn sodium spray (mast cell stabilizer)
  • best for postnasal drip: corticosteroids
  • best for nasal congestion: decongestants (pseudoephedrine >> than phenylephrine), corticosteroids
    o pseudoephedrine can increase BP
  • best for sneezing: antihistamine, corticosteroids
  • best for chronic, nonproductive cough: dextromethorphan
  • nonopioid antitussive for recovering addicts: benzonatate
  • cocktail for acute cough associated with common cold: 1st gen antihistamine + decongestant like pseudoephedrine
    o newer 2nd gen antihistamines are ineffective in this situation
• vitamin C and Zn supplements controversial
• Zicam warning for permanent loss of smell associated with use
• Complications: acute otitis media, chronic middle ear effusions, asthma, dental problems, sinusitis, nasal polyps

7.1.12 Sinus Imaging
• X-ray
  • good for showing air/fluid levels in the maxillary (Waters view) and frontal sinuses (Caldwell view)
  • bad for looking at mucosal thickening or soft tissue abnormalities
  • bones are often obscured and difficult to read
• MRI
• not the preferred modality for sinus imaging but you can get some information from it
• doesn’t detail bones well
• can falsely give the impression of inflamed mucosa
• good for evaluating neoplasms, mucoceles, and encephaloceles

CT
• study of choice for evaluating nasal and sinus structures
• best to do after maximal treatment to reduce inflammation
• coronal CT without contrast is done in the plane of surgical approach and shows the osteomeatal complex best
• evaluation: be sure to look at whole CT, not just the sinuses
  o orbits, orbital wall, maxilla, nasal septum, turbinates, then sinuses anterior to posterior
    ▪ mucus and polyps will be of water density (gray)
    ▪ mucosal thickening indicates chronic sinusitis

Sinusitis: purulent infection of the sinus
• can’t tell whether it is viral or bacterial based on appearance!
• pathogens: Strep pneumo, H. flu, Moraxella, Staph aureus
• complications: facial or periorbital cellulitis, orbital abscess, meningitis, cavernous sinus thrombosis, intracranial abscess

A.) Acute sinusitis: when symptoms do not clear in 7-10 days, due to inflammation from viral URI trapping fluid in sinuses that incubates growth
• bacterial causes make up 90% of cases
• vaccine for influenza may help prevent
• presentation: “double sickening” where pt had viral symptoms, got better, then symptoms returned a week later, localized facial pain, unilateral sinus tenderness, upper tooth pain, purulent foul nasal discharge, fever, cough, fatigue
  o malodorous breath in young children with painless morning periorbital swelling
  o older children have tooth pain, headache, and low-grade fever
• treatment:
  o 10-14 day course of antibiotics
    ▪ try amoxicillin first (Septra if allergic)
    ▪ if severe or with recent antibiotic use use broad spectrum first (unless a child)
      • nasal saline lavage to help move infected mucus out, nasal steroid spray
    o antihistamine, decongestant, mucolytics
    o oxymetazoline (< 4 days) to help pt feel better before antibiotics kick in
    o severe frontal sinusitis needs referral to ENT
    o 63% of cases will be cured without any treatment can just observe mild cases for 7 days for improvement
• follow-up: if antibiotic failure, consider broad-spectrum
  o for failure with max treatment, surgical sinus aspiration
• complications: subperiosteal abscess of the orbit, intracranial abscess, exacerbation of COPD or asthma

B.) Subacute sinusitis: when symptoms last 4-12 weeks
C.) Chronic sinusitis: when symptoms are > 3 months, could be infectious or noninfectious cause
• could be allergic inflammation, cystic fibrosis, immunodeficiencies, ciliary dyskinesia, or anatomic abnormalities
• also consider Klebsiella, Pseudomonas, Proteus, Enterobacter, MRSA, anaerobes, fungus
• investigation: do a culture and sensitivity
• treatment
  o non-antimicrobial therapies that may help with clearance: decongestants, topical vasoconstrictors, nasal saline sprays, topical steroids, NSAIDs, cough suppressants

7.1.13 Pharyngitis
• differential diagnosis: post-nasal drip, virus, group A strep (most common cause), tonsillitis, mono, peritonsillar abscess
• more rarely, gonorrhea, HSV, HIV, or cancer

A.) Viral pharyngitis
• often co-occurs with viral rhinitis
• agents: adenovirus, coronavirus, rhinovirus, influenza, parainfluenza, Coxsackie virus
• presentation: erythema, edema, dysphagia, pain, fever, lymphadenopathy, URI symptoms
  o soft palate is symmetrical, red but not to the extreme
• treatment: supportive meds
• prognosis: self-limiting in 3-7 days

B.) Strep pharyngitis
• presentation: sore throat, dysphagia, odynophagia, erythema, airway obstruction, tender lymphadenopathy
• investigation: must distinguish from viral pharyngitis by rapid Strep test +/- culture
• treatment: penicillin VK or amoxicillin or pen G injection for noncompliant patient, erythromycin if PCN allergic
  but be aware of increasing macrolide resistance

C.) Acute tonsillitis: viral or bacterial
• commonly Strep pyogenes
• presentation: swollen tonsils with white plaques
• treatment: usually antibiotics
  o caution: if it is due to mono, certain antibiotics will cause a rash

D.) Peritonsillar abscess: a collection of mucopurulent material in the peritonsillar space
• often follows tonsillitis
• presentation: bulging, asymmetrical soft palate, “hot potato voice”, severe throat pain, dysphagia, trismus (inability to open jaw), deviated uvula, salivation/drooling, fever, severe malaise
• treatment: I&D by ENT, antibiotics with anaerobic coverage

E.) Mononucleosis: viral disease caused by EBV or CMV
• presentation: fatigue, malaise, sore throat with tonsillar edema/erythema/exudate, lymphadenopathy, hepatosplenomegaly
• investigation: Monospot rapid test (not reliable early in disease), CBC with atypical lymphocytes
• treatment: OTC pain control, possible steroids, splenomegaly precautions

F.) Ludwig’s angina: cellulitis of the floor of the mouth in the sublingual or submaxillary spaces
• angina = Greek for strangling  ❑ an emergency as the airway can become blocked!
• presentation: swollen neck, protruding tongue
• treatment: hospitalization with airway management, IV antibiotics, surgical draining

7.1.14 Laryngoscopy
Two kinds:
• direct laryngoscopy: straight visualization of the larynx (no reflected images)
  • best image quality
  • can palpate vocal cords to distinguish paralysis vs fixation
  • can do injections and biopsies
  • done prior to laryngeal intubation
• indirect laryngoscopy: the use of a mirror, angulated scope, or flexible scope to visualize an image or reflection of the larynx
  • mirror not invasive with no anesthetic but hard to do because of gag reflex and can’t see entire larynx
  • flexible scope goes through decongested/anesthetized nose
    o no gag reflex with better visualization of the upper airway
    o can be done in clinic
    o anesthetic tastes bad
    o can’t do biopsy
When to do?
- complete head and neck exam, hoarseness, mass, foreign body, chronic sinusitis, chronic cough, recurrent otitis media, halitosis, obstructive sleep apnea, referred pain, SOB, hemoptysis, history of neck or cardiac surgery (to evaluate cord mobility)

Reading scope images
- orientation: vocal cords always point to the front/anteriorly!

### 7.1.15 Hoarseness

**Investigation**
- take a good history
- vocal strain?
- recent surgery/intubation?
- thoracic surgery → vocal cord paralysis?
- differential diagnosis
  - if acute → postnasal drip, viral laryngitis, hypothyroidism, vocal fold paralysis, recent intubation, vocal hemorrhage (singers and performers)
    - paralysis a result of viral infection of a nerve or injury
    - bilateral paralysis is an emergency while unilateral paralysis could cause pneumonia
  - if chronic → smoking (Reinke’s edema), vocal strain, GERD, cancer, vocal nodules or polyps
    - nodules are a result of vocal misuse and allow gaps in vocal cords for air to escape
    - polyps are a result of acid reflux
    - could be squamous cell carcinoma
- laryngoscopy
- normal larynx should have sharp vocal cord folds with symmetric opening and closing
- acute laryngitis will cause pink, puffy vocal cords with increased vasculature

**Treatment**
- acute laryngitis is usually self-limiting, treat with rest, fluids, and smoking cessation
- DO NOT use steroids or antihistamines because they may cover up the injury and cause further damage to the vocal cords with permanent injury
- vocal cord nodules can be surgically excised or overcome with voice therapy
- vocal cord polyps heal with treatment of the underlying acid reflux but can be excised if they are large

### 7.1.16 Head and Neck Tumors

**How to evaluate?**
- rule out serious causes first, then think about the benign
- weight loss, chronic ailment, age > 45, previous radiation to head/neck
- rule out infectious cause (most likely) like bartonellosis or TB, congenital abnormalities, and metabolic causes
- look for lymphadenopathy
- postauricular → nasopharynx mets
- submandibular → oral mets
- submental → lip cancer
- superficial cervical → oral/pharyngeal/laryngeal mets
- deep cervical → nasopharyngeal/scalp/ear mets
- supraclavicular → thyroid or upper esophageal mets
- complete skin exam

**A.) Congenital anomalies**
- thyroglossal duct cyst: occurs when duct persists after fetal development
  - a problem because they can cause dysphagia or become infected
  - investigation: have pt tilt head back, then provider takes hold of cyst and has pt stick tongue out
• if action raises the cyst, it is a thyroglossal duct cyst
  • branchial cleft cyst: occurs with abnormal persistence of connections of the URT to the ear canal, upper neck, or lower neck
    o a problem because they can become infected and may need to be excised

B.) Malignant ear tumors
  • squamous cell carcinoma: refer to plastic surgery
  • ear canal tumors: very rare, but ear must be completely excised because they are highly metastatic diagnosis of all ear cancers require biopsy of lesions, surgical excision, radiation, and lymph node dissection if there is metastasis

C.) Benign ear tumors
  • glomus tympanicum: tumor of the tympanic membrane that appears as a bright red mass behind the membrane
    o -causes hearing loss with pulsatile tinnitus
    o -investigation: CT with contrast
    o -treatment: surgical excision
  • glomus jugular: tumor occurs in the jugular foramen

D.) Nasal tumors
  • nasal osteoma: benign tumor of the skull base, usually found incidentally on CT scan
  • leave it alone if pt is asymptomatic
  • squamous papilloma: benign tumor caused by HPV but can transform into malignancy or cause obstruction and bleeding so they are typically excised
  • inverted papilloma: premalignant mass that is often confused for polyps, high chance of cancer conversion
  • juvenile angiofibroma: benign mass that occurs in adolescent males with chronic unilateral nosebleeds
  • squamous cell carcinoma: consider in smokers with history of nosebleeds and nasal pain

E.) Nasopharyngeal masses
  • adenoid hypertrophy: typically occurs in kids as adenoids usually regress by adulthood
  • can cause snoring
  • Tornwald cyst: congenital cyst of the nasopharynx, leave it alone
  • mucocele: cyst caused by buildup of mucus from blocked gland
  • removed only if causing nasal obstruction
  • lymphoma
  • squamous cell carcinoma

7.2 Ophthalmology

7.2.1 Acute Conjunctivitis
  • Bacterial (Staph aureus, Strep pneumo, H. flu, Moraxella), viral, or allergic
  • Presentation: often hard to differentiate bacterial from viral
  • bacterial (Staph aureus, Strep pneumo, H. flu, Moraxella): red conjunctiva with yellow/white/green discharge bilaterally that is consistently purulent
  • viral (usually adenovirus): discharge may be more clear, watery, and stringy, gritty or burning feeling in eye
    o usually one eye affected first with second eye in 24-48 hours
  • allergic: bilateral redness, watery discharge, itching, injected conjunctiva with follicular appearance, may have morning crusting
  • Treatment
  • bacterial □ erythromycin ointment or sulfacetamide drops
    o fluoroquinolone drops preferred in contact wearers due to risk of Pseudomonas
  • viral □ symptomatic relief only with OTC antihistamine drops (Ocuhist, Naphcon-A, Visine AC) compresses, naphazoline, pheniramine
  • allergic □ antihistamine/decongestant drops, mast cell destabilizer drops (olopatadine HCl), NSAID ophthalmic drop
• if severe: lodoxamide drops or cromolyn sodium drops

Prognosis: viral conjunctivitis takes 2-3 weeks to heal

Glaucoma: refers to a group of diseases characterized by damage to the ocular nerve (cupping), with most cases also involving elevated intraocular pressure

• Causes progressive loss of retinal ganglion nerve axons □ loss of visual field with eventual blindness
• Risk increases with age
• Several kinds:

  • secondary glaucoma: caused by injury or infection
  • congenital glaucoma: present at birth, with symptoms manifesting in first few years of life
  • closed (narrow) angle glaucoma: when contact between a malformed iris and trabecular network obstructs outflow of aqueous humor from the eye
    o means angle between iris and cornea is wide = normal
    o most prevalent in Asians
    o presentation is acute with redness and eye pain, headache
      • diagnostic criteria
        • must have 2 of these signs: ocular pain, nausea/vomiting, history of intermittent blurring of vision with halos
        • must have at least 3 of these signs: IOP > 21 mm Hg, injected conjunctiva, corneal epithelial edema, mid-dilated and nonreactive pupil

    o immediate treatment:
      • reduce IOP with carbonic anhydrase inhibitors (CO2 ↔ H20)
        • acetazolamide or methazolamide
        • don’t give to liver/renal pts, adrenocortical insufficiency, or severe pulmonary obstruction
        • side effects: may increase blood sugar in diabetics, transient myopia, nausea, diarrhea, loss of appetite, loss of taste, paresthesias, lack of energy, renal stones, hematological problems
      • reduce IOP with topical beta blocker to decrease aqueous humor production
        • -β-1 selective: betaxolol:
          o -caution: may exacerbate or precipitate heart block, asthma, COPD, or mental changes
        • -nonselective: carteolol, levobunolol, metipranolol, timolol
          o -fewer cardiac and lipid effects
      • add alpha agonist if necessary to decrease aqueous humor production
        • -apraclonidine or brimonidine (interaction with MAOIs, CNS effects, respiratory arrest in young children)
      • suppress inflammation □ topical steroid like prednisolone
      • analgesics for pain
      • antiemetics for nausea/vomiting
      • place pt in supine

o treatment one hour later:
- administer miotics (pull iris away from trabecular meshwork to open up flow) such as pilocarpine (may cause headaches)
- then osmotic agents if unsuccessful in lowering IOP: glycerin or isosorbide if diabetic, IV mannitol
  - but can’t use with pulmonary edema or anuria
- treatment 1-2 days later is focused on creating a new opening in the iris for aqueous humor to drain out of: laser peripheral iridotomy, argon laster peripheral iridoplasty, anterior chamber paracentesis
- meds to avoid in these patients because they will precipitate another attack: pseudoephedrine, phenylephrine, neo-synephrine, chlorpheniramine, diphenhydramine, Detrol, benzos, pupil dilation, tricyclics, hydralazine, citalopram, haloperidol, lithium, paroxetime, topimax
- wide or open angle glaucoma (primary open angle glaucoma): clogged physiologic drain increased intraocular pressure results in sequential damage to the optic nerve progressive loss of visual field
  - means angle between iris and cornea is closed = abnormal
  - most prevalent in blacks
  - causes: idiopathic, steroids, pigment dispersion
  - treatment: want to increase aqueous outflow while decreasing aqueous production to lower the IOP
    - suppress production:
      - beta-blockers
      - alpha agonists
      - alpha + beta agonists (vasoconstriction): dipivefrin (don’t give in angle closure glaucoma), epinephrine
      - topical carbonic anhydrase inhibitors: dorzolamide or brinzolamide
        - can increase glucose in diabetics
    - increase outflow:
      - prostaglandin analogs: latanoprost, travoprost, bimatoprost, unoprostone
      - alpha agonists
      - cholinergic agonists:
        - act as cholinesterase inhibitors (choline ↔ HAc): echothiophate, demecarium, carbachol, physostigmine
    - combination agents available: dorzolamide + timolol, brimonidine + timolol initial therapy is a topical beta-blocker (unless cardiac/pulm contraindications) + topical prostaglandins
      - alternative are alpha/beta agonists, carbonic anhydrase inhibitors, and cholinergic agonists

7.2.2 Refractive Errors

A.) Hyperopia (farsightedness): when the eye does not bend light enough (low optical power) image is in focus behind the retina
  - correct with convex (+) lenses
B.) Myopia (nearsightedness): when the eye bends light too much (high optical power) image is in focus too far in front of the retina
  - correct with concave (-) lenses
C.) **Astigmatism**: abnormal curvature of the cornea causes vision to be out of focus
- correct with a cylindrical lens

D.) **Presbyopia**: symptomatic loss of normal accommodation with age — loss of ability to focus on near objects
- natural aging process
- correct with reading glasses or bifocals

**Amblyopia**: a reduction in vision of one or both eyes that is the result of eye/brain pathways not connecting well at birth and cannot be resolved by the use of corrective lenses
- Causes:
  - sight deprivation such as cataracts or ptosis does not allow for development of correct pathways
  - strabismus
  - refractive errors such as anisometropia (unequal refractive power in eyes) or astigmatism
- Not a result of a lesion in the visual pathway but a developmental problem
- Treatment: close the good eye and force the bad eye to do extra work
- occlusion via pharmaceutical or physical means

**Strabismus (Tropia)**: when eyes are not aligned with each other
- Congenital or develops in early adulthood
- May cause amblyopia
- Eye deviations seen:
  - esotropia: cross-eyes
  - exotropia: walleyed
  - hypertropia: upward deviation
  - hypotropia: downward deviation
- Presentation: no weakness in extraocular eye movements or nerve palsies, no diplopia

### 7.2.3 Disorders of the Lids and Lacrimal System

A.) **Dacrocystitis**: nasolacrimal duct inflammation
- usually due to nasolacrimal duct obstruction or infection (Staph aureus or Strep pneumo)
- presentation: pain, redness, swelling of the inner lower eyelid, constant tearing, recurrent refractory conjunctivitis, abscess in adults
- treatment:
  - infants: massage and observe unless large abscess forms
  - adults: oral antibiotics, warm compress, abscess usually requires surgery

B.) **Ectropion**: eyelid pulls down and away from eyeball
- caused by congenital abnormality, scarring, facial nerve palsy, aging
- presentation: sagging lid with a dull light reflex, irritation

C.) **Entropion**: when the eyelid turns in on itself and lashes rub against the eye
- caused by congenital abnormality, aging, scarring, spasm

D.) **Chalazion**: painless lipogranuloma of the meibomian glands due to trapped oil
- more of a bother than a problem
- treatment: warm compress, lid scrubs

E.) **Hordeolum (stye)**: localized infection of the eyelid involving the hair follicles of exterior or meibomian glands if interior

F.) **Blepharitis**: inflammation of the eyelash follicles due to Staph if anterior and rosacea if posterior
- can progress to chalazion
- presentation: red, itchy eyelids with scales along eyelash bases
- treatment: warm compress, baby shampoo scrubs, topical erythromycin
G.) Lid (pre-septal) cellulitis:
- from insect bite, laceration, fracture into sinus
- presentation: redness, induration of lid, tenderness, pain
  - eyeball itself looks normal
  - no proptosis or limitation of eye movement
- treatment: antibiotics, warm compresses

H.) Orbital (post-septal) cellulitis:
- infection usually originates in infected sinus
- presentation: pain, swelling, proptosis of the eyeball, limited motion of eye, swollen conjunctiva, +/- vision loss
- investigation: visual acuity test, afferent pupillary defect, CT scan
  - consider mucormycosis in a diabetic patient or opportunists in an immunocompromised patient
- treatment: IV antibiotics, surgical draining of abscess

7.2.4 Cataracts: opacification of the eye lens
- Adult causes: age, steroids, diabetes, electrocution, congenital abnormality, trauma
- Childhood causes: metabolic disorder, infection, hereditary, trauma
- Presentation: gradual loss of vision, blurred or smoky vision, glares, decreased vision in bright light or at night
- Treatment: surgical removal of adult cataract when it interferes with ADLs, with replacement by an artificial lens
  - in kids the surgery must be done early to prevent amblyopia

Retinal Detachment: when retinal peels away from underlying support tissue
- Different kinds:
  - rhegmatogenous retinal detachment: occurs due to a tear in the retina that allows fluid to pass from the vitreous space into the subretinal space between the sensory retina and the retinal pigment epithelium
    - progressive unzipping of the retina
  - non-rhegmatogenous retinal detachment: when inflammation gets underneath the retina and causes the detachment
    - may be from fluid buildup (exudative) or from scarring created by the inflammation (tractional)
      - tracional is more common in diabetics
  - Higher risk with cataract surgery, high myopia, aphakia, and peripheral lattice degeneration
  - Presentation: usually acute, with floaters, vision loss, flashing lights, cut or line in vision
  - Treatment: scleral buckle, endolaser, cryotherapy, vitrectomy + endolaser, treatment of underlying cause (diabetes, inflammation, etc)

Age-Related Macular Degeneration: damage to retina causes loss of central vision
- Two forms:
  - non-exudative (dry): when drusen (cellular debris) accumulate between the retina and the choroid
    - loss of cones
    - accounts for 90% of cases
  - exudative (wet): blood vessels grow up from the choroid behind the retina
    - less common but more severe
- Risk factors: age, genetics, smoking, HTN, micronutrient levels, serum lipids?
- Treatment: vitamins and supplementation with zinc, beta carotene, copper, lasering or surgical extraction for neovascularization, macular translocation, antiangiogenesis therapy

7.2.5 Ophthalmic Manifestations of Carotid Atherosclerosis
• **Amaurosis fugax**: 5-10 minutes of unilateral vision loss
  • **Hollenhorst plaque**: cholesterol embolus in retinal arteriole
  • **Central retinal artery occlusion**: severe painless loss of vision due to loss of blood supply to the retina from embolus
    • associated with atrial fibrillation, endocarditis, coagulopathies, CAD, hypercoagulable stages
    • presentation: temporal arteritis (afferent pupillary defect with pale or swollen optic nerve with splinter hemorrhages), cherry-red spot and ground-glass retina, boxcar segmentation of vessels with severe obstruction
    • investigation: cardiovascular exam for murmurs or bruits, examination for temporal arteritis
    • treatment:
      o immediate lowering of IOP with acetazolamide
      o carbogen therapy
      o hyperbaric chamber
  • **Central retinal vein occlusion**: when occluded veins back up and blood fills retina causes painless loss of vision
    • causes: HTN, mechanical compression, glaucoma, inflammation of nerve, orbital disease, hyperviscosity disorders
    • investigation: determine whether it is ischemic or non-ischemic
    • treatment: treat underlying medical condition, aspirin therapy, laser ischemic retina, treat macular edema, treat associated glaucoma
  • **Diabetic retinopathy**: occurs when hyperglycemia damages basement membrane of retinal capillaries leakage of capillaries, macular edema
    • proliferation of weak blood vessels
      o can cause neovascular glaucoma if they grow in the anterior chamber
    • risk with DMI and II frequent eye exams
    • no known increased risk with gestational diabetes
    • presentation:
      o funduscopic exam: serum leakage will form hard exudates while red blood cell leakage will cause hemorrhage, capillary closures, cotton wool spots from retinal ischemia
    • treatment: laser ischemic areas
    • prognosis: diabetics also at increased risk for chronic open angle glaucoma, CN III/IV/VI palsies, early cataracts, orbital mucormycosis
  • **Hypertensive retinopathy**: damage to vessels caused by high blood pressure
    • graded based on extent
      o grade I mild arteriolar narrowing
      o grade II moderate narrowing with AV crossing defects
      o grade III severe narrowing with hemorrhage or exudates
      o grade IV all of the above + optic edema from the hemorrhaging

### Disorders of the Cornea

• **Pterygium**: when sun exposure results in growth of degenerate tissue that digs into the cornea, pulling on cornea as it grows out astigmatism
  • treatment: excision with needle + antifibrotics
  • Corneal abrasions:
    • investigation: stain to view abrasion
    • treatment: topical ointments to prevent infection, will heal with time
  • **Dry eyes**: a result of decreased tear production or abnormal tear content concentrations, or blepharitis
  • Corneal ulcers:
  • Corneal edema:
    • could be from bad cataract surgery or high blood pressure
    • presentation: dull light reflex
  • HSV keratitis:
    • investigation: stain eyes and shine blue light to look for branching pattern
    • treatment: topical or oral antiherpetics
7.2.7 Nerve Palsy
- A semi-emergency
- Presentation:
  - deviation will be greater in direction of action of the weak muscle
    - horizontal diplopia → weak lateral or medial rectus
    - vertical diplopia → weak superior rectus, inferior rectus, superior or inferior oblique
- oculomotor affected → ptosis and a dilated, unreactive pupil, eyes positioned down and out
  - could be a posterior communicating artery aneurysm
  - or if pupil is normal it could be microvascular palsy of CN III (whatever that means)
    - common with HTN and diabetes
- abducens affected → lateral rectus weakness with esotropia
  - caused by increased ICP, tumor, trauma, stroke, microvascular
- trochlear affected → vertical or oblique diplopia
  - hypertropic eye on affected side
  - diplopia and deviation increase on gaze to opposite side
    - head tilt to side to compensate
  - caused by congenital defect or trauma

7.2.8 When to Get an Ophthalmology Consult
When funduscopic exam shows blood, inflammatory cells, tumor cells, or foreign body

7.2.9 Causes of Blindness in the US
- Cataracts, age-related macular degeneration, glaucoma, diabetic retinopathy, retinal detachment, CRA/VO
- Red Eyes

7.3 Common Dental and Oral Mucosal Disorders

7.3.1 Tooth Anatomy
- Crown is what you see, and is covered in enamel
- Root is covered in cementum, which fuses it to the periodontal ligament
- PDL attaches tooth to alveolar bone and limits extent of biting by sensing pressure
- Each tooth contains a neurovascular bundle
- pulp only senses pain = any sensation that stimulates it will be felt as pain

7.3.2 Caries
- More common in children
- Late manifestation of a bacterial infection
- bacterial biofilm produces acid that demineralize and dissolve the enamel
- infection progresses through dentin, cementum, and pulp
  - may create fistulas into the gums for drainage
- can reach periodontal region and beyond to the bone and soft tissue
- Prevention: brushing with fluoridated toothpaste, flossing, drinking water fluoridation, sealants, fluoride treatments
- systemic fluoride supplements only if needed
- Treatment
  - remineralization if early
  - later, drill and fill with synthetic material

7.3.3 Periodontal Disease
- More common in adults
- Also caused by biofilm infections
- Gingivitis occurs in the gums = soft tissue only
- biofilm is mostly anaerobes
- appears as red gingiva near tooth
- after brushing, spit out blood-tinged toothpaste
- may or may not have pain
- leads to destruction of the attachment of gums to teeth
- can cause gum overgrowth
- commonly caused by medications (phenytoin, cyclosporin, Ca channel blockers) or hormonal changes
- can be aggravated by immunosuppression
- reverse with brushing and flossing to prevent progression to periodontitis
- Periodontitis occurs in the soft tissue or bone supporting the teeth
- causes loss of periodontal attachment and bone = gingival pockets that harbor infection
  - depth correlated to severity
- more common in adult males
- not always preceded by gingivitis
- aggravated by smoking, diabetes, osteoporosis, AIDS

7.3.4 Oral Mucosal Infections and Conditions

A.) Oral candidiasis (thrush): yeast infection that occurs when host flora is altered or with immunocompromised host
- forms:
  - pseudomembranous candidiasis: most common, white plaques that you can scrape off with underlying red mucosa
  - erythematous candidiasis: no white component
    - red path under the tongue = median rhomboid glossitis
    - from continual denture wear = denture stomatitis
  - hyperplastic candidiasis: thick white patches that can’t be scraped off
  - angular cheilitis: forms externally, on corners of mouth
    - infection can be mixed, so need to cover both bacteria and fungi
- caused by altered normal flora
- associated with xerostomia, endocrine dysfunction, immunosuppression, medications, trauma, blood diseases, and tobacco
- presentation: mouth burning or soreness, sensitivity to acidic and spicy foods, foul taste, or asymptomatic
- treat with oral antifungals, wash appliances in nystatin

B.) HSV infection
- presentation: may have lymphadenopathy, fever, chills, oral lesions, nausea, irritability
  - kids: gingivostomatitis
  - adults: pharyngotonsillitis
  - can get secondary infections
- treatment: best time to give antivirals is during prodrome
  - late treatment = magic mouthwash (Maalox, Kaopectate, Benadryl, viscous lidocaine), fluids

C.) Recurrent aphthous ulcers
- ulcers of unattached mucosa = not herpes! = not contagious
- caused by immune dysfunction creating breaks in mucosa + varying individual causes (stress, allergies, etc)
- different severities:
  - minor = most cases, 1-2 ulcers that are small
  - major (Sutton's disease) = 6-7 ulcers that are larger
  - clusterform = 10-40 large ulcers
- investigation: must rule out Celiac, cyclic neutropenia, malnutrition, immunosuppression, IBD
- treatment: topical steroids + antibiotic ointment to ease pain until it heals
- D.) Bisphosphonate-related osteonecrosis of the jaw
  - occurs with patients taking IV bisphosphonates (chemo, etc)
  - leads to development of bone that can’t repair itself = limited ability to respond to injury
  - mucosa on top of bone then dies
  - prevention: any patient on bisphosphonates or antiresorptives needs to have a thorough dental exam and cleaning before starting treatment
  - treatment: debridement, pain management, antibiotics, may need to stop chemo

7.4 Oral Cancer and Precancerous Lesions

If you are uncertain about an ulcer/bump, watch it for 3 weeks max, then cut it out!

7.4.1 Oral Lesions

- **Torus:** benign osteoma of the hard palate or mandible
  - no surgery unless they interfere with dentures or eating
- **Leukoplakia:** any mucosal condition that produces whiter than normal coloration (a catch-all term!)
  - includes hyperkeratosis, actinic cheilitis, heat lesions, dysplasias, carcinomas, candidiasis, hairy leukoplakia, lichen planus, lupus, white sponge nevus, hairy tongue, geographic tongue
  - can’t be scraped off
  - considered to be precancerous mucosa = always biopsy
  - smokers and chewers
  - have different stages of dysplasia
- **Oral hairy leukoplakia:** caused by a virus, just watch
- **Erythroplakia:** red, irregular mass
  - frequently dysplastic or carcinomatous = always biopsy
- **Lichen planus:** autoimmune disorder that appears similar to leukoplakia but has a lacy pattern
  - no treatment
  - can biopsy to rule out leukoplakia

7.4.2 Squamous Cell Carcinoma

- Risks: tobacco, alcohol, viruses, genetic, immune dysfunction
- if a smoker develops cancer and has it removed but continues smoking, the chances of developing a 2nd lesion skyrocket
- Prevention: limiting alcohol and marijuana use, quitting tobacco use, use of sunscreen on lips, HPV vaccine
- Presentation: may have many different appearances, including leukoplakia, erythroplakia, ulceration, mass, papillary growth, induration, loose teeth, paresthesias
  - could be on lower lip, lateral or ventral tongue, floor of mouth, soft palate, gingival ridge, buccal mucosa
  - with metastasis, swollen submandibular or superficial/deep cervical chains
- Investigation
  - differentiation
    - called carcinoma in situ if entire thickness of epithelium is involved with intact basement membrane
    - problem with oral cancers is that dysplasia is not as organized and invasion can occur without going through all the steps of dysplasia
- Prognosis: disparity in survival rates between whites and blacks
8 Gastroenterology Exam Notes

8.1 Approach to the Patient with Gastrointestinal Disease

8.1.1 Background

- Main GI tract is mouth, pharynx, esophagus, stomach, small intestines, large intestines, anus
- Accessory organs included in GI system are the salivary glands, liver, gallbladder, and pancreas
- Common GI signs and symptoms (including alarm symptoms):
  - abdominal pain:
    - types:
      - visceral pain is poorly localized
      - somatic pain is initiated by pain receptors in the parietal peritoneum and is sharp, well-localized, and increased by changes in pressure or tension
      - referred pain is a visceral pain felt elsewhere because visceral and somatic afferents frequently converge on the same neurons in the spinal cord
    - investigation:
      - differential: acute pancreatitis, acute cholecystitis, acute appendicitis (begins with periumbilical pain that settles in the RLQ), diverticulitis, intestinal ischemia (great pain after eating), peptic ulcer disease, bowel obstruction, infectious diarrhea, incarcerated hernia
      - must differentiate acute vs. chronic pain
  - altered bowel habits: includes diarrhea, constipation
    - an ALARM symptom that in any patient over 40 is colon cancer until proven otherwise
    - potential non-malignant causes: delayed gastric emptying, gastric outlet obstruction, small bowel adhesions, SBO due to Crohn’s
  - nausea and vomiting
  - bleeding: hematemesis, melena (old blood in stool = maroon or tarry), or hematochezia (BRBPR), coffee ground emesis (old blood from the stomach)
  - pyrosis: heartburn; exposure of the esophageal epithelium to gastric acid
  - dysphagia: an ALARM symptom
  - odynophagia
  - early satiety: an ALARM symptom for pancreatic and colorectal malignancies
  - jaundice
  - anorectal symptoms
  - anemia
  - weight loss > 10% TBW
  - history of PUD
  - FH of gastric malignancy
  - abdominal mass
  - Investigation:
    - GI history: be sure to ask about bowel habits, travel, extra-intestinal manifestations, meds, diet
    - PE: does disease encourage or resist movement by the patient, look for signs of telangiectases or other hallmarks of liver disease, rectal exam if needed
    - diagnosis of GI disease is complex are symptoms can be localized or diffuse
    - many diagnoses must be done by exclusion
    - many disorders are “functional” = lacking laboratory or radiographic evidence of disease
      - causes can be altered gut motility, exaggerated visceral responses to noxious stimuli, altered processing of visceral stimuli
      - ex. atypical chest pain, IBS, dyspepsia, functional bloating, functional constipation or diarrhea
8.1.2 Causes of Chronic Abdominal Pain

A.) GERD

B.) Non-ulcer dyspepsia: chronic or recurrent pain in the upper abdomen
- different from GERD in that pain is the primary feature
- investigation:
  - patients > 55 or with alarm symptoms: prompt endoscopy
  - patients < 55 with no alarm symptoms: test and treat for H. pylori + PPI (or PPI trial only)
- treatment only needed if patients have chronic symptoms

C.) IBS

D.) IBD

E.) Chronic pancreatitis

F.) Infectious diarrhea

8.2 Diagnostic Methods

8.2.1 Common GI Labs

1.) 24-hour urine 5-hydroxyindolacetic acid (HIAA): a breakdown product of serotonin that is associated with carcinoid syndrome when excreted in large amounts
- patient prep: must avoid serotonin-rich foods like bananas, pineapple, avocado, mushrooms, walnuts

2.) Pancreatic labs
- amylase: made by pancreas and salivary glands to break down starch
  - can be obtained from serum, urine, pleural fluid, peritoneal fluid
  - pronounced elevation in acute pancreatitis, pancreatic pseudocyst
  - mod elevation in pancreatic cancer, mumps, salivary gland inflammation, perforated peptic ulcer
- lipase: made mostly by the pancreas to break down TG
  - serum
  - released into the bloodstream with disease or injury to pancreas
  - elevation is highly specific for pancreatic disease
    - pronounced in acute pancreatitis, pancreatic pseudocyst
    - mod in pancreatic cancer

3.) Liver labs:
- total bilirubin: increased production from heme + defective removal
  - bilirubin is a product of RBC breakdown
  - normally the heme □ unconjugated bilirubin by the spleen
    - then the bilirubin is further processed by the liver □ conjugated bilirubin
      - enters the bile
        - most is excreted in feces
        - smaller amount excreted in urine
      - blockage of bile duct □ enters the blood instead
        - insoluble bilirubin = unconjugated = indirect
          - kidneys won’t filter this!
        - soluble bilirubin = conjugated = direct
          - kidneys will filter this, so if urine is dark this is why
  - total and direct bilirubin is what is measured from the blood, and indirect bilirubin is calculated from this number
  - unconj bili elevated from increased heme (hemolysis), hepatitis, drugs
  - conj bili elevated from biliary cirrhosis, drugs, hepatocyte damage, bile duct obstruction
  - elevated from liver cause: impaired uptake, defective bili metabolism, hepatocyte damage, obstruction
- alanine aminotransferase (ALT) and aspartate aminotransferase (AST): enzymes normally within the hepatocytes that are released when they are damaged
  - chronic hepatitis = elevation to the 100s
  - acute hepatitis = elevation > 1000
  - ALT:
    - high content in liver but also in kidney, heart, skeletal muscle
    - low content in pancreas, spleen, lung, RBCs
    - more specific for liver injury than either AST or ALP
    - more elevated injury than obstruction or cirrhosis
  - AST:
    - high content in liver, heart, brain, and skeletal muscle
    - mod content in RBCs
    - can be increased following MI, PE, skeletal muscle trauma, alcoholic cirrhosis, viral or drug-induced hepatitis
    - can be altered by drugs and patient conditions like hemolysis
  - interpreting and ALT/AST elevation:
    - how high are they?
      - if only mildly elevated:
        o repeat labs (half will be normal)
        o review history and consider causes of hepatitis
        o d/c drugs and alcohol and recheck labs
        o consider testing for hepatitis, hereditary diseases
    - if mod-high:
      o think hepatitis, drug injury, toxin injury, muscle injury
      o uncommon: viruses, extrahepatic biliary obstruction
  - if ALP is elevated out of proportion to ALT/AST, evaluate for cholestasis
- alkaline phosphatase (ALP): isoenzymes present rapidly dividing or metabolically active cells in the liver, bone, intestine, and placenta
  - elevated in biliary obstruction, pregnancy, active bone formation
  - if elevated, consider following up with 5’ nucleotidase: more specific to the liver than ALP
    - associated with cholestasis, liver mets
    - not as subject to elevation from drugs
    - if this comes back normal, the source is outside the liver!
- γ-glutamyl transpeptidase (GGT): present in liver and biliary tract, and in low amounts in the kidney, spleen, heart, intestine, brain, and prostate
  - useful in assessing cholestasis and biliary obstruction
  - confirms liver etiology when ALP is elevated
  - elevated in alcohol-induced hepatic changes, and in most liver and hepatobiliary diseases
- serum albumin: the portion of total serum protein formed WITHIN the liver
  - has a half-life of 14-20 days = lags behind disease
    - serum prealbumin has a half-life of 2 days so it is more sensitive to assess acute liver damage
- INR and PT: pertain to liver because clotting factors are synthesized there
  - prothrombin time will not be prolonged until one of the associated clotting factors decreases to < 30-40% of normal
- α-fetoprotein (AFP): elevated with inflammation or hepatocellular carcinoma h.) total protein: includes prealbumin, albumin, globulins
  - increased in dehydration, globulinopathies
  - decreased in pregnancy, excess IVF, cirrhosis, other liver disease, chronic alcoholism, CHF, nephrotic syndrome, burns
- “hepatic function panel”: typically includes Na, K, Cl, CO2, glucose, urea, creatinine, Ca, albumin, P
- 4.) Biliary labs: ALP, GGT, bili
8.2.2 Paracentesis

- Normally peritoneal fluid is ~ 50 mL, clear, and straw-colored
- Paracentesis fluid is evaluated for cells, Gram stain, glucose, amylase, NH3, ALP
- ↑ WBCs and neutrophils indicate bacterial peritonitis
- ↑ amylase indicates pancreatic ascites
- bloody fluid without traumatic tap indicates malignant peritonitis
- Serum albumin : ascites albumin gradient/ratio:
  - high in cirrhosis, CHF, alcoholic hepatitis, myxedema, portal vein thrombosis
  - low in bacterial peritonitis, malignancy, nephrotic syndrome, pancreatitis, TB, peritonitis

Peritoneal Lavage: instillation and aspiration of sterile saline into the abdominal cavity

- Indicated for eval of abdominal trauma, intraperitoneal hemorrhage, intestinal perf, organ perf
- Evaluates cells and chemicals

8.2.3 Fecal Occult Blood Testing

1.) Plain old FOBT:
- qualitatively measures presence of blood by oxidation of guaiac (extract impregnated in the paper) to hydrogen peroxide when exposed to heme blue color
- the “Sensa” brand has an enhancer that gives a more intense blue for greater sensitivity and ease of interpretation
  - requires 3 serial stools
  - can be used to detect bleeding associated with colorectal cancer
  - false + with red meats, NSAIDs, aspirin, excess alcohol, steroids, anticoagulants, chemotherapeutics, iodine preparations
    - = must avoid red meats for 3 days
    - = must avoid NSAIDs (including aspirin over 325 mg) for 7 days prior to collection and during collection
  - false neg with vit C supplements, excess natural vit C,
  - timeframe:
    - wait 3-5 minutes if immediate development of fresh sample is needed
    - specimens should be tested within 14 days of first stool collection
  - green results may be due to bile in specimen

2.) Immunochemical FOBT:
- specific for human globin = fewer false + from red meat, drugs, etc.
- nice because there is no patient prep needed and fewer specimens are needed

8.2.4 Fecal Leukocyte Testing

- Methylene blue stain detects leukocytes (mostly neutrophils)
- neutrophils are indicative of inflammation
  - presence varies by etiology
    - present with Shigella, Campylobacter, EIEC, UC, Crohn’s, radiation colitis, ischemic colitis
    - variably present with Salmonella, Yersinia, Vibrio, C. diff, Aeromonas
    - ABSENT in norovirus, rotavirus, CMV, ETEC, EHEC, Giardia, Entamoeba histolytica, Crypto, Staph aureus, Bacillus cereus, Clostridium perfringens
  - Don’t get in patients hospitalized > 3 days, because they would have manifested symptoms of inflammatory diarrhea by then (unless they got it while in the hospital)

8.2.5 C. diff Testing

- suspect in patients passing 5+ liquid stools per 24 hours

1.) Toxin test
- predominant enterotoxin is toxin A, toxin B is less common
- an ELISA test
false neg is possible, reduce this risk by testing serial stools: 3 specimens on 3 different days

2.) Tissue culture
   - the gold standard but is rarely performed
   - requires anaerobic culture of biopsy

8.2.6 Bacterial Stool Cultures
   - Covers Salmonella, Shigella, and Campylobacter
   - need to specially request media for Vibrio, Aeromonas, Yersinia
   - EHEC is a stool toxin test, so don’t ask for a culture for it!
   - When to order?
     - severe or persistent illness
     - again, don’t get in patients hospitalized > 3 days, because they would have manifested symptoms of infectious diarrhea by then (unless they got it while in the hospital)
   - Takes 3 days for a final negative result

8.2.7 Ova, Cysts, and Parasites
   1.) Fecal acid fast stain for Cryptosporidium parvum and Cyclospora cayetanensis
      - Crypto is a veterinary pathogen seen in immunocompromised patients and kids in daycare
      - Cyclospora stains as “ghost cells”
   2.) Giardia lamblia immunofluorescence assay, need UV microscope to do
   3.) Cryptosporidium parvum immunofluorescence assay
      - Testing caveats:
        - only allowed per hospitalization
        - not indicated in immunocompetent patients over age 6 that have been hospitalized for > 3 days

8.2.8 Summary: Tests to Order in Acute Diarrhea
   - Fecal leukocytes, routine stool culture
   - order with acute diarrhea < 7 days + severe illness:
     - temp > 38.5 C (101.3 F)
     - bloody diarrhea
     - greater than 6 stools a day, dehydration, abdominal pain
   - order with persistent illness for 7-10 days or worsening of symptoms
   - Add C. diff toxin if recent hospitalization or antibiotic use
   - Add ova and parasite testing if diarrhea is > 10 days, travel to endemic area, community water outbreak, HIV infection, homosexual male

8.2.9 Helicobacter pylori Testing
   --- concurrent use of a PPI, antibiotics, or bismuth can cause false neg in these tests!
   1.) Serologic ELISA test that detects IgG or IgA
      - non-invasive test of choice for diagnosing H. pylori in an untreated patient
      - positive in 50% of adults over age 60
      - antibodies persist for years after treatment = can’t discern active vs past infection
   2.) Gastric biopsy urease test
      - best invasive test
   3.) Urea breath test: patient ingests radioactive carbon-13 urea, labeled CO2 is exhaled and detected
      - best non-invasive test for documenting successful treatment of H. pylori
   4.) Stool antigen
8.2.10 Fecal Viral Studies

1.) Rotavirus ELISA
2.) Norovirus PCR: only performed for epidemiology!

**Fecal Fat Studies:** a screening tool for detection of malabsorption disorders resulting in steatorrhea

1.) Quantitative stool fat test: pt is on a high-fat diet for 2 days before and during collection
   - gold standard
2.) Qualitative stool fat test: pt is put on a high fat diet and stool is examined using Sudan stain to look for fat droplets

8.2.11 Common GI Imaging and Procedures

1.) X-ray:
   - plain films
     - abdominal flat and upright
       - ileus: multiple loops of dilated large and small bowel without a transition point
       - SBO: abnormal air-fluid levels with paucity of distal colonic gas
     - CXR: calcifications, foreign bodies, free air, obstruction
       - free air best visualized in LLD or upright ☐ not helpful for evaluation of reflux or colorectal screening
   - + barium = fluoroscopy (aka barium swallow, barium esophagram)
   - evaluate transit times, mucosal abnormalities
2.) CT:
   - indicated for trauma, unexplained pain, infectious or inflammatory lesions, pancreatitis, obstruction
   - indicated for primary malignancies of the liver and pancreas
3.) MR:
   - superior soft tissue resolution
   - good for liver lesions
   - not typically used in acute setting because it takes too long, with the exception of pregnancy
   - magnetic resonance cholangiopancreatogram (MRCP): evaluates biliary tree and pancreatic duct
     - noninvasive and no radiation
4.) Transabdominal US
   - usually test of choice for liver and biliary disease
   - test of choice in pediatric appendicitis and intussusception
   - commonly indicated for cholecystitis, cirrhosis
5.) Endoscopies
   - esophagogastroduodenoscopy (EGD): goes from mouth up through the duodenum
   - colonoscopy: goes from anus to terminal ileum, allows for visualization of entire colon
     - study of choice for colorectal screening
     - also indicated for eval of anemia, bleeding, assessment of IBD
     - extensive patient bowel prep and liquid diet for 24 hours prior to procedure
     - requires sedation
   - sigmoidoscopy: examines descending colon, sigmoid colon, and rectum
     - useful for patients with inflammatory diarrhea who only need a view of the distal colon
     - more effective than fecal occult for colorectal cancer screening, but less effective than colonoscopy
     - less patient prep than colonoscopy
   - endoscopic US: allows for transluminal imaging
     - study of choice for staging of rectal, esophageal, and gastric tumors
     - study of choice for identifying pancreatic tumors
     - can also be used to do aspiration biopsies through endoscope
• endoscopic retrograde cholangiopancreatogram (ERCP): endoscope is inserted from the mouth to the duodenum, and contrast is shot through it while x-rays are taken
  o evaluates the biliary tree and pancreatic duct endoscopically, can also intervene with stents, ductal dilation, or brushings
  o diagnostic uses: choledocholithiasis, biliary strictures, sphincter of Oddi dysfunction, recurrent acute or chronic pancreatitis, pancreatic cancer, pancreatic ampullary adenomas
  o therapeutic uses: removal of gallstones, sphincterectomy, stent placement, stricture dilation, fluid drainage, biopsy
• enteroscopy: small bowel endoscopy
• video capsule endoscopy: pill-sized camera for imaging small bowel
  o small bowel indications: tumors, obscure bleeding, polyposis syndromes, refractory malabsorption syndromes
  o esophageal indications: screening for varices, screening for GERD complications, esophagitis
  o avoid in patients with GI distress, fistulas, pregnancy, or swallowing disorders

6.) Nuclear medicine
• hepatobiliary scintigraphy (aka HIDA scan): injection of radioactive tracer into vein removal by liver tracer enters bile
  o gallbladder not visualized with cystic duct obstruction or inflammation
  o delayed gallbladder emptying with biliary dyskinesia
• tagged RBCs: uses technitum-99 to detect obscure bleeding

8.2.12 Liver Biopsy
• Indicated for evaluation of abnormal LFTs, suspected neoplasm, confirmation of diagnosis (hepatitis C, primary biliary cirrhosis, alcoholic cirrhosis, NAFLD), evaluation of granulomatous disease, unexplained jaundice or suspected drug reaction, management of post-transplant care
• Percutaneous, laparoscopic, or transjugular
• Gold standard for evaluation of liver inflammation or fibrosis
• Outpatient
• Complications rare but serious
• Contraindications: increased PT, thrombocytopenia, ascites, difficult body habitus, suspected hemangioma

8.3 Miscellaneous GI Complaints and Anorectal Disorders

Diverticular Disease
• A 20th century disease associated with the Western lifestyle of low fiber, red meat, obesity, and increasing age
• Includes diverticulosis (presence of small outpouchings of the mucosa and submucosa through the muscular layer of the colonic wall; of unknown pathophysiology) and diverticulitis (inflammation of the diverticula)
• occurs in areas of weakness where the intramural vasa recta penetrate the submucosa
• Presentation of diverticulitis:
  • pain that is LLQ and suprapubic +/- palpable mass = looks like a left-sided appendicitis
  • can be mild to severe
• acute GIB that is painless and maroon in color
• fever, malaise, constipation, diarrhea, nausea, vomiting, dysuria, urinary frequency
• Investigation of diverticulitis:
• leukocytosis with let shift
• CT is imaging of choice to assess severity
• plain films for free air, ileus, or obstruction
• Treatment of diverticulitis:
• 7-10 day course of antibiotics that must cover aerobes and anaerobes: cipro + metronidazole
• clear liquids diet
• surgical consult if no improvement in 72 hours
Complications of diverticulitis:
- lower GIB
- intra-abdominal abscess or peritonitis secondary to diverticula perforation
- fistulas into the bladder, ureter, vagina, or abdominal wall
- obstruction

8.3.1 Diarrhea

- Causes: disordered intestinal motility, malabsorption
- Malabsorption presents as diarrhea with nutrient deficiencies
  - fat malabsorption: bulky, frothy, oily stools
  - CHO malabsorption: bloating, soft diarrhea
  - protein malabsorption: edema, muscle wasting
- Diarrhea may be osmotic, secretory, or inflammatory and weight loss
- Infectious diarrhea is secretory or inflammatory
- Acute if < 6 weeks
  - 80% of cases are infectious: mostly viral, but occasionally bacterial or parasitic
    - diarrhea NOT improving within 3 days of onset is less likely to be viral
  - risk factors: travel, antibiotic use, day care, hospitalization, long-term care facility, immunosuppression therapy, MSM, vigorous/strenuous exercise
- 20% of cases are medication-induced or due to poorly absorbed sugars
- Chronic if > 6 weeks
- Pathogens associated with persistent infection: E. coli, Aeromonas, Yersinia, Giardia, Entamoeba, Cryptosporidium

8.3.2 Constipation

- May refer to infrequent stools (< 3 per week), difficult-to-pass/splashing stools, sense of incomplete evacuation, abdominal distension, bloating, or pain
- Rome criteria: for at least 12 weeks in the past year there is < 3 BMs per week as well as straining, hard stools, sense of incomplete evacuation, sense of anorectal obstruction, or need to use manual maneuvers to facilitate evacuation with more than 25% of BMs
  - loose stools are not present and there are insufficient criteria for IBS
- Generally considered to be a functional disorder with 3 subtypes:
  - slowed transit through colon
  - obstructive defecation
  - constipation-predominant IBS
- Causes:
  - functional: low fiber, sedentary activities, slow transit time
    - consider if there is a long PMH of constipation
  - drugs: Ca channel blockers, diuretics, anticholinergics
  - endocrine/metabolic disorders: diabetes, renal failure, hypercalcemia, hypothyroidism, hypokalemia
  - neuro disorders: MS, Parkinson’s, spinal cord disorders, Hirschsprung’s disease, psychosis
  - structural lesions: anorectal lesions, colonic strictures or lesions
  - recent onset: organic cause: malignancy, meds
- Investigation:
  - PE: rectal and abdominal exam
  - labs: CBC, TSH, metabolic panel
  - procedures rarely needed
- Treatment (after ruling out causes such as drugs or lesions):
  - no data: increase fiber and water intake, regular exercise
  - bowel training
  - increase number of daily meals
  - laxatives
  - severe cases:
    - digital disimpaction
8.3.3 Nausea and Vomiting
- Acute: appendicitis, cholecystitis, pancreatitis, peritonitis, small or large bowel obstruction
- Chronic: esophageal disorders, PUD, gastric malignancy

8.3.4 Anorectal Anatomy
- Sensory fibers end at the dentate line

8.3.5 Common Anorectal Symptoms
A.) Hemorrhoids: occur when increased venous pressure (from straining, prolonged sitting or standing, pregnancy) causes prolapse of the subepithelial pillows of smooth muscle → pain, bleeding, discharge
- internal hemorrhoids: painless bleeding after defecation
  - visible with anoscopy
  - treatment: 1% hydrocortisone, rubber band ligation if prolapsed, infrared coagulation for severe cases
- external hemorrhoids: rare bleeding but extremely painful, especially if thrombosed
  - visible externally on perianal exam
  - treatment: sitz bath, 1% hydrocortisone, stool softeners
    - may need to remove thrombosed clot
  - prolonged recovery
B.) Anal itching: can lead to lichenification, fissures, and infection
- causes: diabetes, malignancies, thyroid disease, or triggers such as diarrhea or constipation, anorectal lesions, wipes, tight-fitting clothes, over-cleansing, ingested irritants (tomatoes, citrus foods, caffeinated drinks), atopic dermatitis, lichen planus, psoriasis, infections (intertrigo, HPV, HSV, scabies, pinworms), meds (colchicine)
  - treatment: good hygiene, removal of offending agents, 1% hydrocortisone, antihistamine, antipruritic
C.) Rectal pain
- causes:
  - fissure: clue is severe pain with or immediately after a bowel movement
  - inflamed internal hemorrhoids: clue is dull, aching pain after a bowel movement
  - proctalgia fugax: spasmodic anal pain unrelated to BMs, may only occur a few times a year
D.) Lump or mass
- causes: external hemorrhoids (painful), skin tags (usually painless), polyps, genital warts, molluscum contagium
E.) Rectal bleeding
- common causes: younger patients: internal hemorrhoids, fissures, polyps (rare)
  - older patients: must also consider malignancy
- causes of BRBPR: hemorrhoids, diverticuli, UC, infectious diarrhea, AVMs, fissures, fistulas, polyps
  - fissures are caused by tears or erosion in the epithelium of the anal canal
    - usually caused by large or hard-to-pass stool, rarely due to trauma
    - very tender and bleed easily
    - most commonly posterior
    - if lateral, think chronic fissuring, TB, syphilis, occult abscesses, or carcinoma
    - diagnosed by appearance
    - treatment: stool softeners, protective ointments, sitz baths, 1% hydrocortisone, 2% NG, Botox
      - if no healing after 6 weeks, need surgical consult
  - fistulas may be caused by cryptoglandular infection, obstetrical injury, TB, Crohn’s, cancer, radiation therapy
- treatment is antibiotics and surgical referral
• abscesses are a medical emergency! can become septic quickly
  ▪ begin as an infection of the anal glands
  ▪ pathogens: E. coli, Proteus vulgaris, Bacteroides, Staph, Strep
• causes of occult blood: gastritis, gastric ulcers, gastric and esophageal malignancies, esophageal varices, diverticuli, polyps, colorectal carcinomas

8.4 Colon Cancer

8.4.1 Background

• 95% of primary colon cancers are adenocarcinomas
• Polyps:
  • some polyps are adenomatous (malignant potential) while some are hyperplastic (not pre-malignant)
    ▪ transformation from adenomatous polyps to colon cancer occurs over many years
    ▪ patients with hyperplastic polyps do not more frequent screening
• Tumors occur in the inner mucosa, muscularis mucosa, and possibly the submucosa
• Incidence decreasing since mid-1980s
• Risk increases with age, FH, DM2, metabolic syndrome, ethnicity, IBD, high red meat/processed meat consumption, inactivity, obesity, smoking, heavy alcohol use
• Genetic risks: up to 30% of colorectal cancers have some familial component
  ▪ FAP: also incurs increased risk of thyroid, pancreas, duodenal, gastric cancers
  ▪ HNPCC: also associated with endometrial, ovarian, gastric, urinary tract, renal cell, biliary, and gallbladder cancers
• Most occur after age 50
• Slightly more common in men
• Prevention:
  • diet with plant foods
  • healthy BMI
  • limit red meats
  • physical activity
  • vit D/Ca?
• screens
  ▪ stool tests: occult blood, stool DNA
    ▪ these generally only detect cancer
    ▪ guaiac-based fecal occult blood test has the best mortality benefit data
      • should be done annually
      • can’t be used with a digital rectal exam sample when used for screening
      • if positive, should always be followed by colonoscopy
  ▪ structural exams: colonoscopy, CT colonography, flexible sigmoidoscopy, double-contrast barium enema
    ▪ these detect polyps as well as cancer
    ▪ colonoscopy: direct inspection of entire colon with conscious sedation
      • extensive and thorough bowel prep needed
      • can miss large adenomas and some cancers
        ▪ but overall much more likely to detect any neoplasia than by fecal immunochemical testing alone
      • complications: bleeding post-polypectomy, perforation
      • should be done every 10 years, or every 3-5 years with detected cancer or polyps, or every 5 years with FH, or yearly once IBD is present for 15+ years
    ▪ flex sig: examines left colon
      • some bowel prep is needed
      • adenomas found will need a colonoscopy follow-up
      • needs to be done every 5 years
    ▪ CT colonography: no sedation
      • requires some bowel prep
• reimbursement varies
• positive results require f/u colonoscopy
• needs to be done every 5 years
• an emerging technology with lower specificity and sensitivity
  - MR colonography: unable to detect lesions < 5 mm
    • non-invasive tests are an option but they are less likely to prevent cancer and a colonoscopy must be done if they come back abnormal
  - ACS guidelines:
    • avg patient begin at 50
    • FH in 1st degree relative or many 2nd degree relatives begin screening 10 years younger than youngest affected family member
    • screening interval determined based on test results and presence of risk factors
  - USPSTF guidelines:
    • use fecal occult blood, sigmoidoscopy, or colonoscopy beginning at age 50 and continuing through age 75

• Presentation: few symptoms!
• rectal bleeding
• iron deficiency anemia
• fatigue and weight loss
• obstruction
• change in stool quality or caliber
• abdominal mass or pain
• weakness
• weight loss

• unusual presentations than can happen:
  • invasion of adjacent organs or formation of malignant fistula
  • fever of unknown origin or intra-abdominal or retroperitoneal abscesses
  • Strep bovis or Clostridium septicum sepsis can be due to underlying colon cancers

• 20% of cases will have metastatic disease, most commonly to the liver and lung
• Investigation:
• evaluation of metastatic disease:
  • colonoscopy is the gold standard for visualization and biopsy of the tumor
  • abd/pelvis CT to help with staging
    • see classic “apple core” lesions
  • CXR
  • labs: CBC, CMP, baseline CEA for follow-up
  • PET
• Treatment
• surgery
  • very early stage tumors may be removed endoscopically
    • polypectomy decreases colon cancer death rate by 53%
  • hemicolecetomy (usually ¼ of the colon) with lymph node dissection
  • may need colostomy
• isolated mets to other organs may be removed
• local treatment of mets
  • radiofrequency ablation
  • ethanol ablation
  • cryosurgery
  • hepatic artery embolization for liver mets to make them necrose
• chemo to eradicate micromets
  • begin considering at stage II
  • standard of care for stage III, metastatic disease, or unresectable tumors
• radiation is not typically used for colon cancer due to high toxicity in the gut, but may be used for rectal cancer
8.5 GI Bleed

8.5.1 Background

- Defined as an intraluminal blood loss anywhere from the oropharynx to the anus
- An "obscure" bleed is one whose source is not identified after upper and lower endoscopies
- An "occult" bleed is detected in an asymptomatic patient
- Occurs more commonly in men
- Acute or chronic, upper or lower (separated by ligament of Treitz)
- Chronic may present as hemoccult + stool, Fe deficiency anemia, or both
- Assessing the GIB patient:
  - how sick are they?
    - vitals
    - resting tachycardia with 10% of intravascular vol lost
    - orthostasis with 10-20% intravascular vol lost
    - shock with 20-40% of intravascular vol lost
  - HPI:
    - frequency, amount of stool
      - blood is cathartic = will accelerate defecation
      - melenic stool means it has been in the GI tract for at least 12-14 hours
      - upper bleeds usually cause bright red blood but can be dark if slower
    - other symptoms
    - meds associated with GIB: NSAIDS (even baby aspirin), Goody or BC powders, steroids in setting of NSAIDs, warfarin, heparin, enoxaparin, clopidogrel
- PMH: prior bleeding episode, underlying disease (liver), history of radiation to the pelvis, results of previous endoscopies/colonoscopies, prior surgical history
- PE: blood in nose or throat, abdominal exam, signs of liver disease (jaundice, ascites, spider angiomas, caput medusiae, palmar erythema), rectal exam
- Investigation:
  - in a known GIB patient, stool guaiac has no utility because it doesn’t tell you where the bleed is coming from
  - labs:
    - H/H: remember that during a GIB the pt is bleeding whole blood, so the hematocrit won’t change until you start adding fluids and compare
      - can also take up to 2 hours for hct to reflect the extent of bleeding
    - MCV should be normal in acute blood loss
    - BUN rises as blood is broken down to urea with digestion
      - differentiate from a kidney cause by a rise without a proportional rise in creatinine
    - INR
    - platelets
    - rectal exam
    - determine source of bleeding and stop active bleeding: EGD, colonoscopy, others
      - NG lavage: dropping an NG tube in to aspirate fluid to look for blood
      - helps delineate upper from lower source
    - problem: false negative in ¼ of upper GIBs, does not give information about etiology
    - endoscopy: EGD, enteroscopy, and/or colonoscopy
      - both diagnostic and therapeutic potential
    - tagged RBC scan; can pick up a slower GIB (0.1 mL/min) in a safe and non-invasive way but can’t intervene with
      - pre-test for angiography
    - angiography: can pick up a bleed of 0.5 mL/min or greater
      - usually only done with positive tagged RBC scan
      - can use to perform coil microembolization of a bleeding vessel
- Treatment:
  - stabilize patient
8.5.2 Upper GIB

- **Causes:**
  - **common:**
    - ulcers: esophageal, gastric, duodenal
      - bleeding occurs from erosion into a vessel
      - risk factors: NSAIDs, *H. pylori*, acid, steroids with NSAIDs, anticoagulation, alcohol
    - esophageal varices
  - less common causes: malignancy, vascular abnormalities, Mallory-Weiss tear (laceration in the mucosa usually from throwing up a lot, usually near the GE junction), tumors, erosions, Dieulafoy’s lesion (dilated submucosal artery erodes into the mucosa with subsequent rupture of the artery), esophagitis, aorto-enteric fistula
- **Presentation:**
  - usually acute
  - most commonly hematemesis, but can also have melena or hematochezia depending on speed of bleed
- **Investigation:**
  - endoscopy to assess risk of re-bleed
- **Treatment:**
  - most are self-limiting and only require supportive care but requires close follow-up
  - if ulcers are present: PPI, *H. pylori* eradication if needed, endoscopic therapy (clips, banding, etc)
    - second-line: angiogram, other surgery
  - if bleed is from varices, this can be massive!
    - airway management
    - octreotide, antibiotics if cirrhosis is present
    - EGD with banding
    - compression with Minnesota tube
    - if EGD fails, treat portal HTN causing the bleed: transjugular intrahepatic portosystemic shunt: establishes communication between the inflow portal vein and the outflow hepatic vein
  - if bleed is from vascular lesions:
    - Mallory-Weiss tears are usually self-limiting
- **Prognosis:**
  - mortality is 8-10%, especially in the elderly

8.5.3 Lower GIB

- **Causes:**
  - common: diverticular disease, neoplasms, colitis (infectious, ischemic, radiation, IBD)
  - less common: angiodysplasia, hemorrhoids, fissures
  - Increased incidence with age
  - Many cases are underreported as most people do not seek medical care
  - Presentation is usually hematochezia
  - if diverticular cause: acute and painless hematochezia
- **Investigation:**
  - procedures:
    - anoscopy
    - flexible sigmoidoscopy
• colonoscopy: role is not well established for acute lower GIB
  o may have poor visibility and may cause bowel purge during active bleeding
• tagged RBC scan: can help localize the bleeding
• angiography
• Treatment:
  • diverticular bleeds usually stop spontaneously but can recur, especially with increasing age
  • fix during scope or angiography
  • further surgical resection: colectomy, hemorrhoidectomy

8.5.4 Iron Deficiency Anemia
• Can result from blood loss, decreased intestinal absorption of iron, or increased red cell destruction
• Check labs
• When unexplained, upper/lower GIB evaluation needs to be conducted

8.6 Liver Disease

8.6.1 Background
• History for liver patient:
  • meds: include herbals
  • FH of hemochromatosis, Wilson’s disease, α-1 antitrypsin deficiency
  • alcohol, drugs
  • HIV status
  • exposures: hepatitis, blood products, sex, IVDU or intranasal, travel
  • PE:
    • HEENT: icteric sclera, Kayser-Fleischner rings
    • chest: gynecomastia from overproduction of estrogen in cirrhosis
    • abdomen: ascites, small liver, splenomegaly, caput medusae
    • GU: testicular atrophy
    • extremities: edema, palmar erythema, spider angiomata from elevated estrogens
    • neuro: asterixis, coma, encephalopathy
• Liver diseases:
  • hepatitis: inflammation of the hepatocytes
    o can be viral (most commonly), alcohol-related, metabolic, toxin, or medication-related
    o can be acute or chronic
  • fulminant liver failure: a progression to liver failure in < 14 days in a patient without previous liver disease
    o can be viral, autoimmune, ischemic, toxin-related
  • cirrhosis: fibrotic bands and nodules as a result of long-standing liver damage
• Common liver disease presentations:
  • jaundice: yellowing of the skin, conjunctiva, and mucous membranes due to increased bilirubin
    o clinically apparent when bilirubin > 2.5 mg/dL
    o first appears in the eyes and oral mucosa
    o may also have dark urine and light stool
    o malaise/fatigue
    o light stools, dark urine
    o pruritus
    o GIB
    o confusion
    o edema
    o weight loss or loss of appetite
    o nausea & vomiting
    o fever
  • Liver labs: AST/ALT, ALP, bili
  • Liver transplant
• indicated for hep C, alcoholic cirrhosis (if abstinent at least 6 months), cryptogenic cirrhosis, NASH, PBC, PSC, autoimmune hepatitis, hep B
• assessments:
  o Child-Pugh score: takes into account ascites, bili, albumin, INR/PT, encephalopathy
    ▪ estimates one and two-year survival rates
  o MELD score: takes into account bili, INR, creatinine
    ▪ used to rank liver transplant candidates and assess surgical risk
    ▪ scores of 12-15 have a better survival living with the disease than getting a transplant but can be put on the list at this time
    ▪ scores of 22+ are ready for transplant
• one year survival is 85%, 3 year 70%

8.6.2 Viral Hepatitis

<table>
<thead>
<tr>
<th></th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
</tr>
</thead>
<tbody>
<tr>
<td>Source</td>
<td>Water- and foodborne, feces</td>
<td>Blood &amp; assoc fluids, parenteral, ex</td>
<td>Blood &amp; assoc fluids, parenteral, sex</td>
<td>Blood &amp; assoc fluids</td>
<td>Water- and foodborne, feces</td>
</tr>
<tr>
<td>Incubation</td>
<td>15-30 days</td>
<td>45-180 days</td>
<td>2-26 weeks</td>
<td></td>
<td></td>
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<tr>
<td>Transmission</td>
<td>Fecal-oral</td>
<td>Percutaneous/mucosal</td>
<td>Percutaneous/mucosal</td>
<td>Percutaneous/mucosal</td>
<td>Fecal-oral</td>
</tr>
<tr>
<td>Prevention</td>
<td>Immunization, esp for travelers, MSM, drug users, chronic liver disease</td>
<td>Immunization of all adolescents and dults in high risk groups, perinatal prevention</td>
<td>Blood donor screening, don't share needles, barrier protection during sex</td>
<td>Immunization for HBV</td>
<td>Safe drinking water</td>
</tr>
<tr>
<td>Presentation</td>
<td>ACUTE RUQ pain, n/v</td>
<td>CHRONIC in 5% unless you clear it</td>
<td>Usually no acute flare, just becomes chronic</td>
<td>Silently progressive</td>
<td>CHRONIC</td>
</tr>
<tr>
<td>Investigation</td>
<td>↑ ALT/AST + IgM if acute + IgG if prior/vacc</td>
<td>+ surface Ag with active infection + surface AB with previous infect/vacc + core AB with active or prior infect (NOT vacc) + E Ag with active viral replication + E AB in chronic infect w/o replication, + blood DNA in infection</td>
<td>+ AB in present or previous infection + RNA in active infection</td>
<td>+ AB in present or previous infection + RNA in active infection</td>
<td>+ AB</td>
</tr>
<tr>
<td>Treatment</td>
<td>IFN, antivirals Usually clears spontaneously</td>
<td>Type 1 ☑️ direct antivirals, pegylated IFN, ribavirin Type 2 or 3 ☑️ pegylated IFN, ribavirin</td>
<td>Benign and self-limiting</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic infection?</td>
<td>No</td>
<td>Yes, especially in kids under 5</td>
<td>Yes in 70%</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Special notes</td>
<td>&quot;Infectious hepatitis&quot; Complications of fulminant hepatitis, cholestatic hepatitis Prevalent in Alaska natives, American Indians</td>
<td>&quot;Serum hepatitis&quot; Chronic increases risk for cirrhosis and HCC</td>
<td>#1 cause for liver transplant 6 genotypes, with 1 most common and hardest to treat Liver biopsy useful for staging chronic</td>
<td>Requires coinfection with hep B</td>
<td>Increased severity in pregnant women Rare in US Endemic in India, Mexico, Iraq, North Africa, etc.</td>
</tr>
</tbody>
</table>

8.6.2 Viral Hepatitis

- Source: Water- and foodborne, feces
- Incubation: 15-30 days
- Transmission: Fecal-oral
- Prevention: Immunization, esp for travelers, MSM, drug users, chronic liver disease
- Presentation: ACUTE RUQ pain, n/v
- Investigation: ↑ ALT/AST + IgM if acute + IgG if prior/vacc
- Treatment: IFN, antivirals Usually clears spontaneously
- Chronic infection?: No
- Special notes: "Infectious hepatitis" Complications of fulminant hepatitis, cholestatic hepatitis Prevalent in Alaska natives, American Indians

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Viral hepatitis labs:
- WBCs normal to low
- super high AST/ALT
- followed by ↑ total bili
- followed by ↑ ALP
- pathogen-specific antigens and antibodies
- proteinuria

8.6.3 Other Causes of Chronic Hepatitis

A.) Hemochromatosis from iron overload
- labs: high ferritin, Fe saturation, HFE gene testing
B.) Autoimmune hepatitis
- labs: ANA, anti-smooth muscle, IgG levels
- treat with prednisone and azathioprine
C.) Wilson’s disease □ copper overload
- labs: low ceruloplasmin
D.) α-1 antitrypsin deficiency
- lung and liver manifestations
E.) Medication side effects

8.6.4 Alcoholic Liver Disease

A.) Acute alcoholic hepatitis
- presentation: RUQ pain, n/v, jaundice
- investigation:
  - labs:
    - AST 2x higher than ALT, but not as high as other etiologies of hepatitis
    - elevated bili
    - elevated INR
- treatment:
  - prednisone +/- pentoxifylline if discriminant function is calculated to be > 32
B.) Alcoholic cirrhosis
- average consumption of 8 12 oz beers, 1L wine, or ½ pint of spirits per day for 20 years

Nonalcoholic Fatty Liver Disease: a spectrum of diseases ranging from asymptomatic fat in the liver to NASH to cirrhosis

A.) Non-alcoholic steatohepatitis (NASH): resembles alcoholic liver disease but patients have no history of significant alcohol consumption
- usually seen in patients with metabolic syndrome
- presentation:
  - mostly asymptomatic, found incidentally in labs or after development of cirrhosis
- treatment: weight loss, exercise, tight glucose control, HTN treatment, hyperlipidemia treatment (can use statins in this case!)
  - current research on use of glitazones, vit E
B.) Non-alcoholic cirrhosis: end result of chronic inflammation from a variety of etiologies = alcoholic cirrhosis will also manifest in same way
- presentation:
  - portal HTN
  - ascites: + fluid wave and shifting dullness
- can have bacterial infection on top of ascites - abdominal pain, fever, renal insufficiency
  - gastro-esophageal varices
  - splenomegaly - thrombocytopenia
  - encephalopathy from lack of toxin clearance - euphoria, confusion, asterixis, coma
    - can be precipitated by infection, bleeding, hyponatremia, hypokalemia, sedatives, azotemia, blood transfusion, TIPS (shunts blood away from the liver, leading to ineffective clearing of toxins)
- investigation:
  - labs:
    - high INR and low albumin from decreased ability to make proteins
      - low total protein
    - elevated conjugated bili followed by elevated unconjugated bili due to inability of liver to process bilirubin
      - initially problems getting the conjugated bili into bile, then problems conjugating at all?
  - US to check for ascites, portal vein thrombosis (cause of acute ascites)
  - diagnostic paracentesis:
    - truly ascites from portal HTN if difference between serum albumin and peritoneal fluid albumin is > 1.1
    - bacterial peritonitis if > 250 neutrophils
  - histology: fibrosis, regenerated nodules, vascular distortion
- treatment:
  - screen for varices with EGD
    - if present, start on β-blocker to reduce portal pressures
  - ascites:
    - salt restriction, but no fluid restriction
    - diuretics
    - therapeutic paracentesis
    - TIPS procedure if refractory
    - if bacterial infection - 3rd gen cephalosporin, hold diuretics
  - encephalopathy:
    - rule out infection
    - correct electrolytes
    - lactulose: decreases pH to favor NH4+ formation with removal by the gut
    - rifaxamin to kill GI tract bacteria and keep NH4+ levels low
  - transplant

8.6.5 Predominantly Biliary Liver Disease
A.) Primary sclerosing cholangitis: inflammation of larger bile ducts leads to scarring and obstruction
B.) Primary biliary cirrhosis: inflammation of the small bile ducts
- labs: + anti-mitochondrial AB

8.6.6 Liver Masses
A.) Benign:
- solid: in most cases, if patient is otherwise healthy, manage expectantly, but if patient has malignancy elsewhere consider a needle biopsy
  - hemangioma: most common benign liver tumor
    - small, asymptomatic, incidental finding
  - hepatic adenoma: associated with long-term estrogen use
    - can rupture and bleed - should be resected
  - focal nodular hyperplasia: may be a response to a congenital vascular malformation
    - resect
  - hamartoma:
- cystic:
simple cyst:
- infectious cyst:
- polycystic liver:
- biliary cystadenoma:
- Von Meyenburg complex:

B.) Malignant
- mets:
  - hepatocellular carcinoma: usually occurs with chronic liver disease or cirrhosis
    - diagnostic imaging shows multiphasic tumor (arterial phase hypervascularity with delayed phase washout)
  - treat by resection, embolization (temporary measure), radiofrequency ablation, or transplantation
  - cholangiocarcinoma:
  - rare tumors:
    - hemangioendothelioma:
    - soft tissue sarcoma:
    - primary hepatic lymphoma:
    - non-Hodgkin lymphoma:

Consideration of liver masses:
- think about underlying liver disease or primary malignancies present
- symptomatic patient vs incidental finding
- risk factors: age, gender, travel, exposures, medications
- imaging is key

8.7 Esophageal Disease

8.7.1 Background
- Anatomy of the esophagus
  - spans from about C6 to T11
  - cricopharyngeus muscle is closed except during swallowing and emesis
  - descends between the trachea and the vertebral column
  - lumen is collapsed at rest and distends with food bolus
  - innervated by the recurrent laryngeal nerve and sympathetic trunks
  - blood supply from aortic branches
- Common esophageal symptoms:
  - pyrosis: heartburn, with pain being substernal, can radiate to the neck
  - dysphagia: difficulty in swallowing liquids and or solids
    - etiology can be oropharyngeal or esophageal, or lie outside of the GI tract
      - esophageal: motility disorder (difficulty swallowing liquids and solids) or mechanical obstruction (difficulty swallowing solids)
      - oropharyngeal: difficult in transferring food bolus to back of mouth
        - may be a neurologic dysfunction (CVA, ALS)
        - can also be caused by Zenker’s diverticulum
  - odynophagia: painful swallowing from inflammation of esophageal mucosa
    - a sign of infectious esophagitis
    - other causes:
      - pill-induced esophagitis
      - meds: doxycycline, tetracycline
      - ingestion of caustic substances
  - chest pain: could be GERD, diffuse esophageal spasm, nutcracker esophagus, achalasia

8.7.2 Esophageal Diagnostic Studies
1.) Barium esophagram: patient swallows barium sulfate to get a better sense of the anatomy of the esophagus and stomach
2.) EGD

3.) **Esophageal manometry:** catheter with multiple pressure-sensing regions is introduced via the nose or mouth into the esophagus to measure swallowing and peristalsis pressures
   - senses pressures in the pharynx, upper esophageal sphincter, esophageal body (3 areas), and the lower esophageal sphincter
   - assesses function of peristalsis and sphincters prior to any surgical or endoscopic correction for reflux

4.) **Ambulatory esophageal pH monitoring:** standard procedure for detecting pathologic acid reflux into the esophagus
   - measures frequency of acid contact and duration to correlate to symptoms
   - indicated for refractory GERD with normal EGD, atypical symptoms, failure to respond to pharmacologic therapy, and patients being considered for antireflux surgery

### 8.7.3 GERD and Complications

- Involves dysfunction of sphincters and reflux of caustic materials (acid, pepsin, bile, pancreatic enzymes)
- Specific causes: incompetent lower esophageal sphincter, transient lower esophageal sphincter relaxation, refluxate, delayed gastric emptying, impaired swallowing, impaired peristalsis (Raynaud’s, scleroderma), impaired salivary secretion (Sjogren’s), hiatal hernia
- Presentation:
  - heartburn 30-60 minutes after a meal
  - sour brash
  - dysphagia
  - relief with antacids
- Esophagitis: does not correlate with severity of heartburn complaint
- Extra-esophageal manifestations: exacerbation of asthma, cough, non-cardiac chest pain, laryngitis, hoarseness, loss of dental enamel

### Investigation:
- Diagnosis is usually clinical
- Procedures:
  - EGD: documents type and extent of tissue damage from GERD, including strictures and Barrett’s
    - Will be normal in up to half of patients with reflux symptoms and won’t detect mild disease
  - Barium studies: limited role in reflux, but will detect strictures, ulceration, and abnormal
    - Reveals abnormal motility or esophageal clearance
  - Esophageal manometry
  - 24 hour esophageal probes

### Treatment/management:
- Uncomplicated PP I empirically
  - No need for further workup unless there is treatment failure, > 10 year duration of symptoms, warning/ atypical symptoms (dysphagia, weight loss, hematemesis, melena, anemia unresponsive to medications)
  - BUT symptom onset after age 50 warrants further invest
- Lifestyle modifications: elevate HOB, lose weight, stop tobacco, no late night eating, limit alcohol/fatty foods/caffeine/chocolate
- Acid suppression: decreases acid but NOT reflux!
- Motility agents
- Surgical procedures:
  - Nissen fundoplication: tightens area around sphincter in an attempt to make it close more tightly
  - Must screen for Barrett’s with EGD in those with symptoms > 10 years, those over 50, white males
- Complications of GERD:
  - Esophageal/peptic stricture: narrowing or tightening of the esophageal lumen that causes dysphagia
may need to be dilated with a balloon to relieve symptoms

- increased risk for adenocarcinoma
  - even symptoms > once per week increases risk by 8x
  - frequent symptoms increase risk by 44x

- Barrett’s esophagus: change from squamous to columnar epithelium in esophagus, puts patient at 30-60x risk for adenocarcinoma of the esophagus
  - chronic reflux esophagitis □ squamous epithelial injury □ metaplasia
  - risk related to extent of Barrett’s
  - on EGD looks like salmon-colored patches with irregular borders, erythema
  - treat with acid suppression therapy, anti-reflux surgery, endoscopic ablation therapy, esophagectomy

8.7.4 Infectious Esophagitis

- Pathogens: CMV, herpes, Candida
- Think AIDS or other immunosuppressive disease with idiopathic ulceration
- Presentation: odynophagia, dysphagia, chest pain, +/- fever
- Investigation: EGD with biopsy, especially if fever

8.7.5 Structural Disorders

A.) Esophageal stenosis/strictures

- causes:
  - rings and webs: vaguely describes lesions that can be found anywhere in the esophagus
    - Plummer Vinson syndrome: symptomatic proximally located webs found in middleaged women with evidence of Fe deficiency anemia
    - Schatzki ring: web occurring in the distal esophagus
  - reflux esophagitis
  - tumors
  - caustic ingestions
  - infections
  - iatrogenic: pills, radiation, sclerotherapy, NG tubes
- treatment: widen stenotic area with balloon
  - can’t be done with active inflammation or ulceration due to risk of perforation

B.) Zenker's diverticulum: herniation of posterior pharyngeal wall

- most common cause of transfer dysphagia
- usually occurs in men over 60
- presentation: regurgitation, dysphagia, halitosis

C.) Eosinophilic esophagitis: allergic or idiopathic infiltration

- associated with asthma, allergic rhinitis, urticaria, hay fever, atopic dermatitis, food or medication allergy
- presentation: dysphagia, food impaction, reflux
- investigation:
  - EGD or imaging shoes strictures, mucosal rings, linear furrowing, “feline” esophagus, eosinophilic abscesses, esophageal polyps
- treatment:
8.7.6 Motility Disorders

A.) Achalasia: absence of normal esophageal peristalsis with increased tone of the lower esophageal sphincter (won’t relax)
- causes: Chagas disease, others?
- develops in patients ages 25 to 60
- presentation: months to years of symptoms
- gradual, progressive dysphagia of both solids and liquids
- regurgitation of undigested foods, sometimes nocturnally
- substernal discomfort or fullness after eating
- poor esophageal emptying
- investigation:
  - manometry is the gold standard
  - shows complete absence of peristalsis, incomplete or absent relaxation of LES
- CXR showing air-fluid level in an enlarged, fluid-filled esophagus
- barium swallow: shows “bird’s beak” from acute tapering of LES at gastro-esophageal junction, esophageal dilation, loss of peristalsis
- EGD to look for cause: stricture, cancer, ring, obstruction
- treatment:
  - meds: smooth muscle relaxers like Ca channel blockers, nitrates
  - balloon dilation of LES: highest perf rate of any esophageal procedure!
  - surgical myotomy
  - Botox injection to relax LES

B.) Diffuse esophageal spasm: simultaneous, nonperistaltic contractions of the esophagus
- uncommon
- presentation:
  - intermittent dysphagia
  - anterior chest pain unrelated to exertion or eating
  - provoked by stress, large food boluses, hot or cold liquids
- investigation:
  - barium swallow shows corkscrew contractions or “rosary bead appearance”
  - manometry shows intermittent, simultaneous contractions of high amplitude not related to swallowing along with periods of normal peristalsis
- treatment: disease is usually self-limiting

C.) Nutcracker esophagus: abnormally high pressures during peristalsis
- presentation: chest pain
- investigation:
  - manometry

D.) Scleroderma esophagus: atrophy and fibrosis of esophageal smooth muscle → loss of LES competence, decreased peristalsis, delayed gastric emptying
- can also occur in progressive systemic sclerosis, Raynaud’s, or CREST
- presentation: severe acid reflux, strictures, erosions, heartburn, dysphagia
- investigation:
  - manometry: diminished peristalsis with low pressures, hyper-relaxed LES
  - barium swallow: very dilated, flaccid esophagus
8.7.7 Esophageal Cancer

- Recent trend towards adenocarcinoma vs squamous cell carcinoma
- Squamous cell carcinoma:
  - risks: alcohol, tobacco, achalasia, caustic-induced esophageal injury, head and neck cancers, Plummer-Vinson syndrome, black ethnicity, male
  - occurs in proximal 2/3 of the esophagus
- Adenocarcinoma:
  - risks: Barrett's esophagus, white ethnicity, males
  - occurs in lower 1/3 of the esophagus
- Usually occurs in ages 50-70
- Presentation: progressive solid food dysphagia, weight loss
  - usually is late stage by the time patient is symptomatic
- Investigation:
  - CXR showing mediastinal widening, lung or bony mets
  - barium swallow showing many infiltrative or ulcerative lesions, strictures
  - chest CT
  - endoscopic US for staging

- Complications:
  - tumor fistula into the tracheo-bronchial tree
  - chest or back pain
  - laryngeal nerve impingement
  - pneumonia
  - malnutrition
- Treatment:
  - surgical resection with gastric pull-up or colonic interposition (5-year survival of 20-50%)
  - palliative radiation (5-year survival of 21%)
  - chemo
  - palliative stenting or photodynamic therapy via endoscopy
- Prognosis: overall 5-year survival is 17%

8.8 Pancreatic Disease

8.8.1 Background

- Anatomy
  - retroperitoneal, lies behind the stomach against the spine
Functions
- exocrine: acinar cells make pancreatic enzymes and zymogens, duct cells make HCO3
- endocrine: alpha cells make glucagon, beta cells make insulin

Acute Pancreatitis: a syndrome defined by inappropriate activation of trypsin within the pancreas resulting in enzymatic damage to the pancreas and discrete episodes of abdominal pain as well as release of systemic pro-inflammatory mediators

Numerous causes
- gallstones are most common
- alcohol use, although temporal relationship is uncertain
- obstructions: gallstones, pancreatic or ampullary tumors, sphincter of Oddi dysfunction, pancreatic divisum (malformation of pancreatic duct)
- medications: diuretics, azathioprine, 6-mercaptopurine, sulfa drugs, ACE inhibitors, HIV meds
- infections: mumps, rubella, Coxsackie virus, echovirus, EBV, HIV
- metabolic: ↑ TG, hypercalcemia
- toxins: ethanol, methanol, scorpion sting in Trinidad
- vascular: vasculitis, ischemia
- abdominal trauma: pancreatic contusion, pancreatic duct damage
- post-ERCP
- inherited causes: hereditary pancreatitis, cystic fibrosis
- idiopathic: microlithiasis?

Presentation: range of severity from mild illness to multiorgan failure
- constant, epigastric pain radiating to the back
- nausea and vomiting
- tachycardia secondary to hypovolemia from leaky blood vessels and third-spacing
- fever within 1-3 days of onset from retroperitoneal irritation or inflammation
- sepsis
- icterus or jaundice with biliary obstruction
- decreased breath sounds with pleural effusion
- abdominal tenderness with guarding and rebound tenderness
- acute interstitial pancreatitis: mild, with pancreatic edema
- acute necrotizing pancreatitis: severe, with necrosis of parenchyma and blood vessels
  - Gray-Turner’s sign: flank ecchymosis from retroperitoneal hemorrhage
  - Cullen’s sign: periumbilical ecchymosis

Diagnosis:
- labs:
  - elevated amylase:
    - problem: not specific, can be elevated in other conditions such as appendicitis, cholecystitis, perforation, ectopic pregnancy, renal failure
    - decreases after the first 24 hours of pancreatitis
  - elevated lipase:
    - more specific for pancreas, but can be elevated in renal failure and other problems
    - elevated for 3-7 days
  - elevated amylase or lipase alone without clinical signs are NOT pancreatitis!
    - bilirubin will be elevated if there is an obstruction blocking it from leaving the liver
    - elevated BUN if there is volume depletion
    - increased hematocrit if there is volume depletion
- US showing enlarged, hypoechoic pancreas
  - also look for gallstones, biliary duct dilation
- CT scan showing pancreatic enlargement, peripancreatic edema
  - imaging of choice for pancreatic parenchyma: can assess necrosis, extrapancreatic fluid, assess complications
  - can be normal in some patients with mild disease
- MRCP
- ERCP
- Treatment:
- NPO? uncertain, feeding the stomach may have an anti-inflammatory effect
- lots of IVF to recover vol from 3rd spacing
- pain meds
- if severe, may need antibiotics (carbapenems) to prevent necrosis, and early jejunal feeds to decrease mortality
- Complications:
  - pro-inflammatory cascade may cause ARDS, sepsis, renal failure
  - fluid collections □ no treatment
  - pancreatic necrosis □ antibiotics
    - if infected tissue, also surgical debridement
  - pancreatic abscess □ antibiotics and CT-guided drainage
  - pancreatic pseudocyst (collection of pancreatic juice encased in granulation tissue) □ drain after 4-6 weeks to allow rind formation

**Chronic Pancreatitis:** chronic inflammation leads to irreversible fibrosis of the pancreas

- Causes: chronic alcohol use, chronic pancreatic duct obstruction (strictures, tumor, papillary stenosis), tropical chronic pancreatitis (due to malnutrition), autoimmune pancreatitis, hereditary pancreatitis, idiopathic
- Presentation:
  - persistent or recurrent episodes of epigastric and LUQ pain
  - steatorrhea due to fat malabsorption
  - fat soluble vitamin deficiency
  - diabetes
- Investigation:
  - labs:
    - no blood tests to diagnose chronic pancreatitis
    - amylase and lipase won’t be elevated because the pancreas is burned out by now
    - fecal fat
    - fecal elastase will be low because it comes from the pancreas
    - secretin stimulation test: give secretin and see if pancreas responds with bicarb secretion
  - imaging:
    - abdominal x-ray showing pancreatic calcifications (classic)
    - CT showing pancreatic calcifications, atrophied pancreas
    - MRCP/ERCP showing “chain of lakes” or areas of dilation and stenosis along the pancreatic duct
    - endoscopic US
- Treatment:
  - abstain from alcohol
  - pancreatic enzyme replacement + PPI + low fat diet
  - narcotics for pain
  - insulin
  - surgical options:
    - ERCP with sphincterectomy or stent placement to open up pancreatic duct
    - Puestow procedure: filleting the pancreas, then hotdogging the jejunum in between and connecting it to the pancreatic duct for ease of pancreatic juice flow into the jejunum
    - subtotal pancreatectomy of the tail or head
    - total pancreatectomy +/- autologous islet cell transplantation into the liver

### 8.8.2 Pancreatic Adenocarcinoma

- Typically occurs in 70s-80s
- Slightly more common in males -Most common location is the head of the pancreas
- Risk factors: tobacco use, chronic pancreatitis, exposure to chemicals in dye manufacturing, DM2 in nonobese person arising after age 50, history of partial gastrectomy or cholecystectomy, genetic factors including BRCA 2
- Presentation: jaundice, weight loss
- cancer in pancreatic head → painless jaundice as it compresses the common bile duct
  - can cause Courvoisier's sign: palpable gallbladder due to compression of bile duct
- cancer in pancreatic tail → abdominal pain due to retroperitoneal invasion into the celiac plexus
- Trousseau's sign: hypercoagulable state created by the malignancy causes a migratory thrombophlebitis = clots forming, resolving and then appearing again elsewhere in the body
- Investigation:
  - labs: ALP, bili, CA 19-9
  - imaging:
    - CT for "double duct sign" = dilation of common bile and main pancreatic ducts
    - MRI
    - endoscopic US if negative CT/MRI but high clinical suspicion
- tissue diagnosis: not always needed if imaging is convincing
  - ERCP with brushings and intraductal biopsy
  - CT-guided biopsy: incurs risk of seeding
  - best option is endoscopic US with FNA
- Treatment:
  - surgical resection + radiation if there is no vascular invasion, lymphatic involvement, or mets
    - cancer of pancreatic head → resection of head, common bile duct, gallbladder, gastric
      antrum, duodenum, proximal jejunum (Whipple procedure)
    - cancer of pancreatic tail → distal pancreatectomy and splenectomy
  - locally advanced disease: radiation only
  - metastatic disease: chemo, pain control, palliative stents
- Prognosis:
  - resectable disease survival is less than 1.5 years
  - locally advanced disease survival is 6-10 months
  - metastatic disease is 3-6 months
    - half of pancreatic cancers are metastatic by time of diagnosis

### 8.9 Biliary Diseases

#### 8.9.1 Background
- Liver makes bile, the gallbladder stores it
- bile is mostly water, bile salts, pigments, a little bilirubin
- functions as fat emulsifier, bactericidal properties, neutralizes stomach acid
Each time bile is released, 95% of it is recycled at the terminal ileum back into the liver multiplied by 5-15x per day = 20-30% of bile excreted in feces each day

- Risk factors for developing disease: obesity, bariatric surgery or rapid weight loss, multiparity, female sex, FH, certain drugs including TPN, Native American or Scandinavian, ileal disease, increasing age

- the “5 F’s” are Fat, Female, Forty, and Fertile, and FH
- the “2 C’s” are Crohn’s, cirrhosis
- the “2 D’s” are diabetes, drugs

### 8.9.2 Labs in Biliary Disease

- Hepatocellular disease:
  - causes very high AST, ALT
  - mildly high or normal ALP
  - increased unconjugated bilirubin
- Biliary disease:
  - high AST, ALT
  - very high ALP
  - increased conjugated bilirubin

### 8.9.3 Imaging in Biliary Disease

- Gallbladder US: good for detecting gallstones and evaluating dilated bile ducts
- less sensitivity with obesity
- hard to assess liver or pancreas
- CT or MRI
- MRI better than CT for detecting gallstones in the bile duct
- ERCP: used before an MRCP for diagnosis
- very sensitive and can use to perform therapy
- requires sedation or anesthesia
- risks of bleeding, infection, pancreatitis, and perforation
- invasive, expensive, and radiation exposure = only use if you plan to do an intervention with it
- MRCP: the most sensitive non-invasive test for detection of gallstones
- costly = used for diagnosis only if there is uncertainty
- **Percutaneous transhepatic cholangiogram (PCT):** needle inserted externally into right hepatic duct, contrast injected, x-rays taken
- can do therapy like ERCP but much more uncomfortable = used when ERCP is not feasible
- Endoscopic US
- HIDA scan

### 8.9.4 Gallbladder Disease

Diseases are on a spectrum:

- asymptomatic cholelithiasis
- **biliary colic** (symptomatic cholelithiasis): gallbladder is contracting against an obstruction in the gallbladder or cystic duct
  - types of stones:
    - cholesterol: located within the gallbladder, think five F’s
    - black pigment stones: located within the gallbladder, made of calcium bilirubinate, think cirrhosis or chronic hemolysis (sickle cell)
    - brown pigment stones: form in bile ducts, made of unconjugated bilirubin, think bile duct infection
      - most common kind of stone
    - presentation: RUQ or epigastric pain for 30 min to several hours (until gallbladder manages to squeeze stone out of the way), nausea or vomiting
      - triggered by fatty foods
o labs are normal
o imaging: no dilated ducts seen with this
  ▪ US to look for hyperechoic mobile stones, acoustic shadow from obstruction of flow
  • test of choice!
  ▪ can also do CT
o treatment: elective cholecystectomy if complications or symptoms are severe enough
  ▪ bile duct is not removed, so patients can still form bile duct stones (choledocholithiasis)

• **acute cholecystitis:** when stone impacts in cystic duct or gallbladder neck □ gallbladder distension, inflammation, and edema □ secondary bacterial infection □ necrosis
  o presentation: fever, nausea, vomiting, RUQ and epigastric pain/rigidity/guarding > 6 hours
  ▪ Murphy's sign: inspiratory arrest with palpation of RUQ
  ▪ referred pain to shoulder not frequently seen
  o labs: ↑WBCs with left shift, mild AST/ALT, bili, ALP, ↑ amylase, ↑ lipase
  o imaging: no dilated ducts
    ▪ US: detects gallbladder wall thickening, pericholecystic fluid, impacted stone
      • can do US Murphy's sign
      • first-line test
  ▪ HIDA scan if US is negative but high clinical suspicion
  o treatment: IV antibiotics, IV fluids, analgesia, cholecystectomy in 2-3 days

• **choledocholithiasis:** when gallstone travels to the common bile duct □ decreased bile flow
  o presentation similar to symptomatic cholelithiasis
  o investigation:
    ▪ labs: mild bili, mod ↑ ALP (distinguish from other causes via elevated ALP), transient ↑ALT/AST
    ▪ imaging: dilated ducts
  o treatment: ERCP with stone extraction followed by cholecystectomy
  o complications: cholangitis, pancreatitis

• **ascending cholangitis:** when choledocholith creates a blockage □ bacterial infection
  o presentation:
    ▪ Charcot's triad: RUQ pain, jaundice from no bile to excrete bilirubin, fever
    ▪ Reynold's pentad: Charcot's + hypotension and mental status changes, suggests sepsis
  o investigation:
    ▪ labs: ↑WBCs, ↑ AST/ALT, ↑direct bilirubin and ALP
    ▪ may have + blood cultures
    ▪ imaging: dilated ducts
  o treatment: IV antibiotics followed by urgent biliary decompression via ERCP, followed by cholecystectomy if etiology was stones

• **gallstone pancreatitis:** when stone blocks pancreatic duct

• Other diseases:
  • **acalculous cholecystitis:** occurs in the absence of gallstones in critically ill patients, progresses to gangrene and perforation if untreated
    o can also present as **emphysematous cholecystitis:** infection of gallbladder with gas-forming organism
      ▪ US will show bubbles in gallbladder wall
      ▪ in this case emergency surgery is required
    o ALP is often elevated unlike typical cholecystitis
  • treatment: IV antibiotics, cholecystectomy or percutaneous cholecystostomy tube if too ill b.) **malignant biliary obstruction:** insidious onset of painless jaundice due to malignancy causing obstruction of the bile duct
    o presentation:
      ▪ overall the presence of Courvoisier's sign is rare
    o investigation:
      ▪ labs: ↑ ALP, ↑ direct bili
      ▪ imaging for dilated duct proximal to obstruction, mass lesions, double duct sign with pancreatic cancer
8.10 Infectious Diarrhea

8.10.1 Background

- What is diarrhea?
- greater than 3 BMs per day (or > 200 g/day) that are loose or liquid
- “acute” diarrhea is present for < 14 days and is infectious
- “persistent” diarrhea lasts 14-30 days
- “chronic” diarrhea has been going on for > 1 month
  - think malabsorption, motility disorders, inflammation

- Kinds of diarrhea:
  - osmotic diarrhea: acts in lumen to suck water into the gut
    - diarrhea should stop with removal of offending agent
      - ex. lactose malabsorption
  - secretory diarrhea: a result of enhanced anion secretion from gut enterocytes
    - can be massive
    - doesn’t stop with fasting - ex. enterotoxin-induced diarrhea

Clinical evaluation of diarrhea:

- most are self-limiting and last < 1 day
- assess severity of disease:
- volume status: general appearance, vitals, mucous membranes, skin turgor, cap refill
- duration of symptoms: concerning if > 2 weeks
- inflammatory components: fever, bloody stools, tenesmus
- alarm symptoms: severe abdominal pain, hospitalized patient, recent antibiotic use, elderly, immunocompromised, systemic signs (especially if pregnant)
- investigation:
  - want to determine viral, bacterial, or parasitic
    - travel, day care, hobbies, antibiotics, sick contacts, recent dietary habits
  - stool studies: only send if diarrhea is persistent or recurring, h/o fever or tenesmus, other warning signs!
    - cultures: costly and diagnostic yield is very low
    - fecal leukocytes can be helpful in determining inflammatory diarrhea
- initial treatment:
- rehydration: oral solutions
- BRAT diet
- avoid lactose

8.10.2 Infectious Diarrhea

- The 3 most common causes are Shigella, Salmonella, and Campylobacter
- Bloody? MESSY CACA!
- M = medical disease
- E. coli:
  - 0157:H7
    - associated with warm weather
    - transmission: undercooked beef, unpasteurized juice, spinach
    - incubation period depends on whether it produces toxin or not
    - presentation: mild or severe symptoms
      - fever
      - toxin □ hemorrhagic colitis: severe abdominal pain, bloody diarrhea
    - treatment: don’t give antibiotics because it can cause/worsen HUS
• complications: HUS, ARF, thrombocytopenia, microangiopathic hemolytic anemia
  • usually in kids < 10
• traveler’s diarrhea = usually ETEC
  • occurs in less developed areas
  • treatment: antibiotics (cipro or rifaximin) may decrease duration of illness
  
  o Shigella:
    • features a Shigatoxin that confers high virulence
    • associated with day care, nurseries, long-term care
    • more common in peds
    • transmission is fecal-oral
    • incubation of 1-3 days
      • low inoculum needed
    • presentation: lower abdominal cramps, diarrhea, fever, bloody and purulent stool, tenesmus
    • treatment: should be self-limiting in less than 7 days, but antibiotics are recommended (cipro or Septra)
      • antibiotics decrease duration by 2.4 days, decrease fever, decrease tenesmus, reduce excretion of organism
  
  o Salmonella:
    • food poisoning salmonellosis (many species)
      • increased incidence in kids < 5 and adults > 60
      • transmission: animals, ingestion of contaminated foods (poultry, eggs, dairy), or fecal-oral
      • high inoculum needed
      • incubation of 6 hours to 3 days
      • presentation: fevers, myalgia, abdominal cramping, headache
      • worse illness in the very old, young, or immunosuppressed
      • complications: septicemia or bacteremia, osteomyelitis (esp sickle cell), endocarditis, arthritis
  
  o Salmonella enterica serovar Typhi
    • bacteria pass through intestinal epithelia to enter the liver, spleen, and bone marrow
    • prevention: vaccine for travelers
    • presentation:
      • typhoid fever = fever with bradycardia
      • 10-14 days after ingestion fever, headaches, myalgia, malaise, anorexia,
      • followed by GI symptoms from colonization of the gallbladder and reinfection of the intestines
    • can become a chronic carrier due to gallbladder colonization
  
  o Yersinia enterocolitica:
    • affects the terminal ileum
    • transmission by ingestion of contaminated food or water
    • presentation: diarrhea, fever, abdominal pain for 1-2 weeks, enlarged lymph nodes
      • may mimic appendicitis
      • can be chronic for months
    • prognosis: high mortality with systemic disease
  
  o Campylobacter jejuni:
    • most produce a toxin that prevents infected cells from dividing and alerting an immune response
    • transmission by animals (esp chickens), contaminated food, milk, or water
    • incubation of 1 weeks
    • presentation: dysentery, bacteremia
    • treatment: illness is usually self-limiting but can last a week or longer
      • consider antibiotics (azithromycin) in AIDS or immunocompromised
        • must be started within 4 hours of onset
    • complications: Guillain-Barre syndrome, reactive arthritis
• Amoeba □ Entamoeba histolytica
  o C. difficile:
    ▪ most common cause of nosocomial diarrhea
    ▪ considered to be an antibiotic-induced diarrhea
    ▪ transmission by spores
    ▪ diagnose with toxin test
    ▪ treatment: Flagyl or oral vancomycin

• Aeromonas:
• Watery?
• viruses: rotavirus, norovirus, adenovirus
  o most common is norovirus
  o usually occurs in winter, except for adenovirus which is year-round
  o fecal-oral, person-to-person, or contaminated foods
  o usually self-limiting
• bacteria: Staph aureus, Bacillus cereus, Vibrio
  o Staph aureus, Bacillus cereus, Clostridium perfringens □ illness caused by ingestion of preformed toxin = fast onset
  o Staph aureus:
    ▪ transmission by ingestion of contaminated food (from carrier’s skin or nose)
      • likes potato salad, meats, custard-filled pastries, ice cream
    ▪ presentation: symptoms within 4 hours that are short-lived
  o Bacillus cereus:
    ▪ prevention: refrigeration
    ▪ transmission by ingestion of contaminated fried rice, meats, sauces
    ▪ presentation: emesis within 1-6 hours of ingestion, longer for diarrheal illness
  o Clostridium perfringens:
    ▪ prevention: heating to destroy toxins
    ▪ transmission by ingestion of contaminated meats and poultry
    ▪ incubation of 8-24 hours
    ▪ presentation: abdominal cramps, watery diarrhea, nausea, vomiting, NO fever
      ▪ lasts less than 24 hours
  o Vibrio:
    ▪ activates intestinal adenylate cyclase □ blocks Na and Cl absorption and promotes Cl excretion □ severe profuse diarrhea
    ▪ transmitted in contaminated seafood or contaminated water (developing countries)
    ▪ incubation of 12-24 hours
    ▪ at risk: patients with liver disease and iron overload
    ▪ presentation: watery “rice-water” diarrhea, abdominal cramping, hypotension
      • can also infect wounds
    ▪ treatment: oral rehydration, single dose fluoroquinolone
    ▪ prognosis: mortality is 50% if untreated!
• parasites: Giardia, Crypto, Entamoeba histolytica
  o diarrhea lasts longer than 7 days
  o Giardia:
    ▪ associated with contaminated streams, day care centers, and well water
    ▪ presentation: diarrhea is foul and watery, also have cramps and farts
    ▪ infection can become chronic in those with hypogammaglobulinemia, IgA deficiency, and even in the immunocompetent
    ▪ diagnose with antigen stool testing
  o Entamoeba histolytica:
    ▪ causes necrosis of the large intestine
    ▪ more common in tropical areas
    ▪ at risk: travelers, MSM
    ▪ presentation: abdominal pain, cramping, colitis, diarrhea (can be bloody), fevers
      ▪ immunocompromised □ think Cyclospora, Isospora, Cryptosporidium, Microsporidia
present in environment and water supply

8.10.3 Anti-Diarrheals

- DON’T use anti-motility agents in inflammatory diarrhea like *Shigella, C. diff, E. coli* 0157
- Loperamide: an opiate without systemic effects that inhibits peristalsis
- helpful to use in conjunction with antibiotics for traveler’s diarrhea
- Bismuth subsalicylate
- good in kids and traveler’s diarrhea, slightly helpful in norovirus
- Antibiotics
- may be used in Shigella, traveler’s diarrhea, C. diff, Campylobacter
- need to weigh risks and benefits
- may prolong shedding of *Salmonella* or C. diff and can worsen Shigatoxin of *EHEC* = make sure there are no risk factors for EHEC before giving (visible blood without fever, June-September presentation, ground beef, petting zoos, etc)
- best if started early
- bottom line: if concerned for severe infectious diarrhea, first choice is cipro or other FQ, second choice is Septra, if Campylobacter use azithromycin
  - otherwise, just treat supportively!

8.11 Inflammatory Bowel Disease

8.11.1 Background

- IBD = Crohn’s disease or ulcerative colitis
- Pathophysiology: exact etiology unknown
- both are autoimmune, chronic inflammatory disorders of the GI tract
- tends to run in families
- may be response to environmental triggers (infection, drugs, other agents) interacting with a genetically susceptible individual
- Epidemiology:
  - incidence is highest in Westernized countries, with a bimodal distribution in 15-40 year-olds and > 60 year-olds
  - Crohn’s more common in Caucasians, with higher risk in Ashkenazi Jews, and lower incidence in Latinos and Asians
  - UC: Ashkenazi Jews and Caucasians have higher incidence rates than other ethnic groups
- Presentation:
  - diarrhea (often bloody), fatigue (may be anemia), weight loss, fever, anorexia, n/v, crampy abdominal pain
  - tend to have a relapsing & remitting course
  - extraintestinal manifestations: generally limited to the eye, skin, liver, and joints
  - **primary sclerosing cholangitis**: a chronic liver disease caused by progressive inflammation and scarring of the bile ducts of the liver
    - usually symptomatic, may have puritus
    - usually initially detected as an ↑ ALP
    - confers high risk for colon cancer! get a colonoscopy ASAP and screen annually
  - **arthritis**: spondylitis & sacroiliitis
    - usually asymptomatic, or pain/stiffness in back and buttocks
  - skin manifestations
    - **erythema nodosum**: raised, tender, red-purplish nodules
      - most commonly on the extensor surfaces of the extremities
      - may parallel IBD therapy
      - may need to treat with steroids
    - **pyoderma gangrenosum**: necrotic inflammation, from papules to widespread necrosis
      - parallels IBD activity half the time
• don't biopsy!
• may require topical therapy
• colectomy may be needed
  o eye manifestations
    ▪ uveitis: inflammation of the middle layer of the eye
      • eye pain, blurred vision, photophobia, headaches
      • requires prompt diagnosis and treatment to prevent complications
        o topical and systemic steroids
    ▪ episcleritis: superficial inflammation of the sclera
      • treat with topical therapy or IBD-directed therapy
  o aphthous ulcers
• Investigation:
  • differential: infectious diarrhea (always think of this if symptoms are less than 2-3 weeks), ischemia (elderly, PVD, thrombosis), meds (NSAIDs, penicillins, mycophenolate), diverticulosis
  • no gold standard for diagnosis!
    o relies on a combination of endoscopy, histology, radiography, labs, and clinical data
    o possible studies:
      ▪ colonoscopy with ileal intubation and biopsy
      ▪ small bowel follow-through
      ▪ entersclysis +/- CT
      ▪ MR enterography
      ▪ capsule endoscopy?
• General principles of IBD management:
  • not everyone needs continued treatment or any treatment at all
    o mild disease may be better than taking daily pills
    o infrequent disease may respond to short steroid treatment
  • treat the affected area: proctitis, ileal disease, etc.
  • not everyone responds to the same treatment
    o response to any given therapy is 30-70%
    o high placebo effect
    o lots of trial and error
• drugs:
  o use as little steroids as possible, and try to get on another therapy as quickly as possible
    ▪ use sparingly to induce remission
      • modest doses are all that is needed
  o patients can become steroid-dependent
  o side effects of steroids: cataracts, hyperglycemia, weight gain, loss of bone density, easy bruising, striae, moon-facies, acne
    ▪ assess risk for osteoporosis using questionnaire
    ▪ may need PCP prophylaxis
    ▪ yearly eye exams
    ▪ bone density monitoring
    ▪ vit D/Ca supplementation
    ▪ blood glucose monitoring
  o 6-mercaptopurine ↔ azathioprine: impair T cell function
    ▪ takes 2-4 months to work, so begin with steroids and wean them off
  o TNF antibodies: inhibit TNF
    ▪ high risk for TB reactivation
    ▪ must adhere to treatment to prevent side effects
    ▪ malignancy risk
• remember that live vaccines are contraindicated for patients on immunosuppressive therapy such as highdose steroids, anti-TNF agents
• screening for colon cancer:
  o begin 8 years after onset of symptoms
  o colonoscopies every 1-2 years
    ▪ or every year if there is concomitant primary sclerosing cholangitis
  o risk increases with time and degree of inflammation
surgical procedures:
  - colectomy may be needed for dysplasia, cancer, toxic colitis

watch for complications!
  - extra-ocular manifestations
  - frequent UTIs/pneumaturia
  - fistula to bladder
  - high fever or abdominal mass
  - abdominal or liver abscess
  - severe abdominal pain
  - perforation
  - nausea and vomiting
  - obstruction
  - severe rectal pain
  - perirectal abscess
  - drug side effects

Management of an acute flare:
  - compare to previous flares to look for worrisome features
  - rule out infection, obstruction
  - check WBCs, H/H
  - consider if it is a medication side effect
  - short course of steroids
  - follow-up
  - endoscopy if not improving

8.11.2 Crohn’s Disease

- Can affect any portion of the GI tract from lips to the anus and can involve entire thickness of bowel wall (transmural)
- Disease tends to skip areas
- Presentation:
  - aggravated by smoking
- Complications:
  - fistulas around the anus and internally
  - abscesses
    - must be surgically repaired
  - abdominal strictures
    - obstruction
- Treatment:
  - drugs:
    - corticosteroids
      - budesonide is directed at the terminal ileum = fewer side effects
    - 6-mercaptopurine/azathioprine
    - methotrexate
    - infliximab, adalimumab, certolizumab, natalizumab (risk of JC virus)
- surgery: general principle is to try to avoid surgery unless absolutely necessary!
  - may need segmental resection for fibrotic structures, obstructions, fistulas

8.11.3 Ulcerative Colitis

- Disease begins in the rectum and is limited to the colon, and has only superficial penetration of the mucosal wall
- Disease is usually continuous
- Characterization:
  - “mild” if ≤ 4 BMs per day, no signs of systemic disease (fever, tachycardia, anemia), normal ESR
  - “severe” if > 6 BMs per day and evidence of systemic disease
- Presentation:
  - proctitis
  - tenesmus, lower abdominal or pelvic cramping
  - bloody diarrhea
- Investigation:
  - H/H showing anemia
  - low serum albumin
  - elevated ESR
  - negative stool cultures
  - sigmoidoscopy
• Treatment:  
  • DOC are 5-ASAs (sulfasalazine, mesalamine, etc)  
    o formulated for delivery to a specific area: colon, small intestine, etc.  
    o highly effective in mild-mod disease or for maintenance after induction of remission  
  • corticosteroids  
  • 6-mercaptopurine/azathioprine  
  • infliximab  
• Complications:  
  • high risk for colon cancer

8.12 Irritable Bowel Syndrome

8.12.1 IBS

• Defined as chronic abdominal pain and altered bowel habits in the absence of any organic cause  
• a function disorder  
• a diagnosis of exclusion, need to rule out IBD, infections, cancer  
• subtypes:  
  o constipation-predominant = IBS-C  
  o diarrhea-predominant = IBS-D  
  o mixed = IBS-M  
• Pathophysiology:  
  • altered bowel motility: motor abnormalities may be detected in IBS such as increased frequency and irregularity of luminal contractions, prolonged transit time, exaggerated motor response after eating (or after being given CCK)  
  • visceral hypersensitivity: IBS patients may experience pain and bloating at lower thresholds than controls  
    o there is also increased cerebral cortex activity during this time  
  • intestinal inflammation: there is an increased number of lymphocytes in the colon and small intestine of patients with IBS  
    o causes release of mediators such as nitrous oxide, histamine stimulation of enteric nervous system  
    o increased mast cells  
    o increased serine protease activity  
• post-infectious: there is a 6x greater risk of developing IBS after an episode of acute infectious gastroenteritis  
  o risk factors: young age, prolonged fever, anxiety, depression  
  o may be due to development of bile acid malabsorption, increased T cells, or altered microflora  
• alteration in fecal microflora and bacterial overgrowth: abnormal breath tests with more hydrogen and methane in some but not all IBS pts  
• food sensitivity: IBS pts with elevated IgG may improve symptoms by eliminating certain food groups  
  o potential overlap of IBS with lactose intolerance and celiac diseases  
• psychiatric: many IBS patients have psych comorbidities  
  o may be exacerbated by stress  
• Epidemiology:  
  • very common, in 10-15% of the population  
  • more common in females  
  • most common in 20s-40s  
  • the #2 cause of work absenteeism  
• Triggers: infection, diet, lifestyle changes, psychological stress  
• Presentation and diagnostic criteria:  
  • Manning criteria: pain relieved with defecation, more frequent stools at onset of pain, looser stools at the onset of pain, visible abdominal distension, passage of mucus, sensation of incomplete evacuation  
    o highly specific but low sensitivity
**Rome criteria**: for at least 3 days a month for at least 3 months (and at least 6 months prior to diagnosis), there is recurrent abdominal pain or discomfort plus >2 of the following:
- improvement with defecation
- change in frequency of stool
- change in form of stool

*other common symptoms supporting diagnosis:* urgency, feeling of incomplete BM, bloating

**Investigation:**
- **differential:** diet cause, infection, inflammatory bowel, psychologic, malabsorption, tumors, endometriosis
- **fecal occult blood**
- **labs:**
  - all: CBC, CMP, ESR, serum albumin, consider TSH
  - IBS-D: celiac panel +/- fecal fat, stool culture

**imaging:**
- IBS-C: abdominal x-ray
- consider flexible sigmoidoscopy if under 45 or colonoscopy if over 45

***red flags for something that is NOT IBS:* abnormal exam, fever, + fecal occult, weight loss, onset in older patient, nocturnal awakening, low hemoglobin, ↑ WBCs, ↑ ESR
  - these patients definitely need a colonoscopy
- **additional specialized studies:** not routinely done in IBS patients
  - IBS-C: colonic transit, anal manometry and balloon expulsion, rectal sensation and emptying, defecography
  - IBS-D: stool osmolarity and electrolytes, laxative screen (if you suspect malingering), small bowel and colonic transit, rectal sensation, cholestyramine trial
  - symptoms of pain and bloating: small bowel series, antidepressant trial, CHO-H2 breath test, small bowel manometry

**General principles for treatment:**
- **develop a therapeutic relationship:**
  - no judgments
  - establish realistic expectations
  - involve patient in decision-making
- **patient education:** no cure but no change in life expectancy
- **dietary modification:** 2 week trial of lactose avoidance, avoiding bloating foods, fiber trial
- **psychosocial therapies:** psychotherapy, biofeedback, hypnosis
- **pharmacologic therapy is tailored to patient symptoms**
  - not usually needed until IBS is moderate to severe
  - for abdominal pain:
    - antispasmodics: for PRN short-term relief
    - ex. dicyclomine, hyoscyamine, peppermint oil, pinaverium
    - antidepressants: reduce pain
    - ex. TCAs (most data), SSRIs, SNRIs
  - for diarrhea:
    - anti diarrheal: PRN, use cautiously if patient has mixed IBS
      - ex. loperamide
    - antibiotics? may improve global IBS symptoms
      - ex. rifaximin
  - for constipation:
    - 1st line are bulking laxatives
      - ex. methylcellulose, psyllium
    - 2nd line are stool softeners, osmotic laxatives, and stimulant laxatives
      - ex. docusate, polyethylene glycol, lactulose, sorbitol, glycerol, mag cit, bisacodyl, Senna
    - for refractory cases lubiprostone twice daily
- **Prognosis:** most remain symptomatic 5 years after diagnosis

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8.13 Peptic Ulcer Disease and Gastric Cancer
8.13.1 Background

- PUD is defined as defects in the gastric mucosa that result from an imbalance between enzymatic activity and mucosal injury
- Epidemiology:
  - typically occurs between ages of 25-64
  - at risk: previous GI event, old age, use of anticoagulants, corticosteroids, NSAIDs, chronic diseases
- Causes: H. pylori, NSAIDs, excess acid
- Prevention: Cox-2 inhibitors vs NSAIDs, mucosal protection with 33isoprostol, PPIs, high-dose H2 blockers
- Presentation:
  - burning pain localized to the epigastrium that is non-radiating
  - gastric ulcers are worse after meals, duodenal ulcers are better after meals
  - pain that awakens patient from sleep between 2-3am
  - can also be asymptomatic
- Investigation:
  - upper GI series
  - EGD to characterize lesions and biopsy
  - H. pylori test
- Treatment:
  - meds:
  - surgery: rarely indicated
    - complete or partial gastrectomy
    - vagotomy
- Complications:
  - ulcer re-bleeding
    - higher for pigmented ulcers and adherent clots
  - hemorrhage
  - perforation of ulcer into adjacent peritoneum or organ
  - gastric outlet obstruction

8.13.2 PUD Caused by H. pylori

- Associated diseases
  - active chronic gastritis: can progress to atrophic gastritis
  - duodenal ulcers: 60-95% of patients with this have HP
  - gastric ulcers: > 80% of patients with this have HP
  - non-ulcer dyspepsia: 50% of patients with functional dyspepsia have HP
  - increased risk for gastric adenocarcinoma, MALT lymphoma
  - Transmitted fecal-oral, with stomach being the only known reservoir
  - Present in 40-50% of the general population
  - chance of getting gastritis from it increases with age
  - more common in blacks, Hispanics, lower SES, institutionalized individuals
- Treatment:
  - eradication of H. pylori
    - triple therapy:
    - confirmation of eradication by urease breath test or stool test
  - Complications: up to 20% of cases may require retreatment
  - Prognosis:
    - eradication reduces duodenal ulcer relapse to near zero, decreases rate of gastric ulcer relapse, and decreases risk of gastric cancer and MALT lymphoma

8.13.3 PUD Caused by NSAIDs

Mechanism of injury:

1.) NSAIDs injure the gastric epithelium □ interruption of mucosal barrier
• occurs within one hour of ingestion
• erosions develop with repeated doses in 24 hours
• patients on chronic NSAIDs will have persistent findings of abnormal mucosa
• degree of mucosal interruption is not predictive of ulcer development

2.) NSAIDs decrease prostaglandin synthesis → decreased mucin production, decreased mucosal blood flow, decreased bicarb production = loss of protective effects

8.13.4 PUD Caused by Excess Acid

• Parietal cells are stimulated to secrete HCl via histamine, Ach, and gastrin
• can act synergistically
• inhibited by somatostatin
• Causes:
  • Zollinger-Ellison syndrome: pancreatic gastrinoma → excess gastrin → excess HCl produced → peptic ulcers
    o causes can be sporadic or associated with MEN I syndrome
    o peptic ulcers will be in the duodenal bulb, distal duodenum, and jejunum = in the “gastrinoma triangle”
    o these ulcers will be resistant to treatment and will recur after gastric surgery
    o also associated with GERD, steatorrhea from large acid load (inactivates pancreatic enzymes)
    o investigation:
      ▪ fasting gastrin or secretin test
        • secretin should have no effect on gastrin in normal patients but will ↑↑ gastrin in ZE
      ▪ endoscopic US + somatostatin-R imaging
    o treatment:
      ▪ high-dose PPI
      ▪ surgical resection if no metastatic disease
      ▪ metastatic disease → chemo, resection of liver mets, hepatic arterial err
    o prognosis: 15-year survival of 83% without mets
      ▪ baseline fasting serum gastrin may have prognostic value
      ▪ think of this in cases of multiple ulcers, refractory ulcers, or distal ulcers

8.13.5 Gastric Cancer

• High incidence in Korea, Japan, China
• More common in men and tobacco users
• Usually occurs after age 60
• Causes: pickled foods, salted foods, smoked meats, H. pylori, atrophic gastritis, polyps, radiation
• Presentation:
  • early disease is asymptomatic
  • indigestion, nausea, early satiety, anorexia, weight loss
• advanced: pleural effusions, GOO (?), gastrointestinal obstruction, SBO, bleeding
• PE: palpable stomach, hepatomegaly, pallor, Virchow’s node and Sister Mary Joseph node
• Investigation:
  • EGD
  • endoscopic US
  • barium swallow
  • CT/MRI
• Treatment depends on stage
  • resection, chemo, radiation, adjuvants if needed
• Prognosis: difficult to cure, most die of recurrent disease even after resection
9 Gynecology Exam Notes

9.1 Gynecologic Anatomy

9.1.1 Pelvic Anatomy

- Pelvic cavity bordered by the abdominal cavity and pelvic floor
- Pelvimetry can be used to describe type of pelvis a woman has
- but not correlated to outcome of childbirth
- most common and “ideal” is gynecoid
- Pelvic ligaments include the anterior & posterior sacroiliac ligaments, pubic symphysis, sacrotuberous ligament, sacrospinous ligament
- loosen during pregnancy due to release of hormones
- Female erectile tissue: corpora cavernosa, bulbs of the vestibule, glans clitoris
- Glands:
  - Skene's (paraurethral) are at 10 and 2 o’clock around the vestibule
  - Bartholin's (greater vestibular) are at 4 and 8 o’clock around the vestibule
  - prone to abscess
- Pelvic cavity muscles:
  - lateral wall: obturator internus, piriformis
  - floor: levator ani, coccygeus
    - weakness here can result in urinary or fecal incontinence
- Perineal body is located between the vagina and rectum
- pelvic floor muscles and perineal membrane attaches here
- where episiotomy is performed
- “Uterine adnexa” = uterine tubes + ovaries
- Pelvic organs are draped in a fold of parietal peritoneum
- All lymphatic drainage in pelvic cavity (except for ovaries) goes from the external iliac nodes to lateral aortic nodes
- Innervation via the sacral plexus (L4 to S4)
- innervates pelvic floor and wall muscles
- branches into the sciatic, gluteal, pudendal nerves
  - pudendal supplies the perineum
    - palpate ischial tuberosities to find right place for pudendal nerve block to perineum

9.1.2 Development of Reproductive Organs

- Male ducts are Wolffian
- testosterone causes regression of Mullerian ducts
- Female ducts are Mullerian
- default sex
- remnants of Wolffian ducts form Gartner’s duct (can form cysts)

9.1.3 Vagina

- Recto-uterine pouch is the deepest fold of parietal peritoneum located between the vagina and rectum
- can be used to surgically access the abdomen via the posterior fornix of the vagina
- Blood supply via vaginal artery and vein
- comes off of anterior trunk of internal iliac
- Innervation:
  - upper 2/3 visceral sensory
  - lower 1/3 somatosensory
- Transverse vaginal septum is a result of incomplete fusion of the urogenital sinus and Mullerian ducts

9.1.4 Cervix
- Made of non-muscular, collagenous tissue
- External os, internal os, and cervical canal
- Contains glands that may form Nabothian cysts (usually self-resolving)
- Effaces (thins/shortens) during pregnancy and dilates before labor

9.1.5 Uterus
- Fundus (top) and body
- Three layers: perimetrium (serosa), myometrium, endometrium
- Variable position: anteflexion (slight is normal), retroversion, retroflexion
- Remains a pelvic organ until 12 weeks’ gestation, then moves into the abdomen
- Uterine ligaments:
  - peritoneum folds over uterus to create the broad ligament
  - round ligament of the uterus connects uterus to labia
    - a remnant of the gubernaculum
    - stretching during pregnancy can cause pain
  - cardinal ligaments (transverse cervical ligament)
    - contains the uterine artery and vein
      - comes off anterior trunk of internal iliac
    - pubocervical ligament connects the uterus to the pubic symphysis
    - uterosacral ligament connects the uterus to the sacrum
- Anomalies:
  - hypoplasia or agenesis
  - unicorneate uterus: missing half of ducts = 1 fallopian tube, 1 cervix, but not necessarily only one ovary
  - didelphys uterus: two cervixes, two uteruses, possibly 2 vaginas
  - bicornuate uterus: one cervix but two separate uteruses
  - septate uterus: uterus divided by septum
  - arcuate uterus: small amount of uterine septum
  - diethylstilbestrol-related anomaly: causes a T-shaped uterine cavity
  - Uterine tubes: isthmus, ampulla, infundibulum, fibrae
    - ligation usually done at the isthmus
- Ovaries:
  - attached to uterus by ovarian ligament (remnant of gubernaculum)
  - attached to ilium via suspensory ligament
    - contains the ovarian artery and vein
      - comes off aorta below the renal artery
  - lymph drains directly into the lateral aortic nodes

9.2 Gynecologic Physiology
9.2.1 Background
- Puberty: series of biologic transitions during adolescence
- ex. development of secondary sex characteristics
- Adrenarche: maturational increase in androgen production
- begins ~6 in both females and males
- causes hair growth, body odor, skin oiliness, acne
- probably unrelated to pubertal maturation of the neuroendocrine-gonadotropin-gonadal axis
- Thelarche: beginning of breast development
- usually age 8 or later
- Menarche: first menstruation
- usually ~2.5 years after onset of puberty
  - average age in US is 12 years, 8 months but is dropping
- may not involve ovulation initially (and can have ovulation before having menstrual periods)
  - irregular bleeding corresponds to irregular ovulation
- Ovary
- **follicles**: oocyte + surrounding follicular cells
  - follicular cells: surround the oocyte to separate from the surrounding connective tissue, shuttle nutrients to the oocytes
    - oocytes arrest in meiosis and remain dormant until adulthood
    - oocytes surrounded by:
      - granulosa cells: stimulated by FSH
        - estrogen secretion & inhibin secretion
        - inhibin suppresses FSH
        - synthesize estrogen from thecal estrogen precursors using aromatase
      - theca cells: stimulated by LH to make estrogen precursors (androgens) for granulosas

### 9.2.2 Menstrual Cycle

- What is normal?
- total cycle length of 28 ± 7 days
- menses for 4 ± 2 days (due to progesterone withdrawal)
  - vol lost of ~ 30mL
- follicular phase of 7-21 days (due to estrogen building the endometrium)
- luteal phase of 14 ± 2 days (due to progesterone stabilization of endometrium)
- Days 1-14: estrogen control, “follicular phase”
- menses occur during ~ first 5 days
  - rupture of spiral arteries, shedding of functional endometrium
- GnRH released from hypothalamus in pulsatile manner
  - release of FSH and LH from ant pit
- GnRH inhibited by stress (high cortisol)
- pituitary tumors can also affect menses
- FSH stimulation of granulosa cells → division & secretion of estrogen
  - estrogen causes upregulation of estrogen and progesterone receptors as well as proliferation of endometrial glands
  - further growth of follicles → more and more estrogen secreted
    - results in negative feedback on hypothalamus (LH & FSH)
    - this is why FSH will be abnormally high in state of estrogen deficiency
- high estrogen results in positive feedback on hypothalamus until estrogen threshold is reached → LH surge from pituitary and ovulation
  - surge then results in negative feedback to stop further GnRH secretion from hypothalamus
  - rising surge precedes ovulation by 24-36 hours
- chosen oocyte is from the follicle with the greatest # of FSH & LH receptors
- Days 14-28: progesterone control, “luteal” or “secretory phase”
  - cervical mucus thickens
  - follicular cells left behind form the corpus luteum
- LH on corpus luteum → secretion of progesterone and estrogen
  - progesterone has negative feedback on estrogen receptors and inhibits release of GnRH
  - ↓ FSH and LH secretion
    - this is how the combined OCPs prevent release of LH and FSH → no follicular development → no production of estrogen by follicle → no LH surge → no ovulation
  - increased body temp just after ovulation due to ↑ progesterone, which is a thermogenic hormone
  - progesterone slows endometrial proliferation but induces secretion of glands in preparation for implantation
  - progesterone levels > 4 at day 21 of cycle indicate that ovulation has occurred
  - degradation of corpus luteum if no fertilization → decreased hormone secretion

### 9.2.3 Premenstrual Syndrome
- Begins with ovulation ~ day 14, lasts 2 weeks then ends with menses
- Symptoms: acne, breast swelling, fatigue, GI, insomnia, bloating, headache, food cravings, depression, anxiety, irritability
- More severe form: premenstrual dysphoric disorder
  - defined as 5+ symptoms of sadness, despair, suicidal ideations, tension, anxiety, panic attacks, irritability that affects others, mood swings, crying, disinterest in daily activities, binge eating, cravings, physical signs
- Treatment: exercise, regular sleep, stress management, proper eating, avoid caffeine/sugar/salt, OCPs
  - PMDD → antidepressants and counseling

### 9.3 Hormone Studies
1.) **GnRH**: released from hypothalamus in pulsatile manner when gonadal hormones ↓
   - aka luteinizing hormone releasing hormone (LHRH)
   - increased GnRH during puberty to induce release of LH and FSH needed for puberty
   - decreased GnRH in hypothalamic hypogonadism, dopamine, and opiates
   - increased in primary hypopituitary hypogonadism, epinephrine
   - GnRH agonists can be used to induce ovulation in setting of infertility
   - labs:
     - serum or plasma
     - can’t have steroids, ACTH, gonadotropin, or estrogen meds for > 48 hours

2.) **FSH**: released from anterior pituitary in pulsatile manner to stimulate development of follicles in granulosa cells; also needed for estrogen production
   - needed for maturation of ovaries
• decreased FSH in secondary gonadal failure, stress, malnutrition, anorexia, severe illness, hyperprolactemia, pregnancy, PCOS
• increased FSH in primary gonadal failure, ovarian agenesis, alcoholism, menopause, gonadotropin-secreting pituitary tumors
• labs:
  o done to diagnose menopause, menstrual irregularities, gonadal failure, predicting ovulation, evaluating infertility, evaluating pituitary disorders
  o plasma or 24 hour urine
  o levels will fluctuate throughout the day

3.) LH: secreted in pulses by the anterior pituitary to stimulate follicular production of estrogen, ovulation, and formation of the corpus luteum
• decreased LH in pituitary failure, hypothalamic failure, severe stress, anorexia, malnutrition, severe illness, pregnancy, hemochromatosis, hyperprolactemia
• increased LH in gonadal failure, precocious puberty, pituitary adenoma, menopause, PCOS
• labs:
  o done to evaluate infertility, endocrine problems with precocious puberty, testicular dysfunction, disorders of sexual differentiation, ovulation prediction
  o plasma or 24 hour urine
    ▪ best time for single specimen is between 11am and 3pm
  o interfering factors: hCG, TSH, drugs (OCPs and many others)

4.) Progesterone: steroid sex hormone produced by the corpus luteum and by the placenta in pregnancy; induces glandular secretion in the endometrium
• converted from a precursor molecule via cholesterol
• decreased progesterone in pre-eclampsia, threatened abortion, placental failure, fetal demise, ovarian neoplasm, amenorrhea, ovarian hypofunction, PCOS
• increased progesterone in ovulation, pregnancy, hyperadrenocorticalism, adrenocortical hyperplasia, luteal cysts, molar pregnancy, choriocarcinoma
• labs:
  o done to monitor ovulation, ectopic pregnancy, infertility, or high risk pregnancies
  o serum only
  o levels rise rapidly after ovulation
  o interference with hemolysis of sample or drugs

5.) Estrogen: made by androgen conversion in the theca cells; causes proliferation of endometrium
• three major types:
  o estrone (E1): converted from ovary-produced androgens by adipose tissue
    ▪ the major circulating estrogen after menopause
    ▪ less potent than estradiol
    ▪ not normally tested
  o estradiol (E2): produced by the ovary before menopause
    ▪ physiologically the most important estrogen
      ▪ feeds back negatively on FSH and LH secretion
      ▪ can be converted by the liver (↔) to E1
      ▪ peaks during ovulation
      ▪ levels drawn to assess menstrual and fertility problems, menopausal status, sexual maturity
    ▪ levels increase throughout pregnancy
    ▪ serial levels drawn starting at 28-30 weeks’ gestation as part of maternal serum quad test
  o estriol (E3): converted by the placenta from fetal DHEAS
    ▪ the major estrogen in pregnancy & an index of fetal wellbeing
    ▪ levels increase throughout pregnancy
  • decreased estrogen in failing pregnancy, Turner’s syndrome, hypopituitarism, hypogonadism, SteinLeventhal syndrome, menopause, anorexia
  • increased estrogen in precocious puberty, ovarian tumor, adrenal tumor, gonadal tumor, normal pregnancy, cirrhosis, liver necrosis, hyperthyroidism
• labs:
6.) **Testosterone**: estrogen precursor that exerts anabolic effects and influences behavior
- made by conversion of DHEA in peripheral fat or in the adrenal gland, or by the ovary
- bound by steroid hormone binding globulin (60%) or albumin, 2% is unbound
- increased testosterone causes masculinization
- decreased testosterone causes decreased libido and mood changes
  - testosterone decreases after menopause
- labs:
  - done to evaluate ambiguous sex characteristics, precocious puberty, female virilization syndromes, tumor marker, hirsutism, monitoring antiandrogen treatment
  - serum only
  - most assays measure total testosterone
    - need special assay to measure free testosterone
  - levels will vary by state of sexual maturity and have slight diurnal variation (max 7am & 8pm)
  - decreased testosterone with primary or secondary ovarian failure, drugs
  - increased testosterone with ovarian tumors, adrenal tumors, congenital adrenocortical hyperplasia, trophoblastic tumors, PCOS, idiopathic hirsutism, drugs
  - interference with drugs and alcohol

7.) **Progesterone withdrawal test**: test for amenorrhea investigation where oral progesterone given to stimulate the hypothalamic-pituitary-gonadal axis then stopped to see if bleeding occurs (like a fake degeneration of the corpus luteum)
- women who bleed must have normal estrogen levels, since they have a thickened endometrium
  - cause of amenorrhea is likely anovulation for one reason or another
- women who fail to bleed must have low levels of estrogen (because there must have been no buildup of the endometrium if there was no bleeding), or have hypothalamic dysfunction, or have an abnormal uterus ❏ repeat test after stimulating endometrium with estrogen

8.) **Prolactin**: anterior pituitary hormone that promotes lactation
- controlled by prolactin-inhibiting and prolactin releasing factors
- can be stimulated by TRH, breast stimulation, pregnancy, nursing, stress, exercise, sleep
- decreased prolactin with Sheehan syndrome, pituitary destruction
- increased prolactin with pituitary adenomas, secondary amenorrhea, galactorrhea, hypothyroidism (results in increased TRH), PCOS, anorexia, paraneoplastic syndromes, hypothalamic or pituitary stalk disease, renal failure, hypoglycemia, dopamine-depleting drugs, ectopic prolactin secretion, high estrogen levels, exercise, stress, sleep, pregnancy, liver disease, nipple stimulation, chest wall injury, TSH ❏ loss of libido, galactorrhea, oligomenorrhea or amenorrhea, infertility, decreased muscle mass, osteoporosis
- labs:
  - serum
  - to be collected 3-4 hours after waking
  - interference with stress (including fear of blood tests), trauma, surgery, drugs

9.) **Human chorionic gonadotropin (hCG)**: placental glycoprotein hormone made up of α and β subunits that is produced after fetal implantation
- concentration in pregnancy rises rapidly, doubles every 2 days for first few weeks
- decreased hCG in threatened or incomplete abortion, fetal demise
- increased hCG with normal pregnancy as well as ectopic or molar pregnancies, choriocarcinoma, germ cell tumors, hepatomas, and lymphoma
- concentration is usually lower in ectopic pregnancies
- labs:
  - serum or urine test for unique β subunit, as the whole hCG has cross-reactivity with pituitary hormones
    - new monoclonal assays can detect small levels of hCG 3-7 days after conception
    - present at higher levels in serum than urine for the first few weeks
• interference with test performed too early, hemolysis, hematuria or proteinuria, dilute urine, drugs
  o quantitative hCG tests are only used to monitor high-risk pregnancies, ensure levels return to normal after ectopic or molar pregnancies or abortion, to monitor hCG-producing tumors, or in patients with cirrhosis

9.4 Gyn Procedures

1.) Pap test: Babes-Papanicolaou test; a speculum is used to open the vaginal canal and allow the collection of cells from the outer opening of the cervix of the uterus and the endocervix; cells are examined under a microscope to look for abnormalities in order to detect potentially pre-cancerous changes usually caused by HPV

- technique:
- appropriate selection of speculum
- adequate sample collection: includes endocervical cells
- results:
  - negative for intraepithelial lesion or malignancy
  - organisms present: yeast, bacterial vaginosis, or trichomoniasis
  - atypical squamous cells of undetermined significance (ASCUS)
  - low grade squamous interepithelial lesion (LSIL)
  - high grade squamous interepithelial lesion (HSIL)
  - atypical glandular cells (AGC)
    o has nothing to do with HPV, it is from inside the uterus or cervix = something that is not considered when formulating screening guidelines
- management protocols:
2.) **Colposcopy:** looking at the cervix under magnification using acetic acid to improve visualization of abnormalities
   - this method has largely replaced diagnostic cervical conization
   - requires referral to a colposcopist
   - woman cannot be on her period
   - premedication with ibuprofen to reduce cramps
   - post-procedure adverse effects: mild cramping, discharge of blood and menses, odor a few days later from mild vaginal infection

3.) **Treatment of cervical abnormalities**
   - cervical cryotherapy
   - laser
   - **cervical conization:** a biopsy of the cervix in which a cone-shaped sample of tissue is removed from the mucous membrane
   - used either for diagnostic purposes, or for therapeutic purposes to remove pre-cancerous cells
   - types:
     - cold knife conization (CKC):
     - loop electrical excision procedure (LEEP): a wire loop through which an electric current is passed at variable power settings is used to excise the lesion and cervical transformation zone to an adequate depth
various shapes and sizes of loop can be used depending on the size and orientation of the lesion. Risks of treatment: formation of sperm antibodies, cervical stenosis, incompetent cervix, missing a significant lesion.

4.) Endometrial cancer testing
- Screening:
  - not routinely recommended
  - not recommended for women on tamoxifen unless there are symptoms or a change in bleeding
- Indications: h/o HNPCC, abnormal uterine bleeding after age 35, atypical glandular cells on pap, benign endometrial cells on pap of postmenopausal woman
- Tests:
  - endometrial biopsy
  - Sensitivity for endometrial cancer in premenopausal women 99.6%, 91% in postmenopausal women
  - can miss focal disease
  - Sensitivity for endometrial hyperplasia 81%
  - Specificity of 98-100%
  - Works best if pathology is global and at least ½ of the endometrium is affected
  - can miss a cancer if it is confined to a polyp
- Pros: office procedure, minimal cervical dilation, no anesthetic, low cost
- Contraindications: pregnancy, pelvic infection
  - Relative: bleeding predisposition, cervical stenosis, cervical cancer
- Technique:
  - Woman not on period
  - Prophylactic NSAIDs to reduce cramping
  - Use of tenaculum makes procedure easier but can cause more cramping
  - Antibiotics not needed
  - Bimanual exam first
  - Then insert speculum to visualize cervix
  - Clean cervix with antiseptic solution
  - Insert sampling device through os and onto uterine fundus, stopping when resistance is met
    - Use tenaculum or lacrimal duct probe to dilate canal if needed
  - Document depth of uterus (avg 6-8 cm)
  - Create negative pressure and rotate sheath to sample uterus
  - Remove device when entire cavity is sampled and catheter is filled with tissue
  - Expel specimen into formalin
  - Perform second pass if needed for insufficient tissue
  - Remove tenaculum
  - Control bleeding with cotton swabs or cauterization if needed
- Risks: cramping, vasovagal reaction, excessive uterine bleeding, uterine perforation, pelvic infection, bacteremia
- Have patient call office for fever, cramping > 48 hours, increasing pain, foul discharge, or heavy bleeding
- Benign pathology results:
  - Atrophy
  - Proliferative endometrium (estrogen effects)
  - Secretory endometrium (progestin effects)
  - Dysynchronous endometrium (unopposed estrogens)
  - Endometritis but if bleeding persists or there are nondiagnostic results or high suspicion of cancer, refer to gyn!
- Non-benign pathology = simple or complex endometrial hyperplasia:
  - Results in unopposed estrogen effects
  - Seen in premenopausal women with obesity, PCOS, eating disorders, thyroid disorders, herbals, other causes of anovulation
  - With or without atypia:
    - Without atypia: risk of cancer progression is < 1-3%
      - Treatment for premenopausal women: Provera (can’t use with nut allergy), micronized progesterone vag cream
      - Re-sampling to document regression
other options: ovulation induction, levonorgestrel IUD, monitoring only if asymptomatic
- treatment for postmenopausal women: r/o ovarian or adrenal tumors, weight loss, d/c hormone replacement, Provera
  - repeat biopsy at 3 months
  - hysterectomy if no regression
  - with atypia: risk of progression 17-53%, risk of co-existing cancer is 25% refer to gyn for D&C or hysterectomy
b.) transvaginal US:
- thin strip < 4-5 mm is associated with low risk of endometrial cancer
  - but can still be estrogen-independent carcinoma
- stripe > 5 mm warrants biopsy
c.) saline infusion sonography
d.) hysteroscopy: thin, lighted tube is inserted into the vagina to examine the cervix and inside of the uterus
- can be diagnostic or operative e.) dilation & curettage
5.) Hysterosalpingogram: x-ray imaging of the internal uterus and fallopian tubes using contrast dye
- for infertility evaluation and detection of uterine defects such as uterine septum, endometrial polyps, uterine fibroids, Asherman’s syndrome
- patient prep: pelvic US, assessment for pelvic infection, drug allergy history, bleeding disorder history, post menses timing

9.5 Abnormal Uterine Bleeding, Amenorrhea, and Dysmenorrhea
9.5.1 Background on AUB and DUB
- Terms
  - menorrhagia: heavy menses > 80 mL
  - intermenstrual bleeding: spotting
  - metrorrhagia: irregular menses
  - menometrorrhagia: irregular and heavy bleeding
  - polymenorrhea: cycle intervals that are < 21 days
  - oligomenorrhea: cycle intervals that are > 35 days
  - dysmenorrhea: painful menstrual cycles
- Abnormal uterine bleeding: bleeding that differs in quantity or timing from a woman’s usual menstrual flow
- structural causes:
  - pregnancy-related structural abnormalities: spontaneous abortion, ectopic pregnancy, abruptio placenta (premature separation of placenta from uterus), trophoblastic disease (pregnancy-related tumors)
  - benign uterine growths: leiomyomata uteri, cervical or endometrial polyps, endometrial hyperplasia, adenomyosis
- iatrogenic causes: IUD or other foreign body, meds (hormones, antipsychotics, anticonvulsants, anticoagulants, NSAIDs, steroids, herbs, SSRIs), trauma (sex, abuse, MVA, straddle injury, pelvic fx)
- systemic causes: disorders of coagulation, disorders of the thyroid, adrenal disorders (hyperplasia or Cushing’s), kidney or liver diseases, stress or intense exercise, pituitary adenoma, hypothalamic suppression, smoking, sudden weight loss or anorexia
- other causes: pregnancy, malignancy, infections
- infections: endometritis, cervicitis, vaginitis, genital warts
- malignancies can occur in the endometrium, cervix, ovary, or vagina
- be aware of non-uterine causes of bleeding such as urethritis, bladder cancer, UTIs, IBD, hemorrhoids
- any cause other than these yields a diagnosis of dysfunctional uterine bleeding rather than AUB
- although some providers consider DUB to be a subset of AUB?
• **Dysfunctional uterine bleeding:** bleeding found in the absence of demonstrable structural or organic pathology that is unrelated to another underlying illness = a diagnosis of exclusion
• usually an endocrine/hormonal disturbances
  o possible causes: pregnancy, menopause, premature ovarian failure, PCOS, prolactinoma, anovulation, immature HPO axis (puberty), perimenopause
• classified as ovulatory or anovulatory (90% of cases), depending on whether or not ovulation occurs
  o anovulatory DUB results in continual secretion of estrogen without egg maturation → no release of progesterone because no corpus luteum forms
    ▪ results in unopposed estrogen hypertrophy of the endometrium = increased risk of endometrial cancer in these patients
      • at risk: patients over age 35, obesity, anovulation > 6 months, h/o breast cancer, h/o tamoxifen use, FH breast/uterine/ovarian/colon cancer
    ▪ eventually the endometrium outgrows its blood supply and sloughs off at irregular intervals
      ▪ no ovulation = patients won’t have symptoms associated with PMS and menses
• further classification of anovulatory causes:
  • **occasional anovulation** is self-limiting and requires no intervention b.)
    • **chronic anovulation**
      o occurs in PCOS when steady unopposed estrogen levels → erratic breakdown and shedding
    • occurs adult-onset adrenal hyperplasia with androgen excess c.)
    • **transitional anovulation** leading to amenorrhea
      o occurs hypothalamus disorders, prolactinomas, and premature ovarian failure
  • **ovulatory dysfunction** (luteal phase defect): occurs with inadequate follicular development and progesterone production

9.5.2 **Bleeding Investigation**
• Differential: hematologic disorders, anatomic or histopathologic disorders, pregnancy, hormonal disorders, trauma, cancer, systemic disease, iatrogenic cause
• Premenopausal patients:
  • always consider pregnancy first
  • then assess ovulatory status:
    o signs of ovulation: predictable menses, cramping, breast tenderness, mood swings, bloating
    o signs of hirsutism, acanthosis nigricans, Cushing’s
    o menstrual calendar
    o basal body temp
    o labs: progesterone levels, urine LH
    o imaging: serial US to view dominant follicle and corpus luteum ($$)
• Postmenopausal patients:
  • check for malignancy first
  • Pelvic exam ± wet prep and cultures
  • Other labs: H/H, TSH ± T4, PT/PTT, liver and renal panel, prolactin, androgens
  • Other imaging: transvaginal US, saline infused sonohysterography
  • Procedures: endometrial biopsy, D&C, hysteroscopy

9.5.3 **Bleeding Treatment**
• Goals are to alleviate acute bleeding, prevent further noncyclic episodes, decrease long-term risks, and improve quality of life
• Pharmaceutical management is preferred:
  • high dose NSAIDs
  • combined OCPs
  • progestins
  • estrogens for acute bleeding only
  • danazol
antifibrinolytic agents
levonorgestrel IUD
desmopressin
GnRH agonists
Surgical options:
hysteroscopic endometrial ablation
nonhysteroscopic endometrial ablation
hysterectomy
  o half of all hysterectomies performed are for AUB, with 1/3 of these cases being DUB
  o types:
    ▪ total abdominal hysterectomy
    ▪ vaginal hysterectomy
    ▪ supracervical hysterectomy
    ▪ laparoscopically assisted vaginal hysterectomy
    ▪ laparoscopic supracervical hysterectomy
    ▪ total laparoscopic hysterectomy

9.5.4 Amenorrhea

• Types:
  • primary amenorrhea: either failure to menstruate by age 16 in presence of 2° sex characteristics, or failure to menstruate by age 14 in absence of 2° sex characteristics
  • secondary amenorrhea: cessation of menstrual flow for a period of time equal to 3 cycles
    o all causes of secondary amenorrhea can also present as primary amenorrhea
• Causes:
  • outflow tract obstruction
    o examine vagina, cervix, and uterus bimanually
    o may need US
    o treatment: surgical if there is an anatomic defect
  • ovarian failure
    o treatment: hormone replacement
  • chronic anovulation
    o treatment:
      ▪ if estrogen is present, need cyclic progestins
      ▪ if estrogen is lacking, need hormone replacement or OCPs
  • pituitary prolactinoma
    o treatment: Dostinex, bromocriptine, surgery if medical therapy fails
  • hypothalamic tumors
    o treatment: surgery
  • hypothalamic dysfunction
    o treatment: hormone replacement
• Investigation:
  o β-HCG
  o TSH, FSH, LH
  o prolactin
  o karyotyping
  o MRI of pituitary with galactorrhea or visual field defects
  o progestin challenge: oral or IM progesterone given to evaluate estradiol and outflow tract status
    ▪ should bleed in 2-14 days

9.6 Sexually Transmitted Infections
9.6.1 Background

- Lifetime risk of 1 in 4
- No development of immunity!
- Can have carrier state
- Risk factors: new sex partner in last 60 days, multiple sexual partners, unmarried, lower SES, h/o STI, substance abuse, early onset of sexual activity, lack of barrier contraceptive use, age 15-24, living in SE US or urban areas, black, commercial sex workers or contact with, sexual abuse victim, incarcerated, juvenile detention center, meeting partners on the internet
- Women who have sex with women can still contract STIs
- Risk varies with number of partners, bisexuality, specific sexual practices
- Prevention: offer vaccination for hep A & B to all patients at risk
- Documenting genital ulcers:
  - location and number
  - pain or friability
  - induration
  - depth, diameter, and base
  - borders: irregular or smooth?
  - related adenopathy: bilateral, consistency, size, tenderness?
- STI PE for women: inguinal adenopathy, skin (including palms and soles), genital inspection, vaginal discharge, cervical exam for mucopus, friability, or pain, adnexal mass or tenderness, pregnancy test
- Prognosis:
  - STI complications: upper genital tract infections, infertility, cervical cancer, enhanced transmission or acquisition of HIV
  - may need to follow up treatment of STIs with a test of cure

9.6.2 STI Testing

- Interfering factors with testing:
  - recent antibiotic therapy
  - some organisms are sensitive to lubricants and disinfectants
  - menses can alter test results
  - female douching within 24 hours of collection can alter pH and ↓ # of organisms
  - voiding with 1-2 hours before collection can wash secretions away and decrease sensitivity
  - fecal material can contaminate rectal cultures
  - some organisms require specific temps, transport media to grow
- Labs available same-day: Gram stain, wet mount, RPR, darkfield microscopy
- Labs available next day or later: cultures, PCR (gonorrhea, Chlamydia, others), MHA-TP for syphilis
- Methods:
  - wet prep: cotton swab rotated over vaginal wall inflammation
    - must avoid cervix and blood
    - pH strip rubbed on swab
    - swab itself is inserted into saline tube to be examined microscopically within 20 min
  - cervical swab: speculum inserted to expose cervix, mucous swabbed away, sterile swab inserted into endocervical canal for 20-30 sec, specimen is inoculated immediately or placed in transport tube
    - gram stain:
      - if discharge is visible, can collect this, otherwise need to insert cotton swab 1-2 cm into urethra
      - can do cervical swab to look for clue cells
  - nucleic acid amplification
    - primarily for gonorrhea and chlamydia
    - can use vaginal swab or urine
    - problem: will still amplify DNA of dead organisms

Pelvic Inflammatory Disease: inflammation of the uterus, fallopian tubes, and/or ovaries as it progresses to scar formation with adhesions to nearby tissues and organs
- Cause is usually polymicrobial, including STIs + endogenous organisms (including anaerobes)
Increased risk with multiple partners, douching, and smoking
Presentation: wide variability of symptoms and signs makes diagnosis difficult
uterine, adnexal, or cervical motion tenderness
Treatment:
treat for PID if no other cause of pelvic or lower abdominal pain can be found in a sexually active woman at risk for STIs
begin while awaiting culture results
hospitalization if there is surgical emergency, pregnancy, nonresponse to oral antibiotics, inability to tolerate orals, severe illness (nausea, vomiting, fever), tubo-ovarian abscess
first line regimen: cefotetan or cefoxitin to cover anaerobes PLUS doxy to cover the chlamydia
  - IV for first 24 hours
second line: clinda + gentamycin
IV for first 24 hours
Prognosis: infertility risk that increases with each episode

9.6.3 Herpes Simplex Virus
Transmission: direct, autoinoculation, herpetic whitlow, perinatal during childbirth
women at higher risk for transmission
can be transmitted while asymptomatic (shedding)
can be reduced by antivirals
Outbreaks can be precipitated by sun, wind, trauma, fever, menses, stress
Presentation:
can be asymptomatic carrier
multiple recurrent vesicles
may have pain with urination due to urine running across lesions, no associated scarring with lesions
Investigation:
diagnosis is usually clinical
viral culture is gold standard if you are uncertain: get it from a fresh vesicle
PCR
serology:
  - controversial as half the population has + herpes antibodies but have no clinical evidence of infection
  - not everyone with + culture will have + serology
  - 4x rise in titer is indicative of acute initial herpes infection
Treatment:
goal is to curtain number of episodic prodromes and minimize antiviral side effects
based on likelihood of patient compliance, whether episode is initial or recurrent, pregnancy status, and host immunity
for first episode:
  - acyclovir, valacyclovir, or famciclovir for 7-10 days
for subsequent episodes: same drugs for 3-5 days
suppressive therapy: same drugs, for up to 1 year
other options for genital herpes: IV foscarnet, topical cidofovir, topical trifluridine
antiviral side effects: headache, confusion, nausea, vomiting, thrombocytopения, renal insufficiency, rash, pruritus, fever, arthralgias, myalgias, TTP, hallucinations, somnolence, depression
Prognosis:
first outbreak is the worst and can last up to 21 days, subsequent outbreaks should be less severe

9.6.4 Syphilis: caused by Treponema pallidum
Cases are increasing, with most being MSM
Presentation:
primary/acute infection: lasts 5-6 weeks
  - contagious chancre (single, usually painless lesion that has a heaped or rolled appearing border)
o associated painless, rubbery regional lymphadenopathy, followed by generalized lymphadenopathy in weeks 3-6

- secondary infection: occurs 6 weeks to 6 months after infection
  o not all patients will develop this
  o symptoms last a few weeks
  o systemic symptoms: fever, malaise, headache, arthralgias
  o bilateral, symmetric papulosquamous rash, especially on palms and soles
  o alopecia
  o denuded tongue
  o condyloma lata: smooth, moist, flat warts of secondary syphilis

- tertiary infection: occurs in disease > 4 years' duration
  o not all patients will progress to this
  o end organ manifestations
  o rarely infectious
  o multi-organ involvement
  o CV symptoms
  o gummas: can be serpiginous appearing, ulcerating
  o neurosyphilis: spirochetes seen in neural tissue

- latent infection: time period after secondary syphilis, with no clinical manifestations
  o serology will be reactive
  o “early” if within first year after secondary infection
    ▪ negative CSF
  o “late” if greater than one year after infection
    ▪ confers reduced risk of transmission
  o 1/3 of patients will have no further consequences

- congenital infection:
- Investigation: negative tests do not exclude diagnosis of syphilis!
- darkfield microscopy of chancre sample
- LP for CSF examination for neurosyphilis: recommended for symptomatic or late-latent infections or with HIV coinfection
- labs:
  o direct fluorescent antibody testing
  o serology:
    ▪ nontreponemal tests detect antibodies to reagin (lipid in treponemal membrane):
      VDRL, RPR, TRUST
      ▪ can have cross-reactivity as reagin is similar to human phospholipids
      ▪ other sources of false + include malaria, leptospirosis, leprosy, mononucleosis, SLE, lymphogranuloma venereum, mycoplasmal pneumonia, typhus, bartonellosis, hepatitis, periarteritis nodosa, acute viral or bacterial infections, hypersensitivity reactions, recent immunizations
      ▪ reported as antibody titers: reflect activity and infectivity
      ▪ use for follow-up at months 1, 3, 6, and 12 until nonreactive
      ▪ 3-6 week latency period
      ▪ venereal disease research lab (VDRL): becomes + 2 weeks after infection and may remain + during further stages of syphilis
      ▪ rapid plasma reagin (RPR): is more sensitive
      ▪ treponemal tests detect antibodies against specific treponemal antigens: FTA-ABS, MHA-TP, TP-PA, TP-EIA
        ▪ will be + for life
        ▪ reported as reactive or nonreactive
        ▪ used for confirmation of nontreponemal tests
  o HIV test recommended as syphilis facilitates this infection

- mandatory reporting within 24 hours
  o partners from the last year are investigated

- Treatment: penicillin G
Chancroid: caused by *Haemophilus ducreyi* infection
- Much less common than other STIs
- Increases risk of contracting HIV
- Presentation: impressive regional adenopathy (unlike syphilis)
- frequent coinfection with herpes, syphilis
- Investigation:
  - culture for gonorrhea won’t grow → suspicion for chancroid
  - PCR
  - gram stain to look for “school of fish” = gram neg diplococci in chains
- Treatment:

Granuloma Inguinale: ulcerative genital lesions caused by *Klebsiella granulomatis*
- Presentation: chronic or recurrent ulcerative vulvitis
- Investigation:
  - PE looking for chronic ulceration (not seen with syphilis or HSV), malodorous discharge, inguinal swelling
  - lesion biopsy
  - Donovan bodies on stained direct smear
- Treatment: antibiotics

9.6.5 Human Papilloma Virus
- High and low risk subtypes
- Risk factors: multiple sex partners, young age at first sexual activity, high risk sex partner, history of STDs, multiparity, young age at first full-term pregnancy, long-term use of OCPs, immunosuppression, lack of screening, uncircumcised male partner, smoking
- invasive cervical cancer is an AIDS-defining illness
- Screening:
  - begin at age 21 or within 3 years of first sexual contact
  - screen annually up to age 30
  - after age 30, screen every 5 years as long as there has been 3 consecutive negative smears
  - stop screening after age 70 as long as there have been 3 consecutive negative smears with no abnormal tests in past 10 years
  - stop screening after total hysterectomy (for benign disease) as long as there is no past history of cervical dysplasia
- never stop screening immunocompromised patients
- Prevention: vaccination against types 6, 11, 16, and 18 available
- offer to females 9-26 years
- Presentation:
  - can be asymptomatic
  - cervical dysplasia
  - cervical cancer
- **condyloma acuminata**: cauliflower, verrucous, dry, bulky warts caused by HPV types 6 and 11
  - can become cancerous
  - treatment:
    - surgical: cryosurgery, electrosurgery, excision, laser vaporization
    - clinic: bichloroacetic acid, trichloroacetic acid, podophyllin, sinecatechins ointment
    - at home: podofilox, imiquimod
- Investigation:
- diagnosis can be clinical
- visual exam with Pap
- colposcopy
- biopsy
- labs: high risk HPV DNA typing
- Prognosis: possible sequelae of cervical adenocarcinoma, squamous cell carcinoma of the vulva, vagina, penis, or anus
9.6.6 Chlamydia trachomatis

- Most commonly reported STI in the US
- Most common in < 20 year olds, nulliparity, nonuse of barrier contraceptives
- Not related to SES
- Increasing incidence
- Can be transmitted perinatally (ophthalmia neonatorum, pneumonia)
- Incubation of 7-10 days, with symptoms < 30 days

Screening:
- every year for women < 26
- with new sex partner in last 60 days
- with > 2 sex partners in the last year

Presentation:
- can be asymptomatic
- vaginal discharge, dysuria
- cervical mucopus, friability, ectropion
- acute urethral syndrome
- pelvic or lower abdominal pain
- frequently coinfected with gonorrhea
- ectopic pregnancy
- perihepatitis

Investigation:
- PCR is best
- EIA cheaper but lower sensitivity
- cell culture only has 60% sensitivity
- urine testing in men

Treatment:
- meds:
  - need to treat gonorrhea + chlamydia
  - first line is azithromycin or doxycycline
    - azithromycin ok for pregnancy
  - alternatives: erythromycin or levofloxacin or ofloxacin
- sexual abstinence for 7 days from initiation of therapy

Prognosis:
- need retesting in 3 months after treatment
- complications:
  - females: PID, related infertility
  - males: epididymitis, urethritis, sterility

Lymphogranuloma venereum: lymphatic infection caused by L serotypes of Chlamydia trachomatis

- More common in males
- Rare in the US
- Presentation: rectal ulceration or stricture, inguinal lymphadenopathy
- Investigation:
- labs: + complement fixation test
- Treatment: antibiotics, stricture dilation, surgery

Gonorrhea: caused by Neisseria gonorrhoeae

- 2nd most common reported STI
- Typically underdiagnosed and underreported
- Increased risk of HIV infection with concomitant gonorrhea
- Presentation:
  - women: vaginal discharge, abdominal pain, half are asymptomatic, cervicitis
  - men: purulent discharge, dysuria, urethritis
  - most men have symptoms with gonorrhea!
- Investigation:
• PCR is optimal
• urethral Gram stain for men
• urethral cell culture
  o needed when women with suspected infection don’t have a cervix
  o must be at least 1 hour after last urination
    ▪ best specimen from first morning urination
  o urethral/prostatic massage may increase culture yield
• may need to culture rectum (press laterally while swabbing to avoid feces)
  o need to repeat sample if stool gets on the swab
• other potential culture sites: oropharyngeal, cervical
• need to culture on special media with no refrigeration
• Treatment
• uncomplicated infection of the cervix, urethra, and rectum:
  o frequent coinfection with Chlamydia
  o first line is ceftriaxone or cefixime or injectable cephalosporin PLUS azithro or doxy
• uncomplicated pharyngitis: ceftriaxone PLUS azithro or doxy
• gonococcal conjunctivitis, meningitis, or endocarditis: ceftriaxone
• disseminated gonorrhea: hospitalization with ceftriaxone, then cefixime
• sex partners (especially with symptoms > 60 days) need to be treated
• Prognosis:
  • complications:
    o females: PID, infertility, ectopic pregnancy, tubo-ovarian abscess, perihepatitis, vertical transmission ophthalma neonatorum
    o males: epididymitis, infertility
    o both: disseminated gonorrhea, septic arthritis

9.6.7 HIV
• Offer HIV test to all patients evaluated for STIs
• Incorporate testing into routine health care
• special emphasis on at-risk populations: MSM, bisexual, IVDU, transfusions, pregnant women
• Legal issues:
  • no longer a national requirement for written informed consent or pre-test counseling, although some states do require it
  • patients still need to be informed of testing
• Investigation:
  • rapid screen test is EIA: tests antibodies to HIV, but not viral antigens
  • confirmatory test is western blot: detects viral antigens
    o if neg after a + EIA, repeat in 3-6 months
• PCR and viral culture also available
• HIV viral load looks for RNA in blood sample
  o used for prognosis, monitoring disease progression, response to therapy
• false + most common with recent immunization
• false neg most common during testing in 2-12 week window period prior to seroconversion
• special considerations for children:
  o definitive diagnosis before 6 months of age is difficult
  o maternal HIV antibodies persist for up to 1 year

Trichomoniases: caused by Trichomonas vaginalis
• Presentation: severe pruritus, musty-smelling green-yellow frothy discharge, dysuria, dyspareunia, cervical petechiae (strawberry markings)
• Investigation:
  • wet prep for motile trophozoites
  • thin prep pap test can reveal trichomonads but is not diagnostic
  • finding on UA is incidental
• culture not common
• Treatment:
  • first line is single dose metronidazole or tinidazole
  • must treat partners
  • frequently need to treat other STIs

9.7 Vulvar and Vaginal Disorders

9.7.1 Vulvar Disease

• Background
  • includes diseases causing pruritus, burning, irritation, or abnormal growth
  • increased risk of malignancy in peri- and postmenopausal women
    • vulvar biopsy of lesions may be needed as they are difficult to differentiate
• infectious and non-infectious causes
  • infectious: ulcerative infections, pediculosis pubis, scabies, candidiasis vulvitis, condyloma, folliculitis, carbuncles, abscesses
  • non-infectious: contact dermatitis, atrophic changes, other dermatitis, neoplasia
• vulvar skin care:
  • good lubricants include petrolatum, olive oil, A&D ointment
  • cold milk or Burow’s solution compresses to decrease itching
• Common vulvar dermatoses:
  • lichen sclerosus: unknown etiology causes white patching and scarring
  • increased risk of transforming into squamous cell cancer
  • presentation: chronic, intense vulvar pruritus with thin, white “onion skin” appearance
    • can lead to disfigurement and stenosis of the vaginal introitus
  • investigation: always biopsy and refer
  • treatment: potent topical steroids, testosterone or progesterone?
  • lichen simplex chronicus: constant itching and scratching leads to thickened, white, localized patches
  • investigation: need to biopsy to rule out malignancy (can look like lichen sclerosus)
  • treatment: topical steroids, hydroxyzine, SSRIs
  • lichen planus: violaceous flat-topped papules, white patches, and ulcerations of unknown etiology
  • presentation: may have both oral and vaginal lesions, burning, itching, atrophy, adhesions, introital stenosis
  • investigation: biopsy
  • treatment: topical steroids, douches, suppositories, vaginal estrogen cream for atrophy
• psoriasis:
  • vitiligo:
  • acanthosis nigricans:
  • nevus:
  • epidermal inclusion cysts:
  • Bartholin’s duct cysts:
• contact dermatitis
  • treatment: 1% hydrocortisone cream
• atrophic changes: erythematous, smooth, shiny, thin mucosa
  • associated with reduced estrogen levels (postmenopausal, minipill, Depo, lactation)
  • investigation: need to differentiate from lichen sclerosus, biopsy for definitive diagnosis
  • treatment: topical estrogens, moderate strength topical steroids
• Paget disease of the vulva: fiery red lesions with white hyperkeratotic areas
  • may have carcinoma beneath the lesions!
  • may also be a sign of carcinoma in the colon, breast, or other areas
  • usually affects women over age 65
  • treatment: wide local excision or vulvectomy
• Vulvar infections:
  • ulcerative vulvar lesions: HSV, chancre
  • parasitic vulvar lesions:
    • pediculosis pubis
- scabies: lesions throughout body
- yeast vulvitis: symmetrical erythematous, confluent lesions with fissures and excoriations
  - can have concomitant yeast vaginitis
- warty lesions: condyloma lata of syphilis, condyloma acuminatum of HPV
- Other vulvar conditions include varicosities, hematoma, edema, masses, and manifestations of systemic disease

9.7.2 Vulvar Cancer

- Background
  - accounts for 4% of all gynecologic malignancies
  - most common cancer type is epidermoid squamous cell carcinoma
  - remains localized for long periods of time then spreads lymphatically
  - posterior vulva drains to inguinal nodes
  - anterior vulva drains to deep pelvic nodes
  - typically occurs in postmenopausal women
  - risk factors: HPV, smoking, lichen sclerosus, VIN lesions, cervical neoplasm or cancer
  - cancer is preceded by skin changes known as vulvar intraepithelial neoplasia (VIN)
    - VIN presentation: vulvar pruritus, chronic irritation, white or gray raised lesions commonly on the posterior vulva and perineum = resembles many benign vulvar conditions
    - treatment:
      - early lesions: local cauterization
      - high-grade lesions: wide local excision, vulvectomy if needed
  - Lesions with risk of malignancy: lichen sclerosus, Paget disease of the vulva, HPV
  - Malignant lesions:
    - vulvar melanoma: raised, irritated, pruritic, pigmented lesions
      - rare but incidence is increasing with tanning bed use
      - investigation: excisional biopsy with wide margins
      - Investigation:
        - lymph nodes
        - biopsy
        - CXR
        - cystoscopy and proctoscopy
        - IV pyelogram
    - Treatment:
      - radical vulvectomy and node dissection more common in the past
      - adjunctive post-op radiation
    - Prognosis: 5-year survival of 75%

9.7.3 Vaginal Disorders

A.) Vaginitis

- presentation: vaginal discharge, dyspareunia, dysuria, urinary frequency, or can be asymptomatic
- cause
  - bacterial vaginosis: a polymicrobial overgrowth of normal flora, especially anaerobes
    - relative absence of Lactobacillus
    - presentation: fishy odor (especially after sex), heavy bubbly discharge that is white or gray
    - investigation: diagnostic criteria with ¾: characteristic discharge, alkaline pH, + whiff test, clue cells on wet prep
    - treatment:
      - first line is PO or intravaginal metronidazole or clindamycin cream
      - second line is tinidazole or PO clinda
  - Trichomonas vaginitis
  - yeast vaginitis. infection with Candida albicans
    - may be precipitated by hormonal changes, oral steroids or antibiotics, nylon underwear, tight clothing, hot weather, obesity
o presentation: pruritus, burning, nonmalodorous cottage cheese discharge, dyspareunia, vaginal or vulvar erythema, or may be asymptomatic

o investigation:
  ▪ KOH wet prep to look for pseudohyphae or budding yeast
  ▪ may need culture

o treatment:
  ▪ first line are 1-day therapies: butoconazole or fluconazole or ticonazole
  ▪ second-line are 3-day therapies or longer

o if recurrent, consider hyperglycemia or diabetes, or HIV

atrophic vaginitis: inflammation of the vagina due to thinning and shrinking of tissues and decreased lubrication

o not infectious, but need to rule out infection, and can have secondary infections

o seen in women with decreased estrogen: postmenopausal, lactation, extreme exercise, progesterone treatment without estrogen

o presentation: pruritus, burning, vaginal dryness, dyspareunia, spotting, no odor, pale and thin vaginal mucosa, no discharge, loss of rugae

o investigation: make sure wet prep is negative

o treatment: estrogen replacement

B.) Bartholin’s gland abscess: can be caused by Neisseria gonorrhoeae, Chlamydia, Strep, E. coli, or anaerobes

• more likely to be gonorrhea if bilateral

• can be chronic

• can also be caused by carcinoma in women over age 40

• presentation: severe vulvar pain and swelling for 2-3 days, uncomfortable walking and sitting

• treatment: I&D, placement of Word catheter for 1-2 weeks, consider antibiotic treatment

• marsupialization (keeping open) if recurrent

9.7.4 Vaginal Cancer

• Background

• rare

• at risk: HPV for squamous cell carcinoma transformation, diethylstilbestrol exposure for clear cell carcinoma, other vaginal intraepithelial neoplasm (VAIN)

• presentation: abnormal bleeding, pain, mass, dyspareunia

• investigation: colposcopy, biopsy or excision

9.8 Cervical Disorders

9.8.1 Cervicitis

• Common infectious causes: Chlamydia, gonorrhea, HSV, HPV, trichomoniasis, Mycoplasma genitalium, CMV, bacterial vaginosis

• less common: TB, lymphogranuloma venereum, cervical actinomycosis (associated with long-term IUD use)

• Noninfectious causes: cervical cap, pessary, or diaphragm use, chemical or latex allergy, cervical trauma

• Presentation: postcoital spotting, intermenstrual spotting, dyspareunia, unusual vaginal discharge, cervical stenosis, salpingitis

• acute cervicitis: mucopurulent endocervical discharge, edematous and/or friable cervix

• chronic cervicitis: leukorrhea, vulvar irritation, granular redness, patchy erythema, cervical stenosis

Nabothian Cysts: mucus-filled cervical cysts

• AKA nabothian follicles, epithelial inclusion cysts, mucinous retention cysts

• Normal, occur when new tissue regrows on cervix, usually after childbirth

• Can also been seen in menopausal women with thinned epithelium
• No treatment necessary

**Endocervical Polyps:** small, red, pedunculated, sessile lesions
• Common in premenopausal or hyperestrogenic women
• Presentation: can be asymptomatic, frequently occurs with postcoital spotting
• Investigation:
  - remove polyp and send to pathology
• Treatment: removal of polyp is curative 90% of the time

9.8.2 Cervical Cancer

- HPV background
- infected epithelium can develop active or latent infection, or undergo neoplastic transformation
  - oncogenic subtypes: 16, 18, 31, 33, 35
    - HPV is found in almost all invasive cervical cancers
- most women will clear HPV infection within 2 years
- Types:
  - **cervical intraepithelial neoplasia:** aka cervical dysplasia; premalignant transformation of cells but not yet cancer
    - most commonly in women in their 20’s
  - **cervical carcinoma in situ:** early cancer that has not invaded surrounding tissue
    - most common in ages 25-35
  - **cervical squamous cell carcinoma:** large cell (keratinizing or non) or small cell
    - most common form, accounts for 75% of cervical cancers
    - usually from HPV 16 or 18
    - verrucous forms associated with HPV 6
    - most develop from intraepithelial layers
    - usually located within 1 cm of the squamocolumnar junction
  - **cervical adenocarcinoma:** derived from glandular elements; mucinous, endometrioid, clear, or serous cell
    - usually from HPV 18
    - more common in women under 35
    - clear cell related to DES exposure
    - develop on endocervical canal and are not visible until more advanced
- **cervical adenosquamous carcinoma:**
- **undifferentiated cervical carcinoma:**
- **neuroendocrine cervical carcinoma:**

- 75% decrease in incidence due to screening programs, but still a leading cause of death in medically underserved countries
- 80% of women will be infected with a strain of HPV by age 50
- Incidence of cervical cancer rises after age 40
- average age of diagnosis is 51
- Presentation:
  - early disease is asymptomatic
  - abnormal vaginal bleeding, postcoital bleeding, vaginal discharge, foul odor, pelvic or flank pain, signs of vesicovaginal or rectovaginal fistula, weakness, weight loss, anemia
  - speculum exam showing cervical lesion, enlarged cervix, ulceration, nodularity, friable tissue, or decreased mobility
  - nodularity of uterosacral ligaments
- Investigation:
  - pap smear
    - limited value for grossly visible invasive disease □ get a biopsy instead
  - for pap showing atypical squamous cells, get HPV testing
  - endocervical curettage
  - imaging to evaluate for mets
- stage by clinical exam results:
  - stage I for carcinoma confined to cervix
- stage II for invasion beyond uterus, but not the pelvic wall or lower 1/3 of the vagina
- stage III for tumors extending to the pelvic wall or involving the lower 1/3 of the vagina or causing hydronephrosis
- stage IV for tumors extending beyond the true pelvis or involving bladder mucosa or the rectum

Treatment:
- pre-invasive: loop electrosurgical excision procedure (LEEP), cold knife conization (CKC), simple hysterectomy
- early stage: radical hysterectomy + pelvic lymphadenectomy, primary radiation with concurrent chemo
- locally advanced: primary radiation with concurrent chemo
- mets or persistent or recurrent cancer: chemo, palliative radiation
- central pelvic recurrence: total pelvic exenteration

Prognosis:
- depends on stage, lymph node mets, tumor volume, invasion, histology, and location of recurrence
- good prognosis for earlier disease responsive to treatment
- nontreatment or nonresponse to treatment yields at 5% 2-year survival
  - causes of death are uremia, PE, hemorrhage, sepsis (from pyelonephritis or fistulas), large bowel obstruction

9.9 Gynecologic Pain Disorders and Sexual Dysfunction

9.9.1 Background
- Sexual dysfunction and pelvic pain disorders are almost always multifactorial and multidimensional
- Must establish reasonable treatment plan and reasonable patient expectations
- Make resources available for patients

9.9.2 Chronic Pelvic Pain
- Pathophys not well understood, may be multisystemic
- Presentation:
  - generally noncyclical pain lasting > 6 months that is localized to the pelvis, anterior abdominal wall below the umbilicus, or to the buttocks
  - functional disability from pain
- Investigation:
  - differential:
    - GI: Celiac disease, colitis, colon cancer, IBS, Crohn’s, chronic constipation
    - gyn: adhesions, adenomyosis, adnexal cysts, endometritis, dysmenorrhea, endometriosis, gyn cancers, fibroids, pelvic congestion, PID
    - msk: degenerative disc disease, fibromyalgia, levator ani syndrome, myofascial pain, peripartum pelvic pain, stress fx
    - psych/neuro: abdominal epilepsy, abdominal migraines, depression, neuro dysfunction, sexual assault or abuse, sleep disturbances
    - urologic: bladder cancer, chronic UTI, interstitial cystitis, radiation cystitis, kidney stones
  - have patient keep a diary of symptoms and their relation to sex, physical activity, meds, psychosocial stressors
  - PE: inspection, speculum exam, bimanual exam, rectal exam
  - transvaginal US
- Treatment:
  - patients want a personalized care plan and evaluation, an explanation for their symptoms, and reassurance regarding findings and prognosis

9.9.3 Acute Pelvic Pain
- Presentation:
  - pain < 3 months duration
- Investigation:
• differential based on age:
  o women of reproductive age: appendicitis, bowel obstruction, diverticulitis, gastritis, ulcer, perirectal abscess, ectopic pregnancy, ovarian torsion, PID, ruptured ovarian cyst, tubo-ovarian
  o abscess, cystitis, pyelonephritis, ureterolithiasis, dissecting aortic aneurysm, poisoning, sickle cell crisis
    ▪ adolescent woman: add imperforate hymen, dysmenorrhea, sexual abuse or assault, transverse vaginal septum
  o pregnant women: ectopic pregnancy, corpus luteum hematoma, postpartum endometritis, ovarian torsion, ovarian vein thrombosis, placental abruption, uterine impaction
  o postmenopausal women with acute pelvic pain: appendicitis, bowel obstruction, diverticulitis, gastritis, ulcer, perirectal abscess, cystitis, pyelonephritis, ureterolithiasis, dissecting aortic aneurysm, poisoning, sickle cell crisis, atrophic vaginitis, vaginal fissures or cuff injuries

9.9.4 Dyspareunia
• Etiology is usually a combination of physiologic, emotional, and relational factors
• possible causes:
  o vulvar pain syndrome (vulvodynia): chronic discomfort in vulvar region with no identified infection or dermatologic cause
    ▪ contributing factors: pelvic floor muscle response, inflammatory response, previous sexual assault or abuse, connective tissue disease
      • vestibulitis: a form of vulvodynia with pain specifically localized to the vaginal opening
    ▪ presentation: pain with gentle pressure to introitus, hymen, or general vulva, pain with attempt at sexual activity
      • vestibulitis: usually unable to do speculum exam or engage in sexual activity, vulvar burning, painful urination
    ▪ treatment: lifestyle modification involving clothing and exercise, biofeedback, SSRIs or tricyclics, perineoplasty
  o vaginismus: painful, involuntary reflex spasm of the pubococcygeus in anticipation of vaginal penetration
    ▪ contributing factors: rape, incest, other sexual assault or trauma, Behcet’s syndrome (autoimmune sores), sexual phobia, decreased lubrication, previous negative experience
    ▪ investigation: sex and menstrual history, psychosocial history, PE
    ▪ treatment: vaginal lubricants, estrogens, physical therapy
  o interstitial cystitis: painful bladder syndrome characterized by negative UA, absence of infectious agent, painful sex, urinary frequency, and nocturia
    ▪ investigation: a diagnosis of exclusion
      • bladder pain diary
      • bladder instillation K+ challenge test to reproduce symptoms
    ▪ treatment
      • low oxalate diet
      • meds: Elmiron

• Investigation:
• PE: inspection, evaluation of skin pigmentation, patient pain response to exam
• Treatment:
  • treat underlying pathology
  • cognitive behavior therapy or desensitization
  • vaginal dilators
  • sexual education and counseling, ± partner
  • pelvic floor physical therapy
  • pharmacologic interventions:
    o local estrogens
    o antidepressants
9.9.5 Dysmenorrhea

A.) Primary dysmenorrhea: painful menses in women with normal anatomy
   - etiology is usually prostaglandins
   - the leading cause of school absences
   - presentation: cramping pelvic pain prior to or immediately following menses
     - usually in adolescent women
     - associated with heavy menstrual flow
   - treatment:
     - meds: NSAIDs (↓ prostaglandins as well as flow), OCPs, progesterone (Depo), Mirena IUD
     - acupuncture
     - thiamine supplementation
     - low fat or vegetarian diet

B.) Secondary dysmenorrhea: painful menstruation as a result of disease or pathology causing recurrent, cyclic pain symptoms
   - etiologies: endometriosis, uterine fibroids, adenomyosis, STIs, endometrial polyps
   - treatment: medical and surgical therapies available

9.9.6 Sexual Dysfunction

A.) Sexual desire dysfunction
   - emotional component
   - relationship component
   - physical fatigue
   - intimacy component

B.) Sexual arousal dysfunction
   - lack of genital response: vaginismus, vestibulitis, recent labor or delivery, surgical trauma, lack of lubrication, meds, stress, decreased estrogen

C.) Orgasmic dysfunction
   - physical or emotional
   - previous sexual trauma or childhood experience
   - partner components
   - environment or circumstances of emotional intimacy
   - sexual aversion

D.) Sexual pain disorders: chronic vaginitis, vaginismus, vulvodynia, vestibulitis, interstitial cystitis

9.10 Female Breast Disorders

9.10.1 Anatomy

- Breasts are composed of fat, glandular tissue, connective tissue
- glandular tissue: lobules, branching ductal system
  - 6-10 ducts converge to empty in the nipple
- Nipple-areolar complex
  - where lactiferous ducts empty
- rich sensory innervation
- Montgomery tubercles are normal external portions of oil glands
- Lymphatics
  - central nodes are usually the most palpable
  - not all breast lymphatics drain the axilla, some drain into the inframammary chain or infraclavicular nodes
9.10.2 Physical Exam

- Inspection
  - arms at side, arms up, hands on hips (contracts pectoralis muscle)
  - make note of breast symmetry, color, contour, prominence of pores, scars, nipple characteristics
  - describe any masses or lesions with reference to clock face and distance from nipple
  - Manual exam: vertical strip method is the most validated
  - palpate axilla with patient in upright position
  - normal findings: dense lobular tissue, hollow ductal area just beneath the nipple, dense or nodular inframammary ridge
  - self-exam can be useful for high-risk women
    - best done on days 5-7 of menstrual cycle

9.10.3 Breast Imaging

1.) Mammogram
   - used for breast cancer screening
   - not needed for patients with total mastectomy who have had a breast implant
   - 2 views
   - unless for diagnostic purposes, in this case 2 additional views are taken
     - indications: symptomatic disease, s/p lumpectomy, f/u abnormal screen, patients with breast implants
   - pros: early detection
   - cons: sensitivity only 85%, high rate false positives
   - abnormalities: microcalcifications (esp in clusters), masses, densities
   - interpretation: BIRADS (breast imaging and reporting database system) standards
     - 0 = needs additional imaging
     - 1 = negative
     - 2 = benign finding
     - 3 = probably benign, needs short interval f/u
     - 4 = suspicious abnormality, biopsy should be considered
     - 5 = highly suggestive of malignancy

2.) US
   - not used as a primary screening tool
   - often used to follow up abnormal area on mammogram, as it can differentiate solid mass vs fluid cyst
   - can be used to guide FNA or core needle biopsy
   - helpful in younger women with denser breast tissue

3.) Breast MRI
   - does not take the place of mammograms
   - uses: supplement to mammogram, evaluation of implants for rupture, breast cancer staging
   - useful in high risk patients with increased breast density
   - ex. BRCA1/2+ in a younger woman
   - pros: more sensitive than a mammogram
   - cons: more false + than a mammogram, unneeded interventions
9.10.4 Pathologic Diagnosis

1.) FNA
- for solid mass or cysts
- diagnostic or therapeutic
- pros: fast, outpatient, quick recovery
- cons: may not be enough material for proper pathologic diagnosis

2.) Core needle biopsy:
- for solid masses or calcifications
- larger needle than FNA
- local anesthetic needed
- multiple samples taken = more likely to have accurate diagnosis than FNA

3.) Surgical or excision biopsy
- done when core biopsy has inadequate results or location of lesion inhibits needle biopsy
- larger amount of tissue removed = scar & deformity created
- guaranteed diagnosis

9.10.5 Common Breast Complaints

A.) Lump or mass
- causes: fibrocystic changes, fibroadenoma, intraductal papilloma, fat necrosis, abscess, malignancy
- investigation differs depending on age of patient
- age under 30:
  - cyst characteristics: monitor for 1-2 menstrual cycles or aspirate
  - persistent cyst or suspicious mass: unilateral US
  - negative US: observe every 3-6 months, consider mammogram
    - simple cyst: observation or aspiration
    - complex cyst: mammogram, may need biopsy
    - solid mass: mammogram followed by further imaging or biopsy
- age over 30:
  - unilateral diagnostic mammogram and US (or bilateral if due)
  - followed by short-term follow-up or biopsy

B.) Mastalgia
- unknown etiology, may be hormonal
- more common in premenopausal women
- rarely a sign of breast cancer
- presentation:
  - cyclic pain: bilateral, poorly localized pain that is worse before menses
    - lasts 1-4 days then resolves spontaneously
  - noncyclic pain: unilateral, sharp, localized pain unrelated to menses that is present < 4 days a month
    - more common in ages 40-50
    - response spontaneously
    - can be associated with cysts or fibroadenomas
- pain may be worsened by menstrual irregularity and emotional stress
- investigation:
  - with no mass, those > 35 should get a mammogram if they haven’t had one in last year
  - majority of women will have negative exams and imaging and pain will resolve spontaneously
- treatment:
  - supportive bra
  - reduction of caffeine intake and avoiding sodium premenstrually
  - NSAIDs
  - evening primrose oil supplements
- severe, persistent pain (mastodynia) may require danazol, which suppresses pituitary gonadotropins
C.) Nipple discharge
- causes:
  - **intraductal papilloma**: benign growths within the ducts
    - presentation: can be palpable or associated with bloody discharge
    - investigation: ductogram
    - treatment: surgical excision
  - **ductal ectasia**: benign thickening and dilation of lactiferous duct than can lead to clogging
    - presentation: thick, sticky discharge (clear, brown, or green), itchy, red, or irritated nipple
    - treatment: warm compresses, antibiotics
  - fibrocystic changes
  - meds: OCPs, HT, psych, opiates
  - infection
  - malignancy
    - hyperprolactinemia: usually due to a benign process, only 2-3% will be due to malignant causes
    - presentation:
    - clear, yellow, white, or dark green
    - spontaneous bloody discharge associated with a mass that is unilateral in a woman over age 40 is suspicious for cancer
    - discharge only on compression with bilateral involvement is usually physiologic
    - investigation:
      - suspected physiologic discharge: breast exam and mammogram if > 35, prolactin levels
      - suspected pathologic discharge: diagnostic mammogram ± US, surgical excision of duct
    - treatment:
      - if discharge is physiologic, avoid stimulating nipple

D.) Breast abscess
- causes:
  - often mastitis from lactation
  - less commonly for other reasons: *Staph aureus*, insect bite, trauma, etc.
- presentation: red, tender, indurated, warm breast, palpable mass, systemic signs of infection
- treatment: antibiotics, I&D
  - often recurs, may need surgical evaluation
  - if no resolution, must consider inflammatory carcinoma

E.) Fibrocystic changes
- the most common benign condition of the breast
- usually happens during age 30-50
- related to menstrual cycle
- can be worsened by caffeine
- uncommon in postmenopausal women, unless on HT
- presentation: pain or tenderness that can be worse prior to menses, cysts, multiple transient painful lumps
- masses are firm, mobile, often tender
- bilateral, single, or multiple masses
- differentiate from malignancy or fibroadenoma by the multiple, transient lesions
- investigation:
  - mammogram or US for masses persistent throughout menstrual cycle
  - FNA or biopsy to exclude cancer
    - warning signs: no fluid or bloody fluid aspirated, mass persisting after aspiration
- treatment:
  - counseling to wear a supportive bra, avoid trauma and caffeine
  - danazol for severe, persistent pain
  - evening primrose oil

F.) **Fibroadenoma**: a common benign neoplasm in young women composed of fibrous and glandular tissue
the most common breast complaint
- hormonally influenced growth
- can be rapid during pregnancy
- occurs in teens to 30’s
- not seen post-menopause unless on HT
- more common in black women
- presentation: round, firm, nontender, mobile 1-5 cm nodules
- investigation:
  - in women > 30, need to consider fibrocystic condition or malignancy
  - US for younger women
  - FNA or needle biopsy for confirmatory diagnosis
- treatment:
  - observation after r/o malignancy
  - surgical excision if unable to r/o malignancy or mass is large
- prognosis: can recur after surgical excision

G.) Fat necrosis: benign inflammatory process as a result of trauma, radiation, or anticoagulation
- presentation: may have a mass, skin retraction, dimpling, ecchymosis, or tenderness
  - can be indistinguishable from malignancy
- investigation:
  - mammogram
  - US
  - biopsy if questionable
- treatment:
  - usually self-limiting

9.11 Female Breast Cancer

9.11.1 Background

- Usually arises from the ducts or lobules
- The most commonly diagnosed female cancer, with a 1/8 chance of lifetime diagnosis
- 2nd leading cause of female cancer deaths
- Most common in white women, but most deadly in black women
- Only 5-10% are due to genetic mutations
- Risk factors: obesity, inactivity, use of HT, nulliparity, first birth after age 30, > 1 alcoholic drink per day, not breastfeeding, increasing age, white, history of chest radiation, history of atypical hyperplasia on previous biopsy, FH breast cancer, inherited genetic mutations
- cancer incidence is NOT related to underwire bras, deodorants, antiperspirants, abortions, miscarriages, breast implants, breast injury
- as many as 75% of women diagnosed with breast cancer will have no obvious risk factors
- can assess risk with Gail model (less accurate for women of color), breast cancer risk assessment tool
- Prevention: avoid weight gain, regular physical activity, minimize alcohol intake, breastfeed, reconsider use of HT
- women with high risk can consider chemoprevention
  - tamoxifen for 5 years
    - reduces risk of invasive and in situ breast cancers by 40-50%
    - only effective for estrogen-R + cancers
    - side effects: DVT, PE, cataracts, hot flashes, endometrial cancer
  - raloxifene
    - reduces invasive estrogen-R + cancers as well as tamoxifen, but no effect on in situ cancer risk
    - better side effect profile
- Breast cancer screening:
  - mammography
    - less prevalent in women with lower education or no health insurance
USPSTF grade C for women 40-49
USPSTF grade B for women 50-74 every 2 years
US ± mammography
clinical breast exam
breast self exam
USPSTF grade D for teaching this to patients
dedicated breast MRI for high risk populations
Presentation:
early:
- single, nontender, firm mass with ill-defined margins
- mammogram abnormality but no palpable mass
later: skin or nipple retraction, axillary adenopathy, breast enlargement, erythema, peau d’orange, edema, pain, fixation of mass to chest wall
late: ulceration, supraclavicular adenopathy, arm edema, mets to bone, liver, lung, or brain
Investigation:
- biopsy
- pathology report: estrogen-R and progesterone-R status, HER-2/neu, nodes, etc.
- 21 genomic assay of tumor tissue
  - provides prediction of chemo benefit, 10 year recurrence risk
  - for individualization of treatments
Chemo is typically 3-6 months
initiated with visceral mets, failed endocrine therapy, or ER-/PR- tumors
can also be used palliatively for pain control with brain, skin, or spinal mets
side effects: cardiomyopathy, infertility, premature ovarian failure, neuropathy, fatigue, weight gain, leukemia or other myelodysplasia
Endocrine therapy:
adjuvant or palliative
duration varies
premenopausal □ tamoxifen
postmenopausal □ aromatase inhibitors
Surgical procedures:
lumpectomy:
  - similar outcomes when combined with radiation vs total mastectomy
  - may not be an option for larger tumors
modified radical mastectomy: removes entire breast and underlying fascia
  - evaluates axillary lymph nodes
lymph node assessment:
  - sampling & dissection: higher morbidity
  - mapping using dyes: less morbidity, faster recovery
reconstruction
  - implants
  - autologous tissue: TRAM using latissimus dorsi
  - can be immediate or delayed
Prognosis:
more favorable outcome with E/P+ tumors because they can be treated with endocrine therapies
HER-2+ tumors are more aggressive
factors influencing survival also include age at diagnosis, stage of disease, race/ethnicity, and SES
survivorship issues: lymphedema, weight management, cognitive changes, menopausal symptom management, bone loss, cardiac issues, fatigue, chronic pain, emotional issues

9.11.2 Types of Breast Cancer
A.) Carcinoma in situ: 80% are ductal, 20% are lobular
- not yet invaded surrounding tissue
- can be associated with occult invasive cancers
- presentation: microcalcifications on mammogram
• treatment: surgery ± radiation ± endocrine therapy
• good prognosis

B.) Invasive: ductal or lobular
• subtypes include medullary, colloid, tubular, papillary
• treatment: surgery, radiation, chemo, endocrine chemo

C.) Inflammatory:
• uncommon but aggressive
• presentation: mets, may look like infection, skin changes, erythema and edema
• prognosis:

D.) Paget's disease: manifestation on skin first
• rare
• usually corresponds to either invasive ductal or DCIS
• presentation:
  o itching, burning of nipple or areola with eczema-like changes or erosion
  o may or may not have mass
• treatment: surgical if caught early
• prognosis: good if there are no + nodes

9.12 Contraception

9.12.1 Background
• Contraceptive counseling
• decreases risk of unintended pregnancy
• must consider drug interactions, especially for patients with seizure disorders
• consider cost and insurance
• is STI protection needed?
• importance of preconception care
• emergency contraception methods
• Most common form of contraception is oral
• Effectiveness of contraception measured by the **pearl index**: failure index of # of unintended pregnancies per 100 women per year
• no contraception has an 85% failure rate/year
• Fertility
• greatest fertility time period is right before the LH surge
  o highest risk of pregnancy 1-2 days before ovulation, 30% chance
• time window is about 6 days per cycle
• sperm can survive inside the female for up to 5 days
• time from ovulation to implantation is about 7 days

9.12.2 Forms of Contraception
1.) Withdrawal: 4-27% failure rate
2.) Douche
3.) Fertility awareness methods: periodic abstinence, symptothermal, rhythm method, ovulation method, natural family planning
• relies on calendar rhythms, temperature change, and cervical mucus changes
4.) Barrier methods:
• spermicide: only manufactured kind available in US is nonoxynol-9
• natural alternatives: lemon juice, lactic acid, and neem oil
• available as a vaginal film, suppository, cream, gel, or lubricant
• no protection against STIs
can cause irritation and allergic reactions in men and women
  o can cause microchafing in females
  □ more prone to STIs
failure rate of 10-29%
costs $0.50 to $1.50 per application
cervical cap: silicone with no hormones that you fill up with spermicide
only one approved in the US is the FemCap
  o only one not associated with abnormal paps
requires prescription and fitting
can be inserted up to 24 hours before sex and can wear for up to 48 hours
no STI protection
increased risk of nonmenstrual toxic shock
failure rate of 7.6-14%
costs $89 plus exam and fitting
diaphragm: rubber that you fill up with spermicide
requires prescription and fitting
needs to be refit after pregnancy or weight changes
no STI protection
increased risk of UTIs, vaginitis, and nonmenstrual toxic shock
failure rate of 10-20%
costs $15-$75 plus exam and fitting
female condom: synthetic nitrile
failure rate of 5-20%
cost $2-$4 each
male condom: latex, polyurethane (more breakable), natural, or “spray on”
natural don’t protect from STIs
often lubricated with spermicide
may cause UTIs in female partners
failure rate 3-15%
cost $0.25-$2 each
sponge: polyurethane with nonoxynol-9
does not prevent STIs
cost $13-19 for 3

5.) Hormonal methods

***absolute contraindications to ALL estrogen-containing birth control: CHF, CAD, afib, mitral stenosis, mechanical heart valve without anticoagulation, smoker > 35, coagulation disorders, h/o DVT or PE without anticoagulation, dyslipidemia, diabetes with CAD or PVD, neurologic disease, known or suspected pregnancies, undiagnosed vaginal bleeding, known or suspected estrogen-dependent neoplasm, active liver disease or adenoma

***relative contraindications to ALL estrogen-containing birth control: HTN, diabetes without CAD or PVD, gall bladder disease, history of cholestatic jaundice in pregnancy, epilepsy, leg injury or cast, elective surgery, sickle cell, migraines, obesity, FH of CVD or coagulopathy

a.) combined oral contraceptive pills:
estrogen portion works by inhibiting ovulation (suppresses FSH surge), altering the endometrium, and causing degeneration of the corpus luteum (potentiates progestin activity)
progestin portion works by inhibiting ovulation (suppresses LH surge), thickening the cervical mucus, and hampering implantation
common myths: OCPs cause infertility, women over 35 shouldn’t take OCPs, they cause weight gain
yet progesterone can have an androgenic effect like testosterone and cause weight gain, hirsutism, and acne?
benefits: improved acne, dysfunctional uterine bleeding, dysmenorrhea, mittelschmerz, endometriosis, ovarian failure, ovarian cysts, uterine fibroids, fibroadenomas and fibrocystic breast disease, iron
deficiency anemia, bleeding associated with blood dyscrasia; decreased risk of ovarian and endometrial cancers, ectopic pregnancy, acute PID

- can help with perimenopausal symptoms like irregular bleeding and PMS
- side effects: nausea, vomiting, weight changes?, change in menstrual flow, spotting, breast changes, migraines, edema, rash (lactose allergy), melasma, depression (due to progesterone), decreased libido
- may increase risk of breast cancer?
- increased risk of benign liver tumors, worsening gallbladder problems, blood clots, stroke
- no protection against STIs
- no age limit as long as not smoking, can continue until menopause
- failure rate of 3-9%
- cost $15-$50 per month

b.) progestin-only oral contraceptive pills (minipill)
- less effective than combined OCPs, must take with obsessive regularity
- can have irregular bleeding
- a good option for breastfeeding women, smokers over 35, or those who can’t tolerate estrogen

c.) injectables: regular injections of ovulation inhibitors by a provider
- medroxyprogesterone acetate (Depo-Provera) available in US
- IM injection every 3 months
- highly effective method of inhibiting ovulation
- results in amenorrhea after a year or so of use
- benefits: good to use if a smoker or nursing, decreased risk of endometrial cancer and PID
- side effects: bleeding abnormalities, weight gain, lipid changes, depression, acne, headache, delay in return to fertility, increased risk of osteoporosis
- osteoporosis may not be reversible ⚠️ new black box warning
- related to duration of use = should only use > 2 years if there are no other options
- most concerning in adolescents and young adults
- no protection against STIs
- failure rate of 1-2%
- Depot costs $35-$75 per injection

d.) implantable rods: progesterone-only devices
- must be trained by company-approved provider to insert and remove
- good for smokers or those who have other contraindications to estrogen
- may be less effective in obese patients
- side effects: menstrual irregularity, amenorrhea, weight gain, acne, depression
- failure rate of 1-4%
- cost $400-$800 for insertion and $75-$150 for removal

e.) patches and intravaginal rings
- Ortho Evra is a progestin/ethinyl estradiol patch
- NuvaRing is ethonogestrel/ethinyl estradiol ring
- less effective for patients weighing > 90 kg
- same contraindications and risks as with other progesterone/estrogen products
- increased risk of venous thromboembolism over OCPs due to higher consistent estrogen blood levels ⚠️ new black box warning
- = use with caution in smokers of any age, and don’t use in smokers over 35
- failure rate of 1-2%
- costs $15-$70 a month

f.) emergency contraception:
- 8/100 women will become pregnant from a single act of unprotected sex
• emergency contraception reduces risk by 75-80% by suppressing ovulation and changing cervical mucus and endometrium
• formulations:
  o Plan B One-Step, Next Choice
    • not an abortifacient and won’t work if already pregnant
    • no evidence of teratogenic effects
    • best if initiated within 72 hours of unprotected sex, but can be taken up to 5 days after
    • rare side effects or risks, even in smokers
    • may need prophylactic antiemetics before taking
    • if given before ovulation, next menses will be early by 3-7 days
    • if given after ovulation, next menses will be on time or late
    • available without a prescription for age 17+
  o Ella (ulipristal acetate): a selective progesterone receptor modulator
    • prescription only
  o mifepristone (RU486)
    • use within 72 hours of unprotected sex
    • inhibits ovulation and changes endometrium
    • effective after implantation has occurred = abortifacient
  o Paragard-T IUD
    • insert within 5 days of unprotected sex
    • toxic effect on sperm and endometrial changes

g.) intrauterine device
• changes mucus and sets up a hostile environment for sperm
• not an abortifacient
• good option for women who can’t take estrogen or are unsure about sterilization
• questionable use in individuals at risk for STIs (issue of string harboring organisms)
• don’t need to remove with PID
• often used in later reproductive years before menopause
• failure rate of 0.5-1.5%
• costs $500-$1000
• brands:
  • Paragard: contains copper
    • can be in place for 10 years
    • benefits: decreased risk of cervical and endometrial cancer
    • side effects: heavy bleeding and cramping
  • Mirena: contains levonorgestrel
    • can be in place for 5 years
    • women may become amenorrheic after a year of use
    • benefits: less bleeding and cramping, no increase in lipids, no increased risk of breast cancer, improvement of anemia, can be used as alternative to hysterectomy in cases of menorrhagia, decreased risk of endometrial cancer, helps with tamoxifen-induced endometrial effects
    • side effects: increased risk of ovarian cysts

6.) Lactation
• most effective if infant is not taking any supplemental formula and mother is nursing at least every 4 hours
• failure rate of 10%

7.) Abortion
• medical abortion has 15% failure rate

8.) Sterilization
• tubal ligation
  • outpatient surgery under general anesthesia with recovery time of 1 week
benefits: decreased risk of ovarian cancer, and possible breast cancer, could be reversible, can be done immediately postpartum
- increased risk of ectopic pregnancy
- need to confirm blockage with hysterosalpingogram
- failure rate of 0.5%
- costs $1500-$6000
- procedures:
  - Essure: non-incision form of tubal ligation using small coils inserted to induce scarring
    - takes 3 months to work but is permanent
  - Adiana: material inserted into fallopian tubes and zapped with radiofrequency energy
    - takes 3 months to work
- vasectomy: cut and sealing vasa deferentia
  - clinic procedure under local anesthesia with recovery time of 2-3 days
  - men will still be fertile for several ejaculations afterwards; need to have a semen sample in one month for surgery to be deemed successful
  - failure rate of 0.15%
  - costs $350-$1000

9.13 Hormone Therapy

9.13.1 Background
- Oral hormone therapy:
  - 1st pass metabolism = need higher doses than systemic therapies
  - results in ↑ synthesis of hepatic proteins and enzymes (including clotting factors, CRP, SHBG, HDL)
  - higher estrone:estradiol ratio
- Systemic hormone therapy:
  - bypasses GI = no 1st pass metabolism = lower doses than orals
  - no effect on hepatic proteins & enzymes
  - more physiologic estrone:estradiol ratio
  - In a woman with a uterus using estrogen, a progestin must be given to prevent endometrial hyperplasia
  - possible exception of low-dose vaginal estrogen formulations
- Hormone therapy in the treatment of menopausal symptoms
  - HT is the most effective treatment for hot flashes!
    - an estrogen effect, progestins have no effect on this
  - HT is also the most effective treatment for urogenital atrophy symptoms such as vaginal dryness and dyspareunia, and also reduces symptoms of overactive bladder
    - vaginal estrogens best for these symptoms vs orals or transdermals
  - HT stabilizes osteoporosis or can prevent it from occurring
    - inhibits osteoclasts and increases calcium absorption
    - supports survival of osteoblasts
    - studies showed decreased risk of hip, vertebral, and arm fx
      - greatest benefit with > 5 years of therapy
      - max protection with > 10 years of therapy
- WHI study showed decreased risk of colorectal cancer with estrogen + progesterone
- WHI study showed that in older postmenopausal women, estrogen + progesterone (Prempro) resulted in increased risk stroke, blood clots, dementia, and breast cancer
- WHI study showed that in older postmenopausal women, estrogen alone (Premarin) resulted in increased risk of strokes, blood clots, and dementia
- North American Menopause Society position is that absolute known risks for HT in women 50-59 are low, but long-term HT or initiation in older women has greater risks
- side effects: breast tenderness, headache, irregular bleeding (↓ over time)
- Heart disease and HT:
• some studies show HT also reduces risk of coronary heart disease
• WHI study showed that HT was neutral in this category black box warning for all HT that it should not be used for prevention of CV disease, and HT should be prescribed at the lowest effective doses and for the shortest duration possible
• Indications for HT:
  • treatment of moderate to severe vasomotor symptoms associated with menopause
  • treatment of moderate to severe symptoms of vulvar and vaginal atrophy associated with menopause
  • prevention of postmenopausal osteoporosis in women at significant risk
• Estrogen contraindications: active breast cancer, estrogen-dependent neoplasia, undiagnosed abnormal genital bleeding, h/o thromboembolic disease, pregnancy, porphyria, active liver disease
• relative: h/o endometriosis, uterine fibroids, PMS, migraines, gallbladder disease, hypertriglyceridemia, seizure disorder, h/o endometrial or breast cancer
• Progestin contraindications: hypersensitivity to progestins, active thrombophlebitis, thromboembolic disorders, or cerebral hemorrhage, liver disease, breast or genital carcinoma, undiagnosed vaginal bleeding

9.13.2 Oral Estrogens
Formulations:
• conjugated equine estrogens (Premarin)
• most data here
• synthetic equine estrogens (Cenestin, Enjuvia)
• esterified estrogens (Menest)
• estropipate (Ogen, Ortho-Est)
• highest estrone:estradiol ratio
• micronized estradiol (Estrace, Gynodiol)
• estradiol acetate (Femtrace)

9.13.3 Vaginal Estrogens
• Background:
  • well-absorbed from the vagina
  • most appropriate for urogenital symptoms
• Formulations:
  • conjugated equine estrogens (Premarin)
  • estradiol (Estrace, Estring, Femring, Vagifem)
  • estropipate (Ogen)

9.13.4 Transdermal and Topical Estrogens
• Varied concentrations of estrogen delivered depending on product
• Patch formulations: Estraderm, Alora, Climara, Vivelle-Dot
• continuous venous delivery of estrogen
• may have application site reactions
• need to rotate application sites
• Topicals include gel, emulsion, spray formulations: Estragel, Elestrin, Divigel, Estrasorb, Evamist
• applied once a day
• issues with washing or bathing sites
• can transfer to others
• approved for vasomotor symptoms Progestins
A.) Oral progestins
• medroxyprogesterone acetate (Provera, Amen, Cycrin)
• norethindrone acetate (Aygestin)
• norethindrone (Micronor, Nor-QD)
• micronized progesterone in peanut oil (Prometrium)
B.) Transdermal progestins: no EBM that these provide endometrial protection in HT
• progesterone gel (Prochieve, Crinone)
• levonorgestrel IUD (Mirena)

9.13.5 Combine Hormone Therapy Regimens
1.) Continuous-cyclic administration: continuous estrogen with progesterone 2\textsuperscript{nd} ½ of month
   • may result in getting periods again
   • formulations: Premphase
2.) Continuous combined administration: continuous estrogen + continuous progesterone
   • formulations: Prempro, Activella, Femhrt, Combipatch, Angeliq, Climara Pro
3.) Intermittent combined administration: continuous estrogen with frequent blips of progesterone
   • formulations: Prefest
4.) Continuous estrogen with progesterone for 14 days every other month

9.13.6 Choosing Products for Management of Menopausal Symptoms
• Vasomotor ± urogenital symptoms:
  • if HT is contraindicated consider alternative therapies
    o ex. venlafaxine, paroxetine, megestrol acetate, clonidine, gabapentin
  • HT acceptable E+P in women with a uterus, E alone in women without a uterus
  • Urogenital symptoms only use vaginal estrogen product
• Asymptomatic woman but osteoporosis risk:
  o begin with Ca/vitD, exercise, bisphosphonate or raloxifene
  o if needed and benefits clearly outweigh risks, E+P or E alone
• Women with osteoporosis Ca/vit D, bisphosphate, denosumab, teriparatide, or calcitonin

9.13.7 Monitoring/Discontinuing HT
• Initial evaluation a few weeks after starting regimen
• assess menopausal symptoms, side effects, blood pressure, weight, compliance
• Re-evaluate every 3-6 months for possible taper or discontinuation
• No hard and fast rules about when to d/c

9.13.8 “Bioidentical” Hormones
• A marketing term denoting hormones that are plant-derived and similar or identical to those produced in the body
• used by some compounding pharmacies to imply that drugs are natural, or have effects identical to those from hormones made by the body
• How does it work?
  • you spit in a tube, send it off, and lab determines what hormones you are deficient in
    o problem: salivary hormone levels don’t correlate to tissue levels or symptoms
• compounding labs make products tailored to individual needs
  • problem: compounding pharmacies are not regulated by the FDA, good manufacturing practices are not enforced, adverse event reporting is not required, and products are not tested for purity, potency, safety, or efficacy
    o E3 is not approved in any form in the US, and the pharmacy needs to make sure prescriber has a valid IND
• Considered investigational or experimental by insurance companies, so it usually isn’t covered

9.13.9 Herbal Products for Menopause
A.) Soy isoflavones: low-level estrogenic activity
• may reduce hot flashes but no RCTs showing + effect
B.) Black cohosh
current trials
side effects: GI, headache, dizziness, CYP 3A4 inhibition
C.) Dong quai: not much data
D.) Evening primrose oil: no published evidence of symptomatic relief, may ↑ HDL
E.) Wild yam: no published evidence
F.) Vitamin E: recent studies show no improvement in vasomotor symptoms

9.14 Menopause

9.14.1 Background

- **Climacteric**: a phase in women transitioning from a reproductive state to a non-reproductive state
- extends for time period before and after perimenopause, and includes perimenopause
- **Perimenopause**: irregular cycles, heavy bleeding, clots, anovulatory cycles, variable length cycles, increased climacteric symptoms
- occurs ~4 years prior to menopause
- average age of 47.5
- women can remain fertile during this time
- **Menopause**: no menses for > 1 year
- different kinds of menopause exist
  - natural: permanent cessation of menstruation as a result of loss of ovarian follicle activity and ovarian estrogen secretion
  - no periods for 12 consecutive months
  - hard to evaluate by lab FSH/LH, no biological markers
  - induced: via surgery, radiation, or chemo
  - temporary: due to diet or GnRH analogues
  - premature: pathologic menopause before age 40, usually autoimmune, known as premature ovarian failure
  - late: after age 55
- average age of natural menopause in US is 51.4 years
  - not changing much over the years (in contrast to menarche)
  - occurs earlier with familial factors, current smoking, alcohol abuse, nulliparity, medically treated depression, h/o shorter adolescent menstrual cycles, h/o DM1, toxic chemical exposure, h/o pelvic childhood irradiation
  - delayed with multiparity, increased BMI, h/o OCP use
- labs:
  - FSH > 35
  - serum hormone levels will not correspond to symptoms
- **Postmenopause**: time period after cessation of menstrual flow for at least 1 year
9.14.2 Menopause Signs & Symptoms

- Symptoms begin several years before cessation of menses, and can last for 2-9 years after cessation of menses
- Symptoms have cultural variation
  - more pronounced in US
- Worsened by fear of aging as well as higher SES
- Ovarian function declines
- Ovaries produce less estrogen, progesterone, androstenedione, testosterone
  - secretion of androgens surpasses estrogen secretion
  - estrone begins to predominate over estradiol
- Increased LH and FSH production in response to low estrogen
- Loss of bone density at 1-2% per year • increased risk of hip and vertebral fractures
- Total cholesterol increases (↓ HDL and ↑ LDL) • increased risk of heart attack and stroke
- H&P findings
  - HEENT: dry hair, facial hirsutism, dry mouth, lower voice,
  - Gyn: menstrual irregularity, menorrhagia, postcoital bleeding, spotting
  - GU: loss of adiposity and collagen in vulva, loss of protective covering of clitoris, thinner vaginal surface, vaginal dryness and atrophy, genital itching or burning, dyspareunia, pale or shiny vaginal epithelium with petechiae and loss of rugae, sparse pubic hair, fusion of labia minora, introital stenosis, pelvic organ prolapse, vulvar dermatoses, vaginitis, ureterovaginal prolapse, cystoureteritis, stress incontinence, urinary frequency/urgency, decreased libido
    - urethral caruncle: benign, bright red urethral lesions seen in postmenopause
    - cystitis, UTIs, dysuria, urgency, and incontinence are NOT improved by HT
    - dyspareunia, vaginal dryness, and decreased libido are associated with decreased estrogen and androgens but won’t improve on estrogen therapy, need to use testosterone instead
- Neuro: hot flashes, vasomotor instability, sleep and mood disruptions
  - hot flashes: sudden onset of warmth and head pressure sensation followed up flushing and temperature elevation
    - not triggered by low estrogen alone, but also related to gonadotropins and altered hypothalamic control of temperature regulation
    - can be aggravated by caffeine, alcohol, hot drinks, eating, spicy foods, food additives, stress, fatigue, drugs, warm or humid climates
    - need to r/o hyperthyroidism, pheochromocytoma, carcinoid, diabetes, TB
    - can last up to 10 minutes
    - most severe during the first 1-2 years
    - usually stop within 5 years of menopause onset, but can continue to age 70+
• decrease incidence by dressing in layers, drinking a cold beverage at onset, using cotton sheets and clothing, regular exercise, relaxation techniques, and avoiding triggers
• other treatment options: estrogen replacement therapy, progestins, SSRIs, gabapentin, clonidine, supplements, biofeedback, acupuncture
  o mood changes: depression, fatigue, anxiety, difficulty concentrating, memory loss
  • Msk: back pain
  • Chest: reduced breast size and loss of ligamentous supports

9.15 Uterine Disorders

9.15.1 Leiomyomas (Uterine Fibroids):
• benign tumors arising from the myometrium
• Risk factors: black ethnicity, obesity, those > 40, nulliparity
• Protective factors: multigravida, postmenopausal, smoker, prolonged OCP use, Depo use
• Presentation: dysmenorrhea, dyspareunia, urinary frequency, infertility, irregular uterus, abdominal mass, bleeding, pelvic pressure or sense of fullness, pelvic pain, or asymptomatic
• acute pain associated with degeneration or torsion of a pedunculated fibroid
• symptoms depend on where the fibroid is
• Investigation:
  • US is diagnostic
  • can also do CT or MRI, and may show up on x-ray if calcified
  • endometrial biopsy is not helpful as fibroids lie below the endometrium
  • laparoscopy to visualize if needed
• Treatment:
  • usually not needed
  • myomectomy via laparoscopy or laparotomy
  • hysterectomy only for extremely large, painful fibroids with intractable bleeding
  • levonorgestrel IUD (Mirena) to decrease bleeding
  • menopause-mimicking treatments such as ulipristal
  • uterine artery embolization to starve off fibroids

9.15.2 Endometrial Polyps:
• usually benign outpouchings of the endometrium
• Presentation: abnormal bleeding, infertility
• Investigation: saline infusion sonogram
• Treatment: polypectomy

9.15.3 Endometriosis:
• location of endometrial tissue any place outside of the uterus
• May be due to “retrograde menstruation” where sloughed off endometrial tissue containing viable hormone cells escapes through the fallopian tubes to implant outside of uterus
• Could also be due to Mullerian cell remnants, lymphatic or vascular dissemination, direct surgical transplantation, altered immune system, genetics, or increased estrogen stimulation
• Usually occurs in the pelvis, but can occur in the ovary, cul de sac, uterosacral ligaments, round ligaments, posterior broad ligaments, fallopian tubes, bladder, rectum, bowel, cervix, vagina, omentum, umbilicus, vulva, ureter, spinal cord, nasopharynx, breast, lung, and kidney
• Most common in tall, thin, Caucasian patients ages 20-30 who have never had a child
• Also associated with early menarche and late menopause
• Genetic component
• Chronic
• Associated with estrogen and improved with suppression of ovulation
• Associated with epithelial ovarian cancer but NOT endometrial cancer
Presentation: a range of symptoms from nothing to debilitating pain, can be unpredictable
- dysmenorrhea
- dyspareunia
- pelvic pain (will be unrelated to degree of endometriosis)
- sacral backache
- pelvic mass
- tenesmus and diarrhea or painful bowel movements
- urinary frequency
- infertility: accounts for 30-50% of women with infertility
- PE: localized tenderness, palpable nodules, pain with uterine movement, painful adnexal masses, fixation of uterus in retroverted position cervix can have lateral displacement or have a stenosed os
- Investigation:
  - US or MRI can help: uterosacral ligament abnormalities, adnexal enlargement
  - laparoscopy needed for definitive diagnosis
    - implants will have variable appearance: black, blue, clear, papular, vesicular, flame-like, stellate, puckered, peritoneal defect
- Treatment:
  - first line is medical therapy
    - combined OCPs, NSAIDS for cyclical pain
    - progestins
    - androgens
    - GnRH agonists: for moderate to severe pain, create a stage of hypogonadotropic hypoestrogenism
      - only approved for use < 6 months
      - can create menopause-like side effects
    - on the horizon: anti-progestins, aromatase inhibitors, selective progesterone receptor modulators
  - acupuncture
  - surgical procedures if medical management fails:
    - excision if focal tenderness is present
    - hysterectomy with bilateral oophorectomy
    - ablation for superficial lesions: laser, electrosurgery, thermal
- Prognosis: recurrence is common

9.15.4 Adenomyosis:
- endometriosis within the muscle of the uterus
- Usually in ages 40-50
- Presentation: severe dysmenorrhea, menorrhagia, chronic pelvic pain
- Investigation:
  - similar symptoms to fibroids/endometriosis, so first rule these out then consider adenomyosis
  - MRI showing large, globular uterus
- Treatment: hysterectomy

9.15.5 Endometrial Hyperplasia:
- when proliferation of endometrial glands results in increased gland:stroma ratio
- Usually caused by chronic unopposed estrogen use
- other risk factors: age 50+, PCOS, DM, obesity, nulliparity, late menopause, tamoxifen use, HNPCC
- Complex hyperplasia with atypica increases risk for endometrial cancer
- Presentation: abnormal bleeding, postmenopausal bleeding
- Investigation:
  - US showing thickened endometrial stripe
  - biopsy for histology
- Treatment:
  - hysterectomy if atypica is present due to risk of progression to endometrial cancer
• no atypica treat with progestins to counter estrogen and cause endometrial sloughing
  o patients should expect massive, medically induced periods

9.15.6 Endometrial Carcinoma

• Most common gyn cancer in US
• Usually adenocarcinoma
• Estrogen-dependent and estrogen-independent varieties
• estrogen-dependent associated with younger, perimenopausal women with history of unopposed estrogen
  o unopposed estrogen can be medical or endogenous (not getting natural periods)
  o begins as endometrial hyperplasia atypia carcinoma
• estrogen-independent associated with thin, older postmenopausal women without h/o unopposed estrogen
  o atrophic endometrium
  o cancers are less well-differentiated
• Risk factors: postmenopausal, FH or h/o ovarian, breast, colon, or endometrial cancer, tamoxifen use, chronic anovulation, PCOS, obesity, estrogen therapy, prior endometrial hyperplasia, diabetes
• Presentation: abnormal bleeding, abnormal pap cytology
• Investigation:
  • transvaginal US to assess endometrial stripe
    o doppler flow if postmenopausal
  • endometrial biopsy
    o do regardless of stripe size if premenopausal
    o histology used for diagnosis
• D&C with hysteroscopy
• Treatment: depends on staging
• primary surgical treatment
  o total hysterectomy
  o bilateral salpingo-oophorectomy
  o node dissection
• adjunctive post-op radiation
• medroxyprogesterone for recurrence
• Prognosis:
  • estrogen-dependent has better outcome

9.16 Urinary Incontinence

9.16.1 Background

• Urogynecology: specialized practice of treating women with pelvic floor disorders
• including urinary incontinence, pelvic organ prolapse, and fecal incontinence
• Causes:
  • detrusor laxity or overactivity
  • outflow obstruction forceful detrusor contractions
    o ex. prostate enlargement: symptoms of weak stream, dribbling, frequent need to urinate, straining, recurrent UTIs, acute urinary retention from stretching bladder out, bladder calculi, atonic bladder, hydronephrosis
  • loss of bladder-urethral angle pelvic prolapse
  • cystocele
    o symptoms of pressure in vagina, bulging at introitus, feeling of incomplete bladder emptying, incontinence, UTIs
  • pelvic floor musculature laxity: as in obesity, childbearing
  • suprasacral spinal cord lesions
    o urge incontinence: MS, Parkinson’s, stroke
    o atonic bladder: diabetes
    o normal pressure hydrocephalus
spinal cord injury

- peripheral lesions: DM, AIDS
- surgical

Reversible causes: delirium, infection, atrophic urethritis/vaginitis (give estrogen cream), pharmaceuticals, psychological, excessive urine output from vol overload, restricted mobility, stool impaction (presses on urethra to prevent voiding), drugs

- drugs causing overflow incontinence: anticholinergics, antidepressants, antipsychotics, sedatives, antihistamines, inhaled respiratory drugs, Parkinson’s drugs
- drugs causing urinary retention: narcotics, alcohol, Ca channel blockers, alpha adrenergic blockers
- drugs causing functional incontinence (can’t get to the bathroom in time): diuretics, caffeine, alcohol, sedatives
- cause depressed central inhibition of urination

9.16.2 Types of Incontinence

A.) Stress incontinence: involuntary loss of urine concomitantly with increased intra-abdominal pressure sufficient to overcome urethral pressure without an associated bladder contraction

- causes: childbirth, pelvic floor weakness, chronic valsalva (smoking, cough, chronic constipation), aging, estrogen deficiency
- contributing factors: short urethra, decreased urethral closure pressure, internal organ prolapse, urethral hypermobility, intrinsic sphincter deficiency
- a failure to store urine
- presentation: loss of urine when coughing, sneezing, laughing, or changing position, no leakage when supine, sensation of heaviness in the pelvic region, low PVR
- can be asymptomatic or masked with concomitant pelvic organ prolapse (causes kinking which prevents the stress incontinence from leaking out) = can appear after surgical reduction of prolapse

- treatment:
  - nonsurgical:
    - topical estrogens if due to atrophic vaginitis
    - Kegels
    - biofeedback
    - weight loss of obese
    - injection of bulking agents around urethra
    - pessary to hold up a prolapse
  - surgery: sling procedures (tension-free vaginal tape is outpatient), anterior vaginal repair

B.) Urge incontinence: involuntary loss of a large amount of urine preceded by the intense feeling of having to void but without sufficient warning

- due to detrusor overactivity or sphincter dysfunction, or secondary to inflammatory conditions or neurologic disorders
- a failure to store urine
- presentation: need to void comes too quickly to reach the toilet, large amount of urine, frequent voiding, loss of urine with sound of running water or waiting to use the toilet or getting to the front door, unrelated to position or activity, normal PVR, nocturia

- treatment:
  - behavioral: fluid restriction after 6pm, frequent voids to retrain bladder, timed voids, relaxation techniques, decrease irritants (caffeine, alcohol, cigarettes, chocolate, acidic or spicy foods, oranges, pineapple, plums, apples, cranberries, onions, tomatoes, peppers, chilies, aged cheese, sour cream, yogurt, rye, sourdough, vinegar, walnuts, peanuts)
  - Kegel exercises
  - PT: pelvic floor muscle training
  - med
  - bladder relaxants: antispasmodics, anticholinergics like oxybutynin (newer ones have no added benefit)
  - posterior tibial nerve stimulation: 12 weekly sessions @ 30 min each
  - surgical: artificial urinary sphincter, other procedures
  - Botox injections or sacral nerve stimulation for refractory cases
C.) **Mixed incontinence:** stress + urge

D.) **Overflow incontinence:** continuous or persistent urine loss through day and night due to chronic urine retention
- causes: urethral blockage, enlarged prostate, urethral strictures, cystocele, stool obstruction, anococntral bladder (DM), neurogenic bladder (spinal cord injury or MS), anticholinergics
- symptoms: incomplete emptying of bladder, dribbling of urine, painful abdomen, unawareness of urine loss
- large PVR = failure to empty bladder
- treatment:
  - alpha blockers to relax bladder neck
  - treat BPH: 5-alpha reductase inhibitors
  - prostate resection
  - balloon dilation of urethra
  - Crede method
  - indwelling, intermittent, or suprapubic catheter
  - scheduled toileting

E.) **Functional incontinence:** inability to toilet due to cognitive impairment, physical disabilities, psychological problems or environmental barriers
- treatment:
  - reschedule meds
  - decrease use of sedatives, alcohol, anticholinergics
  - easy access to toilet, urinal, or bedside commode
  - easy to remove clothing
  - scheduled or prompted toileting

F.) **Extraurethral incontinence:** caused by fistulas
- most commonly seen after surgery, hysterectomy, or long labors
- now less common in the US

9.16.3 Urinary Incontinence Investigation:
- History
- PE: cough stress test, assessment for pelvic organ support
- look for cystoceles, rectoceles, uterine prolapse
- Labs:
  - -UA
  - -urine culture
- Urodynamic testing:
  - determines how well the bladder empties, if bladder filling is associated with normal sensation, if leakage occurs with cough/strain, if leakage occurs with bladder contraction, if there are structural abnormalities of the bladder wall or urethra
- want to reproduce symptoms to be able to direct therapy
- Voiding diary
- Weights of used pads
- Pyridium testing: turns pee bright orange so you can see when you are incontinent

9.17 Induced Abortion and Management of Early Pregnancy Loss

9.17.1 Background
- **Induced abortion:** deliberate termination of pregnancy
- **Missed abortion:** when embryo or fetus dies in utero but products of conception are retained
- presentation: fever, flu-like symptoms, leukorrhea
- Signs of possible miscarriage
- bleeding or abnormal discharge
• abdominal pain
• Normal pregnancy
• feeling like you are going to get your period (Braxton-Hicks contractions)
• Getting a patient to say yes to a pregnancy test
• calling it “routine”
• assuring that you have their best interests in mind
• Counseling for unplanned pregnancy
• this must be a shock for you, since you were not expecting this today, but you don’t need to make a decision today
• I don’t want you to feel abandoned, and I want you to be able to reach me with questions later
• know your community resources!
  o location of resources
  o cost of procedures
  o housing for pregnant mothers
• always have a follow-up appointment
• Legal aspects of induced abortion
• states regulate induced abortion after 3 months
  o North Carolina is 20 weeks
  o can refuse to allow abortion after viability
• Evaluation of patient requesting abortion
• make sure they are really pregnant
• med/surg history for anatomic considerations, pre & post-op considerations, bleeding disorders, etc.
• do STI testing to prevent introduction of disease to uterus during instrumentation
• get a current pap
• labs: hematocrit, Rh status
• may need prophylactic antibiotics

9.17.2 Abortion Procedures

• Background:
• same methods used to remove products from missed abortion
• complications of all procedures include vasovagal reaction, retained products of conception, uterine perforation, cervical injury, incompetent cervix, pelvic infection, hemorrhage, hematoma, DIC
• earlier induced abortions are safer
  o risk of death increases by 38% for each additional week of pregnancy
• pain management:
  o nonmedical: environment, operator technique
  o paracervical block
  o anxiolytics
  o conscious sedation in certain cases
• Methods for induced abortion:
• suction curettage: progressive metal or osmotic dilators are used, followed by suction and sometimes light instrument curettage
  o no anesthesia necessary
  o less blood loss
  o lower risk of uterine perforation, synechiae, or Asherman’s syndrome
• surgical curettage: metal or osmotic dilation followed by sharp curettage with metal instruments
  o results in slower evacuation of uterus
  o not the standard of care d/t greater risk of trauma
  o requires more anesthesia
• manual vacuum aspiration: not done frequently in US
• medical abortion:
  o patient must sign agreement
  o FDA approved regimen:
    • for women less than 49 days since LMP
    • mifepristone given on day 1, followed by misoprostol on day 3
• follow up on day 14 with US
  o non-approved regimen for up to 63 days since LMP

9.18 Ovarian Disorders

9.18.1 Background

• During pregnancy, corpus luteum continues to secrete progesterone until placenta grows large enough to take over
• Benign adnexal masses include:
  - serous of mucinous cystadenoma
  - endometrioma: chocolate cyst
  - leiomyoma
  - tubo-ovarian abscess
• non-gyn inflammatory conditions such as appendiceal or diverticular abscess
• pregnancy related mass: ectopic, theca lutein cysts, luteoma, corpus luteum of pregnancy

9.18.2 Functional Ovarian Cysts:

• exaggerations of normal processes (rather than true neoplasms) that are associated with the menstrual cycle
• Background:
  - aka physiologic ovarian cysts
  - common
  - must be differentiated from malignancy
  o PE:
    ▪ probably benign: mobile, cystic, unilateral, smooth
    ▪ possibly malignant: fixed, solid, bilateral, nodular
  o US:
    ▪ probably benign: < 10 cm, minimal septations, unilateral
    ▪ possibly malignant: > 10 cm, solid, multiple septations, bilateral, ascites
• usually regress spontaneously
• Types:
  - follicular cysts: from continued growth of follicle after failed ovulation
    o can occur in women receiving fertility treatments
    o presentation: can be asymptomatic
      ▪ may be felt on exam
      ▪ can rupture and cause pelvic pain
    o investigation:
      ▪ refer for US to look for free fluid in cul de sac
  - corpus luteum cysts: occurs when corpus luteum fails to involute and continues to enlarge after ovulation, secreting progesterone
    o presentation: adnexal enlargement, one-sided pain, missed menses
  - theca lutein cysts: associated with abnormal pregnancy
    o uncommon
• Treatment: only if recurrent or symptomatic
• OCPs can be used to prevent new cysts but won’t help with existing cysts
• Prognosis: risk of torsion if large or pedunculated

9.18.3 Non-Functional Ovarian Cysts:

• not associated with ovulation

A.) Dermoid cysts (teratoma): contains developmentally mature skin complete with hair follicles and sweat glands, sometimes clumps of long hair, and often pockets of sebum, blood, fat, bone, nails, teeth, eyes, cartilage, and thyroid tissue
• presentation: asymptomatic, unilateral cystic adnexal mass that is mobile, nontender, and often high in the pelvis
• treatment: surgical excision

B.) Endometrioma (chocolate cyst): related to endometriosis

C.) Serous or mucinous cystadenomas

9.18.4 Polycystic Ovary Syndrome:
• complex, heterogeneous disorder of uncertain etiology, but there is strong evidence that it can to a large degree be classified as a genetic disease
• Presentation: oligo or amenorrhea, obesity, infertility, hirsutism, acanthosis nigricans, acne, insulin resistance, DM2, HTN, hyperlipidemia, CV disease, sleep apnea, nonalcoholic steatohepatitis, infertility, depression, dysfunctional uterine bleeding, endometrial hyperplasia or carcinoma
• Investigation:
  • screen for mood disorders
  • labs:
    - glucose and lipids for metabolic abnormalities
    - total and free testosterone
    - DHEA-5
    - HCG, TSH, FSH to r/o other disorders
• pelvic US
• Treatment:
  • obesity □ weight loss, metformin, bariatric surgery
  • insulin resistance □ metformin, thiazolidinediones
  • androgen excess □ OCPs with minimal androgenic activity, spironolactone, hair removal, skin and acne treatments
  • amenorrhea or dysfunctional uterine bleeding □ OCPs, medroxyprogesterone for withdrawal bleeding if contraception is not needed
  • infertility □ clomiphene, aromatase inhibitors, gonadotropin therapy
  • endometrial protection □ OCPs with intermittent progestin

9.18.5 Ovarian Cancer
• Most arise from the epithelium
• 2nd most common gyn cancer
• Leading cause of gyn cancer death (overall 5th cause of cancer deaths in women)
• Risk factors: repeated ovulation (early menarche and late menopause), nulliparity, infertility, PCOS, genetic mutations, endometriosis, obesity, h/o breast cancer
• protective: OCPs, multiparity, tubal ligation, breastfeeding
• Presentation:
  • symptoms can be vague!
  • pelvic pain, bloating, urinary tract symptoms
  • clothing getting too tight
  • enlarging abdomen
  • palpable adnexal mass
• Investigation:
  • must do rectovaginal exam
  • US with Doppler blood flow: helps differentiate malignant vs benign
  • labs: CA-125
  • CT/MRI
• Treatment:
  • total abdominal hysterectomy: not laparoscopic, need to examine entire abdomen for mets
  • bilateral salpingo-oophorectomy
  • surgical staging
  • chemo
• Prognosis: varies by stage
  • early: 76% to 93% 5-year survival
  • late: ~11% 5-year survival
10 Hematology Exam Notes

10.1 Red Cell Disorders & Neutropenia

10.1.1 RBC & WBC Background & Diagnostic Methods

Background

- Cells
- RBCs
  - structure:
    - biconcave
    - any rigidity □ lysis
    - each RBC contains hemoglobin to transport oxygen and CO2
  - hemoglobin types:
    - HbA: normal majority adult; tetramer of α2β2 chains
    - HbA2: minority (1-2%) of adult Hb, tetramer of α2δ2 chains
    - HbF: fetal Hb, majority of Hb until age 1, then HbA takes over
      - normally makes up <1% of adult Hb
    - anemia: when an underlying disease causes a decrease in hemoglobin and/or hematocrit
      - normal hemoglobin ~ 12-17
      - normal hematocrit ~ 35-49%
      - pregnancy normally lowers Hb/Hct because increased plasma volume dilutes RBCs
  - mature cells last 120 days
    - damaged or old RBCs removed by liver & spleen
    - globin, heme, Fe recycled
  - morphologies
    - anisocytosis: presence of variation in RBC size
    - poikilocytosis: variation in shape of RBCs due to deformity or damage
    - schistocytes: RBC fragments due to mechanical injury
    - normochromic: normal Hb
    - hypochromic: low Hb, visualized as increased pallor in cell center
- WBCs
  - last 6-8 hours
- Platelets
  - last 7-10 days
- Processes
  - hematopoiesis: formation of all blood cell components
    - normally coordinated with RBC turnover
    - stresses such as illness, altitude, exercise, and bleeding cause increased production
  - erythropoiesis: formation of RBCs
    - low O2 deliver □ release of kidney erythropoietin (EPO) □ stimulation of erythropoiesis in bone marrow
      - liver is also a small source of EPO in dialysis or nephrectomy patients
    - requires adequate Fe, folate, B12 supply
    - takes 5-6 days to mature RBCs with EPO (would take 30-40x longer otherwise)
      - immature RBCs are blast cells and should only be seen in the bone marrow
      - nucleated RBCs are seen in the final stage of red cell production prior to expelling their nucleus
      - "nucleated RBCs are only released from the bone marrow in times of extreme stress"
    - loss of nucleus □ reticulocyte: immature RBC that has not yet completely lost its ribosomal RNA
      - usually only makes up < 2% of circulating cells
      - exhibit basophilic stippling (residual bands of RNA) upon staining
- in circulation in blood 1-2 days before fully mature

- **Tests**
  - **Reticulocyte count:** usually expressed as a % of total circulating RBC, but in anemia you must make a correction because the decreased # of circulating cells will falsely increase the % retics: \( \text{corrected retic count} = \frac{\text{observed # retics} \times \text{hematocrit}}{\text{avg normal hematocrit}} \)
    - -avg male = 45, avg female = 35
  - **Complete blood count:**
    - - **red cell indices:** calculations that allow characterization of average size & Hb content in individual RBCs
      - mean corpuscular volume (MCV): average size of the RBCs
        - direct measurement or calculation
          \( \text{MCV} = \frac{\text{hematocrit}}{\text{RBC count}} \times 1000 \)
        - falsely normal MCV if cells are widely varied in size, examine smear instead
        - reticulocytes are larger, therefore a larger fraction of reticulocytes will result in a greater MCV?
    - mean corpuscular Hb (MCH): reflects Hb content of RBCs; automated counter gives you the numbers for the calculation
      - \( \text{MCH} = \frac{\text{Hgb} \times 10}{\text{RBC}} \)
    - mean corpuscular Hb concentration (MCHC): indicates mismatch ratio between Hb:hematocrit
      - normally 1:3
      - not often used clinically
      - \( \text{MCHC} = \frac{\text{Hb} \times 100}{\text{hematocrit %}} \)
    - red cell distribution width (RDW): index of RBC size variation
      - higher the RDW, the greater the size variation
      - contributors: abnormally small/large cells, post-transfusion, fragmentation/deformities
  - **WBC count:** given as a total and as a differential
    - typically automated but can be done manually by counting a peripheral smear
    - manual better for identifying immature or abnormal cells
    - **left shift:** increase in banded neutrophils from acute bacterial infection
    - **leukopenia:** decreased WBC in viral infection, radiation, chemical exposure, drugs
    - **leukocytosis:** increased total WBC count, bacterial disease or leukemia
    - **leukemoid reaction:** extreme high WBC count, looks leukemic but is actually caused by severe infection, resolves with treatment

- **Iron studies**
  - - **serum iron:** concentration of serum Fe
  - - **total iron binding capacity (TIBC):** measures the blood's capacity to bind iron with transferrin
  - - **serum ferritin:** measures ferritin, a protein for intracellular storage of Fe to be released in times of shortage
    - concentrated in liver, spleen, and bone marrow
    - ***anemias associated with chronic illness have a false high or normal ferritin because ferritin is elevated in its capacity as an acute phase protein and not as a marker for iron overload
    - anemias associated with iron deficiency have low ferritin

- **Peripheral blood smear**
  - normal WBCs to see:
    - segmented neutrophils: 53-79% of WBCs
    - banded neutrophils (immature)
    - lymphocytes: 13-46% of WBCs
      - increased in acute viral infections
    - monocytes: 3-9% of WBCs
      - increased in chronic infections or recovery from acute infections
- eosinophils: 0-4% of WBCs
  - higher in parasitic infections
- basophils: 0-1% of WBCs
  - higher in CML
  
  **abnormal:**
  - plasma cells
  - abnormal neutrophil inclusions:
    - Auer rods: narrow rod in lymphoblast, suggests AML
    - Dohle bodies: blue irregular patch on edge of neutrophil, suggests infection
    - toxic granulation: prominent granules in neutrophils seen in severe infection & toxic states
    - neutrophil hypersegmentation: 6+ lobes in neutrophils, seen in megaloblastic anemia, B12/folate anemia, myeloproliferative disorders
  - vacuoles in monocytes and neutrophils suggest sepsis
    - clustered bacteria within the vacuoles suggest tickborne erlichiosis
  - pleomorphic lymphocytes suggest EBV infection
  - intracellular fungus may be *Histoplasma*

- **Absolute neutrophil count:** normally 4,800-10,800 cells/µL
  
  \[ \text{WBC} \times (\% \text{ PMNs} + \% \text{ bands}) \]
  - immunocompromised if <1000

- **Bone marrow aspiration:** liquid marrow sucked out
- **Bone marrow biopsy:** larger needle inserted to take out core
- **Lymph node biopsy:** removal of sentinel node

### H&P of Anemias

- PMH of autoimmune disease, malignancy, renal/liver disease, CAD, HTN, organ damage from diabetes, malabsorption or bleeding in GI
- Surgical history of gastrectomy or bowel resection ⊗ impaired absorption
- History of bleeding from menorrhagia, pregnancies, surgeries, melena or hematochezia
- Drugs such as antibiotics, phenytoin, OCPs, chemotherapy, ASA, NSAIDS, anticoagulants
- Exposures to lead or benzene
- Physical exam signs of anemia: jaundice, ankle ulcers, nail changes, pallor, petechiae, palm creases, lead lines, bone pain, pathologic fractures, hypotension, tachycardia, lymphadenopathy from malignancy-associated anemias, splenomegaly, hepatomegaly, peripheral neuropathy, glossitis, gum changes, blood in stool

### Anemias: Production Problem vs Destruction Problem

- Can usually distinguish via reticulocyte count
- Increased retics means body is responding to anemia by trying to increase RBCs
- Usually 90% of anemias are a production problem = typically low retic count
- Ex. B12 deficiency, Fe deficiency, lead poisoning
- Further categorize based on mean corpuscular volume
  - All nutritional anemias will begin as normocytic then progress to micro or macrocytic
  - Microcytic: MCV <80
    - Low Hb content makes cells small
  - Normocytic: MCV 80-100
  - Macrocytic: MCV >100
    - Due to impaired division of RBC precursors in the bone marrow

- Remaining 10% of anemias are a destruction problem = typically high retic count
- Bone marrow can’t compensate for blood loss or destruction
- Can be intrinsic destruction (intracorpuscular) or extrinsic destruction (extracorpuscular)
- Ex. trauma, RBC membrane abnormality, autoimmunity against RBCs, intravascular hemolysis, hemoglobinopathy, hemorrhage compensatory mechanisms dilute RBCs
***Categorization is not always hard and fast! MCVs and retic counts can vary within an anemia category, especially if hemolysis is involved.

10.1.4 Microcytic Anemias: MCV < 80

A.) Thalassemias: inherited defective production of globin chains; can also be interpreted as an intrinsic hemolytic anemia (explains why retics are high when other microcytic anemias have low retics)

- **Alpha thalassemia**: gene deletion decrease or absence in α globins
- mostly in southeast Asian, Mediterranean, or African descent
- severity of disease depends on how many of the four α genes are deleted
  - **HbH disease**: most severe viable form, with unstable Hb and chronic microcytic hemolytic anemia pallor, splenomegaly
    - investigation: abnormal peripheral smear, elevated retic count due to chronic hemolysis?
    - treatments: splenectomy, folic acid, avoidance of Fe, oxidative drugs to avoid hemolysis
  - **A-thal trait**: mildest form with nearly normal erythropoiesis, some mild microcytic anemia normal life expectancy & normal clinical presentation under non-stressful conditions
    - investigation: a diagnosis of exclusion, Hb electrophoresis normal
- **Beta thalassemia**: gene mutation decrease (B^+) or absence (B^0) in β globins
- mostly in Italians, Greeks, Asians, Africans
  - body can compensate by increasing % of HbA2 and HbF
  - excess iron accumulates due to enhanced iron absorption produced by thalassemia, repeated blood transfusions or both
  - all forms have microcytosis with varying degrees of anemia
    - **thalassemia major (Cooley’s anemia)**: homozygous B^0, severe chronic hemolysis jaundice, hepatosplenomegaly, anemia, transfusion dependent, Fe overload, bony abnormalities from hemolysis within BM, chipmunk face, growth retardation
      - investigation: Hb electrophoresis is predominant HbF
      - treatments: transfusion, folate, splenectomy
    - Fe chelation therapy
      - IV or SC deferoxamine (Desferal)
        - possibility of infusion rxn, must be observed for initial dose
        - urine will be orange
        - must initially check Fe levels in 24 hour urine
        - can use in ambulatory infusion pump
        - ascorbic acid needs to be initiated 1-2 months after chelator starts to help excrete the chelated iron
        - also has risks of iron-related cardiac toxicities
      - oral desferasirox (Exjade) is very $$$ and complicated
        - black box: may cause renal/hepatic problems or GI hemorrhage = need to check creatinine clearance, serum transaminases, and bilirubin while on
        - contraindicated with low platelets or poor CrCl
      - cure with allogeneic BMT
      - prognosis otherwise is life expectancy < 20 years
    - **thalassemia intermedia**: homozygous B^+, moderate chronic hemolysis, anemia, occasional transfusions in stress, Fe overload
      - investigation: Hb electrophoresis is HbA2 and HbF
    - **thalassemia minor**: heterozygous, mild anemia, rare transfusions
      - investigation: Hb is mostly normal, with a bump in HbA2 or HbF
B.) Iron deficiency anemia: not enough Fe to make Hb due to decreased intake (diet), decreased absorption (gastric, Celiac disease), increased loss (bleeds, HD, blood donation, malignancy, chronic aspirin use), or increased needs (growth spurts, pregnancy, lactation)

***Fe deficiency in an adult is due to blood loss, likely GI, until proven otherwise!
- normally iron is stored in WBCs, intracellular ferritin, and intracellular hemosiderin in macrophages
- clinical presentation: fatigue, DOE, tachy, cheilosis (cracked corners of lips), spoon-shaped nails, dysphagia d/t webbing of esophagus, pica
- investigation:
  - staging based on length of deficiency:
    - iron store depletion anemia: low iron storage in ferritin but normal iron levels
    - iron deficient erythropoiesis: low ferritin, no marrow ferritin, body iron levels changed, mild normocytic anemia
    - iron deficient anemia: low ferritin, abnormal iron indices, microcytic anemia, abnormal peripheral smear with anisocytosis, maybe increased platelets
- treatment:
  - treat blood loss
  - PO ferrous sulfate supplement with stool softeners
  - consider parenteral iron by hematologist if oral therapy is not tolerated or rapid enough
    - iron dextran (INFeD or Dexferrum) has lower risk of anaphylaxis
      - requires test dose with 60 min observational period
      - then IV does is administered over 4-6 hours or given during dialysis
      - can also be given IM Z-track style to avoid leaching of heavy Fe
    - sodium ferric gluconate complex (Ferrlecit)
      - administered IV or in dialysis
    - iron sucrose injection (Venofur)
      - for use in renal failure pts
- follow-up: check CBC in 3-4 weeks, check ferritin in 8 weeks, continue PO supplement 3-6 months post hemoglobin recovery
- failure to recover after supplementation is often due to poor compliance

C.) Chronic inflammation anemia: usually from reduced erythropoietin stimulation of bone marrow in liver disease, acute/chronic infection like HIV/RA/lupus, hypothyroidism, renal disease from DM or HTN, malignancy
- clinical presentation: mild to moderate anemia, severe anemia in liver disease, symptoms appropriate to underlying disease process
- investigation: microcytic or normocytic, normal peripheral smear, normal retics, low serum Fe, low serum TIBC, normal or artificially elevated ferritin, normal marrow Fe, low EPO
- another disease of exclusion!
- treatment only if pt is symptomatic
- treat underlying cause
- treat Fe, folate deficiencies
- EPO injections ($$$), require adequate iron stores
  - epotin alfa (Procrit or Epoagen)
  - darbepoetin alfa (Aranesp): longer half life, so less frequent injections
- transfusions if severe (minimize to reduce iron overload)

D.) Sideroblastic anemia: enzyme disorder in which the body has enough Fe but can’t make it into Hb accumulation of Fe in mitochondria defective heme synthesis
- inherited, acquired, or idiopathic
- alcohol, lead, myelodysplasia, leukemia, TB, drugs
- clinical presentation: only anemia symptoms (fatigue, pallor)
- investigation: mild-moderate anemia, normocytic or microcytic, high serum Fe
- BM biopsy: ringed sideroblasts (immature erythrocytes containing Fe granules), Fe stains are increased
- treatment based on cause
• acquired = remove offending agent and anemia should resolve
• rule out malignancy
• acquired/idiopathic: transfusions, PRN chelation, vitamin B6

10.1.5 Macrocytic Anemias: MCV >100

Minor causes: inherited disorders, GI surgery/illness, alcoholism, thiamine-responsive anemia, reticulocytosis, hypothyroidism, dietary deficiency, chemotherapy, erythroleukemia, liver disease, Lesch-Nyhan syndrome, splenectomy

Major causes:

A.) Vitamin B12 deficiency: insufficiency of nutrient found only in animal products
• background:
  • normally binds with intrinsic factor in the stomach to be absorbed and stored in the liver
    o liver holds 3 years of storage
  • inadequate intake in vegans
  • inadequate absorption in pts with decreased production of intrinsic factor (pernicious anemia), disorder of ileum, fish tapeworm (competition for B12), taking certain drugs
  • clinical presentation: glossitis, pallor, anorexia, diarrhea, peripheral neuropathy
  • decreased vibration and position sensing
  • stocking-glove paresthesias: abnormal sensations in the hands and feet
  • abnormal balance and dementia
  • investigation: macrocytic, severe anemia, thrombocytopenia, leukopenia, hypersegmented neutrophils on peripheral smear, decreased retic count, low serum B12
  • can also do assays for autoimmune antibodies
  • treatment:
    • oral B12 supplements
    • parenteral
      o IM B12 injections for life with initial front loading
    • nasal spray available
    • follow-up: normal CBC in 2 months

B.) Folic acid deficiency: insufficiency of folate found in fruits and vegetables
• background:
  • body stores a few months of folate
  • caused by inadequate diet, increased requirements (HD), malabsorption, impaired metabolism
    o acalcoholics impaired hepatic function impaired folate metabolism
  • clinical presentation: malnourishment, diarrhea, cheilosis, glossitis, NO neuro symptoms
  • investigation: labs similar to B12 deficiency but show normal levels of B12
  • diagnostic: low RBC folate
  • don’t rely on serum folate which can fluctuate
  • treatment:
    • oral folic acid with initial front loading (indefinitely if anemia is hemolytic)
  • follow-up: anemia should correct in 1-2 months

10.1.6 Normocytic Anemias

A) Pure red cell aplasia: idiopathic or autoimmune-mediated by CD8 cells or IgG against erythroid precursors
• associated with thymoma, lymphoma, lupus, CLL, viral infections, phenytoin
• clinical presentation is general severe symptoms of anemia
• investigation: low or no retics, normal RBC morphology, platelets/WBCs unaffected, normal BM with absence of erythroid precursors
• treatment: end offending meds, treat malignancy, immunosuppression therapy
• if viral, high dose of Ig
B.) Aplastic anemia: from bone marrow failure due to injury or suppression of HSC

- background:
  - most common in young adults or those over 60
  - causes: idiopathic, phenytoin, sulfas, chemo, radiation, chemicals (benzene, solvents, insecticides), viruses, pregnancy
  - can be hereditary as Fanconi’s anemia (diagnosed in childhood)

- clinical presentation: abrupt onset, fatigue, weakness, dyspnea, excess bleeding & bruising, petechiae, purpura, pallor, infections

- absent: hepatosplenomegaly, lymphadenopathy

- investigation: pancytopenia, severe anemia, decreased retics, normal morphology, reduced cells in BM
  - distinguish from MDS or acute leukemia which will have abnormal cells in BM
  - distinguish from hairy cell leukemia which will have splenomegaly and abnormal cells in BM
  - distinguish from normocellular marrow with plain pancytopenia which will have systemic lupus erythematosus, hypersplenism (increased activity of the spleen), and disseminated infection

- treatment based on severity of disease
  - no treatment if mild
  - if severe, BMT or immunosuppression

- prognosis: untreated is rapidly fatal

10.1.7 Hemolytic Anemias: RBCs destroyed sporadically or continually

- Classified based on whether RBC destruction is a result of intrinsic abnormalities of the RBC or extrinsic factors

- Lab results if there is hemolysis will show:
  - low free haptoglobin (binds free Hb released from erythrocytes with high affinity and thereby inhibits Hb’s oxidative activity)
    - normally should be higher due to less free Hb in the blood
    - ***confounder: liver disease can also falsely lower haptoglobin, and haptoglobin also acts as a nonspecific acute phase reactant (false high)
  - high LDH (a marker for cell destruction)
  - elevated indirect bilirubin
  - elevated retics
  - stable or falling Hb depending on how well the BM can keep up with RBC destruction

- How to distinguish etiology of hemolysis:
  - good history
  - Coomb’s test: looks for ABs attaching to RBC to mark for destruction
    - direct Coomb’s test: measures autoantibody attached to RBC surface
    - indirect Coomb’s test: measures free autoantibody in the serum
      - won’t be positive until all RBCs are saturated with autoantibody
  - Hb electrophoresis

- Causes of hemolytic anemias:
  - Hereditary spherocytosis: intrinsic inherited defective spectrins in red cell membrane weak, deformed, spherical RBCs (spherocytes) prone to rupture in blood vessels or spleen
    - clinical presentation: “clinical triad” of anemia, splenomegaly, jaundice
      - may have pigment gallstones (a result of Hb collections)
      - may have chronic leg ulcers
    - investigation: no anemia or mild microcytic anemia, high retics, peripheral smear showing hyperchromic spherocytes, high indirect bilirubin, negative Coomb’s test
      - issue is with RBC itself
      - BM can compensate for hemolysis except in times of stress
    - treatment: folic acid daily, splenectomy if severe
  - Paroxysmal nocturnal hemoglobinuria (PND): acquired stem cell disorder resulting in lack of proteins to protect RBCs against complement-mediated lysis intrinsic hemolysis
    - all stem cell lines affected: WBCs, RBCs, and platelets
    - clinical presentation: sporadic hemolysis sporadic red-brown urine, thrombosis, or pancytopenia
• investigation: variable normocytic or microcytic (if causing Fe deficiency) anemia, variable reticulocytosis, pitted RBCs on peripheral smear, hemoglobinuria, flow cytometry assays showing deficiency or absence of CD50 or CD55 proteins
• treatment: treat Fe deficiency, transfusions, prednisone, BMT if severe, anti-complement AB

Glucose-6-phosphate dehydrogenase deficiency: results in oxidation-prone RBCs → intracellular precipitation of oxidized Hb into Heinz bodies → spleen removal of Heinz bodies → bite cells & intrinsic hemolysis

• background:
  ▪ more likely to affect blacks, Asians, and people of Mediterranean descent
  ▪ X-linked recessive = mostly affects men
  ▪ in most cases only older RBCs are affected but in severe cases hemolysis will also affect younger cells
• clinical presentation: overall healthy, no splenomegaly, only self-limiting episodes of hemolysis triggered by infections, acidosis, or certain drugs
• investigation:
  ▪ during or just following episode: peripheral smear showing bite cells & Heinz bodies, reticulocytosis, increased indirect bilirubin
  ▪ between episodes: normal smear

  • G6PD only low during normal operations (non-stress) because BM will pump out new cells in response to anemia during an episode that will make the G6PD amount WNL = must test G6PD levels 2-3 weeks after episode!
• treatment: avoidance of oxidative stressors such as trigger drugs (screen all meds for reactions with G6PD before prescribing), fava beans, and moth balls
  ▪ meds to avoid: aspirin, sulfas, thiazide diuretics, vitamin K
  ▪ splenectomy in severe cases

Sickle cell disorders: inherited mutation in Hb □ HbS □ chronic intrinsic hemolysis

• background:
  ▪ initially RBCs are morphologically normal but became permanently sickled
  ▪ rate of sickling depends on concentrations of HbS, presence of HbF, dehydration, hypoxemia, and acidosis
  ▪ onset of sickled cells happens early in life, when HbF levels fall and HbS prevails
  ▪ sickled RBCs get stuck in small blood vessels → infarctions
  ▪ episodes can be provoked by infection, folate deficiency, hypoxia, or dehydration
  ▪ common sites:
    o pulmonary → chest symptoms
    o retinal → blindness
    o renal → renal failure
    o brain → stroke
    o spleen → required splenectomy
    o femoral head → aseptic necrosis and infection
  ▪ heterozygous = sickle trait only, with 40% of RBCs sickled
    • carried by 8% of blacks → necessity of newborn screening
    • crises will be rare
  ▪ homozygous = severe sickle cell disease, with up to 98% of RBCs sickled
    • average life expectancy of 40-50 years with good care
    • spleen eventually gets beat up → increased risk of infections
• clinical presentation: pallor, jaundice, splenomegaly, leg ulcers, pigment gallstones, priapism (permanent erection), delayed puberty, infection
  ▪ may have less symptoms than a normal person with these labs would have because the body adjusts to having chronically low Hb and hematocrit
  ▪ acute episodes during infarction = infarctive/pain crisis: severe skeletal pain, fever, but no increased hemolysis
• investigation: chronic hemolytic anemia, low Hb, sickled cells, target cells, Howell-Jolly bodies (DNA fragments), and nucleated RBCs on peripheral smear, reticulocytosis,
leukocytosis, thrombocytosis, high indirect bilirubin, positive Sickledex screen (for both carriers and homozygous disease)
- confirmatory: Hb electrophoresis
  - can’t do until > 3 months old (decline of HbF)
- sickle cell carriers will have normal peripheral smear
  - treatment: preventive or supportive including daily folic acid, up-to-date on vaccinations, counseling (avoid high altitudes, hydration) transfusions if symptomatic, fluids/O2/narcotics/antibiotics during pain crises
  - consider use of hydroxyurea to increase HbF levels, but this has side effects
- genetic counseling

- **Hemoglobin C disorder:** inherited defective β-globin in hemoglobin S intrinsic hemolysis
  - 2-3% of blacks are AC heterozygous carriers
  - CC homozygotes have mild hemolytic anemia
    - peripheral smear shows target cells and Hgb crystals
    - diagnostic test is Hb electrophoresis
  - can also have SC heterozygotes (sickle + HbC) similar but milder clinical course than sickle cell anemia

- **Autoimmune hemolytic anemia:** acquired disorder in which autoimmune IgG binds RBC membrane marked for destruction in the spleen or liver or by macrophages extrinsic hemolysis
  - background:
    - idiopathic or associated with malignancy or lupus
    - more common in women
  - clinical presentation: severe rapid anemia, fatigue, angina, CHF, jaundice, splenomegaly
  - investigation: positive Coomb’s, severe anemia, reticulocytosis, spherocytes on peripheral smear (from macrophage attacks), elevated indirect bilirubin
  - treatment: prednisone (short-term or chronic), splenectomy, immunosuppressants, avoid transfusions if possible (multiple transfusions make it hard to find a good cross-match later)

- **Cold agglutinin disease:** acquired hemolytic anemia due to autoimmune IgM that only reacts in cells 37°C or cooler = binding occurs in extremities, with bound RBCs removed by the liver
  - idiopathic origin, may be associated with malignancies or certain infections
  - clinical presentation: mottled or numb fingers & toes, episodic hemoglobinuria upon exposure to cold
  - investigation: reticulocytosis, peripheral smear showing spherocytes, positive Coomb’s, positive cold agglutination test (chilled blood will clump on the slide)
  - treatment: avoid cold, immunosuppressive therapy in severe cases

### 10.1.8 Iron Overload

**Hematochromatosis:** disease resulting from too much Fe, characterized by increased accumulation of iron as hemosiderin in the liver and other organs hemosiderosis
- can be a result of multiple transfusions
- as in thalassemia
- treat with iron chelators
- can be genetic = hereditary hematochromatosis: recessive mutation common in US Caucasians
  - background:
    - more common in men
    - increased accumulation of Fe in liver, pancreas, heart, kidneys
    - risk factors include alcohol and obesity
- clinical presentation: onset after age 50, fatigue, arthralgias, hepatomegaly, bronzing of the skin, cardiomegaly, diabetes, impotence
- investigation: elevated LFTs (liver damage from Fe), elevated serum Fe, elevated serum ferritin
  - diagnostic: liver biopsy or genetic test
- treatment: avoidance of iron-rich foods/vitamin C/alcohol, bloodletting to decrease iron stores, Fe chelators, treatment of organ damage

### 10.1.9 Neutropenia: neutrophil count < 1500/µL
• Variants:
  - blacks may have lower neutrophil count
  - pregnant women may have slightly higher neutrophil count
  - infants & children will have much higher neutrophil count (normalizes by age 12)

• Clinical presentation: stomatitis, fever, severe infections

• Investigation: CBC with differential, BM biopsy

• Differential diagnosis for neutropenias:
  - bone marrow disorder: aplastic anemia, pure white cell aplasia, congenital, cyclic neutropenia, certain drugs or chemotherapy
  - peripheral disorder: hypersplenism, viral sequelae, sepsis, autoimmune rxn, HIV

• Treatment:
  - discontinue causative drugs,
  - education about neutropenic precautions
  - broad-spectrum antibiotics for infections
  - use of growth factors in severe cases to stimulate bone marrow
    - cytokine colony stimulating factors (CSFs): want to find the minimally effective dosing schedule
      - granulocyte CSFs
        • filgrastim (Neupogen)
        • pegFilgrastim (Neulasta) circulates longer than plain filgrastim
          - contraindicated in infants and small children
        • granulocyte/macrophage CSF choice is sargramostim (Leukine)
        • side effects of CSFs: bone pain, rash, influenza-like illness from the cytokine storm

10.2 Hematologic Malignancies

Myeloproliferative disorders: a group of diseases of the bone marrow in which excess cells are produced, includes CML, polycythemia vera, myelofibrosis, and essential thrombocytosis  □ Polycythemia Vera: too many RBCs

Primary polycythemia vera (true erythrocytosis): true increase in red cell mass

Secondary polycythemia vera (relative erythrocytosis): increase in red cells due to body demanding more oxygen
• in COPD, smoking, CAD, renal disease, high altitude, MI, EPO doping, CO poisoning, renal disorders
• Clinical presentation
• symptoms: headaches, dizziness, itching, weight loss, weakness, joint symptoms and paresthesias
  - symptoms related to hyperviscosity: bleeding, thrombosis, dyspnea, tinnitus, vision problems
    - biggest concern is thrombosis
• signs: splenomegaly, reddened conjunctiva, hepatomegaly
• Investigation: elevated hematocrit, elevated platelets, elevated WBCs, elevated B12
• confirmatory: JAK2 mutation (for janus kinase 2; a change of valine to phenylalanine at the that appears to render hematopoietic cells more sensitive to growth factors such as erythropoietin and thrombopoietin)
• Treatment: phlebotomy, aspirin, myelosuppressive therapy
• cure with stem cell transplant
• mortality is 50% if untreated
• want to reduce complications of thrombosis and hemorrhage without increasing risk of leukemias

10.2.1 Essential thrombocytosis:
• a myeloproliferative disorder resulting in elevated platelet count
• Clinical presentation: thrombosis, hemorrhage, headache, burning toe pain, +/- splenomegaly
• can be asymptomatic
• Investigation:
  • elevated WBCs, normal RBCs
  • differential shows giant platelets, normal RBCs
    o differentiate from polycythemia vera by presence of normal RBCs
• bone marrow
  o increased megakaryocytes
  o JAK2 mutations common
  o can evolve into CML, differentiate from CML by absence of Philadelphia chromosome
  o need to rule out a reactive thrombosis (thrombosis as a result of causes other than myeloproliferation)
• Treatment: aspirin to prevent thrombosis, cytoreductive drugs, platelet pheresis to pull out excess cells

10.2.2 Myelofibrosis
• bone marrow is replaced with scar tissue □ anemia
• Background
  • can be cause by malignant and non-malignant conditions
  • peak incidence in 50-70 year olds
  • life expectancy 2-5 years from onset
• Clinical presentation
• signs: splenomegaly, anemia
• Investigation:
  • bone marrow is dry and difficult to aspirate, biopsy shows fibrosis
  • peripheral blood smear shows splenomegaly, giant platelets, teardrop poikilocytosis, nucleated RBCs
  • may have JAK-2 mutations
  • may have thrombocytosis
• Treatment: supportive; transfusions, EPO, BMT

10.2.3 Myelodysplastic Syndromes:
• hematopoietic stem cell disorders characterized by ineffective hematopoiesis (lack of development or early death) □ peripheral cytopenias
• Background
  • “primary myelodysplastic syndromes” means the cause is unknown, while secondary myelodysplastic syndromes have a known cause (chemical exposure, etc)
  • often occurs around age 70
  • some progress to AML
    o therefore it is sometimes called “preleukemia”
• cytopenias vary between the bone marrow and peripheral blood
• several categories of MDS based on characteristics of anemias and cells
  o fastest killer is refractory anemia with ringed sideroblasts
• Clinical presentation: general symptoms related to bone marrow failure, often a pt presents for a different reason and lab work finds an abnormality
• Investigation
• CBC with differential shows cytopenia, platelet count, retic count
• peripheral blood smear may show ringed sideroblasts and Pelger-Huet cells (hyposegmented neutrophils)
• bone marrow aspirate and biopsy
• EPO, folate, B12, Fe, TIBC, ferritin levels
• Treatment:
  • high risk disease: growth factors, cytokines, immunosuppressive agents, chemotherapy, BMT
  • supportive care: PRBC transfusions for symptomatic anemia, platelet transfusions for bleeding, antibiotics for infections, aminocaproic acid, Fe chelation for overload, cytokines

10.2.4 Multiple Myeloma
• malignancy of plasma cells where replacement of bone marrow with all plasma cells leads to failure
• Background
• etiology is unknown, but increased incidence with history of pesticides, paper production, leather tanning, and nuclear radiation exposure
• higher risk with abnormalities of chromosome 13
• forms lytic lesions on bone, predisposing patient to bone pain, pathologic fractures, and hypercalcemia
• **multi-hit hypothesis:** theory that the development of multiple myeloma requires two oncogenic event:
  o first hit: monoclonal gammopathy of unknown significance (MGUS; a common, age-related medical condition characterized by an accumulation of bone marrow plasma cells derived from a single abnormal clone)
    ▪ MGUS will show moderate spike in IgG on electrophoresis
  o second hit: more severe multiple myeloma
    ▪ 25% of MGUS cases progress to multiple myeloma
    ▪ no treatment for MGUS, just monitor for transition
• Clinical presentation: renal failure from excretion of proteins, fatigue, bone pain (back and ribs), recurrent infections, spinal cord compression, **hyperviscosity syndrome** from high circulating Ig of all kinds
• Investigation
• the “classic triad”
  o 1.) bone marrow biopsy shows > 5% plasma cells = plasmacytosis
  o 2.) bone lytic lesions on metastatic bone survey (x-ray studies, NOT a bone scan)
  o 3.) spikes in **M protein** (abnormal protein produced in high amounts by the malignant plasma cells) in protein electrophoresis
    ▪ differentiate from MGUS, where the M protein will have normal spike
• will also see spikes in IgG and/or IgA on the serum protein electrophoresis
• peripheral blood smear shows rouleaux formations (lining up like poker chips)
• urine has Bence-Jones proteins (produced by malignant plasma cells)
• plasma hypercalcemia
• anemia
• Treatment
• chemotherapy
• local radiation for pain control
• autologous BMT
• bisphosphonates for hypercalcemia
• Prognosis: average survival with chemo 3 years, with BMT 7 years
• especially poor outcome with elevated **β-2 microglobulins** (from MHC I on malignant plasma cells)

10.2.5 Waldenstrom’s Macroglobulinemia
• malignancy of B-cells involving the bone marrow, lymph nodes, and spleen, where IgM is overproduced
  □ hyperviscosity
• Median age of onset is 64
• Clinical presentation: fatigue, hyperviscosity syndrome, weight loss, headache, cold hypersensitivity, peripheral neuropathy, hepatomegaly, splenomegaly, engorged retinal veins, anemia
• Investigation:
• decreased RBCs and decreased platelets
• abnormal monoclonal IgM spike in protein electrophoresis
• differentiate from MGUS by the presence of plasmacytic lymphocytes on bone marrow biopsy
  ▪ MGUS will not infiltrate the bone marrow?
• normal bone survey
• Treat only if symptomatic
• plasmapheresis for hyperviscosity syndrome
• BMT
• chemotherapy
• Prognosis: median survival 3-5 years
10.2.6 Hodgkin’s Lymphoma

- a group of cancers characterized by the orderly spread of disease from one lymph node group to another and by the development of systemic symptoms with advanced disease
- Background
- two peak ages of onset: 20-40, and after age 50
- rare in children
- most common in men 15-45 years old
- associated with Epstein-Barr virus
- usually arises in a single node and spreads to contiguous nodes = “next-door disease”
- extranodal presentation in the lung, liver, bone marrow in 5-10% of cases
- staging based on number and location of lesions, and presence of organ involvement
- Clinical presentation: cervical/supraclavicular/mediastinal lymphadenopathy → SOB, “B-cell symptoms” (fever, night sweats, weight loss)
- Investigation
  - peripheral smear shows Reed-Sternberg cells (bilobed nuclei)
  - CT scans of chest, abdomen, pelvis
  - PET scan
  - bone marrow biopsy
  - lymph node biopsy
  - Treatment
  - chemotherapy followed by re-scan
  - radiation after chemo
  - consider stem cell transplant if relapse occurs
- Prognosis: 80% survival rate is 5+ years

10.2.7 Non-Hodgkin’s Lymphoma

- a diverse group of blood cancers that include any kind of lymphoma except Hodgkin’s lymphomas
- Background
- single or multiple areas of involvement
- low, intermediate, and high grades based on apoptosis, proliferation, and rate of accumulation
  - low grades further classified based on location of lesions
- includes CLL, Waldenstrom’s macroglobulinemia, multiple myeloma
- most common kinds are follicular lymphomas and diffuse large B-cell lymphomas
- follicular non-Hodgkin’s lymphoma can have Richter’s transformation to aggressive form
- Symptoms: lymphadenopathy, B-cell symptoms, abdominal pain, vomiting, bleeding, edema
  - lymphadenopathy may cause jaundice, hydronephrosis, bowel obstruction, wasting, obstruction of superior vena cava (SVC syndrome)
- Investigation
  - usually normal blood counts
  - may occasionally see lymphomas on peripheral blood smear
  - increased LDH
  - can use CT scans of chest, abdomen, pelvis
  - need to do lymph node biopsy for staging & diagnosis
- Treatment
  - depends on type of non-Hodgkin’s and grade
    - ranges from monitoring to aggressive chemotherapy with radiation
      - if using chemo give tumor lysis prophylactic
- BMT
- Prognosis: cure possible in half of patients

10.2.8 Leukemias Background

- Includes CML, AML, CLL, CML, hairy cell leukemia
- CLLs & CMLs characterized by gradually increasing numbers of mature cells in marrow
  - slow onset, may be asymptomatic
• Investigation: formal leukemia evaluation checks WBC morphology, special stains on peripheral smear to show cytochemistry, genetic analysis, and serology
• peripheral blood smear shows blasts
• CBC shows increased WBC, decreased platelets, normocytic anemia
• definitive diagnosis made with bone marrow biopsy showing predominance of blasts

10.2.9 Acute Leukemia

• immature, abnormal blasts in the bone marrow (> 20%) and peripheral blood (> 10%), and often in the liver, spleen, lymph nodes, and other organs
• Patients become sick over days and weeks vs months
• Two major types:
  • Acute lymphocytic leukemia (ALL): cancer of the lymphoid progenitor, affecting B or T-cells
    ▪ most common leukemia in children 3-7 years old
    ▪ clinical presentation: malaise, fatigue, fever, bleeding gums, lymphadenopathy, splenomegaly, petechiae, weight loss, meningitis, lethargy, anorexia, dyspnea
    ▪ investigation
      ▪ bone marrow biopsy shows > 30% blasts
      ▪ pancytopenia
    ▪ treatment:
      ▪ aggressive chemotherapy for ~2 years
        ▪ need to prophylax CNS intrathecally (chemo won’t cross blood-brain barrier)
        ▪ induction phase of 4-6 weeks
        ▪ consolidation phase of several months
        ▪ maintenance phase weekly for 2-3 years
      ▪ possible BMT
    ▪ prognosis:
      ▪ 80% cure rate for children with chemotherapy
      ▪ 20-40% cure rate for adults with chemotherapy
  • Acute myeloid leukemia (AML): cancer of the myeloid progenitor, where cells do not mature and do not die
    ▪ classified based on morphology and histochemistry
    ▪ clinical presentation:
      ▪ from cell deficiencies: pallor, fatigue, dyspnea, thrombocytopenia with petechiae, hematomas, and bleeding, neutropenia with sepsis, cellulitis, and pneumonia
      ▪ from hyperleukocytosis: obstruction to capillaries and small arteries with high numbers of blasts
      ▪ from CNS involvement: headache, altered mental status, issues with cranial nerves
      ▪ leukemia cutis: the infiltration of neoplastic leukocytes or their precursors into the skin cutaneous lesions
      ▪ DIC with any form of leukemia
      ▪ tumor lysis syndrome
    ▪ investigation:
      ▪ pancytopenia with hyperleukocytosis
      ▪ differentiate from ALL by peripheral blood smear showing Auer rods
    ▪ treatment:
      ▪ different if AML is classified at M3 (promyelocytic)
      ▪ aggressive chemotherapies tailored to classification
    ▪ prognosis: differs with which chromosomal abnormalities are present, average survival of 30%

10.2.10 Chronic Lymphocytic Leukemia

• clonal proliferation and accumulation of mature-appearing B lymphocytes
• Background
• most commonly occurring leukemia
• mostly occurs in those > 50 years old
- more common in males
- RAI system for staging
- slow growing
  - possible Richter's transformation to aggressive
- worse prognosis with deletion on chromosome 17
- Clinical presentation: fatigue, night sweats, weight loss, persistent infections, lymphadenopathy, hepatomegaly, splenomegaly
- Investigation
- lymphocytosis with WBCS > 20,000/µL
- anemia
- coexpression of CD19 and CD5
- high IgG
- peripheral blood cell shows mature small lymphocytes and cobblestone-appearing smudge cells
- Treatment: observation, chemotherapy, BMT, tumor lysis prophylaxis (to prevent kidney failure from killing of WBCs during chemo), radiation for lymphadenopathy

10.2.11 Chronic Myelogenous Leukemia
- disorder of myeloblast progenitor cell, resulting in excess proliferation of myeloblast and/or its subsequent progeny
- Background:
  - normally, progeny of the myeloblast (neutrophils, etc) feedback negatively to inhibit the myeloblast progenitor but it is lost in CML
  - usually occurs in young to middle age adults
- three categories of CML:
  - chronic: < 15% blast component of bone marrow or peripheral blood
  - accelerated: peripheral blood > 15% blasts or > 30% blasts + promyelocytes, or > 20% basophils
    - also see thrombocytopenia
  - acute: when blasts comprise >30% of bone marrow cells
- Clinical presentation
- signs & symptoms: fever, bone pain, LUQ pain with splenomegaly, weakness, night sweats, bleeding & bruising, petechiae
- Investigation
- detection of Philadelphia chromosome via FISH or RT-PCR
- leukocytosis
- thrombocytopenia
- Treatment: BMT, chemotherapy
- Prognosis: average survival 6 years with treatment

Hairy Cell Leukemia: malignancy of small B-cells found in the bone marrow, peripheral blood, and spleen
- Background
- median age of onset is 50 years
- affects males much more than females
- slow course that is very responsive to treatment
- Clinical presentation: fatigue, abdominal discomfort from splenomegaly, persistent infections
- Investigation:
- pancytopenia
- peripheral smear shows hairlike projections from B-cells with fried egg appearance of cells
- anemia
- Treatment/prognosis: oral agent for 5-7 days with 90% chance of complete remission

10.2.12 Oncologic Emergencies
- Febrile neutropenia: get to ER within 4 hours for antibiotics
- SVC syndrome in non-Hodgkin's lymphoma
- Tumor lysis syndrome
• Hypercalcemia in multiple myeloma
• Cord compression in multiple myeloma

10.3 Hemostasis: Platelets & Coagulation

Hemostasis: blood coagulation; collective term for all physiologic mechanisms the body uses to protect itself from blood loss

• Need to maintain balance of coagulation and blood fluidity
• hemorrhage: failure to maintain hemostasis
• thrombosis: failure to maintain fluidity
• Four systems of hemostasis
• vessel wall: disruption of endothelia □ vasoconstriction □ decreased blood flow
  - only significant in arterioles and downstream capillaries
  - vessel wall can be broken by trauma, infection, medications, or autoimmunity
    □ may result in purpura: extravasation of blood to skin surface
  - vessel wall can be weakened by scurvy, amyloidosis, hereditary telangiectasia, neurofibromatosis, or collagen disorders such as Marfan’s or Ehler-Danlos

• platelets
  - keep endothelia smooth
  - initiate repair when blood vessel walls are damaged
  - large supply reserved in spleen
  - normal amount and functioning required for primary hemostasis: stickiness of platelets with platelet adherence to damaged vessel wall
    □ primary hemostasis (the activation of platelets): reversible initial aggregation of platelets
    □ secondary hemostasis (the coagulation cascade): irreversible subsequent layers of aggregated platelets
      - initiated by release of platelet factor 3 (PF3) and increased intracellular Ca
      □ thromboxane A2 release
      - would require fibrinolytic system to break up
  - decreased platelet numbers occur as a result of decreased production (bone marrow problem), increased destruction (meds, autoimmune, or DIC), or sequestration (splenomegaly)
  - decreased platelet functioning occurs as a result of membrane defects (Glanzmann’s, BernardSoulier), pathway defects (arachidonic pathway defect or aspirin use), or other reasons such as myelodysplastic syndrome
  - sometimes platelet numbers or functioning decrease as a result of many factors!
• coagulation system: 2 pathways that converge
  - extrinsic pathway initiates process
  - intrinsic pathway enhances thrombin formation
• fibrinolytic system: natural anticoagulant defense mechanism
  - coactivated with coagulation cascade to provide balance
  - results in plasmin digestion of fibrin □ clot dissolution

10.3.1 Diagnostic Methods: Platelet Studies

• Platelet count: automated
• can also estimate on peripheral smear
• Bleeding time studies: how long to clot
• rarely done, hard to reproduce and standardize
• prolonged with low platelet counts, abnormal platelet functioning, or with use of antiplatelet drugs
• Platelet aggregation studies: evaluation of patterns in the presence of known aggregation inducers
• different pathologic conditions produce different patterns of aggregation
  □ ristocetin will agglutinate large multimers of vWF
• measured as plasma turbidity
• Platelet function assay: evaluates platelet adhesion as well as aggregation
• common causes of decreased platelet function: uremia, von Willebrand disease, antiplatelet drugs
• measures function with collagen/epinephrine as well as with collagen/ADP
  o prolonged closure for collagen/epinephrine suggests aspirin-like defect
  o prolonged closure for collagen/ADP suggests true platelet defects
• lets you know when you really need to order an agg study
• von Willebrand factor (vWF): plays a large role in promoting blood coagulation by binding certain members of the cascade to mediate platelet adhesion to endothelia
• ***only active in the large multimer form!
• synthesized in endothelia and megakaryocytes, with storage in platelets
• acts as a carrier for factor VIII
• ADAMTS13: a protease required for cleavage and inactivation of vWF
• D-dimer: a small protein fragment present in the blood after a blood clot is degraded by fibrinolysis
• negative result rules out thrombosis
• positive result MAY indicate thrombosis or other causes
• only significant at high and tiny amounts, numbers in the middle don’t mean much
• Fibrin split products (FSP): products of degradation of fibrin clot
• Prothrombin time (PT): a measure of the extrinsic pathway of coagulation, specifically tests factor 7
• tissue factor is added to the vial so that it will follow the extrinsic pathway
• useful in monitoring warfarin/Coumadin therapy
• typically takes 11-13 seconds
  o prolonged in liver disease, warfarin therapy, vitamin K deficiency, factor 8a inhibitors, deficiencies in factor 7 and common pathway factors
• Activated partial thromboplastin time (aPTT or PTT): a measure of the intrinsic pathway of coagulation, specifically tests factors 12, 11, 9, 8
• no tissue factor in vial means it only measures the intrinsic pathway
• useful in monitoring heparin therapy
• typically takes 25-35 seconds
  o prolonged in deficiencies in intrinsic and common pathway factors, in heparin therapy, hemophilia A (factor 8 deficiency), hemophilia B (factor 9 deficiency)
• Activated clotting time (ACT): beside test done in OR or cath lab to monitor heparin treatment
• performed to determine if it is safe to pull catheters or A-lines
• Plasma fibrinogen
• 1Factor 10a assay: measures LMWH therapy
• LMWH directly inhibits 10a

10.3.2 Heparin Therapy

Unfractionated heparin: binds antithrombin III to accelerate its activity, while inhibiting factor 10a and thrombin
• purified from animal tissues
• used to initially treat DVT or PE and for prophylaxis
• weight-based dosing
• big people require big doses!
• monitor with aPTT
• therapeutic range is 1.5-2.5x normal length
• watch platelets for heparin-induced thrombocytopenia
• watch urine and stool for signs of bleeding
• kinetics: quick onset and elimination
• peak absorption in 2-4 hours after injection
• metabolized by liver and macrophages/monocytes
• non-dialyzable = can’t pull it off if you give too much
• elimination half life of 1.5 hours
• adverse effects
• antidote is protamine
Low molecular weight heparin (LMWH): a fragment of unfractionated heparin that inhibits factor 10 and thrombin

- response is more predictable
- given subcutaneously
- used to treat DVT/PE and to prophylax against
- initiate therapy with heparin, then transition to warfarin
- weight-based dosing
- kinetics
- time to peak is 2-4 hours post injection
- not dialyzable
- elimination half life of 5-7 hours
- same adverse effects as UF heparin
- monitor the same as UF heparin
- measure levels of LMWH in “anti-factor 10a” level
  - peaks 4 hours after last injection = get peak level now in a heavy person if you’re wondering if they’re getting enough LMWH
  - trough just prior to last injection = get trough level now if you’re wondering if renally impaired patient is clearing LMWH ok
- kinds:
  - enoxaparin (Lovenox): renal dosing guidelines available
  - dalteparin (Fragmin): no specific renal dosing guidelines
  - fondaparinux (Arixtra): contraindicated in renal insufficiency
    - renally excreted

10.3.3 Warfarin Therapy

- Brand name Coumadin
- Acts as a vitamin K antagonist
- Used in treatment of DVT and PE, A-fib, mechanical heart valves, left heart failure, and myocardial reinfarction
- Contraindicated in active cancer, pts with unstable vitamin K intake, or noncompliant pts
- Dosing
  - need to get factors in order first, so achieve therapeutic anticoagulation via UF heparin or LMWH prior to starting warfarin
    - need to be careful with initial therapy because protein C and protein S are indirectly made more active by the affects of warfarin
  - adjust warfarin by INR and PT
    - check twice a week!
    - once stable monitor every 4-6 weeks
  - treat an active thrombosis with UF heparin or LMWH + warfarin at least 5 days or until therapeutic INR
  - need to transition back to heparin for a surgery or procedure
    - because warfarin inhibits both sides of the pathway while heparin only inhibits one?
- Interactions
  - antibiotics, antifungals, amiodarone, anticonvulsants, NSAIDs, any herbal preparation
  - educate patients about vitamin K consumption
  - Adverse effects: alopecia, skin necrosis, supra or subtherapeutic levels
  - Warfarin is teratogenic = category X = transition to LMWH prior to attempting pregnancy

Direct Thrombin Inhibitors: use if suspecting heparin-induced thrombocytopenia

- Dabigatran (Pradaxa)
- oral direct thrombin inhibitor
- FDA approval for use in non-valvular a-fib
- dosage need to be adjusted for renally impaired pts
- kinetics
  - absorption peak in 1-2 hours
  - metabolism makes it active!
• then excreted renally
  o half life of 12 hours
  o acts as a PGP substrate
• no monitoring needed
• no antidote
• fussy, has to be kept in original container, no pill crushing
• adverse effects: GI
  Lepirudin (Reflduran)  
  IV or SC
• contraindicated in renal insufficiency
  Bivalirudin (Angiomax)
• IV
• best option for multi-organ dysfunction
• Fondaparinux
• for use when platelets normalize

Monitor all direct thrombin inhibitors similarly to UF heparin monitoring
• they may cause a falsely elevated INR due to chromogenic factor 10a

10.3.4 Rivaroxaban
• Trade name Xarelto
• FDA approval in post-op hip/knee prophylaxis
• No monitoring needed
• Adverse effects: bleeding
• Kinetics
  peak absorption in 2-4 hours
• CYP and PGP substrate
  o renal excretion
• half life of 5-9 hours
• No antidote

10.3.5 Thrombocytopenias: too few platelets
• must distinguish from pseudo-thrombocytopenia in patients that are “EDTA clumpers”
  EDTA clumpers need blood draws in blue vs lavender tubes
• some meds can have anti-platelet effects: aspirin, clopidogrel, prasugrel, NSAIDs A.) Acute thrombocytopenia: a sudden decrease in platelets
  background:
    o causes could be decreased production, increased destruction, or sequestration
    o need to do a thorough history asking about meds, autoimmunity, recent surgeries, alcohol, menstrual characteristics, any abnormal bleeding or bruising
    o in physical exam need to look for dried blood in nose, wet purpura in the mouth, splenomegaly, petechiae
• labs
  o platelets < 150,000
  o was there a normal count before?

Immune (idiopathic) thrombocytopenic purpura (ITP): abnormally low platelet count due to anti-platelet antibodies
• background:
  • children: can be from self-limiting viral infection
  • adults: typically chronic with no preceding viral infection
    o may be secondary effect of other disease states: HIV, Hep C, autoimmune, Rocky Mtn spotted fever
    o may be secondary effect of surgeries such as valve replacement or cardiac cath
    o may be secondary effect of drugs: heparin, sulfa
see heparin-induced thrombocytopenia below

- clinical presentation: neurologic symptoms, fever, +/- renal insufficiency
- investigation: PT/PTT normal, normal cell lines, normal marrow, normal spleen  diagnosis of exclusion!
  - reduced ADAMTS13 due to reduced platelets

- adult treatment:
  - immunosuppression with steroids
  - immune modulation via IV Ig or splenectomy
  - plasma transfusion with plasmapheresis
  - give EPO to stimulate platelet production

- adult prognosis: 90% fatal without treatment!

Heparin-induced thrombocytopenias: occur as a result of heparin therapy

- heparin-induced thrombocytopenia type I: non-immune mediated, is only transient
  - platelet counts ~100,000
  - treatment: improves upon D/C of heparin

- heparin-induced thrombocytopenia type II: results in autoimmune IgG against PF4 formation of
  - immunogenic complexes that activate platelets to form microthromboses in small vessels throughout body
  - background:
    - RBCs may bang against microthromboses and become damaged  microangiopathic hemolytic anemia (MAHA)
    - occurs 4-10 days after first exposure via heparin infusion
      - will occur 1-2 days after subsequent exposures
      - reduce risk by using LMWH
    - clinical presentation: microthromboses cause necrosis of limbs, pulseless extremities
    - investigation:
      - platelet counts ~50,000
      - normal PT/PTT
      - evidence of heparin/PF4 antibody
      - if MAHA has happened, peripheral smear shows schistocytes from chewed up RBCs as well as anemia
      - confirm with serotonin release assay
    - treatment: stop all heparin, then use alternative anticoagulant such as direct thrombin inhibitors, and begin warfarin after platelet counts have normalized

Thrombotic thrombocytopenic purpura: a rare disorder of the blood-coagulation system usually caused by inhibition of ADAMTS13  extensive microthromboses in small blood vessels throughout the body

- associated with certain meds
- clinical presentation: mental status changes, fevers, chest pain, trouble breathing, trouble urinating
- physical exam findings similar to acute and idiopathic thrombocytopenias
- investigation
  - decreased platelets < 20,000
  - normal coagulation tests
  - MAHA signs: peripheral smear shows schistocytes from chewed up RBCs as well as anemia
  - another diagnosis of exclusion
  - want to rule out DIC
  - treatment
  - plasmapheresis to remove anti-ADAMTS13 antibodies
  - maybe immune suppression with steroids

Hemolytic uremic syndrome: a disease characterized by hemolytic anemia, acute renal failure  uremia, and thrombocytopenia

- classical HUS = with diarrhea:
  - E. coli toxin causes damage to endothelia  activation of platelets  thrombocytopenia
    - also damages kidney arterioles  acute renal failure  uremia also inactivates ADAMTS13
    - accumulation of large VWF chunks with increased activation of clotting cascade  thromboses  MAHA & anemia
• investigation: rule out other causes of coagulopathy
  o anemia with schistocytes
  o thrombocytopenia
  o very similar to TTP, distinguish it by renal dysfunction vs neuro impairments
    ▪ no distinctive HUS test
• treatment is supportive
  o only give PRBCs if anemia is severe
  o volume repletion and pressors
  o plasma exchange
  o NO antibiotics, will worsen HUS
  o NO platelets, will worsen AHA
• prognosis:
  o 5% mortality rate
  o 25% may develop ESRD

Disseminated intravascular coagulation (DIC): a pathological activation of coagulation that happens in response to a variety of diseases
• background
• always associated with an underlying illness!
  o often in widespread infections (Gram- sepsis), burns, cancer, head trauma, snake bite, vasculitis
    ▪ Trouseau’s syndrome: when a malignancy causes hypercoagulability, resulting in recurrent DVTs, can progress to DIC
• begins with a clot and ends in consumptive coagulopathy
• investigation
  • thrombocytopenia
  • schistocytes on blood smear
  • positive D-dimer and positive FSP
  • decreased fibrinogen (all used up)
  • prolonged PTT and PT (factors all used up)
• treatment: treat underlying disease state
  • replace blood products PRN
  • certain cases warrant the use of heparin or LMWH to inhibit further clot formation
• prognosis depends on underlying disease

Other causes of thrombocytopenia
• from liver disease: occurs when a sick liver does not manufacture enough coagulation factors (responsible for all but factor 8) □ low thrombopoietin □ platelets remain sequestered in spleen □ thrombocytopenia
• investigation: prolonged PT and aPTT
• treat with FFP infusion
• from vitamin K deficiency □ can’t activate vitamin-K dependent factors 2, 7, 9, 10, or protein C & S
• causes: destruction of vitamin K-synthesizing gut bacteria by antibiotics, malnutrition, biliary tract disease
• investigation: prolonged PT and aPTT
• treatment:
  o if due to high INR, hold warfarin, give IV vitamin K supplemented with FFP □ differentiate between the two by testing levels of factors 5 & 7
    ▪ in liver disease, both are low
    ▪ in vitamin K deficiency, only 7 is low

Thrombopathies: bleeding disorders characterized by prolonged bleeding time despite normal platelet count
A.) Von Willebrand disease: the most common hereditary coagulation abnormality, arising from a functional or quantitative deficiency of vWF
• background:
• comes in several forms
  o type I is the mildest
vWF important in bridging platelets together and with the endothelium, and to carry factor 8
investigation
low levels and low activity of vWF
electrophoresis shows decreased vWF multimers (opposite of TTP which is all multimers)
platelet agg studies: ristocetin will cause hyperagglutination (abnormal) while other agents (ADP, thrombin, collagen) show normal agglutination
normal coagulation
platelet function assays show prolonged closure time for collagen & ADP (true platelet defect)
treatment: only severe cases with vwF + factor 8 concentrates, or desmopressin for quick release of vWF from endothelial stores

B.) Glanzmann's thrombasthenia: an extremely rare where the platelets lack glycoprotein IIb/IIIa no fibrinogen or vWF bridging can occur prolonged bleeding time
background
rare, autosomal recessive
investigation
platelet agg studies OPPOSITE vWFD: ristocetin will cause normal agglutination with diminished aggregation with ADP, collagen, thrombin

C.) Bernard-Soulier syndrome: a rare autosomal recessive coagulopathy that causes a deficiency of the receptor for vWF (glycoprotein Ib)
giant platelets dominate over functional normal platelets = functional thrombocytopenia
investigation
thrombocytopenia
reduced or abnormal vWF-R on platelets
prolonged bleeding time
differential shows giant platelets
do not differentiate from polycythemia vera by ?
platelet aggregation studies show no aggregation with ristocetin (again OPPOSITE vWFD)
can be corrected with addition of normal platelets

D.) Hemophlias
background
hemophilia A: factor 8 deficiency
hemophilia B: factor 9 deficiency
X-linked inheritance
clinical presentation: abnormal bleeding, bleeding into joints (hemarthroses) and muscle
investigation
prolonged aPTT
decreased factor 8 or 9 levels
treatment: infusion with factor concentrates

E.) Decreased factor 8 due to autoimmunity
investigation:
do not differentiate from hemophilia in that it is not corrected by a mixing study!
decreased factor 8 levels
treatment: steroids to immunosuppress

E.) Acquired thrombopathy from drugs, infection, renal disease, hepatic disease, AIDS, NSAIDS
via inhibition or reduced synthesis of normal clotting factors

Hypercoagulable States: most thromboemboli result from a combination of genetic predisposition and an acquired precipitating event

I.) Hereditary
factor V Leiden: hereditary resistance to factor 5 inactivation by protein C
PTT may be shortened and does not correct
definitive PCR test
- **prothrombin G20120A**: inherited mutation that causes increased prothrombin levels  
  - definitive DNA test
- **protein C/S deficiency**: deficiency of natural vit K-dependent anticoagulants  
  - death if homozygous  
  - C deficiency associated with warfarin hypersensitivity
- **antithrombin III deficiency**: reduced inhibition on the conversion of fibrinogen to fibrin  
  - death if homozygous

II.) Acquired  
- **Virchow's triad**: presence of these signs predisposes patients to venous thrombosis  
  - vascular damage, hypercoagulability, vascular stasis
- **anti-PL syndrome**: circulating IgG or IgM against self phospholipid  
  - prolonged PTT  
  - recurrent spontaneous abortions  
  - presence of livedo reticularis: lacy netlike rash on limbs  
  - treat indefinitely with warfarin
- **hormonal**: pregnancy, birth control pills increase levels of clotting factors  
- malignancy
- smoking
- immobilization
- surgery

10.4 Transfusion Medicine  
- Donated blood is screened for: HIV, HBV, HCV, HTLV ½, West Nile, syphilis  
- future screening for Chagas disease  
- greatest risk for transmitted virus is West Nile  
- potential transmission of but no screening for CMV, EBV, parvovirus B19, HHV-8  
- Greatest risk in platelet transfusion is bacterial contamination  
- Blood typing and infection testing is done by the collection agency, while the hospital performs additional tests on site of transfusion  
- Most people are type O or type A and Rh+  
- Can make use of therapeutic hemapheresis to remove desired blood component and re-transfuse everything else back  
- for hyperviscosity syndrome, TTP, leukemia, sickle cell, thrombocytosis, lymphoma, hairy cell leukemia

10.4.1 Important Tests  
1.) **Direct antiglobulin test (Coomb’s test)**: detects presence of IgG or complement coating the red cell  
  - detects in-vivo sensitization of RBCs  
  - will be positive if there is a hemolytic transfusion reaction, in autoimmune hemolytic anemia, and with transfusion of passive immunity Ig
2.) **Indirect antibody test (antibody screen)**: detects presence of serum antibodies other than anti-A and anti-B  
  - used to screen patients prior to transfusion to prevent reaction  
  - also used during pregnancy to assess risk of hemolytic disease of the newborn
3.) **Type & screen**: determines ABO blood type and Rh status  
  - used for a pt when there is a low but possible necessity of transfusion  
  - pt’s blood is drawn, tested, and held in case crossmatching with donor may be needed in the future
4.) **Crossmatch**: pt’s serum mixed with donor blood to look for agglutination
5.) **HLA testing**: matches HLA of pt with HLA of donor  
  - done for a pt who has had multiple transfusions and may have developed antibodies  
  - requires multiple assays
10.4.2 Blood Components

- Whole blood
  - rarely used, only for acute massive bleeding
  - given with 5-7 units pRBCs
  - risk of transfusion reactions and volume overload
- Packed RBCs
  - for severe bleeding or anemia
    - only needed with bleeding loss of > 30% blood volume
- may cause hemolysis
- Washed RBCs
  - with history of leukocyte antibodies or reaction
  - for sepsis in unresponsive granulocytopenias
  - risk of graft vs host disease
- Leukocyte concentrates
- Platelet concentrates
- for bleeding due to thrombocytopenia, thrombocytopenia, DIC, massive transfusions
  - short shelf life!
- Cryoprecipitate
  - for factor 8, factor 13, fibrinogen, vWF deficiencies, and for DIC
  - risk of anaphylaxis
- FFP
  - for coagulation disorders and massive transfusions
  - anaphylaxis risk
- Factor 8 concentrates
  - for treatment of hemophilia A
  - risk of infection because it is pooled from up to 30,000 donors
  - Autologous blood: transfusing with your own blood

10.4.3 Transfusion Reactions

- Nonimmune-mediated acute:
  - fevers from pyrogenic substances in IV solutions & sets
  - bacterial contamination
  - circulatory overload (TACO)
  - air embolism
  - thrombophlebitis
  - mechanical hemolysis by IV pump
  - aggregates pulmonary infiltrates
  - Nonimmune-mediated delayed:
    - infection
  - Fe overload
- Acute immune-mediated
  - hemolysis low BP, fever, shaking, redness at infusion site DIC
  - anaphylaxis
  - TRALI from immune aggregates
  - graft vs host
11 Infectious Disease Unit Exam Notes

11.1 Pathogens By Site of Infection

- Mouth: Peptococcus, Peptostreptococcus, Actinomyces
- Skin/soft tissue: Staph aureus, Strep pyogenes, Staph epidermidis, Pasteurella
- Bone & joint: Staph aureus, Staph epidermidis, strep, Neisseria gonorrhoeae, Gram negative rods
- Abdomen: E. coli, Proteus, Klebsiella, Enterococcus, Bacteroides
- Urinary tract: E. coli, Klebsiella, Enterococcus, Staph saprophyticus
- URT: Strep pneumo, Haemophilus influenzae, Moraxella catarrhalis, Strep pyogenes
- LRT-community: Strep pneumo, Haemophilus influenzae, Klebsiella pneumoniae, Legionella, Mycoplasma, Chlamydia
- LRT-hospital: Klebsiella pneumoniae, Pseudomonas aeruginosa, Enterobacter, Serratia, Staph aureus
- Meningitis: Strep pneumo, Neisseria meningitidis, Haemophilus influenzae, group B strep, E. coli, Listeria

11.2 Antibiotics

- Antibiotics used for prophylaxis, empiric therapy, or documented/specific therapy

11.2.1 Cell Wall Synthesis Inhibitors:

β-Lactams: compete for cell wall synthesis components in the bacteria creation of bacteria with weakened cell wall death

- characteristics of all β-lactams:
  - bactericidal
  - variable oral absorption
  - distribution in the body is wide
  - typically eliminated by the kidney need renal dosing for pts with decreased kidney functioning
    - exception: nafcillin, oxacillin, ceftriaxone eliminated by the liver
    - elimination half life is short, under 2 hours frequent dosing required
- adverse effects
  - sensitivities in 3-10%, with cross-reactivity between all penicillins and some other β-lactams
  - neurologic symptoms with penicillins and carbapenems
  - hematologic: penicillins
  - liver: can increase LFTs
  - GI: nausea, vomiting, diarrhea (including C. diff)
  - interstitial nephritis with methicillin and nafcillin
- bacterial resistance
  - reduced bacterial membrane permeability (some Gram negatives in Septra)
  - drug efflux (macrolides and quinolones)
  - β-lactamases
  - modification of target protein (MRSA in penicillin, macrolides, quinolones)
  - metabolic bypass of drug target

1.) Penicillins

- natural penicillins: mainly narrow spectrum against Gram positives; defeated by β-lactamases
- DON’T: not active alone against Staph aureus, don’t cover Gram negatives
- DO:
  - Gram positives: strep, Enterococcus, Listeria, Clostridium
    - Strep pneumo IM injection
  - Gram negatives: Neisseria
  - anaerobes: Clostridium if above the diaphragm
  - other: Treponema pallidum (long acting IM injection)
• penicillin G: IV
• penicillin VK: PO
• penicillinase-resistant penicillins: narrow-spectrum against Gram positives
  • nafcillin, oxacillin, dicloxacillin, cloxacillin, Methicillin
• DO: renal patients (hepatically eliminated), skin and skin structure infections
  o Gram positives: MSSA, strep
• DON'T: CA-MRSA
• aminopenicillins: broad spectrum with some Gram negative activity; alone defeated by β-lactamases
• ampicillin: can come + sulbactam (β-lactamase inhibitor)
• amoxicillin: can come + clavulanic acid (β-lactamase inhibitor)
  o DO: UTIs, respiratory infections, skin and skin structure infections, animal bites (with inhibitor)
    • ALONE:
      • Gram neg: Proteus, Salmonella, Shigella, E.coli, Haemophilus influenzae
      • Gram pos: strep, E. coli, Listeria, Enterococcus, strep
      • some anaerobes
    • WITH INHIBITOR: add *Staph aureus*
• extended-spectrum penicillins: anti-pseudomonal = activity against Gram negatives, alone defeated by β-lactamases
  • ticarcillin + clavulanic acid:
• piperacillin + tazobactam (another β-lactamase inhibitor): UTIs, abdominal infections, nosocomial infections
• DON'T:
  o weak staph activity and no MRSA
• DO:
  o Gram neg: Pseudomonas
  o Gram pos: strep
  o Anaerobic activity
• β-lactamase inhibitor combos: ampicillin + sulbactam, amoxicillin + clavulanic acid, piperacillin + tazobactam, ticarcillin + clavulanic acid
  -Gram pos: *Staph aureus*

2.) Cephalosporins
• first generation: narrow spectrum similar to aminopenicillins, defeated by β-lactamases
  o cefazolin or cephalaxin: IV for surgical prophylaxis, skin and skin structure infections, UTIs
    • no value in adding inhibitor because??
    • DO:
      • Gram neg: E. coli, Klebsiella, Proteus
      • Gram pos: staph, strep
• second generation: increased activity towards Gram negs, increased stability in presence of β-lactamases
  o cefoxitin: good anaerobe activity
  o cefuroxime: community acquired pneumo iii.) cefotetan: good anaerobe activity
  o cefuroxime axetil: PO; community acquired pneumo, LRT infections, UTI infections, skin and soft tissue infections
  o cefaclor: PO; respiratory tract infections, UTIs, skin and skin structure infections
  o cefprozil: PO; respiratory tract infections, otitis media, skin and skin structure infections, UTIs
  o DO: respiratory tract infections, otitis media, sinusitis, pharyngitis, tonsillitis, skin and skin structure infections, UTIs, surgical prophylaxis = activity of 1<sup>st</sup> gen plus:
    • Gram neg respiratory pathogens *Haemophilus* (newer only), *Moraxella, Neisseria*
    • cefoxitin, cefotetan, cefmetazole also cover anaerobes = use for treatment of pelvic/abdominal infections and prophylaxis
DON'T: MRSA, *Enterococcus*, *Pseudomonas*, suboptimal CNS penetration

- **third generation**: broader spectrum; more resistant to β-lactamases
  - *cefotaxime*: good against *Haemophilus*, good CNS penetration, PRSP ii.) *ceftriaxone*: CA-pneumo, meningitis, PRSP
    - no dose adjustment for renal dysfunction
  - *ceftazidime*: *Pseudomonas*, *Serratia*, best at PRSP
  - *cefixime*: PO; UTIs, otitis media, tonsillitis, pharyngitis, acute bronchitis or chronic exacerbation, uncomplicated gonorrhea
    - DO: hospital-acquired and polymicrobial infections
        - *Pseudomonas* and *Serratia* only if ceftazidime
      - Gram pos
    - ORALS ok for: URT & LRT infections, otitis media, skin and skin structure infections, UTIs
  - DON'T: MRSA, *Enterococcus*, *Pseudomonas*, suboptimal CNS penetration

- **fourth generation**: extended Gram neg and pos activity, especially *Pseudomonas*, stable against β-lactamases
  - excellent against Gram pos and Gram neg, but WEAK against anaerobes!
    - *cefepeime*: LRT infections, UTIs, skin and skin structure infections, abdominal/pelvic infections, bacteremia, sepsis, febrile neutropenia, pediatric cystic fibrosis, meningitis
    - Gram neg activity of ceftazidime: *Pseudomonas*, *Serratia*
    - Gram pos activity of cefotaxime: PRSP
    - ceftaroline: MRSA
    - DON'T: *Pseudomonas*

3.) **Carbapenems**: β-lactams for use febrile neutropenia, consolidation therapy, resistant infections
- *imipenem* + *cilastatin*: stable against β-lactamases, covers anaerobes, and is extremely broad, should only be used in complicated and polymicrobial infections
  - adverse effects: GI, nausea, seizures, cross reactivity with penicillins and cephalosporins!
  - DON'T: MRSA
- *meropenem*: similar to imipenem but with less seizure potential c.) *ertapenem*: no *Pseudomonas* or *Acinetobacter*

4.) **Monobactams**: new class of β-lactams
- *aztreonam*
  - adverse effects: rash
  - no cross reactivity with penicillins & cephalosporins
  - DO: gram negs resistant to first-line agents including *Pseudomonas*, or in patients with hypersensitivity to β-lactams
  - DON'T: Gram pos

11.2.2 **Cell Wall Synthesis Inhibitors: Non β-Lactams**

1.) **Vancomycin**: prevents polymerization of bacterial peptidoglycans; used for resistant, serious Gram positive infections in β-lactam-allergic patients
- adverse effects: renal, ototoxicity, “red man” allergy reaction
- DO: bacteremia, empyema, endocarditis, pneumonia, peritonitis, skin and soft tissue infections, osteomyelitis, surgical prophylaxis, refractory *C. diff* colitis
  - Gram pos such as MRSA, MSSA, coag-negative staph, PRSP, strep, *Enterococcus*, *Clostridium*, *Peptococcus*, *Peptostreptococcus*
- DON'T: Gram neg, aerobes

2.) **Daptomycin**: similar to vanco; used in settings of vanco failure or contraindication
- DO: Gram pos endocarditis, bacteremia, MSSA, MRSA, VRSA, PRSP, VRE
- DON'T: no Gram negs, don’t use to treat CNS or pneumonia (inactivated by surfactant)
**Fluoroquinolones**: inhibit DNA synthesis by acting on Gram neg DNA gyrase and on Gram pos DNA topoisomerase

- characteristics of all fluoroquinolones
- broad spectrum
- bactericidal
- great oral absorption
- good tissue penetration
- long half life
- pretty safe
  - some adverse effects: GI, CNS especially in the elderly, hepatotoxicity, phototoxicity, may have QT prolongation, articular damage/joint swelling, tendon rupture, dysglycemia, hypersensitivities
- lots of drug and micronutrient interactions = take on an empty stomach to avoid poor oral absorption
  - warfarin interaction
- DO:
  - Gram neg: all Enterobacteriaceae, *Haemophilus, Moraxella, Neisseria*
    - excellent activity against Gram negs, with cipro = levo > moxi
  - Gram pos: MSSA, *Strep pneumo* including PRSP
  - atypicals: Legionella, Chlamydophila, Mycoplasma, Ureaplasma
  - others: Mycobacterium tuberculosis, Bacillus anthracis
  - DON’T: pediatrics, pregnant, breastfeeding

1.) 2nd generation
- **ciprofloxacin**: IV or PO; best against *Pseudomonas*, also for LRT infections, UTIs, bone /joint/skin/skin structure infections, gonococcal infections, infectious diarrhea
  - drug interaction with theophylline and cyclosporine (inhibits cipro metab → toxicity)
- **floxin**: best against *Chlamydophila*, also for LRT infections, skin structure infections, UTIs, gonococcal infections, prostatitis

2.) 3rd generation: enhanced activity against *Strep pneumo, Staph aureus*, and anaerobes = “respiratory quinolones”
- **levofloxacin**: CA-pneumo, acute exacerbations of chronic bronchitis, sinusitis, skin & skin structure infections, complicated UTIs
  - renal elimination
- **moxifloxacin**: CA-pneumo, acute exacerbations of chronic bronchitis, sinusitis
  - some anaerobe activity
  - hepatic elimination
  - no activity in urine = don’t use to treat UTIs
- **gemifloxacin**: CA-pneumo, Strep pneumo, Haemophilus, Moraxella, Klebsiella

11.2.3 **Protein Synthesis Inhibitors**

1.) Aminoglycosides: gentamicin, tobramycin, amikacin
- characteristics of all aminoglycosides:
  - bactericidal
  - toxicity: renal and oto
- DO: UTIs
  - mainly Gram neg activity
  - use in combination with β-lactams for Gram pos activity
- DON’T: anaerobes

2.) **Macrolides**: inhibit protein synthesis by binding to 50s ribosomes
- adverse effects of all macrolides: GI effects, ototoxicity, QT prolongation, allergy
- DO:
  - upper airway anaerobes
  - atypicals: Legionella drug of choice, Chlamydia, Mycoplasma, Ureaplasma
o others: MAC, Treponema pallidum, Campylobacter, Borrelia, Bordetella, Brucella, Pasteurella a.) first generation: erythromycin
o PO or IV
  ▪ if IV be careful about thrombophlebitis
o interactions: CYP450 inhibitor increased concentrations of other drugs
o DOC: Legionnaires Camp on My Border
• second generation: improved absorption, longer half life, less GI effects, broader spectrum
  o clarithromycin: sinusitis, pharyngitis, tonsillitis, otitis, bronchitis, CA-pneumo, skin & skin struct infections
    ▪ interactions: CYP450 inhibitor increased concentrations of other drugs
    ▪ DO: Mycobacterium avium intracellulare
  o azithromycin: pharyngitis, bronchitis, CA-pneumo, skin & skin struct infections, with less food/drug interactions
    ▪ be careful about thrombophlebitis when giving IV
    ▪ DO: Mycobacterium avium intracellulare, chlamydial infections (single dose)
  o dirithromycin: acute exacerbation of chronic bronchitis, pharyngitis, tonsillitis, skin & skin struct infections
    ▪ DO: Campylobacter jejuni, Borrelia burgdorferi
    ▪ DON’T: Haemophilus
c.) ketolides (macrolide derivatives): bacteria resistant to macrolides may still be sensitive to these
  o telithromycin: CA-pneumo, pharyngitis, tonsillitis, sinusitis, acute exacerbation of chronic bronchitis
    ▪ adverse effects: GI, QT prolongation, acute hepatic failure, death = why it’s not used much
  o contraindicated in myasthenia gravis ii.) fidaxomicin: very expensive
    ▪ DO: for use in adults to treat C. diff as well as other Gram pos aerobes and anaerobes
    ▪ DON’T: Gram negs
3.) Clindamycin: penetrates most tissues, including bone, and is active against anaerobes
• adverse effects: GI, elevated ASTs, one of the worst propagators of C. diff colitis
• DO: for skin and skin struct infections, malaria, above the diaphragm anaerobes
  o Gram pos: CA-MRSA, MSSA, Strep pneumo (PSSP only), other strep
  o fungi: Pneumocystis jiroveci
  o others: Toxoplasma gondii, Plasmodium
4.) Chloramphenicol: broad spectrum, covering most aerobes and anaerobes
• associated with rare bone marrow depression and aplastic anemia that is usually fatal = reserve only for serious life-threatening infections
• DO: for Rocky Mountain spotted fever
  o Gram neg: Rickettsia, Salmonella, Haemophilus, Neisseria
  o Gram pos: covers
  o anaerobes
• DON’T: Pseudomonas
5.) Tetracyclines: broad spectrum
• doxycycline:
  ▪ bacteriostatic
  ▪ adverse effects: GI, rash, hepatic, photosensitivity
  ▪ DO: Rocky Mountain spotted fever, Lyme, CA-MRSA skin infections
    ▪ Gram neg: Rickettsia, Treponema, Leptospira, Borrelia, Coxiella, Chlamydophila, Chlamydia, Vibrio, Brucella, Burkholderia
    ▪ Gram pos:
    ▪ atypicals: Mycoplasma pneumoniae, Mycobacterium marinum
    ▪ others: Plasmodium, Entamoeba
  ▪ DON’T: pediatric patients
6.) Oxazolidinones: inhibits bacterial translation
• linezolid: for vancomycin-resistant Gram pos
11.2.4 Folate Antagonists

*Trimethoprim/sulfamethoxazole* (trade name Septra or Bactrim): inhibits bacterial folate synthesis

- **adverse effects:** rash, GI, hematologic, renal, CNS
- **DO:** Gram neg urinary pathogens, respiratory tract infections, CA-MRSA, protozoa, PCP, some Gram pos
- **DON’T:** anaerobes

11.2.5 Antiprotozoals

*Metronidazole*: inhibits DNA replication in protozoa and bacteria

- **adverse effects:** GI, stomatitis, metallic taste, CNS (including seizures, peripheral neuropathy, encephalopathy)
- **drug interactions with warfarin and alcohol**
- **DO:** vaginal trichomoniasis, giardiasis, amebiasis, anaerobes, DOC for *C. diff* colitis

11.2.6 Antifungals

1.) *Azoles*: inhibit ergosterol synthesis = fungicidal

- **systemic mycoses:** drugs for these provide variable coverage against a spectrum of organisms
  - **fluconazole:** IV or PO; will cover most things you’ll see in clinic
    - adjust for renal dysfunction
  - **itraconazole:** PO
    - erratic oral absorption requires serum concentration monitoring
    - use caution with heart failure patients
  - **voriconazole:** IV or PO
    - small changes in dose can result in large changes in drug exposure
    - greatest degree of side effects
  - **posaconazole:** PO
    - no adjustments available for renal dysfunction
  - **topicals:** clotrimazole
    - **DO:** tinea corporis, tinea pedis, tinea versicolor, oral and mucocutaneous candidiasis

2.) *Polynenes*: bind ergosterol = disruption of membrane function

- **amphotericin B**: used to treat serious disseminated fungal infections, especially in the immunocompromised
  - **adverse effects:** nephrotoxicity, infusion-related toxicities, electrolyte imbalance, nausea/vomiting, hematologic
    - why it is called “ampho-terrible”
  - **DO:** cryptococcal meningitis, zygomycosis, disseminated histoplasmosis, other refractory invasive fungal infections
  - **DON’T:** *A. terreus*, *C. lusitaniae*

- **nystatin**: topical; for mucocutaneous fungal infections and oral candidiasis

3.) *Echinocandins*: inhibit synthesis of fungal β-(1,3)-D-glucan; IV only

- **DO:** most *Candida* infections (fungicidal), *Aspergillus* (fungistatic), some CNS and UTIs, some endemic mycoses
- **DON’T:** dimorphs, *Cryptococcus neoformans*, trichosporosis, zygomycetes a.) anidulafungin
- **caspofungin**: used for empiric prophylaxis of febrile neutropenia c.) micafungin

4.) *Flucytosine*: potent antifungal but has rapidly developing resistance

- use in combination therapies
• adjust for renal dysfunction
• monitor serum concentrations to maintain therapeutic level

5.) Terbinafine:
• DO: topical for various tinea infections, oral for dermatophytic onychomycosis

11.2.7 Antivirals

1.) Other antivirals: inhibit viral DNA polymerase
• adverse effects: renal failure
• cross resistance amongst group
• DO: herpes infections (1 and 2), VZV, EBV
• acyclovir: IV or PO; activated by triple phosphorylation
  o poor oral absorption
  o valacyclovir = prodrug, preferred form
    ▪ oral only, but with better absorption
• famciclovir: similar to acyclovir
• ganciclovir: IV, intraocular implant, PO; activated by triple phosphorylation
  o poor oral absorption
  ▪ improve with valganciclovir
  o adverse effects: nephrotoxicity, bone marrow suppression; why use is limited to treatment of CMV
• foscarnet: does not require triple phosphorylation for activation
  o adverse effects: renal impairment, headache, seizures, electrolyte abnormalities, but less risk of bone marrow toxicity
  o DO: only for ganciclovir-resistant CMV, and resistant HSV
• cidofovir: requires intracellular activation
  o adverse effects: renal toxicity, anemia, rash, headache, hair loss, chills, abdominal pain
  o requires premedication with probenecid

2.) Influenza
• influenza A only (H1N1 resistant to these, increasing resistance makes them no longer recommended)
  o amantadine
  o rimantadine
• influenza A and B: neuraminidase inhibitors
  o zanamivir
  o oseltamivir: H1N1 resistance

11.2.8 Antimalarials
For acute attack: chloroquine, mefloquine, primaquine, quinine sulfate, fansidar

11.3 Introduction: Principles of Infectious Disease
• Biggest killer in human history thus far was the Spanish Flu Pandemic of 1918
• effects overshadowed by WWI
• Current concerns
• aging infrastructure, contaminated water supply
• pandemic flu
  o at greater risk if born after 1950
• bioterrorism: anthrax, plague, tularemia, botulism, smallpox

11.3.1 Inflammation
• Classic signs: rubor, calor, dolor, tumor, functio laesa (loss of function)
• Results in vasodilation and increased permeability, leukocyte mobilization, synthesis/release of acute phase liver proteins, release of cytokines, prostaglandins, and bradykinins
• if host becomes overwhelmed by inflammation sepsis
• Not all inflammation is infectious!
• can be uric acid from gout or from reactions to certain drugs
• From peripheral or systemic infection
• systemic presentation: fever, chills, myalgias, headache, anorexia, hypotension shock

11.3.2 Fever: elevation of core body temperature

• Background on fever
• body temp regulation is in the thermoregulatory center of the hypothalamus
  o temp varies over course of the day with max normal oral temp 98.9f at 6am and 99.9f at 4pm
  o prostaglandins can reset body temp
  o don’t confuse typical fever with hyperthermia, which is uncontrolled body temp due to thermoregulatory center dysfunction (heat stroke, drug rxn etc)
  o inability to mount an immune response in certain populations mean low grade fevers may be significant
    ▪ sometimes a subnormal temperature in these populations can indicate severe infection
    ▪ ex. children and the elderly
• causes:
  • acute of chronic infection
  • connective tissue disease
    o ex. RA or gout
  • malignancy
  • drug reaction
    o ex. Septra or doxycycline
• hyperthermia
• FUO: fever of unknown origin
• Approach to immunocompetent patients presenting with a fever
• which group do they fall into?
  o fever + localizing symptoms
  o fever only
    ▪ viruses: EBV, CMV, enteroviruses (+ headache think meningitis), various respiratory viruses
    ▪ bacteria:
      • no animal exposure: Salmonella Typhi or Paratyphi, Listeria, Staph aureus
      • animal exposure: Coxiella, Leptospira, Brucella, Ehrlichia
      • Mycobacterium tuberculosis, Histoplasma capsulatum
  o fever + rash
    ▪ viruses
      • maculopapular rash: EBV, CMV, HIV, measles, mumps, rubella, roseola, parvovirus B19
      • vesicular rash: coxsackie A, HSV, VZV
    ▪ bacteria: Salmonella Typhi, Treponema pallidum, group A strep = Strep pyogenes (with TSS, scarlet fever), Staph aureus (with TSS), Neisseria meningitidis, Neisseria gonorrhoeae, Borrelia, rickettsial diseases (petechiae)
  o fever + lymphadenopathy and/or hepatosplenomegaly
    ▪ a node of clinical significance is > 2 cm
    ▪ reactive lymph nodes take 6-8 weeks to go away
    ▪ hard, mobile, nontender node think malignancy
    ▪ generalized nodes think viral
    ▪ EBV, CMV, HIV
    ▪ localized nodes think bacterial or protozoa
    ▪ bacterial: TB, cat-scratch fever (Bartonella), tularemia, plague
• protozoan: toxoplasmosis
  • fever + musculoskeletal symptoms
    • ex. arthritis, bursitis, tendonitis
  • viruses:
    • symmetric polyarthritis □ parvovirus B19
    • dengue
    • looks like RA □ Hep B
  • bacteria: Staph aureus (#1 cause), Neisseria gonorrhoeae, group A strep, Borrelia burgdorferi □ Lyme
    • peds: Kingella kingae
• Approach to fever in special populations
• neonates
• hospitalized patients: nosocomial infections or postoperative infections
• immunocompromised patients: HIV, neutropenia, immunosuppression therapy, elderly, pregnant
• travelers
• Approach to fevers of unknown origin
  • differential:
    • neoplasms: leukemia, Hodgkin’s lymphoma, non-Hodgkin’s lymphoma, solid tumors
    • collagen vascular diseases
    • drug fevers
    • granulomatous disease
    • smoldering, potentially silent infection
      • disseminated TB
      • abscesses: abdominal, pelvic, dental
      • endocarditis
      • sinusitis
      • osteomyelitis
      • viral infections: EBV, CMV, HIV, Hep B, Hep C
      • STD’s: Chlamydia, HPV, syphilis
      • gastritis: Helicobacter pylori
      • systemic febrile syndromes
    • rule out Munchausen’s or other self harm
      • fever may be constant vs diurnal with Munchausen’s?
• need to do meticulous history and exam
  • HPI: onset, duration, characterization of symptoms
    • meds, alternative therapies, drugs/alcohol
    • travel
    • food poisoning
    • occupational exposures or hobby exposures
    • sick contacts
    • sexual activities
  • exam: when symptoms aren’t focal, investigate skin and lymph nodes
  • investigation:
    • offer HIV test biopsy any suspicious lesions, consider bone marrow biopsy as well
    • labs: CBC with differential, urine culture, routine chemistries, blood cultures,
      • erythrocyte sedimentation rate (nonspecific marker of inflammation increased with malignancy), CSF exam, joint fluid exam, serologic studies (IgM or IgG)
    • radiology: CXR
    • septic workup: done to determine site of infection, typically includes CBC, CXR, UA, +/- LP

11.3.3 Treatment of Infectious Disease

Empiric therapy: treatment for suspected microbial disease without microbiologic confirmation testing
necessary in life-threatening or rapidly progressing infections
antimicrobials selected to cover microbes most likely to be causing the infection
tests and cultures ordered before initiation of antimicrobial
antimicrobial of choice may change depending on results of labs
specific therapies for isolated organisms

Diseases to Know

Infections of HEENT

Eye
- conjunctivitis: most common eye infection; the more dramatic, the more likely to be bacterial
- viral conjunctivitis is usually adenovirus
- bacterial: Strep pneumo, Haemophilus, Moraxella, Pseudomonas
  - if infant, also think of Neisseria gonorrhoeae and Chlamydia trachomatis
- verno: allergic conjunctivitis
  - treatment for all: typically self-limiting, but topical antibiotics often used
- dacrocytis: infection of the lacrimal sac secondary to infection
- treat with systemic antibiotics
- blepharitis: infection of eyelid margins
- fungal
- treatment: shampoo wash with antifungal
- sty: abscess of eyelid
- always Staph aureus
- treatment: warm compress
- keratitis: infection of the cornea
- viral keratitis: usually HSV
  - treatment: avoid steroids!
- bacterial keratitis: Pseudomonas aeruginosa, Strep pneumo, Moraxella, staph
  - aggressive course
  - at risk: contact lens users, corneal trauma
  - treatment: topical quinolones
    - always give some kind of antibiotic
    - do not patch, it will incubate the infection (same for ointments)
- fungal keratitis: Fusarium, Aspergillus, Candida
  - at risk: those with corneal injury involving plant material, patient with chronic disease of the ocular surface, contact users
  - clinical presentation: eye pain, foreign body sensation, corneal scraping culture
  - treatment: antifungal eyedrops (polyenes) or oral azoles iv.
    - parasitic keratitis: Acanthamoeba
      - causes suppurative keratitis in contact lens wearers as a result of improper handling or use (hot tubs, showers, swimming)
      - treatment is difficult due to cysts, use chlorhexidine or azoles

Ear
- otitis externa: infection of external auditory canal
- bacterial: Pseudomonas aeruginosa ("swimmer's ear"), Proteus, Staph aureus
  - Pseudomonas has slower onset, Staph is acute
  - more common in the summer
  - at risk: activities leaving water in the ear or mild mechanical trauma to ear
  - clinical presentation: severe pain, itching, may have discharge, decreased hearing, swelling
  - treat with topical antibiotics + hydrocortisone
- fungal: Aspergillus most likely, Candida
  - acute or chronic
  - at risk: can be a sequelae of treatment with antibiotics
  - clinical presentation: fungal debris in ear
treatment: use acetic acid if unsure of etiology (covers fungus and bacteria), otherwise azoles

- **acute otitis media**: infection of middle ear
- usually bacterial: Haemophilus influenzae, Moraxella catarrhalis, Strep pneumo, Staph aureus, group A strep
  - occasionally viral
- commonly secondary to viral URT infection
- at risk: more common in children, but can occur in adults
- clinical presentation: pain, sometimes purulent drainage
- treatment
  - first resort: high dose amoxicillin
    - if penicillin allergic → macrolides
  - second resort if unresponsive to treatment
    - amoxicillin + clavulanic acid
    - 2nd or 3rd gen cephalosporin
      - IM ceftriaxone

**Nose & Sinuses:**
- rhinitis: mucopurulent or watery nasal discharge
- usually rhinovirus
- clinical presentation: headache, nasal congestion, sore throat
- treatment is symptomatic and supportive
- antibiotics have no role in preventing secondary infections, unless patient has COPD
- **acute rhinosinusitis**: rhinitis with involvement of infection in paranasal sinuses
- bacterial: Strep pneumo, Moraxella catarrhalis, Haemophilus influenzae, Staph aureus
  - secondary to previous viral URT infection
  - clinical presentation: headache, localized sinus pain & pressure, may have nasal discharge, fever
  - kids may not exhibit sinus pain, but have more runny nose/cough
  - treatment: amoxicillin, SMZ/TMP, cephalosporins (remember ability to cover Strep pneumo varies), macrolides, quinolones
    - if fever present, treat more aggressively
- fungal
  - immunocompromised (esp transplants, diabetics) = acute and invasive → mucormycosis caused by the zygomycetes (Mucor, Absidia, or Rhizopus)
    - can spread from sinuses to brain
  - immunocompetent → chronic and noninvasive → Aspergillus, Penicillium, Alternaria, Cladosporium, Bipolaris
  - allergic: fungal balls in the sinuses

**Oropharynx**
- pharyngitis:
- accounts for large amounts of antibiotics used inappropriately
- commonly caused by group A strep
  - other possible etiologies:
    - bacteria: group C strep, Neisseria gonorrhoeae, Chlamydia trachomatis, Mycoplasma
      - less common: Corynebacterium diphtheriae, Clostridium haemolyticum, anaerobic strep
    - viruses: EBV
- affected population: mostly a disease of 5-17 year olds, rare in children < 2
- clinical presentation: beefy red throat, increased WBCs with neutrocytosis, may have bad smell
  - maculopapular rash if it has progressed to scarlet fever
  - kids: nausea and vomiting due to inflamed mesenteric nodes
- diagnosis for strep
  - Centor criteria: if fever > 38c, tender anterior cervical nodes, presence of exudate, and lack of other respiratory symptoms, good bet it’s strep
treatment:
  - drug of choice: penicillin (single IM injection)
    - penicillin allergy: erythromycin/azithromycin
  - short course cephalexin
  - if penicillin failure (recurrence): clindamycin
  - Infections of the Lower Respiratory Tract

Pneumonia: etiology is age-related, typically bacterial BUT viral pneumonias are common in the young and the old
  - bacteria pneumonia: Strep pneumo, Mycoplasma pneumoniae, Chlamyphila pneumoniae, Legionella
  - rarely Staph aureus
  - if aspiration mixed with anaerobes
  - clinical presentation: pleuritic chest pain (pain worsens with deep breath), productive cough, fever, rales
  - investigation: CXR (may be ahead of or lag behind exam findings), CBC, sputum stain & culture
  - treat empirically and tailor as needed
    - community acquired: doxycycline, cefotaxime + azithromycin, or fluoroquinolone alone if severe
    - postoperative or nosocomial (making Staph aureus suspect): cefepime
    - aspiration: clindamycin
  - fungal pneumonia: distinguish from allergic pulmonary aspergillosis
  - immunocompetent: endemic dimorphs, most commonly Coccidioides, Histo, Blasto
    - clinical presentation: may be asymptomatic, typically self-limiting unless large dose inhaled or patient is immunocompromised
      - immunocompromised dissemination to skin, bones, CNS
    - investigation & treatment
      - Midwest & exposure to bird poop Histo
        - treat with itraconazole or amphotericin
        - pts with chronic pulm disease may have persistent infection
      - CA, TX, AZ, travel to S/Central America, fever, cough, pleuritic pain, arthralgias Coccidioides
        - pregnancy increases risk of disseminated disease
      - N. America, travel to Africa Blasto
        - can resolve, become chronic, or disseminate (bones, skin, GU)
        - treat with itraconazole for 3 months
  - immunocompromised: zygomycetes, hyphomycetes, yeasts like PCP
    - Pneumocystis jiroveci
      - worldwide distribution
      - transmission by inhalation
      - clinical presentation: subacute onset, SOB for several weeks, severe hypoxemia
      - investigation: CXR shows patchy infiltrates
  - Bronchiolitis: usually just in kids
  - Bronchitis

11.3.4 Musculoskeletal Infections

Acute infective monoarthritis (septic arthritis), osteomyelitis, and septic bursitis:
  - bacterial = most common etiology for all
  - most times it is Staph aureus
    - unless young adult or adolescent that is sexually active Neisseria gonorrhoeae
    - IV drug users Pseudomonas aeruginosa
    - osteomyelitis: also consider Pseudomonas aeruginosa and Pasteurella multocida
      - ulcers are often polymicrobial with anaerobes
      - kids Kingella kingae
      - bursitis preceded by trauma or skin infection
    - osteomyelitis a result of spread of distant infection
• investigation:
  o joint aspiration to check for sensitivities
  o osteomyelitis: x-rays and blood cultures
• treatment: if not getting better with treatment, think fungal!
  o osteomyelitis: naftillin or cefazolin
  o septic arthritis: ceftriaxone
• fungal arthritis & osteomyelitis
• immunosuppressed: Candida, Aspergillus
• immunocompetent post-surgery, post-trauma, or post-steroid joint injections: Candida

Polyarthritis:
• rarely infectious!
• a sequelae of infection with bacteria or viruses (group A strep, *Chlamydia*, enteric bacteria, Hep B, Hep C, rubella, parvovirus B19)

### 11.3.5 Infections of the Skin

• scale □ fungal
• scale + pain □ *Staph aureus*
• MRSA will look more purply with a fine scale

**Superficial and cutaneous infections**

a.) *folliculitis*: superficial infection of hair follicle
• usually *Staph aureus*
  o other etiology: HSV, fungus, molluscum contagiosum
  ▪ hot tub: *Pseudomonas aeruginosa*
• treatment is topical if localized or systemic if not
  o MRSA: mupirocin
  o MSSA: retapamulin
  o cephalxin or dicloxacillin
  ▪ azithromycin if PCN allergy
  o NOT amoxicillin; it doesn’t cover staph!

b.) *intertrigo*: inflammation of body folds
  -treatment: nystatin

c.) infections of occluded skin (bandages, casts, backs of bedridden patients)
• treatment: nystatin

d.) nail infections caused by *Candida*
• **paronychia:** infection where nail and skin meet along length of finger
  o at risk: occupational exposure to water
• **onychia:** infection of nail/skin fold on side of nail
• investigation: culture if infection involves nail
• treatment: topical or oral triazoles

e.) hair/skin/nail infections (*tineas*) caused by the **dermatophytes** (*Epidermophyton, Trichosporon, Microsporum*)
• transmission: person-to-person, animal-to-person, fomites, soil
• presentation: head (*tinea capitis*), skin (*tinea corporis*, lesions are round and well-demarcated with central clearing)
• investigation: by clinical presentation or KOH scrape
• treatment: azoles, allylamines
• lamisil is anti-dermatophyte but not anti-*Candida*
• tinea capitis must be treated systemically

f.) *tinea versicolor*: *Malassezia furfur*
• at risk: high humidity, lots of sebum, use of oil-containing cosmetics
• clinical presentation: hypo or hyperpigmented flat lesions on face, trunk, and upper extremities, with no scale
• investigation: clinical presentation or KOH scrape
• treatment: azoles, Rx-strength Selsun Blue
g.) mucosal infections: *Candida*
• presentation for mild to moderate immunosuppression: oropharynx, vagina, cheilitis
• presentation for severe immunosuppression: esophagus, bronchial tree, bladder (an AIDSdefining illness!)
  o can progress to invasive disease
• treatment: nystatin, triazoles

II.) Abscesses, furuncles, carbuncles
• almost always *Staph aureus*
• clinical presentation: very tender with central indentation
• at risk: those with family history of furuncles (due to genetic T-cell defect)
• treatment
• I&D (incise and drain):
• dicloxacillin

III.) Impetigo:
• usually group A strep
• if bullous □ Staph aureus
• clinical presentation: oozing lesions, may be pruritic
• treatment:
• topical mupirocin or retapamulin
• oral cephalaxin
  o macrolide if PCN allergic
• if suspecting MRSA, add Septra

IV.) Herpes virus skin infections
• triggers: stress or sun exposure
• clinical presentation: labialis, whitlow, gladiatorum, folliculitis
• non-skin presentations: encephalitis/meningitis, Bell’s palsy, esophagitis, keratitis
• prodrome: tingling or burning
• treatment:
• topical penciclovir
• oral valacyclovir
• OTC Abreva

V.) Cellulitis: bacterial infection of deeper layers of the skin
• usually group A strep
• staph tends to stick to superficial layers of skin?
• also consider Gram negatives in immunocompromised
• at risk: anything causing a break in the skin
• interdigital tinea pedis can be a source of lower extremity cellulitis
• clinical presentation: poorly defined borders, commonly on lower extremities
• treatment:
• cephalaxin
• amoxicillin + clavulanic acid
• expanded spectrum quinolones
• macrolides

VI.) Erysipelas: superficial cellulitis-like infection of the skin
• caused by group A strep
• common in kids and older adults
• clinical presentation: raised borders, usually on face or legs
• treat same as cellulitis

VII.) Necrotizing cellulitis, necrotizing fasciitis, myonecrosis
  • etiology: trauma, surgery, or idiopathic
  • pelvic surgery: see Fournier’s gangrene from normal flora of perineum (high mortality rate)
  • bacteria involved: group A strep +/- Staph aureus, can be polymicrobial with anaerobes
  • clinical presentation: pain is disproportionate to physical findings
  • treatment: debridement followed by multiple antibiotic regimens

11.3.6 Infections of the GI Tract
I.) Intra-abdominal abscesses: may involve a solid organ or be extravisceral
  • etiology: secondary to other GI infection, trauma, or transplantation
  • mixed Gram negative anaerobes and aerobes, enterococci
  • clinical presentation: commonly involves the liver, spleen, or pancreas
  • treatment: drainage followed by multiple antibiotics

II.) Peritonitis:
  • primary peritonitis: spontaneous
  • almost exclusively only in ascites
  • most E. coli, other Gram negatives, enterococci
  • secondary peritonitis: a result of bowel leakage from trauma or surgery, or from peritoneal dialysis catheter infection
  • in peritoneal dialysis, infection is skin normal flora (Staph epi or other staph)
  • high mortality rate

III.) Gastritis

IV.) Appendicitis:

V.) Diverticulitis:

VI.) Gastroenteritis:
• could be any one of many microbes, or non-infectious etiology
• determine which one based on history, exposures, presentation
  o acute = typically viral
  o blood, fever > 101, greater than 6 stools/day, fecal leukocytes, tenesmus, severe abdominal pain = bacterial
  o chronic = rarely bacterial
  o fungal etiology is rare
  o consider parasites
    ■ most commonly Giardia lamblia
• dysentery: invasive diarrheal disease with blood + fever
• Salmonella, Shigella, Campylobacter, C. diff, Yersinia, Vibrio parahaemolyticus, EHEC
• also consider parasitic Entamoeba histolytica in travelers or immigrants
• investigation:
  o if suspecting amebiasis □ stool exam, antigen detection assays
  o amebiasis can progress to hepatic abscesses
• treatment
  o Shigella: Septra or quinolone
  o C. diff or Entamoeba histolytica: metronidazole
  o also treat severe cases of Campylobacter and Salmonella
• toxin-mediated non-invasive diarrheal disease
• ETEC, Vibrio cholerae
  o could also be viral (rotavirus or norovirus), has same clinical presentation, but invasion of colonic epithelia present
  o clinical presentation: water, secretory diarrhea
• food intoxication: ingestion of preformed toxins
- Staph aureus, Bacillus cereus, Clostridium perfringens
- clinical presentation: less diarrhea and more vomiting, fast onset of symptoms
- parasitic diarrhea
  - giardiasis: most common
    - at risk: homosexual men
    - transmission: fecal-oral, person-to-person, ingestion of contaminated food or water
    - incubation period of 1-4 weeks
    - clinical presentation: asymptomatic or foul smelling, frothy stools, steatorrhea, acute or chronic diarrhea
    - investigation: direct stool exam or immunoassay
    - treatment: metronidazole, treat the whole family!
  - cryptosporidiosis: 2nd most common
    - transmission: fecal-oral, person-to-person, ingestion of contaminated food or water
    - investigation: immunoassay, PCR
    - treatment: usually none because it is self-limiting, but if severe use nitazoxanide
  - isosporiasis or cyclosporiasis less common but with similar epidemiology
- VII.) Rectal itching is parasitic: *Enterobium vermicularis* ("pinworms")
  - the most common parasitic intestinal infection
  - transmission is fecal-oral or by inhalation
  - clinical presentation: severe rectal itching, can cause UTI or vaginitis in female children
  - investigation: tape test or diagnose by clinical presentation
  - treatment: chewable albendazole
- VIII.) Waxing/waning burning GI pain +/- pulmonary symptoms: think *Strongyloides stercoralis*
  - distribution: southern US, Appalachia, Puerto Rico
  - transmission: initially via larval penetration of skin with circulation to GI tract, patient coughs up larvae and swallows, where GI infection occurs as the larvae mature to lay eggs, which are expelled in feces
  - autoinfection from stool means this can persist for years
  - diagnosis: immunoassay, stool exam
  - treatment: ivermectin

11.3.7 Infections of the CNS
- most present acutely (fever, headache, stiff neck, lethargy)
- some present subacutely/chronically (headache, focal neuro symptoms over days or months)
- how to determine etiology:
- meningitis is usually bacterial or fungal
  - asplenia think viral
  - focal abscesses on imaging think parasitic
- I.) Meningitis
- bacterial meningitis
- children and adolescents < 15 years old account for majority of cases
- etiology is age dependent
  - neonates: group B strep, E. coli, Listeria
    - 0-5 and 14-21 year olds: most commonly Neisseria meningitidis
  - also consider Strep pneumo if < 5 years old
  - ages 1 month-50 years overall most common is Strep pneumo
  - ages > 50 years: Strep pneumo is also #1 cause but consider Listeria as well
- clinical presentation
  - higher mortality associated with abrupt presentation
- investigation
  - LP with CSF exam showing high numbers of neutrophils, decreased glucose, protein
  - Gram stain
- treatment:
  - under 50: cefotaxime or ceftiraxone + vanco
  - over 50: ampicillin + cefotaxime (or ceftiraxone + vanco)
If suspecting Staph aureus: vanco + cefepime
- prophylax any contacts of patient with meningococcal meningitis with cipro?

- aseptic meningitis: implies viral cause
- majority of the time it’s an enterovirus
  - also coxsackie, ECHO, mumps, HSV, HIV
- more common in younger patients
- higher incidence in summer and early fall
- clinical presentation: severe headache, fever, photophobia
  - but no focal neurologic signs
- investigation
  - CSF exam and culture negative for bacterial growth
  - CSF shows lower numbers of neutrophils with normal glucose, normal to slightly increased protein
- treatment is supportive and symptomatic unless it’s HSV meningitis
  - HSV  acyclovir, valacyclovir

- subacute/chronic meningitis: headache, focal neuro symptoms over days or months
  - can be viral, bacterial, fungal, or parasitic
    - HIV, Mycobacterium tuberculosis, Treponema pallidum
    - also late-stage Lyme (Borrelia burgdorferi), which presents along with arthritis
    - fungal: Cryptococcus neoformans, endemic dimorphs (esp Histo and Coccidioides)
    - parasitic: cysticercosis (Taenia solium)

II.) Encephalitis

- almost always viral
- most commonly HSV
- if vector-borne, will have seasonal distribution that aligns with vector life cycle
- ex. WNV
- clinical presentation: altered mental status, unusual behavior, decreased level of consciousness, seizures
- more focal neurologic signs
- HSV may have upper respiratory prodrome
- investigation
- CSF exam shows lymphocytes, normal glucose, increased protein
- diagnostic: nucleic acid amplification

III.) Meningoencephalitis

- usually viral
- could be amebic
- clinical presentation: more focal neurologic signs
- Acanthamoeba results in granulomatous encephalitis
- Balamuthia has a subacute presentation
- treatment
- Naegleria  amphotericin B

11.3.8 Genitourinary Infections

I.) Cystitis & pyelonephritis

- usually E. coli
- ascending infections are endogenously acquired
- more frequent in women than men
- male recurrent UTI needs workup
  - especially if < 35, then it’s an STD
- infant male: any UTI needs workup
- increased incidence with age, catheterization, pregnancy, anatomic abnormalities of GU tract
- clinical presentation:
• cystitis: frequency, urgency, dysuria, no back pain
  o older patients may have no symptoms other than altered mental status, and a UTI in this population can be life threatening and quickly progress to urosepsis
• pyelonephritis: fever + CVA tenderness
• investigation
• UA: WBCs, bacteria, +/- RBCs
  o with suspect pyelonephritis, culture also done if pregnant, male, pediatric (= anyone not female 18-35 and sexually active)
• treatment
• length:
  o minimum 3 days for cystitis
  o minimum 7-14 days for pyelonephritis
• hospitalized with pyelonephritis: ceftriaxone
• uncomplicated cystitis: fluoroquinolones or nitrofurantoin
  o alternative: Septra (don’t use if high E. coli resistance in the community)
  o quinolone not approved if < 18 years old

III.) Prostatitis

IV.) Epididymitis: treat with ceftriaxone

V.) STDs: treat syphilis with penicillin

11.3.9 Invasive Disease

• At risk:
• transplants: molds are the most common cause of invasive disease in stem cell and solid organ transplants!
• extremes of age
• immunosuppressive therapy or disease
• major surgery
• Consider dissemination from original site of infection
• from TB
• from fungal pneumonia in the immunocompromised
• pregnant women with Coccidoides
• disseminated Blasto
• dissemination from sinuses: mucormycosis in immunocompromised
• progression of Candida mucosal infections = fungemia
  o know it’s disseminated by isolating organism from a second site (retina, CNS, myocardium, liver, spleen)
• dissemination of Toxoplasma in reactivation disease = brain, eye, lung
• Treatment of disseminated fungal disease requires long-term systemic therapies!

11.3.10 Nosocomial Infections:

• develop within 48 hours of hospital admission
• Etiology: flora changed by colonization of hospital organisms
• most commonly viral: RSV, influenza, para influenza, rotavirus, enterovirus
• bacterial: UTIs most common, less common MRSA, resistant Gram negatives (enterobacteria, Pseudomonas, Acinetobacter), C. diff
• fungal: rare but increased incidence in immunocompromised
• At risk: those with invasive devices (foleys, shunts, drains, IVs, central lines)
• Presentation: fever, elevated WBC, change in mental status, tachypnea, decreased urine output, hypotension
• most to least common:
  o UTI: E. coli, other enterobacteria, Candida, Enterococcus
  o pneumonia, can be secondary to aspiration or intubation
ventilator-associated pneumonia is *Pseudomonas*
- early onset: Staph aureus, Haemophilus influenza
- late onset: gram negative enterics (aspiration)
  - surgical site infection
  - sepsis
  - diarrhea

11.3.11 Sepsis
- **Bacteremia**: presence of bacteria in the blood, can be transient
- **septicemia**: a more severe bacteremia
- When host becomes overwhelmed by inflammation: **sepsis** or systemic inflammatory response syndrome (SIRS)
- diagnosis if meeting 2+ criteria: temp > 38°C or < 36°C, HR > 90, RR > 20, WBC > 12,000 or with > 10% bands
- **severe sepsis** (sepsis syndrome): sepsis + organ dysfunction from hypoperfusion
  - hypoxia, altered mental status, decreased urine output, fever, leukopenia, thrombocytopenia, organ failure, **septic shock** (sepsis-induced hypotension)
- etiologic agents:
  - specific bacteria
    - 50% Gram negatives: E. coli, Klebsiella, Pseudomonas, Proteus, Serratia, Neisseria meningitidis
    - 40% Gram positives: Staph aureus, coag neg staph, Strep pneumo, group A strep, Enterococcus
    - 10% fungal
    - seeding infection: pneumonia, UTI, wounds, cellulitis, abscesses, sinusitis, IV, meningitis
- treatment: empiric IV therapy with maximal doses
  - 3rd generation cephalosporin + aminoglycoside
  - if PCN allergic or suspected *Enterococcus*: nafcillin or vanco
  - suspected anaerobe: add clindamycin or metronidazole
  - hemodynamic and respiratory support

11.3.12 Emerging Pathogens
- Agents of human monocytic disease (ehrlichiosis/anaplasmosis)
- EHEC
- Hep C: the most common chronic bloodborne infection in the US, also the #1 cause of primary hepatocellular carcinoma
- risks: IVDU, sex
- TB
- WNV
- Antibiotic-resistant bacteria: mostly Enterobacteriaceae, VRE, MRSA, MDRTB, PRSP, *C. diff*
- beta lactam hydrolyzers: Enterobacter, Klebsiella, Pseudomonas, Acinetobacter
- H1N1

11.3.13 Travel Medicine
- Pertinent infections: Hep A, dengue, rabies, viral hemorrhagic fevers, SARS, bird flu, rotavirus, norovirus, cholera, bacterial meningitis, E. coli, Salmonella, Shigella, cryptococcosis, coccidioidomycosis, giardiasis, malaria, amebiasis, cryptosporidiosis, filariasis
- Consider chemoprophylaxis, vaccination (Hep A, polio, Hep B, typhoid, Japanese encephalitis, yellow fever, meningococcal), or "in case" antibiotics
- Educate about traveler’s diarrhea: use of pepto Bismol, fluid/electrolyte replacement, when not to use anti-motility agents (bloody diarrhea or fever), risk of IBS sequelae
- Plasmodium
- 4 species with different geographic distribution
- at risk: travel to endemic areas
- transmission via mosquito vector (*Anopheles*)
- clinical presentation: malaria = intermittent attacks of fever, chills, sweats, nausea, vomiting, diarrhea, headache, malaise, dizziness, arthralgia, myalgias
  - can progress to hypotension, CNS involvement, organ failure, pulmonary edema, metabolic derangement
- investigation: thick and thin blood films
- treatment or prophylaxis based on species/geographic distribution
  - If traveling to chloroquine or MDR area, use atovaquone or doxycycline

### 11.4 Prevention of Disease

#### 11.4.1 Prophylaxis

- Pre-surgical: cefazolin or vanco if PCN allergic
- Endocarditis risk (prosthetic valves or congenital deformities)
- Exposures
  - labor: group B strep
  - sexual assault: gonorrhea and chlamydia
  - HIV: depends on source pt and viral load
  - Hep A: Ig
  - Hep B: Ig and vaccine
  - bacterial meningitis: cipro, ceftriaxone, or rifampin
  - influenza: oseltamivir, zanamivir, or vaccine
- Animal bites: penicillin + clavulanic acid, rabies vaccine or Ig if indicated

#### 11.4.2 Screening

- Chlamydia: all sexually active women < 25, all pregnant women < 24
- Gonorrhea: sexually active women with increased risk
- Hep B: all pregnant women
- Syphilis: all persons with increased risk, all pregnant women
- HIV: all high risk persons, all pregnant women

#### 11.4.3 Highly Recommended Vaccines

- Adults
  - flu shot every year
    - kids getting first shot ever need 2 doses that season
  - Tdap once followed by Td booster every 10 years
    - if > 65, skip the Tdap
    - can give Td booster with acute dirty injuries
  - 2 doses of varicella vaccine
    - don’t give to pregnant or immunocompromised
  - females: 3 doses of HPV
  - HZV once > 65, 1 dose
    - don’t give if immunocompromised
  - MMR: 2 doses up to age 49
    - skip if born before 1957, immunocompromised, or pregnant
    - only one dose if born 1957-1967
    - high risk: give 2 doses 4 weeks apart
  - pneumococcal: 1 dose after age 65 or earlier of high risk (smokers, chronic lung disease, chronic renal failure, chronic liver disease, asplenia, sickle cell, cochlear implant, alcoholics, diabetics, immunosuppressed)
    - only revaccinate if < 60 when first vaccinated, or once between the ages of 19-64 for persons vaccinated 5+ years earlier

#### 11.4.4 Suggested Vaccines
- 2 doses of Hep A (typically given in childhood)
- especially if traveling or high risk (IVDU, MSM, chronic liver disease, parents of international adopted children)
- can give combined HepA/B vaccine
- 3 doses of Hep B
- especially if high risk (MSM, sex workers, IVDU, multiple partners, other STI, health care workers, public safety workers, inmates)
- meningococcal
- if less than 56 use Menactra
  - revaccinate after 5 years if at increased risk
- if older than 56 use polysaccharide vaccine
12 Men’s Health Exam Notes

12.1 Male Genitourinary Anatomy

12.1.1 Abdominal Wall

Superficial to deep:
- Camper’s fascia
  - extends to cover scrotum and penis and anchors to the inguinal ligament
    - possible route for spread of infection
- Scarpa’s fascia
- external oblique muscle
- makes up exit to inguinal canal (superficial inguinal ring)
- internal oblique muscle
- transverse abdominal muscle
- transversalis fascia
- makes up entrance to inguinal canal (deep inguinal ring)
- parietal peritoneum

12.1.2 Inguinal Canal

- Formed as the testes descend into the scrotum
- drags along layers of external oblique aponeurosis (external spermatic fascia), internal oblique (aka cremaster muscle), and transversalis fascia (aka spermatic fascia)
- does not bring along layer of transverse abdominal muscle!
- Upper opening to processes vaginalis should be pinched off and obliterated
- Spermatic cord travels through it

12.1.3 Hernias

- **Direct inguinal hernias**: plowing “directly” through weak tissue
  - less common
  - mechanism: increased intra-abdominal pressure (coughing, constipation, urinary retention, ascites), weakening of tissue due to age or smoking
  - results in a bulge medial to inferior epigastric vessels
  - can protrude all the way down through superficial inguinal ring, but rarely enters the scrotum
- **Indirect inguinal hernias**: slipping through an abnormally open inguinal canal
  - more common
- mechanism: a result of a patent processus vaginalis
  - common in kids
- results in a bulge lateral to the inferior epigastric vessels
- may protrude all the way into the scrotum
- **Femoral hernia**: occurs via the femoral canal and will appear as a bulge BELOW the inguinal ligament

### 12.1.4 Testes
- **Function**: testosterone secretion (via Leydig cells), spermatogenesis
- Covered in tunica albuginea to keep the seminiferous tubules together
  - connect to epididymis
    - pathological accumulation of fluid in the epididymis is called a spermatocoele
- Partly covered in tunica vaginalis (remnant of processus vaginalis)
  - may be attached to a variably present appendix testis (a remnant of the Mullerian duct)
    - can become torsioned
      - visible in babies as a blue dot on the back of the testis
- Connected to urethra via the vas deferens
- vas deferens is what is cut during vasectomy
- Failure to descend is called cryptorchidism
  - usually unilateral
  - more common in preemies
  - will usually self-resolve but can be fixed surgically or hormonally
- Pathological accumulation of fluid in the testis is called hydrocele

### 12.1.5 Scrotum
- Divided into right and left compartments by the median septum
- Asymmetry is common, with left lower than the right
- Houses spermatic cord and testes
  - spermatic cord is made of layers from the anterior abdominal wall
    - contains the testicular artery (from renal artery), vas deferens, and lymphatics and nerves to the testes
    - wrapped by the pampiniform plexus of veins, which serves to cool arterial blood
    - pathological dilation of the veins of the spermatic cord is known as varicocele
- Scrotal disorders:
  - epidermal (sebaceous cysts)
  - elephantiasis: from filarial worms

### 12.1.6 Prostate
- Separated into central, transitional, and peripheral zones of cells
  - most cancers originate in the peripheral zone
  - central zone surrounds ejaculatory ducts

### 12.1.7 Penis
- Corpus spongiosum contains the urethra and makes up the glans penis
- Corpora cavernosa
- Meatal abnormalities:
  - **hypospadias**: opening of urethra on underside of penis
  - **epispadias**: opening of urethra on top of penis
  - **megameatus**: enlarged meatus
- Prepuce (foreskin):
  - inner surface of foreskin is a mucus membrane that secretes smegma
  - attaches to glans via the frenulum
  - normally fused to glans until retraction ~ 10 years
  - abnormalities:
    - **phimosis**: nonretraction
    - **paraphimosis**: when foreskin becomes trapped behind the glans and can't be pulled back over
      - necrosis risk
    - **balanoposthitis**: inflammation of the foreskin
- Shaft abnormalities:
  - **Peyronie's disease**: buildup of fibrous plaques in fascial layers leads to a curved penis
  - **chordee**: tightening of fascia on underside of penis makes it curl downward
- Erection:
  - arterial supply for erection comes from the dorsal artery, deep artery, and artery of the bulb of the penis
  - venous drainage via deep dorsal vein
  - erection is a parasympathetic response
    - increased arterial flow with decreased venous drainage
  - ejaculation is a sympathetic response
  - contraction of internal urethral sphincter prevents semen backflow

12.1.8 Seminal Pathway

1.) Testes
2.) Epididymis
3.) Vas deferens
4.) Ampulla of vas deferens
5.) Ejaculatory ducts
  - contribution from seminal vesicles (make up 60% of ejaculate)
6.) Prostatic urethra
  - contribution from prostate glands
7.) Cowper's glands: only contribute pre-ejaculate prior to ejaculation to neutralize any remaining urine in urethra
7.) Penile urethra

12.2 H&P of Male Genitalia, Hernias, Lymphatics, Anus, Rectum, and Prostate

12.2.1 History

- Remember to ask:
  - sexual orientation
  - gender identity
  - relationship status
  - sexual activity
• sexual response & function
• penile discharge or lesions
• scrotal pain, swelling, or lesions
• h/o STIs
• urological ROS
• Screen for substance abuse, prostate, testicular, penile, and colorectal cancers
• Counsel on:
  • nutritional
  • exercise
  • sleep
  • safety and injury prevention: prevention of STIs and HIV, contraception, testicular self-exam
  • mental health
• young adult: risk-taking behaviors, body image
• mid-life adult: occupation, relationships, stress
• geriatric: retirement transition

12.2.2 Physical Exam

A.) Penis
• can be supine or standing
  • inspect: skin, prepuce, glans, urethral meatus, shaft, base
    o document: skin, discoloration, circumcision, prepuce retraction or replacement, urethral position, urethral discharge
  • palpate: glans, any abnormal areas
    o document: induration or tenderness

B.) Scrotum
• can be supine or standing
• inspect: skin contours
  o document: skin, discoloration, contours, degree of testicular descent
  o transilluminate swollen areas
• palpate: testis, epididymis, spermatic cord
  o document: size, shape, consistency, tenderness

C.) Hernias
• first standing, then supine
• inspect: inguinal regions, genitalia
• document: bulging, asymmetry, changes with straining, changes with supine position
• palpate:
  • inguinal canal: deep ring and internal ring (1 cm above midpoint of inguinal ligament)
  • femoral canal
• document: bulging, asymmetry, changes with straining, changes with supine position

D.) Inguinal lymphatics
• do while patient is standing
• inspect for lymphadenopathy
• palpate: horizontal and vertical groups of the superficial inguinal nodes
• horizontal groups drain lower abdomen, buttock, external genitalia (except tests), anal canal, perianal area
• vertical groups drain portions of lower extremity

E.) Cremasteric reflex
• evaluates genitofemoral nerve (L1-L2)
• normal: ipsilateral contraction of the cremasteric muscle, elevation of scrotum and testes
• abnormal: absent reflex
• may indicate testicular torsion, L1-L2 cord injury, upper or LMN injury, or epididymitis
F.) Anus
- upright/bent over or left lateral decubitus
- inspect: perianal and sacrococcygeal areas
- document: lumps, ulcers, inflammation, rashes, excoriations
- palpate: abnormal areas
- document: lumps or tenderness

G.) Rectum
- upright/bent over or left lateral decubitus
- “windshield wiper” over the prostate and palpate each half
- document: consistency, tenderness, induration, nodules
- have patient bear down as you exit to check sphincter tone
- any tenderness stop palpation, inspect anal canal while patient is straining
- document: sphincter tone, tenderness, induration, nodules, fissures

12.3 Miscellaneous Male Diagnostic Methods

Remember that reference ranges vary between men and women
- men have higher Hb
- men have higher uric acid

1.) Testosterone
- to evaluate hypogonadism, delayed or precocious puberty
- to monitor testosterone replacement therapy, antiandrogen therapy
- evaluation of infants with ambiguous genitalia

2.) Semen analysis
- male partner contributes to ~40% of cases of infertility
- need to refrain from sex for 2-5 days
- results give appearance, liquefaction, pH, motility, concentration of sperm, morphology

3.) LH
- elevated in testicular dysfunction, primary testicular failure, CNS dysfunction, precocious puberty,
- postviral orchitis
- decreased in testicular tumors, secondary testicular failure, hypopituitarism

4.) FSH
- pulsatile secretion
- elevated in primary gonadal failure, testicular agenesis, alcoholism, gonadotropin-secreting tumors
- decreased in anterior pituitary hypofunction, hypothalamic disorders

5.) Antispermatozoal antibody

6.) Seminal plasma fructose
- evaluation of azoospermia
- absence implies obstruction or nonpresence of ejaculatory ducts

12.4 Topics In Men’s Health

12.4.1 Erectile Dysfunction
- the consistent or recurrent ability of a man to attain/maintain an erection sufficient for sexual performance
- Mainly neurovascular cause, but with contribution factors
  - could be inhibited production of cGMP □ no stimulation of parasympathetic sexual response
  - vascular endothelial dysfunction: HTN, dyslipidemia, smoking, hyperglycemia
  - cavernosal issues: significant penis curvature
  - neuro: diabetic neuropathy, MS
• endocrine: low testosterone (from high prolactin or other causes)
• psychological factors: excessive sympathetic input
• Affects 22% of US men ages 20-75
• Associated with age
  • however, it is normal for men to slowly decrease in hardness of erection and to have longer refractory periods between orgasm as they age
• Likely an early marker of vascular disease
  • men with ED more likely to have CV event than men without ED
  • study showed 19% of ED men have silent, asymptomatic CAD
• ED precedes onset of angina by 2-3 years and adverse CV events by 3-5 years
• Investigation:
  • history:
    o circumstance surrounding ED
    o ask about libido
    o problem with getting an erection vs maintaining it
    o does patient have normal morning erections, any problems with masturbation
    o premature ejaculation
    o contributing comorbidities: CV disease, diabetes, depression, alcohol, smoking
    o surg history: pelvic, radiation, trauma
    o contributing prescription drugs, recreational drugs, or herbs
      ▪ antihypertensives: thiazides, beta blockers
      ▪ antidepressants
      ▪ hormones: antiandrogens, anabolic steroids
  • PE:
    o BP
    o testicular exam
    o penis exam
    o vascular & neuro exam: peripheral pulses
    o prostate: can be done but rarely plays into ED
  • labs:
    o early morning testosterone with free testosterone
    o lipids
    o fasting blood glucose
    o if nipple discharge prolactin
• Treatment:
  • treat organic comorbidities
  • treat psychosexual dysfunctions
  • counseling:
    o good book: The New Male Sexuality
  • medications and devices:
    o phosphodiesterase type 5 inhibitor: interfere with cGMP breakdown continued dilation of inflowing blood vessels
      ▪ sildenafil: should be taken on empty stomach, interaction with fatty foods
      ▪ tadalafil: can be taken daily
      ▪ vardenafil:
      ▪ caution with prolonged QT
    • first-line agents in the treatment of ED
      • all are similarly effective, with 75% of men being able to have satisfactory erection for intercourse
      • may need 6-8 tries before meds will work max efficacy in 1 hour
      • side effects: headache, indigestion, flushing, nasal congestion, loss of blue-green color vision, significant hypotension
      • contraindications: concomitant nitrates, severe CV disease causes of treatment failure:
        o still need stimulation to have an erection after taking
        o heavy alcohol use
        o relationship problems
12.4.2 Prostatitis

Inflammation of the prostate due to a variety of possible causes

- occurs in all ages of men
- a common complaint

A.) Acute bacterial prostatitis:
- organisms: mostly gram negs (E. coli, Enterobacter, Serratia, Pseudomonas, Enterococcus, Proteus), also Neisseria gonorrhoeae and Chlamydia trachomatis in sexually active young men
- etiologies: sexually acquired, seeding by urine reflux, hematogenous or lymphatic spread from distant source, contiguous spread from adjacent infection
- least common form
- easiest to diagnose
- can be life-threatening
- consider in septic males without an obvious source of infection
- risk factors: GU instrumentation, anal intercourse, immunocompromised, DM, neuro disorders affecting GU tract
- presentation: urinary frequency, urgency, dysuria, nocturia, change in urine stream, pain in lower back, genitals, or abdomen, systemic signs of fever, chills, nausea, vomiting, hypotension, changes in level of consciousness with sepsis
- investigation:
  - PE: vitals, LOC, abdomen, GU, neuro, CVA tenderness
  - UA and urine cultures to look for organism
  - gonorrhea/chlamydia testing
  - blood cultures if septic
  - CT if abscess suspected

- treatment:
  - hospitalization if septic, other comorbidities, no support at home
  - pain management
  - urinary diversion if urine retention is present
  - suprapubic catheter preferred over urethral catheterization to avoid abscess formation
  - broad-spectrum antibiotics until sensitivities come back
    - gram negs: Septra, fluoroquinolones, aminoglycosides
    - gram pos: amoxicillin, ampicillin, cephalixin, cefazolin, vanco if MRSA
  - IV for 3-4 days, then switch to orals
    - usually fluoroquinolones orally for 2-6 weeks

B.) Chronic bacterial prostatitis:
similar to acute bacterial prostatitis, but not life-threatening
presentation: symptoms wax and wane
recurrent UTIs with same organism and no explanation
investigation:
- DRE: prostate may appear normal
- UA and culture for organism (may be harder to do)
  o Meares-Stamey 4 glass test: multiple samples taken for localization cultures
    ▪ initial 10 mL void is from the urethra
    ▪ midstream void is from the bladder
    ▪ then do prostate massage for prostate secretions
    ▪ next 10 mL contains urethral and prostatic fluid
treatment:
- prolonged course of antibiotics: fluoroquinolones
- suppressive antibiotic treatment: consider if 3+ recurrences each year
  o Septra, tetracycline, amoxicillin, or nitrofurantoin
C.) Chronic prostatitis and chronic pelvic pain syndrome: urinary or genital pain with no evidence of infection, with symptoms for 3 of the last 6 months
etiology not well understood
- nanobacteria that we can’t find? Ureaplasma, Mycoplasma hominis, etc.
elevated prostatic pressures
voiding dysfunction
pelvic floor myalgia (like IBS or fibromyalgia)
functional somatic syndrome
emotional disorder
the most common form of prostatitis
affects all ages of men
inflammatory: WBCs present
noninflammatory (aka prostatodynia, may be a misnomer)
presentation: waxing and waning symptoms
investigation:
- differential: infection, GU cancer, urinary tract disease, urethral stricture, neurologic disease
  need to do a complete H&P
- imaging: US, MRI
- biopsy
- bladder function tests: cystoscopy, flow dynamics
- blood tests
- formal psychological testing?
treatments:
- meds:
  o NSAIDs may not alter course of disease, only help for pain
  o alpha blockers for urinary symptoms
  o muscle relaxants for painful ejaculations
  o finasteride to shrink prostate
  o antibiotics: may or may not help
- sitz baths
- lifestyle modifications
- physical therapy: need a pelvic floor specialist
- counseling
D.) Asymptomatic inflammatory prostatitis:
- often found when working up men for infertility or during biopsy for presumed prostate cancer
- no treatment needed

12.4.3 Benign Prostatic Hyperplasia:
- benign proliferation of the prostatic stroma and epithelium → palpable prostate with possible urinary symptoms
- Histologic presence of BPH increases with age
  - prostate undergoes a growth spirt after age 40
  - present in 90% of men age 85 years
    - only 50% of these men will have macroscopic findings and only 30-50% of these will have symptoms
    - more likely to have symptoms with higher PSA or larger prostate
- Presentation:
  - bladder storage problems = irritative symptoms
    - urgency, frequency, nocturia, urge incontinence, stress incontinence
  - bladder emptying problems = obstructive symptoms
    - voiding symptoms: hesitancy, poor flow, intermittency, straining, dysuria
    - postvoid symptoms: terminal dribbling, postvoid dribbling, incomplete emptying of bladder
- Investigation:
  - give pt AUA BPH symptom score sheet to fill out
    - can also be used as a screen and for f/u
    - mild = 0-7
    - moderate = 8-19
    - severe = 20-30
  - history: any recent instrumentation
  - PE: DRE, abdomen for distension, neuro, PVR
  - labs: glucose, electrolytes, UA, PSA in select patients
- Treatment:
  - always based on patient symptoms rather than scores, etc.
  - watchful waiting if patients is not bothered and there are no complications
    - AUA score < 7
    - monitor every 6-12 months
  - medical therapy:
    - AUA score > 8
    - alpha-1 blockers: decrease muscle tone in stroma and capsule
      - rapid symptom relief
      - do not decrease prostate size
      - nonselective: terazosin, doxazosin, prazosin
        - not recommended for use in BPH with concomitant HTN
        - full effect in 2-4 weeks
        - side effects: first dose syncope, orthostatic hypotension
      - selective: tamsulosin, alfuzosin
        - no effect on BP
        - effects in days to one week
        - side effects: fatigue, asthenia, slight risk of ejaculatory dysfunction, nasal congestion
    - 5-alpha reductase inhibitors:
      - for those who can’t take or tolerate alpha-1 blockers
      - shrink prostate
      - can take 6-9 months
      - pregnancy category X = women must not handle pills!
      - side effects: erectile and ejaculatory dysfunction (greater than alpha-1 blockers), nausea, abdominal pain, asthenia
  - surgical interventions
    - indicated for renal insufficiency, urinary retention, recurrent UTIs, bladder calculi, hydronephrosis, large PVR
    - transurethral resection of prostate (TURP): prostate tissue removed via urethral scope
      - longer, more complicated procedure but best outcome
    - transurethral incision of prostate (TUIP): crack open prostate a little bit to allow more room for urethra
• less invasive, less complications, quicker recovery, but prostate must be small
  o open prostatectomy: good option for cases requiring several operations in the same area
  post-surgical issues: erectile dysfunction, urinary incontinence, 5 year recurrence rate
• minimally invasive procedures: going through urethral to prostate but not cutting or removing the prostate in any way
  o transurethral needle ablation (TUNA): pierce urethral wall and transmit radiofrequencies to liquefy parts of prostate
  □ sloughing of tissue via urethra
  o transurethral laser-induced prostatectomy (TULIP): same as TUNA but using laser
  o transurethral microwave thermotherapy:
  o water-induced thermotherapy:
  o intraprostatic stent placement: quicker recovery, need temporary catheter, can’t use these procedures for tissue sample

12.5 Orchitis, Benign Scrotal Disease, and STIs

12.5.1 Orchitis
A.) Mumps orchitis
  • mostly in kids and adolescents
  • occurrence in the spring
  • presentation: abrupt fever, testicular swelling and tenderness, may be bilateral, parotitis (7-10 days before onset of orchitis)
  • treatment: bed rest, NSAIDs, scrotal elevation and ice packs
  • prognosis: rare chance of sterility
B.) STI orchitis
  • agent is usually Neisseria gonorrhoeae or Chlamydia trachomatis in sexually active heterosexual men under 35
  • can be related to epididymitis from same agent = epididymo-orchitis
  • consider enterobacteria in men > 35 with voiding dysfunction
  • treatment:
    • scrotal support, ice, pain relief, injection of spermatic cord with 1% procaine
    • admission if there is priapism or uncontrolled pain

12.5.2 Epididymitis
  • Follows a STI, UTI, or can inflammatory only without infection
    • commonly Neisseria gonorrhoeae or Chlamydia trachomatis in sexually active heterosexual men under 35
    • older men: coliforms, Pseudomonas
    • noninfectious causes include trauma, autoimmune disease, vasculitis, or irritative urine reflux
      □ incited by prolonged periods of sitting, vigorous exercise
  • Most common cause of adult scrotal pain
  • Acute, subacute, or chronic
  • Risk factors: recent instrumentation, anal insertive intercourse, heavy physical exertion, bicycle or motorcycle riding
  • Presentation: -usually subacute
    • may be associated with urethritis and hemospermia
    • if bacterial □ severe swelling, exquisite pain, high fever, rigors, irritative voiding symptoms, acute prostatitis
Investigation:
- need to r/o torsion, tumor, incarcerated or perforated appendix
- PE: urethral discharge, swollen, tender, indurated scrotum
- cremasteric reflex present
- UA and culture
- urethral swab if discharge
- US to r/o testicular torsion
- prepubertal boys with recurrent epididymitis need evaluation for structural abnormalities of the urinary tract

Treatment: varies with severity
- hospitalization if acute febrile and septic
- oral antibiotics for 3-6 weeks
  - treat empirically until cultures come back
- ice, scrotal elevation, NSAIDs

Prognosis:
- complications of oligospermia and infertility

12.5.3 Hydrocele:
- collection of peritoneal fluid between the parietal and visceral layers of the tunica vaginalis
- In adults, may be due to fluid imbalance between secretion/absorption in the tunica vaginalis
- can be related to injury or inflammation
- can be associated with neoplasm or torsion
- Presentation: soft, painless, cystic scrotal mass
  - could also have pain
  - mass transilluminates
  - can be bilateral
- Treatment:
  - not necessary unless symptomatic
  - surgical excision of hydrocele sac
  - simple aspiration has high recurrence rate
  - surgical repair of patent processus vaginalis
- Investigation:
  - US

12.5.4 Varicocele
- dilation of pampiniform plexus
- Valve insufficiency in gonadal veins may contribute
- More common on left side
- Presentation:
  - bowl of spaghetti appearance in scrotum
    - increases with valsalva, deceases when supine
  - oligospermia or asthenospermia
  - painful, dull, or heavy sensation in scrotum
    - increased when standing, relieved by laying down
- Treatment: scrotal support, analgesics, surgical repair

12.5.5 Testicular Torsion:
- twisting of spermatic cord within a testicle, cutting off blood supply
- A result of inadequate fixation of the testis to the tunica vaginalis
- Can occur after trauma or spontaneously
- A medical emergency, needs surgical treatment within 4-6 hours
  - irreversible damage after 12 hours
- More common in neonates and postpubertal males
- More common in colder seasons
- Presentation: scrotal pain, nausea, vomiting, abdominal pain
  - often awakens kids in the middle of the night
- Investigation:
  - PE: tender testicle, scrotal swelling, tender epididymis, elevated testis, scrotal discoloration
  - absent cremasteric reflex
  - color Doppler US if PE is equivocal
- Treatment:
  - surgical correction
  - manual detorsion if surgery not available
    - sedation or cord block followed by external rotation of testis
    - need to f/u with surgical fixation to prevent recurrence
- Prognosis: infertility possible

12.5.6 Torsion of Appendix Testis

- Occurs in boys age 7-14
- Presentation:
  - gradual onset of pain
  - early point tenderness localized to appendix testis
  - reactive hydrocele
  - "blue dot sign" from infarction and necrosis
- Investigation:
  - US
- Treatment:
  - rest, ice, NSAIDs
  - surgery if persistent pain
- Prognosis: pain will last several days to months

12.5.7 STIs in Men

A.) Chlamydia trachomatis
- in men, most common ages 25-34
- most common notifiable disease in US
- presentation: urethritis, urethral discharge, itching, dysuria
- complications: infertility, chronic prostatitis, reactive arthritis, urethral strictures

B.) Lymphogranuloma venereum
- caused by Chlamydia trachomatis
- more common in Asia, South America, Africa, tropical environments
- higher risk with MSM
- presentation: shallow painless ulcer, then painful adenopathy, then buboes

C.) Gonorrhea
- second most common notifiable disease in US
- presentation: urethritis, conjunctivitis, pharyngitis, proctitis, dysuria, purulent discharge, fever
  - can be asymptomatic

D.) Trichomoniasis
- lives in male urethra
- presentation: most males are asymptomatic, some get urethritis

E.) HSV
- presentation: pain, pruritus, soreness, external dysuria, inguinal adenopathy, characteristic vesicles
F.) Syphilis
- presentation: painless chancre, signs of secondary or tertiary syphilis if late

G.) Chancroid
- presentation: multiple painful genital ulcerations

H.) Granuloma inguinale
- caused by Klebsiella granulomatis
- presentation: chronic painless ulcers that are beefy red

12.6 Male Cancers

12.6.1 Prostate Cancer
- Usually adenocarcinoma
- Most commonly diagnosed male cancer and 2\textsuperscript{nd} leading cause of male cancer deaths
- Incidence increases with age
- More common in black patients
- Risk factors: age, race, high fat diet, FH, genetics, obesity
- no association with smoking, sexual activity, prior infections, or BPH
- protective: well-balanced diet, physical activity, weight control
  - chemoprevention not recommended
- Screening and available prostate tests:
  - USPSTF: any prostate cancer screen for men under age 75 is grade I, and grade D for men over 75 = let patients make the decision
    - if yes, do it every 2 years if normal or every year if abnormal
  - DRE: low detection rate for tumors
    - refer if abnormal
  - transrectal US: no role as a screen
    - high cost and low specificity
    - can be used to assess elevated PSA
    - best for staging and for guiding biopsies
    - can also be used to estimate prostate volume
    - not accurate in determining local tumor extension
  - cystourethroscopy: for visualization of abnormalities of the bladder, prostate, ureters
    - can also be used to do biopsy, retrograde pyelogram, or transurethral surgery
  - prostate biopsy:
    - indicated for early diagnosis of prostate cancer, active surveillance during conservative management of prostate cancer, or for evaluation of men with azoospermia
  - labs:
    - serum prostate specific antigen: protein produced by healthy and malignant prostate cells
      - elevated in cancer, inflammation, or BPH
      - not diagnostic of cancer
      - low detection rate
      - false + and negs
      - will rise as men age
      - unknown if its use reduces mortality
      - refer if > 4.0 ng/mL
    - free PSA: PSA that is not protein bound
      - healthy men have a higher free PSA %
      - lower % free PSA = increased cancer risk
      - may be useful in differentiating cancer from BPH in patients with borderline high total PSA
    - PSA velocity:
      - if > 0.75 ng/mL \uparrow per year, this increases likelihood of cancer
    - PSA density: serum PSA/prostate vol (from US)
      - adjusts PSA level for prostate size
- increased density = increased cancer risk
  - prostatic acid phosphatase: enzyme produced by the prostate
    - may be elevated in adenocarcinoma, manipulation of prostate, inflammation, BPH, other nonprostatic disease
    - questionable role in diagnosis of prostate carcinoma
    - can be used for monitoring chemotherapy
    - can’t be ordered immediately after DRE, TURPs, or prostatic massage

- Presentation:
  - no signs early in disease
  - advanced disease: obstructive urinary symptoms, hematuria, hematospermia
  - mets to bones, inguinal lymph nodes

- Investigation:
  - prostate biopsy by transurethral US
    - look for hypoechoic areas
    - 8-12 core are sampled from the apex, mid-portion, and base of both lobes
  - MRI: look for capsular extension and invasion to seminal vesicles, lymphadenopathy
  - PET scan if suspecting mets
    - consider for PSA > 20, high-grade histology, or bone pain
  - scoring of biopsy by Gleason system
    - higher score = more aggressive, worse prognosis

- Treatment:
  - based on patient life expectancy, general health, tumor characteristics, risk of tumor progression and recurrence
  - controversial if disease is localized
  - radical prostatectomy: open or laparoscopic
    - cavernosal nerve sparing to preserve potency
    - risks: urinary incontinence
    - follow up operation with PSAs, should be 0
  - radiation: external beam or brachytherapy
    - results in impotence in many patients
  - advanced or metastatic disease: hormone therapy
    - androgen deprivation via surgical or medical castration
      - meds: GnRH analogues, antiandrogens, ketoconazole, steroids
    - side effects: hot flashes, osteoporosis, impotence, decreased facial hair, weight gain, loss of muscle mass, gynecomastia
  - if refractory to hormone treatment:
    - docetaxel
    - targeted immunotherapy using patient’s own WBCs is now available
      - costs $93,000
      - side effects: infusion reactions, CV events

- Prognosis:
  - localized disease that is actively surveyed has a < 10 year life expectancy
  - localized disease that is treated has a > 10 year life expectancy

12.6.2 Penile Carcinoma

- Most commonly squamous cell
- Rare
- Diagnosed almost exclusively in uncircumcised men
- Risk factors: lack of neonatal circumcision, HPV 16 or 18, tobacco use, poor hygiene
- Presentation:
  - painless, non-indurated, ulcerated mass
  - may be on the glans penis, coronal sulcus, or foreskin
  - inguinal adenopathy
- Investigation:
- lesion biopsy
• Treatment:
  • depends on tumor histology, size, location, and presence of lymphadenopathy
  • surgical removal is the gold standard
    o goals are to preserve glans sensation and maximize penile shaft length
    o may need total penectomy with perineal urethroscopy for proximal tumor
    o Mohs microsurgery for low grade tumors
  • other options: topical chemo, radiation, laser ablation

• Prognosis:
  • directly related to grade of tumor and extent of invasion
  • poor prognosis: high histologic grade, vascular invasion, advanced pathologic grade, lymph node involvement, mets above the inguinal ligament
  • if untreated can lead to auto-amputation

12.6.3 Testicular Tumors

• Risk factors: cryptorchidism, abnormalities in spermatogenesis, FH or personal history of testicular cancer

• Screening:
  • USPSTF recommends against screening in asymptomatic adolescents and adult males

• Presentation: firm, painless mass arising from the testis
  • scrotal pain in 10% of cases, due to tumor hemorrhage or epididymitis
  • usually unilateral, but 2-3% have bilateral involvement
  • advanced disease: cough, GI, back pain, neurologic signs, supraclavicular lymphadenopathy

• Investigation:
  • scrotal US: distinguishes benign vs malignant and intra vs extratesticular
  • excisional biopsy with inguinal orchiectomy
    o pathology: germ cell (most common) or stromal tumor
      • if germ cell: seminoma or nonseminoma
  • labs:
    o β-HCG: will be elevated in choriocarcinomas, embryonal carcinomas, and in some seminomas
    o AFP: elevation excludes diagnosis of seminoma
  • CT of chest, abdomen, pelvis for mets
    o especially to retroperitoneal lymph nodes, lungs, and mediastinum

• Treatment:
  • inguinal orchiectomy with follow-up of tumor markers
    o need chemo if they don’t decrease post-op
  • seminomas are radiation sensitive
    o also need chemo if above IIb
  • non-seminomas are usually cured by orchiectomy alone

• Prognosis:
  • seminoma 5-year survival rate is 98% if early, 55-80% if advanced
  • non-seminoma 5-year survival rate is 96-100% if early, 90% if advanced
  • consider sperm banking prior to treatments
13  Microbiology Exam Notes

13.1  Background & Classification

- **eukaryotes**: have organelles (Mt, ER, Golgi), 80s ribosomes, no cell wall or chitin/cellulose cell wall, cell membrane contains sterols, nucleus contained in membrane
- **prokaryotes**: no organelles, 70s ribosomes, complex cell wall, no sterols in cell membrane, no nuclear membrane
- **commensal**: organisms of different species that live together in a close relationship; one benefits while the other neither benefits nor is harmed
- **normal flora**: the endogenous population of microbes that inhabit the external and internal surfaces of healthy humans
  - permanent or transient
  - in constant change from birth to death
  - create barrier to invasion from pathogenic bacteria
  - only cause disease by disruption of normal balances or through contamination of a normally sterile site
- **strict pathogen**: always causes a disease
- **pathogenicity**: ability to cause disease
- **virulence**: degree to which an organism causes disease

13.2  Viruses

**DNA viruses**

- Group I: viruses possess double-stranded DNA.
- Group II: viruses possess single-stranded DNA.

<table>
<thead>
<tr>
<th>Virus Family</th>
<th>Examples (common names)</th>
<th>Virion naked/enveloped</th>
<th>Capsid Symmetry</th>
<th>Nucleic acid type</th>
<th>Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Adenoviridae</td>
<td>Adenovirus</td>
<td>Naked</td>
<td>Icosahedral</td>
<td>ds</td>
<td>I</td>
</tr>
<tr>
<td>2. Papillomaviridae</td>
<td>Papillomavirus</td>
<td>Naked</td>
<td>Icosahedral</td>
<td>ds circular</td>
<td>I</td>
</tr>
<tr>
<td>3. Paroviridae</td>
<td>Parovirus B19</td>
<td>Naked</td>
<td>Icosahedral</td>
<td>ss</td>
<td>II</td>
</tr>
<tr>
<td>4. Herpesviridae</td>
<td>Herpes simplex virus, varicella-zoster virus, cytomegalovirus, Epstein-Barr virus</td>
<td>Enveloped</td>
<td>Icosahedral</td>
<td>ds</td>
<td>I</td>
</tr>
<tr>
<td>5. Poxviridae</td>
<td>Smallpox virus, vaccinia virus</td>
<td>Complex coats</td>
<td>Complex</td>
<td>ds</td>
<td>I</td>
</tr>
<tr>
<td>6. Hepadnaviridae</td>
<td>Hepatitis B virus</td>
<td>Enveloped</td>
<td>Icosahedral</td>
<td>circular, partially ds</td>
<td>VII</td>
</tr>
<tr>
<td>7. Polyomaviridae</td>
<td>Polyoma virus: JC virus (progressive multifocal leucoencephalopathy)</td>
<td>Naked</td>
<td>Icosahedral</td>
<td>ds circular</td>
<td>I</td>
</tr>
<tr>
<td>8. Circoviridae</td>
<td>Transfusion Transmitted Virus</td>
<td>Naked</td>
<td>Icosahedral</td>
<td>ss circular</td>
<td>II</td>
</tr>
</tbody>
</table>
**RNA viruses**

- **Group II**: viruses possess double-stranded RNA genomes
- **Group IV**: viruses possess positive-sense single-stranded RNA genomes.
- **Group V**: viruses possess negative-sense single-stranded RNA genomes.

<table>
<thead>
<tr>
<th>Virus Family</th>
<th>Examples (common names)</th>
<th>Virion naked/enveloped</th>
<th>Capsid Symmetry</th>
<th>Nucleic acid type</th>
<th>Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Reoviridae</td>
<td>REO virus, Rotavirus</td>
<td>Naked</td>
<td>Icosahedral</td>
<td>ds</td>
<td>III</td>
</tr>
<tr>
<td>2. Picornaviridae</td>
<td>Enterovirus, Rhinovirus, Hepatovirus, Cardiovirus, APhthovirus, Poliovirus, Parechovirus, Erbovirus, Kobovirus, Teschovirus, Coxsackie</td>
<td>Naked</td>
<td>Icosahedral</td>
<td>ss</td>
<td>IV</td>
</tr>
<tr>
<td>3. Caliciviridae</td>
<td>Norwalk virus, Hepatitis E virus</td>
<td>Naked</td>
<td>Icosahedral</td>
<td>ss</td>
<td>IV</td>
</tr>
<tr>
<td>4. Togaviridae</td>
<td>Rubella virus</td>
<td>Enveloped</td>
<td>Icosahedral</td>
<td>ss</td>
<td>IV</td>
</tr>
<tr>
<td>5. Arenaviridae</td>
<td>Lymphocytic choriomeningitis virus</td>
<td>Enveloped</td>
<td>Complex</td>
<td>ss(-)</td>
<td>V</td>
</tr>
<tr>
<td>6. Flaviviridae</td>
<td>Dengue virus, Hepatitis C virus, Yellow fever virus</td>
<td>Enveloped</td>
<td>Icosahedral</td>
<td>ss</td>
<td>IV</td>
</tr>
<tr>
<td>7. Orthomyxoviridae</td>
<td>Influenzavirus A, Influenzavirus B, Influenzavirus C, Isavirus, Thogotovirus</td>
<td>Enveloped</td>
<td>Helical</td>
<td>ss(-)</td>
<td>V</td>
</tr>
<tr>
<td>8. Paramyxoviridae</td>
<td>Measles virus, Mumps virus, Respiratory syncytial virus</td>
<td>Enveloped</td>
<td>Helical</td>
<td>ss(-)</td>
<td>V</td>
</tr>
<tr>
<td>9. Bunyaviridae</td>
<td>California encephalitis virus, Hantavirus</td>
<td>Enveloped</td>
<td>Helical</td>
<td>ss(-)</td>
<td>V</td>
</tr>
<tr>
<td>10. Rhabdoviridae</td>
<td>Rabies virus</td>
<td>Enveloped</td>
<td>Helical</td>
<td>ss(-)</td>
<td>V</td>
</tr>
<tr>
<td>11. Filoviridae</td>
<td>Ebola virus, Marburg virus</td>
<td>Enveloped</td>
<td>Helical</td>
<td>ss(-)</td>
<td>V</td>
</tr>
<tr>
<td>12. Coronaviridae</td>
<td>Coronavirus</td>
<td>Enveloped</td>
<td>Helical</td>
<td>ss(-)</td>
<td>IV</td>
</tr>
<tr>
<td>13. Astroviridae</td>
<td>Astrovirus</td>
<td>Naked</td>
<td>Icosahedral</td>
<td>ss</td>
<td>IV</td>
</tr>
<tr>
<td>14. Bornavirus</td>
<td>Borna disease virus</td>
<td>Enveloped</td>
<td>Helical</td>
<td>ss(-)</td>
<td>V</td>
</tr>
</tbody>
</table>

- require intracellular host to actively function
- classify based on type of genome, tropism, geographic location of discovery, body site of discovery, clinical manifestations, or structure/size/morphology
- structure:
  - **genome/core**: nucleic acid that directs synthesis of viron components within an appropriate host cell, may be linear or circular
  - **viron**: the extracellular, inert phase of the virus that acts as the spaceship taking the genome to infect a host cell (vs active virus that is intracellular)
    - DNA or RNA
      - DNA viruses share replication and gene expression with the host cell
        - single or double stranded
      - RNA viruses have devised a way to replicate without host cell machinery
        - **+ sense RNA**: describes RNA that is in the message-sense orientation, 5' to 3'
        - **retroviruses**: single-stranded + sense RNA viruses that have reverse transcriptase (RNA dependent DNA polymerase) that can make DNA out of RNA
        - **- antisense RNA**: describes RNA that is anti-sense in orientation, 3' to 5'
        - means these kinds of viruses must package an active RNA-dependent RNA polymerase into their virion to be able to make proteins in the host cell (host cell polymerases won’t read in antisense)
  - **capsid**: protein coat that surrounds the core
    - helical (cylinder, more easily evades innate immunity) or icosahedral (more spherical)
    - may have capsid to resist phagocytosis and dessication
    - may have lipid envelope
      - makes them more delicate and labile vs being beneficial in bacteria

DNA or RNA
clinical considerations:
- DNA viruses and retroviruses are capable of persistent or latent infection
  - **persistent**: an infection that often lasts the lifetime of the individual and virus can always be isolated from the host
  - **latent**: an infection which lasts the lifetime of the host but rarely produces virus particles although the viral genome exists in dormancy in certain cells
- some viruses can be **oncogenic**: viral infection does not kill the host cell but all or some of the viral genome is stably inherited by the infected cell and affected growth
  - can inactivate host cell tumor suppressor genes, inhibit apoptosis, or increase proliferation
- RNA viruses are very prone to mutation and constant evolution of virus, evasion of immunity, evasion of vaccination efforts, reinfection multiple times possible due to changing antigens
- antivirals aim to block entry of virus, block viral uncoating, block cell-to-cell spread, or inhibit viral replication
- medically important DNA viruses
  - herpesviruses: HSV 1&2, varicella, EBV, CMV
  - parvoviruses: parvovirus B-19
  - adenoviruses
  - hepadnaviruses: hep B
  - papovaviruses: HPV
  - poxviruses: smallpox
- medically important RNA viruses
- parmyxoviruses: parainfluenza, measles, mumps, RSV
- orthomyxoviruses: influenza
- caliciviruses: norovirus
- retroviruses: HIV
- picornaviruses: rhinovirus, polio, Coxsackie
- others: coronavirus, rubella, Hanta virus, rotavirus, Ebola

### 13.3 Bacteria

- prokaryotic
- classified by:
  - shape: bacillus, cocci, spirochete
  - arrangement: pairs (diplococci), chains (streptococci), clusters (staphylococci)
- Gram stain
  - Gram positives are purple because their thick peptidoglycan cell wall layer retains crystal violet dye
  - Gram negatives are pink because their peptidoglycan is very thin and protected from dye by a lipopolysaccharide (LPS) in their outer membrane, so they take up the pink safranin dye instead
  - LPS functions as an **endotoxin** that stimulates a powerful immune response but is poorly antigenic
- some bacteria don’t stain with Gram stain
  - ex. Mycobacteria
- nutritional and oxygen requirements
  - **autotroph**: eats only inorganic compounds
  - **heterotroph**: eats organic compounds
  - **obligate aerobe**: requires oxygen to grow
  - **obligate anerobe**: can’t grow in the presence of oxygen
  - **facultative anaerobe**: can grow with or without oxygen
  - **microaerophile**: grows best in low amounts of oxygen
- pathogenicity: some have extra structures that enhance virulence
  - **plasmids**: extrachromosomal DNA elements encoding virulent traits such as antibiotic resistance
  - **spores**: form intracellular hard protective coats that lay dormant and resist heat, dessication, and irradiation
  - only seen in Bacillus and Clostridium
capsules: slimy outer layer composed of polysaccharide or protein that resist phagocytosis and facilitate adherence to human cells
  - encapsulated microbes: Staph aureus, Strep pneumo, Group A & B Strep, Neisseria gonorrhoeae, Neisseria meningitidis, Haemophilus influenzae, E. coli, Klebsiella pneumoniae, Salmonella, Yersinia pestis, Pseudomonas aeruginosa
flagella: single or multiple tails that allow movement, mostly in bacilli
pili (fimbriae): hairlike filaments projecting from cells that mediate attachment to human cells and conjugation, mostly in Gram negatives
  - may have adhesin proteins to attach to host cells
  - endotoxins
exotoxins: proteins secreted by both Gram positives and negatives that stimulate an antigenic response
biofilm: describes layers of bacterial communities that work together to secrete a sticky polysaccharide which enables them to escape host defenses and antibiotics
invasion enzymes to lyse host cells
taxonomy

13.4 Fungi: yeasts & molds

eukaryotic
  - all fungi stain Gram positive but it is due to chitin in their cell wall vs peptidoglycan
  - some have capsules
  - most are obligate aerobes and none are anaerobes
  - some exhibit thermal dimorphism: grow as a mold in the environment (cooler 25°C) and a yeast in the host (warmer 37°C)
  - Histoplasma capsulatum, Blastomyces dermatitidis, Sporothrix schenckii, Coccidoides immitis, Paracoccidioides brasiliensis, Penicillium marneffei
  - yeasts characterized by: lack of filaments (aka hyphae), unicellular, reproduce by budding, look creamy on media
    - ex. Candida, Torulopsis glabrata, Cryptococcus neoformans, Pneumocystis
  - molds characterized by: multicellular filaments (septate or no-septate), asexual reproduction (conidia = asexual nonmotile fungal spores, conidiophores = stalks bearing conidia) and sexual reproduction, look fuzzy when grown on media
    - conidia come in many forms and can be used to identify a mold
      - dermatophytes (= love to eat and grow on skin): Trichophyton, Malassezia
      - dematiaceous fungi (grow dark on a plate): Alternaria, Cladosporium
      - hyaline fungi (grow pale or white on a plate): cause opportunistic disease
    - fungi cause disease via metabolic toxicity (ingestion - how you take a shroom trip!), hypersensitivity/allergies, or host colonization with subsequent disease (infrequent if you’re healthy)
    - fungal infection = mycosis
  - disease is classified by level of tissue invasion:
    - superficial mycoses: limited to outermost layers of hair and skin b.) cutaneous mycoses: extend into the dermis or nail
    - subcutaneous mycoses: extend to muscle and fascia
  - systemic mycoses: typically originate in the lung and disseminate to organs and skin □ lesions
    - caused by certain thermal dimorphs found in soil or bird poop: Histio, Blasto, Coccidioides, and Paracoccidioides
  - opportunistic fungi only cause disease in immunocompromised hosts
  - Candida: most common opportunistic fungi
    - changes to more pathogenic form with hyphae once inside human
    - not a dimorph but a polyphenic yeast
  - Cryptococcus neoformans: thick capsule protects it from immune system
    - □ can infect both immunocompetent and immunocompromised hosts
    - tropism for CNS □ meningitis
    - □ always a yeast
Aspergillus: common worldwide environmental mold that colonizes the human airway and can invade tissue
  o virulence factors: conidia bind fibrinogen

Zygomycetes: Mucor, Rhizopus

Fusarium and other hyaline fungi

Pneumocystis jiroveci
  o route of infection is inhalation
  o causes PCP: *Pneumocystis jiroveci* pneumonia
    • common in AIDS patients

13.5 Parasites: protozoa & helminths

- eukaryotic
- protozoa: unicellular
- metazoa: multicellular
  - can form cysts to survive harsh environmental conditions
  - plays a key role in most disease transmission
  - in US, consider in patients with travel to remote or exotic areas, in immigrants or refugees, in the immunosuppressed, and in AIDS patients
  - acquisition of disease is fecal/oral or through direct penetration
  - can have arthropod vectors
  - important pathogens grouped by site of disease or morphology:
    - intestinal protozoa: *Entamoeba histolytica*, *Giardia lamblia*, *Coccidia*
    - urogenital protozoa: *Trichomonas vaginalis*
    - blood and tissue protozoa: *Plasmodium*, *Naegleria*, *Acanthamoeba*, *Toxoplasma gondii*
    - nematodes (roundworms): *Enterobius vermicularis*, *Ascaris lumbricoides*, *Strongyloides stercoralis*, *Trichinella spiralis*, *Ancylostoma*, *Necator americanus*
    - cestodes (tapeworms): *Taenia*, *Echinococcus*
    - trematodes

13.5.1 Unusual Bacteria that are Hard to Classify

A.) *Spirochetes*: the pathogenic genera are *Borrelia*, *Treponema*, *Leptospira*
  - differentiate *Leptospira* from *Treponema*: *Leptospira* can be grown in vitro

B.) *Mycoplasmas*: the smallest free-living bacteria, slow growers, no cell wall, sterols in cell membrane
  - *Mycoplasma spp* have a fried egg appearance when grown on media
  - *Mycoplasma pneumoniae*: always a pathogen!
    o causes URT and LRT infections
    o has superantigen adhesin protein (P1) that kills cilia
  - *Mycoplasma hominis* & *genitalium*: colonize GI tract, may play a role in genital infections and spontaneous abortions
  - *Ureaplasma urealyticum*: colonizes GU tract, the most important cause of urethritis C.) *Chlamydias*: small parasitic Gram negatives
    o extracellularly form elementary bodies that are like spores
    o intracellularly form metabolically active reticulate bodies that replicate

D.) *Rickettsias/Orientias*: poorly staining Gram negative rods that are maintained in animal and arthropod reservoirs, humans are accidental hosts (except for *Rickettsia prowazekii*)

E.) *Ehrlichias/Anaplasm*: intracellular bacteria similar to Gram negatives but nonstaining, associated with tickborne diseases
  - also have elementary and reticulate bodies

F.) *Coxiella burnetii*: causes Q fever
  - small cell variants and large cell variants, *Anaplasma*, actinomycetes
  - human exposure from contaminated environment (inhalation?)
• similar to Rickettsias, distinguish by LPS antigens

G.) **Aerobic actinomycetes**: Gram positives that resemble fungi
• found in soil, decaying vegetation, ventilation systems
• will only cause disease in immunocompromised
• don’t confuse with anaerobic actinomycetes that are usually normal flora in URT, GI, GU
• medically important genera:
  o *Nocardia*: infection acquired by inhalation or traumatic implantation, spectrum of disease based on immunocompetency
  o *Tropheryma, Gordonia, Tsukamurella*

13.5.2 **Sites of Antibiotic Activity**

1.) **Bacterial cell wall**: Gram characteristics, mycobacteria, or mycoplasma
• cell wall inhibitors:
  o **β-lactams**: antibiotic confuses bacteria into using it to make their cell wall, but it results in a faulty cell wall that does not cross link peptidoglycan
    • ex. penicillins, cephalosporins, carbapenems, monobactams
    • ***older β-lactams only work on Gram positives but newer versions work on Gram negatives as well***
  o others: vanco, bacitracin, anti-TB agents

2.) **Bacterial cell membrane**
• ex. polymixin

3.) **Bacterial ribosomes**: disruption of protein synthesis
• ex. erythromycin

4.) **Antimetabolic agents**: mimic structure of a required metabolite
• ex. Septra

5.) **DNA or RNA synthesis inhibitors**
• ex. Cipro

13.5.3 **Anaerobic Infections**

• Always occur **endogenously**: when normal flora are introduced to inappropriate sites
• anaerobes are normal flora in the GI tract, vagina, URT, skin
• Risk factors: trauma, decreased vascular supply
• Clues of an anaerobic infection
  • near site where anaerobes are normal flora
  • foul smelling discharge
  • no bacterial growth on culture grown in normal air
  • presence of gas
  • failure to improve on antibiotics covering aerobic bacteria

13.5.4 **Immune Response to Microbes**

• First line of defense: intact skin
• Second line of defense: intact mucous membranes
• Neutrophils destroy bacteria
• Macrophages destroy all pathogens
• NK cells destroy virus infected cells

13.6 **Respiratory Pathogens**

13.6.1 **Respiratory Pathogens**
• URT = eye, ear, pharynx, sinuses
• normal respiratory flora complete with pathogens for attachment sites and produce bactericidal substances
• etiology of disease:
  o wiping out ciliary mechanisms
  o introduction to sterile site in large numbers
  o if you have no antibody to streptococcal M proteins
  o transient colonization leads to infection
  o having risk factors: smoking, allergies, or preceding viral infection
• LRT = trachea, bronchioles, lungs
• historically thought of as a normally sterile environment (may or may not be true)
• majority of pathogens are the same pathogens that cause URT disease, as well as Gram negatives normally found in the GI tract (from aspiration)

13.6.2 Clinical Pearls
• Influenza C, parainfluenza, RSV, human metapneumo all look the same clinically
• Haemophilus influenzae, Strep pneumo, and Moraxella catarrhalis look similar clinically
• Neonatal pneumonia is bacterial (group B strep)
• Childhood pneumonia up to age 5 is almost always viral
• Bronchitis in non-smoking adults is almost always viral
• General considerations:
  • in infants and children, LRT pathogens are usually viral, only consider bacteria if child does not get better: Strep pneumo, Haemophilus influenzae, rarely Staph aureus
  • in adolescents and adults, consider Strep pneumo, Mycoplasma pneumoniae, Chlamydophila pneumoniae, Haemophilus influenzae, Legionella
• causative agents of hospital-acquired pneumonias: aerobic Gram negatives (multi-resistant Gram negative bacilli or MRGN), Enterobacter, Klebsiella, Acinetobacter, Pseudomonas, Legionella
  o rarely Staph aureus
  o have plasmids encoding resistance to β-lactams
• in immunocompromised patients, consider fungal pneumonias: Candida, Aspergillus
  o in HIV patients, consider PCP

13.6.3 Viral URT Pathogens Overview
• some can also be seen in LRT
• Common colds: rhinovirus, coronavirus
• Conjunctivitis: adenovirus, enterovirus
• Keratitis: adenovirus, HSV-1, HSV-2, Herpes zoster
• Influenza: influenza A & B (both URT and LRT), influenza C (URT only)
• Laryngitis: parainfluenza virus, influenza virus, EBV, adenovirus
• Otitis media: adenovirus, rhinovirus
• Pharyngitis: adenovirus, rhinovirus, coronavirus, EBV, Herpes simplex, Coxsackie A virus, parainfluenza, influenza, HIV

13.6.4 Viral LRT Pathogens Overview
• Bronchiolitis: RSV
• Bronchitis
• age < 2: adenovirus
• ages 2-5: RSV, parainfluenza 1-3
• adolescents & adults: adenovirus, influenza
• Pneumonia
• infants & children: RSV, parainfluenza
• adolescents & adults: influenza, adenovirus, RSV, Hanta virus

13.6.5 Hanta Virus
• ss RNA
• An emerging pathogen first seen in Four Corners
• Transmission
• carried by rodents
• humans exposed via rodent droppings, urine, or nests
• Disease: pneumonia
• at risk: hikers and campers in rodent-infested areas

13.6.6 Picornaviruses
• one of the largest and most important groups of viruses
A.) Enteroviruses
B.) Rhinoviruses
• habitat: likes to replicate in cooler places like nasal cavities
• transmission: direct, inhalation, fomites
• disease:
  o most important cause of the common cold!
  o many serotypes = multiple colds over lifetime
  o at risk: greatest prevalence in infants and children
C.) Heparnavirus = Hep A

13.6.7 Coronavirus
• Encapsulated RNA virus
• Transmission: aerosols
• Disease:
• cause of SARS
• at risk: affects all ages, greatest in children and infants
  o exacerbates asthma & pulmonary disease
  ▪ may cause bronchospasms for months

13.6.8 Adenovirus
• DNA virus with multiple serotypes
• Worldwide distribution with no seasonal incidence
• Transmission: inhalation or fecal/oral
• Disease: URT and LRT
• less than age 2: bronchitis
• major cause of conjunctivitis
• capable of latent infection

13.6.9 Influenza
• Enveloped RNA orthomyxovirus
• Typing based on antigenic variation on viral surface antigens hemagglutinin and neuraminidase
• antigenic drift: small changes in the virus that happen continually over time, causes epidemics
• antigenic shift: an abrupt, major change in the virus resulting in a totally new hemagglutinin or neuraminidase, causes pandemics
• influenza type A infects humans, birds, mammals
  o changes occur via antigenic drift and shift
  o important in Asian cultures, where there is close contact of humans and animals □ reassortment of virus
• influenza type B infects only humans
  o changes occur via antigenic drift only
• influenza type C only causes mild respiratory illness and does not cause epidemics
Seasonal influenza is caused by types A and B
Pandemic influenza is only caused by a major antigenic shift in type A only!
Influenza A & B can cause URT and LRT problems
can be followed by a secondary bacterial infection
clinical presentation: fever > 101.5, painful dry cough, myalgias

13.6.10 Paramyxoviruses
A.) Parainfluenza
• disease: LRT
B.) Respiratory syncytial virus (RSV)
• induces syncytia: fusion of adjacent cells into giant cells
• worldwide distribution
• seasonal incidence: winter
• transmission: highly contagious via aerosols, fomites
• disease: causes a spectrum of disease from colds to pneumonia, URT and LRT
  • at risk: all children become infected at some point, virus is mild in adults
    • most frequent cause of fatal, acute respiratory infections in infants and young children
  • causes bronchiolitis in children
  • ages 2-5 bronchitis
• treatment: supportive
• prevention: can prophylax high risk infants with Synagis, a monoclonal antibody
C.) Human metapneumovirus
• newly discovered
• disease:
  • clinical presentation very similar to RSV if the RSV test is negative, it’s probably human metapneumo
  • probably everyone gets it at a young age
  • can cause URT & LRT disease
  • will exacerbate asthma and pulm disease
  • causes serious illness in immunocompromised patients
D.) Measles
• -still a major cause of morbidity and mortality in developing nations
• -only one serotype
• -causes giant cells similar to RSV
E.) Mumps
• eradicated in developed countries due to vaccination
• only one serotype
• clinical presentation:
  • can cause asymptomatic infections
  • bilateral parotitis and fever

13.6.11 Streptococci Background & Lancefield Groupings
• Group A strep = GAS = Strep pyogenes
• exhibits β-hemolysis on blood agar plate
• normal flora in carriers in low numbers on skin, URT
• disease: pharyngitis, skin infections, scarlet fever, bacteremia, endocarditis
  • especially exudative pharyngitis in 5-15 year olds
  • sequelae: rheumatic fever (if untreated) or acute glomerulonephritis
• virulence factors:
  • M proteins: surface proteins that facilitate spread through host tissue
  • adhesins: facilitate adherence to host tissue
- encapsulated to resist phagocytosis
- many exotoxins
- many proteins that inactivate antibiotics
- superantigens: able to bind directly to MHC on T-cells and activate without an APC
  - massive release of cytokines
  - fever, shock, endothelial dysfunction
  - also produced by *Staph aureus* and some other pathogens

- Group B strep = *Strep agalactiae*
- exhibits β-hemolysis on blood agar plate
- normal flora of perineum in some adults
- disease: neonatal infections (sepsis, meningitis), compromised adults
  - ***why we test women for group B strep before labor***
- Group C strep = many kinds, not normal flora in humans, primarily veterinary pathogens
- exhibits β-hemolysis on blood agar plate
- Group D strep = *Strep bovis*
- Group F strep
- Group G strep = *Strep canis*
- exhibits β-hemolysis on blood agar plate
- infections of skin
- No Lancefield group = *Strep pneumoniae* = “the diplococcus”
- worldwide distribution with greater prevalence in spring/winter
- normal flora in low numbers in URT, nasopharynx
  - transmission via endogenous spread to distal site
- many serotypes
- disease: #1 cause of sinusitis, otitis media, pneumonia, meningitis, and suppurative conjunctivitis in ages 5-65
  - risk factors for disease: preceding viral illness, children and the elderly, immunocompromised
- treatment: worsening drug resistance is a problem
- Alpha hemolytic strep aka “viridans strep” (area of hemolysis looks green) are normal flora in the URT and GI tract
- *Strep sanguis*, *Strep mutans*, *Strep mitis*, *Strep salivarius*
- cause of bacterial endocarditis from dental work
- Enterococcus faecalis and Enterococcus faecium are also considered to be streptococci

### 13.6.12 Bacterial URT Pathogens Overview

- **Otitis media**: *Strep pneumoniae*, *Haemophilus influenzae*, *Moraxella catarrhalis*
- less common: *Staph aureus*, group A strep
- **Otitis externa**: *Pseudomonas aeruginosa*, Gram negative rods, *Staph aureus*
- **Conjunctivitis**
- neonates: *Chlamydia trachomatis*, *Neisseria gonorrhoeae*
- children and older adults: *Haemophilus influenza*, *Strep pneumoniae*, *Staph aureus*
- Keratitis (inflammation of cornea): *Staph aureus*, Gram positive cocci & rods, Gram negative cocci, coccobacilli, and rods. *Pseudomonas aeruginosa*, *Chlamydia trachomatis*
- **Styes** (hordeolum): *Staph aureus*
- Pharyngitis/tonsillitis: groups A/C/G strep, Acinetobacter haemolyticum, *Mycoplasma pneumoniae*
- rare: Corynebacterium diphtheriae
- Rhinosinusitis: *Haemophilus influenzae*, *Strep pneumo*, *Moraxella catarrhalis*, *Staph aureus*, group A strep, Gram negatives
- anaerobes if chronic

### 13.6.13 Bacterial LRT Pathogens Overview

- **Bronchitis in smokers**: *Chlamyphilia pneumoniae*, *Mycoplasma pneumoniae*, Bordetella pertussis
- Pneumonia
- neonatal: group A/B/G strep, *Staph aureus*, *Pseudomonas*, *Chlamydia trachomatis*, *E. coli*
• typical or “pneumococcal”: Strep pneumo
• atypical or “walking pneumonia”: Chlamyphila pneumoniae, Mycoplasma pneumoniae, Legionella
• Acute bacterial exacerbation of chronic bronchitis (ABECB): only in patients with chronic pulm disease
• Strep pneumo, Haemophilus influenzae, Moraxella catarrhalis
• Tuberculosis: Mycobacterium tuberculosis, Mycobacterium leprae

13.6.14 Bacterial Respiratory Pathogens: Gram Negatives
A.) Haemophilus influenzae
• may exhibit pleomorphism on stain, fastidious to grow
• normal flora of mucous membranes
• transmission by endogenous spread from URT to eye, ear, or sinuses
• disease
• at-risk: asplenic persons (can’t attack capsule), elderly, unvaccinated children
• virulence factors: LPS, capsule
• treatment: may be resistant to β-lactams
• pediatric vaccine available
B.) Moraxella catarrhalis
• Gram negative cocci
• normal flora of oropharynx
• transmission by endogenous or droplet spread
• disease: sinusitis, otitis media, suppurative conjunctivitis, bronchitis
• virulence factors: LPS, capsule, pili
• treatment: may be resistant to β-lactams
C.) Pseudomonas aeruginosa
• Gram negative rod, grows blue-green on agar with distinct fruity odor
• ubiquitous in soil, water, and vegetation
• normal flora of skin and mucosa
• transmission: direct spread after colonization
• disease: URT infections limited to eye and ear
• at-risk: hospitalization
• virulence factors: exotoxins, endotoxins, pili, capsule
D.) Bordetella pertussis
• xs Gram negative coccobacilli
• disease: whooping cough, associated with dry coughs > 2 weeks
• suspect in patients with history of post-cough emesis
• at risk: adults with waning immunity
• prevention: adult booster
E.) Legionella pneumophila
• poorly staining pleomorphic Gram negative
• habitat: forms biofilms in air conditioners, cooling towers, shower heads
• transmission: inhalation of aerosols or aspiration of contaminated water
• reservoir in amoeba
• disease
• community as well as nosocomial infections
• at risk for fatal infections: older age, male
• Pontiac fever: a milder form of legionellosis
• virulence: LPS, proteolytic enzymes

13.6.15 Bacterial LRT Pathogens: No Gram Reaction
A.) Chlamydophila pneumoniae
• obligate intracellular bacteria
- elementary bodies and reticulate bodies
- will only grow in cell culture
- transmission
- droplet
- human reservoir because it is a pathogen of humans only
- disease
- virulence: LPS, elementary body
- diagnosis: blood test
- but treat prior to positive results

B.) Mycoplasma pneumoniae
- fried egg appearance on agar
- facultative anaerobe
- worldwide distribution with no seasonal incidence
- disease
- virulence factors: no cell wall = antibiotic resistance, adhesins

C.) Mycobacterium spp
- Mycobacterium *tuberculosis*
- transmission: droplet, low infectious dose
  - humans are the only reservoir
- disease: TB
  - may be asymptomatic or latent
  - at risk: HIV, immigrants
- treatment: multidrug resistance
- Mycobacterium avium-intracellulare
- disease:
  - immunocompetent: pulmonary disease
  - immunocompromised: systemic

13.7 Pathogens of Skin, Mucous Membranes, and Bone

- Normal flora of the skin
- bacteria: Staph, Corynebacterium, Propionibacterium, Strep, Clostridium perfringens
  - Gram negatives in moist areas: *Enterobacter, Klebsiella, E. coli*
- yeast: Candida, Malassezia furfur, Torulopsis glabrata

13.7.1 Viral Skin Infections Overview

- Exanthems: cutaneous manifestation (rash) of systemic viral illness, usually with fever
- seen in measles, rubella, roseola, fifth disease (parvovirus B19), enteroviruses, hand-foot-and-mouth disease, Scarlet fever, herpangina (sores in the mouth)
- Mucocutaneous infections: herpes simplex
- oral & genital, pharyngitis, whitlow, gladiatorum
- Molluscum contagiosum from pox virus
- Chicken pox or shingles from varicella zoster virus
- Verrucae (genital or plantar warts) from HPV

13.7.2 Enteroviruses

- Resistant to detergent, acid, dessication, temperature
- Worldwide distribution
- Increased incidence in summertime
- Transmission is fecal-oral
- Disease: wide clinical spectrum
- at risk: neonatal meningitis
13.7.3 Herpes Viruses

- Large enveloped DNA virus
- New classification system
- HHV 1 & 2: herpes simplex 1 & 2, vesicular lesions on an erythematous base
  - genital herpes on anything covered by underwear
  - herpes labialis: on mouth; tingling is prodrome of outbreak because it resides in nerves
  - herpes gladiatorum: looks like genital herpes but is anywhere not covered by underwear
  - herpetic whitlow: around fingernail or hand
- HHV 3: varicella zoster virus
  - should see lesions in all phases on an infected person
  - can be fatal in adolescents/adults
- HHV 4: EBV
- HHV 5: CMV
- HHV 6 & 7: associated with roseola
- HHV 8: associated with Kaposi’s sarcoma

13.7.4 Poxviruses

- Large DNA viruses
- Transmission: strictly human to human
- Direct: sexual and auto-inoculation possible
- Disease: molluscum contagiosum: pearly umbilicated papules
- Treatment: self-limiting but may take 2 years

13.7.5 Papovaviruses: HPV

- ds DNA viruses
- Transmission: direct (sexual or perinatal)
- Disease
  - infects and replicates in squamous epithelium of skin and mucous membranes → proliferation → warts
    - may cutaneous, mucosal, or anogenital
  - persistent or latent infections
  - oncogenic

13.7.6 Bacterial Skin Infections Overview

- Superficial
- Acne: Propionibacterium acnes
- Rosacea
- Bites
  - incidence of infection in cat bites > human bites > dog bites
  - incidence of infection extremities > head & neck
    - hand bite is always a medical emergency!
    - early cat bite is Pasturella multocida → start antibiotics
    - later bite (Staph or Strep prevails) or swelling → ED
- Incidence of infection in punctures > lacerations
- Impetigo: Staph aureus, group A strep; could be either, always cover for both!
- Erythrasma: Corynebacterium minutissimum
- Intertrigo (areas of skin on skin): groups A&B strep
- Pyodermas (closed area of pus): Staph aureus always!
- Folliculitis: Staph aureus, treat with antibiotics
  - from hot tub: Pseudomonas, usually don’t treat
- Soft tissue infections
- Erysipelas (deep infection of epidermis, a type of impetigo): group A strep
- Cellulitis (group A strep, Staph aureus
- Rarely: Strep pneumo, Erysipelothrix rhusiopathiae, Pseudomonas
• secondary to water exposure: Vibrio vulnificus, Aeromonas hydrophila
• necrotizing: group A strep, polymicrobial anaerobic (Bacteroides, Peptostreptococcus)

13.7.7 The Staphylococci
• Gram positive cocci in clusters, nonmotile
• Facultative anaerobes
• Disease is opportunistic
• ranges from superficial skin infections, toxin-mediated food poisoning, septic arthritis, pneumonia, sepsis

A.) *Staphylococcus aureus:* most important member!
• coagulase +
• normal flora in nasopharynx, skin, GI, GU
• likes moist skin folds
• transmission
• direct contact
• fomites: hangs out on dry surfaces
• increased incidence in hospitalized patients, medical personnel, needle users, those with underlying dermatoses
• disease
• #1 cause of bacteremia and sepsis, endocarditis, osteomyelitis
  • at risk:
    • MSSA: hospitalized patients post-op or post-trauma, foreign body, or on antibiotic regimen
    • MRSA: children, athletes, blacks, Native Americans, immunocompromised
• virulence factors: enterotoxin, TSS toxin, exfoliatin, beta-lactamases, proteolytic enzymes

B.) Coagulase-negative staphylococci
• normal flora on skin, oropharynx, GI, GU
• disease
• at risk: hospitalized patients with indwelling devices, joint or heart prostheses
• virulence factors: glycocalyx capsule, proteolytic enzymes, cell wall structures

13.8 Corynebacterium
• Gram positive rods, irregularly shaped
• Ubiquitous, so culture may not be clinically significant
• Some species are normal flora on skin, GI, GU, respiratory tracts
• Skin disease: erythrasma

13.8.1 *Erysipelothrix rhusiopathiae*
• Slow grower in vitro
• Habitat: colonizes many animals
• Disease in humans is mostly zoonotic
• may progress to systemic endocarditis
• at risk: farmers, butchers, veterinarians

13.8.2 *Propionibacterium acnes*
• Small Gram positive rods in clumps or chains
• Anaerobes
• Normal flora on skin, oropharynx, female genital tract

13.8.3 Vibro spp
- Gram negative rods
- Habitat: free standing water
- Disease
  - *Vibrio cholerae*: GI from contaminated water
  - *Vibrio vulnificus*: skin and soft tissue infections, cellulitis
  - *Vibrio parahemolyticus*: acute gastritis from contaminated seafood

13.8.4 Pasteurella multocida
- Small Gram negative rods/coccobacilli
- Normal flora in oropharynx of animals
- Disease from bites
- Immunocompromised can develop systemic infection
- Virulence factors: capsule, endotoxin

13.8.5 Capnocytophaga canimorsus
- Gram negative rod, fastidious slow grower
- Normal flora in respiratory tract/saliva of humans, dogs, and cats
- Disease from bites
- At risk: severe infection of asplenic patients
- HACEK Group: *Haemophilus aphrophilus*, *Actinobacillus actinomycetemcomitans*, *Cardiobacterium hominis*, *Eikenella corrodens*, *Kingella kingae*
- Gram negative rods that colonize human oropharynx, fastidious

13.8.6 Bacteroides spp
- Pleomorphic Gram negative rods, anaerobic
- Growth enhanced in the presence of bile
- Normal flora in URT, GI, GU
- Disease: commonly seen in polymicrobial infections of the pelvis, peritoneum, abdomen
- Virulence factors: capsule, fimbriae, adhesins, destructive enzymes

13.8.7 Fungal Skin Infections Overview
- Superficial: Malassezia furfur, Candida
- Cutaneous
  - dermatophytes: *Trichophyton*, *Epidermophyton*, *Microsporum*
  - non-dermatophytes: Candida, others

13.8.8 Superficial Fungal Infections
A.) Malassezia furfur
- Lipophilic yeast
- Worldwide, especially in tropical climates
- Can be normal flora
- Disease
  - Tinea versicolor: hypo or hyperpigmented macular lesions, especially on trunk
    - Rim of fine scale
  - Diagnosis: skin scraping in KOH prep thick walled yeast with short pseudohyphae (spaghetti and meatballs)
B.) Candida
- Normal flora of skin, oropharynx, GI tract, female GU tract
- Disease is opportunistic
- Intertrigo (if it’s beefy red plaque with satellite lesions it’s *Candida* vs bacteria), diaper rash, paronychia (nail fold), onychomycosis (nail)
- Treatment is topical except for onychomycosis
• always culture to find the right antifungal, meds are pricey and hard on the liver

13.8.9 Cutaneous Fungal Infections
• Dermatophytes: restricted to keratinized layers of the skin □ varying ringworms of the head, beard, nails, skin
  A.) Epidermophyton
  B.) Trichophyton
  C.) Microsporum

13.8.10 Subcutaneous Fungal Infections:
• uncommon, require risk factors to get such as traumatic implantation, inhalation, or iatrogenic inoculation
  A.) Chromoblastomycoses or phaeohyphomycoses
    • dematiaceous fungi
    • disease: progressive granulomatous infection of skin and subcutaneous tissue
    • Xylomypha particularly deadly as it as a tropism for the CNS
  B.) Mycotic mycetoma: a chronic, granulomatous, purulent, progressive inflammatory disease □ puffy, lumpy extremities, including “madura foot”
    • associated with tropical areas
  C.) Sporothrix schenckii
    • habitat: ubiquitous in soil and decaying vegetation
    • disease: causes subcutaneous mycosis from thorny injury
    • initial lesion is small and painless but enlarges to an ulcer and progresses along direction of lymph drainage
    • “Rose grower’s disease”

13.8.11 Systemic Mycoses
• when infection of the skin is actually a sign of disseminated disease; can happen in immunocompetent individuals
  A.) Histoplasma capsulatum
    • a thermal dimorph
    • yeast: intracellular and extracellular oval budding yeast with narrow neck, “shipwheels”
    • mold: multinucleated branched hyphae with tuberculate macro and microconidia
    • worldwide distribution with niches in the Midwest and Southern US
    • associated with construction projects, spelunkers, bird roosts, farmers cleaning barns, prisoners cleaning roadsides
    • also common in Latin America and Africa
    • transmission by inhalation of conidia or fragments □ conversion to yeast form in host within hours and intracellular replication
    • can live within macrophage phagolysosome to avoid destruction
    • disease: pulmonary □ pericarditis, disseminated disease (with skin & mucocutaneous manifestations), eye
    • can travel to meninges
  B.) Blastomyces dermatitidis
    • a thermal dimorph
    • yeast: broad based buds of blasto
    • mold: septate with lollipop conidia
    • distribution is mostly in southeast, southcentral, Midwest US
    • associated with waterways and disruption of wet soil
- most common route of transmission is inhalation
- disease: acute or chronic pneumonia disseminated infection in many cases to skin, bone, GU, CNS

C.) Coccidoides spp
- a thermal dimorph
- yeast: spherules containing uninucleate endospores
- mold: multinucleate barrel-shaped conidia alternating with empty cells
- prevalent in desert areas in US, as well as Central and South America
- transmission by inhalation
- risk factors: dust storms, construction, military training ops, earthquakes, archeological digs
- disease
- may be asymptomatic
- pulmonary disease with sequelae
- disseminated disease is rare but will involve any organ, usually skin, CNS, bone
  - causes nonspecific erythematous rashes
- increased risk: blacks, Filipinos

D.) Cryptococcus neoformans
- always a yeast, is encapsulated (protects from phagocytosis)
- worldwide distribution
- major route of transmission is inhalation
- disease is acute or chronic
- usually a slow, simmering onset
- pulmonary dissemination to CNS, raised skin lesions
  - mostly in immunocompromised (otherwise healthy people usually get bacterial meningitis)

13.8.12 Infections of the Mouth and Mucous Membranes

A.) Lactobacillus
- normal flora of the mouth, GI, GU tract = frequent contaminant of urine specimens
- disease: transient bacteremia, endocarditis, opportunistic septicemia

B.) Actinomyces
- filamentous bacteria
- normal flora in URT, GI, female GU
- disease: causes infection when mucosal barriers are disrupted chronic infections
  - “lumpy jaw”

C.) Other opportunists: viridans strep, Peptostreptococci, Fusobacterium, Neisseria, Haemophilus
   D.) Viral causes of oral syndromes:
   - HSV stomatitis, mucocutaneous ulcers
   - Coxsackie herpangina, hand-foot-mouth disease

E.) Bacterial causes of oral syndromes:
- Gram positives gingivitis & plaque
- *Strep, Eikenella corrodens* parapharyngeal space infections
- Gram negatives periodontal infections
- *Strep mutans* dental cavities

13.8.13 Muscle Infections: Clostridium perfringens
- Anaerobic spore former
- Ubiquitous in soil, water, human GI tract
- Disease: range from mild gastroenteritis to severe myonecrosis (gas gangrene)
- pain will be disproportionate to physical findings
- virulence: A toxin
- risk factors: penetrating trauma
13.8.14 Bone Infections
- Agent is usually *Staph aureus* if in long bones
- emerging pathogen in kids is *Kingella kingae* (normal flora of oropharynx)
- Transmission: blood carries pathogen from cutaneous site
- At risk
- sickle cell patients: *Salmonella* osteomyelitis
- IVDU patients: *Pseudomonas* osteomyelitis

13.8.15 Breast Infections
- Common agent is *Staph aureus*
- also: group A or B strep, *E. coli, Bacteroides*, coagulase negative staph

13.9 Gastrointestinal Pathogens

13.9.1 Gastroenteritis Background
- Normal flora
- stomach: low numbers of Lactobacilli and strep
- small intestine: many organisms, including fungi, bacteria, and parasites
  - mostly *Bacteroides fragilis* and other anaerobes such as *Peptostreptococci* and enterobacteria
  - in polymicrobial infections of the abdomen, *Bacteroides* always overgrows and is part of the problem
  - always provide anaerobic coverage for antibiotics in abdominal infections
  - transient viruses: adenoviruses, enteroviruses
  - Candida
  - parasites: Blastocystis hominis, Entamoeba coli, Endolimax nana, Trichomonas hominis
- When to suspect bacterial gastroenteritis
  - if greater than 6 per day 
  - if bloody
  - severe abdominal pain
  - fever > 101
  - fecal leukocytes
  - rectal urgency (*tenesmus*)
  - bloody diarrhea with fever is dysentery!
  - 80% of acute diarrhea is infectious and 80% of infectious diarrhea is viral
  - disease is usually self-limiting
    - unless infants are affected, because the younger the child, the more prone to fluid imbalance (smaller total body water)
- treatment is symptomatic unless diarrhea is unresolved for 3+ days then do a stool workup

13.9.2 Viral Pathogens Causing Gastroenteritis Overview
- Infants
- rotavirus A: yellow stools, little emesis, prolonged diarrhea without fever
- adenovirus
- coxsackie virus
- sapovirus
- Children & adults
- caliciviruses
- heat & freeze resistant viruses:
  - norovirus
  - astrovirus
  - reovirus
13.9.3 Rotavirus
- Disease: prolonged diarrhea for weeks but children otherwise don’t look sick
- at risk: children 0-2 years
- Treatment: fluid & electrolyte replacement
- Prevent with vaccines

13.9.4 Astroviruses
- RNA
- Worldwide distribution with no seasonal pattern
- Transmission: fecal-oral or direct
- can have asymptomatic shedding
- multiple serotypes
- Disease
- at risk: more common in children than adults
- Bacterial Pathogens Causing Gastroenteritis and Intoxications Overview
- Gastroenteritis
- traveler’s diarrhea: enterotoxic E. coli
  - an exogenous strain, not your own!
- food intoxication (ingestion of toxin): Staph aureus, Clostridium botulinum, Bacillus cereus, Vibrio cholerae, Clostridium difficile, Clostridium perfringens, enterohemorrhagic E. coli
- food infection (ingestion of vegetative bacteria):
  - The Big Three: most labs only test for these 3, let them know if you’re looking for something else
    - Campylobacter jejuni
    - Salmonella
    - Shigella
  - others: Listeria monocytogenes, Yersinia, Vibrio
- Peritonitis
- primary/spontaneous peritonitis: Enterobacteriaceae, Strep pneumoniae, Enterococcus, other anaerobes
- secondary peritonitis (from trauma, surgery, or catheters): Enterobacteriaceae, Bacteroides, Pseudomonas aeruginosa
- continuous ambulatory peritoneal dialysis: Staph aureus, Staph epidermidis
- Cholecystitis/biliary disease: e, Enterococcus, Bacteroides, Clostridium
- Gastritis/peptic ulcer disease: Helicobacter pylori
- By location:
- disease inside and outside of GI tract: E. coli, Salmonella, Vibrio
- disease mostly within GI tract: Shigella, Campylobacter, Helicobacter, Yersinia
- disease mostly outside GI tract: Klebsiella, Enterobacter, Serratia, Proteus, Providencia, Morganella, Bacteroides

13.9.5 Helicobacter pylori
- Gram negative curved rod
- Common in developing countries
- Transmission: fecal-oral
- human GI tract is the only reservoir
- Disease: gastritis, peptic ulcers, gastric malignancies, enteric disease
- virulence factors: urease, motility, adhesins, flagella, LPS
- Treatment only if symptomatic

13.9.6 Enterobacteriaceae
- A family of coliforms or enteric bacteria
- Ubiquitous in soil, water, vegetation, human GI tract
• Transmission of disease
  • reservoirs are typically in animals, humans, or self
  • Disease when in wrong place at the wrong time = many are opportunists or nosocomials
  • account for 1/3 of all septicemias and 2/3 of all UTIs
• virulence factors: exotoxin, LPS, capsule, flagella, pili, antibiotic resistance
  o endotoxin causes fever, WBC count changes, decreased platelets, decreased circulation and perfusion, shock
A.) Escherichia coli
  • transmission: infecting strains originate in self GI tract
  • exception: traveler’s diarrhea is exogenous strain
• disease:
  • #1 cause of UTIs
    o infecting strains are endogenous
  • also causes bacteremia, sepsis, neonatal meningitis
• gastroenteritis
  o enterotoxigenic E. coli: small intestine; causes traveler’s diarrhea, low fever
    • severe watery diarrhea with involvement of enterotoxins
    • treat with quinolone or antibiotics
    • mild diarrhea only requires supportive treatment
    • no prophylaxis recommended, prevent with cooking and drinking only bottled water
    • at risk: infants in developing countries and travelers
  o enteropathogenic E. coli: small intestine, watery diarrhea, fever, vomiting
    • disease is self-limiting
    • can be a part of normal flora
    • at risk: children in daycare
  o enteroaggregative E. coli: small intestine, persistent watery diarrhea, vomiting, dehydration, low fever
    • adheres vigorously to mucosa
    • self-limiting
    • at risk: children, infants in developing countries, travelers
  o enterohemorrhagic E. coli: large intestine, mild to severe hemorrhagic colitis large numbers of stools, prolonged diarrhea
    • other than the rectal bleeding, most people feel fine, no fever
    • small infectious dose
    • sequelae: HUS, ARF, thrombocytopenia
•  enteroinvasive E. coli: large intestine, invades and destroys colonic epithelia fever, cramping, watery diarrhea, may have a few bloody stools
  • all except hemorrhagic not seen in the US without history of travel
• virulence factors: exotoxins, adhesins
• treatment: increasing resistance to antibiotics
B.) Salmonella enterica
  • multiple serotypes based on presentation
  • typhoid serotypes = systemic disease
    o typhoid fever = Salmonella enterica Typhi and Salmonella enterica Paratyphi A and B
      • worldwide distribution
      • prevalence in warmer months
      • transmission is strictly human-to-human via fecal-oral route
      • small infectious dose
      • chronic carrier state possible
      • disease: systemic, no GI presentation
      • at risk: travelers to SE Asia, Africa, latin America
• non-typhoid serotypes = gastroenteritis
  o foodborne = Salmonella enterica Enteritidis
    • transmission by ingestion of contaminated eggs, poultry, dairy
- reservoir in animals
- large infectious dose required
  - disease
    - at risk for severe disease: infants, elderly, immunosuppressed
      - children may have prolonged shedding

C.) Shigella
- transmission: fecal-oral person-to-person
- human GI tract is reservoir
- low infectious dose
- disease: mild to severe
- at risk: children in daycare, workers in custodial facilities, anyone working with kids
- treatment: even though prolonged shedding is rare, treat with antibiotics to completely eradicate even for mild disease

D.) Yersinia
- Gram negative rods
- disease
- gastroenteritis from ingestion of contaminated food
  - *Yersinia enterocolitica* or *Yersinia pseudotuberculosis*

E.) Klebsiella
- may be normal flora in the colon
- disease: not enteric disease but causes pneumonia from aspiration, also *Klebsiella pneumoniae* causes UTIs
- virulence factors: LPS, capsule, beta-lactamase, large production urease
- treatment of UTI requires multiple antibiotics

F.) Enterobacter and Serratia
- disease: not enteric disease but causes UTIs and aspiration pneumonia
- treatment: common resistance to drugs

G.) Proteus
- motile: swarthy stinky growth on plate
- disease: community acquired UTIs
- renal calculi
- virulence factors: large amounts of urease

H.) Providencia stuartii and Morganella
- disease: nosocomial UTIs

I.) Campylobacter jejuni
- curved Gram negative rod
- requires microaerophilic environment
- worldwide distribution
- increased incidence in warm weather
- transmission: ingestion of contaminated food, milk, or water; also fecal-oral or direct contact with pets and farm animals
- reservoir in animals
- disease: bacterial gastroenteritis
- typically self limiting
- virulence factors: adhesins, cytotoxic enzymes, enterotoxin
- at risk: those ingesting large dose, those lacking gastric acid, males, ages < 5 years, ages 20-30 years
- sequelae: Guillain-Barre syndrome
- treat if severe with antibiotics

13.9.7 Bacterial Pathogens Causing Food Intoxication
A.) Vibrio
- transmission via ingestion of contaminated water
- *Vibrio parahemolyticus* via consumption of contaminated seafood
- gastroenteritis mediated by toxin causing hypersecretion of water and electrolytes

B.) Clostridium botulinum
- transmission via food or wound contamination (rare in US)
- honey in infants
- disease mediated by neurotoxin

C.) Bacillus cereus
- gastroenteritis mediated by certain endotoxins:
  - heat stable enterotoxin □ upper GI disease
    - ingestion of spores in contaminated rice
    - toxin-mediated diarrhea onset within 2-6 hours
  - heat labile enterotoxin □ lower GI disease
    - ingestion of spores in reheated meats and vegetables
    - vegetative-cell mediated diarrhea onset within 24 hours

D.) Clostridium difficile
- can be normal flora in some people
- disease: antibiotic associated colitis = explosive diarrhea, can be bloody, leukocytosis, fever
- mediated by enterotoxin A and cytotoxin B

13.9.8 Parasitic Pathogens Causing Gastroenteritis Overview
- AIDs patients or those with prolonged diarrhea: (*Mycobacterium avium intracellulare*), *Giardia lamblia*, *Cryptosporidium parvum*, *Isospora belli*
- Diarrhea: *Giardia lamblia*, *Cryptosporidium parvum*, *Blastocystis hominis*
- Intestinal amoebiasis: *Entamoeba histolytica*

13.9.9 Cryptosporidium parvum
- Worldwide distribution
- More prevalent in summer
- Transmission is fecal-oral, ingestion of contaminated water or food, or oral-anal
- sources: contaminated water, apple cider, raw produce
  - resistant to chlorination
- asymptomatic carriage possible
- Disease: mild to severe gastroenteritis
- self-limiting in immunocompetent
- at risk: AIDs patients □ chronic diarrhea

13.9.10 Isospora belli
- Worldwide distribution
- Transmission is fecal-oral, ingestion of contaminated water or food, or oral-anal
- asymptomatic carriage possible
- Disease: mild to severe gastroenteritis

13.9.11 Giardia lamblia
- More prevalent in late summer and fall
- Transmission
- low infectious dose
- many antigenic variants
- can have asymptomatic carriage
• Disease: most common cause of parasitic diarrhea in the US
  may result in acute or chronic diarrhea
    o can have malabsorption as well (looks like IBS)
• Diagnosis: since parasite comes out in stool in infrequent showers, check at least 3 stools

13.9.12 Entamoeba histolytica
• Cysts and trophozoites
• Worldwide distribution with increased prevalence in tropical climates
• Transmission
  vectors: flies and cockroaches
  can be asymptomatic carrier
• Disease: gastroenteritis or spread to liver, lungs, brain, heart
  stools are bloody vs nonbloody for Giardia
• risk factors: travel to foreign countries, disruption of water supply

13.10 Genitourinary Pathogens
13.10.1 Genital Tract Pathogens Background
• Female normal flora of vagina (varies with hormonal influence): Lactobacillus, Staph, Strep, Gardnerella vaginalis, Mycoplasma, Ureaplasma, Enterobacteriaceae
• anaerobes: Bacteroides, Clostridium, Peptostreptococcus
• Female normal flora of anterior urethra
• indigenous: Lactobacillus, Corynebacterium, coagulase negative Staph
• transient: Enterobacteriaceae, Candida, Enterococcus
• Male normal flora: little colonization if circumcised

13.10.2 Viral Genital Pathogens Overview
• Genital warts or cervical dysplasia: HPV
• Genital herpes: HSV-2 or HSV-1
• HIV
• Hepatitis viruses

13.10.3 HPV
• Many types
• most genital warts caused by types 6 and 11
• cervical dysplasia associated with 16, 18, 31, 45
• Transmission: fomites or sexual
• asymptomatic shedders
• Disease can be cutaneous, mucosal, and/or anogenital, or result in cervical dysplasia
• many dysplasias spontaneously regress and some develop into cancer

13.10.4 Genital Herpes
• From HSV-1 or HSV-2
• HSV-1 traditionally oral
• HSV-2 traditionally genital
• Transmission: sexual or during birth process
• prior infection with HSV-1 inhibits infection with HSV-2
• Disease: painful vesicular lesions on an erythematous base
• Diagnose by appearance but always culture
• blood test is a bad idea, almost 100% of people have antibodies and will be positive

13.10.5 Bacterial Pathogens Overview
I.) Genital:
- gonococcal infections from Neisseria gonorrhoeae
- male urethritis
- cervicitis
- disseminated infections to joints and skin
- non-gonococcal urethritis or cervicitis: Chlamydia trachomatis (most of the time)
- others: Mycoplasma hominis, Ureaplasma, Mycoplasma genitalium
- more common than gonococcal urethritis & cervicitis
- gonorrhea and Chlamydia present similarly and can be asymptomatic
- gonorrheal discharge is thick and yellow
- chlamydial discharge is watery
- syphilis: Treponema pallidum
- chancroid (different from chancre!): Haemophilus ducreyi
- vaginitis:
  - bacterial: polymicrobial with Gardnerella vaginalis, Mobiluncus, non-fragilis Bacteroides, Actinomyces
    - STD vaginitis: Trichomonas vaginalis
  - yeast: Candida
  - epididymitis/prostatitis
- if male < 35: Chlamydia trachomatis with or without Neisseria gonorrhoeae
  - in males < 35 UTIs are STDs until proven otherwise
- if male > 35: Enterobacteriaceae
- proctitis: Chlamydia trachomatis, Neisseria gonorrhoeae
- balanitis: nonspecific inflammation of the penis
- Candida, HPV, Treponema pallidum, Gardnerella, Group A or B strep
- need to treat partners!

II.) Urinary
- acute cystitis (lower UTI): uropathic strains of E. coli, Staph saprophyticus, Enterococcus, Enterobacteriaceae (Klebsiella pneumoniae, Proteus)
- pyelonephritis (upper UTI): same as lower UTI

13.10.6 Neisseria gonorrhoeae
- Small Gram negative diplococci with flattened sides ☐ coffee bean appearance
- Very fastidious
- Transmission: strictly human to human
- asymptomatic women provide reservoir for perinatal spread
- urethra and cervix are most common sites of infection
- Disease: untreated ☐ male urethritis or ascension of female genital tract and cervicitis
- possible dissemination to blood, skin, joints
  - knees in females
- virulence factors: LOS, pili, outer membrane proteins I, II, and III
  - facilitates intracellular survival
- Diagnosis: urethral discharge with Gram negative intracellular diplococci
- Prevention: erythromycin ointment on eyes of all newborns to prevent gonococcal ophthalmia neonatorum

13.10.7 Chlamydia trachomatis
- Obligate intracellular bacteria, nonstaining
- Prevalence: nearly epidemic in sexually active teenagers
- Transmission: sexual or infection during birth process
- Disease:
  - alters vaginal normal flora ☐ PID ☐ scarring of fallopian tubes
    - recurrent or persistent infection
    - can be asymptomatic
#1 cause of infertility
- developing countries: trachoma
- adult and neonatal conjunctivitis
- neonatal pneumonia during 2 weeks - 3 months of life
  - vs neonatal pneumonia during first day of life = *Neisseria*
- urethritis reactive arthritis
- lymphogranuloma venereum: certain serotypes can disseminate from genital tract to lymph nodes
  - three stages:
    1.) ulcerations
    2.) papular lesions, systemic symptoms
    - proctitis via lymphatic spread
    - may have buboes: swollen painful inguinal nodes
    3.) extensive scarring, chronic lymphatic obstruction, genital elephantiasis
- virulence factor: LPS

13.10.8 Treponema pallidum
- Gram negative thin spirochete
- Labile
- Transmission: strictly human-to-human via sex, birth, transplacental, or transfusion
- low infectious dose
- Disease: syphilis, balantitis
- but certain subspecies not in the US cause non-venereal disease
- three stages:
  1.) painless chancre at site of infection
  2.) secondary disease: flu-like symptoms followed by diffuse rash including palms and soles
  3.) tertiary disease involving any organ as well as CNS manifestations and gummas (granulomatous lesions)
- virulence factors: endotoxin, outer membrane, hyaluronidase
- Diagnosis: non-treponemal followed by confirmatory FTA?

13.10.9 Haemophilus ducreyi
- Slide shows “school of fish” pattern
- Prevalence: rare in developed countries but still happens occasionally in US
- Transmission is strictly sexual
- Disease: chancroid: a softer chancre that is painful
- exudate is yellow necrotic and foul-smelling
- characterized by buboes

13.10.10 Klebsiella granulomatis
- Small pleomorphic intracellular rods
- Can’t be grow outside of cell
- Transmission sexually or via trauma to the genital area
- Prevalence is rare in US
- endemic in warmer climates
- Disease: granuloma inguinale (*donovanosis*): genital ulcerative disease
- long incubation period

13.10.11 Vaginitis and Balantitis
A.) Mobiluncus & Gardnerella
- will stain Gram negative or variable but are actually Gram positive
- obligate anaerobes
- normal flora in large numbers in female genital tract
- disease
- females: overgrowth → vaginitis
- males: balantitis
- diagnosis: clue cells

B.) Candida, typically albicans
- typically opportunists
- disease: vaginitis or balantitis
- treat with azoles or nystatin

C.) Trichomonas vaginalis
- a flagellated protozoan parasite, only in trophozoite form
- high prevalence in developed countries
- transmission mostly sexual, can be fomites
- asymptomatic men serve as a reservoir
- disease:
  - women: can cause vaginitis
  - can be asymptomatic
  - will see strawberry cervix (frangible cervix) upon examination
  - must treat partners!

13.10.12 Other Parasitic Genital Pathogens
A.) Pthirus pubis = pubic lice
B.) Sarcoptes scabei = scabies

13.10.13 Staphylococcus saprophyticus
- Prevalence: common in sexually active healthy women
- Transmission via poor hygiene
- Disease: UTI
- virulence factors: antibiotic resistance, hemagglutinin

13.11 Pathogens of Sterile Sites
- Sterile Sites Background: infections here are never normal flora and have high mortality rates
- Any infant < 3 months old with a fever is seriously ill with a life-threatening illness until proven otherwise
- CNS:
  - meningitis
    - incidence
      - viral: warmer months due to vectors breeding
      - mumps: winter
    - etiology:
      - most common fungal meningitis is cryptococcal meningitis
      - age is a factor
        - in children and young adults, usually viral meningitis
        - 90% of the time it will be an enterovirus
      - aseptic is usually viral
        - determine with negative bacterial culture
        - could be fungal or parasitic if immunocompromised
  - encephalitis
    - most commonly is HSV encephalitis
- Blood: septicemia
  - intermittent septicemia: when focus of infection is at a distal site
  - continuous septicemia: when infection is mostly intravascular
- viral sepsis tends to be transient
- bacterial sepsis:
- age is a significant factor in etiology
  - Peritoneum
  - Pleura
  - Pericardium
  - Joints
  - Urine from a catheter

### 13.11.1 Viral Pathogens of Sterile Sites Overview
- Viral encephalitis: HSV-1, HIV, togavirus, rabies, flavivirus, CMV, WNV
- Aseptic viral meningitis:
  - most commonly enteroviruses (ECHO, Coxsackie A & B)
  - mumps with CNS involvement

### 13.11.2 Viral Encephalitis

A.) HSV
- disease: 7-10 day prodrome of upper respiratory symptoms followed by sudden onset of fever and headache
- frequently altered mental status with confusion and delirium

B.) Rabies virus
- disease
- long incubation period depends on distance of bite from CNS
- near 100% mortality rate
- treat with prophylaxis based on local health department recs
- always prophylax with any contact with a bat, even if skin is unbroken

C.) West Nile virus
- increased incidence in summer and early fall
- transmission by mosquito vector, contaminated blood products, transplanted organs
- disease symptoms: severe frontal headache, fever and chills, myalgias
- can be asymptomatic
- at risk: > 60 years old
- can have neurological sequelae

### 13.11.3 Bacterial/Fungal/Parasitic Pathogens of Sterile Sites Overview
- Bacterial meningitis
  - neonates: group B strep, E. coli, Listeria monocytogenes
  - ages > 1 month through 50 years:
    - #1 cause is Strep pneumoniae
    - others: Neisseria meningitidis, Haemophilus influenzae
  - ages > 50 years
    - #1 cause is Strep pneumoniae
    - others: Listeria monocytogenes, misc Gram negative rods
    - if chronic: Mycobacterium tuberculosis, Treponema pallidum, Borrelia burgdorferi
    - from underlying immunosuppression
- Fungal meningitis
  - *Cryptococcus neoformans* infects immunocompetent as well as suppressed
  - Coccioidoides immittis
  - Histoplasma capsulatum
  - Parasitic meningitis or meningoencephalitis
  - Toxoplasma gondii
  - amoebas: Naegleria, Acanthamoeba, Balamuthia
  - Taenia solium
  - Sepsis
- neonates:
  - group B strep
  - acquired from birthing process: *E. coli, Enterobacter, Klebsiella*
  - in infants < 1 week old: *Haemophilus influenzae*
  - rarely, Staph aureus
- children: *Haemophilus influenzae*, Strep pneumo, Neisseria meningitidis, Staph aureus
- immunocompetent adults:
  - Staph aureus is the #1 cause
  - others: group A strep, *Legionella, Salmonella, Enterococcus*, viridans strep, *E. coli*
- immunocompromised adults: coagulase negative *Staph, Listeria monocytogenes, Strep pneumoniae*
- neutropenic adults: Enterobacteriaceae, Candida, Aspergillus, Staph aureus
- Septic arthritis
  - infants < 3 months: Staph aureus, Neisseria gonorrhoeae, group B strep, Enterobacteriaceae
  - children: Staph aureus, group A strep, Strep pneumo, Kingella kingae, Gram negative rods
- adults
  - acute & monoarticular & sexually active: Neisseria gonorrhoeae, Staph aureus, strep
  - not sexually active: Staph aureus, strep, Gram negative rods
  - chronic & monoarticular: Brucella, Nocardia, mycobacteria, fungi
- Pericarditis: *Staph aureus, Strep pneumo*, group A strep, Enterobacteriaceae
- Pleural effusion/empyema:
  - infants and children up to 5 years: *Strep pneumo*, group A strep
  - children over 5 years and adults: Staph aureus, Haemophilus influenzae
- chronic presentations: *Mycobacterium tuberculosis, Strep milleri, Bacteroides*, anaerobic strep, Enterobacteriaceae from aspiration

### 13.12 Listeria monocytogenes

- Gram positive rod in singles or pairs
- Exhibits tumbling motion on broth
- Habitat: widely found in animals, as well as soil, water, vegetation
- Transmission from ingestion of contaminated food, zoonosis, or transplacental
- high infectious dose required
- can have asymptomatic carriers or colonizers
- Disease: varies from mild self-limiting flu-like symptoms with or without GI symptoms to meningitis if immunocompromised
- at risk: neonates, elderly, pregnant women, cancer or transplant patients
  - makes it the most serious foodborne disease
  - pregnant women: stillbirth, spontaneous abortion, premature delivery
  - neonates
    - early onset listeriosis: contracted in utero, characterized by widespread abscesses/granulomas
    - prevents within 7 days of life
    - late onset listeriosis: acquired at birth or shortly after, presents as meningitis or meningoencephalitis with sepsis
    - presents after 7th day of life
  - elderly account for half of all diagnosed cases, with the most common presentation being meningitis
- virulence factors: intracellular growth, *listeriolysin* O facilitates escape, survives cold temperatures

### 13.12.1 Neisseria meningitidis

- Encapsulated, intracellular
- Fastidious
- Transmission: direct or droplet
- can have transient colonization or carriers
- Disease: hematogenous spread from nasopharynx → septicemia, meningitis, possibly pneumonia
- solely septicemia is less threatening
- symptoms can look very GI!
- virulence factors: pili adhere to receptors in nasopharynx, endotoxin
- at risk:
  - endemic in 0-5 year olds, peaks again in late adolescence
  - “meningitis belt” in sub-Saharan Africa
    - prophylax travelers to this area

13.12.2 Toxoplasma gondii
- Humans are infected almost ubiquitously
- Transmission: ingestion of cysts in cat feces or ingestion of contaminated meat, transplacental
- reservoir in cats
- Disease is flu-like
- often asymptomatic
- can have reactivation of latent disease in immunocompromised → brain, eye, lung

13.12.3 Naegleria fowleri
- Habitat: free-living amoeba in water
- Transmission usually from swimming in contaminated water
- travels up olfactory nerve
- Disease from amoeba eating your brains → acute meningoencephalitis
- fatal in children and young adults
- at risk: neti pot users using unsalinated tap water
- Diagnosis: motility in CSF or mouse inoculation

13.12.4 Taenia solium
- Pork tapeworm
- Prevalent in SE Asia, Africa, Latin America, Mexico
- Transmission is by ingestion of cysticerci in undercooked pork
- Disease: mild abdominal symptoms but cysticerci travel to brain → meningitis, hydrocephalus, seizures
- Diagnosis: proglottids in feces, calcified cysticerci seen on CT or US

13.12.5 Brucella
- Small Gram negative coccobacilli
- Transmission: zoonotic, from ingestion of contaminated or unpasteurized milk or dairy
- Disease: ranges from mild to severe
- severe: relapsing and remitting fevers
- rare but potential is there as a bioterrorism agent

13.13 Systemic Febrile Syndromes

13.13.1 Systemic Febrile Syndromes Overview
I. Vector-borne: Bartonella, ehrlichiosis, anaplasmosis, Lyme disease, babesiosis, plague, relapsing fever, Rocky Mountain spotted fever, tularemia
- Lyme, RMSF, ehrlichiosis, anaplasmosis are all treated the same, so if you suspect treat, don’t order serologies because they are very expensive
II. Sepsis and shock syndromes, typically seeding from a distant site
- bacterial sepsis or shock
- staphylococcal TSS
- streptococcal TSS
III. Misc febrile syndromes
- Kawasaki fever
- rheumatic fever

IV. Infections presenting with febrile syndromes
- pyelonephritis, hepatitis
- in travelers: typhoid fever, dengue, malaria

13.13.2 Bartonella
- Gram negative rod
- Transmission via arthropod vectors
- reservoir in animals
- Disease depends on species
- *Bartonella bacilliformis* □ bartonellosis or Aroya fever
  - Central and South America
- *Bartonella quintana* □ trench fever, bacillary angiomatosus (nodules with proliferation of capillaries) involving skin, subcutaneous tissue, and bone
  - may cause endocarditis
- *Bartonella henselae* □ bacillary angiomatosus involving skin, lymph nodes, and liver or spleen, as well as *cat scratch fever* (lymphadenopathy, headache, chills)
  - may cause endocarditis
  - most common presentation in US is *cat scratch fever*
    - typically self-limiting
- Diagnose *cat scratch fever* with biopsy of nodule

13.13.3 Borrelia
- Large spirochete, weakly staining Gram negative
- Seasonal incidence
- Lyme: May-Sept
- Transmission via louse or tick vector
- Lyme: nymph tick
  - reservoir in mice and deer
- endemic relapsing fever: tick
- epidemic relapsing fever: louse
- Disease depends on species
- *Borrelia burgdorferi* □ Lyme disease
  - may see telltale *erythema migrans* (must be > 5 cm)
- *Borrelia recurrentis*
  - epidemic relapsing fever
  - endemic relapsing fever
- Diagnosis
- of Lyme: serology or clinical features
- of relapsing fever: microscopy

13.13.4 Babesia microti
- Intracellular blood protozoan
- Forms rings in infected RBCs
- Endemic in NE coastal areas
- Transmission via tick bite or blood transfusion
- reservoirs: deer, cattle, rodents
- Diagnose by looking at blood films

13.13.5 Rickettsia
- Small weakly staining intracellular Gram negative rods
• Transmission via bite of infected arthropod
• reservoirs in animals and arthropods
• Tick vectors are geographically distributed
• Disease depends on group
• spotted fever group: Rickettsia rickettsiae
  o Rocky Mountain spotted fever: fever, headache, myalgias, nausea, vomiting, macular rash 2-14 days after tick bite
    ▪ sequelae: neurologic, cardiac, renal
    ▪ most common rickettsial disease in US
    • most common vector: American dog tick
    ▪ high mortality rate if treatment is delayed □ always treat with doxycycline if presenting with headache and fever
• typhus group: Rickettsia prowazekii, Rickettsia typhi

13.13.6 Ehrlichia chaffeensis
• Intracellular in neutrophils, monocytes, RBCs, platelets
• elementary and reticulate bodies
• reticulate bodies converge to form morulae
• Common in SE US
• Seasonal in April-Sept
• Transmission via bite of lone star tick
• Disease: human monocytic ehrlichiosis (HME): fever, headache, rash on chest/abdomen (vs extremities like RMSF), pancytopenia, increased LFTs
• Diagnosis: serology or PCR

13.13.7 Anaplasma phagocytophilum
• Most common in New England, northcentral US, some sites in California
• Transmission: bite from tick vector
• Disease: anaplasmosis: very similar to HME
• resolves if immunocompetent

13.13.8 Francisella tularensis
• Small Gram negative intracellular coccobacilli
• Transmission: zoonotic infection
• Disease: many clinical presentations depending on route of exposure
• virulence factors: capsule

13.13.9 Miscellaneous Febrile Syndromes
• Kawasaki disease: acute onset of rash, fever, conjunctivitis, stomatitis (strawberry tongue), swollen erythematous hands and feet
• agent may be viral?
• associated with carpet cleaning
• no specific treatment, just watch for later cardiac abnormalities
• Acute rheumatic fever: sequelae of group A strep infections, when antibodies to M proteins cross react with heart valve tissues □ scarring

13.13.10 Infections Presenting with Febrile Syndromes
• Hepatitis viruses: tropism to the liver
• can be RNA or DNA
• similar: Hep A, Hep E
  o Hep A = heparnavirus
    ▪ transmission from ingestion of contaminated seafood or water
    ▪ disease
• abrupt in adults with moderate to severe symptoms
  o 30 day incubation period
• mild disease or asymptomatic carriers in children
• no chronic liver disease
• at risk: daycare centers
• prevent with vaccine
  o Hep E
    • common in developing countries
    • transmission is fecal-oral or via consumption of undercooked meat
    • infection serious in pregnant women
    • no chronic disease
• similar: Hep C, Hep G
  o Hep C is “emerging”
    • often coexists with Hep B
    • disease
      • rapid and progressive course possible
      • usually, chronic liver disease is likely, #1 cause of hepatocellular carcinoma
      • at risk: IV drug users
• Hep D only occurs in presence of Hep B
  o Hep B = hepadnavirus
    • transmission via contaminated needles or sexual disease
      • mild in kids, can be asymptomatic carriers
      • chronic disease associated with liver cancer
      • at risk: IV drug users, homosexual males, immigrants
    • prevent with vaccine
  o Hep D will only replicate in Hep B infected cells ⧫ increases severity of infection
    • transmission same as B&C
    • disease will be chronic
• Dengue virus
• worldwide distribution, most common in Central and South America and the Caribbean
• transmission via mosquito vector
  o most common mosquito-borne viral infection
• disease ranges from asymptomatic to hemorrhagic fever and shock
  o can have severe joint or back pain = bone-break fever
14  Nephrology Exam Notes

14.1  Nephrology Tidbits

14.1.1  Background

Nephrology is an internal medicine subspecialty that deals with kidney function
- ex. acute kidney failure, chronic kidney disease, glomerular disorders, tubular disorders, interstitial disorders

Urology is a surgical subspecialty that deals with more structural urogenital tract problems
- ex. kidney stones, UTI from structural abnormality, urinary incontinence, prostate issues, erectile dysfunction, genitourinary cancers

Upper urinary tract = ureters & kidneys
Lower urinary tract = bladder & urethra

Common disorders
- outpatient: UTIs, kidney stones, CKD (from DM or HTN)
- inpatient: ARF, fluid/electrolyte disorders, pre-existing CKD on top of other comorbidities

Think of nephrotic/nephritic syndrome as being signs or symptoms that help guide your diagnosis

Nephrotic syndrome: protein abnormally leaking through glomerulus is excreted in the urine
- kidney is spilling protein, with too much excretion of the wrong proteins
  - but serum creatinine may be normal
- massive proteinuria, hypoalbuminemia (liver can’t keep up with amount peed out), edema (not enough protein in blood to keep fluid in capillaries), dyslipidemia (because some proteins lost are the ones that process lipids)
- can occur in liver failure, protein deficiency/malnourishment

Role of PCP in nephrology
- prevention of CKD by treating DM and HTN, minimizing nephrotoxic meds
- spotting kidney disease and knowing when to consult a nephrologist
- maintaining early stage CKD patients, consulting with nephrology when necessary
- Bladder cancer
  - more common in men than women
  - major risk factor is cigarette smoking, followed by exposure to industrial dyes and solvents
  - presentation: hematuria, urinary frequency/urgency, or asymptomatic
  - investigation:
    o urine cytology (repeats due to poor sensitivity), cystoscopy +/- transurethral resection
  - staging:
    o based on biopsy results and imaging
  - treatment:
    o superficial +/- resection +/- intravesicular chemo
    o advanced +/- combo chemo +/- radiation
  - prognosis: early disease has > 80% survival
    o rare survival with metastatic disease
- Renal cell carcinoma
  - presentation: hematuria, flank pain, abdominal mass, cough, bone pain with mets, paraneoplastic syndromes
    o often found incidentally on other imaging
  - treatment: nephrectomy, low response rates with chemo
  - prognosis:
    o good for cancers confined to renal capsule
    o 50-60% for tumors extending beyond the renal capsule
    o 0-15% for node positive tumors

14.2 Diagnostic Methods: Renal Chemistries, UA, Urine Cultures

14.2.1 Background
- Renal function testing is ordered to estimate kidney health, monitor renal function changes over time, evaluate patient need for dialysis or transplant, and for adjustment of nephrotoxic kidney meds
- Kidney functioning tests are included in the basic metabolic panel (BMP or Chem 7/8/9/etc)
- Centers for Medicare & Medicaid approve (will reimburse for) these specific tests: Na, K, Cl, CO2, BUN, Cr, glucose, Ca, albumin, phosphorus
- Normal urine components are NH3, sulfate, phosphate, Cl, Mg, Ca, K, Na, creatinine, uric acid, urea, and water

14.2.2 Metabolic Panel Components
1.) Sodium
2.) Potassium
3.) Chloride
4.) CO2
5.) Ca
6.) Blood urea nitrogen (BUN): a measure of the amount of nitrogen in the blood in the form of urea
   - derives from breakdown of protein (mostly dietary)
   - ↑BUN is known as “uremia”
     o begins when kidney function is < 10% of normal
     o prerenal cause (decreased renal blood flow) when there is shock, dehydration, or increased protein catabolism
     o postrenal cause when urea is backed up into the blood from a lower urinary obstruction (kidney stones, etc)
     o renal cause when diseased glomeruli/renal vasculature/tubules don’t remove urea as normal
7.) Serum creatinine: product of creatinine breakdown (mostly muscle)
• usually stable from day to day
• amount is proportional to muscle mass = higher in men than women at baseline
• ratio of BUN:creatinine is usually 10:1 (range from 12-20)
  o lowered in liver disease, starvation, acute tubular necrosis
  o increased + normal Cr in prerenal uremia, high protein diet, GI bleed
  o increased + high Cr (azotemia) in renal disease and renal failure

8.) Glucose

9.) GFR (MDRD formula)
• should be at least 37 in Caucasian patients and at least 45 in black patients

14.2.3 Urinalysis

• Components:
  • appearance: color, clarity, specific gravity (concentration)
  • chemical composition:
    o pH: normally 5-8
      ▪ acidic with crystals, high protein diet, medications, uncontrolled diabetes
      ▪ alkaline after eating, vegetarian or dairy-rich diet, in UTIs, with certain medications, with crystals
      ▪ neutral normally or in renal tubular acidosis
    o protein: should normally be 0 in urine
      ▪ composed of 1/3 albumin, 2/3 LMW globulins
      ▪ LMW globulins are mostly Tamm-Horsfall protein (produced by the kidney, normal if < 2.5 mg/dL)
    o usually need a 24 hour sample for best assessment
    o causes of proteinuria include preeclampsia, multiple myeloma, temperature extremes, fever, exercise, position, stress
    o glucose: there should only be a small, undetectable amount in the urine
    o ketones: normally should be 0 in the urine
      ▪ positive in fasting, exercise, poorly controlled diabetes, fever, alcoholism
    o blood
    o nitrites: a bacterial product that is normally negative in the urine
      ▪ positive in most UTIs, although not all bacteria are nitrite producers
    o leukocyte esterase: WBC enzyme that is normally negative in the urine but is made by neutrophils in response to bacteria
      ▪ positive in UTIs and some STIs
    o bilirubin: product of Hb breakdown, normally should be 0 in the urine
      ▪ positive in liver disease or biliary obstruction
    o urobilinogen: a colorless product of bilirubin reduction that formed in the intestines by bacterial action, normally at very low levels in the urine
      ▪ increased in hemolytic and liver disease
      ▪ low or absent in biliary obstruction
  • microscopic visualizations (centrifuged sample): RBCs, WBCs, epithelial cells, casts, crystals, bacteria
    o rare squamous epithelial cells, renal epithelial cells, WBCs, or RBCs is normal
    o casts enumerated on low power
      ▪ hyaline: normal in low numbers, otherwise indicative of CHF
      ▪ RBC = acute glomerulonephritis
      ▪ WBC = pathognomonic for acute pyelonephritis
      ▪ epithelial = tubular necrosis
      ▪ granular = nephrotic syndrome, pyelonephritis
      ▪ waxy = tubular atrophy, renal failure
      ▪ bacterial = pyelonephritis
      ▪ fatty = proteinuria, nephrotic syndromes
    o all other cells enumerated on high power
    o crystals
      ▪ can be normal
- triple phosphate crystals associated with alkaline urine and UTIs
- cystine crystals present in acidic urine cystinuria

- Urine collection over 24 hours usually needed to measure protein and creatinine

### 14.2.4 Urine Cultures

- Caveats to diagnosis based on UA
  - WBCs in urine (pyuria) does not always correlate to infection
    - can be a result of inflammation, renal calculi, neoplasms, interstitial nephritis, polycystic kidney
  - infection may be present without WBCs in immunocompromised patients UA alone not sufficient in diagnosis
    - also need history, culture, sensitivities for accurate treatment
- Methods
  - always get UA and culture sample before initiation of empiric treatment
  - urine specimen sources
    - clean catch
    - straight cath
    - indwelling cath sample
    - suprapubic aspirate
  - antibiotic susceptibility testing may be done
    - determines the MIC: lowest concentration of a drug that will significantly inhibit bacterial growth
  - plates are incubated 24-48 hours for final call on growth
- Interpretation
  - pathogens isolated depends on type of infection
    - acute = single organism
      - chronic = potentially 2+ pathogens
      - nosocomial = high probability of resistant organism
    - acute cystitis, pyelonephritis, and acute prostatitis all have the same end result (same pathogens) = base diagnosis on history as well as results in order to differentiate
  - significant growth:
    - if 1 or 2 organisms, must be > 100,000 CFU/mL to be significant
    - if male, any organism > 10,000 CFU/mL is significant
    - greater than 3 organisms = mixed flora/contamination = insignificant, repeat specimen needed
  - no growth on culture of urine with WBCs?
    - consider other causes of WBCs and atypical infections that won’t grow on traditional media (Mycobacterium, herpes, Chlamydia, Trichomonas, Ureaplasma)

### 14.2.5 Glomerular Filtration Rate

- Renal clearance: volume of plasma from which a substance is completely removed by the kidneys in a given amount of time, reflects the level of overall glomerular functioning
  
  clearance of X = (mass of X secreted per min)/[plasma X]

  clearance of X = ([urine X] (urine volume per min))/[plasma X]

  need to measure using a substance that is with 100% excretion in the urine
- GFR indicates level of kidney function
  - can estimate using inulin clearance
    - since inulin is neither reabsorbed nor secreted its clearance is proportional to GFR
  - can estimate using creatinine clearance in a 24 hour urine sample as it should be 100% excreted
    
    \[
    \text{mL/min rate} = \frac{(\text{urine Cr} \times mL \text{ urine collected/time})/\text{[plasma Cr]}}{(1.73/\text{body surface area})} \]
    
    - body surface area should be in m$^2$
    - creatinine concentrations should be in mg/dL
plasma Cr levels and 24 hour urine should be taken on same day
- normal clearance:
  - 80-125 ml/min/1.73m² in a healthy young woman
  - 90-130 ml/min/1.73m² in a healthy young man
- disadvantage: can overestimate GFR by 10%
  - if a 24 hour urine is not feasible, you can estimate Cr clearance with the Cockcroft-Gault formula:
    \[
    \text{GFR} = \frac{(140 - \text{age}) \times \text{wt in kg}}{[\text{plasma Cr}] \times 72}
    \]
    - multiple by 0.85 in females to account for less muscle mass
    - normal ranges are 90-140 ml/min/1.73m²
  - can also use Modification of Diet in Renal Disease (MDRD) formula for GFR estimation
    - more accurate than Cr clearance
    - takes into account serum Cr, gender, race, and age
  - can’t use these estimations in situations where the GFR is changing rapidly or with patients on dialysis!

14.2.6 Spot Urine Albumin:Cr Ratio
- random urine specimen used to estimate results of a 24-hour urine collection by comparing levels of albumin to creatinine
  - Microalbuminuria if ratio is 30-300 mg albumin to 1 g Cr
  - Albuminuria if ratio is > 300 mg albumin to 1 g of Cr
  - Need >2 positive tests spaced by 1-2 weeks to meet criteria for persistent proteinuria
  - Used in pregnancy to assess for pregnancy-induced HTN and risk of preeclampsia
  - Recommended over a 24-hour sample in order to prevent patient error

14.2.7 Chronic Kidney Disease
- Chronic kidney disease is defined by a GFR < 60 mL/min/1.73m² for ≥ 3 months
- But kidney damage has occurred by the time GFR is < 90

14.3 Diagnostic Methods: Urinary Tract Imaging

14.3.1 Use of Contrast
- Iodine-based
  - excreted by the kidneys
  - two kinds:
    - ionic (hypertonic) contrast: adverse reactions in 5-12%
    - nonionic (isotonic) contrast: adverse reactions in 1-3%
      - more expensive but more widely used now
  - mild to severe adverse reactions: urticaria, nausea, vomiting, laryngeal edema, bronchospasm, arrhythmia, death
    - for mild allergies, can prep with steroids before giving contrast for imaging
      - standard prep is prednisone beginning 13 hours before scan
      - emergency prep is solu-medrol 4 hours before scan or IV Benadryl 1 hour before scan
  - In renal insufficiency: contrast ok for use with creatinine < 1.8
    - higher threshold for more urgent studies
    - can give renal protectants such as n-acetylcysteine or NaHCO₃ beforehand

14.3.2 Studies and Indications
1.) Kidney, ureters, bladder (KUB) x-ray
- frontal abdominal x-ray
  - indicated for follow up on chronic renal calculi, r/o bowel obstruction or ileus, detection of free intraperitoneal air (an emergency), screening for renal calculi
  - can visualize bones, bowel gas, liver, spleen, kidney, psoas, bladder
• interpretation: look at bowel gas pattern, free gas, bones, soft tissues, lung bases, and calcifications
• gas in bladder wall is a sign of **emphysematous cystitis**: infection of bladder by gas producing organisms, particularly common in DM and neurogenic bladder conditions

2.) IV pyelography = KUB + tomograms
• contrast is injected and x-rays are taken at specific time intervals to capture the contrast as it travels through the different parts of the urinary system
• indicated for post-op complications, f/u on chronic renal calculi or obstruction
• can also visualize transitional cell carcinomas, schistosomiasis, calyceal diverticula (often an incidental finding but can cause stones), filling defects of the ureters
• goblet sign: appearance of a full goblet in the ureter that is a sign of transitional cell carcinoma
• stones will appear radiopaque, but radiolucent masses are often tumors

3.) Renal US
• indicated in ARF to r/o urinary obstruction, initial imaging of renal masses and cysts, f/u in renal transplant complications, screening for renal masses, imaging of first febrile UTI in young children
• fast, inexpensive, no radiation
• quality depends on sonographer, details decreased
• obstructed kidney □ view dilated calyces, dilated pelvis

4.) Lasix renal scan
• first, radioactive compound injected via IV, and imaging is taken
• then IV Lasix is given and more imaging is taken
• pt voids with imaging also taken afterwards
• for use in determining renal function and assessing obstruction

5.) DMSA (dimercapto succinic acid) scan
• radioactive DMSA is injected
• useful in performing cortical imaging or assessing scarring
• used as a screening test in kids with prior infection

5.) Retrograde pyelography
• indicated with IV pyelography failure

6.) Urine flow studies (uroflowometry)
• indicated for lower urinary tract obstruction

7.) Cystography (voiding cystourethrography)
• catheter is used to fill bladder with radiocontrast, and images are obtained as pt voids it out
• indicated for vesicoureter reflux, post-op complications, assessment of anatomy, and for first febrile UTI in a young child
• if contrast is seen refluxing into the ureters, there is an increased risk of infection
• children with this are given prophylactic antibiotics until they outgrow the condition

8.) Cystometry
• indicated for misc. voiding difficulties such as detrusor-sphincter dyssynergia

9.) Cystoscopy
• indicated when atypical cells are found in urine sample, or for unusual growth, polyp, tumor, or cancer

10.) Renal CT
• initial imaging of renal masses and cysts, acute renal or ureteral calculi, suspected asymptomatic renal calculi, suspected pyelonephritis (UTI with fever and flank pain), renal trauma
• no contrast for renal stone imaging
• with and without contrast for renal mass imaging
• can also image anatomic abnormalities like horseshoe kidneys

14.4 Kidney Physiology
• **diffusion**: movement of a solute from an area of higher concentration to an area of lower concentration with no restriction of movement
• **osmosis**: movement through a selectively permeable membrane

### 14.4.1 Functions

- **Fluid & electrolyte balance**
  - regulation of plasma ions
  - stabilization of blood pH
- **Endocrine functions:**
  - renin: regulation of volume and blood pressure
  - erythropoietin secretion
  - activation of vitamin D3
- **Removal of waste**
- **Detox and excretion of drugs**

### 14.4.2 Basic Renal Processes

- Urine formation begins with **glomerular filtration**: filtration of plasma from glomerular capillaries into Bowman’s capsule  
  - what gets filtered to form the filtrate?
    - 100% of Na, K, Cl, HCO3-, urea, glucose, inulin
    - 75% of myoglobin (muscle breakdown)
    - 3% of hemoglobin and 1% of albumin, because these are large proteins that should not be making it through the filter
  - Glomerular filtration rate is typically 125 mL/min  
  - concentration of waste by 36x from blood concentrations
  - a bulk flow process
  - uses up a lot of energy, more than the heart, brain, or skeletal muscle
  - proteins are restricted by Bowman’s capsules and their negative charge
    - since Ca and fatty acids are bound by proteins they don’t end up in the glomerular filtrate either
  - forces involved in filtration:
    - **Starling forces** (balance between water pressure and protein concentration): net filtration must be positive for urine formation
      - glomerular hydrostatic pressure favors filtration
      - makes up greatest force
      - Bowman’s fluid hydrostatic pressure opposes filtration
        - regulated by renal arterioles
        - can also be increased by blockage of urinary tract
      - glomerular osmotic (aka oncotic) pressure opposes filtration
      - Bowman’s fluid osmotic pressure is 0 because there is no protein in there
glomerular filtration rate: can be regulated by neuronal or hormonal input to efferent/afferent arterioles
- caffeine dilates afferent arteriole → increased pressure in glomerular caps → increased GFR
- intense exercise leads to increased vascular resistance (vasoconstriction of afferent arteriole) which decreases GFR
- hemorrhage will increase vascular resistance and decrease GFR
- can measure filtration of a substance in Bowman’s by multiplying its plasma concentration by GFR
  - compare result to amount of substance excreted to determine if net filtration or reabsorption occurred
- not affected by MAPs of 80-180 mm Hg because GFR is autoregulated
  - dilation/constriction of arterioles, tubular-glomerular feedback, reflex feedback

- Filtrate passes down tubules to interact with capillaries
- Tubular reabsorption: movement is from tube lumen to capillary plasm
  - occurs to 99% of all filtrate volume
    - in normal states, glucose, Cl, and water are always reabsorbed by almost 100%
      - but glucose transporters can only handle 300 mg/dL of glucose, concentrations beyond this result in abnormal excretion of glucose in the urine
    - K is also high reabsorbed
    - urea is 50% reabsorbed
  - reabsorption rates for water and important ions are under physiologic control
  - important steps do not occur by bulk flow because there is not enough difference in pressures, rather they occur by diffusion or mediated transport
    - reabsorption of many substances is coupled to Na cotransporter
    - many mediated transport systems are limited by saturation of binding sites
      - ex. glucose max transport is 400 mg/100 mL filtrate
      - this is why there is glucose in the blood in DM
  - not affected by MAPs of 80-180 mm Hg because GFR is autoregulated
  - important steps do not occur by bulk flow because there is not enough difference in pressures, rather they occur by diffusion or mediated transport
  - transport systems are limited by saturation of binding sites
    - ex. glucose max transport is 400 mg/100 mL filtrate
    - this is why there is glucose in the blood in DM

- Tubular secretion: movement is from plasma to tube lumen
  - occurs mostly in proximal tubule
  - can also occur by diffusion or mediated transport
  - toxins are always secreted
  - commonly secreted substances: H+, K+, choline, creatinine
    - usually coupled to reabsorption of Na
  - Amount of substance excreted in urine = (amount filtered) + (amount secreted) - (amount reabsorbed)
  - change rates of filtration, reabsorption, and secretion to regulate amount of substances in body

- Metabolism by the tubules: renal tubule epithelia can use peptides taken up from lumen or capillaries for gluconeogenesis during fasting
- Regulation of membrane channels and transporters
  - hormones and paracrine/autocrine agents regulate activity and concentrations of transport proteins

14.4.3 Structure of the Kidneys and Urinary System
- Nephron: the kidney subunit
  - there are two different kinds of nephrons:
    - juxtamedullary nephrons: ~15% of nephrons; glomeruli lie close to cortical medullar junction in kidney → loops of Henle go deep into medulla
      - help generate osmotic gradient for H2O reabsorption
    - cortical nephrons: most nephrons; glomeruli are on outer cortex and loops of Henle only superficially penetrate the medulla
      - involved mainly in secretion and reabsorption
- Other regions of the kidney
  - renal cortex: outer portion; contains all glomeruli as well as parts of loops of Henle and collecting ducts
  - renal medulla: inner portion containing thin descending and ascending loop of Henle, part of the thick ascending loop, and medullary collecting duct
• Nephron pathway:
  - **Bowman’s capsule**: forms filtrate from blood free of cells and proteins, and is surrounded by a **glomerulus** (capillary bed)
    - each glomerulus is supplied with blood by an afferent arteriole (from the interlobular artery)
    - blood leaves glomerulus by efferent arteriole (becomes hairpin loop of vasa recta and then joins the interlobular vein)
    - glomerulus is encased in podocytes to provide support functions and only allow entry of certain molecules, plasma, and water
  - **tubule**: extends from renal corpuscle
    - adds or removes substances from glomerular filtrate
    - capillaries continue from glomerulus to surround tubule
    - made of up of a single-layer epithelium containing segments cells with different functions:
      - proximal tubule: drains Bowman’s capsule; contains proximal convoluted tubule and proximal straight tubule
        - where 60-70% of the reabsorption of water, ions, glucose, HCO3-, and all organic nutrients happens
        - also secretion of NH3 and H+
        - contains 3Na+/2K+ countertransporters and Na/HCO3- cotransporters
      - **loop of Henle**: contains descending limb and ascending limb
        - reabsorption of water in the descending limb
        - reabsorption of Na and Cl in the ascending limb
          - via Cl-/K+ cotransporters and Na+/K+ countertransporters
        - ascending limb results in creation of an osmotic gradient as the nephron goes deeper into the medulla, which facilitates reabsorption of water = counter current multiplier system
      - distal convoluted tubule: has special macula densa cells that sense [Na] and volume in tubule fluid
        - secretion of K+, H+, other acids, drugs, and toxins
        - variable reabsorption of water, NaCl, and Ca under hormonal control
        - reabsorption of HCO3-
      - collecting duct system: contains cortical collecting duct and medullary collecting duct
        - variable reabsorption of water
        - variable reabsorption or secretion of Na, K, H+, HCO3-
          - via Na+/K+ countertransporters, Cl- channels, and HCO3-/Cl-countertransporters
          - results in final urine pH as low as 4.5
        - also descends into medulla osmotic gradient to facilitate further water reabsorption
        - each nephron is separate from another but all merge at the cortical collecting ducts
        - from here urine empties into minor and then major calices
        - additional merging occurs until everything drains into the renal pelvis (the kidney’s central cavity)

14.4.4 Diuretic Sites of Action

A.) Carbonic anhydrase inhibitors such as acetazolamide interfere with reabsorption of bicarb → decreased ability to exchange Na+ for H+ in proximal convoluted tubules → mild diuresis

B.) Loop diuretics such as furosemide act on the Na+/K+/2Cl- cotransporter in the thick ascending limb of the loop of Henle to inhibit Na and Cl reabsorption
  - because Mg and Ca reabsorption in the thick ascending limb is dependent on Na and Cl concentrations, loop diuretics also inhibit their reabsorption.
  - prevent the urine from becoming concentrated and disrupt the generation of a hypertonic renal medulla - water has less of an osmotic driving force to leave the collecting duct system → increased urine production

C.) Thiazide diuretics block the Na+/Cl- cotransporter in the distal convoluted tubule
also cause loss of K+ and an increase in serum uric acid

D.) Aldosterone antagonists like spironolactone compete with aldosterone in the cortical collecting duct, decreased reabsorption of Na and water, decreases the secretion of potassium

14.4.5 Hydrogen Ion Regulation in the Kidney

- body gains H+ from: increased CO2, metabolites, loss of bicarb in diarrhea or urine
- body loses H+ from: using H+ for metabolism, losing H+ in vomit or urine, hyperventilation
- Kidneys are the main regulators of [H+] and act by altering [plasma bicarb]
  - bicarb is freely filtered at the glomeruli and actively reabsorbed
  - buffers H+ secreted into the tubule into H2CO3 which then dissociates to form H2O and CO2 which diffuse or transport out of the tubule and into the renal epithelial cell
    - epithelial cell then makes a new bicarb out of these and secretes it into the interstitial space
      - when all bicarb has been used up by excess H+ present:
        - different buffer like HPO4^-2 is used
        - carbonic anhydrase works to generate bicarb from H2O and CO2
• more bicarb can also be made from glutamine (produced by the proximal convoluted tubule) □ NH3 and HCO3-
  ▪ NH3 buffers secreted H+ in the cortical collecting duct □ NH4+, which should then be excreted in the urine
  ▪ loss of collecting duct function means NH3 just goes back into the blood and travels to the liver to be made into urea
  ▪ kidney failure results in increased blood urea nitrogen content (BUN)
• kidneys pee out a lot of the acid that is put into them

14.5 Salt and Water

14.5.1 Basic Renal Processes for Sodium and Water

• Sites losing water to external environment: skin, respiratory airways, GI tract, urinary tract = alter excretion of water and salt by the kidneys to offset loss of water
• Sodium reabsorption
  ▪ occurs mainly in proximal tubules but can occur in all tubular segments except descending loop of Henle
  ▪ achieved by Na/K ATPase pumps that keep Na in tubule epithelial cells low so that Na always moves out of tubule lumen to be reabsorbed
    ▪ Na diffusion into interstitial fluid is often coupled with glucose, amino acids, etc in proximal tubules
• Water reabsorption
  ▪ occurs by diffusion and is dependent on Na reabsorption
    ▪ as Na and Cl are reabsorbed, water will follow by osmosis
    ▪ also occurs with glucose, amino acids, bicarb
  ▪ water movement across tubule epithelium is dependent on presence of aquaporins
    ▪ permeability is highest in proximal tubule
    ▪ permeability in cortical and medullar ducts (last tube segments) is varied by physiologic control
      ▪ major control is by antidiuretic hormone (ADH aka vasopressin) secretion
        ▪ ADH secreted by posterior pituitary in response to hypothalamus sensing low blood volume or increased serum osmolality
        ▪ increased ADH □ increased water reabsorption by more opening up more aquaporins
          ▪ water diuresis: large urine flow, possibly from decreased ADH
            ▪ decreased plasma osmolarity
          ▪ osmotic diuresis: large urine flow due to increased solute concentration
            ▪ ex. excess urine in diabetes mellitus
            ▪ any loss of solute in the urine must be accompanied by water loss!
          ▪ diuretics: drugs that increase loss of body water by inhibiting Na+ reabsorption in the tubules
            ▪ be careful when increasing Na/Cl cotransporters, because loss of Na will also be loss of K+ □ need to give KCl supplement so K+ in ECF doesn’t get too low
• Urine concentration
  ▪ terms:
    ▪ hypoosmotic: urine [solute] < normal extracellular fluid (dilute)
    ▪ hyperosmotic: urine [solute] > normal ECF (concentrated)
    ▪ isoosmotic: urine [solute] = ECF [solute]
  ▪ process of urine concentration:
    ▪ descending loop of Henle does not reabsorb NaCl but is permeable to water □ water diffuses out as it passes down deeper into the medulla into more solute-concentrated areas until osmolalities of solute within descending loop and in ECF are equal
      ▪ medulla ECF has increasingly hyperosmotic gradient due to nearby ascending loop of Henle being impermeable to water but actively reabsorbing NaCl via Na/K ATPases
at end of ascending loop of Henle the tubular fluid is hypoosmotic because so much NaCl has been pumped out

tubule fluid is then enters distal convoluted tubule, where more active reabsorption of NaCl creates an even more hypoosmotic fluid

tubule fluid then enters cortical collecting duct
  - action of vasopressin makes the cortical collecting duct permeable to water, so water leaves tubule because ECF has higher osmolarity than tubule

tubule fluid then enters medullary collecting ducts
  - also acted on by vasopressin: more water reabsorption by diffusion of final small amount of urine (about 15% of original volume of urine) that is hyperosmotic
    - without influence of vasopressin, final urine is hypoosmotic

14.5.2 Renal Regulation of Sodium

- Overview:
  - urinary excretion of Na will increase or decrease in order to maintain normal total body Na
  - Na is actively reabsorbed but never secreted
  - baroreceptors sense pressure changes (don’t directly sense [Na])
    - low [Na] → low plasma volume (water exits vessels) → low BP → baroreceptor reflex on renal arterioles to lower GFR and increase Na reabsorption
  - macula densa cells in the distal convoluted tubule directly sense decreased [Na] or decreased flow/volume of tubule fluid

- Control of GFR
  - control of Na reabsorption
    - aldosterone and the renin-angiotensin system
      - renin: acts on angiotensin in the blood to cleave it to angiotensin I
        - secreted by juxtaglomerular cells lining the afferent arteriole in response to macula densa sensing low [Na] or in response to sympathetic firing d/t low plasma vol sensed by baroreceptors
      - angiotensin converting enzyme (ACE): cleaves angiotensin I to angiotensin II
        - angiotensin II stimulates secretion of aldosterone and constriction of arterioles
          - high during salt deficiency and low in salt excess
      - aldosterone: secreted by the adrenal cortex; stimulates production of Na/H and Na/K countertransporters in the distal convoluted tubule and the cortical collecting ducts so that Na is reabsorbed and Na excretion is close to 0%
        - also stimulated by hyperkalemia
        - acts more slowly because it’s a steroid and requires de novo protein synthesis of the transporters (vs fast peptide ADH) → treat high BP by manipulating this system
        - ACE inhibitors, angiotensin II blockers, aldosterone blockers
      - atrial natriuretic peptide (ANP): secreted by atrial cells in response to distension from excess plasma vol
        - acts on medullary collecting duct to inhibit Na reabsorption (less Na in plasma = less vol)
        - acts on renal blood vessels to increase GFR

- What happens in hypernatremia?
  - high [plasma Na]:
    - stimulates thirst and release of ADH → water retention in the kidney
      - angiotensin II and aldosterone are inhibited by high Na because we don’t want to reabsorb more Na
    - increases plasma vol → stretches atria → release of ANP
      - ANP inhibits ADH (want to lose water to lose salt)

14.5.3 Body Water and Fluid Compartments

- Total body water
• measured in kg
• younger males have 60% of their total weight being water
• males over 60 □ 50%
• younger females have 50% of their total weight being water
• females over 60 □ 40%
• Fluid compartments: water passes freely between these compartments to maintain osmotic equilibrium
  • intracellular fluid: all fluid inside of cells, makes up 60% of body water
    o dehydration causes fluid loss here to keep up the BP
  • extracellular fluid: all fluid outside of cells, makes up 40% of body water
    o this is where loss causing hypovolemia occurs
    o 20% of this is the intravascular fluid (within vessel walls)
    o 80% of this is interstitial fluid or “third space” (surrounding vessels and at tissue interfaces)
      ▪ does not contribute to circulation or cell volume!
• Na generates the most osmotic force here
• Circulating volume
  • decreased in hyponatremia because there is less drawing of water into the vessels
  • decreased in heart failure because pooling of blood in the oversized heart causes a loss of fluid to the interstitium
  • lost in areas with an arterio-venous fistula
  • decreased in advanced hepatic cirrhosis due to loss of albumin □ loss of circulating fluid to the interstitium
• Fluid movement between compartments
  • molality: the number of moles of a solute per kilogram of solvent in a solution
  • molarity: the number of moles of solute per litre of solution
  • osmolarity: the total concentration of solutes (including ions) in a solution
    o takes into account the total concentration of penetrating solutes and non-penetrating solutes
    o does not depend on whether the solutes can cross the cell membranes or not
  • tonicity: relates to the osmotic gradient created by solutes that affects a semi-permeable membrane
    o only solutes that can’t freely cross the membrane contribute to this effect
    o example: high BUN makes the blood serum hyperosmotic (more solutes) but it can cross cell membranes to equalize its concentration between the serum and cell, so it has no ability to generate oncotic pressure and draw water out of cells = serum remains isotonic to the body cells
    o example: hyperglycemia makes the blood serum hyperosmotic as well as hypertonic because glucose can’t freely diffuse into the cells (requires transporters) = water leaves cells to equilibrate glucose concentrations between the cells and blood
• Plasma osmolality calculation:
  • plasma osmolality = 2\(Na\) + glucose/18 + BUN/2.8

14.5.4 H&P Assessing Volume Status
• Significant history:
  • volume overload: fluid retention, weight gain, heart failure symptoms
  • volume deficit: prolonged fever, profuse sweating, vomiting, diarrhea, thirst, decreased fluid intake, weight loss, weakness, confusion, lethargy, seizures, coma, third spacing of fluids, use of diuretics, adrenal insufficiency or Addison’s disease, ketonuria
• PE:
  • volume overload: pulmonary edema, peripheral edema, ascites, S3, JVD, rales
  • volume deficit: tachycardia, orthostatic hypotension, decreased turgor, dry mucosal membranes, oliguria

14.5.5 IV Fluids
• normal blood serum is 300-310 mOsM
• fluids will re-distribute in body fluid compartments like water distributes
  A.) 5% dextrose in water (D5W)
• 252 mOsm = slightly hypotonic in relation to the body shift of water into cell until osmolarity equilibrates across all compartments= good for rehydration of intracellular fluid
dextrose is rapidly metabolized by the liver, so you are essentially just giving the patient water
• pH = 3.5-6.5

B.) 0.9% NaCl (normal saline or NS)
• 308 mOsm = isotonic in relation to the body
• no fluid shifts, no change in osmolarity, just restoration of intravascular volume
eventually results in ADH being turned off with excretion of excess water
• pH = 4.5-7
good for maintenance fluid
calculate need:
  o 100 mL/kg/day for the first 10 kg
  o 50 mL/kg/day for the next 10 kg
  o 20 mL/kg/day for every kg over 20 then divide by 24 for hourly rate

C.) Lactated Ringer's solution
• 273 mOsm = ~ isotonic in relation to the body
• contains Na, K, Ca, Cl, and lactate
• used in the first 24 hours post-op, then replaced with NS because the lactate can cause metabolic alkalosis if used for too long

D.) ½ NS
E.) ¼ NS
F.) 3.0% Na Cl
• for initial treatment of severe hyponatremia

14.5.6 Hyponatremia
• Normal serum Na mOsm is 280-295; low if < 280
• Categories
  • isotonic hyponatremia: low serum Na with normal ECF osmolality and tonicity
    o probably due to high blood levels of triglycerides or protein (multiple myeloma) that push Na intracellularly to prevent increased serum osmolality
    o a kind of pseudohyponatremia
    o no treatment
  • hypertonic hyponatremia: low serum Na with high ECF osmolality and tonicity
    o caused by a highly osmotic molecule like glucose or mannitol in the ECF, which draws water out of cells and dilutes the Na concentration
      [Na] will fall by 1/6 mEq/L for every 100 mg/dL increase in [glucose]
    o also pseudohyponatremia
    o treatment with NS until hemodynamically stable, then ½ NS
  • hypotonic hyponatremia: true hyponatremia that is the most common form, there is an increase in ADH causing water and Na retention in the tubule
    o further characterize based on volume status:
      • hypervolemic hypotonic hyponatremia: third spacing of fluid leads to reduced circulating volume (even though total body water is hypervolemic), fluid is hypotonic because too much Na is retained in the urine
        • ex. CHF, liver failure, nephrotic syndrome, advanced renal failure
        • treatment: water and Na restriction
      • euvolemic hypotonic hyponatremia: due to excessive ADH release
        • ex. SIADH, postoperative hyponatremia, hypothyroidism, psychogenic polydipsia, excess beer drinking, idiosyncratic drug reactions
        • treatment: water restriction with hypertonic NaCl infusion
      • hypovolemic hyponatremia:
        • an extrarenal cause when kidneys are attempting to resuscitate volume by saving Na and water
Treatment of hyponatremia
- depends on whether patient is symptomatic and if it is acute or chronic
  - chronic asymptomatic mild-moderate hyponatremia may not need any treatment
  - correct to magic number 125
  - severe symptoms 1.5-2 mEq/L/hour for first 2-4 hours
    - don’t exceed 12 mEq/L/day
  - asymptomatic patients < 0.5 mEq/L/hour
- definitive treatment based on underlying cause of impaired renal water excretion

14.5.7 Hypernatremia
- When serum Na mOsM > 145
- Usually from loss of water with failure to adequately replace water loss
  - extrarenal water losses: sweat, fever, severe burns
  - renal losses:
    - osmotic diuresis,
    - diabetes insipidus (central or nephrogenic): deficiency of ADH or insensitivity to ADH
      - treat with slight volume depletion to increase water absorption at the proximal tubule, low salt diet, thiazide diuretic
      - don’t use loop diuretics or NSAIDs
    - iatrogenic: administration of hypertonic NaCl)
- Categories:
  - hypovolemic hypernatremia:
    - non-renal causes: excess water loss from skin, diarrhea low urine Na with high urine osmolarity
    - renal causes: osmotic diuresis with mannitol, glucose, or diuretics high urine Na with normal? urine osmolarity
    - treatment:
      - severe NS to lower the serum osmolality back to normal
      - mild D5W + ½ NS
  - euvolemic hypernatremia:
    - non-renal causes: excessive sweating from skin or respiratory system water loss
    - renal causes: lack of ADH
    - treatment: increase PO water or use IV D5W
      - also use diuretics if GFR is decreased
  - hyperpervolemic hypernatremia:
    - non-renal causes: treatment of previous hypotonic fluid loss with higher sodium fluids, sea water ingestion, overuse of NaHCO₃ in CPR
    - renal causes: rare, due to Na addition from hyperaldosteronism, Cushing’s syndrome
    - treatment: D5W to reduce hyperosmolality
      - may also need dialysis if pt has renal failure
  - chronic hypernatremia:
    - treatment: slow correction to prevent cerebral edema by decrease serum Na by 0.5-1 mEq/L/hour, with complete correction accomplished over 36-72 hours
      - calculate water deficiency: normal TBW = (present TBW) (present serum Na)/(normal serum Na = 140)
- Presentation: lethargy, weakness (brain cell shrinkage), irritability, twitching, seizures, coma, focal intracerebral and subarachnoid hemorrhages (due to vessel attachment to shrinking cells)
- Treatment fluid tips:
  - D5W will replace water without adding Na
    - caution: not good at restoring ECF in hypovolemic patients, can develop hyperglycemia or glucosuria, can aggravate the hypernatremia by causing an osmotic diuresis?
• 1/2 NS will replace water and Na
  o less efficient than D5W but ok to use when patient is both hypernatremic and hyperglycemic
  o can be used to restore ECF in hypovolemic patients

14.5.8 Serum Anion Gap
• Law of conservation of charge: sum of cations and anions must equal each other!
  • Cations in the blood:
    o routinely measured: Na+, K+
    o not usually measured (“unmeasured cations”): Ca2+, Mg2+
  • Anions in the blood:
    o routinely measured: Cl-, HCO3-
    o not usually measured (“unmeasured anions”): albumin3-, PO43-, SO42-, lactate, ketoacids
    \[ \text{Na}^+ + \text{K}^+ + \text{UC} = \text{Cl}^- + \text{HCO}_3^- + \text{UA} = \text{UA} - \text{UC} = \text{anion gap} \]
    o but K+ normally is a very small amount in the blood (ECF), so it is not accounted for

- Anion gap < 0
  • can’t be due to no UA because there are always albumin, lactate, ketoacids as long as metabolism is going on = must be due to a lot of UC
  o ex. Li toxicity, multiple myeloma (IgG and IgM are + charged)

- Anion gap > 0 = positive anion gap
  • can’t be due to having 0 unmeasured cations, so must be due to having a lot of unmeasured anions
  o ex. albumin3-
  • normal anion gap is 10-12 due to having normal amounts of albumin
    o above this is pathological (“increased anion gap”)
      . ex. multiple myeloma with - charged IgA, methanol, ethylene glycol, ketoacids, acute
      . renal failure □ high PO43- and SO4

14.5.9 Urine Anion Gap
• Also based on the law of conservation of charge
  • Urine cations:
    o measured: Na+, K+
    o unmeasured cations: Li+, Ca2+, Mg2+, NH4
  • Urine anions:
    o measured: Cl-
    o unmeasured anions are the “titratable acids” =concentration fluctuates/unpredictable:
      HCO3-, PO43-, SO42-, lactate □ urine anion gap = Na+ + K+ UC = Cl- + UA
    o K+ counted here because it exists in large concentrations in the urine □ UAG = urine Na+ + urine K+ + urine Cl = UA - UC

- UAG equation can only be used in a patient with metabolic acidosis
- UAG > 0 = positive
  • either no/low unmeasured cations or too many unmeasured anions
    o usually due to low number of unmeasured cations, typically low NH4+
      . ex. renal tubular acidosis (kidney can’t make NH4+)
  • UAG < 0
    • due to either no unmeasured anions (rare) or lot of cations generated
      o usually due to lots of NH4+ generated
      . a normal response when there is a high acid load for the kidney to get rid of
      . can also be due to GI losses of bicarbonate □ acidosis

14.6 Nephrolithiasis

14.6.1 Background
• Epidemiology
• peak age of incidence is 30-60 years
• historically males 3x more likely to develop a stone, but female incidence is catching up
• FH incurs a 3x greater risk of development
  • increased risk with increased weight, metabolic syndrome, immobility, gastric bypass
  • recurrence of stones is common, with 80% suffering a second stone within 10 years of the first
  • a "stone belt" exists in the South, including North and South Carolina, Georgia, Kentucky, and Tennessee
  • overall incidence increasing due to changes in diet, lifestyle, and increasing obesity
• Types of kidney stones: calcium oxalate, calcium phosphate, uric acid, struvite, cystine, medication crystallization (antiretrovirals, laxatives)
  • most common is calcium oxalate?
• Presentation of patient with kidney stones:
  • flank pain secondary to obstruction, hematuria, nausea, vomiting, lower UTI symptoms
  • intermittent/colicky pain that may "move" with stone movement
  • tend to move around/anxious vs. being still
• Investigation
  • labs:
    • UA: look for blood, leukocyte esterase, nitrates, WBCs, crystals
      ▪ there will almost always be hematuria with kidney stones!
    • urine culture: look for Proteus, which likes to make stones
    • BMP: check Cr (determines feasible treatments), Ca levels (hyperparathyroidism is a risk factor for stone development
    • CBC with differential to look for infectious cause
  • imaging:
    • CT without contrast considered (aka spiral CT, kidney protocol, stone protocol) the gold standard
      ▪ highly sensitive and specific, fast, can assess non-stone problems
      ▪ cons: costly, involves radiation
    • US: good for evaluation of secondary signs of obstruction
      ▪ low cost, no radiation
      ▪ cons: decreased sensitivity, hard to detect stones that are mid-ureter, tend to overestimate stone size, can’t be done on an obese patient
    • kidney/ureter/bladder (KUB) x-ray +/- tomograms
      ▪ good place to start for imaging
      ▪ decreased sensitivity, requires IV contrast, can be time consuming
    • IV pyelograms
    • MRI
• Treatment of symptomatic stones:
  • home treatment:
    • always give a pain med
    • strain urine to check for stones (don’t always get instant relief with stone passage)
  • surgery for intractable pain, significant obstruction, fever, infection, severe bleeding, when patient only has one kidney, and if patient is immunocompromised/deterioration is imminent
    • open surgical nephrolithotomy: incision into renal pelvis to completely remove stone
    • percutaneous nephrolithotomy: retrieval of stones using a catheter
      ▪ indicated for large stone mass, certain stone shapes (staghorn) anatomic abnormalities such as horseshoe kidney or diverticulum, obesity, obstruction, previous lithotripsy failure, cystine stones, and whenever total removal needs to be 100% guaranteed
    • ureteroscopy
    • shock wave lithotripsy
      ▪ stone must be surgical, there must be no obstruction to passage of fragments created, stone < 1.5 cm, mid/upper pole or renal pelvis location, normal renal anatomy, no distal obstruction below the stone
      ▪ obese patients do not do well with this
      ▪ can result in shoving stone deeper into kidney
contraindicated with active UTI, irreversible bleeding/anticoagulation, large stones, cystine stones, or presence of obstruction distal to stone
  - the larger the stone, the more likely it will recur if lithotripsy is used
    - medical expulsive therapy
    - laparoscopic surgery
- Treatment of asymptomatic stones
- if only involving one kidney, typically just watch (other kidney can take over if stone becomes an obstruction)
  - exceptions: occupations such as pilot or businessperson frequently on travel (someone who can’t have an acute attack safely), or someone who only has one kidney
  - any treatment must involve the unaffected kidney as well
- Follow-up
- if no improvement with home treatment in 48-72 hours, refer to nephrology

14.6.2 Ureteral Calculi
- Most common locations are at the ureteropelvic junction, at the crossing of the iliac artery midureter, and at the uretero-vesicular junction
- Treatment options:
  - observation +/- medical expulsive therapy: most stones will pass spontaneously within 6 weeks
    - studies show that giving alpha blockers help stones pass sooner, but this is not FDA approved
  - shock wave lithotripsy for any ureteral stones < 1cm
  - ureteroscopy for stones > 1 cm

14.6.3 Medical Management of Nephrolithiasis
- Recurrent stones are preventable!
  - reduce new stone formation by reversing underlying physiochemical and physiologic abnormalities
  - contributing to stone formation, overcoming nonrenal complications of stone formation, and staying free of serious side effects
- Do metabolic evaluation for all stone formers
  - simplified eval for first time stoners or rare stones over lifetime
    - serum Ca and phosphate to look for hyperparathyroidism
    - serum electrolytes to look for renal tubule acidosis
    - serum uric acid to look for gout or HUCU
    - UA to look for crystals, signs of infection
    - history for fluids, diet, meds
    - x-rays to look at stone shape
  - stone composition analysis
    - calcareous (Ca carbonate) calculi with hypercalciuria, hyperuricosuria, hypocitraturia, hyperoxaluria, hypomagnesuria
    - non-calcareous calculi with low urine pH (uric acid), cystinuria, or infection (struvite stones)
  - comprehensive eval for recurrent stoners or stoners with risk factors such as FH, intestinal diseases, surgeries, pathologic fractures/osteoporosis, gout, poor health, solitary kidney, anatomic abnormalities or urinary diversion, renal insufficiency, cystine stones, uric acid stones, certain occupations (pilots, truck drivers, business travelers), medications (topiramate, acetazolamide)
  - truck drivers at increased risk d/t less hydration to avoid urination
  - includes all elements of the simplified eval + 2x 24-hour urine collections
  - also check Na, Mg, K, Cr, sulfate, NH4
- General dietary recs: increase fluid intake, goal urine output of 2.5 L/day, decrease Na and animal protein intake
  - increase Ca intake (will bind oxalate to help it pass in stool rather than urine)
  - increased vit D intake controversial and probably doesn’t help maintain Ca
• Medications that may help prevent recurrent stones
  • potassium citrate: regulates urinary pH and binds Ca
  • thiazide diuretics: reduce Ca
  • allopurinol: lowers urinary uric acid
  • tiopronin/D-penicillamine: reduces cystine levels
  • acetohydroxamic acid with antibiotic: reduces struvite stone formation
• Prognosis: selective treatment to prevent stone formation has greater benefit than conservative treatment

14.7 Acute Renal Failure

14.7.1 Background

• Definitions
  • acute renal failure: an abrupt decrease in GFR sufficient to result in azotemia and perturbation of ECF volume, electrolyte, and acid-base balance = kidney is not removing proteins that should normally be removed from the blood
  • azotemia: abnormally high levels of nitrogen-containing compounds, such as urea, creatinine, various body waste compounds, and other nitrogen-rich compounds in the blood
    o can result from many disorders including renal failure
  • acute tubular necrosis: abrupt and sustained decline in GFR occurring within minutes to days in response to an acute ischemic or nephrotoxic insult
    o most common cause of ARF
    o proximal convoluted tubule has the highest energy and oxygen requirements, so it is the first to be damaged
    o nephrotoxins: contrast, aminoglycosides, amphotericin B
  • Slow decline in renal function as measured by GFR is normal with aging
  • Presentation of ARF:
    • accumulation of urea and other substances □ fatigue, loss of appetite, headache, nausea, vomiting
    • flank pain from stretching of fibrous capsule surrounding kidney during blockage situation
    • accumulation of K+ □ irregular heartbeat
    • dehydration □ thirst, signs of fluid depletion
    • inability to excrete fluid in urine □ signs of volume overload such as peripheral edema, pulmonary edema (dyspnea, orthopnea, decreased oxygenation, respiratory failure), pulmonary rales, elevated right atrial pressure/increased JVP, cardiac tamponade, low urine output, pulsus paradoxus (abnormal drop in pulse pressure upon inspiration)
    • other presentations: mental status changes, pruritus, seizures, SOB, asterixis (hand flap pathognomonic for uremia, hepatic failure, and hypercapnea) and other myoclonus, pericardial or pleural friction rub, Kussmaul respirations (acidosis)
  • Investigation
    • labs: elevated BUN and Cr
    • see EKG changes with diffuse ST elevation in uremic pericarditis

14.7.2 Prerenal Azotemia

• a result of interrupted blood flow to the kidneys □ ischemia of the proximal tubular cells
• Decreased renal perfusion □ release of renin by the kidneys □ maximal retention of Na and water
  • Common causes:
    • decreased effective circulating volume: heart failure, cirrhosis, nephrotic syndrome
    • cardiac arrest
    • low BP: anorexia, GI illness or bleed, cardiac surgery
    • renal artery stenosis, renal vein thrombosis, diuretic use in heart failure or edema
    • any of these events can lead to acute tubular necrosis (= prerenal cause becomes a renal cause of azotemia)
  • Investigation:
    • hypotension
- decreased urine output with concentrated urine
  - very low urine Na (< 10 mM) due to water conservation
- rise in urea out of proportion to rise in Cr
- Treatment: IV NS, treatment of underlying illness, d/c of any antihypertensives or diuretics, octreotide in patients with cirrhosis

14.7.3 Renal Azotemia
- a result of direct damage to the kidneys
- Common causes:
  - vascular: renal infarction, renal artery stenosis, renal vein thrombosis, malignant HTN, scleroderma renal crisis (thickened kidneys with HTN), thrombotic microangiopathy, atheroembolic disease (cholesterol embolus from cath procedure lodges in renal artery)
  - tubular: ischemia from sepsis/systemic HTN/long-term pre-renal state, nephrotoxicity from aminoglycosides/methotrexate/contrast/myoglobin/chemotherapeutics
  - glomerular: acute glomerulonephritis, vasculitis, thrombotic microangiopathy
  - interstitial: acute interstitial nephritis secondary to drugs/systemic disease/tumor infiltration/infection
    - can also occur with transplant rejection
    - common offending drugs: cephalosporins, penicillins, rifampin, sulfonamides, NSAIDs, diuretics, allopurinol

- Presentation
  - acute tubular necrosis: volume overload
  - vascular damage: flank pain, abdominal bruit, hematuria, retinal hemorrhages, acute nephrosclerosis
    - atheroembolus, livedo reticularis rash
  - acute interstitial nephritis: abrupt deterioration in renal function with inflammation and edema of the renal interstitium
- Investigation
  - ATN: oliguria or anuria, rise in Cr and urea in = proportions, metabolic acidosis with hyperkalemia, casts
  - acute interstitial nephritis:
    - UA: proteinuria, pyuria, hematuria, renal tubular epithelial cells or casts, eosinophiluria
    - labs: ↑BUN, ↑Cr, hyper or hypokalemia, hyperchloremic metabolic acidosis, fractional excretion of sodium, anemia, eosinophilia, elevated LFTs, elevated serum IgE
- Treatment
  - ATN: conservative or renal replacement therapy if volume overloaded, unresponsively acidic, hyperkalemic, uremic, encephalopathic, azotemic, or with significant bleeding (platelets don't work well in uremia) or uremic pericarditis
    - involves dialysis to remove urea, K, phosphate, Cr, while replacing HCO3-, Ca, erythropoietin, and vit D
  - treat underlying causes:
    - HTN: antihypertensives
    - scleroderma: ACEI
    - thrombotic microangiopathy: plasmapheresis, treatment of underlying anemia or thrombocytopenia, cessation of meds causing it

14.7.4 Postrenal Azotemia
- a result of obstruction of urine flow
- Common causes: enlarged prostate, kidney stones, bladder tumor, injury, obstructed urinary catheter, GYN cancers, retroperitoneal fibrosis
  - can also be caused by drug crystallization: amoxicillin, indinavir, acyclovir
    - especially in settings of volume depletion and hypoalbuminemia
- Presentation
• obstruction secondary to drug crystallization (crystalluria, hematuria, leukocyturia, obstructive uropathy, ARF from intratubular ppt of crystals)
• Investigation: US, UA

14.8 Urinary Tract Infections

14.8.1 Cystitis in Women

• Risk factors: sexual intercourse, spermicide use, diaphragm use, DM on insulin, history of recurrent UTIs, recent antibiotic use
• Pathogen is usually E. coli or Staph saprophyticus
  • others: Proteus mirabilis, Klebsiella, enterococci
  • ascension into urinary tract via colonization of vaginal entrance
• Presentation:
  • lower UTI: dysuria with muscle spasm before or after urination, frequency with small volume, urgency, suprapubic pain, +/- hematuria, midline suprapubic tenderness
  • upper UTI: lower symptoms + fever > 100.4, flank pain, CVA tenderness, nausea, vomiting
• PE: fever, suprapubic tenderness, CVA tenderness, may need to do pelvic exam if suspecting urethritis or vaginitis
• Investigation:
  • if acute and likely to be uncomplicated (= healthy young nonpregnant female) proceed to empiric treatment
  • if acute and possibly of being complicated (= anyone other than a healthy nonpregnant female) further diagnostic testing
    • especially with history of catheterization, post void residuals, azotemia, or renal transplant patients
    • may need to r/o dysuria secondary to STI urethritis (gonorrhea or chlamydia)
      • risks: history of STI, new sex partner, partner with urethral symptoms, gradual onset
    • need to r/o vaginitis: external dysuria but no frequency or urgency
      • also has symptoms of vaginal discharge, itching, and dyspareunia, which are not seen in UTI
  • UA: midstream catch for pyuria
    • clean catch not necessary
    • hematuria common in UTI but not present in urethritis or cervicitis
  • culture urine in complicated infections, with symptoms atypical of UTIs, with persistent symptoms following a treatment, if symptoms recur < 1 month after treatment
    • also get susceptibilities
• Treatment
  • acute uncomplicated UTI:
    • no long term adverse effects if UTI is left untreated, but it may progress to pyelonephritis
    • typically a 3-5 day short antibiotic course (no proven benefit to extending > 3-5 days)
      • DOC is nitrofurantoin or fluoroquinolone
        • nitrofurantoin inactive against certain gram negs
        • fluoroquinolone used with nitrofurantoin allergy, complicated infections, or with severe symptoms
      • can use TMP-SMX if not allergic, no antibiotics in last 3 months, no recent hospitalizations, and local E. coli resistance is not > 20%
      • ***advise patients that any antibiotic use may decrease effectiveness of oral contraceptives
        • single dose available (fosfomycin) but is less effective
        • cranberry juice may have a role in prevention of recurrent UTIs
          • acidifies urine, prevents uropathogens from adhering to epithelia
        • probiotics being researched as a UTI prevention
        • phenazopyridine (Azo) is used to treat symptoms only for severe dysuria
          • can’t be used chronically due to risk of toxicity, hemolytic anemia, ARF, hepatitis, skin pigmentation changes
  • complicated UTI:
14.8.2 Recurrent Cystitis

- Hard to distinguish reinfection from relapse
- Usually a genetic predisposition: blood group antigen nonsecretor enhances uropathogen adherence, IL-8 deficiency decreases neutrophil chemotaxis
- Strongest predictor is frequency of intercourse
  - others: spermicide use in last year, new sex partner, first UTI before age 15, mother with history of UTIs
  - postmenopausal risk factors: urinary incontinence, cystocele, postvoid residual, history of UTI before menopause, nonsecretor status
- Prevention strategies:
  - change contraception and eliminate use of spermicide
  - urinating after sex
  - increase fluid intake
  - cranberry juice
  - may need antibiotic prophylaxis for women with ≥ 2 UTIs in last 6 months or ≥ 3 UTIs in last year
    - first clear urine of UTI with negative culture results
    - then initiate TMP-SMX, nitrofurantoin, cefaclor, cephalexin, or fluoroquinolone
    - length of therapy:
      - 6 months continuous use provides a 95% decrease in recurrence
        - may cause resistance, vaginal candidiasis, GI symptoms
        - then re-evaluate and trial a time period without prophylaxis
      - can also use a single dose after sex
    - postmenopausal women may benefit from an vaginal estrogen cream increased Lactobacillus population and decreased E. coli
      - vagina gets drier post-menopause
- Self-treatment of a short course of TMP-SMX or fluoroquinolone is effective
- UTIs occur more frequently than with prophylactic antibiotics but less antibiotics are used overall
  - requires motivated and compliant patients
- Consider urologic evaluation if suspecting a structural problem as the cause for recurrence
  - CT or renal US, then cystography

14.8.3 Pyelonephritis

- Pathogens involved are frequently uropathogenic strains of E.coli
  - traits including hemolysin, aerobactin, and special pili
- Presentation: ranges from cystitis symptoms to mild flank pain to gram neg septicemia
- progression to sepsis more common than in cystitis
- Investigation:
  - urine microscopy
  - UA for pyuria
  - urine culture
  - blood cultures if hospitalized
- Treatment:
  - mild symptoms (no nausea or vomiting) outpatient oral med like cipro or levofloxacin
    - can use TMP-SMX if susceptibilities are known
  - moderate-severe symptoms or pregnancy inpatient treatment with IV ceftriaxone, aminoglycosides
    - switch to orals in 2-3 days if symptoms improve
    - otherwise, repeat cultures and consider US or CT
    - always get f/u culture 2 weeks after therapy
14.8.4 UTIs in Men
- Very rare in men under age 50 due to having a drier periurethral environment, longer urethra, and antibacterial substances in the prostatic fluid
  - uncomplicated infections can occur in young males (typically E.coli)
  - the elderly or infants tend to get complicated infections with urological structure abnormality
- Risk factors: homosexuality, lack of circumcision, sexual partner with uropathogens, low CD4 count
- Investigation:
  - must r/o urethritis, prostatitis as these are more likely in a male
  - always do a culture!
- Treatment:
  - longer course (7 days) of TMP-SMX or fluoroquinolone

14.8.5 Catheter-Associated UTI
- Most common source of gram neg bacteremia in a hospitalized patient
- Prevention: replace indwelling catheters every 2 weeks, use sterile insertion techniques, ensure collecting systems are closed
- Treatment:
  - frequently resistant to antibiotics due to biofilm growth

14.8.6 Asymptomatic Bacteruria
- No benefit in treatment except in pregnant women, before TURPs procedure, or before a procedure that will cause mucosal bleeding

14.9 Glomerulopathies and Other Renal Diseases
14.9.1 Approach to a Patient with Renal Disease
- Serum creatinine
- Serum urea
- CBC for Hb, platelets
- Coagulation profile
- Lipid disorders: cholesterol panel
- Abnormalities in mineral metabolism: Ca, phosphate, PTH
- Autoimmune serologies
- Infectious serologies: HIV, hepatitis
- UA for protein, sediment/casts
  - **nephritic sediment**: a result of active inflammation with leukocyte infiltrate □ damage of capillary walls □ escape of RBCs into the urine
    - another hallmark is cellular casts such as RBC casts, WBC casts
    - HTN also results as kidneys become ischemic and release renin
    - some edema
    - occurs in presence of renal failure
    - may be associated with renal cell cancer, trauma to the urologic system, or other malignancies of the bladder and ureter
  - **nephrotic sediment**: loss of massive amounts of protein in the urine □ hypoalbuminemia □ peripheral edema
    - also causes hyperlipidemia
    - occurs in absence of renal failure
    - oval fat bodies in fatty casts and hyaline casts
    - Maltese cross crystals
    - has an “o” in it because there is loss of protein, oval fat bodies, it is an “oh shit” bad thing to happen
must follow up this kind of finding with a biopsy to find out what is going on.

14.9.2 Glomerular Disease:

A.) Minimal change disease:

B.) Focal segmental glomerulosclerosis: sclerosis of selected glomeruli → impairment of kidney function

- ESRD
  - accounts for ¼ of adult nephropathies
  - affects black patients more than white patients
  - affects men more than women
  - presentation:
    - proteinuria
    - renal insufficiency
    - HTN
  - investigation:
    - labs: serum albumin < 2 g/dL, hyperlipidemia, decreased immunoglobulins
    - histology shows one of several pathologies including glomerular hypertrophy or a collapsing variant
  - treatment: slows disease down but does not ultimately prevent it from causing ESRD
    - prednisone
    - alternatives: cyclophosphamide, cyclosporine, ACEI & ARB
  - prognosis: spontaneous remission in some

C.) Membranous glomerulopathy: an immune-mediated disease characterized by immune complex deposition in the subepithelial portion of glomerular capillary walls

- may occur secondary to hep B, syphilis, endocarditis, thyroiditis, carcinoma, gold?, penicillamine, captopril, carcinoma, autoimmune disease, formaldehyde exposure, graft vs host disease
- the most common association with nephrotic syndrome
- affects males more
- presentation:
  - microscopic hematuria
  - HTN
  - normal or slightly decreased renal function
  - acute renal failure
- investigation:
  - histology shows diffuse thickening of basement membrane with subepithelial immune complex deposits
- treatment:
  - pulse methylprednisone + cyclophosphamide or chlorambucil
  - azathioprine
  - cyclosporine
  - mycophenolate mofetil
  - ACEI or ARB
- prognosis: 1/3 have spontaneous remission, 1/3 respond to treatment, 1/3 develop ESRD

D.) Membranoproliferative glomerulopathy (mesangial capillary glomerulonephritis):

E.) IgA nephropathy (Berger’s disease): glomerulonephritis with deposition of IgA in the glomerulus

- uncommon
- less common in black patients, more common in Asian and Australian patients
- can occur secondary to cirrhosis, Celiac disease, HIV, CMV
- presentation: gross hematuria 1-3 days after URT infection, may have flu-like symptoms or GI illness
  - IgA deposits in tubules can cause acute kidney failure
  - Henoch-Schönlein purpura: rash resulting from IgA deposition in other blood vessels
    - can progress to ESRD in adults
• treatment: disease is on a spectrum, with some cases only requiring monitoring and other more severe cases needing biopsy and full workup
  • control blood pressure to < 125/75
  • ACEI or ARB or both
  • prednisone for proteinuria > 1g
  • fish oil
  • Cellcept?
• prognosis:
  • 1/3 will achieve clinical remission
  • 2/3 will develop renal insufficiency, with 20% going on to develop ESRD

F.) Goodpasture syndrome: rare disease characterized by “crescentic” glomerulonephritis and hemorrhaging of the lungs due to production of an anti-basement membrane antibody
• usually presents as a nephritic syndrome
• affects males more
• associated with influenza A, hydrocarbon solvent exposure, HLA-DR2, and B7 antigen
• investigation:
  • labs for anti-basement membrane antibody
  • CBC shows Fe deficient anemia
  • normal complement
  • sputum with hemosiderin-filled macrophages
• treatment only works if patients is not on HD yet or if Cr is < 4
  • plasma exchange
  • steroids
  • cyclophosphamide
  • often requires intubation
• prognosis: may progress to rapidly progressive glomerulonephritis

G.) Glomerulopathies secondary to systemic diseases such as SLE, multiple myeloma, DM, HTN, sickle cell, infections
• post-infectious glomerulonephritis: glomerular inflammation secondary to any infection with deposition of IgG in the glomerulus
  • particularly Strep pyogenes but can also occur after TB, HIV, hepatitis, MRSA, meningococcal infection
  • damage is immune-mediated by IgG antibody deposition in the glomerulus
  • more common in children and males
  • onset is 1 to 3 weeks after infection
  • presentation: edema, HTN, gross hematuria, renal failure
• investigation:
  • labs: ↑ anti-streptolysin O titer if due to streptococcal infection, ↑ serum creatinine
  • UA: RBC & WBC casts, RBCs, but no bacteria
  • biopsy shows neutrophils, hypercellular mesangial cells, obliteration of capillary lumens, antibody clumps
    • can do immunofluorescence stain to visualize IgG depositions
• prognosis: good in children, poor in adults (go on to develop CKD or remain dependent on renal replacement therapy)

14.9.3 Tubulointerstitial Disease
• Affects the medulla
• Acute or chronic
  • acute associated with toxins, allergies, and ischemia
    • offensive drugs: beta-lactams, cipro, erythromycin, tetracycline, vanco, Bactrim, rifampin, ethambutol, NSAIDs, diuretics, allopurinol, cimetidine, phenytoin
    • systemic infections with bacteria, viruses, or parasites
    • also idiopathic
• chronic a result of acute or progressive disease □ fibrosis
  o associated with analgesics, heavy metals, multiple myeloma, and gout
  o small, contracted kidneys
  o decreased urine concentration
  o hyperchloremic metabolic acidosis
  o hyperkalemia
  o reduced GFR
  o obstructed uropathy
  o vesicoureteral reflux □ UTIs in childhood or young adulthood

14.9.4 Cystic Disease
• Background
  • affects both cortex and medulla
  • cysts develop from renal tubular elements
  • common after age 50 and most are asymptomatic
  • Pathological in autosomal dominant polycystic kidney disease: characterized by multiple cysts, usually present in both kidneys
  • mutations of ADPKD2 and ADPKD2 (longer life expectancy with this one)
  • can develop secondary infections of cysts
  • predisposes to development of stones, UTIs
  • increases risk of renal cell carcinoma
  • half develop ESRD by age 60
  • presentation: abdominal or flank pain, hematuria, history of UTI, history of stones, FH, HTN, abdominal mass
  • cysts can rupture
  • may also see cerebral aneurysm, mitral valve prolapse, aortic aneurysm, colonic diverticulosis
• investigation:
  • UA: hematuria and proteinuria
  • US is diagnostic:
    ▪ < 30 years old with 2+ cysts
    ▪ between 30-59 with 2+ cysts on each kidney
    ▪ greater than 60 with 4+ cysts on each kidney
• treatment usually requires transplant with removal of cystic kidneys

14.10 Chronic Kidney Disease and Management of Potassium, Calcium, and Phosphorus

14.10.1 Background
• Definitions
  • kidney “disease” means that there is an abnormal marker of kidney damage with diminished kidney function to a GFR < 60
  • CKD is also known as chronic renal failure (CRF) or chronic renal insufficiency (CRI) must be present for > 3 months
• Staging
  • stage 1 = GFR ≥ 90 and with kidney damage but asymptomatic
  • stage 2 = GFR 60-89 and with kidney damage but asymptomatic
  • stage 3 = GFR 30-59, still asymptomatic
    ▪ BUN and serum Cr begin to elevate
    ▪ mild anemia
  • stage 4 = GFR 15-29, symptoms begin
    ▪ fatigue
    ▪ altered electrolytes
    ▪ acidosis
    ▪ anemia
• stage 5 = GFR ≤ 15 or dialysis-dependent

Epidemiology
• increasing in incidence and prevalence due to aging population, increased rates of diabetes, and changing racial distributions in the U.S.
• relative risk of CKD varies by racial ethnicity
  o blacks have 3.8x greater relative risk
  o native Americans have 2x greater relative risk
  o Hispanics have 1.5x greater relative risk
• common comorbidities include diabetes, HTN, glomerulonephritis, cystic kidney disease
• Presentation of CKD relates to interruption of normal kidney homeostasis
• inability to properly filter blood
  o imbalance of salt and water □ fluid accumulation, HTN, peripheral edema, hypo or hyperten
  □ maternal effects, subsequent neurologic effects
  o imbalance of potassium affects cell membrane potential and cardiac conduction
  o imbalance of Ca and phosphorus affects bone metabolism and cell membrane stability
  o acid/base imbalance affects functioning of cells and enzymes
• inability to excrete
  o buildup of uremic toxins □ nausea, anorexia, abnormal metallic taste in mouth, insomnia, seizures, coma, bleeding, immune dysfunction, arrhythmias, accelerated atherosclerosis, cardiomyopathy, pruritus
  o inability to metabolize certain drugs
• loss of hormones and enzymes normally produced in the kidney
  o no erythropoietin □ anemia
    □ 90% prevalence in CKD
  o no activation of vit D □ hyperparathyroidism, renal osteodystrophy, fractures
  o loss of bone Ca with deposition of Ca in the wrong places, such as soft tissue and arteries
    □ osteoporosis and 4x increased fracture risk
• CKD patients are also at higher cardiovascular risk
  o 60% have CAD lesions at time of CKD diagnosis, without having prior history of CAD
  o increasing risk with progression to later stages of CKD
  o most patients will die of a cardiac-related cause before ESRD develops

Prognosis
• patients with ESRD face a 1:5 chance of dying each year
• common causes of death are arrhythmias, CHF, acute MI, and other cardiac issues
• degree of proteinuria predicts rate of disease progression

14.10.2 Managing CKD Patients

A.) At-risk population
• recognize the disease!
• look for associated risk factors of DM, glomerular diseases, vascular diseases, tubulointerstitial diseases, cystic diseases, transplant complications, FH of severe kidney disease, cardiovascular disease
• regularly screen these populations for CKD
  • diabetics: use spot urine:creatinine test yearly
  • all others: spot urine test or dipstick, estimate GFR based on serum Cr using MDRD prediction

B.) Early CKD stages: delay or prevent progression to ESRD
• diagnosis at an early stage can add 2+ ESRD-free years to a patient’s lifespan
• first goal is to achieve BP < 130/80 □ use ACEI and ARBs
• data shows that ACEI are kidney protective
• sodium restriction if needed
• Ca channel blockers and beta blockers if needed
• smoking cessation
• lipid management
• tight control of A1C in diabetics (higher levels = greater risk of developing CKD)
• want to keep it under 7!
• avoid nephrotoxins: contrast, NSAIDs
• but low dose NSAIDs are cardioprotective and don’t cause much harm, so these are recommended for use in CKD patients
• drug-induced nephropathy: defined as an increase in serum Cr of 0.5 for pts normally < 2, or an increase of 30% for patients normally > 2 after implementation of a drug
• monitor for anemia
• if deficient, first replace folate, B12, Fe if that is the cause
• then consider adding EPO
• check GFR 1-2 times per year
• stage 3 and above every 3 months monitor PTH, phosphorus, Ca, bicarb, vit D
• concern is for bone health
• may need activated Ca supplements if kidney function is very low
• also need to be careful to not oversupplement Ca to avoid tissue calcification
• diet:
  • low protein diet may lessen progression but may not be significant, falling out of favor
    o currently moderate protein intake is recommended
    o low salt
    o good Ca intake
    o minimize phosphorus intake to avoid hyperphosphatemia
    o fluid restriction to 2 L/day
• prep patient for ESRD to improve outcomes
• recognize and manage CKD complications consult with nephrology as needed!
• should be referred to a nephrologist when GFR < 30

C.) Later stages
• refer for renal replacement therapy
• begin replacement once uremic
• screen for hyperkalemia, GFR decline, and metabolic acidosis every 2-3 months

14.10.3 Managing CKD Complications and Other Electrolyte Disturbances
A.) Anemia:
• from iron or vitamin deficiency secondary to kidney disease, failure of kidney to produce erythropoietin, or inhibition of erythropoietin due to inflammatory cytokines released by the kidney
• begins to develop once GFR drops below 30
• leads to volume overload in an attempt to compensate for decreased oxygen carrying capacity LVH
• treatment: goal Hb is 11-12, not to exceed 13 (associated with more heart events and death above this)
• first try to correct Fe, folate, B12 deficiencies if present
• Epogen or darbopoietin for Hb < 11
• monitor serum ferritin and transferrin saturation
B.) Renal osteodystrophy: a bone pathology, characterized by bone mineralization deficiency, that is a direct result of the electrolyte and endocrine derangements that accompany chronic kidney disease

- **hypocalcemia:** occurs with ↑phosphorus and vit D deficiency
  - **treatment:** goal is serum levels at 9-10 mg/dL
    - IV calcium gluconate, PO calcium carbonate
    - PO calcium carbonate, PO calcium gluconate, or PO calcium citrate
  - **time to implement a vit D supplement when Ca supplements aren’t effective in correcting serum Ca and PTH, and when active vit D level is < 30 ng/mL with PTH above target**
    - if patient has adequate inactive vit D levels but ↑PTH, need to use active vit D
      - calcitriol:
      - calcijex (IV)
      - doxercalciferol: less incidence of hypercalcemia, requires functioning liver
      - paricalcitol: less incidence of hypercalcemia
      - ergocalciferol: requires functioning kidney, use up to stage 3 or 4 OK □ D/C once PTH is at goal
- **hyperphosphatemia:** phosphate excretion decreases as GFR falls below 25
  - **other causes:**
    - massive phosphate load: ingestion, rhabdomyolysis, tumor-lysis syndrome
    - increased absorption: hypoparathyroidism, acromegaly
  - **higher phosphorus increases risk for death (may accumulate in arteries) □ treat with phosphorus restrictions and phosphorus binders if necessary**
  - **treatment:** goal phosphate is 2.5-5.5 mg/dL
    - ***should be corrected before Ca and PTH!***
    - dietary restriction
    - hemodialysis
    - if chronic □ phosphate binders with meals
      - can use certain Ca preparations as a binder: Ca carbonate, calcium acetate (best)
      - sevelamer carbonate: also decreases total cholesterol and LDL
      - only use in combination with Ca when monotherapy is not effective
      - lanthanum carbonate: chewable tablet for use when Ca alone is not effective
      - Al(OH)₃ or aluminum carbonate: used 2nd line for short-term only when phosphate is really high (toxicity issues)
    - hypocalcemia and hyperphosphatemia both stimulate the release of PTH □ secondary hyperparathyroidism □ breakdown of bone and continuation of renal osteodystrophy, increased vascular calcification, and cardiovascular disease □ also want to keep PTH at 150-300 pg/mL, and insoluble Ca phosphate ppt < 55
      - can use PTH inhibitor cinacalcet (makes parathyroid receptor more sensitive to Ca)

C.) Other electrolyte abnormalities

- **hyperkalemia:** [K+] > 5.5
  - usually K+ balance is maintained until GFR < 10
  - prevent by avoid K-sparing diuretics and cautious use of ACEIs and ARBs in later stage CKD
  - causes:
    - acidosis, which causes K+ to shift out of cells and into the ECF
  - investigation: peaked T waves on EKG
  - treatment depends on EKG findings
    - EKG changes □ concern for arrhythmias
      - IV calcium chloride or calcium gluconate to modify myocardial excitability
      - onset in 1-3 min with duration of 30-60 min
      - repeat every 30-60 minutes until EKG normalizes
      - won’t lower the hyperkalemia!
    - use a K+ binder to lower total body potassium
      - sodium polystyrene sulfonate exchanges Na+ for K+ in the colon
      - takes 2-3 hours to work
    - dialysis to remove excess potassium
    - get K+ back into cells
• glucose (or not if hyperglycemic) and insulin to increase intracellular uptake of K+
  • onset in 5-10 min with duration of 2 hours
• sodium bicarb IV over 5 minutes if acidosis is present
• albuterol to increase intracellular uptake of K+ (stimulates β-cells in pancreas to make insulin)
  • onset of 30-40 min with duration of 2-6 hours
  • may not work in 20% of people

• hypokalemia:
  • causes:
    • decreased K+ intake
    • increased entry into cells: alkaline pH, insulin, stress, β-agonists, increased RBC production, hypothermia, chloroquine toxicity
    • increased GI losses: vomiting, diarrhea, tube drainage, laxative abuse
    • increased urinary losses: diuretics, mineralocorticoid excess, loss of gastric secretions, nonreabsorbable anions, metabolic acidosis, hypomagnesemia, amphotericin B, saltwasting nephropathies, polyuria
    • increased sweat losses
    • dialysis
    • plasmapheresis
  • investigation:
    • EKG □ flattening of T waves into U waves

• hypercalcemia:
  • potential causes:
    • excess bone resorption: too much PTH, malignancy, bony mets, hyperthyroidism, vit D toxicity
    • excess Ca absorption or intake: milk alkali syndrome, vit D toxicity, sarcoidosis
    • Li or theophylline toxicity, Addison’s disease, thiazides
  • presentation: fatigue, weakness, lethargy, hyporeflexia, altered mental status
  • investigation:
    • EKG: shortened QT interval
  • treatment:
    • NS followed by loop diuretic if there is resulting volume overload
    • IV bisphosphonates to inactivate osteoclasts

• hypophosphatemia:
  • causes:
    • decreased intake: aluminum-containing antacids, sucralfate, alcoholism, starvation, malabsorption
    • intracellular uptake: alcohol withdrawal, acute asthma, respiratory alkalosis, sepsis, refeeding, recovery phase of malnutrition, hyperparathyroidism, hypomagnesemia, IV glucose infusions
    • renal losses: post-op or post-trauma, diuretics, dialysis, Fanconi’s syndrome, cystinosis, amyloidosis, myeloma, Wilson’s disease, nephrosis, cadmium toxicity, lead toxicity, hyperparathyroidism, vit D-resistant rickets

D.) Acid/base disruptions:
• acidosis occurs because ability to excrete H+ by the sick kidney is decreased
• respiratory compensation by hyperventilating □ ↓CO2
• goal is to maintain serum CO2 at 23-29 mMol (normal range for adults) and pH between 7.35-7.45
• maintaining CO2 □ maintaining HCO3- □ prevention of excess protein catabolism
• in event of symptomatic or severe acidosis (CO2 < 8 or pH < 7.2), must replace with bicarb
• calculate base deficit:
  \[ \text{base deficit} = 24 - \text{[serum bicarb]} \]
• calculate bicarb dose:
  \[ 0.5 \text{L/kg x (wt in kg) x (base deficit)} \]
• dose should be given over several days, with 12-20 mEq daily thereafter
• in event of asymptomatic /mild acidosis (CO2 12-20 or pH 7.2-7.4), give 2-3 sodium bicarb tabs daily
E.) HTN

F.) Malnutrition

G.) Volume overload
   - diuretics (if not on dialysis) to take off excess water
   - thiazides for stages 1-2
   - loop if stages 4-5 because they're better at diuresing
   - loop + thiazide if needed
   - caution in using K-sparing diuretics as these can cause hyperkalemia

H.) Cardiovascular effects
   - give baby aspirin daily unless contraindicated
   - aggressive lipid lowering? statins?
   - if not already done: beta-blockers, ACEI, smoking cessation
15 Neurology Exam Notes

15.1 Neuroanatomy Review

![Nervous System Diagram]

15.1.1 Organization of Nervous System

I. CNS: brain and spinal cord

II. PNS: spinal nerves and 11/12 cranial nerves (except for the optic nerve)

- **Sensory division**: carries sensory signals from receptors  
  - CNS = AFFERENT
  - **viscerosensory**: sensation from the organs
  - **somatosensory**: sensation from skin, muscles, bones, joints

- **Motor division**: carries signals from CNS  
  - glands, muscles, effectors = EFFERENT
  - **autonomic (visceromotor)**: innervations in motor muscles, cardiac muscles, smooth muscles, glands, GI neurons
    - neurons originate in brain or lateral horn
    - two neuron pathway
      - CNS ganglion → target cell
    - usually involuntary
    - uses Ach and norep as NTs
    - excitatory or inhibitory effects
    - primary function is to regulate blood flow to where you need it

- **sympathetic division**: automatic control for crisis reactions, fight or flight responses
  - cell bodies in the thoracolumbar region of spinal cord, sympathetic neurons exit this area to form a line of ganglia called the sympathetic trunk next to spinal cord
    - length of sympathetic trunk extends entire length of spinal cord
    - first synapse is in sympathetic trunk
  - postsynaptic neuron is adrenergic = communicates with target cell using norep (or epinephrine in the special case of the adrenal medulla)

- **parasympathetic division**: predominates with maintenance functions
  - cell bodies are in the brainstem and sacral regions
    - parasymp neurons exit from these regions
  - first synapse is in ganglia that are closer to or within target tissue
  - postsynaptic neuron is cholinergic = only uses Ach to communicate with target cell
  - dual innervation of smooth muscle by symp and parasymp = fine level of control

- **enteric division**: acts independently in the gut but can but can be modulated by sympathetics / parasympathetics

- **somatomotor**: innervations of motor muscle and skeletal muscle
  - one neuron from CNS to target with NO ganglia = long neurons
  - neurons originate in ventral horn
  - usually voluntary
  - uses only Ach as NT
  - always excitatory effect
15.1.2 Brain Anatomy & Physiology Refresher

- Supporting cells are glial cells
- Meninges: surround entire CNS including the optic nerve and spinal cord
  - layers:
    - dura mater is the thick outer layer
    - arachnoid mater is thin middle layer
    - pia mater is the delicate, highly vascularized inner layer that adheres tightly to the brain
  - isolate/pad brain from hard bones of the skull
  - CSF travels through the pia and arachnoid maters
  - innervation by CN V (trigeminal)
- Blood supply via the circle of Willis:
  - using this information + neurologic deficits will help you to locate a stroke
  - CSF nourishes neuronal tissue and removes waste
  - penetrates into the subarachnoid space surrounding the cranial nerves and spinal cord
  - produced by the choroid plexus in ventricles
- Cerebral cortex contains cell bodies and interneurons of the CNS → gray matter
  - association fibers connect the same hemisphere
  - commissural fibers connect contralateral hemispheres = corpus callosum
  - regions of fine discrimination (smallest receptor fields) take up more area in the cerebral cortex and tend to be located more laterally
    - ex. fingers, lips
    - regions can also be trained to be more sensitive
- Internal capsule makes up the main passageway for ascending and descending tracts
  - most neural traffic will pass through it
  - contains most of the fibers connecting the cerebral cortex to the thalamus, basal ganglia, and other deep structures
- Cerebellum coordinates voluntary body movement and muscle tone → smooth movements
  - influence is not directly on lower motor neurons, but indirectly via the cortex and brainstem
  - does not initiate movement, so damage does not lead to paralysis but does cause slow, clumsy, tremulous movements
  - damage → ipsilateral effect on movement
    - awkwardness with intentional movement = intention tremor
    - hypotonia, decreased DTRs, asthenia (muscle fatigue), dysmetria (inability to gauge distance, power, or speed of movement), dysdiadochokinesis (impaired ability to stop one action and start another - RAMs), speech disorders, ataxia
- Basal ganglia fine-tunes movement as it is constantly informed about most aspects of cortical function
  - damage → contralateral effect on movement
    - unexpected, meaningless, unintentional movement, tremors at rest
    - uncontrollable abnormal movements: chorea (sudden jerky, purposeless movements), athetosis (slow, writhing, snakelike movements of mostly the fingers and wrists), hemiballismus (sudden, wild flailing movement of one arm)
Thalamus is the train station and connection center for the cortex, basal ganglia, hypothalamus, and brainstem
  - integrates information and relays directional changes
  - the final point where information can be transferred, modified, or coordinated before reaching the postcentral gyrus
  - all sensory tracts synapse here before being directed to the cortex
    - exception: those involved in smell
  - Hypothalamus controls autonomic functions, regulates homeostasis, coordinates neuroendocrine functions, and integrates information with the limbic system and frontal cortex to express physical changes associated with emotion
    - anterior = parasympathetic response
    - posterior = sympathetic response
      - synthesizes ADH and oxytocin
  - Limbic system functions in drive-related emotional behavior and memory
    - acts as the bridge between the autonomic/automatic and voluntary responses to changes in the environment
  - Brainstem controls neurological functions necessary for breathing, digestion, HR, BP, awake/alertness
    - most cranial nerves originate here
    - forms the pathway for all fiber tracts traveling from peripheral nerves and spinal cord to the cerebral cortex
    - contains the reticular activating system: plays a central role in bodily and behavioral alertness
      - has ascending connections that affect the function of the cerebral cortex and descending connections that affect bodily posture and reflexes
      - route of action for many psychotropic drugs and general anesthesia
      - bilateral damage can lead to permanent coma
    - not a lot of space but a lot going on = major consequences with damage
  - Aphasia and language centers
    - Broca's is a motor and expression center
      - damage: inability to express words and great difficulty producing them
        - words come out in a telegraphic manner - most important words only!
        - can comprehend but can't respond
    - Wernicke's is a sensory and reception center
      - damage: inability to comprehend and respond in a meaningful way
        - words come out as a salad and don't pertain to the conversation
  - can have both kinds of aphasia
  - Spinal cord
    - ends at L1-L2
    - spinal nerves exit above vertebrae up to C7, then C8 exits below C7
    - Spinal nerves: all are mixed sensory-motor
      - dorsal root contains afferent sensory fibers going towards the CNS
      - ventral root contains efferent motor fibers going away from the CNS
        - remember: the motor is in front of the car!
    - several spinal nerves can reassort into plexi so that all fibers going to a specific body travel together in one plexus (T1-T12 are independent)
      - cervical plexus = C1-C4
      - brachial plexus = C5-T1
      - lumbar plexus = L1-L4
      - sacral plexus = L4-S1
      - coccygeal plexus = S5-Co - provides for efficiency, but also leads to increased risk of injury
  - Major peripheral nerves:
    - upper extremity: axillary (deltoid), musculocutaneous (biceps), radial (triceps, wrist & hand extensors), median (most of the forearm flexors & pronators), ulnar (intrinsic hand flexors and extensors)
    - lower extremity: obturator (adductors), femoral (iliopsoas and quadriceps), common fibular nerve/peroneal (tibialis anterior, fibularis), tibial (gastrocnemius, posterior tibialis)
Check functioning of PNS with the CNS via reflex testing
- Dermatome = area of skin supplied by a single spinal nerve
- considerable overlap between dermatomes
- landmarks that are regular on most people despite body habitus:
  - C4 = shoulder
  - T4 = nipple line
  - T10 = umbilicus
  - L1 = groin
- Myotome = portion of skeletal muscle innervated by a spinal cord level
- most are innervated by more than one level for protection of function
- shoulder = C5-C6
- elbow = C6-C7
- hand = C8-T1
- hip flexion = L1-L2
- knee extension = L3-L4
- knee flexion = L5-S2
- plantarflexion of the foot = S1-S2
- Spinal tracts
  - rules for ascending pathways:
    - they always synapse in the thalamus on their way to the cortex
    - exception: those involved in smell
    - they always cross
- Spinal tracts
  - rules for ascending pathways:
    - they are subject to the controls of descending neurons via interneurons
- dorsal column-medial lemniscus tract: ascending tract that carries sensory information regarding fine touch, vibration, stereognosis, conscious proprioception
  - PE: light touch, joint position sense, vibration, two-point discrimination
  - pathway:
    - first order neuron picks up information from specialized receptor
      - for fine touch = Merkel or Meissner’s
      - for vibration or pressure = Pacinian corpuscle
      - cell body of first order neuron is in DRG
    - first order neuron synapses at medulla on 2nd order neuron = damage at level of 1st order neuron will cause ipsilateral loss of sensation
    - 2nd order neuron crosses medulla and ascends to thalamus where it synapses on a 3rd order neuron = damage at level of 2nd order neuron or above will cause contralateral loss of sensation
    - 3rd order neuron ascends to the cerebral cortex
      - spinothalamic tract: ascending tract of axons through which pain and temperature information travels; includes lateral and anterior tracts
        - lateral spinothalamic tract senses pain and temperature
        - anterior spinothalamic tract senses light touch and pressure
        - no special receptors, only free neuron endings sit in periphery

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- **PE:** pinprick, temperature testing
- **pathway:**
  - 1st order neuron picks up info and synapses right away in dorsal horn onto 2nd order neuron - where "referred pain" can happen
  - 2nd order neuron crosses spinal cord and ascends to thalamus = any damage here will cause a contralateral loss below the level of the lesion synapse onto 3rd order neuron in thalamus
  - 3rd order neuron ascends to the cerebral cortex (or synapses throughout midbrain in the case of slow pain)
  - fast pain response utilizes αδ fibers that are myelinated • response in 0.15 sec
    - ex. pin prick
  - slow pain response uses C fibers • response in 1 min
    - ex. appendicitis
- **spinocerebellar tract:** an ascending tract that senses unconscious proprioception
  - connects cerebellum with the same side of the spinal cord = any damage will have ipsilateral effects
- **corticospinal tract:** a descending tract of mostly motor axons that travel between the cerebral cortex of the brain and the spinal cord
  - PE: graphesthesia, two-point discrimination testing
  - impulses originate in the precentral gyrus in large cell bodies (pyramidal cells)
  - axons pass down through the internal capsule to the midbrain and then to the medulla
  - at the medulla 80-90% of the axons cross over and descend in the lateral (dorsal) corticospinal tract, while 10-20% descend on the same side as the anterior (ventral) corticospinal tract

- **Motor neurons:**
  - **upper motor neurons:** motor neurons that originate in the motor region of the cerebral cortex or the brain stem and carry motor information down to the final common pathway = any motor neurons that are not directly responsible for stimulating the target muscle
  - disease here causes spasticity, hypertonic reflexes, and possibly a Babinski reflex, clonus
    - ex. tumors of the brain and spinal cord, strokes, multiple sclerosis, meningitis, cerebral palsy, ALS
• **lower motor neurons**: the motor neurons that connect the ventral horn to muscle fibers, bringing the nerve impulses from the upper motor neurons out to the muscles
  o disease here causes flaccidity, atrophy, fibrillations or fasciculations, and hypotonic reflexes
    ▪ ex. trauma, polio, birth injuries, muscular dystrophies, Guillain-Barre syndrome, carpal tunnel, myasthenia gravis, ALS

• **Spinal reflexes**

  - can test somatosensory and somatomotor nerves in an unconscious patient
    - anesthesia eliminates reflexes in a predictable sequence, helping to determine if a patient is sufficiently sedated
  - absence indicates damage to sensory
  - function, internuclear connections, or motor function
  - Cranial nerves
  - those originating in the:
    - forebrain: I & II
    - midbrain: III & IV
    - pons: V
    - junction of pons/medulla: VI, VII, VIII
    - medulla: IX, X, XII
    - superior spinal cord: XI
  - sensory: I, II, VIII
  - motor: III, IV, VI, XI, XII
  - mixed: V, VII, IX, X

15.2 **Approach to the Neurologic Patient and Diagnostic Methods**

15.2.1 **Neuro H&P**

  - Good history
• PMH: trauma, meningitis, congenital abnormalities, cardiovascular disorders, neurologic disorders, cancer, surgeries or anesthetic complications
• FH: known hereditary disorders, congenital cognitive deficits, seizure disorders, headaches, Alzheimer’s or other dementia, learning disorders, weakness or gait disorders, metabolic disorders, alcoholism
• SH: environmental or occupational hazards, hand/eye/foot dominance, ability to care for self and ADLs, sleeping and eating habits, sexual contacts, alcohol use, illicit drug use, caffeine intake
• ROS, allergies, and meds may reveal clues or missed information
• Good physical
• complete PE: includes general appearance, mental status, gait/coordination tests, cranial nerve exam, motor system exam, sensory testing, reflex testing, cerebral vascular exam, GI exam (autonomic function)
  o note speech: aphasia affects understanding, thought, and word-finding while dysarthria affects voice production (UMN or CN dysfunction)
  o mental status: visual spatial skills (drawing or copying), judgment, mood, memory, language
  o gait: Parkinsonian, marche a petit pas, asymmetrical, ataxic, hemiplegic, decreased arm swing, spasticity, broad-based, festination, waddle, foot-drop, dystonia, start-hesitation
  o extremities:
    ▪ generalized weakness: disease of the nerve (polyradiculopathy), neuromuscular junction (myasthenia gravis), or muscle (myopathy)
    ▪ weakness in all limbs: UMN (cervical or brainstem) or LMN (polyradiculopathy, peripheral neuropathy)
    ▪ unilateral limb weakness: hemisection of cervical cord, brainstem lesion, cerebral lesion, UMN (lesion above highest involved level), LMN (mononeuropathy if a single nerve, radiculopathy if a single nerve root)
    ▪ weakness in both legs: UMN (spinal cord lesion), LMN (cauda equina lesion)
  o reflexes:
    ▪ UMN lesion □ increased DTRs, clonus, + Babinski
    ▪ LMN lesion □ decreased DTRs
    ▪ isolated decreased reflex □ peripheral neuropathy or nerve root lesion
• screening PE: inspection, mini mental status, CN II-XII, muscle strength, RAMs, Romberg, pronator test, gait & heel-toe walking, superficial pain, touch, vibration, DTRs bilaterally
  o pronator: one arm pronates and drifts down □ ipsilateral weakness, both arms drift □ bilateral weakness, arm rise □ cerebellar disease, fingers continuously move up and down (pseudooathetosis, deficit of joint position sense)
• want to know if there is a motor deficit, sensory deficit, or both
• want to determine location: CNS or PNS?
  o CNS: unilateral weakness or sensory complaints, language dysfunction, spatial disorientation, hemivisual loss, flattening of affect or social disinhibition (frontal lobe), alteration of consciousness, memory deficits
    ▪ motor deficits:
      • if UMN is damaged above the medulla □ contralateral deficit with increased muscle tone and DTRs
      • if damage is below the medulla □ ipsilateral deficit with weakness, paralysis, decreased muscle tone, and decreased DTRs
    ▪ cerebellar damage: limb clumsiness, unsteady gait or posture, impaired intentional movement
    ▪ basal ganglia damage: involuntary movements
    ▪ brain stem damage: contralateral weakness, sensory complaints with ipsilateral weakness, sensory complaints in the face, double vision, vertigo, alterations of consciousness
    ▪ spinal cord damage: weakness, spasticity, anesthesia below a specified level, unsteadiness of gait, deficits are usually bilateral, weakness and sensory complaints in multiple contiguous radicular distributions
  o PNS: weakness, spasticity, anesthesia below a specified level, unsteadiness of gait, bilateral or asymmetric weakness, sensory complaints in multiple contiguous radicular
distributions, distal weakness, unilateral special sensory loss or facial weakness = difficult to
differentiate from spinal cord deficits
  ▪ cranial nerve deficits: vision and eye movements, movement disorders, vertigo,
    sensorineural hearing loss, anosmia

15.2.2 Confirmatory Diagnostic Studies:

1.) Lumbar puncture for CSF:
  • CSF background:
  • CSF is produced by the choroid plexus in the ventricles, circulates to bathe the spinal cord, and is
    reabsorbed back into blood vessels by the arachnoidal villi in the brain’s sagittal sinus
  • functions to enhance brain nutrition, remove metabolic byproducts, and protect against mechanical
    injury
  • 500 mL produced per day, with a total vol of 140 mL at any given time
  • less rapid but more specific than serologies
  • indications for LP:
    • diagnosis: lab analysis, determine spinal fluid pressure, administer imaging dyes
      ▪ encephalitis
      ▪ meningitis: do immediately with suspected meningitis unless contraindicated
        ▪ delayed LP □ start antibiotics immediately
      ▪ subarachnoid hemorrhage with headache
      ▪ pseudotumor cerebri with idiopathic intracranial hypertension: the only time an LP is done
        despite presence of papilledema
      ▪ MS
      ▪ normal pressure hydrocephalus and prediction of response to surgical shunting
    • therapeutic: administer drugs into CNS, remove excess CSF
    • headaches: severe, rapid-onset, recurrent, worst headache of life, or intractable
      ▪ only do LP after normal CT and normal platelet count
  • contraindications:
    ▪ due to risk of brain herniation:
      ▪ suspected brain abscess
      ▪ elevated intracranial pressure
    ▪ suspected mass lesion, ventricular obstruction, local infection at puncture site, suspicion of
      epidural abscess, thrombocytopenia or anticoagulation therapy, position-related
      cardiorespiratory compromise, acute spinal trauma or prior lumbar surgery
  • risks: headache (25%), back pain, allergic reaction, brain herniation, infection, bleeding, paralysis
    ▪ headache due to decreased CSF volume from slight leakage, can last several days
      ▪ can give an epidural blood patch (injection of autologous blood into the epidural
        space) for severe cases
  • procedure:
    ▪ may use sedative
    ▪ insert needle into L3-L4 to reach the lumbar cistern (cauda equina region)
      ▪ need to go lower in kids
    ▪ elderly may need a cisternal procedure
  • interpretation: most constituents of CSF will be present in = or lower levels than in plasma
    ▪ opening pressure
      ▪ high elevation in purulent meningitis or intracranial tumors
      ▪ moderate elevation in mild inflammation, encephalitis, neurosyphilis
    ▪ appearance and color:
      ▪ normal is clear and colorless
      ▪ cloudy with increased WBCs or protein
      ▪ yellow (xanthochromia) with ↑ bilirubin or carotene or melanoma
      ▪ red-tinged from traumatic tap or bleeding into subarachnoid space
    ▪ consistency
    ▪ tendency to clot
    ▪ cells:
      ▪ count and differential
- normally 0-5 lymphocytes or monocytes per mL
- granulocytes, macrophages, and RBCs are never normal

- **WBCs:**
  - high but under 100 = inflammation but not necessarily infection
  - greater than 100 = likely infection
  - neutrophil predominance = bacterial
  - lymphocyte predominance = viral or something else
  - eosinophils seen in shunt, parasitic infections, and allergic reactions

- **protein:**
  - elevated protein means something is wrong but is not specific for infection
  - could be tumor, trauma, inflammation
  - decreased in CSF leak, hyperthyroidism, water intoxication

- **glucose:** compare to plasma values, should be 70%
  - low glucose = bacterial or fungal

- **lactate:** increased in CVA, intracranial bleed, bacterial meningitis
  - normal in viral meningitis = how to differentiate from bacterial

2.) Nerve conduction studies
- **electromyogram (EMG):** measurement of electrical activity arising from muscle fibers; a needle is inserted into the muscle and the electrical activity is recorded during muscle rest and contraction
- used to distinguish disorders of the neuromuscular junction or muscle
- **nerve conduction study (NCS):** measurement of electrical activity arising from peripheral nerves; electrodes are placed on the skin overlying a muscle or nerve, and the area is stimulated by an electric shock
- electrical stimulation of the muscle provides a measurable response that is recorded and compared to normal values
  - used to distinguish peripheral nerve disorders (axonal vs demyelinating)
- repetitive stimulation used to diagnose neuromuscular junction disorders
  - numbers subject to change with temperature and technique skill and insight = careful judgment needed regarding utility of these tests
- there are times when the EMG/NCS absolutely proves the existence of a problem and there are times when they are useless or misleading
- consider this study to be an extension of the neuro exam when to use these studies: suspicion of peripheral nerve or muscle injury, detection of carpal tunnel, investigation of polyneuropathy, investigation of radiculopathy or muscle diseases

3.) **Evoked potential studies:** electrical studies used to study the conduction of CNS pathways; electrodes are placed on the scalp and brain potentials are recorded in response to a stimulus
- values are compared to normal values
- three kinds of tests: visual (switching checkerboard), brainstem/auditory (clicks), somatosensory (shocks)
- used more commonly in the past before development of imaging
- still useful for diagnosing MS, spinal cord diseases, optic neuritis, hearing abnormalities, balance difficulties

4.) **Electroencephalography (EEG):** electrodes are placed on a pattern on the scalp to create a graph comparing electrical potentials at 2 different points on the scalp over time
- specific patterns of electrical activity have been identified as normal or pathological patterns
- normal background is ~18 oscillations
- abnormal: sharp wave followed by slow wave = epileptiform
- not all variation is abnormal, it is all about the patterns, and interpretation is an art
  - not all spikes are epileptic
- only works during a seizure
- when to order: looking for evidence of epilepsy, trying to tell if shaking episode is true epilepsy, to determine state of consciousness, to detect absence of brain activity
- EEG won't be flat in brain death until the cerebral cortex has died, which takes several days after brainstem death
• can also be used to determine if there is an intracranial mass, as EEG tracings are muted or slow over the mass
• currently not used frequently as imaging techniques are more precise

5.) Tissue biopsy

6.) CT scan
• without contrast best for lesions

7.) MRI

8.) PET

15.2.3 Synthesis of Findings:
• what levels are affected, and how many lesions are there?
• small lesions in areas of high traffic (internal capsule, spinal cord, brainstem) cause widespread neurologic dysfunction
• small lesions elsewhere may be asymptomatic
• can the findings be grouped together to form a known syndrome?
• which is the etiology: genetic, congenital, infectious, inflammatory, neoplastic, degenerative, metabolic, endocrine, or vascular?
• temporal clues: degenerative diseases progress gradually while vascular diseases progress rapidly

15.3 Neurogenetics

15.3.1 Background
• Most diseases probably result from a combination of one or more genes interacting with environmental factors vs monogenetic inheritance (where a single defective gene causes disease)
• Expressivity: variation in degree of expression of the phenotype
• Penetrance: percent of individuals with the mutation who will show any clinical manifestation
• Non-allelic genetic heterogeneity: a clinical syndrome caused by more than one gene
• Allelic heterogeneity: when one gene causes > 1 clinical syndrome
• Lyonization: a normal biological process in females (or Klinefelter’s) where one X chromosome is inactivated in every cell
• Trinucleotide repeat expansion/anticipation: a biological phenomenon in neurologic disorders where disease severity increases in subsequent generations with expansion of trinucleotide repeats
• associated with multiple modes of inheritance
• includes fragile X syndrome, Huntington’s, myotonic dystrophy, Kennedy’s disease, spinocerebellar ataxias, Friedrich’s ataxia

15.3.2 Autosomal Dominant Disorders
• Characteristics:
  • multiple affected generations
  • males and females equally affected
  • parents of affected child have a 50% risk that subsequent child will be affected
  • male to male transmission is seen
  • variable expressivity
  • in neurology, generally involves late onset degenerative diseases

A.) Neurocutaneous disorders
• tuberous sclerosis:
• neurofibromatosis: a genetically-inherited disorder in which the nerve tissue grows tumors that may be benign or may cause serious damage by compressing nerves and other tissues
• NF 1 is autosomal dominant with 100% penetrance but variable expressivity
- half the mutation is inherited and the other half is caused by a de novo NF1 mutation in the neurofibromin gene inactivation of Ras
- diagnostic criteria (must have 2/7): 6+ café au lait macules, freckling in the axillary or inguinal region, 2+ neurofibromas of any type or one plexiform neurofibroma, 2+ Lisch nodules in the iris, optic glioma, distinctive osseous lesion such as sphenoid dysplasia or pseudoarthrosis, 1st degree relative with NF1
- other presentations: astrocytoma, vestibular schwannoma, ependymoma, meningioma, congenital hydrocephalus, seizures, learning disabilities, glaucoma, pheochromocytoma, renal artery stenosis, GH deficiency, short stature, scoliosis, precocious puberty, cutaneous neurofibromas
- management:
  - kids: regular physical exams, track development, correct skeletal abnormalities, annual eye exams, MRIs for suspected lesions
  - adults: regular physical exams, regular BP screening to catch renal artery stenosis, MRIs for suspected lesions
  - prognosis: main cause of death is malignant nerve sheath tumor

- NF2 is also autosomal dominant and is a result of mutation of the schwannomin gene
- diagnostic criteria: bilateral vestibular schwannomas (may exhibit facial nerve issues as this also runs through the external auditory meatus); FH of NF2 + unilateral vestibular schwannoma; two of the following: meningioma, glioma, neurofibroma, schwannoma, posterior subscapular lenticular opacities (looks like a cataract)
- management: many teams, VEGF inhibitors
- prognosis: depends on age of symptom onset, degree of hearing deficit, and number and location of tumors
  - now usually greater than 15 years
- Von Hippel-Lindau:
  B.) Myotonic dystrophy:
  C.) Huntington’s disease: see movement disorders lecture
  D.) Hereditary spinocerebellar ataxias
  E.) Hereditary neuropathies
  F.) Dementias
    - Alzheimer’s disease: the most common form of dementia that causes problems with the temporal and parietal lobes
      - results in decreased parenchymal volume, hippocampal atrophy, neurofibrillary tangles with tau, neuritic plaques with amyloid deposition, granulovacular degeneration, Hirano bodies
      - all cases are autosomal dominant and involve abnormal cleavage of amyloid precursor protein
      - risk factors: age, FH, Down’s syndrome, apolipoprotein E4 genotype (E2 is protective)
        - but < 10% of cases are familial, with familial Alzheimer’s associated with an earlier onset of presentation
      - presentation: memory impairment, language deficits, acalculia (difficulty performing simple mathematical tasks), depression, agitation, apraxia (inability to perform skilled movements)
      - investigation: diagnosis is by exclusion
        - genetic testing is to provide information only, less sensitive than clinical dx
        - MRI or CT will show hippocampal atrophy
        - PET to detect amyloid
        - lumbar puncture to detect increased hyperphosphorylated tau
      - treatment:
        - cholinesterase inhibitors: tacrine, donepezil, rivastigmine, galantamine
        - NMDA receptor antagonist: memantine
      - prognosis: death usually occurs within 5-10 years secondary to aspiration pneumonia or infection
      - frontotemporal dementia: degenerative illness of the frontal and temporal lobes as a result of accumulation of tau in neurons
        - genetic subtypes: frontotemporal dementia with Parkinsonism
presentation:
- usually begins around ages 55-65 and runs a shorter course than Alzheimer’s
ggradual onset of confusion with personal neglect, apathy, aphasias, personality
changes, abulia (lack of will or initiative), frontal release signs, echolalia

15.3.3 Autosomal Recessive Disorders

- Characteristics:
  - greater than 1 family member affected within a single generation
  - males and females equally affected
  - history of consanguinity
  - parents of affected child have a 25% risk that future child will be affected
  - carriers are usually asymptomatic
  - in neurology, usually seen in childhood inborn errors of metabolism
  - Inborn errors of metabolism
  - phenylketonuria:
    - Tay-Sachs disease: lysosomal enzyme deficiency □ ganglioside accumulation in brain
  - more common in certain populations: Ashkenazi Jews, French Canadians of Quebec, southern
Louisiana Cajuns
  - presentation:
    - begins around 6 months
    - deterioration of mental and physical abilities: deafness, blindness, dysphagia, paralysis
    - cherry-red spot from degeneration of the fovea
  - investigation: blood test for hexosaminidase A activity
  - prognosis: death by age 4

15.3.4 Maple syrup urine disease

B.) Friedrich’s ataxia: see peripheral neuropathies lecture

C.) Wilson’s disease: see movement disorders lecture

D.) Homocystinuria:

E.) Sickle cell disease □ X-Linked Recessive Disorders

- Characteristics:
  - female-to-male transmission of disease
  - males tend to have more severe disease
  - females tend to be carriers or have a mild, late-onset phenotype
  - affected males will have carrier daughters
  - carrier females have a 50% chance that sons will have the disease and a 50% chance that
daughters will be carriers

A.) Duchenne/Becker’s muscular dystrophy: see muscular dystrophy lecture

B.) Adrenoleukodystrophy:

C.) Kennedy’s disease: spinal bulbar muscular atrophy

D.) Menkes disease:

E.) Lesch-Nyhan disease:

F.) Fragile X syndrome: the most common inherited form of mental retardation

15.3.5 X-Linked Dominant Disorders

- Characteristics:
  - multiple generations affected
  - female-to-male disease transmission
usually lethal in males

A.) **Rett’s syndrome**: mutation in MeCP2 gene □ progressive neurodevelopmental disease
- only in females (or males with Klinefelter’s)
- presentation:
  - normal until 6-18 months of age, then decreased head growth, autistic behavior, writhing hands, ataxia, loss of speech, seizures
  - later cardiac issues, scoliosis
- investigation: clinical and genetic testing
- prognosis: patients may live into their 40s

B.) Aicardi syndrome:

C.) Lissencephaly 2: smooth brain with no sulci or gyri □ severe mental retardation, seizure syndromes

15.3.6 **Mitochondrial Inheritance Disorders**
- Characteristics:
  - affects multiple generations but transmission is by females only due to cytoplasmic inheritance (only ovum contributes cytoplasm in the zygote)
  - equal numbers of males and females affected
  - variable expressivity and severity
  - affected males won’t transmit it to future offspring, but all affected females at risk of transmission to future offspring

A.) Monoclonic epilepsy with ragged-red fibers syndrome:

B.) Mitochondrial encephalopathy, lactic acidosis, and stroke (MELAS): point mutation in tRNA for leucine
- presentation:
  - onset before age 40
  - recurrent headaches, stroke-like episodes, seizures, short stature, progressive dementia
- diagnosis: elevations in serum pyruvate and lactate, stroke lesions that don’t conform to normal vascular distributions
- treatment: no proven therapy, but can give mitochondrial cocktails with antioxidants and coenzyme Q10

C.) Leber’s hereditary optic neuropathy (LHON):

D.) Kearns-Sayre syndrome: bad ophthalmoplegia

15.3.7 **Genetic Testing**
- Should only be done on well-informed, consenting ADULTS
- May be done for diagnosis, prediction, risk assessment, or pharmacogenetic purposes

15.4 **Movement Disorders**

15.4.1 **Background and Abnormal Movements**
Movement disorders commonly occur as a result of lesions in the basal ganglia or cerebellum and their connections.

Acetylcholine and dopamine act in opposing directions.

- Adding dopamine is equivalent to blocking Ach.

Abnormal movements:

- tremors:
  - contraction (action) tremor: occurs when trying to maintain a fixed position; the most common kind of tremor
    - physiologic tremor: seen with fatigue, anxiety, hypoglycemia, hyperthyroidism, drug withdrawal, caffeine use, and in normal people with movements requiring a high degree of precision or power
    - essential tremor: a slower frequency physiologic tremor with varying mechanisms that is common later in life
      - can involve the extremities, head, and voice
      - called familial tremor if there is a FH
      - treatment: first line is a β-blocker, primidone, benzos for anxiety, alcohol
  - intention (ataxic) tremor: absent at rest and at the start of a movement but increases when fine adjustments are required
    - impaired finger-to-nose coordination
    - caused by disease of the cerebellum or its connections, including MS
    - treatment: meds are usually ineffective but surgery is last resort

- athetosis and chorea
  - athetosis can be seen in cerebral palsy or as a result of kernicterus (elevated bilirubin at birth) or hypoxia
  - chorea can be the result of untreated strep infection (Sydenham’s chorea), pregnancy (chorea gravidum), or Huntington’s
    - can be cause by a state of dopamine excess

- tics: quick, coordinated, repetitive movements
  - can occur alone or with other syndromes
    - Tourette’s syndrome: the onset of tics from ages 2-13 as well as involuntary whistles, grunts, and coughs
      - may exhibit echolalia or coprolalia (uncontrolled use of offensive language)
    - treatment: haloperidol or pimozide, but limited by side effects

- hemiballismus
  - if unilateral, usually the result of a contralateral subthalamic nucleus of Luys infarct

- myoclonus: shock-like contraction of a group of muscles (or generalized) that is irregular in rhythm and amplitude
  - from anoxic damage, spinal cord injury, uremia, hepatic encephalopathy, or rare neurologic disorder
  - treatment: clonazepam, valproate (limited efficacy)

- dystonia: maintenance of a persistent extreme posture in one or more joints
  - generalized dystonia (dystonia musculorum deformans): a rare hereditary dystonia most commonly affecting Jewish families
  - focalized dystonias: includes torticollis, writer’s cramp, and blepharospasm
15.4.2 Parkinson’s Disease

- a degenerative disorder of the central nervous system as a result of the death of dopamine-generating cells in the substantia nigra in the midbrain and accumulation of Lewy bodies in neurons
- Degeneration of connection between substantia nigra and the striatum, as well degeneration of the raphe nuclei, locus ceruleus, and the motor nucleus of the vagus nerve
- results in decreased dopamine and increased Ach
- Most cases are idiopathic
  - monogenic forms only represent 5% of cases
    - may be autosomal dominant or autosomal recessive
      - dominant forms involve the PARK1, 4, and 8 genes
        - PARK1 and PARK4 involve the α-synuclein gene (α-synuclein is the main component of Lewy bodies)
          - rare but involve early onset disease with dementia and rapid progression
        - PARK8 is the most common genetic form of Parkinson’s, and is associated with late-onset disease with psychiatric features
          - recessive forms involve the PARK2, 6, 7, and 9 genes
    - risk factors: age, exposure to MPTP (byproduct of synthetic heroin), manganese exposure, flu epidemic
      - caffeine and nicotine may be protective
- Presentation:
  - usually begins after age 65
  - most cases have unilateral symptoms: resting tremor (pill-rolling), bradykinesia, stiffness, fatigue, stooped posture, cogwheel rigidity, shuffling steps, festinating gait (unwanted acceleration of gait once commenced), masked facies, memory loss, micrographia, postural instability, difficulty initiating movements, disturbance of postural reflexes (can’t adjust upon being pulled upright)
    - if bilateral, it is more likely that the disease is a result of pharmacologic exposure
- Investigation:
  - genetic testing is available but should be performed only after careful consideration due to inconclusive testing results and lack of specific treatment for the disease
- Treatment:
  - meds:
    - levodopa: dopamine precursor that can cross the blood-brain barrier to replace the dopamine deficit
      - problem: levodopa will be converted in the periphery to dopamine, so you must also give carbidopa to prevent this and allow for more availability of levodopa in the CNS
        - can’t cross the BBB
        - also helps to minimize nausea and vomiting
      - can be administered to help diagnose Parkinson’s
      - treatment should begin when patient experiences functional impairment
      - first-line therapy in older patients (> 65) as its efficacy decreases over time
      - 80% of patients significant improve on it
      - won’t improve postural instability, dementia, autonomic dysfunction, or "freezing", or prevent progression of the disease
      - side effects: nausea, vomiting, anorexia, postural hypotension, cardiac arrhythmias, mental disturbances, dyskinesias (increase with duration of treatment), overactivity, restlessness, agitation, hypomania
      - drug interactions: nonselective MAOIs, antipsychotics, iron salts, metoclopramide, phenytoin
      - contraindications: narrow angle glaucoma, melanoma, undiagnosed skin lesions
- **dopamine agonists**: act directly on dopamine receptors in the corpus striatum
  - first-line therapy for younger patients with milder disease
  - may delay need for levodopa
  - can be used as additional therapy for patients already on max dose levodopa
  - two generations:
    - 1st gen derived from ergot alkaloids
      - bromocriptine:
    - 2nd gen
      - pramipexole:
      - ropinirole:
      - apomorphine: rescue therapy for “off” episodes
        - must monitor BP with test dose
      - rotigotine: currently being reformulated for the US
  - side effects: retroperitoneal, pleural, pericardial, cardiac valve fibrosis, dizziness, headache, insomnia, somnolence, confusion, hallucinations, GI, orthostatic hypotension, syncope, dyskinesias
  - because dopamine is involved in the reward center of the brain, people on these may start showing impulsive behaviors such as gambling and hypersexuality
  - drug interactions: lots, including serotonin modulators, can increase risk of serotonin syndrome
- **COMT inhibitors**: prevent breakdown of levodopa by another pathway and increased levodopa avail to cross BBB
  - allows for decreased levodopa use (which will help decrease side effects)
  - types:
    - entacapone:
    - tolcapone: watch for liver failure
  - side effects: dyskinesias, nausea, dizziness, hallucinations, urine discoloration, abdominal pain, diarrhea, orthostasis, somnolence, headache
  - drug interactions: nonselective MAOIs, ethanol
- **MAO-B inhibitors**: inhibit metabolism of dopamine
  - can help delay need for levodopa
  - types:
    - selegiline: acts centrally to prevent destruction of dopamine
    - rasagiline: can cause headache, dizziness, nausea, dyskinesias
  - side effects: insomnia, nausea
  - drug interactions: lots including SSRIs- risk of serotonin syndrome
- **amantadine**: antiviral agent that increases dopamine release from the nerve terminals
  - can help reduce dyskinesias with levodopa use
  - side effects: tachyphylaxis develops within 3 months, may need to d/c and re-initiate later, insomnia, cognitive, convulsions, ankle edema, orthostasis, livedo reticularis
- **anticholinergics**: block Ach
  - no longer considered 1st line
  - may be more effective for treatment of resting tremor in younger patients
- **other treatments**:
  - vitamin E supplementation not shown to be beneficial
  - coenzyme Q10 not shown to be beneficial
  - creatine and minocycline still being studied

15.4.3 Huntington’s Disease

- abnormal CAG repeats on chromosome 4
- loss of caudate and squared-off lateral ventricles
- Presentation:
  - onset by ages 20-40, which is affected by anticipation
• symptoms often begin with a psychiatric disorder
• subcortical dementia, chorea, dystonia, motor impersistence, incoordination, gait instability, depression, anxiety, impulsivity, apathy, OCD, athetosis
• Investigation: diagnosis is clinical, but CT or MRI will show cerebral atrophy and loss of caudate
• Treatment: no cure, but symptomatic control and genetic counseling are important
  • chorea is like a dopamine-excess state: give dopamine-R blockers such as haloperidol or risperidone or dopamine reserve depleters such as reserpine
    o but may cause depression
• SSRIs for depression and anxiety
• tetrabenazine decreases monoamine uptake into synaptic vesicles and depletes monoamine stores
• Prognosis: death within 10-15 years of onset of symptoms

15.4.4 Wilson’s disease
• impairment of ceruloplasmin synthesis due to hepatolenticular degeneration: copper accumulation in tissues and basal ganglia: neurological or psychiatric symptoms and liver disease
• Presentation:
  • usually in teenage years
  • first sign is hepatitis which leads to cirrhosis
  • neuro: tremor, slowness, dysarthria, dysphagia, hoarseness, chorea/dystonia, psychiatric disturbances, “wing-beating” tremor with arms held out
  • progressive disease: limb rigidity, fixed empty smile
• Investigation:
  • labs: low serum ceruloplasmin, low serum copper, high copper on liver biopsy, Kayser-Fleischer rings (brown ring around cornea)
• Treatment:
  • reduce copper intake: avoid chocolate, mushrooms, shellfish, nuts, and take sulfured potash with meals to prevent copper absorption
  • chelating agents: beware, may cause rebound freeing of copper reservoirs
  • may need liver transplant
  • early treatment prevents neurologic sequelae

15.4.5 Tardive Dyskinesia
• abnormal buccal-lingual, head, and sometimes limb movements from long-term treatment with neuroleptics
• May be the result of dopamine-R supersensitivity
• Treatment: stop offending drug, use dopamine-depleting agents or vitamin E
• Prognosis: symptoms can fluctuate and may take months to years to resolve, can be permanent

15.5 CNS Infections

15.5.1 Meningitis
• inflammation of the meninges that is typically acute, evolving over hours to days
• General presentation:
  • fever, headache, neck stiffness, lethargy
  • usually without any focal neuro signs
A.) **Purulent meningitis**: the typical meningitis, a medical emergency
- **typical organisms**: Neisseria meningitidis, Strep pneumo, H. flu
- **presentation**:
  - meningococcal: petechial rash is common, also associated with DIC
  - TB: gradual onset with listlessness and irritability, CN palsies, abnormal CXR
- **investigation**: lumbar puncture → increased WBCs with left shift, low glucose, high protein, markedly elevated opening pressure
- **treatment**:
  - get blood cultures then start on empiric antibiotic coverage: ceftriaxone
  - meningococcal → Pen G or ceftriaxone
    - nasal carriers: rifampin
    - contacts may need prophylaxis
  - pneumococcal → add vanco
  - consider H. flu if developed in the setting of otitis or sinusitis → ceftriaxone
  - TB → standard pulm TB treatments will work
- special consideration: patients with purulent meningitis who have received antibiotics for something else may have a milder clinical course and less severe CSF abnormalities (resembling aseptic meningitis) = always consider this possibility in a meningitis patient who has recently received antibiotics

B.) **Chronic meningitis**: usually not due to typical organisms, but fungi or TB
- **investigation**: lumbar puncture → mildly elevated WBCs that are mostly lymphocytes, low glucose, high protein, mildly-moderately elevated opening pressure

C.) **Aseptic meningitis**: any acute meningitic syndrome not caused by acute bacterial infection, usually viral
- **presentation** may initially look just like purulent meningitis
- **investigation**: differentiate from purulent meningitis by lumbar puncture → more lymphocytes than PMNs, glucose not as low, total WBCs not as high, opening pressure not as high
- **treatment**: empiric antibiotics until cultures are negative

15.5.2 **Encephalitis**
- generalized or diffuse inflammation or infection of the brain tissue itself
- Usually caused by a virus (herpes or arboviruses)
- arbovirus encephalitis is spread by insects, so it is more common in the spring and early summer
- herpes encephalitis is more common in the elderly
- **General presentation**:
  - usually with fever, headache, lethargy, confusion, seizures, sometimes coma
  - usually without any focal neuro signs
  - herpes encephalitis often involves the medial temporal lobes and may be confused for stroke!
- **Investigation**: assays generally not done as they are not widely available and don’t change the course of treatment
- **Treatment**: IV antiherpetics are given empirically for nearly all patients with clinical syndrome suggesting viral encephalitis

15.5.3 **Brain Abscess**
- a localized infection in the brain which typically presents with focal signs due to abscess compressing brain tissue and mass effect
- **Common organisms**: Strep, Staph, anaerobes
- Initially begins as a focal area of inflammation = cerebritis
- Progresses to form a pocket of pus with surrounding capsule
- **Presentation**: may have fever, chills, or other signs of infection, focal deficits with increased ICP, may have concomitant sinusitis or history of surgical procedure to the area
- **Investigation**:
  - CT showing ring-enhancing lesions with surrounding edema
- **Treatment**:
  - surgical drainage
• prolonged IV antibiotics with serial scan monitoring

15.5.4 Other Conditions

A.) Meningitis-like inflammatory conditions such as sarcoidosis, carcinoma, lupus, and chemicals or drugs can cause meningeal injury
• tend to be more subacute but can cause CSF abnormalities

B.) Rabies: rhabdoviral infection transmitted in infected animal saliva via bite
• most common carriers are bats, skunks, foxes, and raccoons
• infected dogs are unlikely as they usually die within 5-7 days
• incubation period is usually 3-7 weeks as the virus travels up the nerves into the CNS
• presentation:
  • prodrome of pain at the bite site, fever, malaise, nausea and vomiting
  • later delirium, painful swallowing, rage alternating with calm, or acute ascending paralysis
  • progression to coma, autonomic dysfunction, and death
• treatment:
  • keep biting animal in isolation for 7-10 days of observation
  • post-exposure immunization with rabies Ig administered around the wound and IM

C.) Prion diseases
• slow replication and long latency
  • Creutzfeld-Jakob disease: prion disease transmitted through infected tissue or genetically inherited
    • cases can be sporadic or in a familial autosomal dominant pattern
    • presentation: rapidly progressive dementia, myoclonus, ataxia, and somnolence
    • investigation: may have epileptiform EEG

15.6 Multiple Sclerosis

15.6.1 Background
• Pathophysiology: infectious agents, genetic predisposition, and environmental factors may all play a role in causing an abnormal immunologic response that leads to MS
• Course: inflammation □ demyelination □ axonal loss
• there will be a period of time with no clinical features prior to first attack
• can’t diagnose MS from just one attack, need to have at least 2
• demyelination continues to occur during the clinically silent periods between relapses
• as disease progresses, MRI lesion burden and disability increase as cognitive function decreases
• Forms:
  • relapsing-remitting: partial recovery from disability between relapses
    • accounts for 55% of cases
    • all meds are for this form of MS!
    • may convert to a progressive form
  • secondary progressive: increasing disability with distinct relapses
    • accounts for 30% of cases
  • primary progressive: nearly continuous worsening of disability
    • accounts for 10% of cases
• Average age of onset is 20-40 years
• More prevalent in women and in individuals living further from the equator
  • prior to puberty, you will inherit the incidence of the place you move to
  • if moving after puberty, your risk will remain the same as where you grew up
• Common manifestations: optic neuritis (retro-orbital with patchy loss of vision), transverse myelitis (one level of the spinal cord vs all the way down), paresthesias, ataxia, weakness, incoordination, spasticity (LMN lesions), cognitive impairment
• Investigation:
• diagnostic criteria: none are very good, really all they say is you must look for other explanations, and that there needs to be occurrence in > 1 area of the brain > 1 time = only used for defining cohorts for research purposes
• history of episodes that come and go - must be separated in space and time!
• MRI of brain and spinal cord showing multiple characteristic lesions or plaques (periventricular or subcortical U-fibers, corpus callosum lesions)
  o T1 weighted imaging makes use of gadolinium contrast that can penetrate the blood-brain barrier to enhance areas of inflammation (active lesions)
    ▪ “black holes” seen on this kind of imaging represent areas of serious brain injury such as axonal loss
  o T2 weighted imaging does not use contrast and shows various lesions to represent the cumulative disease burden
    ***remember that may healthy individuals have incidental white spots, so these spots need to be in the characteristic places for MS, such as the cervical spinal cord and ventricles
• CSF: evidence of oligoclonal bands or increased IgG index
• evoked potentials may be helpful

Treatment:
• may be most effective early in disease to prevent brain atrophy
• goals are to treat the whole disease, slow down disability, reduce relapse rate, reduce CNS inflammation, reduce brain atrophy, and improve patient’s quality of life
• meds:
  o immunomodulators: IFN, glatiramer acetate injections
    ▪ problem is they don’t make you feel better and sometimes make you feel worse (flu-like symptoms), although they will make you better long-term
  o immunosuppressants: azathioprine, methotrexate, cladribine, fingolimod, mitoxantrone, cyclophosphamide, IV IgG, mycophenolate mofetil, natalizumab (must test for JC virus before giving or risk causing a demyelinating process worse than original MS!)
    o large-dose corticosteroids for relapses or aggressive disease
• vitamin D supplementation (association between low vit D and MS attacks)

Prognosis:
• if untreated, brain atrophy will occur and half of all MS patients will need an assistive device to walk within 5 years, relapsing MS will give way to progressive MS within 10 years, and most patients will experience cognitive impairment
• early intervention at time of diagnosis associated with better outcomes

15.7 CNS Neoplasms

15.7.1 Primary Brain Tumors

• Originate in the CNS
  • ex. non-Hodgkin lymphoma confined to the CNS
  • 100+ types, arising from different cells of the CNS
• focus today is on malignant neoplasms, but even histologically benign tumors can cause mass effect
• Incidence is rising (may be due to increased detection or environmental factors)
  • associated with level of economic development of a population
  • higher incidence in Caucasians, uncommon in Asians and Native Americans
  • slightly more common in males
  • risk increases with age and peaks at age 50
• Risk factors: healthcare and lab research worker, electrical worker, oil refinery worker, agricultural worker, exposure to ionization radiation (including atomic bomb survivors), history of head trauma, exposure to N-nitroso compounds (diet or tobacco), genetic predisposition
  • potential risk factors: viral infections, *Toxoplasma* infection, alcohol, tobacco, radiofrequency and EMF radiation exposure (microwaves, radar)
  • cell phone use for > 10 years doubles chance of getting a glioblastoma or acoustic neuroma
• Presentation: aphasia, sensory loss, focal weakness, may cause obstructive hydrocephalus
• Headaches are usually secondary to increased ICP, with progressive increase in frequency and severity.
  o Classically occur as a headache upon waking or a headache that wakes pt up.
  o Occur in 20% of brain tumor patients.
• High grade tumors tend to present more as headaches due to mass effect, while low grade tumors tend to present more as seizures because they irritate synapse sites.
• Seizures are often what precede the diagnosis.
  o Occur in 35% of brain tumor patients.
• Cognitive dysfunction is probably the most common problem in patients with brain tumors:
  o Frontal personality: impulsiveness, hypersexuality, irritability, etc.
  o Memory problems, especially short-term.
  o Depression from altered brain chemistry.
  o Language dysfunction in left hemispheric tumors.
  o Problems with visual perception and scanning in right hemispheric tumors.
  o Focal neuro deficits: hemiplegia, hemiparesis, ataxia, nystagmus, CN palsies = can mimic a stroke!
• Nausea and vomiting secondary to increased ICP.
  o Higher incidence with posterior fossa tumors.
• Symptomatic endocrine dysfunction from effects on hypothalamus: hypothyroidism, decreased libido.
• Visual disturbances from pressing on optic nerve: contralateral flashing lights, visual field loss, diplopia.
  o Transitory episodes of altered consciousness and visual disturbances known as plateau waves.
• Investigation:
  o Full neuro PE: CN, DTRs, strength.
  o CT +/- MRI.
  o Work up for metastatic disease of suspected: chest or abdomen CT, breast mammogram.
  o EEG if there are seizures.
  o Serial LPs: the old school way of detecting tumors.
  o PET: Help distinguish active lesions from old/dead lesions.
  o Biopsy: Primary tumors are classified by their predominant cell type and are graded low or high by presence or absence of standard pathologic features.
• Treatment:
  o Surgery +/- radiation +/- chemo.
  o Quality of life issues.
  o Anti-epileptics only needed for patients with seizures at time of diagnosis.
    o Be aware of side effects and metabolism interactions with chemotherapeutics.
    o Increased seizures aren’t always a sign of tumor progression.
  o Steroids are a mainstay of treatment of symptoms.
    o Consider prophylaxis after 2 months due to risk of PCP.
    o Need to prophylax against thromboembolic events (increased risk in cancer and treatment): LMWH, heparin, warfarin, IVC filters.
• Cognitive dysfunction secondary to tumor and treatment.
  o Need neuropsych eval.
  o Drugs avail for memory deficits and attention deficits.
• Poor prognosis with an average 5 year survival rate of 33%.
• Survival has not improved significantly over the last 50 years.

15.7.2 Secondary Brain Tumors
• Originate as solid tumors in other parts of the body that then metastasize to the brain.
• Frequently carcinomas from the breast, lung, and colon, and melanoma.
• More common than primary brain tumors.

Gliomas
• Arise from support cells of the CNS, including astrocytes and oligodendrocytes.
• Most primary brain tumors are this kind.
• Most are malignant.
• Grade 1:
  • pilocytic astrocytomas: usually found in kids, tend to occur in cerebellum or 3rd ventricle, rarely invasive
    o treatment of choice is surgery
    o prognosis: 10-year survival rate is 80%
  • pleomorphic xanthoastrocytoma:
    o treatment: surgery +/- radiation

• Grade 2: diffuse or well-differentiated astrocytomas or oligodendroglomas
  • well-differentiated astrocytoma: occurs around age 35, usually located in cerebral hemispheres or cerebral cortex, slow-growing
    o prognosis: avg survival is 7 years because malignant transformation to aplastic astrocytoma or glioblastoma is common
  • well-differentiated oligodendrogloma: occurs in young to middle-aged adults
    o investigation: histology shows characteristic “fried egg” cells
    o prognosis: survival is ~10 years
    o treatment: surgery, observation, chemo if progression or intractable seizures

• Grade 3: considered high-grade due to ability to invade normal brain via white matter tracts, with spread to contralateral brain via corpus callosum
  • anaplastic astrocytoma: occurs around age 45, most commonly located in cerebral white matter, fast-growing
    o prognosis: average survival is about 3 years with high incidence of progression to glioblastoma
  • oligodendrogloma: occurs around age 40-60, chemosensitive but almost universally fatal
    o treatment: surgery, radiation with temozolomide, consider clinical trials

• Grade 4: glioblastoma or gliosarcoma
  • characterized by necrosis with vascular proliferation
  • glioblastoma: accounts for half of all astrocytomas and is the most common primary brain neoplasm, usually arises after age 60, usually located in cerebral white matter
    o spreads rapidly, will double in size in 14 days if left untreated
    o investigation: appears on CT as a ring of tissue around a necrotic core
    o prognosis: survival with appropriate treatment is 1 year
  • treatment: surgery, radiation with temozolomide, 1 year chemo +/- bevacizumab, consider clinical trials

• Glioma treatment:
  • if low grade:
    o if no symptoms other than well-controlled seizures, defer treatment until disease progression with progressive symptoms
    o resection +/- chemo
      ▪ radiation only in refractory cases
  • if high grade surgical resection, radiation therapy, chemo
    o goals of surgery: confirm pathological diagnosis, rapid improvement of symptoms, reduce # of cancer cells requiring treatment (especially the core that is relatively resistant to radiation and chemo)
    o can surgically implant chemo wafer (Gliadel- 2 month survival benefit), use radiolabeled antibodies, or use intratumoral gene therapy
    o radiation: focal or conventional high-dose (intensity-modulated or stereotactic)
      ▪ side effects:
        • acute encephalopathy in first few days: give steroids
        • early delayed encephalopathy in weeks to months: steroids
        • focal cerebral necrosis in months to years
          o hard to distinguish from tumor recurrence
          o steroids, hyperbaric oxygen therapy
        o chemo limited by blood-brain barrier
          ▪ dexamethasone use may close tumor-brain barrier to chemo
          ▪ consider interactions with anti-epileptics pt may be on
          ▪ temozolomide shown to improve survival in studies
          ▪ VEGF antibodies may be useful (bevacizumab) to inhibit tumor angiogenesis
new therapies: vaccines, inhibitors of resistance, growth factor inhibitors, anti-angiogenesis therapies
ideal future therapies: targeted to high percentage of gliomas, activated in tumor, something that is important to the tumorigenic process, ability to penetrate blood-brain barrier, P450 metab
Overall prognosis: most important factors are extent of surgical resection, age, and performance status
skill of neurosurgeon may be most important treatment decision
better outcome with gross total resection

15.7.3 Other Cranial Neoplasms
A.) Ependymomas: arise from cells lining the ventricles or spinal canal, with most tumors being in the brain
- slow growing
- affects children and young adults
- prognosis: significantly worse if under age 3
B.) Meningiomas: slow-growing tumors arising from the meninges that are attached to the dura mater
- benign?
- account for 1/3 of primary brain tumors
- prior radiation is a risk factor
- presentation: often asymptomatic, visual complications if affected optic nerve tract
- investigation: consider neurofibromatosis
- treatment: surgery is mainstay of therapy
C.) Nerve sheath tumors: arise from Schwann cells, which are the glial cells of the PNS
- ex. vestibular schwannoma
D.) CNS lymphomas: affect lymphoid tissue confined to the CNS and eyes, usually are multifocal and very deep in the brain parenchyma
- majority are non-Hodgkin
- risk factors: immunodeficiency, AIDS, organ transplant, older adults
- treatment: steroids, methotrexate-based chemo regimens
- prognosis: survival without treatment is less than 1 year, with treatment is about 4 years

15.8 Motor Neuron Diseases, Disorders of Neuromuscular Transmission, and Muscular Dystrophy

15.8.1 Motor Neuron Diseases
- Background
- presentation of UMN disease: loss of dexterity, increased muscle tone, spasticity, hyper DTRs, + Babinski, spastic dysarthria, pseudobulbar affect (pathological over-response to emotional situations)
- presentation of LMN disease: weakness, decreased muscle tone, muscle atrophy, fasciculations, reduced or absent DTRs

15.8.2 Amyotrophic Lateral Sclerosis
- aka Lou Gehrig's disease; caused by the degeneration of upper and lower neurons located in the ventral horn of the spinal cord and the cortical neurons that provide their efferent input
- Highest incidence in ages 65-74, with average age of onset 56-63
  - rarely occurs before age 20
- Slightly more common in males
  - 10% of cases are familial, with some of them due to the SOD1 mutation
- autosomal dominant inheritance
- Presentation
  - focal, painless limb weakness that spreads to contiguous areas over several months
- distal to proximal spread: foot drop, hand weakness, head drop
- some start with corticobulbar weakness (this tract contains UMN of cranial nerves): slurred speech, difficulty swallowing or choking
- cramps
- fasciculations
- cognitive changes such as frontotemporal dementia
- no sensory symptoms or problems with coordination (cerebellum), this is purely a motor disease!
- PE:
  - UMN signs: hyperactive reflexes, abnormal reflexes such as Babinski, decreased RAMs, increased tone/spasticity, pseudobulbar affect
  - LMN signs: weakness, fasciculations, muscle atrophy
- Investigation:
  - differential: cervical myelopathy, motor neuron disease secondary to HIV, multifocal motor neuropathy, HTLV-1 infection, adult-onset hexosaminidase deficiency, Lyme disease, lead intoxication, vit B12 deficiency, paraneoplastic syndromes (lymphoma), hyperthyroidism, benign cramp-fasciculation syndrome
- diagnosis:
  - upper and lower motor neuron signs in at least ¾ regions: bulbar, cervical, thoracic, or lumbosacral regions
  - UMN signs as detected in PE
  - LMN signs as detected by EMG: denervation (fibrillations, + sharp waves), small fasciculations not visible on PE, reinnervation □ large, complex motor units
- labs: serum CK may be normal or elevated
- Treatment:
  - goals: slow disease progression, maintain function, maintain safety, maintain comfort
  - what needs to be managed: sialorrhea (drool), secretions, pseudobulbar affect, depression, laryngospasm, head drop, communication, hypoventilation, contractures, cognitive impairment, foot drop, quads weakness, ADLs, dysphagia, constipation, urinary urgency, muscle cramps = may need multidisciplinary clinic referral
  - meds:
    - botox for refractory sialorrhea
    - dextromethorphan or quinidine for pseudobulbar affect
    - riluzole: slows progression by reducing presynaptic release of glutamate ▪ costly with little increase in survival but improves quality of life
    - baclofen, benzos, tizanidine for spasticity
    - SSRIs for pseudobulbar affect, depression
  - early PEG placement to prevent aspiration, stabilize weight and lengthen survival
    - anticholinergics to reduce secretions
  - RT:
    - noninvasive ventilation to treat respiratory insufficiency
    - cough assist devices and chest physical therapy
    - tracheostomy and mechanical ventilation
  - communication devices for dysarthria
- Prognosis: 60% of patients die within 5 years of symptom onset (not diagnosis), but many live beyond 10 years

15.8.3 Upper Motor Neuron Diseases

A.) Primary lateral sclerosis: a rare neuromuscular disease characterized by progressive voluntary motor muscle weakness
- onset is typically in middle age
- slight male predominance
- presentation:
  - common: leg stiffness or weakness that eventually spreads to the arms and bulbar muscles
  - other: hyperreflexia, unilateral onset, dysphagia, dysarthria, late emotional lability, urinary urgency, subclinical frontal lobe abnormalities
- treatment: supportive only as there is no evidence for riluzole
- prognosis: disease itself lasts 8+ years, and many patients go on to develop LMN symptoms and transition to the diagnosis of ALS (could take as long as 27 years)
- can do serial EMGs to monitor LMN function

B.) Pseudobulbar palsy: an upper motor neuron lesion to the corticobulbar pathways in the pyramidal tract

C.) Hereditary spastic paraplegia: a group of inherited diseases whose main feature is progressive stiffness and contraction in the lower limbs as a result of damage to dysfunction of the nerves

D.) Adrenomyeloneuropathy: a rare inherited disorder that is a milder form of X-linked, where young children generally exhibit cerebral dysfunction, with rapid progression to dementia and quadriplegia.

15.8.4 Lower Motor Neuron Diseases

A.) Progressive muscular atrophy: a slower-progressing relative of ALS that affects only the LMNs
- presentation: focal and asymmetric distal extremity weakness, atrophy, and fasciculations, hyporeflexia
- bulbar musculature often spared
- investigation:
- differential: ALS, multifocal motor neuropathy, adult onset spinal muscle atrophy
- diagnosis is done by exclusion, takes 3+ years from onset
- labs: CK elevated up to 10x the normal

B.) X-linked spinal-bulbar atrophy: a recessive, slow progressing, neurodegenerative disease associated with mutation of the androgen receptor
- onset from adolescence to mid-80s
- presentation: facial fasciculations, weakness of mouth and tongue, dysphagia, proximal limb weakness, gynecomastia, diabetes mellitus, oligospermia

C.) Hereditary spinal muscular atrophy:

D.) Poliomyelitis:

15.8.5 Myasthenia Gravis

- an autoimmune neuromuscular disease leading to fluctuating muscle weakness and fatigability due to circulating antibodies that block acetylcholine receptors at the postsynaptic neuromuscular junction, inhibiting the excitatory effects of the neurotransmitter acetylcholine on nicotinic receptors
- Presentation:
  - fluctuating weakness of specific muscles that worsens with repetition and improves with rest
    - repeated strength tests will progressively weaken
  - asymmetric proximal or distal extremity weakness
  - difficulty holding up head
  - shortness of breath
  - ocular: fatigable and fluctuating ptosis that is often asymmetric, double or blurry vision, fluctuating ophthalmoplegia (paralysis of 1+ extraocular muscles)
    - symptoms worse at end of the day
  - bulbar/facial: difficulty chewing or swallowing, tired facial appearance, difficulty smiling or whistling, difficulty keeping food in mouth
- Investigation:
  - administer Tensilon (Ach converting enzyme inhibitor) temporarily overcome neuromuscular junction Ach deficit
  - labs: Ach-R antibody, MuSK (muscle specific kinase) antibody
  - repetitive nerve stimulation showing amplitude drop off over time
  - single fiber EMG: the most sensitive test for myasthenia gravis
  - CT chest to rule out thymoma
Treatment:
- meds:
  - cholinesterase inhibitors (pyridostigmine) for symptoms
  - immunosuppressants: steroids to induce remission (high dose with slow taper), then mycophenolate mofetil, azathioprine, and cyclosporine to maintain remission
- thymectomy: best response in younger patients with hyperplasia
- MG exacerbation or crisis: acute worsening of symptoms that can lead to respiratory failure
  - occurs with infection, pregnancy, medication noncompliance, steroid use, illness, surgery, or certain medications
    - meds to avoid: neuromuscular blocking agents, quinine, quinidine, procainamide, aminoglycosides, azithromycin, telithromycin, quinolones, botox, β-blockers, Ca channel blockers, Mg, iodinated dyes (including IV contrast)
  - treat with plasmapheresis to remove pathologic antibodies or IV Ig, as well as supportive respiratory care

15.8.6 Lambert-Eaton Myasthenic Syndrome
- a rare autoimmune disorder that is characterized by muscle weakness of the limbs as a result of antibody formation against presynaptic voltage-gated calcium channels in the neuromuscular junction, or as a result of a neoplasm
- Half of the cases are autoimmune, 2/3 are paraneoplastic
- Presentation: proximal weakness and autonomic symptoms such as dry mouth, hypo or absent reflexes
- Investigation:
  - labs: voltage-gated Ca channel antibodies
  - EMG with decrementing pattern similar to myasthenia gravis
- Treatment:
  - treat underlying malignancy if present
  - meds:
    - diaminopyridine: blocks K+ efflux → increased Ca influx in nerve terminal → greater Ach release at synapse
    - acetylcholinesterase inhibitors such as pyridostigmine
    - immunosuppressants

15.8.7 Botulism
- blockade of Ach release due to botulinum toxin → flaccid paralysis
- Caused by ingestion of contaminated canned foods, or in kids, contaminated honey
- Can also be iatrogenic from bad Botox injections
- Wound botulism possible in trauma cases where soil is involved
- Potential for airborne bioterrorism agent
- Presentation:
  - symptoms begin within 24 hours of ingestion
  - diplopia, ptosis, dilated pupils
  - facial and respiratory weakness
  - descending paralysis
  - autonomic dysfunction
- Treatment: supportive, horse serum antitoxin from CDC
- Prognosis: recovery takes months

15.8.8 Muscular Dystrophies
Inherited muscle disorders characterized by muscle weakness and asting
- abnormalities in ultrastructural proteins
- progressive vs. congenital myopathies which are stable
- classified by distribution, inheritance, and clinical features
• muscle biopsy reveals necrosis of muscle fibers
• presentation and evaluation:

- look for stiffness, cramps, and myalgias
- temporal evolution and age at onset
- FH
- precipitation factors: meds, toxins, exercise, fever, carbs, cold
- systemic manifestations: cardiac disease, respiratory failure, hepatomegaly, cataracts, hearing loss, dysmorphic features, contractures
- weaknesses: evaluate distribution
  - facial: inability to bury eyelashes, horizontal smile, can’t whistle
  - ocular: double vision, ptosis, dysconjugate eye movements
  - bulbar: nasal speech, weak cry, nasal regurgitation of liquids, poor suck, difficulty swallowing, recurrent aspiration pneumonia, cough during meals
  - neck: poor head control
  - trunk: scoliosis, lumbar lordosis, protuberant abdomen, difficulty sitting up
  - shoulder girdle: difficulty lifting objects overhead, scapular winging
  - forearm/hand: inability to make a tight fist, finger or wrist drop
  - pelvic girdle: difficulty climbing stairs, waddling gait, Gower’s sign (hard to get up off floor)
  - leg/foot: foot drop, inability to walk on heels or toes
  - respiratory: use of accessory muscles

A.) Duchenne/Becker muscular dystrophy: X-linked or sporadic disease characterized by absent dystrophin (Duchenne’s) or reduced dystrophin (Becker’s)
- dystrophin is a muscle membrane protein needed for stabilization
- mutation in dystrophin gene → progressive muscular degeneration leading to loss of ambulation and death
- presentation:
  - mostly males but females can rarely have it due to lyonization or Turner’s syndrome
  - begins in childhood around age 6 (a little later for Becker’s) with weakness in lower extremities, Gower’s sign, pseudohypertrophy of calves, cardiomyopathy (dystrophin in heart)
  - braces by age 10
  - wheelchair by age 12 (later for Becker’s)
- diagnosis: muscle biopsy with immunostain for dystrophin, genetic testing, elevated CK, EMG
- treatment:
  - supportive care
  - meds:
    - corticosteroids
    - new: gene therapies, losartan, pentoxifylline, aminoglycosides
• Eval by PT, ortho, cardiology, and pulm
  o Cardiac transplant for Becker’s (cardiomyopathy may be more disabling than the weakness)
• Prognosis:
  o Duchenne: lifespan of 20-40 years
  o Becker: milder course of disease

B.) **Myotonic dystrophy type 1:** A chronic, slowly progressing, highly variable inherited multisystemic disease characterized by distal myopathy with myotonia
• Inherited in an autosomal dominant pattern
• Onset can occur at any age
• 2nd most common muscular dystrophy
• Presentation: Wasting of the muscles, endocrine changes, myotonia (cramping in hands with slowed relaxation), cardiac conduction defects, frontal balding, early cataracts, diabetes mellitus, infertility, cognitive impairment
• Investigation: Electrical myotonia with myopathy on EMG
• Treatment:
  • Meds: Phenytoin, mexilitine for myotonia
  • DM management
  • Annual EKG

C.) Limb-girdle dystrophies: a host of diseases characterized by slowly progressive symmetric proximal muscle weakness
• Dominant and recessive inheritance
• Requires specialist referral

D.) Facioscapulohumeral muscular dystrophy: A usually autosomal dominant inherited form of muscular dystrophy that initially affects the skeletal muscles of the face, scapula, and upper arms
• 3rd most common muscular dystrophy
• Onset in childhood to age 50
• Presentation: Asymmetric weakness, scapular winging, sleeping with eyes open, sensorineural hearing loss, vascular retinal disease, rarely epilepsy or cognitive impairment
• Investigation: Genetic testing and FH are most helpful
• Muscle biopsy is rarely helpful

E.) Emery-Dreifuss muscular dystrophy: A condition that chiefly affects skeletal muscles and cardiac muscle, resulting in contractures of the ankles, neck, and elbows
• An X-linked mutation in the emerin gene or an autosomal dominant mutation in lamin gene
• Onset in adolescence
• Presentation: Humeroperoneal or scapuloperoneal weakness with early contractures, cardiac arrhythmias
• Treatment: Early pacemaker placement

15.9 Epilepsy and Coma

15.9.1 Background
• **Seizure:** Paroxysmal, excessive, synchronous discharge of a group of neurons
• Risk factors: Head trauma, CNS infections, cerebrovascular disease, alcohol, drug overdose or withdrawal, metabolic disorders, genetics, malignancy
• Focus: The location of the original group of firing neurons
  o Propagation of seizure activity from focus to other structures determines symptoms at the onset of seizures (aura) and the activity that occurs during the seizure’s evolution
• Common seizure mimics: Hyperventilation, migraine, panic attack, pseudoseizure, syncope, transient global ischemia, TIA
• Pseudoseizure: An episode that clinically looks like a seizure but occurs for emotional or psychological reasons and is not accompanied by EEG evidence of a seizure during the episode
- can occur as a result of prior physical, sexual, or emotional abuse

  
  **investigation:**
  
  o proper diagnosis requires EEG
  o no response to epilepsy meds

  **complication:** can have both seizures and pseudoseizures

  **Epilepsy:** documented history of 2+ seizures that are not temporally related to an obvious metabolic or febrile cause

  febrile seizures, even several, do not mean that the patient has epilepsy!

  incidence is highest in first year of life, drops off up to age 30-40, then begins to increase again

  most epileptics who will go into remission do so within 3 years of their first seizure
    o factors against remission: FH of epilepsy, psychiatric comorbidity, h/o febrile seizures, > 20 seizure history, adult age (except for the elderly), failed monotherapy due to lack of efficacy

  1/3 of epileptics who being taking a single anticonvulsant will never have another seizure

  seizures may increase or decrease during pregnancy

  H&P for seizures: investigate feeling before the seizure, aura, onset of seizures, incontinence, tongue-biting, length of post-ictal confusion, provoking factors, predisposing conditions (DM, uremia, lupus, arrhythmia, hyponatremia, hypocalcaemia), history of substance abuse, trauma, use of seizure-inducing prescription drugs

  common provoking factors: sleep deprivation, excessive use of stimulants, withdrawal from sedatives or alcohol, substance abuse (cocaïne & amphetamines), high fever, hypoxia, hypoglycemia, electrolyte disturbance

  Investigation:

  differential: seizure mimics like syncope, pseudoseizures, breath holding spells, REM behaviors like sleep walking, panic attacks (can involve numbness and tingling around the mouth and fingers and dropped CO2)

  EEG is what determines seizure type

  labs: electrolytes, glucose, anticonvulsant levels, alcohol and tox screen, ABG if suspecting hypoxia

  LP to rule out meningitis

  CXR, CT, or MRI

  Treatments

  drugs are selected based on type of seizure, adverse effects, toxicity potential, cost, and patient-specific considerations like gender and family planning

  patients with newly diagnosed epilepsy can be placed into categories of treatment responsive or treatment resistant
    o 2/3 of patients will become seizure-free after the first or second drug is tried and will be on it for several years = want to select the drug that is most tolerable with least side effects

  monotherapy is preferred due to risks of toxicity and drug interactions

  consider second agent if inadequate trial of 2 different single agents

  monitor drug levels, but treat the patient, not the level

  when to treat after a single seizure:
    o TREAT: patients with a structural lesion (tumor, AVM, herpes encephalitis, stroke) or recognized abnormal EEG pattern, person with focal seizure
    o DON’T TREAT: patients without structural or EEG abnormality, alcohol withdrawal, drug abuse, provoked seizure, single seizure after head injury without structural abnormality.
      ▪ because 5-year risk of recurrent after a single unprovoked seizure is only 30% in both cases, most patients can’t drive for 6-12 months, and some states have mandatory reporting

  important drugs:
    o **carbamazepine:** inhibits voltage-gated Na channels
      ▪ for seizure as well as bipolar disorder, trigeminal neuralgia, and glossopharyngeal neuralgia
      ▪ side effects: diplopia, dizziness, drowsiness, nausea, unsteadiness, lethargy, Stevens-Johnson syndrome (= don’t use in patients of Asian descent), hypocalcaemia, hyponatremia, SIADH, hematologic, hepatitis
      ▪ drug interactions: acts as an enzyme inducer will lower levels of warfarin, decreased efficacy of oral contraceptives
- contraindications: pregnancy (D), hypersensitivity to TCAs, bone marrow depression
- monitoring: CBC, LFTs, mental status, bone mineral density, levels
  - oxcarbazepine: blocks voltage-gated Na channels, modulates Ca channels, increases K conductance
    - for partial seizures
    - side effects: sedation, dizziness, ataxia, nausea, Stevens-Johnson, hyponatremia
    - drug interactions: decreases bioavailability of estrogens, increases phenytoin
    - contraindications: pregnancy (C)
    - monitoring Na
  - clonazepam: a benzo that modulates GABA-related transmission in the brain
    - not a first-line choice
    - a schedule IV controlled substance
    - frequently added as a second agent with levetiracetam
    - abrupt d/c may ppt withdrawal and seizures
  - ethosuximide: increase seizure threshold and suppress paroxysmal spike and wave pattern, depresses nerve transmission in the motor cortex
    - indicated for absence seizure
    - side effects: ataxia, drowsiness, GI, unsteadiness, hiccups, Stevens-Johnson, hematologic, SLE
    - drug interactions: lowered levels with concomitant carbamazepine use, increased levels with concomitant valproic acid use
    - contraindications: pregnancy (C)
  - felbamate: glycine receptor agonist
    - indicated for partial and generalized seizures
    - side effects: anorexia, nausea, vomiting, insomnia, headache, Stevens-Johnson, aplastic anemia, hepatic failure-it WILL destroy your liver! = reserve for patients that don’t respond to any other therapy!
    - drug interactions: inhibits clearance of carbamazepine, phenytoin, valproic acid, and phenobarbital
    - contraindications: pregnancy (C)
      - requires signing an informed consent
    - monitoring: weekly LFTS, bilirubin, CBC
  - gabapentin: modulates Ca channels
    - indicated for combination therapy for seizure and also for neuropathic pain
    - renal dosing needed
    - side effects: dizziness, fatigue, somnolence, ataxia, nystagmus, tremor, headache, peripheral edema, Stevens-Johnson (rare)
    - contraindications: pregnancy (C)
  - pregabalin: similar to gabapentin
    - indicated for partial seizures and neuropathic pain
    - titrate initial dose slowly to avoid sedation
    - a schedule V controlled substance
  - lamotrigine: blocks voltage-gated Na channels, inhibits glutamate release
    - indicated for seizure, bipolar disorder
    - side effects: nausea, diplopia, dizziness, unsteadiness, headache, hypersensitivity rash (titrate slowly to avoid), Stevens-Johnson, hematologic, liver failure
    - drug interactions: valproic acid inhibits clearance big time
    - contraindications: pregnancy (C), caution in renal, hepatic, and cardiac impairment
  - levetiracetam: inhibits Ca channels, facilitates GABA, reduces K currents, modulates NT release
    - indicated for partial seizure, tonic-clonic, and myoclonic seizure
    - side effects: sedation, behavioral, suicidal ideation, pancytopenia, liver failure
    - contraindications: pregnancy (C)
  - phenobarbital: decreases post-synaptic excitation
    - indicated for seizure and sedation
- side effects: ataxia, hyperactivity, headache, unsteadiness, sedation, nausea, cognitive impairment, blood dyscrasias, Stevens-Johnson, hepatic injury, osteopenia
- many drug interactions
- contraindications: pregnancy (D), hepatic impairment, dyspnea, airway obstruction, caution in renal and hepatic impairment
- monitoring: CBC, LFTs, mental status, levels
  - primidone: similar to phenobarbital
    - may be used more frequently in familial tremor but also indicated for tonic clonic, psychomotor, and focal seizures
  - phenytoin: stabilizes neuronal membranes by altering Na efflux
    - may be given as fosphenytoin for faster effects
    - indicated for generalized tonic-clonic and complex partial seizures
    - side effects: ataxia, nystagmus, behavior changes, dizziness, headache, sedation, lethargy, incoordination, cognitive impairment, fatigue, blurred vision, blood dyscrasias, rash, immune rxn, gingival hyperplasia, skin thickening, hirsutism, coarsening of facial features, folate deficiency, peripheral neuropathy
    - many drug interactions
    - contraindications: pregnancy (D)
    - monitoring: levels, hypotension/bradycardia after administration
  - tiagabine: inhibits GABA reuptake
    - indicated as adjunct therapy for partial seizures
    - contraindications: pregnancy (C)
    - side effects: dizziness, fatigue, difficulty concentrating, nervousness, tremor, blurred vision, depression, weakness
  - topiramate: modulation of Na channels, enhances GABA, antagonizes glutamate-R
    - indicated for partial or generalized tonic-clonic seizure or for migraine prophylaxis
    - side effects: difficulty concentrating, psychomotor slowing ("dopamax"), speech or language problems, somnolence, fatigue, dizziness, headache, metabolic acidosis, kidney stones
    - drug interactions: decreases efficacy of oral contraceptives
    - contraindications: pregnancy (C)
    - monitoring: electrolytes
  - valproic acid: increases GABA
    - indicated for absence, complex partial, or mixed-type seizures, as well as bipolar disorder and migraine prophylaxis
    - side effects: GI upset, sedation, unsteadiness, tremor, thrombocytopenia, palpitations, immune hypersensitivity, ototoxicity
    - many drug interactions
    - contraindications: pregnancy (D), hepatic dysfunction
    - monitoring: mental status, CBC, LFTs
  - vigabatrin: irreversibly inhibits GABA transaminase, increased GABA in brain
    - indicated for infantile spasms, refractory complex partial seizures, refractory generalized seizures
    - side effects: permanent visual loss, psychiatric disturbances including acute psychosis, acute abnormal MRI findings in infants = in a restricted distribution program
  - zonisamide: mechanism unknown
    - indicated for adjunct therapy for partial seizure
    - side effects: sedimentation, dizziness, cognitive impairment, nausea, kidneys tones, Stevens-Johnson, schizophreniform disorder
    - contraindications: pregnancy (C)
- special considerations for women on antiepileptics:
  - many AEDs can decrease efficacy of oral contraceptives
  - estrogen in oral contraceptives can decrease lamotrigine levels
  - estrogen is seizure-triggering while progesterone is seizure-protective = women can be more vulnerable to seizures around ovulation and menstruation
  - pregnancy:
• if AED must be used, use monotherapy at lowest possible dose and supplement with folic acid
• adverse fetal effects greatest with valproic acid, phenytoin, and carbamazepine
• lamotrigine may be the safest
• vitamin K is given from week 36 to delivery to prevent hemorrhagic disease
  o special considerations for the elderly on antiepileptics:
    ▪ start low, go slow
    ▪ the lower the albumin, the greater the amount of free drug
  o elderly are more susceptible to adverse neuro and cognitive effects
    kids:
    ▪ neonates need lower doses
    ▪ kids ages 2-3 have a more active liver, so they need higher doses

Partial Seizures: when electrical discharge begins in a small region of the brain

A.) Simple partial seizure: no alteration of consciousness
• alternating contraction and relaxation of muscle groups
• eye movements and turning of head to the same side
• speech arrest, vocalization
• may see flashes of light or colors, hallucinations
• may hear humming, buzzing, or hissing
• may experience unpleasant odors and tastes
• dizziness
• autonomic symptoms: flushing, incontinence, nausea, vomiting, goose bumps, pupillary dilatation, sweating, tachycardia
• psychiatric symptoms: detachment, memory distortion, time distortion, unprovoked emotion
• can manifest in a continuous form known as epilepsia partialis continua
• can turn into a complex partial seizure

B.) Complex partial seizure: involves an alteration of consciousness
• will have automatisms: coordinated, involuntary motor activity such as lip smacking, picking, patting, chewing, swallowing
• inability to carry out simple commands or execute willful movement
• lack of awareness of surroundings and events
• can secondarily generalize to tonic clonic seizures = patient jerking all 4 extremities does not rule out partial seizure onset
• most common kind of seizure
• usually begins between ages 10-30
• may be seen in 30-60 year olds with brain tumors (?)
• may be a stroke in > age 60 (?)
• common after head trauma
• many of these patients will have abnormal tissue in their temporal lobe: sclerosis, hamartomas, tumors, infections, vascular lesions
• in patients with seizures of the temporal lobe, surgery has a better outcome than meds
• investigation:
  • EEG may reveal a small, focal unilateral abnormality or may look normal
• abnormal imaging due to metabolic abnormality may be present in half of these patients

15.9.2 Treatment for partial seizures
• first line: carbamazepine, phenytoin, lamotrigine, valproic acid, oxcarbazepine
• alternatives: gabapentin, topiramate, levetiracetam, zonisamide, tiagabine, phenobarbital, felbamate

15.9.3 Generalized Seizures
• when electrical discharge occurs simultaneously in multiple areas of both sides of the brain
A.) **Absence (petit mal) seizure**: 5-10 second recurrent episodes of staring, sometimes associated with minor motor automatisms
- patients have no memory of the spells but are normal immediately at completion
- may be brought on by hyperventilation
- not associated with any other seizure type
- begins around age 4-8
- patients are of normal intelligence
- investigation: EEG shows 3/sec spike and wave with no other abnormalities
- considered to be diagnostic, and will be present even when individual is not having an absence seizure
- treatment:
  - first-line: valproic acid, ethosuximide
  - alternatives: lamotrigine, levetiracetam
- prognosis: most cases will resolve spontaneously

B.) **Tonic-clonic seizure**: tonic phase begins with loss of consciousness, tensing of skeletal muscles, and often a loud moan or yell from forceful exhalation of air, clonic phase commences with convulsions of muscles, eyes rolling back, and strong jaw contractions
- patient may have an aura
- lasts 5-20 minutes
- there may be incontinence
- patient may remain unconscious for a period of time after the seizure and awaken confused and sleepy
- most common cause with onset before age 30 is idiopathic epilepsy
- treatment:
  - first-line: phenytoin, carbamazepine, valproic acid
  - alternatives: lamotrigine, levetiracetam, topiramate, phenobarbital, primidone, oxcarbazepine

C.) **Myoclonic seizure**: brief major motor seizure with quick, lightning-like jerking movements of the trunk or extremities associated with a paroxysmal EEG abnormality
- may occur throughout body or limited to certain muscle groups
- onset may be so sudden that patient falls to the ground
- so brief that consciousness may not be lost
- causes: metabolic abnormalities (hepatic or renal failure)
- treatment:
  - first-line: clonazepam, valproic acid
  - alternatives: lamotrigine, levetiracetam, topiramate, felbamate, zonisamide

D.) **Clonic seizure**: impaired consciousness followed by asymmetric bilateral jerking, with muscles relaxing completely then returning to produce rhythmic jerks

E.) **Tonic seizure**: relatively rare alone; involves stiffening of the body, upward deviation of the eyes, dilation of the pupils, and altered respiratory patterns

F.) **Atonic seizure**: sudden loss of muscle tone that may cause a fall, lasting 1-4 seconds but without a detectable loss of consciousness
- ranges from mild and affecting only one body area to a severe loss of all body tone
- treatment:
  - first-line is valproic acid
  - alternatives: lamotrigine, topiramate, zonisamide

G.) **Infantile spasms**: characterized by a particular jack-knife posturing of the child’s body
- spasms occur throughout the day or may be continuous
- most children are found to have neurologic problems eventually

15.9.4 **Other Kinds of Seizures**
A.) Unclassified seizure: incomplete data to say whether seizure is partial or generalized
B.) Status epilepticus: prolonged or recurrent seizures without regaining consciousness
   - does not apply to simple continuous seizures
   - EEG can be helpful in determining a seizure etiology if there are no convulsions
C.) Febrile seizures: also known as a fever fit or febrile convulsion, is a convulsion associated with a
   significant rise in body temperature
   - often patients have a FH of febrile seizures
   - slightly increases risk for later epilepsy
   - especially if there are multiple seizures during one illness, focal seizures, an abnormal neurological
     exam, or delayed development
   - treatment: supportive, anticonvulsants are not routinely given
   - prophylax at first sign if illness with antipyretics to prevent seizures
D.) Alcohol withdrawal seizures: usually a generalized seizure but can be focal
   - if focal, patients can be left with a temporary focal deficit (Todd’s postictal phenomenon)
   - treatment: anticonvulsants can be used to temporarily break seizures, but long-term resolution depends
     on cessation of alcohol use

15.10 Coma

15.10.1 Coma Background

- Defined as an inability to sense or respond to external stimuli or inner needs
- Not a disease itself but an expression of underlying pathology
- Consciousness:
  - awareness: a high level function residing in the cerebral cortex that permits understanding of self
    and environment
  - arousal: a more primitive function residing in the brainstem that involves a set of primitive responses
  - loss of consciousness means that either both cerebral hemispheres must be damaged or there must
    be a brainstem lesion
- Causes of coma: cerebral infarction, cerebral hemorrhage, metabolic causes, drug ingestion,
  hypoglycemia, psychiatric
  - sudden onset □ think cardiac arrest, subarachnoid hemorrhage secondary to aneurysm, brainstem
    infarct or hemorrhage, bicerebral hemispheric infarction
  - onset in minutes to hours □ think drug overdose, hypoxia, hypoglycemia, subarachnoid
    hemorrhage, acute hydrocephalus, vascular malformation, meningitis, encephalitis, metabolic
    (uremia or hepatic failure), hypertensive encephalopathy
- History for the comatose patient:
  - ask everyone who was around what happened
  - check previous medical and psychiatric history
  - trauma?
  - medication use, alcohol, and other drugs
  - timeframe for onset
- PE:
  - skin: look for trauma, signs of liver disease, needle marks (insulin), rash (infection), signs of
    embolism
  - head: trauma (Battle’s sign at mastoid), raccoon eyes (orbital fracture), CSF rhinorrhea or otorrhea
    (basilar skull fracture),
  - eyes:
    - funduscopic exam: look for signs of bleeding or increased ICP
      - Roth spots: retinal hemorrhages with white or pale centers composed of coagulated fibrin, usually
        caused by immune complex mediated vasculitis often resulting from bacterial endocarditis but may
        also be observed in leukemia, diabetes, subacute bacterial endocarditis, pernicious anemia, and
        ischemic events
- **Hollenhorst plaques**: a cholesterol embolus seen in the retinal vessels, often from plaque broken off from neck vessels
  - papilledema from increased ICP
- **reactive pupils**
  - usually indicates that the midbrain is intact and that the cause of coma is a metabolic abnormality (hypoglycemia or drug ingestion (barbiturates)
  - small + reactive = pontine damage or drugs (opiates, pilocarpine)
- **unreactive pupils**: make sure light source is adequate!
  - if truly unreactive = midbrain damage
  - if bilaterally unreactive + midposition = hypothermia
- **dilated or "blown" pupil**:
  - if unilateral + nonreactive = CN III compression, DM, or some drugs
- **eye movements**:
  - eye deviates TOWARDS a unilateral hemispheric lesion
  - eye deviates AWAY from a unilateral brainstem lesion
  - **tests**:
    - **Doll's head (oculocephalic) reflex**: rapidly turning the head from side to side
      - normal: eyes move in direction opposite to the movement of the rotating head
      - abnormal: absent or asymmetric eye movement suggests disease of the midbrain or pontine level (or barbiturate toxicity)
    - **oculovestibular reflex (ice water calorics)**: irrigation of cold water into the auditory canal to see if eyes deviate
      - normal, conscious response: tonic (sustained) deviation of the eyes
      - toward the stimulated side, with quick nystagmus towards the opposite side
      - comatose with intact brainstem response: tonic deviation towards stimulus without nystagmus
      - comatose with brainstem dysfunction: loss of tonic deviation
      - ***does not distinguish between metabolic and structural causes of coma!***
    - corneal sensation: checks CN V (trigeminal); abnormal response suggests pontine lesion
- **neck**: stiffness (meningitis or subarachnoid hemorrhage)
- **breath**: ketoacidosis, fetor hepaticus (liver disease), alcohol, uremia
- **cardiac**: murmurs or arrhythmias
- **neuro**:
  - sensation: noxious stimuli like a sternal rub is applied to the face, trunk, and extremities bilaterally
    - potential responses: purposeful withdrawal bilaterally, absent response unilaterally, facial grimace, posturing
    - **decorticate posturing**: painful stimuli flexion of arms, clenching of hands into fists, and extension of legs with feet turned inward
      - correlates to a hemispheric or diencephalic dysfunction due to destructive lesions or metabolic abnormality
      - better outcome than decerebrate
    - **decerebrate posturing**: painful stimuli involuntary extension of the upper extremities, head arches back, arm and leg extension with internal rotation, elbow extension; patient is rigid, with the teeth clenched
      - correlates to midbrain or upper pons dysfunction due to a metabolic or structural abnormality
- **lungs**:
  - **Cheyne-Stokes**: small breaths going up incrementally to a crescendo then back down
    - seen with bilateral hemispheric lesions, as well as non-neurologic disorders such as CHF
- **central neurogenic hyperventilation**: commonly has a metabolic cause such as sepsis or DKA
- **apneustic**: deep breaths held for prolonged periods of time
  - associated with pontine infarction
- **ataxic breathing (Biot's respirations)**: irregular breathing seen with damage to the medullary respiratory centers

### 15.10.2 Glasgow Coma Scale

- **Made up of three tests, with values considered separately as well as conglomeratively:**
  - **eye response**
    - 4 = spontaneous opening
    - 3 = opening to speech (if they were just sleeping they are a 4!)
    - 2 = opening in response to pain
    - 1 = no eye opening
  - **verbal response**
    - 5 = fully oriented
    - 4 = confused
    - 3 = inappropriate words, no conversational exchange
    - 2 = incomprehensible sounds
    - 1 = no sounds
  - **motor response**
    - 6 = obeys commands
    - 5 = localizes to painful stimuli
    - 4 = withdrawal from painful stimuli
    - 3 = decorticate response to painful stimuli
    - 2 = decerebrate response to painful stimuli
    - 1 = no motor response
  - **Lowest possible GSC is 3 = deep coma or death**
  - **Highest is 15 = fully awake and responsive**

### 15.10.3 Coma Investigation

- **Labs**: glucose, Na, K, Cl, CO2, renal functions, Ca, P, ABG, CBC, tox screen
- **EEG**: can help determine presence and degree of coma but won’t tell you about the etiology
- **EKG**
- **CXR**
- **Neuroimaging**

### 15.10.4 Coma Prognosis

- **Lower the Glasgow score, the lower the chance for making a recovery of any kind**
- **almost all comatose patients will eventually wake up to some degree in 2-4 weeks**
  - most will develop a sleep wake cycle
  - they may open their eyes in response to verbal stimuli or appear to follow a light, but there is no response to visual threat
  - they do not discreetly localize motor responses, follow commands, or speak comprehensibly
- **“Brain death” means that the patient does not make any purposeful movements, has no pupillary responses, no extraocular movements (spontaneously or with stimulation), no corneal reflexes, no spontaneous respirations or movements**
- **a clinical diagnosis**
- **DTRs may be present**
- **there are no documented recoveries from brain death in an adult patient**
- **EEG may be completely flat but there are some patients who meet the clinical criteria for brain death that still have some EEG activity**
15.11 Stroke

15.11.1 Background
- Defined as an acute neurological deficit of vascular etiology with symptoms lasting longer than 24 hours
- Causes: infection, autoimmunity, metabolic disorder, neoplasm, trauma, epilepsy, demyelinating disease, psychiatric disease
- 4th leading cause of death in the US
- More common in women
- More prevalent in the “stroke belt” in SE US
- Diagnosis is based on history, PE, and selected labs
  - correlate patient’s symptoms and signs with brain anatomy
  - CBC, PT/PTT, electrolytes, glucose, and renal function
  - EKG for signs of cardiac ischemia
  - brain CT or MRI

15.11.2 Types of Stroke
1.) Hemorrhagic: accounts for 15-20% of strokes
- parenchymal intracranial hemorrhage: bleeding within brain itself
  - primary ICH originates from the spontaneous rupture of small vessels damaged by chronic hypertension or amyloid angiopathy
    - ICH from chronic hypertension:
      - tend to occur in weaker deep vessels of the thalamus, basal ganglia, pons, and cerebellum
      - presentation: history of HTN, currently severely hypertensive, severe headache, nausea, vomiting, focal neuro deficits
      - investigation: CT showing white mass
        - remember that 3 things are white on a CT: blood, rocks, or contrast
    - ICH from amyloid angiopathy: brain arterioles weaken from deposition of amyloid
      - presentation: dementia, episodic worsening, no history of HTN
  - secondary ICH occurs in association with trauma, vascular abnormalities, tumors, impaired coagulation, or vasculitis
  - presentation:
    - if in the thalamus or basal ganglia  □ contralateral motor and sensory deficit, aphasia, language or spatial neglect, depressed level of consciousness due to mass effect, intraventricular extension □ hydrocephalus
    - if in the cerebellum □ ipsilateral ataxia, depressed level of consciousness
    - if in the pons □ vertigo, diplopia, crossed signs, depressed level of consciousness

- subarachnoid hemorrhage: bleeding outside the brain
most common cause is a ruptured aneurysm
  - most common location is the anterior communicating artery
  - can also occur at the bifurcation of the carotid artery, PCCM, MCA, basilar tip artery, PICA
  - risk factors: hypertension, smoking, heavy alcohol, genetics (Ehlers-Danlos, inherited polycystic kidney)
  - presentation: abrupt, severe headache, meningismus (inflammation consciousness, non-focal neuro exam (because it’s outside the brain)

less common causes: vasculitis, infection, neoplasms, blood coagulopathies

- treatment: general emergency management, blood pressure control, aneurysm occlusion, surgical evaluation

2.) Ischemic: accounts for 80-85% of strokes
- atheroembolic: occlusion of artery supplying brain or within the brain due to CAD stenosis or cholesterol embolus; the most common kind of stroke
  - lacunar stroke: a type of stroke that results from occlusion of one of the penetrating arteries that provides blood to the brain's deep structures
  - presentation: there will be warning signs with a stepwise progression to full-blown stroke!
    - history of HTN or CAD
    - transient language disturbances and weaknesses
    - vertebrobasilar stroke: affects CN III (oculomotor) \(\downarrow\) dilated pupils
    - the more subcortical the stroke location, the more areas of the body will be affected because the tracts begin to run together as they go deeper into the brain
    - lacunar strokes can appear as a pure motor stroke, pure sensory stroke, ataxic hemiparesis, or dysarthria + clumsy hand

- investigation:
  - head CT: caution, may look normal
  - doppler US to look for carotid stenosis
  - catheter angiography: an invasive test that is not first-line

- cardioembolic: embolus thrown from the heart goes to the brain
  - sources: afib, cardiomyopathy, acute MI, valvular heart disease
  - most common lodges in the middle cerebral artery
  - presentation: history of afib, aphasia, focal neuro deficits with max deficits occurring at onset
    - can break up into many clots and travel to multiple vascular territories

- investigation:
  - carotid US will be normal
  - brain CT will be normal during first few hours of stroke
- 24-48 hour EKG to check for intermittent afib
- echo: transthoracic or transesophageal

- embolic strokes can cause a hemorrhagic infarction as the ischemic blood vessels die and split open, but you must differentiate if cause of a detected hemorrhage is primary/secondary ICH vs embolism
- cause is primary/secondary ICH — can’t give blood thinners or lytics ever again because you will kill them if they bleed again
- cause is truly embolic — must be put on a blood thinner regimen to prevent future embolic strokes
  - a transient ischemic attack (TIA) is an acute focal neurologic deficit as a result of ischemia that resolves within 24 hours
  - incurs a greater risk of having a stroke in the near future
- treatment for ischemic stroke (or TIA with symptom recurrence):
  - start TPA if within 4.5 hours of onset of symptoms (cutoff point for prevention of disability)
  - must make sure head CT has no evidence of hemorrhage or other complication
  - within 3 hours of onset relative contraindications: recent head trauma or stroke, prior ICH, recent arterial puncture, active bleeding or acute trauma, on oral anticoagulants with high INR, normal aPPT if recent heparin, low platelets, hypoglycemia, HTN >185/>110, CT with hypodensity in > 1/3 of cerebral hemisphere, rapidly improving symptoms, seizure with postictal impairment, recent MI, recent GI or urinary tract hemorrhage, recent major surgery
  - further contraindications after 3 hours of onset: over age 80, oral anticoagulant therapy regardless of INR, history of prior stroke + diabetes
  - TPA increases risk of hemorrhage by 10x but the benefit generally outweighs this risk as long as the protocol is followed
- if TPA is not an option, consider endovascular repair or mechanical removal of clot
- give fluids but avoid D5W as glucose crosses the blood-brain barrier and is quickly metabolized to water, creating greater free water in a brain already at risk for swelling
- blood pressure management
  - want to keep MAP up as brain blood vessels are maximally dilated during a stroke = reduce resistance in blood vessels
  - consider lowering BP in severely hypertensive patients (>220/>120) or with other concomitant organ system injury by 15-2% within the first day
- temperature: induction of hypothermia in febrile stroke patients may lessen ischemia (still being researched)
- antithrombotic agents
Later PT, OT, speech therapy
pharmacologic therapy for recovery is being researched

- everyone improves to some degree after a stroke
- where you end up depends a lot on starting severity
- quickest period of recovery after a stroke is in the first 30-60 days

15.11.3 Stroke Primary Prevention

- Healthy lifestyle
- Assess and treat modifiable risk factors for ischemic stroke:
  - HTN:
  - afib:
    - for clinical benefit, dabigatran (direct thrombin inhibitor) > warfarin = rivaroxaban > aspirin
    - but dabigatran and rivaroxaban are not reversible
  - carotid stenosis:
    - screen for with carotid bruits, US, MR or CT angiography
    - surgery if asymptomatic is generally not indicated as the risk now outweighs benefit
  - diabetes:
    - even diabetics with well-controlled blood glucose are at same risk of macrovascular complications as poorly controlled DM
    - puts greater emphasis on need for tight HTN control and statin use in this population
  - hyperlipidemia:
    - diet, niacin, cholestyramine, etc not shown to reduce stroke risk
    - statins reduce risk of stroke by 20% in patients with CAD or risk factors
    - aspirin or other antiplatelet
- Assess and treat modifiable risk factors for hemorrhagic stroke:
  - biggest risk factor is HTN!
  - smoking
  - alcohol
  - can consider prophylactic clipping or endovascular coiling in patients with FH stroke in > 2 1st degree relatives

15.11.4 Stroke Secondary Prevention

- Based on mechanism for initial stroke
- Platelet antiaggregants: warfarin > aspirin
- Anticoagulants
- Blood pressure control
- Lipid lowering: statin proven to reduce risk of recurrent stroke
- Endarterectomy for patients with carotid disease
- may be useful in carotid artery stenosis
- Prevent complications of hospital admission and treatment: UTI, DVT, pneumonia, etc.

15.12 Headache

15.12.1 Background

- Headache differential: systemic infection, HTN, vision decline, cervical radiculopathy, occipital neuralgia, temporal arteritis, TMJ, trigeminal neuralgia, tumor, mass lesions, chronic subdural hematoma, ischemia, arteriovenous malformation, aneurysm, pseudotumor cerebri (young, obese females with papilledema & compressed ventricles)
- Primary headache: not a symptom or caused by another disease or condition
- includes tension-type headaches, cluster headaches, chronic daily headaches
- Secondary headache: a symptom or result of another underlying disease or condition such as brain tumor or infection
- when to be concerned: systemic symptoms, risk factors like HIV or cancer, odd neurologic symptoms, sudden onset, new headache in an older patient, progressively worsening headache in a middle-aged
patient, major change in attack frequency or severity, different headache than before, headache precipitated by exercise, coughing, sneezing, bending over, or sexual arousal
  o imaging not necessary with:
    ▪ no abnormal neuro findings
    ▪ patient has history of recurrent headache
    ▪ no history of seizures
  o get an MRI with:
    ▪ abnormal neuro findings
    ▪ progressively worsening headache
    ▪ new persistent headache
    ▪ new, rapid onset headache
    ▪ headache not responding to standard therapy

15.12.2 Tension-Type Headache

- Most common type of headache
- More common in women than in men
- 2 major forms:
  - episodic tension headache: attacks occur on average 3 days a month
  - chronic tension headache: 15+ attacks per month
- Presentation:
  - no aura, nausea, or vomiting
  - with or without photophobia or phonophobia
  - may have head muscle tender points
- Investigation:
  - diagnostic criteria = at least 2 of the following along:
    ▪ bilateral head pain from 30 minutes to 7 days (like a “tight hat”)
    ▪ steady, non-pulsating pain (dull, tightness, or pressure)
    ▪ mild to moderate pain intensity
    ▪ normal physical activity does not aggravate the headache
- Treatment:
  - if episodic:
    ▪ DOC are OTC analgesics: ibuprofen, naproxen, aspirin, acetaminophen, Excedrin tension headache
    ▪ non-responders may require prescription NSAIDs like diclofenac
    ▪ last-line treatments for non-responders: butalbital + aspirin or acetaminophen + caffeine, isometheptene + dichloralphenazone + acetaminophen, acetaminophen + opioid
      ▪ can result in chronic daily headache if overused, especially with butalbital and codeine
  - consider prophylaxis if meds are needed > 2 days/week:
    ▪ tricyclics:
      ▪ amitriptyline: very sedating = take at bedtime
        ▪ start low and titrate up
      ▪ nortriptyline: moderately sedating
        ▪ also start low and titrate up
      ▪ side effects: weight gain, dry mouth, constipation contraindicated in severe heart disease
    ▪ duloxetine: for patients with major depressive disorder + chronic daily headache
      ▪ usually an 8 week course for improvements in both depression and headache
    ▪ skeletal muscle relaxants: cyclobenzaprine, methocarbamol, tizanidine
      ▪ to be taken at first sign of head or neck tension as prophylaxis
      ▪ can cause liver disease if used for long periods of time
      ▪ can help with weaning from other analgesics like narcotics
      ▪ tizanidine has a lot of drug interactions and can cause hypotension and sedation, needs LFT monitoring
    ▪ botox injection into CN muscles at tender points
15.12.3 Migraine Headaches

- More common in women
- but increased incidence in men as they get older
- Usually beings in teens or perimenopausal
- Highest prevalence in 25-45 year olds
- decreased incidence during childbearing years
- Genetic component that can incur vascular abnormalities as well as hypercoagulability = migraine can increase risk for future stroke
- High incidence with concomitant depression
- Common precipitators: stress, hormones, hunger, sleep deprivation, odors, smoke, alcohol, meds, high tyramine foods
- may be a load factor requiring presence of multiple triggers to provoke a headache
- very common triggers to avoid in all migraine sufferers: sleep disturbance, skipping meals, caffeine, alcohol
- May begin with sensitization of peripheral nociceptors that pass this on to central nociceptors
- patients may have sensitivity to things like touch and combing hair
- Often begin in the morning with gradual onset of pain
- 5 phases: prodrome □ aura □ headache □ termination □ postdrome
- May be confused for a “sinus headache”
- Types:
  - migraine without aura: accounts for most migraine cases; headaches last 4-72 hours
    - the most common kind of migraine
    - presentation: nausea, vomiting, photophobia, phonophobia, unilateral, pulsating frontotemporal pain
    - investigation:
      - usually need 5+ attacks for a diagnosis along with 2+ of the following:
        - unilateral location
        - pulsating quality
        - moderate or severe pain intensity
        - aggravated by physical activity
  - migraine with aura: headaches will begin during the aura or within 1 hour of it
    - most common kind of aura is a scintillating scotoma
    - up to 50% of patients with this also have a patent foramen ovale
    - presentation: visual, sensorimotor, speech, or brainstem disturbances
    - investigation:
      - diagnostic criteria involve having an aura for a minimum of 5 minutes and 1+ of the following:
        - fully reversible visual symptoms
        - fully reversible sensory symptoms
        - fully reversible dysphasic speech disturbance
      - never use a triptan during an aura because there is diminished cerebral blood flow and you could cause a stroke = wait til the pain starts before taking
  - complicated migraine: headache accompanied by major neurologic dysfunction
    - presentation: looks like a stroke
    - neurologic changes can outlast headache by 1-2 days
  - confusional migraine:
  - ophthalmoplegic migraine: occurs with changes in vision
  - basilar migraine: severe episode headache that accompanies or precedes cerebellar dysfunction
    - typically occurs in teenage girls
    - presentation: diplopia, tinnitus, bilateral vision abnormalities, ataxia, dysarthria, bilateral sensory or motor disturbance, CN deficits, coma
  - menstrual migraines: occur prior to, during, or after menstruation, or during ovulation
    - treatment:
    - abortive: triptans
    - prophylaxis:
• begin NSAIDs 2-7 days prior to menses, continue through last day of flow
• also consider oral contraceptives in women who do NOT have an aura

• **chronic migraine:** chronic daily headache with migraine qualification at least 8 days a month that is not caused by drug overuse or secondary cause
  o may develop from episodic migraine due to snoring, sleep apnea, obesity, caffeine, medication overuse, and psychiatric comorbidities

• **Migraines in kids:**
  o kids have symptoms like abdominal pain, motion sickness, sleep disturbances, and cyclic vomiting

• **Treatment**
• exercise shown to be just as good as meds
• patients with chronic migraine need to be given a prophylactic therapy, an abortive therapy, and a rescue med if the abortive underperforms or fails

• **abortive therapy**
  o goals are to treat attacks early and consistently, restore ability to function, minimize use of rescue meds, emphasize self-care, use cost-effective therapy, and avoid side effects
  o non-opioids that can be used: NSAIDS or acetaminophen, rectal indomethacin, IM ketorolac, Excedrin migraine
    o **MOA:** inhibition of prostaglandin synthesis
    o **side effects:** GI tox with prolonged use, possible rebound headache, sodium and water retention, renal dysfunction, exacerbation of CHF, antiplatelet effects
    o **contraindications:** GI bleed or history, renal insufficiency, hepatic failure
      • caution in PUD
  o triptans: constrict intracranial blood vessels, inhibit vasoactive neuropeptide release, interrupt pain signal transmission centrally
    o cost per trade name for oral dose is $20-$28 unlikely health plans and hospitals will usually have contracts for a preferred agent
      • **types:**
        • **sumatriptan:** good place to start as insurance covers it as a generic
          o avail subq for fast onset
          o may cause HTN in the elderly
        • **zolmitriptan:** wafer form avail
          o caution in hepatic impairment
        • **naratriptan:**
          o can’t use MAOIs, caution in renal and hepatic impairment
        • **rizatriptan:** wafer avail
        • **almotriptan:**
          o can’t use MAOIs
        • **frovatriptan:**
          o can’t use MAOIs
        • **eletriptan:**
          o can’t use MAOIs
      • **side effects:** paresthesias, fatigue, dizziness, flushing, warm sensations, somnolence, chest tightness, possible rebound headache with overuse
      • **drug interactions:** MAOIs, ergot, caution with SSRIs (serotonin syndrome)
        • also monitor for serotonin syndrome with SNTRIs, TCAs, and linezolid
      • **contraindications:** ischemic heart disease, uncontrolled HTN, stroke, basilar or hemiplegic migraines
        - patients at risk for unrecognized heart disease should be assessed prior to triptan use
  o **ergots:** direct smooth muscle vasoconstriction, non-selective 5-HT1-R agonist
    • **ergotamine:**
      • **dihydroergotamine:** most common form, avail injection, nasal, oral, rectal, sublingual
        • side effects: vasoconstriction, HTN, peripheral ischemia, nausea, vomiting, diarrhea, pruritus, vertigo, cramps, paresthesias, cold skin, decreased
pulses in extremities, rebound headache, fibrosis if long-term = this is a last-resort medication!

- drug interactions: triptans in last 24h, CYP 3A4 inhibitors
- contraindications: CAD, PVD, HTN, renal or hepatic failure, protease inhibitors, pregnancy (X)
  - combination sympathomimetics: isomehtepene + dichloralphenazone + acetaminophen
  - opioids: transnasal butorphanol, Percocet, Vicodin
    - overuse can lead to chronic daily headache or rebound headache
  - combination products with barbiturates: butalbital + aspirin or acetaminophen
    - decreased cognition and high abuses potential
  - antiemetics: prochlorperazine, metoclopramide
    - give 15-30 minutes before abortive therapy
    - when used alone can stop the migraine
  - intranasal lidocaine
  - corticosteroids
  - droperidol
  - nitrous oxide
  - propofol

- consider prophylactic therapy for patients with incomplete response to acute therapies, with contraindications to acute therapies, with migraine significantly affecting quality of life, of those with frequent attacks requiring medication > 2x per week
  - patients with rebound headaches with acute treatments may also benefit
  - β-blockers: propranolol, timolol, metoprolol, nadolol, atenolol
    - MOA: central/serotonergic, β-1 mediated
    - helpful in patients with anxiety, HTN, or angina
    - side effects: sedation, fatigue, dizziness, depression, orthostatic hypotension, impotence
    - contraindications: 2nd or 3rd degree heart block, asthma, decompensated CHF, bradycardia, PVD, IDDM (mask hypoglycemia)
  - Ca channel blockers: verapamil
    - MOA: prevent vascular spasm
    - β-blockers work better
    - these take up to 8 weeks to work
    - side effects: edema, bradycardia, tachycardia, hypotension, constipation, dizziness, fatigue, CHF exacerbation
    - caution in 2nd or 3rd degree heart block, systolic heart failure
  - NSAIDS: aspirin, ibuprofen, naproxen
    - for use with migraines that have a predictable pattern (menstrual)
    - start 1-2 days before expected onset and continue for expected duration
  - TCAs: amitriptyline, imipramine, doxepin, nortriptyline, protriptyline
    - best evidence is with amitriptyline
    - side effects: anticholinergic, sedation, postural hypotension, arrhythmias, tremor, weight gain
    - contraindications: MAOIs, recent MI
      - caution in elderly, BPH, glaucoma
  - SSRIs: fluoxetine, fluvoxamine, sertraline
    - not as much data
  - atypical antidepressants: bupropion, venlafaxine
    - also not a lot of data
  - MAOIs: phenelezine
    - can’t eat tyramine-containing foods
    - side effects: anticholinergic, hypotension, impotence, skin rash, hypertensive crisis
    - we should not use this
    - drug interactions: severe and potentially fatal with SSRIs, meperidine, triptans
  - antiepileptics: carbamazepine, gabapentin, tiagabine, topiramate, valproic acid or divalproex, oxcarbazepine, lamotrigine, vigabatrin, zonisamide
    - valproic acid and divalproex are FDA approved
      - requires monitoring of LFTs, blood
- carbamazepine requires monitoring
- newer anticonvulsants still being researched
  - Botox: approved for chronic migraine prophylaxis (15+ days/month of migraine)
    - 5U injected IM into 31 different sites = costs $2000
      - needs to be done every 12 weeks
  - must give 6-8 week trial for each therapy
  - prolonged headache-free intervals can signal time for dose reduction or discontinuation with slow taper
- behavioral strategies: relaxation training, thermal biofeedback, EMG biofeedback, cognitive behavioral therapy
- insufficient evidence for acupuncture, TENS, chiropractic, hyperbaric oxygen, hypnosis, avoidance of triggers, and lifestyle/stress management
- When to refer: symptoms are refractory to treatment efforts, worsening disability, status of symptomatology changes and no longer fits diagnostic criteria, comorbid conditions requiring polypharmacy, habituated patient/rebound headaches
- most migraine patients can be effectively managed in primary care

15.12.4 Chronic Daily Headache:
- Headache of any kind occurring 15+ days out of the month
- includes chronic migraines, chronic tension headaches
- hemicrania continua: a daily strictly unilateral primary headache associated with miosis, ptosis, eyelid edema, lacrimation, nasal congestion, and rhinorrhea
  - similar to paroxysmal hemicrania, which goes through bouts of 2-30 minute attacks
  - only responds to indomethacin!
- May be primary or secondary, usually primary
- episodic migraine and tension headaches can transform into this
  - promoted by medication overuse
- Causes: disrupted sleep regulation, sleep apnea, insomnia
- Treatment:
  - give bridge therapy when d/c analgesic that has been overused

15.12.5 Cluster Headaches
- Characterized by unilateral excruciating, steady pain in the eye, periorbital region, or temple
- increased sweating on ipsilateral side of face
- lasts 15-180 minutes untreated and typically occurs every other day, or up to 8 attacks per day
- usually occurs in bouts lasting for weeks or months following by remission for months or years
- More common in spring and fall
- Can be precipitated by sleep, occurring 90 minutes after falling asleep
- More common in men
- Presentation: patients often complain of “worst headache of life”
- Diagnostic criteria: 5+ attacks along with at least 1 of the following:
  - ipsilateral conjunctival injection and/or lacrimation
  - ipsilateral nasal congestion or rhinorrhea
  - ipsilateral eyelid edema
  - ipsilateral forehead and facial sweating
  - ipsilateral miosis or ptosis
  - a sense of restlessness or agitation
- Treatment:
  - abortive therapy:
    - 100% O2 on a non-rebreather @ 6-12L/min for 15 min
    - subq sumatriptan
    - nasal sumatriptan or zolmitriptan
    - dihydroergotamine: IV, sublingual, or rectal
    - nasal lidocaine
  - prophylaxis:
DOC is verapamil: remember it takes 8 weeks to work
- lithium
  - big side effects
- ergotamine: can be used for brief periods sublingually or injected to prevent nighttime attacks
- corticosteroids: prednisone taper over 2-3 weeks
  - takes 1-2 days to work
  - headaches may recur after d/c of therapy

- nerve block

15.12.6 Thunderclap Headache
- Presentation: severe headache of abrupt onset, “worst headache of life”, mimics pain of ruptured cerebral aneurysm
- pain from 1 hour to 10 days
- Treatment: send to ER no matter what to rule out subarachnoid hemorrhage

15.12.7 Mass Lesions and Headache
- 1/3 of patients with an intracranial mass will have headache as a symptom
- Presentation:
  - pain stays in same location and progressively gets worse
  - subtle changes in mental status
  - increased ICP when laying down or bearing down

15.13 Peripheral Neuropathies
15.13.1 Background
- Physiology
- neuronal APs are mediated by Na
- NTs at the synapse:
  - motor/sensory: nicotinic Ach, L-glutamate, GABA
  - homeostatic: muscarinic Ach, serotonin, histamine, adenosine
- Classification of peripheral neuropathies:
  - by location: mononeuropathy vs polyneuropathies
  - by course of disease:
    - acute: vasculitic, toxic, porphyria, AIDP/GBS
    - chronic: diabetic, uremic, HIV, CMTD
  - by pathophysiology:
    - axonal: normal or slightly slowed conduction velocity
    - demyelinating: slow or absent conduction velocity
    - vasculitic: normal or slightly slowed conduction velocity
    - mixed pattern
- by cause: hereditary, physical, endocrine, infectious, inflammatory, toxic, paraneoplastic, critical illness
  - there are 1,000,000 ways to get a peripheral neuropathy!
- Common neuropathic presentations:
- motor: weakness, incoordination or ataxia, muscle wasting
- sensory: numbness, tingling, loss of sensation, pain, ataxia
- autonomic: dizziness, lightheaded, loss of consciousness, exercise intolerance, difficulty digesting foods, constipation, urinary symptoms, sexual dysfunction, visual symptoms
- Important components of the complete history:
- allergies
- meds: HIV, chemo
- PMH: diabetes, hypothyroidism, sarcoid, amyloid, uremia, anemia, liver failure, cancer, previous radiation, recent infection, nutritional deficiencies
  - recent surgeries
FH: neuropathy, gait problems, foot deformities, similar symptoms
SH: alcohol use, exposure to toxins, occupational activities
comprehensive ROS needed
PE: vitals, HEENT, CV, pulm, abdominal, complete neuro, derm
Investigation:
formation of differential diagnosis:
  - try to localize the lesion
    - unilateral extremity affected
    - symmetric disease
    - portion of limb or trunk affected
    - dermatome or myotome affected
  - determine pathophysiology
    - axonal: sensory symptoms > motor symptoms, greater distal weakness, decreased DTRs
    - demyelinating: motor symptoms > sensory symptoms, greater proximal weakness, decreased or absent DTRs
    - vasculitic: varied clinical features
    - mixed: varied clinical features
  - determine pattern of nerve involvement
    - if focal:
      - acute, EMG/NCS needed
      - subacute or chronic, EMG/NCS needed
      - if multifocal, EMG/NCS needed
    - if symmetric, EMG/NCS needed
    - if axonal or demyelinating, unusualness of features determines referral
    - if demyelinating, neuro consult needed
- diagnostics:
  - common tests: EMG/NCS, B12 levels, CBC, glucose tolerance, rapid plasma reagin, CMP, serum protein electrophoresis, thyroid function tests
  - tests for select cases: anti-Hu, ESR, ANA, RF, SS-A, SS-B, genetic studies for HMSN, HIV, Lyme, phytanic acid, 24 hour urine for heavy metals, CSF, nerve biopsy
up to 1/3 of patients with neuropathy remain undiagnosed

15.13.2 Single Peripheral Mononeuropathies
A.) Carpal tunnel syndrome: compression of median nerve
- risk factors: repetitive wrist motion, pregnancy, diabetes, rheumatoid arthritis, wrist injury, inflammatory tenosynovitis, myxedema, localized amyloidosis, sarcoidosis, acromegaly, hyperparathyroidism
- presentation: median nerve distribution, early pain/burning/tingling, later weakness/thenar atrophy, worse at night
- atypical: proximal radiation
- investigation:
  - Phalen’s, Tinel’s
  - EMG/NCS rarely indicated
- treatment: want to relieve pressure on the median nerve
  - conservative: modify hand activities, extensor wrist splint for a month, carpal bone mobilization, yoga
  - invasive: steroid injection, surgical decompression
B.) Ulnar neuropathy: stretching or compression of ulnar nerve
- may be caused by cubital tunnel syndrome or Guyon’s canal syndrome
- risk factors: pressure, trauma, bone spurs, congenital tumors or cysts
- presentation: early pain/burning/tingling, later weakness of hand and forearm
- worsened by elbow flexion (cubital tunnel) or wrist extension (Guyon’s) at nighttime
• atypical: proximal radiation
• investigation: EMG/NCS can help differentiate site of lesion
• treatment: want to relieve pressure on ulnar nerve
  • conservative: modify elbow or wrist activities, extensor splint at nighttime, NSAIDs
  • invasive: surgical nerve transposition or ligament release
    o can’t do steroid injections due to high risk of nerve injury!

C.) Radial neuropathy: stretching or compression of the radial nerve

![Radial Nerve Image]

• risk factors: injury to the axilla (crutches), Saturday night palsy (falling asleep on outstretched arm), wrist restraints, humeral fx
• presentation: motor deficits > sensory, weakness on finger/wrist/forearm extension, weakness on external rotation of the arm, forearm atrophy
• investigation: EMG/NCS, x-ray of shoulder + humerus
• treatment:
  • patient education & behavioral changes, braces, splits, PT/OT
  • surgery

D.) Meralgia paresthetica (Bernhard-Roth syndrome): compression or stretching of the lateral femoral cutaneous nerve

• a sensory nerve
• risk factors: obesity, diabetic peripheral neuropathy, pregnancy, hyperextension of the hip, lumbar lordosis, tight clothing
• presentation: pain, paresthesia, numbness on outer aspect of thigh
• usually unilateral, sometimes relieved by sitting
• no motor symptoms
• further investigation by EMG/NCS rarely indicated
• treatment: not always needed as symptoms can resolve spontaneously
  • anticonvulsants, hydrocortisone injection, nerve decompression by transposition

E.) Femoral neuropathy: compression or stretching of the femoral nerve

• risk factors: lithotomy position (pressure on inguinal ligament), diabetic peripheral neuropathy, retroperitoneal neoplasm or hematoma, pelvic fx, nerve trauma from femoral artery catheterization
• presentation: weakness and atrophy of quads, buckling of the knee, sensory deficits over thigh and leg to the medial malleolus, depressed or absent patellar DTRs
• investigation: EMG/NCS, CT, MRI
• treatment: aimed at etiology
  • splints and braces
  • PT
F.) Sciatic nerve palsy (sciatica): stretching or compression of the sciatic nerve
- causes: misplaced deep IM injections, trauma to butt/hip/thigh, piriformis syndrome, hip replacement surgery, pelvic injury, degenerative disk disease, spinal stenosis, CNS or PNS tumor, lumbar disc herniation
- presentation:
  - weakness with leg flexion/foot dorsiflexion/foot eversion, depressed or absent ankle DTRs
  - sensory deficits on the posterior thigh, leg, and foot
    - tingling, burning, or lanceting
    - aggravated by prolonged sitting or standing, nighttime, when sneezing, coughing, or laughing
- patients can usually draw a line down affected dermatome to help the provider localize which nerve root is being impinged
- investigation:
  - EMG/NCS to distinguish from peroneal neuropathy
  - x-ray of spine, pelvis, hip, femur
- treatment: based on cause
  - patient education and behavioral changes
  - anti-inflammatory meds
  - PT
  - surgery

G.) Peroneal (common fibular) nerve palsy: stretching or compression of the peroneal nerve
- may be caused by crossing legs for a long period of time, trauma or injury to the knee, fracture of the fibula, use of tight casts on the lower leg, wearing high boots, knee positions during deep sleep or coma, knee surgery
- presentation:
  - motor deficits: weakness on dorsiflexion and foot eversion
  - sensory: paresthesias or sensory loss on anterolateral calf and top of foot
- investigation:
  - diagnosis is usually clinical
  - must distinguish from sciatic nerve palsy (EMG/NCS)
- treatment: based on cause
- patient education and behavioral changes
- anti-inflammatories
- PT
- splints and braces

H.) Tibial neuropathy:

I.) CN VII (facial nerve) palsy (Bell’s palsy): impairment due to compression, ischemia, or inflammation

- causes: mostly idiopathic, can also be HIV, sarcoid, Lyme, tumors, reactivation of HSV
- risk factors: diabetes, pregnancy
- presentation: abrupt onset that may progress over several days
  - motor deficits: facial paralysis, ptosis
  - sensory disturbances: ear pain, taste disturbance, hyperacusis
- investigation:
  - must distinguish peripheral cause from central
    - peripheral cause will result in complete paralysis of frontalis muscle
    - central cause will result in partial sparing of frontalis because there is bicortical input from the brain, so half the input is still functioning
  - EMG/NCS will indicate severity but won’t guide treatment
    - treatment: controversial
      - prednisone taper
      - artificial tears
      - NOT HELPFUL: surgical procedures or nerve decompression
    - prognosis: 60% recover completely without treatment, 10% have permanent dysfunction
      - best indicator of severity of palsy is progress in first 2-3 days
      - poor prognosis with complete palsy at onset, advanced age, hyperacusis, severe initial pain

15.13.3 Multiple Peripheral Mononeuropathies

A.) Discogenic neuropathies: caused by impingement of a spinal nerve by lateral disc protrusion or arthropathy
- presentation: motor, sensory, and autonomic dysfunction
  - location and severity differs based on nerves involved and degree of impairment
- investigation:
  - neuroimaging: MRI, CT myelogram
  - EMG/NCS
- treatment:
  - rest, immobilization
  - PT
  - surgical intervention

B.) Plexopathies: compression or invasion of a neuronal plexus (cervical, brachial, lumbar, sacral)
- causes: trauma, diabetic peripheral neuropathy, congenital anomalies, neoplastic involvement, radiation injury
• presentation: motor, sensory, and autonomic dysfunction that corresponds with nerves involved and degree of invasiveness
• investigation: labs, EMG/NCS
• treatment depends on cause
• prognosis is variable

C.) Mononeuritis multiplex

15.13.4 Peripheral Polyneuropathies

A.) Hereditary peripheral polyneuropathies
• Charcot-Marie-Tooth disease type (HMSN): inherited disorder of nerves characterized by loss of muscle tissue and touch sensation
• results in myelin damage (type I) or axonal damage (type II)
• usually inherited autosomal dominant but can be sporadic X-linked recessive
• onset in childhood or early adulthood
• presentation: slow progression
  o motor deficits > sensory
    ▪ muscle wasting and secondary weakness: pes cavus, hammer toes, foot drop, slapping gait
    ▪ postural tremor
    ▪ lower extremities more affected than upper
    ▪ deficits less prominent in type II
  o numbness and vibratory sensory losses
  o depressed or absent DTRs
  o kyphosis
  o peripheral nerve hypertrophy (not present in type II)
• investigation:
  o nerve or muscle biopsy is confirmatory
  o genetic testing
  o EMG/NCS to differentiate type I from type II
    ▪ type I □ reduced conduction velocity
    ▪ type II □ normal or slightly reduced conduction velocity, reduced or absent sensory action potential
• treatment:
  o no cure, goal is to maintain independent functioning
  o casts, braces
  o orthopedic surgery
  o PT & OT

• Dejerine-Sottas disease (aka Charcot-Marie-Tooth disease type III or HMSN III): abnormal phytanic acid metabolism leads to progressive demyelinating neuropathy
• onset in infancy or childhood
• presentation:
  o motor weakness and ataxia
  o loss of sensation
  o global hypoactive DTRs
• investigation:
  o labs: elevated CSF protein
  o EMG/NCS: reduced motor velocity and sensory conduction
• treatment is supportive
  o plasmapheresis to remove excess phytanic acid
  o dietary restriction: cow products, fish

• Refsum disease (aka Charcot-Marie-Tooth disease type IV or HMSN IV): progressive demyelinating neuropathy
• onset in early childhood
• presentation: same as type III plus retinitis pigmentosa
• investigation:
o labs: normal CSF protein
o nerve biopsy
o EMG/NCS same as type III

- treatment is supportive
- Friedrich's ataxia:
- porphyria:

B.) Endocrine peripheral polyneuropathies
- diabetic peripheral neuropathy: axonal involvement that can affect DM1 or DM2
  - presentation can take many forms:
    o distal symmetric polyneuropathy such as stocking-glove paresthesias
      - sensory proceeds motor disease
      - lower extremity disease precedes upper extremity disease
    o isolated peripheral neuropathy
      - focal, sudden onset, complete recovery in 6-12 weeks
    o painful diabetic neuropathy
    o autonomic neuropathy
  - investigation:
    o Semmes Weinstein filament test on bottom of feet
    o lab confirmation of DM
    o EMG/NCS showing normal to mildly slow conduction
  - treatment: symptomatic, glycemic control won't improve symptoms but will delay progression
  - complications:
    o Charcot arthropathy: arthritic foot change from peripheral neuropathy, autonomic dysfunction, and trauma
      - acute presentation: pain and swelling
      - chronic presentation: "rocker bottom" deformity, ulceration
      - diagnosis is clinical
      - treatment: daily foot care, custom molded shoes, management of ulcers
  - uremic peripheral neuropathy: probably from a combination of metabolic and toxic factors
  - presentation: symmetric sensory-motor deficits
    o lower extremities > upper
    o distal > proximal
    o severity correlates with degree of renal insufficiency
  - investigation:
    o labs: CMP
    o EMG/NCS
  - treatment: supportive/symptomatic, long-term dialysis, kidney transplant
  - alcohol and nutrition deficiency peripheral neuropathy: neuronal dysfunction secondary to inadequate nutrition
    - axonal > myelin involvement
    - presentation: slow progression of distal symmetric polyneuropathy
      o sensory precedes motor involvement
      o lower extremity precedes upper involvement
      o sensory disease: cramps, painful paresthesias, tenderness
      o CNS symptoms often precede PNS symptoms
  - investigation:
    o labs: B12, CBC, LFTs
    o EMG/NCS
  - treatment: stop alcohol, nutritional supplementation, management of malabsorption, PT
  - paraproteinemias

C.) Infectious peripheral polyneuropathies
- acute inflammatory demyelinating polyneuropathy (Guillain-Barre syndrome): an immune-mediated progressive demyelinating neuropathy
- subtypes: acute motor axonal neuropathy and acute motor-sensory axonal neuropathy
- risk factors: recent infective illness or immunization, recent surgery
• presentation:
  o motor deficits: symmetric weakness
    ▪ proximal precedes distal
    ▪ lower extremities precede upper
    ▪ advanced: respiratory muscle compromise, CN involvement
  o sensory deficits: paresthesias, loss of sensation
    ▪ distal precedes proximal
  o global hyporeflexive DTRs
  o autonomic dysfunction: tachycardia, cardiac irregularities, BP changes, pulm dysfunction, loss of rectal tone

• investigation:
  o elevated CSF protein 2-3 weeks after onset
  o EMG/NCS showing demyelination with delayed conduction 3-4 weeks after onset

• treatment indicated for gait or respiratory impairment or progressive weakness
  o plasmapheresis
  o IV Ig
  o mechanical ventilation

• prognosis: mortality rate of 10%, lasting disability in 10-20% of cases, can become chronic

• HIV-related peripheral neuropathy: may be caused by infection of nerve root ganglion or involvement with CMV
  o presentation may be acute, subacute, or chronic
    ▪ motor deficits > sensory, may also have autonomic dysfunction
  o treatment is supportive

• leprosy
• Lyme
• sarcoidosis
• polyarteritis:
• rheumatoid arthritis

D.) Inflammatory peripheral polyneuropathies

E.) Toxic peripheral polyneuropathies
  • from exposure to neurotoxins such as industrial agents, pesticides, heavy metals, medications
  • presentation: motor, sensory, autonomic, and mixed features depending on agent
  • treatment: prevent further exposure, PT, OT, time

F.) Metastatic peripheral polyneuropathies
  • result of invasion of plexus or peripheral nerves by malignant cells
  • investigation:
  • EMG/NCS
  • MRI for soft tissue
  • treatment: radiation, less commonly surgery

G.) Paraneoplastic peripheral neuropathies
  • immune-mediated response to neoplasm
  • investigation: paraneoplastic antibody panel
  • treatment: management of primary tumor

G.) Peripheral polyneuropathies as a result of critical illness
  • a result of axonal dysfunction, mechanism uncertain
  • presentation:
    • associated with ICU admission, sepsis, multi-organ dysfunction, and difficulty weaning from ventilator
    • motor deficits > sensory
    • weakness and muscle wasting
  • investigation: EMG/NCS
  • treatment is supportive
16 Oncology Exam Notes

16.1 Imaging Studies in Oncology

- **Spatial resolution**: ability to define objects of a certain size; greater the spatial resolution, greater the detection of smaller objects
- **Contrast resolution**: ability to resolve differences between tissue types (tumor vs organ)

16.1.1 Radiographs

- 5 basic densities: air, fat, soft tissue/water, bone, metal
- Good spatial resolution
- Contrast resolution depends on differing densities of objects of interest
- Detection of cancer
  - when mass is surrounded by a different density material
    - ex. lung or breast masses
  - with enlargement of a normal appearing structure or displacement of near structures
    - ex. renal, pelvic, or liver masses
  - destruction of a structure
    - ex. bone masses
  - detection of malignancy-associated densities
    - ex. calcification patterns in breast cancer

16.1.2 Sonography

- Reasonable contrast and spatial resolution
- Allows for detection of blood flow
- Limitations based on skill of sonographer, patient size, and inability to transmit signals through air
- Detection of cancer

16.1.3 Computed Tomography

- Generates sections of tissue with varying densities represented
- Better contrast resolution than radiographs
- Improved contrast resolution over radiographs, can use injected contrast to enhance (usually always used for malignancy imaging)
- allows for identification of vascular structures
- tumors are typically hypervascular and will enhance more than a solid organ (but can be opposite this also)
- timing of imaging after contrast injection needs to be concerted to optimize tumor detection in organ of interest

16.1.4 Magnetic Resonance Imaging

- Uses magnets to evaluate proton spin characteristics of tissues
- Excellent contrast resolution
- injected contrast also used for evaluation of a malignancy

16.1.5 Nuclear Medicine

- Different in that you are imaging physiology vs structures
- Radioactive material is injected into the patient and cameras detect emission from the patient
- Material used varies and depends on area being imaged
- planar imaging: bone scans, parathyroid scans
- SPECT imaging: MIBG, octreotide scans, parathyroid scans
- PET scans: most malignancies
red blood cell study tags RBCs to look for liver mass vs hemangioma

16.1.6 Which Study to Use

- depends on what you want to do, are you just screening for a malignancy, does the patient have symptoms with an unknown cause, or does the patient have a known malignancy that you want to stage?

A.) Screening test: must meet the guidelines for a good screen

B.) Symptomatic investigation: should use ACR appropriateness criteria to decide which study is best, which takes into account amount of ionizing radiation involved

- CNS symptoms: headache, neurologic deficit, new onset seizures
- headache CT scan (frequently negative)
- chronic headache with new features MRI with or without contrast
- suspected hemorrhage: CT without contrast
- beware of tumor mimics: hemorrhagic infarction, abscess, tumefactive MS, aneurysm
- musculoskeletal tumors
- bone responds to pathology by breaking down or forming more bone
- lytic bone lesion could be primary tumor, mets, cyst, tumor from hyperparathyroidism, or infection
- benign and malignant lesions can both result in pathologic fracture
  - imaging options:
    - CT
    - MRI: best for anything you think is malignant, can examine any soft tissue components of bone lesions

- lung tumors
- CXR for initial imaging
- CT looking for other things sometimes incidentally detect nodules follow Fleischner Society recs for follow up
  - takes into account level of patient risk for lung cancer
  - solitary pulmonary nodule: round opacification < 3cm, hard to determine benign vs malignant on film
    - stability over 2 years suggests benign (except for bronchoalveolar cell carcinoma)
  - ground glass nodule: area of opacification but can still see underlying lung parenchyma
    - will be persistent if it is a neoplasm or focal fibrosis
    - will resolve if it is infectious, inflammatory, or hemorrhagic in nature

- gastrointestinal tumors: liver, pancreas, esophagus, stomach, bowel
- CT or MRI for specific organs (used more for staging)
- lower stage/mucosal based lesion: CT less specific than endoscopy
- suspect esophageal mass must use US!
- suspect gastric mass: endoscopy best, CT is very subtle
- genitourinary tumors: kidney, adrenal gland, bladder, ureter
- US best for initial assessment of kidney
- CT good for complex cysts
- MRI good for troubleshooting (or staging)
- remember pyelonephritis can look like a mass!
- adrenal adenoma: a common, benign tumor that may be hormonally active; can be confused for metastatic disease
  - visualized on MRI or CT
- ovarian or endometrial mass
- US good for screening
• breast mass
• mammography with 2 views (top/bottom and oblique)
  o additional views + US ordered for suspicious finding
  o mass only if it is present on 2 views
    ▪ “asymmetric density” if only present on 1 view
  o calcifications: most are benign, but they become suspicious when very small, tightly clustered together, or irregular in size and shape
  o only sign of mass may be architectural distortion: can’t see the mass itself but can see the lines of other tissue displaced by it or pulled in another direction
  o radiologist classifies result based on Breast Imaging Reporting and Data System (BIRADS) from 0-6 (2 view screening should be 0-2)
    0 = needs further assessment
    1 = normal
    2 = benign
    3 = probably benign
    4 = suspicious abnormality □ biopsy recommended
    5 = high suggestive of malignancy
    6 = known malignancy previously proven by biopsy
  o US supplements the mammogram and further characterizes the lesion on size, border, composition
    ▪ however, fat necrosis can look worrisome on US!
  o MRI used for screening high risk patients, screening contralateral breast in newly diagnosed breast cancer, neoadjuvant therapy monitoring, monitoring for recurrent disease, evaluating metastatic disease with suspected breast primary

C.) Staging: use cancer-specific guidelines

• CXR: evaluation of lung mets
• CT:
  evaluation of brain/liver/lung mets, can also evaluate tumor invasion or nodes
    o add contrast to see spine mets
• GI staging
• endoscopic US: evaluation of tumors and nodes for gastric, pancreatic, or colorectal masses
• PET scan: a full-body survey of cells utilizing glucose, with hypermetabolism corresponding to brightness of image
  limitation: inflammation or infection are also metabolically active processes
• used for evaluation of melanoma or lung mets
• bone scan: evaluates bony metastatic disease such as osteosarcoma
• endoscopy with or without ultrasound
• MRI
• GI staging
• evaluation of extent of breast cancer
• mammogram

16.2 Radiation Therapy

16.2.1 Background

• Application:
  60% of patients receiving radiation therapy for cancer have breast, prostate, or lung cancer
  used for treatment of cancer as well as some benign conditions
• Mechanism:
  ionization radiation can be x-rays (people made via electrons striking target) or gamma rays (nuclear decay)
    o both are photons = exponential absorption, deep penetration
    o electron bombardment better for superficial sites like skin
• radiation therapy causes direct DNA damage (30% of the time) and produces free radicals from water in the area of the tumor (70% of the time) which then damage the DNA
• free radicals will live longer in the presence of oxygen
o rapidly proliferating cells and those without adequate DNA repair mechanisms are preferentially damaged by the radiation - cell cycle arrest and death
   ▪ killing is logarithmic vs 1:1 = increased delivery of radiation increases killing exponentially
     • problem is that many tumors are hypoxic so they may require greater dose to kill
o but normal cells will also be damaged
   ▪ rapidly growing tissue of the mucosa, marrow, and skin will die early in treatment
   ▪ slower growing tissue of the lung, CNS, muscle, nerve, and vasculature will die later
• goal is to balance killing of tumor cells with sparing of normal tissue
• target tumor tissue
• use largest total dose tolerated, but break it up into small fractions
  o but the greater the fractionation, the lesser the tumor kill
  o smaller dose per fraction preferentially spares late-responding tissues
• treat area over shortest time possible
• want normal cells to be able to repair sublethal damage, reassort into normal cell cycle, repopulate the irradiated area, and establish reoxygenation
• Dose delivered is based on complex calculations

16.2.2 Techniques of Radiotherapy
advances leading to these kinds of therapies have decreased the need for fractionation of treatments, as normal tissue is greatly spared

A.) 3D conformal radiotherapy: makes use of CT images going in direction of beam when the treatment volume conforms to the shape of the tumor, the relative toxicity of radiation to the surrounding normal tissues is reduced, allowing a higher dose of radiation to be delivered to the tumor than conventional techniques would allow
• can also use PET scans to help generate 3D model
• radiation oncologists look at location of tumor in cm and volume to determine how many radiation beams will be needed, orientation/type of beams, dosing plans
• clinical target volume: area of tumor to treat that we can and can’t see
  • perfectly round target want to go through least amount of normal tissue
  • non-spherical target treating along the long axis of the target is better, regardless of how much normal tissue is gone through?
• target near critical structure reorient beams to best avoid critical structure
  o ex. whole breast radiotherapy: orient beams to miss heart and lungs
• maximum dose is area where beams intersect
B.) Intensity-modulated radiation therapy (IMRT): an advanced type of high-precision radiation that is the next generation of 3D conformal radiotherapy; improves the ability to conform the treatment volume to concave tumor shapes via computer-controlled x-ray accelerators - Both 3DCRT and IMRT make use of image-guided radiotherapy: using real-time imaging to make real-time beam adjustments
  -can visualize tumor, match imaging with previous imaging, and adjust patient position or beams to refine target
C.) Stereotactic radiation: a specialized type of external beam radiation therapy that uses focused radiation beams targeting a well-defined tumor using extremely detailed imaging scans
• stereotactic radiosurgery (SRS): using a stereotactic radiation treatments for the brain or spine to inactivate or eradicate a target without needing to make an incision
• requires team of neurosurgeon, radiation oncologist, and medical physicist
• requires 1-5 sessions
• precision may be enhanced with imaging and robotics
• brand-name systems include the GammaKnife, CyberKnife, and Novalis Tx
• indications for intracranial SRS: brain mets, meningiomas, acoustic neuromas, AV malformations, chemodectomas, recurrent gliomas
  o studies indicate increased survival vs using whole brain radiotherapy
16.3 Chemotherapy

16.3.1 Background

- Chemotherapy is based off of the principle that faster growing cells are more sensitive to cytotoxic drugs
- not as useful for larger tumors, where fewer cells are actively growing
- good response to chemo with leukemias, lymphomas, germ cell tumors, breast cancers
- poor response to chemo with pancreatic cancer, melanoma, soft tissue sarcomas
- Factors influencing success of chemotherapy include tumor type, tumor burden, genetics/tumor resistance, and drug availability
- Combination therapy increases proportion of cells killed per cycle over monotherapy
- reduces drug resistance
- may provide drug synergy
- best drugs have minimal overlapping toxicities
- Dosage of chemo is most limited by myelosuppression effects

16.3.2 Traditional Chemotherapy

- Acts on different parts of the cell cycle to ultimately attack rapidly dividing cells
- cell cycle phases:
  - G0 = resting/gap phase
  - G1 = post-mitotic phase: enzymes for DNA synthesis are manufactured, and RNA synthesis is occurring
  - S = synthesis phase: DNA is replicated in preparation for mitosis
  - G2 = pre-mitotic phase: production of RNA proteins for cell division
  - M = mitotic phase: active cell division
- cell cycle-specific drugs: exert their effects within a particular cell cycle phase
  - these drugs are schedule-dependent
  - nadirs in 7-14 days, with recovery in 7-21 days
  - provide the greatest tumor cell kill
- kinds:
  - antimetabolites: S phase specific; incorporate into cell to make it unable to divide
    - capecitabine: cutaneous side effects
    - methotrexate: toxicity issues, will build up in 3rd spacing as it competes with many other drugs such as NSAIDs for metabolism
    - gemcitabine: risk of thrombocytopenia
    - fluorouracil: GI effects
    - fludarabine: side effects: myelosuppression
  - camptothecins: plant alkaloids; act in S phase to inhibit topoisomerase I (needed for DNA unraveling and rezipping)
    - irinotecan: diarrhea
    - topotecan: constipation
    - side effects: myelosuppression, alopecia
  - epipodophyllotoxins: plant alkaloids; act in G2/S phases to inhibit topoisomerase II
    - etoposide: myelosuppression, GI, hypotension (depends on freshness/temp of product), hypersensitivity
  - taxanes: plant alkaloids; act in G2/M phases to inhibit microtubules
    - paclitaxel:
    - docetaxel: risk of thrombocytopenia - side effects: myelosuppression, cutaneous, neuro toxicities, hypersensitivities
    - vinca alkaloids: plant alkaloids; act in G2/M phases to inhibit microtubules
    - vincristine:
    - vinorelbine: myelosuppression
    - vinblastine:
    - side effects: constipation, peripheral neurotoxicity
  - cell cycle nonspecific drugs: exert effects in all cell cycles, including the resting phase
these drugs are dose-dependent
nadirs in 10-14 days, with recovery in 21-24 days
best for treatment of tumors with few dividing cells
kinds:
  • alkylating agents: alkylate DNA
    • cyclophosphamide:
    • cisplatin:
    • carboplatin: risk of thrombocytopenia
    • oxalaplatin:
    • chlorambucil:
  • side effects: myelosuppression, renal, GI, hypersensitivities, secondary malignancies
  • antitumor antibiotics: from Streptomyces; bind DNA to cause breakage and also inhibit RNA synthesis
    • doxorubicin: side effect of cardiac toxicity (permanent), thrombocytopenia
    • bleomycin: side effect of pulmonary fibrosis
    • epirubicin: side effect of cardiac toxicity
    • idarubicin:
    • side effects: myelosuppression, GI, cutaneous
  • Endocrine therapy (hormonal therapy): given to block a hormone promoting the growth of the cancer
    • makes use of molecular profile techniques to specifically target cancers bearing receptors for certain hormones for more effective treatment that is individualized to the patient
    • multiple mechanisms, including stopping production of the receptor, blocking the receptor, or substituting chemically similar agents that will bind the receptor but can’t be utilized by the cancer cell
    • kinds:
      • antiestrogens
        • tamoxifen: increased risk of blood clots, increased risk of endometrial cancer
        • toremifene:
      • aromatase inhibitors: block conversion of androgens to estrogen
        • anastrazole:
        • letrozole:
        • exemestane:
        • contraindications: can’t use unless post-menopausal or have had ovaries artificially blocked
      • antiandrogens: inhibit the binding of testosterone to the androgen receptors in the prostate
        • bicalutamide:
        • flutamide:
        • nilutamide:
      • GnRH agonists: simulate continuous release of GnRH, which downregulates the release of LH and FSH due to negative feedback of deprivation of tumors of needed hormonal stimulation
        • leuprolide: bone mineral density loss
        • goserelin:
    • side effects for all: GI, gynecomastia, menstrual irregularity, libido changes, hot flashes, myalgias, bone pain

16.3.3 Targeted Chemotherapy: Other Cancer Tissue Characteristics That Can Be Targeted

1.) evasion of apoptosis
  • apoptosis-inducing drugs
    • ex. Velcade, Genasense
  • biologic therapy: uses the body’s immune system to fight the cancer by stimulating NK cells, T-cells, macrophages, or cytokine production
    • includes IFN, IL, monoclonal ABs, colony stimulating factors, gene therapies, or stimulating self-immune system against a cancer antigen
    • monoclonal antibodies: target cancer cells for immune destruction; less toxicity issues than traditional chemo
      • trastuzamab: anti-HER2+ breast cancer
      • cardiac toxicity
- **rituximab**: anti-CD20 non-Hodgkin’s lymphoma
- **bevacizumab**: anti-VEGF; effectiveness seems to vary by patient; high cost due to drug company
  - risk of bleeding or wound dehiscence
- **alemtuzumab**: anti-CD52 CLL
  - high rxn risk in the Carolinas!
- **cetuximab**: metastatic colon cancer
  - high rxn risk in the Carolinas!
- **panitumumab**: metastatic colon cancer
  - side effects: infusion reaction including anaphylaxis
- **conjugated monoclonal antibodies**: Abs attached to drugs, toxins, or radioactive substances to deliver them directly to the cancer cell
  - risk of increased toxicity

2.) self-sufficiency of growth signals
- small-molecule drugs to block specific enzymes or growth factor receptors
  - signal transduction (tyrosine kinase) inhibitors:
    - **imatinib**: used for CML, GI stromal tumors
    - **lapatinib**: used for HER2+ breast cancers
  - epidermal growth factor receptor blockers:
    - **gefitinib**: non-small cell lung carcinoma
    - **erlotinib**: non-small cell lung carcinoma
  - proteosome inhibitors:
    - **bortezomib**: multiple myeloma
      - side effects: skin, GI

3.) insensitivity to growth inhibition signals

4.) tissue invasion and metastasis

5.) sustained angiogenesis
- **antiangiogenesis agents**: inhibit vascular endothelial growth factor to rob cancer of nutrients
- available for metastatic colon cancers, and breast?, brain, lung, and renal cancers
- oral only

6.) unlimited reproduction

16.3.4 Chemotherapy-Induced Nausea and Vomiting
- Can be acute, delayed, or anticipatory
- Multifactorial in nature, not just the chemo, but the radiation, opioids, metabolic abnormalities, etc. too
- Best management is to treat prophylactically for entire duration of anticipated nauseous period
- Classes of antiemetics:
  - **serotonin antagonists**: relieve the nausea but may cause headache, diarrhea, or constipation
  - **phenothiazines**: block dopamine receptors
    - may cause sedation, hypotension
  - **corticosteroids**: mechanism unknown
    - side effects: insomnia, hyperglycemia, increased appetite, euphoria, agitation, anxiety
  - **cannabinoids**: mechanism unknown, but improves appetite and pain as well
  - **benzodiazepenes**: anxiolytic and sedative properties
    - side effects: sedation, hypotension, disinhibition, motor incoordination

16.3.5 Summary of Drug Side Effects
- Diarrhea with irinotecan, fluorouracil, topotecan, capecitabine
- Constipation with vincristine, vinblastine, vinorelbine
- Mucositis is common, manage by avoiding irritants
- Hypersensitivities with the monoclonal antibodies and bacterial antibiotics
• Cardiac toxicities with anthracyclines, trastuzumab

16.4 Introduction to Medical Oncology

• Cancer is the leading cause of death in Americans under age 85
• Top cancer types: lung, breast, prostate, colorectal, pancreas
• Neoplasm: an abnormal growth of tissue that may be benign or malignant
• Malignancy: a tumor that is malignant = can invade and destroy nearby tissue and can metastasize

16.4.1 Advances in Oncology

• Movement from inpatient to outpatient treatment
• Can be managed as a chronic disease
• Minimally invasive procedures for diagnosis and treatment
• Higher cure rates
• Improved symptom management □ better quality of life
• Prolonged life

16.4.2 Types of Cancer

• Carcinoma: cancer derived from epithelia (skin or internal organs)
• Sarcoma: cancer of a tissue derived from the embryonic mesoderm (bone, cartilage, fat, muscle, blood vessels, connective tissue)
• Leukemia: abnormal proliferation of malignant cells in peripheral Blood
• Lymphoma and myeloma: abnormal proliferation of malignant cells in the tissues, primarily the lymph nodes (bone in the case of myeloma); these are a solid tumor neoplasms
• CNS cancers

16.4.3 Tumor Markers

• Cellular products that can be helpful in detection, diagnosis, and therapeutic management of certain cancers
• May be present in blood, other body fluids, or in the tumor tissue
• Can be normal products that are over-expressed
• Can be produced by the body in response to malignant cells
• Not available for all cancers and no standardized method
• Information not taken into account in formal staging
• Downfalls: none are unique to cancer cells, different markers are found in different kinds of cancer while some are the same between cancers, sometimes the associated tumor marker is not elevated in a known cancer = can’t use them to rule out cancer, diagnose cancer, or identify a specific cancer!
• How to properly use tumor markers:
  • extremely high levels can be pathognomonic for a particular cancer
  • to confirm a diagnosis you already suspect through history, exam, and imaging
  • helps narrow your differential in cancer with unknown primary tumor
  • to help determine prognosis and treatment
  • some tumor markers are associated with a more aggressive course or higher relapse rate
  • some tumor markers that are tissue receptors can be a target for therapies
  • to evaluate how well a treatment is working
  • tumor markers should be low or undetectable if therapy is effective
  • best use is for patients with widespread disease
  • to follow treated cancer patients for disease recurrence
  • post-treatment levels can be used to establish baseline for surveillance
  • rise above baseline may alert to a recurrence faster than clinical symptoms or radiographic findings
  • use in screening
  • usually not good as they often lack enough sensitivity and specificity given the low prevalence of cancer in most populations
only used when early detection of the cancer improves prognosis and mortality
5 categories of tumor markers:
- **antigens (oncofetal proteins):** proteins normally found in larger amounts during fetal development
  - since cancers contain undifferentiated cells, they may express more fetal surface markers, and can manufacture increased quantities of antigen protein
  - **alpha-fetoprotein (AFP):** normally found in fetal GI tract but is increased in most patients with hepatocellular carcinoma
    - higher levels correlated to greater tumor burden
    - can be used as a screen for patients with high risk of developing HCC
    - caveat: can also be increased in patients with non-seminoma germline cancers
  - **Bence-Jones proteins:** urine electrophoresis protein used for detection and monitoring of multiple myeloma
    - amount of protein correlated to extent of disease
    - caveat: also elevated in leukemia, lymphoma, bone mets, high dose aspirin or penicillin
  - **cancer antigen 19-9 (CA-19-9):** useful in diagnosis, evaluation, and surveillance of pancreatic and hepatobiliary cancers
    - high levels in pancreatic cancer indicate unresectable disease
  - **CA-125:** elevated in most women with ovarian cancer, can be used for evaluation of therapy and surveillance
    - blood levels correlate to extent of disease
    - BAD as a general screen with a positive predictive value of 2%
  - **carcinoembryonic antigen (CEA):** produced by fetal GI tract but elevated in GI cancers, useful for determining extent of disease, prognosis, and evaluation of therapy
    - can also be used to evaluate other malignancies such as breast, pancreas, hepatobiliary, and small cell lung cancers
    - caveat: elevated baseline levels in smokers
  - **prostate specific antigen (PSA):** screening test for early detection of prostate cancer with high sensitivity but low specificity
    - levels correlate to tumor size and can be used evaluate therapy and post-therapy monitoring
    - caveats: not all prostate cancer is clinically significant
  - **HER2:** gene encoding synthesis of epidermal growth factors, protein levels are increased in more aggressive breast cancers = useful in making treatment decisions
    - can be used as a target for trastuzumab
  - **CA 15-3:** blood levels elevated in many patients with metastatic breast cancer, can be used to monitor therapy
  - **CA 27.29:** blood levels elevated in some patients with early breast cancer and in many patients with metastatic breast cancer, can be used to monitor therapy
- **enzymes:** blood levels may be increased in presence of malignant tissue
  - measured by immunoassay
  - ex. prostatic acid phosphatase, galactosyl transferase II
- **hormones:** can be increased levels of hormone normally secreted by a tissue, or ectopic secretion of hormone by a tumor
  - **paraneoplastic syndrome:** a disease or symptom that is the consequence of the presence of cancer in the body, but is not due to the local presence of cancer cells
    - mediated by hormones or cytokines excreted by tumor cells or by an immune response against the tumor
  - **beta-HCG:** glycoprotein produced by placental tissue in pregnancy, but also produced in hydatidiform mole of the uterus, choriocarcinoma of the uterus, germ line tumors of the uterus, germ cell neoplasms in males
    - caveat: also elevated in hepatoma
  - others: human calcitonin
- **oncogenes:** genes that are useful in fetal development but trigger tumor growth in mature cells
  - **BRCA1 or BRCA2** indicate increased susceptibility to breast and ovarian cancer in women, and prostate or colorectal cancer in men
o others: Philadelphia chromosome genes

- **tissue receptors:** cell surface proteins that affect the rate of tumor development by binding hormones and growth factors
  - can be present on tumor tissue or secreted into blood
  - **estrogen receptor assay (ER assay):** a tissue receptor that can be targeted for hormonal therapy and helps determine prognosis of breast cancer
    - ER+ tumors are twice as likely to respond to hormonal therapies
  - **progesterone receptor (PR assay):** a tissue receptor that can be targeted for hormonal therapy and helps determine the prognosis of breast cancer
    - more frequently + in postmenopausal breast cancer patients
  - greatest to least response to hormonal treatment: ER+/PR+, ER-/PR+, ER+/PR-, ER-/PR-

- others: EGFR

### 16.4.4 Cancer Prevention

- **Primary prevention:** keeps disease from occurring by reducing exposure to risk factors - lifestyle modification, removing environmental risks, or giving drugs to prevent cancer from developing
- ex. HPV and Hep B vaccines
- drugs are used for high risk populations
  - ex. selective estrogen receptor modulators like tamoxifen to reduce risk of breast cancer
  - ex. oral contraceptives
  - ex. sunscreen
- prophylactic surgery for patients with hereditary cancer syndromes
- **Secondary prevention:** detects a disease before it is symptomatic, when early intervention can change the course of the disease
- proven screens: mammography, pap smear, colonoscopy

### 16.4.5 Diagnosing Cancer

I.) **History & physical exam**
- ask about weight loss, fatigue, pain, SOB, blood in stool
- examine for masses, bumps, sounds, reactions, appearances

II.) Order imaging if needed — suspicion of diagnosis

III.) Histologic diagnosis made by a pathologist — confirmation of suspicion
- determines type of cancer
- therapy can’t proceed until this information is obtained
- remember that benign bone lesions are difficult to distinguish from malignant under the microscope, so make judicious use of biopsies here
- methods:
  - **fine needle aspiration:** a small bore needle is introduced into a mass and cells are removed for microscopic evaluation
    - CT guided for lung or abdominal soft tissue masses
    - US guided for breast or testicular masses
    - endoscopic US for pancreatic or rectal masses
    - a very efficient procedure with same-day results, but can’t do a lot of staining techniques with a sample like this = if you need to know specific tumor markers present, do a tissue biopsy instead
    - pros: minimally invasive, low risk
    - cons: small sample size, does not reveal extracellular architecture, can get nonrepresentative samples
  - **punch biopsy:** under local anesthetic, a circular needle is used to excise a full-thickness piece of tissue for evaluation
    - procedure of choice for suspected melanomas, as the seriousness of the tumor corresponds to the depth of the tumor penetration = can’t do shave biopsy!
    - pros: can be done in clinic, provides full tissue architecture
    - disadvantages: limited application
incisional or excisional biopsy: requires OR
  o US guided for thyroid, breast, renal, or liver biopsies
  o pros: best tissue for diagnosis, excision biopsy may be therapeutic
  o cons: most invasive with most risk for bleeding and infection
  ***sometimes tissue diagnosis is unnecessary before proceeding with surgery, as in pancreatic mass vs abscess

IV.) Staging of cancer: determine local vs systemic disease, as cancer may spread lymphatically to regional nodal basins or hematologically to the lung, liver, brain, or bones
  • get imaging: site of primary tumor will guide imaging studies to look for metastases
  • formal staging by tumor/node/metastasis method to guide treatment and prognosis makes use of information gathered from imaging and/or pathology report
  • T = size and extent of invasion of primary tumor
    o Tis = tumor in situ (tumor has not moved, sometimes called “precancer”)
    o T1-T4 based on size or invasion of adjacent structures
  • N = number and location of involved regional lymph nodes
    o Nx = can’t assess lymph node involvement
    o N0 = no nodes involved
    o N1-N3 based on levels of lymph nodes
    o lymph node mets will be treated differently than other mets
  • M = presence or absence of distant mets
    o Mx = can’t assess presence of mets
    o M0 = no mets
    o M1 = presence of mets
  • use this information to come up with numerical stage
  • stage I would be early, T1 or T2 tumors, N0
  • stage II would be T1/T2 + N1, or T3N0
  • stage III would be T1/T2/T3 + N1-N3
  • stage IV is any metastatic disease

16.4.6 Initial Oncology Visit
  • What happens: tissue diagnosis, staging, discussion of treatment options, referral for surgery or radiation, clinical trials discussion
  • Treatment goal may be cure, control, or palliation
  • Must take into account patient’s performance status (organ functioning and whether or not they will be able to handle or survive certain therapies)
  • especially important if treatment is palliative vs curative
  • poorly functioning lungs/liver/kidneys = poor performance, may not derive benefit from therapy
  • clinical measures of performance status:
    o Karnofsky scale: 10-100, with 10 being close to death and 100 being no evidence of disease with ability to perform ADLs
    o Zubrod scale: 0-4, with 0 being ability to perform ADLs, and 4 being bedridden
  • Must also think about patient’s support system and social situation, and how that will affect treatment
  • Choosing therapy: regional or systemic?
  • considerations:
    o remember that established data will be far behind the cutting edge therapies
    o tumor type, growth rate, location, and invasiveness
    o metastatic potential of tumor
    o quality of life issues as a result of treatment
  • regional therapy: treats cancer confined to a certain area; includes radiation and surgery
  • brachytherapy: intraoperatively sealing a radiation source near the site of the tumor
    o surgery: removes the primary tumor and allows for biopsy or remove regional nodes for complete pathologic staging
      • extent of resection will depend on preoperative and intraoperative findings of tumor invasion and nodal spread
• local excision removes the grossly visible tumor but can leave behind microscopic extensions
  o adding radiation therapy to area can remove microscopic disease while sparing normal tissue and patient function
• wide excision removes more normal tissue around the gross tumor and can catch the microscopic extensions, but may result in greater patient impairment or losses
  ▪ find which nodes the tumor site drains to by injecting blue dye and lymphoscintigraphy (a radioactive substance) into the primary tumor site
    o use a Geiger counter to identify nodes that radioactive and blue
    o typically about 3 nodes are removed ■ information from sentinel nodes determines if complete dissection of other nodes is needed
  ▪ removal of primary tumor must be done without disruption of the tumor capsule to avoid spilling tumor cells
    o formal anatomic resections preferred
• risks of surgery in cancer patients:
  • poor healing due to nutrition, radiation fibrosis or vasculitis
  • immunosuppression ■ high infection risk
  • bleeding or thrombosis risk as cancer can cause anemia, thrombocytopenia, or hypercoagulability ■ DVT, MI, PE
    o radiation therapy: increased indication for use with fast-growing but locally restricted tumors
      ▪ increased efficacy when combined with chemo, especially for tumors that are fast-growing and fast-spreading
        o ex. rectal, head/neck, lung, cervical, and brain tumors
      ▪ can use drugs to sensitize cancer tissue to radiation prior to therapy
    • systemic therapy: treats cancer anywhere in the body; includes chemotherapy, hormone therapy, immunotherapy
      o presence of mets, large-size tumor, or nodal involvement may indicate systemic therapy prior to or instead of surgery
    • myeloablation therapy: drugs given to obliterate the bone marrow just before transplantation
• risks of surgery in cancer patients:
  • poor healing due to nutrition, radiation fibrosis or vasculitis
  • immunosuppression ■ high infection risk
  • bleeding or thrombosis risk as cancer can cause anemia, thrombocytopenia, or hypercoagulability ■ DVT, MI, PE
    o radiation therapy: increased indication for use with fast-growing but locally restricted tumors
      ▪ increased efficacy when combined with chemo, especially for tumors that are fast-growing and fast-spreading
        o ex. rectal, head/neck, lung, cervical, and brain tumors
      ▪ can use drugs to sensitize cancer tissue to radiation prior to therapy
    • systemic therapy: treats cancer anywhere in the body; includes chemotherapy, hormone therapy, immunotherapy
      o presence of mets, large-size tumor, or nodal involvement may indicate systemic therapy prior to or instead of surgery
    • myeloablation therapy: drugs given to obliterate the bone marrow just before transplantation

16.4.7 Oncology Visits Throughout Therapy
• What happens: assessment of tolerance, side effects, response
• did the disease respond completely or partially, or is it just stable, or has it progressed?
• Decide if adjuvants or neoadjuvants are needed
• neoadjuvants (induction therapy): preoperative therapy, such as hormones, chemo, or radiation in an attempt to downsize tumor before resection and treat regional affected lymph nodes
  o often given to patients with more advanced tumors who are at risk for microscopic mets
• adjuvants (systemic therapy): postoperative therapy in order to eradicate any micrometastases not caught by the surgery
  o regimen is tailored for a specific malignancy, may be radiation, chemo or hormonal therapy
  ▪ may use established standard of care or drugs from clinical trials
• Manage side effects: anticonvulsants, antidepressants, benzodiazepines, antihistamines, steroids, antibiotics, radiation, bisphosphonates, surgery, neurolytic blocks or neurosurgery, acupuncture, relaxation techniques, therapeutic touch, radiopharmaceuticals

16.4.8 Follow Up Oncology Visits After Therapy
• What happens: long-term observation and restaging studies to rule out recurrent disease
• Address survivorship issues

16.4.9 Palliative Care Visits
- What happens: symptom management, hospice if needed, end of life issues
- Definitely consider whenever the health care provider would not be surprised if the patient died within the next 12 months
- Dying from cancer can be an expected decline, or an unexpected catastrophic deterioration
- Goals are to enhance quality of life for patient and family, optimizing patient’s function, helping with decision making (advanced care and end of life plans), providing opportunities for personal growth and a sense of peace, and strengthening relationships with loved ones
- Need to address the psychological, physical, social, and spiritual needs of patients in order to properly address their pain and administer therapy
  - Need to openly speak with patient about their emotional state
  - Need to speak to caregivers and family about what to expect, and address their concerns as well, referring to hospice as needed
- Advance care planning: communication between the patient, the family, and staff to clarify treatment preferences, identify a surrogate healthcare decision maker, and develop individual goals and priorities for end of life care
  - Filling out legal advance directives
  - Start the discussion between patient and their caregivers, and make sure they know the likely outcomes of alternative care plans
- Can be delivered concurrently with life-prolonging care or can be the therapy
- Can be delivered regardless of the stage of the disease
- Alleviates symptoms such as pain, dyspnea, dehydration without curing underlying disease
- Dyspnea worsens during the dying process, with anxiety greatly aggravating it
  - Patient’s report often seems out of proportion to physical findings, but treat it based on how the patient reports it
  - Treatment using opioids and oxygen, or benzodiazepines if it is anxiety-related
  - Antitussives for coughing
  - Anticholinergics to minimize secretions
  - Diuretics
  - Bronchodilators
  - Corticosteroids
  - Give psychosocial support to friends and family to alleviate anxiety and distress
    - Thirst is estimated to be highly prevalent at end of life, but uncertain association with true dehydration
    - Risks in providing hydration include pulmonary congestion, peripheral edema, ascites, increased need to urinate, need for diuretics, artificial prolongation of dying process
    - Alternatives: sips of water, ice chips, oral care
    - Nutritional supplementation frequently provided to ally families’ fears and anxieties
      - But no benefit for alleviating cachexia, increasing activity or survival, or preventing aspiration
    - Other symptoms of concern at end of life: nausea and vomiting, diarrhea, GI obstruction, confusion, insomnia, depression, constipation, ascites, delirium, sedation, anxiety

16.4.10 Oncologic Emergencies

I.) Neurologic oncologic emergencies
- Spinal cord compression: impingement of spinal cord or cauda equina, usually in thoracic region
- Cancers most likely to lead to this are breast, lung, thyroid, kidney, prostate (BLT + kosher pickle)
- Majority of compressions are a result of metastasis
- Clinical presentation: localized, dull, constant back pain that is worse when supine
  - May have neurologic symptoms
    - Parasthesia or ataxia
    - Weakness signals that an urgent intervention is necessary!
    - Bowel and bladder dysfunction are later signs
- Investigation: total spine MRI better than myelogram or spinal CT
• treatment: steroids (dexamethasone) to decrease swelling into spinal cord, neuro consult to see if lesion can be removed, radiation oncology consult for quick radiation treatment to prevent further damage to spinal cord
• goal is to prevent loss of function, palliate pain, prevent local recurrence, and preserve spinal stability
• prognosis: severity of weakness is correlated to outcome
• ambulatory on diagnosis will most likely remain so post-treatment
• rapid onset of neuro symptoms and rapid progression indicates poor prognosis
• brain metastasis
• -occurs in 1/3 of cancer patients
• -frequently in junction between gray and white matter
• -clinical presentation:
  o cerebral edema, increased intracranial pressure, headache
  ▪ headaches usually worse in the morning due to pressure of laying down
  o -also may have focal weakness, behavioral changes, seizures
• -investigation:
  o -head CT with and without contrast to check for hemorrhagic/blood cause
  ▪ -hemorrhage common with melanoma, gestational cancer, and testicular cancer
  o -MRI with and without contrast, better for evaluating lesions of the cerebellum, temporal lobes, or brainstem
• -treatment:
  o -steroids
  o -radiation therapy consult: whole brain irradiation vs stereotactic radiosurgery
  o -traditional surgery?
  o -not indicated: anticonvulsant therapy
• carcinomatous meningitis: spread of cancer to the CNS
• -most commonly occurs with lymphoma, leukemia, breast cancer, lung cancer, and melanoma
• -usually affects more than one structural area
• -clinical presentation: visual changes, facial numbness, nausea, headache, weakness, bowel or bladder dysfunction = can mimic spinal cord compression!
• -investigation: LP with CSF cytology
• -treatment: intrathecal chemo, radiation, palliative care

II.) Cardiovascular oncologic emergencies
• pulmonary embolism or DVT: cancer is a hypercoagulable state
  o greater risk in black patients
  o -clinical presentation: systolic BP <90 indicative of massive PE with high mortality
  o -investigation:
    ▪ high resolution CT angiography
    ▪ EKG to rule out coronary event
  o -treatment: give oxygen, heparin, fibrinolytics if PE is massive
    ▪ lifelong anticoagulation needed for cancer survivors
• heart failure
  o -clinical presentation:
  o -investigation:
  o -treatment:

III.) Infectious oncologic emergencies
• neutropenia: cancer treatment causes immunosuppression
• most commonly occurs during first cycle of chemotherapy
• -prevention: prophylactic colony stimulating factors, reduced-dosing chemo, breaks in treatment regimen
• -clinical presentation: +/- fever (varying ability to mount immune response)
• -investigation: CBC, blood cultures, UA, examination of sinuses, skin, and mucosa
• -treatment: broad spectrum empiric antibiotics, consider antifungals or antivirals if not better in 5 days
  o transition to oral antibiotics to go home
• prognosis: without treatment, febrile neutropenia has a 95% mortality rate
• anemia
• clinical presentation:
• investigation:
• treatment:
• thrombocytopenia
• clinical presentation:
• investigation:
• treatment:

IV.) Metabolic/endocrinologic oncologic emergencies: cancer causes metabolic dysregulation
• tumor lysis
• clinical presentation:
• investigation:
• treatment:
• hypercalcemia: bony lesions break down calcium and release it into the blood, or the cancer releases substances that cause bone to release calcium into the blood, and decreased renal calcium excretion
• most commonly occurs with breast cancer or multiple myeloma
• clinical presentation: constipation, loss of appetite, nausea, vomiting, sleepiness, muscle weakness, confusion, coma
• investigation:
  o Ca levels + albumin to generate corrected Ca levels
• treatment:
  o aggressive fluid resuscitation
  o bisphosphonates to interfere with osteoclastic activity
  o calcitonin to decrease bone breakdown and increase urinary Ca excretion
  o furosemide to block Ca resorption
  o treat underlying disorder
• hyper or hypoglycemia induced by treatment of tumor
• clinical presentation:
• investigation:
• treatment:
• hyponatremia: a patient who has no relevant PMH for this has a malignancy until proven otherwise
• could be syndrome of inappropriate antidiuretic hormone (SIADH): a paraneoplastic syndrome associated with certain cancers, where ectopic ADH is produced excessive water reabsorption and dilution of blood Na
• clinical presentation: nausea, malaise, headache, lethargy, altered mental status (excess water third spaced to the brain), obtundation, coma, respiratory arrest, death
• investigation: BMP, imaging for suspected malignancy
• treatment:
  o treat the underlying malignancy
  o water restriction
  o possibly demeclocycline, and expensive antibiotic that results in Na retention
  o hypertonic saline only if case is very severe

V.) Urologic oncologic emergencies
• urinary tract obstruction
• clinical presentation:
• investigation:
• treatment:
• hemorrhage
• clinical presentation:
• investigation:
• treatment:

VI.) GI oncologic emergencies
• intractable nausea/vomiting
• clinical presentation:
• investigation:
- treatment:
- bowel obstruction from mass
- clinical presentation:
- investigation:
- treatment:

16.4.11 Pain and Cancer

- Risk of having pain with cancer is correlated to type and stage of tumor, increased age, race, gender, therapy modality, and provider lack of belief in the patient's pain
- chemotherapy especially causes a lot of pain
- Pain is nociceptive as well as subjective
- can be aggravated by psychological suffering and dilemmas, anxiety, spiritual distress
- can also be worse from loss of appetite or medical crisis
- Causes of pain:
  - progression of tumor
  - further tissue damage
  - iatrogenic from procedures
  - toxicity from chemo
  - infection
  - musculoskeletal issues
- When considering pain meds, think about age of patient, whether or not they can swallow, whether they are opioid naïve or tolerant, renal function, and drug cost and availability
- addiction is rare in this patient category
- transdermal or transmucosal medications are helpful in end of life patients with pain
- Pain is much better managed with scheduled dosing with PRN available on top, rather than just PRN
- short-acting opioid for breakthrough pain

16.5 Types of Solid Tumor Malignancies

16.5.1 Breast Cancer

- Background
  - 30% of cases are hereditary or familial
    - BRCA genes play a 40-50% role
- Prevalence
- Prevention
  - discuss chemoprevention in high risk population: USPSTF Grade B
  - Screening in general population
    - Gail model: used to assess the risk of a women developing an invasive breast cancer over the next 5 years, also assesses her lifetime probability of developing breast cancer
      - takes into account current age, age at menarche, previous biopsies and results, age at first live birth, and FH of breast cancer in first-degree relatives
      - disadvantages: doesn’t take into account age of family member diagnosis and extent of disease
  - breast self exam
    - USPSTF Grade D
  - clinical breast exam
  - mammogram: radiologist compares to last 2 mammograms
    - USPSTF Grade B recommendation for ages 50-74, every 2 years
    - other agencies still recommend beginning at age 40 evaluate on case-by-case basis
  - mammogram + US
  - Screening in high risk population
  - dedicated breast MRI
  - genetic counseling & testing: USPSTF Grade B
- Clinical presentation:
- palpable mass
16.5.1 Breast Cancer

- fibroadenomas common in younger women
  - Investigation:
  - could just be cyst or fat necrosis
  - suspicion additional mammogram views, US, biopsy
    - if woman is < 30, begin with US
  - Treatment:
  - no hormonal target for therapy in triple negative tumors (ER-/PR-/HER2-)
    - more frequently seen in black women

16.5.2 Cervical Cancer

- Prevalence
- Screening
- pap smear: begin at age 21 or within 3 years of 1st sexual encounter
  - USPSTF Grade A for every woman with a cervix who has been sexually active
  - but stop at age 65 if previous exams have been normal and risk is average
  - after age 30, average risk, and 2-3 normal tests, screening can drop to every 3 years
  - high risk patients (HIV, abnormal paps, immunosuppressed) = annual exams
- HPV test: USPSTF Grade I

16.5.3 Colorectal Cancer

- Prevalence
- Screening in general population (begins at age 50):
  - fecal occult blood test yearly: USPSTF Grade A
  - colonoscopy every 10 years or flexible sigmoidoscopy every 5 years: USPSTF Grade A
  - digital rectal exam
  - barium enema every 5 years
  - CT colonography (virtual colonoscopy) every 5 years: USPSTF Grade I

16.5.4 GI Cancer

- prevalence
- clinical presentation:
- investigation:
- treatment:

16.5.5 Head and Neck Cancers

- CNS tumors
- malignant: metastatic disease, glioblastoma multiforme, anaplastic astrocytoma, low-grade glioma
- benign: pituitary adenoma, Schwannoma, meningioma, arachnoid cyst
  - may be benign but can still be fatal or debilitating!
  - prevalence
  - clinical presentation:
  - investigation:
  - treatment:
  - prevention:

16.5.6 Lung Cancer
• Background
• **non-small cell lung cancer**: includes adenocarcinoma, squamous cell carcinoma, bronchoalveolar cell carcinoma
• small cell lung cancer:
• Prevalence
• Risk factors: smoking, asbestos exposure, exposure to other carcinogens (uranium, beryllium, vinyl chloride, nickel chromates, coal, mustard gas, chloromethyl ethers, gasoline, diesel exhaust, radon gas), FH, air pollution, arsenic in drinking water, radiation therapy to the lungs
• Screening: all are USPSTF Grade I
• CXR
• sputum cytology
• low-dose/helical/spiral CT: more than 4x sensitivity of a CXR, but greater cost, more radiation, and increased false positives
• Clinical presentation: dyspnea, hemoptysis, chronic coughing, change in regular coughing pattern, wheezing, chest or abdominal pain, cachexia, fatigue, loss of appetite, dysphonia, clubbing of the fingernails, dysphagia
• Investigation:
• Treatment:
• can surgically address all the way up to stage IIIB

16.5.7 Melanoma
• prevalence
• clinical presentation:
• investigation:
• treatment:

16.5.8 Ovarian Cancer
• Background
• 10% of cases are hereditary
  • BRCA genes have a role in 90% of these cases
• Prevalence
• Screening: all USPSTF Grade D for average risk women
• options for high risk women:
  • Ca-125
  • transvaginal US
  • pelvic exam
• Clinical presentation:
• Investigation:
• Treatment:

16.5.9 Prostate Cancer
• Prevalence
• Screening
• under age 75 ▶ USPSTF Grade I for any screens
• over 75 ▶ USPSTF Grade D
• digital rectal exam
• PSA
• Clinical presentation:
• Investigation:
• Treatment:

16.5.10 Cancer Genetics
• Metastasis can occur via blood or lymph
• cancer escapes epithelium by secreting chemicals to break down the basement membrane

16.5.11 Genetic Damage
• Can be inherent or environmental damage such as UV light, tobacco smoke, ionizing radiation, or nitrites
• Somatic mutations will only be found in the cancerous tissue, while germline mutations are inherited and thus will be present in every cell in the body
• Genes involved in cancer:
  • proto-oncogenes: normal genes that stimulate growth, but can be abnormally activated if mutated to become an oncogene
    o these genes are special in that only ONE copy needs to be mutated to induce tumorigenesis
    o ex. BRC-ABL is mutated in many leukemias
  • tumor suppressor gene: normally suppresses cellular growth or mediates differentiation, but mutation causes it to be inhibited in cancers
    o often the culprits in hereditary cancers
    o requires both copies of the gene to be mutated to lose function
    o ex. Rb, p53, p16, BRCA1, BRCA2
• DNA repair genes: when turned off accumulation of mutations in genes
• Knudson’s two-hit cancer hypothesis: since every gene has 2 copies, it takes a mutation in each copy to release the cell from normal regulatory processes
  • so if someone has a germline mutation, all of their cells only have 1 good copy left
  • most cancers need multiple mutations in genes to proceed to metastasis
  • Genetic damage leading to carcinoma
    • loss of tumor suppressor gene such as APC  
    • activation of RAS oncogene
    • loss of tumor suppressor gene DCC  
    • loss of tumor suppressor gene p53
    • additional mutations  

16.5.12 Sporadic Cancers
• Occur by chance in individuals who have no known hereditary risk factors and usually no family history of cancer
• Genetic mutations are only seen in the affected tissue type, with no germline representation
• Accounts for about 60% of all cancers

16.5.13 Hereditary Cancers
• Associated with a susceptibility gene (such as BRCA1 or BRCA2)
• Mutated susceptibility gene is passed down in an autosomal dominant fashion
• risk of cancer in person with mutated gene is as high as 85%
• but not everyone inherited the mutation will get the cancer due to reduced penetrance
• Accounts for about 10% of all cancers
• Hereditary cancer syndromes:
  • neurofibromatosis I: causes tumors in the form of optic gliomas, neurofibrosarcomas
    o highly prevalent, affects 1/3000 people
  • tuberous sclerosis: causes brain tumors, Wilms’ tumors, renal cell carcinoma
  • retinoblastoma: causes retinoblastomas, osteosarcomas
  • multiple endocrine neoplasia II: causes thyroid pheochromocytomas
  • neurofibromatosis II: causes vestibular schwannomas, meningiomas
  • Von Hippel Lindau: causes clear cell renal carcinoma, hemangioblastoma
    o dominantly inherited VHL mutation
  • neurofibromatosis: causes basal cell carcinoma, pancreatic tumors
  • juvenile polyposis: causes tumors of the small intestine, stomach, colon, pancreas
• **Peutz-Jeghers**: causes tumors of the colon, breast, ovary, pancreas, uterus
• **multiple endocrine neoplasia I**: causes tumors of the parathyroid glands, pituitary, pancreas

16.5.14 Familial Cancers

• Caused by multiple genes and environmental factors
• each gene variant causes an increase in risk, with overall risk of cancer depending on the number of inherited variants, and which environmental factors interact with the genes
  o results in more cases of cancers in families than would be expected by chance alone
• Also passed down in an autosomal dominant fashion
• Accounts for about 30% of all cancers

16.5.15 Other Dominantly Inherited Cancer Syndromes

• Familial retinoblastoma: RB1 mutation
• Familial adenomatous polyposis: APC mutation
• Hereditary nonpolyposis colorectal cancer: MLH1/2/6, PMS1/2 mutation
• Wilms tumor: WT1 mutation

16.5.16 Breast and Ovarian Syndromes

• **Hereditary breast/ovarian cancer syndrome**: most commonly involves BRCA1 and BRCA2 mutations
  increased risk of breast and ovarian as well as other cancers
• a dominantly inherited cancer syndrome
• **BRCA1** mutation associated with greatest risk of bilateral breast tumors (each one primary)
  o also carries greatest risk of ovarian cancer
  o other associated cancers are male breast, prostate, stomach, colon, pancreatic
• **BRCA2** mutation associated with greatest risk of male breast cancer
  o other associated cancers are prostate, melanoma, throat, pancreas, colon
• risk management by screening for these patients:
  o beginning age 18: monthly self breast exams
  o beginning age 25: complete breast exam every 6 months
  o beginning age 30-35: transvaginal ultrasound every 6 months, serum CA-125 every 6 months, pelvic exam every 6 months
  o men beginning age 40: digital rectal exam & PSA annually
  o case specific: 6 month mammograms, annual MRIs, full body derm exams (BRCA2 only)
• other ways to manage increased risk:
  o prophylactic mastectomy and/or oophorectomy
  o chemoprevention by tamoxifen (BRCA2 only)
  o oral contraceptives (lowers ovarian cancer risk but may increase breast cancer risk)
• **Cowden syndrome**: PTEN mutation increased incidence of breast cancer, thyroid cancer
• other associated diseases: macrocephaly, Lhermitte-Duclos disease (gangliocytoma), endometrial carcinoma, mental retardation, hamartomatous intestinal polyps, fibrocystic disease of the breast, lipomas, fibromas, genitourinary tumors or malformation
• **Li-Fraumeni syndrome**: dominantly inherited p53 mutation osteosarcomas, soft tissue sarcomas, premenopausal breast cancer, brain tumors, adrenal cortical tumors, acute leukemia
• other associated cancers: melanoma, stomach cancer, colon cancer, pancreatic cancer, gonadal germ cell tumors, Wilms tumor

16.5.17 Gastrointestinal Syndromes

• Colon cancer:
  • genetic causes account for 15-35% of cases
    o **familial adenomatous polyposis (FAP)**: an inherited condition in which numerous polyps form mainly in the epithelium of the large intestine
      ▪ polyps start out benign but malignant transformation occurs when not treated, starting in adolescence, with every untreated individual affected by age 35
diagnosis made with > 100 polyps detected
extracolonic signs of FAP: adenocarcinoma of the small intestine, periampulla, stomach, bile ducts, or adrenal glands; papillary thyroid cancer; hepatoblastoma; medulloblastoma; osteoma; fibroma; dental abnormalities; desmoid tumors; congenital hypertrophy of the retinal pigment epithelium
prevention: prophylactic colectomy indicated
  hereditary non-polyposis colon cancer (HNPCC): inherited mutations in DNA mismatch repair proteins predispose individuals to colon cancer as well as endometrial or ovarian cancer, small bowel cancer, gastric cancer, biliary duct cancer, urinary tract cancer, sebaceous skin tumors
  associated with colorectal cancer diagnosis before age 45 and cancer located in proximal colon
diagnosis of HNPCC:
  Amsterdam criteria: more strict diagnostic criteria for HNPCC; 3 family members with confirmed colorectal cancer, affecting 2 successive generations, with 1+ of these cancers diagnosed under age 50, FAP excluded
  Amsterdam criteria II: less strict; 3 family members with HNPCC-related cancer, affecting 2 successive generations, with 1+ of any of these cancers diagnosed under age 50, with FAP excluded
risk management after diagnosis: studies show that 3-year screening reduces mortality by 65% and halves the colorectal cancer rate in affected families

16.5.18 Identifying At-Risk Families and Individuals

- Take a 3-generation FH with information about all family members and ethnicities
- features of FH suggesting possible hereditary syndromes
  - cancer in 2+ close relatives on same side of family
  - cancer diagnosis at early age
  - multiple primary tumors on same individual
  - bilateral disease in paired organs
  - tumors with rare histology
  - tumors occurring in sex usually not affected
  - multiple family members affected with same type of tumor or related tumor
  - patterns of autosomal dominant transmission
- Genetic testing
  - ideal candidate: individual with early-onset cancer syndrome in direct line of hereditary descent, who is the most likely candidate to carry the mutation
    - then if this individual is positive, consider testing other family members for mutation-specific testing
  - psychosocial concerns?
  - positive test with known FH: altered self-perception, adjustment challenges, strained family relationships
    - negative test with known FH: relief, guilt, or disbelief, gap between those who have the gene and family that don’t
    - negative test with no FH: risk of false negative test is increased
    - seems to be no increase in stress, anxiety, or depression after knowledge of test results
    - conversely, in BRCA-linked families, persons with high levels of cancer-related stress who decline genetic testing may be at risk for depression require education, counseling, and monitoring for depression
- insurance and employment discrimination
  - some legal protections conferred by HIPAA, state laws, Genetic Information Non-Discrimination Act
- Risk assessment and patient counseling
  - go over patient’s motivation for and expectations of a genetic assessment
  - review medical and genetic facts
  - assess patient coping and support
  - consider privacy and confidentiality
• communicate risks to patient
• refer to medical geneticist or hereditary cancer center if needed
17 Ortho Exam Notes

17.1 Introduction to Orthopedics

17.1.1 Bone

- organic matrix makes up 40% dry weight of bone
- includes type I collagen, proteoglycans, matrix proteins
- inorganic matrix makes up the other 60%
- includes minerals such as Ca hydroxyapatite, osteocalcium P
- diaphyseal blood supply via arteries entering through nutrient foramen
- epiphyseal blood supply via arteries arising from periarticular vascular plexus
- periosteal blood supply via capillaries
- metabolism of Ca and P and osteocytes maintain bone
  - but vit D needed for Ca absorption
  - parathyroid hormone increases osteoclastic bone breakdown
    - signs of hyperCa: stones, groans, abdominal moans
- remodeling is in response to physical stress
  - more stress → bone deposition
  - less stress → bone breakdown

Steps in fracture healing
- inflammation: hematoma, osteoclast removal of necrotic bone, secretion of growth factors by hematopoietic cells
- repair: soft callus as fibrous tissue unites bone fragments, then hard callus with conversion to bone
- remodeling for several months

17.1.2 Articular Cartilage

- Types
  - fibrocartilage: area for bone and tendon insertion
  - elastic cartilage:
    - fibroelastic cartilage: deepens articular surface and stabilizes joint
    - ex. menisci
  - articular cartilage: load distribution and friction reduction

17.1.3 Complications of Musculoskeletal Trauma

A.) Fat embolism syndrome: when marrow fat forms an embolus that lodges in the pulmonary capillary beds
- acute respiratory distress
- usually a result of trauma, most commonly in femoral shaft fracture
- occurs within several days of fracture
- presentation: hypoxia, dyspnea, AMS, tachycardia, petechiae
- treatment: oxygen or mechanical ventilation, inotropes, maintain proper hematocrit, correction of metabolic acidosis

B.) Rhabdomyolysis: breakdown of muscle fibers with release of cellular contents
- caused by blunt trauma, seizures, burns, strenuous exercise, electrocution, drugs, viruses
- presentation: muscle pain, dark urine, hypovolemia, hyperkalemia, metabolic acidosis, ARF, DIC
- investigation: labs showing CK elevated 5-10x normal, UA showing myoglobinuria
- treatment: fluids, correction of imbalances, treatment of underlying cause

C.) Nerve injuries
- nerve compression syndromes: include carpal tunnel, ulnar nerve palsy, peroneal nerve palsy, sciatic nerve neurapraxia
- fracture or overuse injuries
- neurapraxia: a temporary loss of motor and sensory function due to nerve contusion
• associated with fractures
• resolves in 6-12 weeks as long as nerve is not severed
• axonotmesis: crush injury of nerve axon, can also happen in traction injuries
  • recovers at rate of 1 inch per month
• neurotmesis: trauma injury creating severed nerve
  • surgical repair needed

D.) Reflex sympathetic dystrophy (chronic regional pain system): persistent pain and hyperesthesia after an injury, that anyone with a nerve injury is at risk of developing
• clinical presentation: intense burning pain, edema, stiffness, skin discoloration, atrophy
• treatment: refer to pain specialist, neuroleptic drugs, regional nerve blocks, PT

E.) Venous thromboembolism: most common in spine, pelvic, hip, and femur fractures
• increased risk with trauma, smoking (decreases vessel elasticity), bedrest, hormone therapy, or surgery
• prevention: prophylactic anticoagulation in all trauma admissions and some ortho surgeries
• clinical presentation: PE may be the first sign, calf pain in post-op hip or knee pt
• investigation: duplex doppler venous ultrasound

F.) Myositis ossificans: laying down bone in the muscle belly
• caused by focal trauma to muscle □ calcified hematoma □ ossification
• clinical presentation: hard muscle mass
• investigation: must rule out malignancy
• treatment: ice, compression, last resort is surgical excision

G.) Fracture complications:
• delayed union due to slow callus formation (normal adults should only take 6-10 weeks)
• nonunion of fracture after 3 months
• infection
• nerve/vascular injury: must evaluate circulation and sensation distal to injury site

17.1.4 Approach to the Orthopedic Patient
• HIPROT!
  1.) history: mechanism of injury, handedness are important
  2.) inspection
  3.) palpation
  4.) ROM: measure in degrees
  5.) other tests

17.1.5 Important Motor Nerve Roots and Actions
• C1-C2 □ neck flexion
• C3 □ lateral neck flexion
• C4 □ scapular movements (shoulder shrug)
• C5 □ deltoids and biceps (shoulder abduction)
• C6 □ wrist extensors, elbow flexion
• C7 □ triceps, wrist pronation, elbow extension
• C8 □ finger flexion (hand grip), interossei
• T1 □ finger abduction, interossei
• L1 □ hip flexion
• L2 □ hip adductors
• L3 □ knee extension
• L4 □ ankle dorsiflexion
• L5 □ hallucis longus extension
17.1.6 Soft Tissue Injuries

- can be acute or overuse

A.) Sprains: stretched or torn ligaments, graded 1-3
   1 = partial tear
   2 = partial tear or instability
   3 = complete tear

B.) Strains: muscle or tendon injuries, also graded 1-3

C.) Tendonitis: an overuse, mechanical injury of the tendon
   - vs tenosynovitis: mechanical irritation of the tendon sheath
   - includes the injuries known as should supraspinatus, epicondylitis, DeQuervain’s, trigger finger, ITB, patellar, quadriceps, peroneal tendon, posterior tibial tendon, Achilles, plantar fasciitis
   - treatment: rest, stretch, ice, NSAIDS, correction of biomechanics
   - if no improvement, PT, ROM, iontophoresis, corticosteroid injection

17.1.7 Basic Musculoskeletal Therapeutics

- PRICEMMM!
  - protect from further damage
  - rest for 24-48 hours
  - ice for 20 min for 2-3 days
  - compression to prevent further swelling
  - elevation to drain fluid
  - motion early on to speed recovery
  - medication
  - modalities:
    - iontophoresis: electric current applied to transport anti-inflammatory drugs across the skin to the affected tendon
    - phonophoresis: same as iontophoresis but using US
    - sonorex: extracorporeal shock wave therapy, promotes neovascularization and local anesthesia

17.1.8 Pain

- Characteristics:
  - simple sprains & strains • nonspecific pain
  - nerve root pain • brief, sharp, shooting pain increased by cough, standing, or sitting
  - neoplasm or infection pain • severe, constant, persisting through the night pain

- Management:
  - NSAIDS appropriate for impingement and inflammation
  - COX-2 inhibitors NOT appropriate for soft tissue injury
  - acetaminophen good for soft tissue injuries
  - narcotics
  - non-narcotics: ketorolac and tramadol
  - joint injections
    - limit to 4 per year, per site
    - avoid intra-tendinous injections to avoid rupture
    - NO corticosteroids into septic joint
    - side effects: tendon rupture, infection, hypopigmentation, fat atrophy, steroid flare

17.1.9 Arthritis
A.) Osteoarthritis:
- presentation: must be > 40 years old, asymmetric stiffness < 1 hour, decreased joint space and bony spurring
- treatment: NSAIDS, ROM, glucosamine, steroid injections, visco-supplementation

B.) Rheumatoid arthritis:
- presentation: early and sudden onset bilaterally, bony erosion with preservation of joint space, systemically affected
- treatment: disease-modifying antirheumatic drugs (DMARDs), steroids

C.) Crystal arthropathies
- **gout**: monosodium urate crystals
- **pseudogout**: calcium pyrophosphate deposition

D.) **Ankylosing spondylitis**: chronic autoimmune inflammation of the spine and sacroiliac joint

17.1.10 Musculoskeletal Imaging
- X-rays: get at least 2 views
- CT: defines bony anatomy
- MRI: defines soft tissues
- Nuclear medicine studies: defines tumors
- EMG: evaluates denervation of muscles
- NCS: evaluates conduction velocities

17.1.11 Describing Fractures

I.) Anatomic location

II.) Region of bone: diaphysis, metaphysis, epiphysis

III.) Direction of fracture: transverse, oblique, spiral

IV.) Condition of bone: comminuted, incomplete

V.) Condition of soft tissue: closed, open, open joint

VI.) Deformities of fracture: displacement, angulation

VII.) Pediatric classifications: greenstick, torus, Salter-Harris

- **Salter-Harris classification**: defines growth plate injuries in peds
  - I (S) = straight/directly through growth plate
  - II (A) = above
  - III (L) = lower
  - IV (T) = through
  - V (R) = ram/ramming together of bones fractures growth plate

17.1.12 Fracture Management
- Splinting
- Casting: fiberglass
- Closed reduction: use hematoma and digital block
- Surgery
  - **open reduction internal fixation (ORIF)**: use of screws and plates to hold reduction together
  - **open/closed reduction percutaneous pinning (O/CRPP)**: use of pins going through the skin into fractured area

17.1.13 Musculoskeletal Tumors
- Bone
- benign: osteoblastoma, osteoid osteoma
- malignant: Ewing’s sarcoma, osteosarcoma, chondrosarcoma

- Soft tissue
  - benign: ganglia, giant cell tumor, lipoma, hemangioma, antiomyoma
  - malignant: fibrosarcoma, liposarcoma, rhabdomyosarcoma

17.2 Cervical Spine

17.2.1 Background
- C-spine has two segments: the craniocervical junction between the atlas/axis/occiput (skull base), and the lower cervical vertebrae C3-C7
- each segment allows for half of the total range of motion of the c-spine
- atlanto-occipital joint = “yes” motion
  - atlanto-axial joint = “no” motion
- Movements: flex/ext, lateral flexion, rotation, axial compression, distraction
- Review anatomy of atlas, axis, vertebral ligaments
- Spinal stability
  - created when both columns are intact
    - anterior column includes the vertebral bodies, anterior and posterior longitudinal ligaments, and the annulus fibrosis
    - posterior column includes the pedicles, facet joints, laminar spinous processes, ligamentum flavum, interspinous and supraspinous ligaments
  - injury to one column means the spine is still stable, but injury to both means the injury is unstable
- Spinal alignment
  - **anterior marginal line**: drawn along anterior vertebrae
  - **posterior marginal line**: drawn along posterior of vertebral bodies
  - **spinal laminal line**: drawn along bases of the spinous processes (just posterior to spinal cord)
  - **posterior spinous line**: drawn along tips of spinous processes

17.2.2 Innervation from the C-Spine
- Motor:
  - C1-C2: neck flexion
  - C3: lateral neck flexion
- C4 □ scapular movements (shoulder shrug)
- C5 □ deltoids and biceps (shoulder abduction)
  - level of biceps reflex
- C6 □ wrist extensors, elbow flexion
  - level of brachioradialis reflex
- C7 □ triceps, wrist pronation, elbow extension
  - level of triceps reflex
- C8 □ finger flexion (hand grip), interossei
  - T1 □ finger abduction, interossei
- Sensory: see dermatome map

17.2.3 How to Look at a C-Spine Radiograph

- Any trauma = must order lateral, AP, odontoid (open mouth) views
  - lateral view:
    - look for the 4 smooth lines of spinal alignment
    - must see all vertebrae through C7 for image to be informative
  - AP: look for vertical row of spinous processes, vertebral body height and width should be uniform
  - odontoid: space in atlanto-axial joint should be symmetric bilaterally

17.2.4 Clinically Ruling Out C-Spine Fractures

- Patient must be mentally stable to evaluate = no drugs, alcohol, trauma creating alt ment status!
- Patient must have no other injuries distracting from neck injury
  - No neck pain
  - No neck pain when palpated
  - No loss of consciousness
  - No referable symptoms to neck injury: paralysis, sensory changes (even transient)

17.2.5 C-Spine Injuries
A.) Jefferson fracture (atlas burst): a fracture of the anterior and posterior arches of the atlas, resulting from an axial load on the back of the head or hyperextension of the neck
- may be accompanied by a break in other parts of the cervical spine or a fracture of the axis
- forces lateral masses of C1 outward
- investigation:
  - radiograph: lateral masses of C1 aren’t lining up with their facets in C2, and distance between dens and C1 lateral masses is asymmetric
- treatment depends on stability of injury
  - stability = whether or not transverse ligament of the atlas is intact
    - stable □ rigid cervicothoracic collar for 3 months with f/u x-rays
    - unstable □ halo (cranial traction) for 3 months
      - large degree of displacement between atlanto-axial joint = spinal fusion needed

B.) Odontoid fracture: break at the dens from hyperflexion or hyper extension
- may also be associated with Jefferson fracture
- in one of three places
  - type I: rare avulsion fracture of the alar ligament
  - type II: most common fracture at neck of dens
    - watershed area of blood compromises bone healing
  - type III: fracture around base of dens
- treatment: reduce fracture and halo immobilize for 3 months
  - C1/C2 spinal fusion may be needed for severe displacement or nonunion
  - prognosis: can have neurologic injury

C.) Traumatic spondylolisthesis of C2 (hangman’s fracture): fracture of both pedicles of the axis
- can occur in one of four places
- unstable but neuro deficits are rare
- treatment: immobilization in halo with traction, anterior fusion/screw fixation/internal fixation if severe

D.) Cervical strain or sprain
- trapezial strain: pain will be localized to posterior C-spine and is reproducible on palpation
  - may see torticollis (twisted neck)
• treatment is supportive
• **whiplash**: from hyperextension or hyperflexion
  • can injur ligaments
  • investigate with x-rays to check for stability
• **acute cervical sprain**: injury to the restraining ligaments of the cervical spine
  • grade I-III depending on disruption of ligaments
  • can occur alone or with muscle strain, fracture/dislocation, or instability
  • investigation: x-rays in flexion and extension
  • treatment: if x-rays are negative normal activities after painless ROM and axial compression, subluxation hard collar, instability immobilization or possible surgery

E.) **Cervical spondylosis**: degenerative osteoarthritis of the vertebral discs from repetitive strain or trauma
• most commonly in C5-C6
• risk factors: frequent lifting, smoking, excessive driving (truck drivers)
• clinical presentation: neck pain, radiculopathy, myelopathy (location will tell you where the problem is)
• investigation: MRI or CT myelogram
• treatment: supportive; facet injections, surgical decompression via discectomy or laminectomy (allows nerve to breathe) +/- fusion for stability

F.) **Cervical stenosis**: narrowing of the cervical spinal canal
• may be congenital or acquired (weight lifting or spondylosis)
• most commonly in C5-C6
• presentation: often asymptomatic until neuro signs
• investigation:
  • assess severity with **Torg’s ratio**: ratio of canal to vertebral body width, should be 1, < 0.8 predicts neuro involvement

G.) **C-spine injury in an athlete**
• football players: 10-15% incidence
• greatest % of head injuries in hockey players
• injured athlete that is unconscious has a spinal cord injury until proven otherwise
• injured athlete with neck pain must be treated as unstable fracture
• don’t allow to return to play until flex/ext radiographs in full ROM have been taken (may not be able to do full ROM until pain is better)

H.) **Cord injuries**
• **cervical cord neurapraxia**: a temporary loss of motor and sensory function due to blockage of nerve conduction, typically caused by a blunt neural injury due to external blows or shock-like injuries to muscle fibers and skeletal nerve fibers, which leads to repeated or prolonged pressure buildup on the nerve ischemia neural lesion spinal edema temporary damage to myelin sheath
  • will last 6-8 weeks • **transient quadriplegia**: a more serious but temporary injury to the cervical spinal cord, with numbness or pain, weakness, or complete paralysis.
  • lasts 15 min-36 hours
  • investigation: c-spine films, CT scan, MRI if everything else looks normal
• **brachial plexus neurapraxia (stinger or burner)**: sudden burning pain or numbness in lateral arm, thumb, and index finger due to stretch injury on the brachial plexus
  • lasts 1-2 minutes
  • investigation with MRI if symptoms persist > 15 min or are repeated
  • treatment: ROM, strengthening, protection
  • most common in young males
  • mechanism could be MVA, fall, diving, gunshot wound
  • 5-10% due to sports or recreational activity
  • frequently missed in patients with decreased level of consciousness
  • treatment: methylprednisone within 8 hours of occurrence

17.3 **Common Shoulder Disorders**
17.3.1 Background

- Four important joints:
  - sternoclavicular
  - acromioclavicular
    - acromion process has different formations, with certain types predisposing to certain conditions
      - type I is normal, flat, smooth
      - type II is hooked, with mildly decreased subacromial space
      - type III is hooked + spur, significantly decreased subacromial space
  - glenohumeral: large range of motion = inherently unstable
  - scapulothoracic

- H&P key findings
  - scapular winging/trauma – serratus or trapezius dysfunction
  - can’t externally rotate – posterior dislocation
  - supra/infraspinatus wasting – rotator cuff tear or suprascapular nerve palsy
  - decreased cervical ROM with pain below elbow – cervical disc disease
  - throwing athletes with anterior pain – instability
  - pain or clunk with motion – labral tear
  - night pain – impingement or frozen shoulder
  - generalized laxity – multidirectional instability

17.3.2 Shoulder-Related Injuries: See Chart for Tests

A.) Rotator cuff injury
- muscles involved are SIT(minor)S
- very unusual for pt under 25 to have rotator cuff tear
- tear vs. tendinopathy?
- tear usually = weakness
- remember that shoulder exams are not very sensitive, history more important!
- treatment: conservative with NSAIDs, ice, injections, potential surgery

B.) Biceps tendonitis
- usually associated with other pathologies such as rotator cuff injury or SLAP tear
- treatment: NSAIDs, corticosteroid injections, PT

C.) Biceps rupture
- usually in patients over age 50
- almost always long head
- imaging: MRI only if uncertain
- treatment: if proximal rupture – conservative management, if distal – tenodesis (surgical reattachment)

D.) AC joint separation
• usually from direct blow to shoulder
• 6 classifications
• presentation: step deformity, tenderness over joint
• investigation:
  • tests: + crossover sign
  • imaging: AP, Zanca (10° cephalic tilt), axillary radiographs
• treatment: grade 3+ surgery, below grade 3 conservative E.) Anterior instability

F.) Cervical radiculopathy: really a neck injury from compression of a cervical nerve root, but can cause pain to occur in the shoulder, arm, neck, or chest
• any exam for neck pain with arm/shoulder involvement should assess motor functioning and reflexes in movements associated with cervical spine roots

G.) Circulation problems associated with the anatomy of the shoulder
• thoracic outlet syndrome: compression of a neurovascular bundle passing between the anterior scalene and middle scalene → numbness or tingling down arm

H.) Clavicle fractures
• typically in the middle 1/3 of clavicle
• usually from FOOSH
• distinguish from AC separation
• presentation: look for clavicle prominence, tenderness/edema over fracture site
• investigate with AP X-ray at a 45° cephalic tilt
• treatment: sling, immobilization (longer for adults), periodic ROM, avoid contact sports for 6 weeks
• surgical fixation if needed
• refer if there is neurovascular compromise, open fracture, nonunion after 12 weeks, fracture involving distal or proximal 1/3 of clavicle (could involve other joints)

I.) Anterior SC dislocation
• usually from MVA
• presentation: tender over SC joint, deformity
• investigation: radiographs in AP and 40° cephalic views
• treatment: sling, ROM

J.) Posterior SC dislocation
• usually from fall on flexed/adducted shoulder
• can be life-threatening → immediate referral needed!
• investigation: CT
• treatment: closed or surgical reduction K.) Anterior shoulder (GHJ) dislocations
• accounts for majority of shoulder dislocations
• presentation: shoulder stuck in external rotation/abduction
• investigation: radiographs in AP, axillary, Y views
• treatment: reduction, sling, possible surgical repair
• complications: recurrent dislocations, bony injury, rotator cuff tear, neurovascular injury, arthropathy

L.) Posterior shoulder (GHJ) dislocations
• very rare
• associated with high velocity trauma, seizure, electrocutions

M.) Adhesive capsulitis (“frozen shoulder”): contraction of GHJ capsule
• usually secondary to immobilization after an injury
• less commonly due to diabetes, thyroid issues, chemo, radiation
• more frequently in women due to increased estrogen-R around shoulders
• presentation: decreased shoulder ROM, 1 of 3 stages
• painful stage (0-3 months): pain with movement, generalized ache, muscle spasm, pain at night and with rest
• adhesive stage (3-6 months): less pain but increased stiffness and reduced movement, pain felt at extreme ranges of motion
- recovery stage (6+ months): decreased pain, slow increase in ROM, spontaneous but often incomplete recovery
- investigation: rule out rotator cuff tear
- treatment: PT, NSAIDs, injections, potentially surgical lysis of lesions

N.) SLAP lesion: superior labral tear from anterior to posterior
- presentation: pain in shoulder, clicking, popping, may have instability or biceps tendonitis
- investigate with MRI
- treat with NSAIDs, PT, rest, surgery if needed depending on type of tear

17.3.3 Shoulder Imaging
- Radiographs: get scapular AP (AP at an angle for clearer view of GHJ) and axillary views
  - special view is the “Y” view that tells you what kind of acromion the patient has (positioning if the humeral head with the scapula makes a Y shape)
    - taken when dislocation or scapular fracture is suspected
  - look at humeral head, greater tuberosity, glenoid, clavicle, acromion
- possible findings:
  - bony Bankart lesion: a pocketing of the anterior (inferior) glenoid labrum due to repeated (anterior) shoulder dislocation
  - Hill-Sachs: a cortical depression in the posterior head of the humerus from anterior dislocation of the shoulder
  - spur, tumor, or fracture
  - elevated humeral head \( \Rightarrow \) rotator cuff tear
  - AC separation
  - degenerative joint disease
- MRI: imaging of choice for soft tissue when appropriate
  - best for rotator cuff tear but is expensive, typically CT arthrogram is done instead
  - CT good for bone abnormality such as tumor
  - Ultrasound is an MRI alternative in older or claustrophobic individuals

17.3.4 Treatment for Shoulder Injuries
Injections: short acting (depo Medrol, celestone) vs intermediate (dexamethasone) vs long acting (Kenalog)

17.4 Elbow, Wrist, and Hand

17.4.1 Elbow Background
- Carrying angle: how far away from body your forearms naturally fall
  - typically 5° in men, 10-15° in women
- cubitus varus (gun-stock deformity): decreased angle so that the arm points toward the body

17.4.2 Elbow Imaging
- Radiographs
  - anterior fat pad sign (“sail sign”: usually normal
  - posterior fat pad sign: always pathologic, indicative of fracture until proven otherwise
    - adults = radial head fracture
    - kids = supracondylar fracture

17.4.3 Common Elbow Problems
A.) Lateral epicondylitis: elbow pain from repetitive wrist extension
- treatment: ice, stretch, strap, iontophoresis, surgical release, injections
B.) Medial epicondylitis: elbow pain from repetitive wrist extension
- treatment: same as lateral epicondylitis, but be cautious of ulnar nerve in injection use
C.) Nursemaid's elbow: radial head slides out of annular ligament
   • investigation: assess neurovascular involvement, x-ray
   • treatment: usually reduced by positioning of arm for x-ray

D.) Elbow instability: due to ulnar collateral ligament strain or tear
   • seen in throwing athletes
   • presentation: medial elbow pain, hand paresthesia, pain with valgus testing
   • investigation: x-ray, MRI to rule out fracture
   • treatment: rest, NSAIDs, PT, Tommy John surgery (UCL reconstruction) if needed

E.) Olecranon bursitis: inflammation due to trauma or with insidious onset
   • seen in truck drivers from repetitive leaning
   • presentation: red, swollen joint, +/- pain
   • investigation: rule out infection, gout, triceps rupture
   • treatment: compression sleeve, anterior splint, rarely bursectomy if chronic, high threshold for aspiration or injection

17.4.4 Elbow Fractures & Dislocations

A.) Distal humerus fracture
   • many kinds
   • supracondylar fx: is the most common kind in peds
     o check for neurovascular involvement
   • epicondylar fx: most commonly medial
   • treatment: send to ER or urgent care
   • stable/non-displaced □ splinting or cast immobilization, protected ROM
   • unstable □ ORIF or CRPP

B.) Radial head fracture
   • from FOOSH
   • presentation: lateral swelling, pain over radial head, limited supination and extension
   • investigation: AP, lateral, and oblique radiographs
   • treatment: depends on Mason classification:
     • Mason I = undisplaced □ splint/sling with early ROM
     • Mason II = displaced □ splint/sling if minor, ORIF if major
     • Mason III = comminuted □ excision of fragments or radial head Mason IV = dislocated □ same as III

C.) Olecranon fracture
   • investigation: check neurovascular function and ulnar nerve
   • treatment: nondisplaced □ 45° splint, displaced □ ORIF

D.) Olecranon dislocation
from FOOSH
almost always posterior dislocation
investigation: check for neurovascular function and any associated radial head or distal humerus fractures
treatment: reduction

17.4.5 Wrist Imaging
Radiographs
- lateral view to see normal 2-20° palmar tilt of articular radius, smooth dorsal aspect of distal radius, capitate sitting in lunate
  - bulge or density at the epiphyseal line is just an old scar from previous fx
- PA view to see radius is distal to ulna, radial border of scaphoid intact, < 2mm intercarpal joint space, no cortical abnormalities
- clenched fist view to see scapholunate dissociation

17.4.6 Common Wrist Problems
A.) DeQuervain's tenosynovitis: tendinosis of sheath surrounding abductor pollicis longus and extensor pollicis brevis tendons
- common in new moms picking up babies
- presentation: radial wrist pain
- treatment: ice, thumb spica, rest, iontophoresis, injection, last resort surgical release

B.) Carpal tunnel: pain, numbness, paresthesia in the median nerve distribution
- treatment: ergonomics, splinting, injection

C.) Ganglionic cysts: swelling at wrist from leakage of joint fluid
- most commonly dorsal at the scapholunate joint
- presentation: +/- pain
- treatment: aspiration, compressive bandage, surgical excision if recurrent

D.) Scapholunate dissociation: traumatic scapholunate ligament tear
- presentation: wrist pain and instability
- investigation: radiograph shows > 2 mm joint space at the SL joint ("Letterman sign")
- treatment: SL ligament repair, proximal row carpectomy, arthrodesis (surgically induced joint ossification), wrist fusion
- complications: lunate will move around without ligament to stabilize it (dorsal intercalated segment instability) □ degenerative arthritis □ scapholunate advanced collapse (SLAC)

E.) Triangular fibrocartilage complex (TFCC) tear: acute or from repetitive use
- presentation: tenderness over TFCC
- investigation:
  - radiograph showing ulnar variance
  - MRI arthrogram if considering surgery
- treatment: splint, NSAIDs, PT, injection, surgical repair

F.) Ulna impaction syndrome: when ulnar head punches into carpi 🟢 swelling, weakness, pain 🟢 lunotriquetral ligament attrition (strength reduction)
- investigation: radiograph showing sclerotic changes of the lunate/triquetral
- treatment: ulnar shortening

G.) Kienbock’s disease: lunatomalacia from repetitive microtrauma with vascular insufficiency 🟢 avascular necrosis and lunate collapse
- presentation: radiating wrist pain and swelling over the lunate, pain in middle finger in flexion
- investigation: x-ray findings are subtle, may need MRI
- treatment: surgical unloading, fusion, vascular implantation
- prognosis: the earlier the diagnosis, the easier to mitigate damage

17.4.7 Forearm Fractures

- Monteggia fracture: fx of ulnar shaft + proximal radius dislocation
  - treatment: ORIF vs long arm cast
- Galeazzi fracture: radial fracture + distal ulnar dislocation
  - treatment: same as Monteggia

17.4.8 Mnemonic MUGR

- Greenstick fracture: incomplete fracture of a forearm bone in peds due to thick periosteum
  - treatment: reduction, short arm cast
- Nightstick fracture: isolated ulnar fracture
  - historically refers to criminals putting their arms up in defense against beating with a police nightstick
  - treatment: cast or splint
- Forearm fracture of radius + humerus
  - from fall or direct hit
  - treatment: little displacement 🟢 long arm cast, displacement > 10° 🟢 ORIF

17.4.9 Wrist Fractures

A.) Colles fracture: distal radial fracture with dorsal angulation 🟢 “dinner fork deformity”
• FOOSH
  • most common fracture of distal radius
  • treatment: minimal angulation □ short arm cast, significant angulation/displacement □ ORIF or CRPP

B.) Smith fracture: involves ventral angulation of distal fragment; opposite of Colles
  • fall on back of hand
  • treatment same as Colles

C.) Barton fracture: intra-articular fracture of the distal radius
  • treatment is ORIF

D.) Chauffeur’s fracture: oblique fracture through the styloid process of the radius
  • historically happened when chauffeurs were out cranking the engines of cars when the engine backfired and would hit the crank into their arm
  • treatment: long arm cast followed by short

E.) Torus fracture: buckle fracture of the distal radius with intact periosteum
  • common in ped
  • treatment: short arm cast in adults, long arm in kids so they won’t take it off

F.) Scaphoid fracture:
  • FOOSH
  • most common carpal fracture
  • categorized as distal, waist, proximal
  • imaging: radiographs with AP, lateral, oblique, and scaphoid views; MRI
    • if initial imaging is negative, immobilize and repeat films in 10-14 days
  • treatment: percutaneous screw fixation or ORIF with bone graft
  • complications: osteonecrosis a problem due to reduced blood supply, proximal fracture takes wayyy longer to heal
17.4.10 Hand Imaging

- Radiographs
  - AP, lateral, oblique, and finger-specific views
  - check films for joint alignment, cortical defect, joint space narrowing, periarticular bony erosions, sclerosis, or spurs

17.4.11 Common Hand Disorders

A.) Carpometacarpal osteoarthritis:
- presentation: pain over CMC at thumb
- investigation: radiograph shows marginal osteophytosis, joint space narrowing, and sclerosis
- treatment: try thumb spica and NSAIDs, injections, CMC arthroplasty with tendon interposition

B.) Depuytren’s contracture: occurs when thickened palmar fascia forms nodules over the flexor tendons → flexion contracture
- most commonly in ring and pinky fingers
- more common in men > 40 years with FH
- treatment: surgery or microcuts in fascia indicated for contractures > 30°, new injection also available

C.) Trigger finger (stenosing tenosynovitis): congenital thickened flexor tendon or nodule at pulley → locking, stiffness, pain in finger
- more common in RA, OA, DM
- treatment: injection at the finger flexor crease into sheath, if no response then surgical release

D.) Osteoarthritis of the fingers: creates hard but painless bony overgrowths
- Heberden’s nodes: affects DIP joint
- Bouchard’s nodes: affect PIP joint
- treatment: NSAIDs, injections, arthrodesis, rarely arthroplasty

F.) Mucous cyst: a type of ganglion cyst associated with osteoarthritis
- refer to ortho hand specialist for surgical removal

E.) Rheumatoid arthritis of the fingers: causes ulnar deviation of the fingers

- presentation: chronic swelling, decreased ROM
- boutonniere deformity: hyperextension of DIP + flexion of PIP
  - can also happen acutely due to rupture of extensor digitorum tendon over PIP, unrelated to RA, treat with serial casting
- swan neck deformity: opposite of boutonniere
- treatment: DMARDs, surgery

F.) Skier’s thumb (gamekeeper’s thumb): torn ulnar collateral ligament of finger due to abduction stress
- historically in gamekeepers breaking rabbit necks
- may x-ray prior to examination!
- treatment: nondisplaced/mild thumb spica, avulsion/displaced or complete tear surgical fixation
- complications: aponeurosis of adductor pollicis may sneak into site of broken UCL and prevent its healing (Stener lesion)

G.) Mallet finger: traumatic rupture of extensor tendon distal to DIP
- treatment: splint

H.) Jersey finger: traumatic rupture of flexor digitorum profundus at DIP
- as when football player grabs another’s jersey to stop them and they pull away
- treatment: surgical repair within 2 weeks or it will be permanent!

17.4.12 Hand Infections

- any laceration between distal palmar crease and PIP joint crease is no man’s land! get to a hand surgeon!

A.) Septic tenosynovitis: bacterial infection of a tendon and its sheath
- etiology: puncture or bite wound infected with staph or strep
- presentation: rapid swelling and pain over 1-2 days
- if flexor tendon, may see Kanavel’s signs: fusiform swelling of finger, tenderness along course of tendon, pain on passive extension, flexed finger at rest
- treatment: antibiotics, incision and drainage if progressing

B.) Felon infection: abscess in the fleshy pad of the distal phalanx
- presentation: localized erythema, swelling, throbbing pain
- treatment: ED for I&D, antibiotics
C.) **Subungual hematoma**: crush injury → bleeding under fingernail
   - treatment: trepanation (drill a hole) unless > 50% of nail affected, then remove the whole nail

**17.4.13 Hand Fractures**

A.) **Bennet's fracture**: fracture of the thumb at the metacarpal base → abductor pollicis pulls fragment away
   - abduction stress on the thumb
   - treatment: ORIF if unstable

B.) **Boxer's fracture**: fracture of the 5th metacarpal neck
   - treatment: angulation > 40° → CRPP, angulation < 40° → splint or cast

C.) **Hook of the hamate fracture**: bust in hamate due to forceful impact as in racquetball
   - investigation: be sure to check ulnar nerve
     - radiograph needs CT view
     - may need to do CT scan
   - treatment: excision of fragment or casting

D.) **Phalangeal fractures**
   - distal: splint or CRPP if displaced
   - middle or proximal: buddy tape or ORIF if displaced

**17.5 Lumbar Spine**

17.5.1 **Background**

- 90% of low back pain will be self-limiting within 6-12 weeks regardless of treatment
- Waddell signs: non-organic physical signs (unexpected or physically inexplicable patient reactions)
  - tenderness over wide area or non-localized deep tenderness
  - simulations tests: axial load should not cause low back pain
- distraction tests such as the FLIP
- widespread muscle pain in various groups
- pain out of proportion

17.5.2 **Innervation from the Lumbar Spine**

- Motor:
  - L1 → hip flexion
  - L2 → hip adductors
  - L3 → knee extension
  - L4 → ankle dorsiflexion
- level of patellar reflex
- L5 □ hallucis longus extension
- S1 □ hallucis longus flexion
  - level of Achilles reflex
- Sensory: see dermatome map

17.5.3 Spinal Imaging

- Rarely indicated for nontraumatic, recent onset low back pain
  - image if conservative therapy fails
- Radiographs: AP, lateral, obliques, flex/ext views
  - AP view: look for
    - vertical alignment of vertebral bodies
    - distance between vertebral bodies
    - vertebral body itself (“owl”):
      - “eyes” are the pedicles □ missing eye with destruction of peduncle, crack in eye with fracture, increased space between eyes or increased head height with burst fracture,
      - “beak” is the spinous process □ open beak or decreased distance between 2 beaks is fracture
  - oblique view: look for the “scotty dog”
    - any collars on the pars interarticularis (neck)
    - front and hind legs are the inferior intervertebral articular processes
    - ears and tails are the superior intervertebral articular processes
    - body is the lamina
    - eye is pedicle
    - nose is transverse process
  - lateral view: look for
    - alignment of vertebrae
    - intervertebral disc space
    - comparison of A/P vertebral cortex for change in height
    - look for black fracture lines in the spinous processes
- MRI: study of choice for discopathy
  - Bone scan for primary tumors, metastatic disease, or infection

17.5.4 Common Problems in the Lumbar Spine

A.) Lumbar strain: injury to muscle
- accounts for 70% of low back pain
- presentation: tender paravertebral or erector spinae muscles with minimal radiation
- investigation: labs or x-rays are not indicated
• treatment: pain relief, modified activity with exercise, education, encouragement

B.) Herniated nucleus pulposus: flexion + rotation or tears in the annulus → impingement of nucleus on spinal cord
  • L5 most common site
  • presentation: sciatica, positive straight leg raise + FLIP, pain worse on back extension
  • neuro deficits specific to root involved
    - ex. L5 → weak extensor hallucis longus, numbness on top of foot and 1st web space
  • investigation: rule out infection or tumor, MRI/CT
  • treatment: NSAIDs, muscle relaxants, exercise, education, some will need surgery
  • pain relief: NSAIDs (ibuprofen or Naprosyn), COX-2 inhibitor like Celebrex, narcotic (Percocet or Vicodin), Lidoderm patch
  • anti-inflammatory: NSAID, COX-2 inhibitor
  • muscle relaxant: Flexeril, Skelaxin, Soma or Robaxin
  • steroids? hold NSAIDs

C.) Sacroiliac dysfunction: acute or chronic injury to the SI joint
  • presentation: pain in SI area, + FABER, no discogenic pain
  • investigation: CBC, eosinophil sedimentation rate, antinuclear antibody, rheumatoid factor, HLA-B27
  • treatment: ice, stretch, NSAIDs, injections

D.) Cauda equina syndrome: compression of L2-L4 nerve roots causes paralysis without spasticity
  • could be central disc herniation, abscess, or hematoma
  • presentation: loss of bladder and bowel control, bilateral lower extremity weakness and sensory deficits
  • treatment: emergency surgical decompression

E.) Lumbar spinal stenosis: progressive degeneration of disc and facet joints → narrowing of the canal and compression of nerve roots
  • presentation: cramping in legs, radicular symptoms, pain increased with sitting or spinal extension, pain relieved with flexion, patient walks stooped over, sensory changes, decreased DTRs, mild weakness
  • investigation: x-ray, MRI
  • treatment: PT, core strength, NSAIDs, decrease impact and bending, surgical decompression if disease is progressive

F. Spondyloysis: stress fracture of the pars interarticularis
  • most commonly in L5
  • dancers, gymnasts, lifters
  • presentation: pain is adjacent to midline and is aggravated with extension and rotation
  • investigation: x-ray showing “scotty dog with collar”
  • treatment: modification of activities, core strength

G.) Spondylolisthesis: displacement of a vertebra anteriorly or posteriorly
  • grade I-V depending on degree of displacement
  • seen in dancers and gymnasts
  • investigation: x-ray showing slip
  • treatment:
    - if asymptomatic → no restrictions, core exercises
    - if symptomatic → same but with brace
    - progressive with deficits → surgery

H.) Piriformis syndrome: irritation of the sciatic nerve beneath the piriformis muscle
  • from trauma, spasm, or anatomic defect
  • presentation: sciatic notch tenderness
  • investigation: rule out herniated nucleus pulposus
  • treatment: rest, ice, meds, stretching, injection
I.) **Scoliosis**: lateral curvature of the spine in the thoracic or lumbar region
- frequently idiopathic
- much more common in girls
- investigation: forward flexion for asymmetry, x-ray at Cobb angle
- treatment: if < 10° watch it, if < 20° conservative management
- if severe, surgical fixation with fusion and rod

J.) **Tumor**
- highest prevalence in BLT-kosher pickle
- presentation: night pain, nerve root compression

K.) **Lumbar spine osteoarthritis**: degeneration of articular cartilage with growth of new bone around facet joint
- presentation: brief stiffness in the morning
- can lead to facet syndrome: nerve root compression by loss of disc height and facet hypertrophy
- investigation: x-ray showing joint narrowing, sclerosis, osteophytosis
- treatment: weight reduction, education, pain relief

L.) **Ankylosing spondylitis**: chronic autoimmune inflammation of the spine and sacroiliac joint
- presentation: chronic low back pain, morning stiffness that improves with movement
- investigation: seronegative spondyloarthropathy, x-rays showing erosion and sclerosis of SI joint and calcification between vertebral bodies (“bamboo stalks”), decreased Schober’s test mobility
- treatment: PT, NSAIDs, sulfasalazine, infliximab

M.) **Osteoporosis**: reduction in bone mass → vertebral compression fracture
- treatment: calcium and vitamin D, exercise, smoking cessation, postmenopausal estrogen therapy, bisphosphonates, raloxifene

N.) **Lumbar spine infection**: osteomyelitis, septic discitis, paraspinous abscess, shingles
- accounts for 0.01% of all low back pain cases
- presentation: fever + low back pain
- investigation: leukocytosis

O.) **Referred pain to the lumbar spine**: gallbladder, pancreas, abdominal aortic aneurism, endometriosis, chronic pelvic inflammatory disease, prostate cancer, renal stones, pyelonephritis

17.5.5 **Vertebral Fractures**

A.) **Chance fracture**: a compression injury to the anterior portion of the vertebral body and a transverse fracture through the posterior elements of the vertebra and the posterior portion of the vertebral body
- from MVA where seatbelt immobilizes pelvis while thorax is thrust forward
- unstable!
- investigation: lateral view x-ray best

B.) **Burst fracture**: collapse of a vertebral body
- from high height fall with landing on feet or buttocks
- unstable!
- presentation: may have neuro symptoms from fragments extending into the spinal canal
- investigation: lateral view x-ray shows smaller than expected vertebral body, AP x-ray shows distance between pedicles

C.) **Wedge fracture**: collapse of anterior vertebral body with intact posterior wall
- from hyperflexion +/- osteoporosis
- stable

D.) **Spinous process fracture** ("Clay shoveler's fracture if at C7"):
- from sudden forceful ligamentous traction on or below the spinous process
- stable
- investigation: lateral x-ray shows lucency through spinous process
E.) Coccyx fracture
- from fall on coccyx
- presentation: pain over coccyx
- investigation: rule out hematoma or displaced fracture with rectal exam
- x-rays not indicated in mild trauma

17.5.6 Low Back Rehab
- Pain control
- Reduce inflammation
- Relative rest with aerobic conditioning, flexibility, core strengthening
- Weight reduction
- Good biomechanics
- Goal towards pain-free ROM

17.6 The Hip

17.6.1 Gait Analysis
1.) Width: normal is 2-4” from heel to heel
   - wider [instability]
   - as in cerebellar disease or peripheral neuropathy
2.) Center of gravity: normal lateral oscillation is < 2”
   - hip pain or weakness [shift in center of gravity over affected hip]
3.) Knee and foot position: knee should be flexed in all phases of stance except on heel strike
   - abnormal: patient hikes up affected leg or swings it out and around to the front
   - steppage gait: weak ankle dorsiflexors result in increased knee and hip flexion
   - flat foot gait: from gastroc or soleus weakness (S1/S2 radiculopathy)
   - back knee gait: from quadriceps weakness, patient must push on thigh to lock the knee during stance phase
   - foot drop: weakness of the tibialis anterior
4.) Pelvic shift: normal is 1” lateral shift to weight bearing side
   - weak glutes (hip abductors) [lateral shift accentuated to side involved]
   - Trendelenberg gait (abductor lurch): gluteus medius weakness, patient lurches toward weak side to help place center of gravity over that hip
   - Extensor lurch: gluteus maximus weakness, patient thrusts thorax posteriorly to maintain hip extension
5.) Length of step: 15” on average
   - age, fatigue, pathology [shortened stride]
   - antalgic gait: limping from pain
6.) Cadence: 90-120 steps per minute on average
   - age, fatigue, pain [cadence decreased to save energy]
7.) Pelvic rotation: normally 40° in leg moving forward in swing phase
   - pain or stiffness in swinging hip [abnormal rotation]

17.6.2 Pelvis Imaging
- Radiographs
- AP interpretation:
  - inspect inner and outer main ring cortices
  - inspect the 2 small obturator rings
  - SI joint spaces should be equal
  - alignment of pubic symphysis with < 5 mm joint space
- inspect acetabulum for step off
  - lateral view
  - all views:
    - smooth femoral neck cortex with normal trabecular pattern and no transverse sclerotic lines
    - compare intertrochanteric region with other hip
- CT if fracture identified or suspected
- a high-energy pelvic fracture is associated with organ and vascular laceration

17.6.3 Common Hip Injuries

A.) Fractures:
- most cases are > 65 years old
- caused by falls or MVA
- types
  - Garden classification: for femoral neck fracture; has implications for treatment
    - Garden type I: incomplete fx ORIF
    - Garden type II: complete fx with no displacement ORIF
    - Garden type III: complete fx with partial displacement prosthetic replacement
    - Garden type IV: complete fx with total displacement prosthetic replacement
- intertrochanteric region fracture
- subtrochanteric region fracture
- femoral shaft fracture
- distal femur fracture
- prevention: exercise, calcium supplements, activity, safety precautions
- presentation: pain, shorter or rotated leg
- investigation: screen with x-ray, MRI if needed
- complications: pneumonia, pulmonary embolism, femoral neck fx/hip dislocations prone to avascular necrosis
- treatment: screws, partial or total hip replacement

B.) Femoral stress fracture: most commonly in the neck
- seen in thin, young, female endurance athletes
- presentation: groin pain with running that progresses to ADL pain, pain limits extremes of internal and external hip rotation
- investigation: x-ray may be negative, bone scan in 2-8 days
- treatment: displaced or lateral fx ORIF, nondisplaced no weight bearing for 6-8 weeks

C.) Hip dislocation
- almost always posterior
- often in from MVA and knee slamming dashboard
- presentation: hip stuck in flexion/adduction/external rotation
- investigation: x-ray, assess for neurovascular involvement
- treatment: pain relief and reduction with Allis maneuver

D.) Hip osteoarthritis: achy pain over hip and anterior groin with loss of ROM
- investigation: x-ray showing decreased joint space, sclerosis, osteophytosis
- treatment: NSAIDs, intra-articular injection, hip replacement

E.) Hip apophysitis: inflammation at sites of muscle attachment to hip apophyses (growth plates)
- separation or widening apophysis

F.) Avulsion fracture of the ASIS: where the sartorius originates
- caused by knee flexion with hip hyperextension
- presentation: pain over ASIS and with resisted hip flexion
- investigation: x-ray
- treatment: RICE, progressive weight bearing, splint in knee flexion, ORIF if displaced
G.) Avulsion fracture of the ischial tuberosity: where hamstrings originate
- caused by vigorous hip flexion with knee extension
- presentation: pain in buttock, tenderness at ischial tuberosity
- treatment: RICE, progressive weight bearing, ORIF if displaced

H.) Groin pull:
- from forced abduction during fall or collision
- presentation: pain at origin of hip adductors, increased pain on resisted hip adduction
- investigation: rule out hernia or torsion
- treatment: rest, ice, meds, stretching, strengthening

I.) Hip pointer: contusion of the iliac crest
- from direct blow
- presentation: swelling, tenderness, ecchymosis at iliac crest
- investigation: x-ray to rule out fracture
- treatment: ice, compression, pain meds, progressive stretching

J.) Legg-Calve-Perthes disease: avascular necrosis of the femoral head in peds
- ages 2-11
- presentation: limp, insidious groin pain, thigh pain, loss of internal/external rotation
- investigation: x-ray shows mottled femoral head
- treatment: containment of femoral head with bracing or casting
- prognosis: typically self-limiting, some with spontaneous revascularization

K.) Slipped capital femoral epiphysis: separation of femoral head from femur at growth plate
- seen in obese, pre-pubescent boys and girls, but otherwise idiopathic
- commonly bilateral
- presentation: limp, hip/thigh/knee pain, loss of internal rotation/flexion/abduction
- treatment: surgical fixation with no weight bearing

L.) Snapping hip syndrome: ITB or iliopsoas tendon snaps or ASIS
- presentation: hip pain is worse with activity, snapping with flexion, increased pain with resisted hip flexion
- treatment: ice, meds, activity modification, strengthening & stability, injections

M.) Trochanteric bursitis: inflammation of bursa of greater trochanter
- presentation: extreme point tenderness, pain at night when lying on affected side, pain with flexion/extension movement, crepitus over greater trochanter
- treatment: hip stretches, meds, injections

N.) Transient synovitis of the hip: inflammatory response to upper respiratory infection synovial fluid buildup in hip joint and pain
- presentation: hip pain for 3-7 days, painful ROM, joint held in flexion/abduction/internal rotation
- investigation: must rule out septic hip and Legg-Calve-Perthes with bone scan (would need antibiotics and I&D)
- CBC showing normal WBC and sed rates
- joint aspiration showing normal fluid
- x-ray will show capsular swelling
- treatment is symptomatic

O.) Meralgia paresthetica: lateral femoral cutaneous nerve entrapment as it exits the pelvis at the ASIS
- caused by obesity, tight clothing, repetitive trauma/activity
- presentation: burning pain over lateral thigh
- treatment: correct offending source, pain relief, injections or surgical release if

17.7 The Knee

17.7.1 Assessment of Injury
Swelling within a few hours — think hemorrhage
ACL tear
patellar dislocation
fracture
meniscus tear
Intermittent swelling — meniscus tear, gout, chondral lesions
Localization of pain (see Betsy's sheet)
  • anterior patellofemoral dysfunction, patellar tendonitis, plica or fat pad irritation, tibial plateau fx
  • posterior meniscal tear, medial gastroc strain, distal femoral fx
  • lateral meniscal tear, LCL injury, ITB syndrome, posterolateral corner, chondral lesion
  • medial meniscal tear, DJD, MCL injury, pes anserine bursitis, chondral lesion
Instability — ACL, PCL, PLC, ITB, plica syndrome
Other causes of knee pain: infection, arthritis, referred pain, neoplasm

17.7.2 Imaging of the Knee

Radiograph
  • AP/lateral views: good for visualizing tumors, fractures, DJD, surgeries, hardware
    o DJD see "Fairbanks changes" of flattened tibial plateau, decreased joint space, osteophytosis, subchondral cysts
  • merchant or "sunrise" views: good for visualizing instability, DJD, chondral lesions
  • tunnel view: osteochondral defect
MRI
  • excellent for soft tissue injuries such as ACL, meniscus, chondral lesions
  • also for bone contusions, edema, tumors
  • fracture imaging is getting better
CT
  • excellent for fracture characterization
  • not so good for evaluation soft tissue injuries

17.7.3 Common Knee Problems

A.) Meniscal tears:
  • presentation: +/- swelling, locking, catching, joint tenderness, may have Baker’s cyst
  • investigation: + Apley’s grind test
B.) Medial collateral ligament tear:
  • from valgus stress
  • graded I-III depending on degree of tear
  • presentation: medial pain on and around joint line
  • investigation: + valgus stress test
  • treatment: NSAIDs, ice, rest, bracing, PT, rarely is surgery needed
C.) Osteochondritis dissecans: avascular necrosis — death of bone — loss of support for articular cartilage
  • particles of bone and cartilage rub around in joint space
  • presentation: swelling after exercise, locking, catching, vague pain, small effusion, tender femoral condyles
  • treatment: no weight bearing for 6+ weeks
D.) Plica syndrome: when fold of synovial membrane gets stuck in joint spaces — catching
  • presentation: painful snapping, local swelling, palpable plica
  • investigation: imaging to rule out other causes of injury
  • treatment: PT, ice after exercise, NSAIDs, injection, surgical excision
E.) Lateral collateral ligament tear:
  • from varus stress
  • graded I-III depending on degree of tear
• treatment: conservative for grades I&II, consider surgical repair for grade III

F.) IT band syndrome: irritation of the IT band when it rubs at the femoral head or lateral femoral epicondyle
• presentation: snapping hip or knee, instability
• treatment: PT, injection, orthotics, running on different surfaces or using different shoes

G.) Patellar dislocation
• investigation: AP, lateral, merchant, sunrise, Laurin x-ray views
• treatment: extension brace, quad strengthening, consider surgical repair with multiple occurrences

H.) ACL tears
• investigation: MRI to rule out other injuries
• a Segond fracture (avulsion fx at the tibial plateau) is strongly associated with ACL tears
• treatment: PT prehab, surgical repair, post op brace, NSAIDs

I.) PCL tears
• investigation: + posterior draw, + sag sign, + recurvatum, + quad active test

J.) Patellofemoral instability/malalignment: a spectrum of disorders usually due to anatomic abnormalities
• almost always involves lateral instability of the patella damage of medial retinacular tissue and medial patellofemoral ligament
• aggravated with walking stairs or prolonged sitting
• treatment: PT, short course NSAIDs, patellar brace, orthotics, activity modification, surgery last resort

17.8 The Ankle

17.8.1 Ankle Background

- Lateral ligaments
  - anterior talofibular ligament: primary source of restraint to anterior ankle translation, internation rotation, and inversion
    - but is the most commonly injured ligament during ankle inversion injuries
  - posterior talofibular ligament:
  - calcaneofibular ligament: prevents inversion when the foot is in the neutral or dorsiflexed position
    - deep to fibularis tendon sheath
  - relative ligament strength: calcaneofibular > posterior talofibular > anterior talofibular

- Medial ligaments
  - deltoid ligament: the largest, prevents abduction/eversion of the ankle
  - anterior tibiofibular ligament:
  - posterior tibiofibular ligament:

- Prepubescent ankle injuries have increased risk of growth plate injury over ligamentous injury, as ligaments are stronger at this stage in development

- Grading of ankle sprains (depends mostly on degree of instability)
  - type I sprain: ligaments are overstretched
  - type II sprain: ligaments are slightly torn
  - type III sprain: ligaments are torn completely
17.8.2 Ankle Imaging

- Radiographs
  - when to order go by Ottawa Rules: get x-ray with any bone tenderness or inability to bear weight
  - views: AP, lateral, mortise (10-15° internal rotation)
  - look for: medial clear space, lateral clear space, tibiofibular clear space, symmetry

17.8.3 Common Ankle and Foot Injuries

- order of rupture is always anterior talofibular, then calcaneofibular, then posterior talofibular

A.) Lateral ankle sprain: usually anterior talofibular injury
- most common ankle injury
- most commonly from ankle inversion stretch of tear of lateral ligaments
- treatment: PRICE, NSAIDs, elevation, crutches until weight bearing without limp

B.) Medial ankle sprain: injury to deltoid ligament
- rare!
- may co-occur with medial fx = make sure you palpate the knee area as well
- Maisonneuve fracture: occurs from excessive external rotation tearing of syndesmosis and spiral fx of proximal fibula
- treatment: conservative in absence of fx; theraband exercises, stretching

C.) Syndesmosis sprain: “high ankle sprain”
- presentation: minimal swelling, pain over anterior tibiofibular ligament
- investigation: + squeeze and external rotation tests
- treatment: non-weight bearing, then walking boot

D.) Achilles rupture: sharp pain with shot-like sound when it happens
- presentation: + Thompson test
- treatment: serial casting with PT, surgical repair

E.) Achilles tendonitis:
- presentation: gradual onset of posterior pain with activity
- treatment: short-term heel lift, NSAIDs, ice after activity, PT

F.) Medial tibial stress syndrome (shin splints): posterior tibial muscle tendonitis
- presentation: pain is worse with activity
- investigation: point tenderness or night pain consider stress fx, numbness/pain/swelling consider compartment syndrome
- treatment: ice, NSAIDs, decrease mileage, orthotics, stretch & strengthen
- compartment syndrome surgical release

G.) Injuries to the rear foot
- Sever’s disease (calcaneal apophysitis): repetitive microtrauma to the calcaneal growth plates
- common in 7-15 year olds
- presentation: pain at the calcaneus and Achilles tendon insertion, heel pain worse with activity
- treatment: ice, massage, stretch heel cord, heel cups, orthotics
- Haglund’s deformity (“pump bump”): overgrowth of bone on lateral and posterior calcaneus due to recurrent friction
- treatment: change shoes, padding, ice, excision of overgrowth

H.) Plantar fasciitis: excessive pull at origin of plantar fascia on calcaneus inflammation heel spur
- treatment: orthotics, higher heeled shoes, ice, heel cord stretch, NSAIDs

I.) Sesamoiditis: repeated or direct trauma to the sesamoids at the 1st metatarsal
- treatment: metatarsal lift pad

J.) Turf toe: 1st metatarsophalangeal joint sprain
- from hyperextension of big toe
• graded 1-3 based on degree of tear
• presentation: swelling, tenderness, decreased ROM at 1st MTP joint
• treatment: PRICEMM

K.) Morton’s neuroma: fibrosis of plantar nerve from injury
• often from repeated irritation of tight, high-heeled shoes
• presentation: feels like walking on a marble
• treatment: injections or excision

L.) Gouty toe: urate crystal deposition in the 1st MTP joint
• from hypercalciuria due to disorder of purine metabolism
• presentation: red, hot, swollen big toe that is exquisitely tender
• treatment: Indocin, Toradol, steroids, chlophoprine

M.) Pes planus: flat feet
• congenital or acquired from posterior tibialis tendon weakness
• treatment: arch supports, heel cord stretching, orthotics

N.) Bunion (hallux valgus): lateral deviation of the big toe at the MTP joint
• caused by tight shoes
• treatment: shoe modification, osteotomy

O.) Onychocryptosis: ingrown toenail
• most commonly on the lateral border of the big toe
• due to trauma or nails cut too short
• can lead to infection of soft tissue around the nail
• treatment: antibiotics, soaks, debridement, nail removal if chronic

P.) Toe deformities
• usually caused by ill-fitting shoes
• hammer toe: fixed flexion of PIP
• mallet toe: fixed flexion of DIP
• claw toe: fixed flexion of both
• claw toes can also be caused by rheumatologic disorders
• treatment: Girdlestone-Taylor tendon transfer

17.8.4 Ankle Rehab
• Phase I: RICE
• Phase II: active and passive ROM, muscle strengthening, inversion & eversion exercises, proprioceptive training
• Phase III: plantarflexion stretching program, continued proprioception and strengthening
• Can return to play when there is pain-free ROM, can complete functional testing, and can do 10 strong painless toe raises on affected ankle

17.8.5 Foot and Ankle Fractures
A.) Proximal 5th metatarsal fractures
• Jones fracture: fracture of the diaphysis of the 5th metatarsal of the foot (between insertion of fibularis brevis and fibularis tertius)
  • from plantarflexion + adduction force
• treatment: non-weight bearing immobilization, ORIF if displaced
• avulsion (dancer’s) fracture: secondary to pulled plantar aponeurosis
• treatment: boot, PT
• stress fracture:
  • Be aware of the commonly missed “FLOAT” fractures

B.) Distal fibula fractures
• most common kind of ankle fx
• inversion injury
• presentation: tenderness over lateral malleolus
• treatment based on Weber classification:
  • Weber A = below mortise \(\rightarrow\) short leg cast, then boot
  • Weber B = spiral fx at mortise \(\rightarrow\) refer
  • Weber C = above mortise \(\rightarrow\) refer

C.) Lower leg stress fracture: most commonly tibia, navicular, metatarsal
• presentation: localized pain
• investigation: x-ray (but will look normal until 2-3 weeks after injury), bone scan (+ sooner than x-ray)
• treatment: rest, immobilization in pneumatic air cast

D.) Lisa Frank fracture! (actually Lisfranc): fracture where lateral dislocation of the metatarsals occurs in relation to the cuneiforms
• historically from foot of soldiers getting caught in stirrups
• treatment: ORIF

17.9 Pharmacology: Management of Musculoskeletal Pain

17.9.1 Kinds of Pain
• Acute: describes post-op, procedural, and trauma-related pain
• a protective response to injury
• well-defined starting point
• improves as healing occurs
• good response to analgesics: acetaminophen, NSAIDs, muscle relaxers, benzos, tramadol, opioids
• Chronic: maladaptive pain that is out of proportion to injury
• a non-protective response
• injury is often not apparent
• can be neuropathic or nociceptive
• variable response to analgesics, may require multiple drug classes: acetaminophen, NSAIDs, antidepressants, benzos, tramadol, opioids

17.9.2 NSAIDs
• Includes aspirin, ibuprofen, naproxen, diclofenac, indomethacin, ketorolac
• ibuprofen: IV available
• naproxen sodium:
• acetaminophen: first-line therapy for osteoarthritis, IV available
• aspirin: anti-platelet effects
• indomethacin:
• diclofenac K:
• diclofenac:
• sulindac: less renal toxicity
• ketorolac: IV available
• COX selective:
  • o meloxicam: but COX-2 activity \(\geq\) COX-1 activity at low doses
  • o etodolac: more COX-2 selective
  • o celecoxib: COX-2 specific, $$, cardiovascular toxicity, sulfa allergy caution
    • increased risk of CV thrombotic events
    • GI protective only up to 6 months
• long-acting: all have slow onset
  • o oxaprozin: useful for chronic pain
  • o nabumetone:
  • o piroxicam:
• non-acetylated salicylates: less like to cause GI bleed but are $$
  • o diflunisal:
17.9.3 Opioids

- Usually not for acute pain, only if it is severe or unresponsive to NSAIDs
- Common kinds:
  - codeine:
  - hydrocodone:
  - oxycodone:
- tramadol: reduced dosing in elderly/liver/renal patients, seizure risk with concomitant antidepressants
  - serotonin syndrome risk with SSRIs
  - contraindicated with alcohol or drug intoxication
- Kappa opioids/agonist-antagonists
  - generally try to avoid because:
    - they will act like Narcan on someone who is opioid-dependant and make them go crazy on you
    - they have high risk of psychiatric side effects
    - there is a ceiling effect
- more effective in women than men
- Side effects: respiratory depression, CNS, nausea, vomiting, constipation

17.9.4 Skeletal Muscle Relaxants

- Antispasitics: used for neuromuscular conditions, not really musculoskeletal
- NOT effective for CP, MS, stroke
- baclofen:
- dantrolene:
- Tizanidine: both an antispastic and antispasmodic
  - needs renal/hepatic dosing, hypotension, sedation, dry mouth, constipation
  - may be effective for chronic pain, headaches
  - Antispasmods: used for msk spasms related to injury
  - short-term use only = first 2-7 days post injury
  - really more sedative than truly muscle relaxing
- cyclobenzaprine: potential cardiac effects, dry mouth
- methocarbamol: available IV for tetanus
- carisoprodol: may be habit forming
- chlorzoxazone: fatal hepatocellular injury with use > 1 month
- metaxalone: nausea, hypersensitivity, LFT elevations
- orphenadrine: injection available, dry mouth, urinary retention, constipation, elderly confusion
- diazepam: may be habit forming
17.9.5 Combos

- **Combunox**: ibuprofen + oxycodone
- **Vicoprofen**: ibuprofen + hydrocodone

17.9.6 Other Pain Relief Agents

- Capsaicin creams or patches
- work by depleting substance P
- uber-dose patch requires topical anesthetic to administer but relieves pain for 3 months
- Topical salicylates

17.9.7 Specific Therapies

- Back pain
- acute: NSAIDs (nonspecific or COX-2 inhibitors), muscle relaxers, opioids
- chronic: tricyclic antidepressants
- Fibromyalgia: pregabapentin, gabapentin, SNRIs, milnacipran
18 Pulmonology Exam Notes

18.1 Pulmonology H&P

18.2 Physiology Refresher

- Control of ventilation
- Autonomic control via the brainstem
  - Primarily involuntary, but voluntary control can be achieved through descending pathways from the cerebral cortex to respiratory muscles
  - Coordinated through phrenic, intercostal, cranial, and cervical nerves
  - Positive and negative feedback loops via chemoreceptors and mechanoreceptors
- Inspiration is a result of muscles creating negative air pressure
  - Primary muscle is the diaphragm
-Expiration is normally a passive process as a result of natural recoil and elasticity of the lungs
- O2 unloading at the tissues follows the oxygen/Hb dissociation curve
- Measured by pulse oximetry
  - May be inaccurate in severe anemia, abnormal Hb, presence of intravascular dyes, and lack of pulsatile arterial blood flow
- PO2 falls with increasing altitude

18.2.1 Physical Exam Refresher

- Inspection
- Palpation
- Percussion
- Auscultation

 Normal breath sounds:
  - Vesicular: soft, low pitched, over most lung fields, inspiration > expiration
  - Bronchovesicular: med pitched, over main bronchus and R posterior lung, inspiration > expiration
  - Bronchial: loud, high pitched, over manubrium only, expiration > inspiration
  - Tracheal: very loud, high pitched, over trachea only, inspiration > expiration

 Adventitious sounds: extra sounds, always abnormal
  - Crackles or rales: discontinuous, fine/medium/coarse, not cleared by coughing, heard more often on inspiration
    - Dry or wet
    - Due to small airways being forced open in a disruptive fashion
    - Also heard in atelectasis from disuse of the lung
  - Rhonchi: continuous, foghorn, low-pitched, cleared on coughing
    - From air passing through an obstructed airway
  - Wheezes: continuous, tea kettle high pitch, usually diffuse and bilateral
    - Heard diffusely in asthma
    - Unilateral = foreign body aspiration
    - From air being forced through a constricted airway
  - Rub: pleural sound that is like leather rubbing together
    - Caused by inflamed pleural surfaces rubbing together
    - Come and go depending on amount of fluid in pleural space
    - Documentation: loudness, pitch, quantity, location on lung fields, inspiratory/expiratory, effect of coughing, effect of position change

 Vocal resonance: egophony ("E" ∆ "A"), bronchophony, whispered pectoriloquy
18.3 Common Pulmonary Symptoms

18.3.1 Dyspnea

- Acute or chronic

- Causes
  - respiratory: bronchospasm, bronchitis, pneumonia, pulmonary embolism, pulmonary edema, pneumothorax, upper airway obstruction
  - cardiovascular: acute MI, CHF
    - cardiac tamponade: water bottle appearance of heart on CXR
  - something else: anemia, DKA, deconditioning, anxiety, etc.
  - if chronic: asthma, COPD, interstitial lung disease, cardiomyopathy

- Investigation
  - good history & PE leads to accurate diagnosis 2/3 of the time
  - oximetry or ABG
  - CXR
  - spirometry
  - CBC to r/o dyspnea from anemia
  - ECG

- Treatment
  - treat the cause!
  - oxygen
  - pulmonary rehab: improves exercise capacity, reduces perceived breathlessness, improves quality of life, reduces anxiety and depression, improves survival
  - treat anxiety

18.3.2 Cough

- Acute if less than 3 weeks
- Persistent if 3-8 weeks
- Chronic if greater than 8 weeks
  - women more likely to develop

- Causes: URI, pneumonia, aspiration, pulmonary embolism, pulmonary edema
  - in smokers it is usually low-grade chronic bronchitis
    - with increased intensity ⊗ lung cancer
  - in nonsmokers is usually postnasal drip, asthma, GERD, or ACE inhibitors
  - ROS may include: fatigue, insomnia, headache, urinary incontinence, rib fx

- Investigation
  - CXR in smokers, fevers, and weight loss
  - Treatment: care for underlying cause, elimination of irritants

18.3.3 Hemoptysis

- expectoration of blood originating below the vocal cords
- Usually comes from bronchial arteries (high pressure)
- Be aware of mimics: upper respiratory tract bleed, upper GI bleed
- Causes: most commonly bronchitis, bronchogenic carcinoma, pneumonia
  - other causes: infection, Goodpasture’s syndrome, Wegener’s granulomatosis, autoimmune, iatrogenic, cocaine, AV malformation, pulmonary embolism, elevated pulmonary capillary pressure, foreign body, airway or parenchymal trauma, fistula formation, idiopathic

- Investigation: CXR, hematocrit, UA, renal labs, coag profile, bronchoscopy
  - tumor workup with strong history of smoking and > 1 week hemoptysis

- Treatment: treat cause
18.4 Pulmonary Imaging

18.4.1 Imaging Techniques
- Radiation dose
  - too much white = not enough radiation used/underexposed
  - too dark = too much radiation used/penetrated objects too much
- Densities
  - air = black
  - fat = charcoal
  - water = gray
  - calcium = pale gray
  - metal = white
- Silhouettes
  - borders of objects next to each other can’t be distinguished unless they are of different densities
  - if you are uncertain of which lobe a consolidation is in or whether it is anterior/posterior you can figure it out by looking at where normal borders of the heart are lost in the consolidation = silhouette signs

18.4.2 Systematic Approach to Reading a Chest Radiograph
1.) Adequacy: is it a good image on the right person?
- symmetric clavicles
- midline spinous processes
- exposure: should be able to see through trachea to vertebral processes
2.) Mediastinum and hila
- check mediastinal contours
- heart size should be less than half the thorax diameter
- cardiophrenic angles
- retrocardiac shadows: should be able to see heart lung through the heart
- check hilar contours for adenopathy
- look at vessel size for pulmonary hypertension
3.) Airways and lungs
- foreign bodies?
- count ribs to make sure there is no crowding
- tracheobronchial tree
- examine air spaces for masses, nodules, or consolidations
- look at interstitium (between air spaces)
  - look for thickening or nodules of the pulmonary vessels and lymphatics
- hyperexpansion of lungs in COPD and asthma
4.) Pleura and diaphragm
- look for hemothorax, empyema, effusion (simple fluid), pneumothorax
  - pleural effusion: see blunting of costophrenic angles, air/fluid level
    - large effusions may cause mediastinal shift
    - minimum effusion amount for detection is 75 mL on lateral view or 200 mL on frontal view
- air in pleural space occurs with tension pneumothorax
  - also pushes diaphragm down (deep sulpus sign), shifts mediastinum to the left, and causes intercostal widening
- slivers of air underneath diaphragm are called pneumoperitoneum
  - normal post-operatively
  - if no history of chest surgery, may be perforated bowel
5.) Bones and soft tissue
- bones:
  - architectural distortion
  - cortical discontinuity
  - clavicles and shoulders
  - ribs
  - vertebrae
- soft tissue:
  - neck base
  - axilla
  - breast shadows
  - subcutaneous gas
    - due to penetrating injury or rib fracture in a trauma patient
  - upper abdomen

6.) Tubes, lines, and drains
- check for proper positioning
- widened mediastinum indicates vascular injury from device

18.4.3 Chest CT
- Indications: CXR abnormality, lung tumor, mediastinal mass, aortic injury, dissection, aneurysm, complicated infection
- When to use contrast:
  - not usually needed for pulmonary imaging as most things will be of differing density than lung tissue
  - best for vessel enhancement as in PE, aortic aneurysm or dissection, some tumor protocols
  - See interlobular septal thickening in interstitial lung disease
  - Can visualize thrombus in pulmonary artery during PE
  - CXR frequently normal

18.4.4 Ventilation-Perfusion Scans (VQ Scans)
- Benefits: less radiation than CT
- Disadvantages: time consuming, doesn’t provide as much anatomic information as CT
- Involves inhalation as well as venous injection of a radiotracer
- Detects areas of the lung that are being perfused and those that are being ventilated for comparison
- Imaging is graded based upon probability of PE
- Use over a CTA if patient has a contrast allergy or is pregnant (less radiation)

18.4.5 Cardiothoracic Angiography
- Preferred over VQ scan

18.4.6 Thoracentesis
- Ultrasound or CT guided
- Can be diagnostic and/or therapeutic
- Short or long-term
- drain is promptly removed if there is no purulent fluid draining (no evidence of infection)

18.4.7 Lung Biopsy
- Guided by bronchoscope or CT
- Fine-needle aspirate or core sample
- core provides more tissue for testing
- Contraindicated for lesions < 1cm or high bleed risk
- Small pneumothorax always occurs as a result
- resolves if tissue is healthy
needs to be followed by a chest tube with unhealthy lung tissue

18.5 Sputum Cultures

- Defining the respiratory tract
  - upper = nose, nasal cavity, nasopharynx
  - lower = larynx, trachea, bronchi, bronchioles, alveoli
- Specimens
  - sputum specimen: expectorated matter from the trachea, bronchi, and/or lungs through the mouth
  - endotracheal specimen: suctioned sputum from an endotracheal or tracheostomy tube
    - ideal because you are bypassing the mouth flora
  - bronchoalveolar lavage specimen: wash collected from an area of the lung during a bronchoscopy
- Cultures
  - LRT specimen should be sterile when directly sampled (induced sputum, BAL, bronchial brush, etc) = don’t need to screen with Gram stain before culturing
  - sputum will always have some normal oral flora in it = Gram stain will evaluate sample for quality
    - needs to have < 10 squamous epithelial cells per low power field to be acceptable
- when to culture?
  - bronchitis □ never, almost always viral
  - pneumonia □ must ask for different culture medium when suspecting anaerobes (aspiration), atypicals, pertussis, fungi
  - acid fast bacilli: requires serial (3) early morning sputum cultures because there will be a low yield of bacteria in each sample
    - long incubation period, up to 6 weeks
- Stains
  - Gram stain
    - too many squamous epithelial cells are indicative of oral mucosal contamination
    - numerous neutrophils are indicative of infection
      - although the absence of neutrophils in a neutropenic or immunocompromised patient does not rule out infection
    - macrophages common in fungal, acid-fast, and other atypical bacterial infections
    - eosinophils indicate allergic reaction or parasitic infection
    - mucus strands indicate direct attack (antibodies and lysosomes) of inhaled bacteria
  - acid fast stain: special stain to look for Mycobacterium and other acid fast bacteria
    - low sensitivity, but a positive indicates treatment should begin as long as there is an appropriate clinical picture
      - must also report to health department

18.6 Tuberculin Skin Testing

- Mantoux tuberculin skin test (PPD): tuberculin antigen is injected beneath the skin, with presence or absence of reaction measured in 48-72 hours
- induration (bump) not erythema measured
- will only catch a developed immune response against TB
  - takes 2-12 weeks to develop a response after an exposure
  - problem if someone does not have a strong enough immune system to mount a response = potential false negative
    - prevent by using a control that everyone is exposed to, such as Candida albicans antigen
  - problem when someone has latent TB or old BCG vaccine with waning immunity against it
    - first PPD test will be negative but will stimulate memory T-cells
    - second PPD will be positive
    - this person is a “converter” = why you frequently have to get “two-step” TB tests to protect against this being missed
- positive readings
- patients at high risk for developing active TB: immunosuppressed, recent contacts, CXR demonstrating past infection
  - positive if their skin test is ≥ 5 mm
- other high risk groups: injection drug users, residents/employees of hospitals/nursing homes/prisons/shelters, lab workers, children under 4, comorbid conditions
  - positive if their skin test is ≥ 10 mm
- patients with no risks
  - positive if their skin test is ≥ 15 mm
- potential for false positives as this test has cross-reactivity with all mycobacterial exposures
- anyone who has had the BCG vaccine for TB or latent TB will probably test positive also = need to use a different test to check for active infection vs antigenic memory
  - **Interferon gamma release assay**: uses a blood sample from a patient to detect release of interferon in response to TB antigens not present in the BCG vaccine or in other mycobacterial infections
    - means this test can distinguish between a positive PPD as a result of previous vaccination and latent TB

### 18.7 Respiratory Tract Infections and Antibiotic Therapy

#### 18.7.1 Pulmonary Defenses
- Mechanical: epiglottis, cough reflex, mucociliary clearance
- Immune: lysozyme, lactoferrin, IgA, collectins, alveolar macrophages

#### 18.7.2 Antibiotics and LRT Infections
- Shorter courses of high dose antibiotics is gaining popularity
- reduced resistance with better drug penetration to the infection site
- increased compliance
- Amoxicillin, Augmentin, and oral cephalosporins
- plain amoxicillin good for most Strep pneumo
- clavulanate adds active against β-lactamase producers (H flu, Staph aureus, anaerobes)
  - but less well tolerated
- no activity against atypicals
- low potential for drug interactions
- can use in pediatrics
- may have GI effects
- Macrolides: azithromycin, clarithromycin, erythromycin
  - active against most common pathogens including atypicals
  - but erythromycin not active against *H. flu*
- **Strep pneumo** resistance around 20-30%
  - risk factors for resistance: young children, daycare, recent hospitalization, recent β-lactams, HIV, alcoholism, age > 65, URT disease, inadequate dose or duration
- can use with penicillin allergies
- can use in pediatrics
- frequently have drug interactions (unless using azithromycin) with common meds like statins
- side effects of GI intolerance, QT prolongation
- Fluoroquinolones: gatifloxacin, levofloxacin, moxifloxacin, gemifloxacin
  - great activity against **Strep pneumo** but resistance is emerging
- active against *H. flu*, atypicals, *Staph aureus*
- short course, once daily
- can use with penicillin allergies
- expensive
- some safety concerns: tendon rupture, arthropathies in pediatrics, caffeine interaction, QT interval effects
- Doxycycline: rarely used but may be gaining popularity
  - active against **Strep pneumo**, *H. flu*, atypicals
- inexpensive
- Clindamycin
• active against *Strep pneumo*, anaerobes, group A strep with TSS
• not active against H. flu or atypicals
• causes *C. diff* diarrhea

18.7.3 Acute Sinusitis
• Consider: *Strep pneumoniae*, H. flu, Moraxella, Staph aureus: Bronchitis

A.) *Acute bronchitis*: symptoms for < 3 weeks where cough is the predominant feature
• may have purulent sputum
• investigation: must rule out pneumonia
• treatment: almost always viral = no antibiotics, just supportive therapy with antitussives

B.) *Chronic bronchitis*: symptoms persist for > 3 months each year for at least 2 years with other causes excluded
• common in COPD, smokers
• acute bacterial exacerbation of chronic bronchitis
• presentation with deterioration in respiratory function, increased dyspnea, increased sputum, purulent sputum
• could be *Strep pneumoniae*, H. flu, Moraxella, Mycoplasma, Chlamyphila
• treatment
• antibiotics are useful in: patients with > 4 exacerbations/year, comorbidities, on home oxygen, steroid-dependent, marked airway obstruction
• amox/clav, cephalosporins, macrolides, respiratory fluoroquinolone (NOT cipro)
• do not use antibiotics for long-term prophylactic therapy!

18.7.4 Pertussis
• Treatment
• isolation for 5 days from start of treatment
• antibiotics: macrolides, TMP-SMZ

18.7.5 Non-TB Pneumonia
A.) Types
• community: most commonly *Strep pneumo*
• if < 60 and no comorbidities, also consider: H. flu, Klebsiella, Mycoplasma, Chlamyphila, Legionella
• if > 60 with a comorbidity, also consider: H. flu, Moraxella, Klebsiella, Staph aureus, Legionella
• smokers: H. flu pneumonia more common
• Chlamyphila pneumoniae associated with chronic inflammatory diseases
• Staph aureus pneumonia rare but more common following illness with influenza
• 5-15% of these cases will be due to aspiration
• health care-associated: those in extended care, on home infusion therapy, long term HD in last 30 days, home wound care, exposure to family members with resistant organisms, recent hospitalizations
• hospital = pneumonia onset > 48 hours after admission
• also most commonly *Strep pneumo*, but increased incidence of gram neg enterics (E. coli, Klebsiella), Acinetobacter, Citrobacter, Proteus, Serratia, Pseudomonas, and Staph aureus
  -ventilator (> 48 hours after intubation)

B.) Presentation: fever or subnormal temp, rigors, sweats, cough +/- sputum, dyspnea, pleuritic chest pain, fatigue, myalgias, abdominal pain, anorexia, headache, altered mental status
• no symptom is sensitive or specific for pneumonia
• *Mycoplasma pneumoniae* may have CNS symptoms, anemia, bullous myringitis

C.) Investigation
• PE demonstrating rales or pulmonary consolidation
• CXR: remember that it can lag behind physical findings!
• new infiltrate on lung
• gram neg pneumonias may cavitate or produce empyema
• *Staph aureus* may cause necrotizing infiltrates or pneumatoceles in children
• aspiration pneumonia: necrotizing pneumonia, empyema, lung abscess
• urine test available for *Legionella*, but not useful for kids
• if hospitalized blood cultures, sputum stain and culture
• check CBC for leukocytosis, BUN, glucose, electrolytes, LFTs, O2 sats, HIV status
• induce sputum for detection of atypicals and PCP
• *Strep pneumo* urinary antigen test
• sputum examination & culture
• need 3 samples 8 hours apart

D.) Treatment

• determine outpatient vs inpatient
• can use PORT or CURB-65 score to gauge risk of mortality
  ○ PORT class I are < 50, have no sig comorbidities, relatively normal vitals, and normal mental status
• ICU with septic shock requiring vasopressors and intubation, maybe for RR > 30, multilobar infiltrates, confusion, uremia, leukopenia, thrombocytopenia, hypothermia, hypotension requiring aggressive fluid resuscitation
• antibiotic regimen
• outpatient pneumonia:
  ○ low risk advanced generation macrolide (azithromycin or clarithromycin)
    ▪ doxycycline if PCN allergic
  ○ higher-risk (cardiopulmonary disease) = need to cover resistant *Strep pneumo*, enterics, *Moraxella*, anaerobes
    ▪ antipneumococcal fluoroquinolone
    ▪ macrolide + β-lactam (cefloxacin, cefuroxime, HD amoxicillin, ceftriaxone)
  ○ suspected CA-MRSA add vanco or linezolid
• inpatient pneumonia:
  • patients being admitted for pneumonia through the ED should get their first dose of antibiotics while still in the ED
  • inpatients need to continue therapy until ≤ 1 of the following is present: temp of 37.8+, pulse 100+, RR 24+, SBP < 90, spO2 < 90%, inability to take fluid PO
  • transition to oral meds with patient is hemodynamically stable, improving clinically, able to take meds PO, and has a normally functioning GI tract
  • non ICU inpatient: same as higher-risk outpatient
• ICU without *Pseudomonas* risk:
  ○ β-lactam (aztreonam if PCN allergic) + macrolide (azithromycin)
  ○ fluoroquinolone
• ICU + *Pseudomonas* risk:
  ○ antipneumococcal/antipseudomonal β-lactam (cefepime, imipenem, meropenem, piperacillin/tazobactam, or aztreonam) + ciprofloxacin
  ○ aminoglycoside + azithromycin
  ○ aminoglycoside + antipneumococcal fluoroquinolone
• hospital-acquired pneumonia
• early onset, no MDR risk factors:
  ○ ceftriaxone
  ○ respiratory fluoroquinolone
  ○ ertapenem
• late onset and/or MDR risk factors
  ○ antipseudomonal cephalosporin: cefepime, ceftazidime
  ○ antipseudomonal carbapenem: imipenem, meropenem
  ○ piperacillin-tazobactam + antipseudomonal fluoroquinolone
  ○ aminoglycoside + vanco
• special cases:
  • consider infection with enterics in nursing home residents, those with underlying cardiopulmonary disease, multiple comorbidities, and recent antibiotic therapy
  • consider infection with *Pseudomonas* with bronchiectasis, corticosteroid therapy, recent use of broad-spectrum antibiotics, malnutrition, cystic fibrosis, recent hospitalization
  • extended therapy should be considered for *Chlamydophila*, *Legionella*, pathogens that cause pulmonary necrosis (*S. aureus*, *Pseudomonas*, *Klebsiella*, anaerobes)
• resistance issues:
  • consider increased risk of drug-resistant *Strep pneumo* with patients > 65 years, recent β-lactam therapy, alcoholism, immunosuppression, multiple comorbidities, exposure to child in daycare
  • consider risk of multi-drug resistant pathogens with recent use of antibiotics, current hospitalization > 5 days, immunosuppressive disease or therapy, nursing home residency, home infusion therapy, chronic dialysis, home wound care
E.) Prognosis:
  • response to antibiotic therapy should occur within 3 days of starting treatment
  • fever should disappear within 2-4 days of starting treatment
  • leukocytosis should resolve within 4-5 days of starting treatment
  • CXR should clear in about 30 days or up to 6 months if elderly
  • causes of treatment failure:
    • resistant organism ☐ do drug susceptibility tests
    • effusion or empyema
    • nosocomial superinfection
    • misdiagnosis
    • drug fever
  • causes of deterioration:
    • if early (< 72 hours): severe illness, resistant organism, metastatic infection, ARDS
      • misdiagnosis, could actually be a PE, vasculitis, or CHF
    • if delayed: nosocomial superinfection, exacerbation of underlying illness
      • intercurrent acute illness such as PE, MI, renal failure
  • outpatient mortality is < 1% while 12% of hospitalized pneumonias and 40% of ICU pneumonias are fatal
  • most patients with CAP should respond within 3 days of therapy, but 10% do not respond to initial treatment
  • change antibiotics if deterioration occurs or if specific organism is identified
18.7.6 Tuberculosis
  • TB most common in foreign-born US residents
  • especially Mexico, Philippines, Vietnam, India, China
  • Presentation:
    • asymptomatic if infection is latent (no symptoms, nothing in the sputum, not infectious, normal CXR)
    • usually asymptomatic during the primary infection
    • active infection: cough, fever, weight loss, night sweats, hemoptysis, fatigue, decreased appetite, chest pain
    • can also be present in CNS, lymphatic system, genitourinary system, bones, joints, disseminated (miliary TB)
  • Investigation
    • CXR
      • active TB: infiltrates in mid or lower fields, hilar adenopathy, cavitation, empyema
      • miliary pattern if there is hematogenous spread
    • past TB: pulmonary nodules +/- calcification, apical fibrosis and volume loss, upper lobe bronchiectasis, Ghon lesion (calcified granuloma), apical thickening, or normal
  • TB skin test
  • AFB smear if looking for TB
  • Treatment for active TB
  • initiate treatment after positive AFB smear or with high clinical suspicion
• may need to observe therapy to reduce rates of relapse and resistance
• meds given in phases
  o initial, for 2 months: isoniazid, rifampin, pyrazinamide, ethambutol
    ▪ isoniazid can cause peripheral neuropathy
    ▪ pyrazinamide can have GI effects, arthralgias, arthritis
    ▪ anything rif- can cause thrombocytopenia, GI effects, drug interactions
      • new drug rifabutin can be substituted for rifampin if there are drug interactions
        o ex. HIV+ on antiretrovirals
      • can substitute fluoroquinolone when first-line drugs are not tolerated or when there is resistance
    o continuation, for 4-7 months: isoniazid and rifampin
      ▪ extend if there is cavitary disease or sputum is still +
      ▪ can substitute new drug rifapentine
    o monitor throughout with sputum smears and cultures + sensitivities
      ▪ vision checks and color vision testing if using ethambutol
      ▪ renal, liver, bilirubin, and platelet monitoring if baseline abnormal
    o for culture-negative but high clinical suspicion, initial phase is given, then re-evaluation with CXR
• antibiotic resistance:
  o remember that cases of TB in foreign-born patients have higher rates of resistance
  o always add drugs to failing regimens in 2’s!
• Treatment for latent TB:
  • when to treat:
    o when skin test is positive according to their risk
    o standard treatment: 9 months of isoniazid or 4 months of rifampin
    o make every effort to treat HIV+ patients with something that has a rif- in it!
    o new option: isoniazid + rifapentine once a week for 3 months
      ▪ for healthy patients > 12 years, HIV patients not taking antiretrovirals
      ▪ avoid in children < 2, HIV patients on antiretrovirals, pregnant women
    o therapy monitoring needed in HIV, pregnant women, chronic liver disease, regular alcohol users
      ▪ may see reactivation syndrome with HIV where reconstitution of immune responsiveness causes surge of TB symptoms early in therapy ❌treat with steroids

18.7.7 Lung Lesions
• Parapneumonic effusion: a type of pleural effusion that arises as a result of a pneumonia, lung abscess, or bronchiectasis
  • three types: uncomplicated effusions, complicated effusions, and:
  • empyema: a collection of pus within a naturally existing anatomical cavity
• here, the lung pleura
• investigation: effusions big enough should be tapped right away
• treatment:
  o pH, protein, LDH, and glucose of fluid (Light’s criteria) used to determine whether the effusion might become complicated
  o adequate drainage must be done to prevent formation of a pleural rind and trapped lung (pleural thickening with mediastinal involvement that eventually scars and restricts the lung’s movement)
• Lung abscess: a collection of pus in a newly formed cavity
  • usually a complication of aspiration
  • treatment: 4-6 weeks of antibiotics covering anaerobes

18.7.8 Pneumonia and Viruses
• Many patients hospitalized for CAP have a viral pneumonia or viral co-infection on top of bacterial pneumonia
• no difference in outcomes or mortality
• Viruses involved: influenza A/B, human metapneumovirus, RSV, parainfluenza, adenovirus
• Only RSV and influenza have rapid antigen tests
• Influenza: presentation: abrupt onset, with fever, myalgia, headache, malaise, nonproductive cough, sore throat, rhinitis
• incubation period is 1-4 days, symptoms may last 2 weeks
• kids may have otitis media, nausea, vomiting
• Complications of viral pneumonia:
  • common: febrile seizures
  • uncommon: encephalopathy, transverse myelitis, myositis, myocarditis, pericarditis, Reye’s syndrome
  • exacerbation of underlying pulmonary and cardiac conditions
  • secondary bacterial pneumonia
    • MRSA superinfection in peds

18.7.9 Influenza
• Pandemic influenza characteristics:
  • highly infectious
  • rapidly fatal
  • activity in summer and fall
  • pulmonary edema and hemorrhage
  • hemagglutinin antigen shift
  • Prevention
    • vaccinate everyone over 6 months old (inactivated form)
    • especially 6 mos-18 years, or > 50 years, pregnant women, those on aspirin therapy, those with chronic medical conditions, caregivers, and nursing home residents
    • can use live vaccine if 2-49 years old and healthy
    • can’t be in contact with immunocompromised individuals (viral shedding possible)
    • first-time vaccination in kids under 9 requires two doses
    • proper use of vaccines prevent 70-90% of disease in healthy individuals 30-70% of influenza-related hospitalizations in the elderly/infirm, and 80% of influenza-related mortality in nursing home residents
  • Influenza diagnosis
    • nasopharyngeal swab with viral cell culture
    • can also do rt-PCR, immunofluorescence, EIA
    • rapid test is 70% sensitive and 90% specific
    • some can’t detect B or differentiate A from B
  • Treatment
    • only drugs effective against A & B are oseltamivir and zanamivir
    • increasing resistance of H1N1 to oseltamivir
    • must be taken with 48 hours of onset to do anything and only decreases symptoms by 1-2 days
    • can’t use zanamivir with COPD
    • really not helpful unless prophylaxing select populations (nursing home outbreaks etc.)

18.8 Pulmonary Function Testing & Sleep Studies
• Obstructive lung disorders include COPD (chronic bronchitis/emphysema), bronchiolitis, tumors, sarcoidosis, lung damage from prior infection (scarring)
• Restrictive lung disorders include disorders of the chest wall or pleura (obesity, pleural effusion), interstitial lung disease, acute pneumonitis, neuromuscular disorders

18.8.1 When to Get Pulmonary Function Testing
• DO for:
  • chronic persistent cough, wheezing, dyspnea, exertional cough, chest discomfort (but not pain?)
  • chronic fatigue for smokers
  • objective assessment of bronchodilator therapy
  • evaluation of occupation exposures
- pre-operative risk assessment
- objective assessment of impairment or disability

CONTRAINDICATED for:
- chest or abdominal pain of any cause
- oral or facial pain that will be exacerbated by using a mouthpiece
- stress incontinence
- dementia or confusion
- hemoptysis of unknown origin
- pneumothorax
- recent MI
- thoracic/abdominal/cerebral aneurysms
- recent eye/abdominal/thoracic surgery
- history of syncope with forced expiration
- Spirometry also contraindicated with BP > 140/90 or URI

18.8.2 Types of PFTs

- **Spirometry**: measurement of breathing patterns including amount and rate of air being moved
  - readily available, little risk, takes 10-15 minutes
  - results are very useful
  - quality affected by operator and patient performance
  - numbers generated:
    - FEV1/FVC: proportion of the forced vital capacity that can be forcefully expelled in the first second of expiration
    - FEV25-75%: average flow rate of the middle 50% of expired volume during a maximal forced expiration
      - these are compared to reference values based on age, height, gender, and race
      - volumes are corrected to control for body temperature saturated with water vapor (BTPS), ambient spirometer temp, and barometric pressure
- **Pulse oximetry**: uses spectrometry to measure peripheral oxygen Hb saturation (ear, finger, or toe)
  - oxygen therapy indicated with sats < 88% at rest
  - beware: not accurate to use for O2 titration for advanced COPD
    - because they are CO2 dependent and giving them too much oxygen will suppress their respiratory drive
- **Diffusing capacity (DLCO)**: the carbon monoxide uptake from a single inspiration in a standard time, usually 10 secs
  - measured during expiration
  - high if > 140% predicted
  - seen in:
    - polycythemia vera: more RBCs = more Hb = increased uptake
    - morbid obesity: upregulation of RBCs due to greater body mass & blood vol
    - asthma: breath with CO2 is held in lungs longer (obstructive expiration) = longer time for CO2 to bind to Hb
    - pulmonary hemorrhage: because there is more blood available for CO2 to bind to
    - left-to-right intracardiac shunting: increased vascular congestion
    - mild left heart failure
    - exercise just prior to test: getting rid of CO2 built up from greater oxygen burn
  - normal if 81-140% predicted
  - low:
    - borderline low if 65-80%
    - mildly decreased diffusing ability if 61-75% predicted
    - moderate decrease if 41-60%
    - severe decrease if < 40%
    - causes:
      - if spirometry is normal:
        - anemia: low Hb causes lower uptake
• pulmonary vascular disease: clots blocking blood flow to the lungs
• early interstitial lung disease: less CO2 diffusion across tissues due to fibrosis
• altitude
• carboxyhemoglobin (higher in smokers)
  ▪ if spirometry indicates obstruction:
    • emphysema: alveolar breakdown provides less surface area for CO2 diffusion
    • cystic fibrosis or bronchiolitis: mucus impedes diffusion
  ▪ if spirometry indicates restriction:
    • advanced interstitial lung disease
    • pneumonitis

• Peak flow: measures maximum speed of expiration
  • used for daily monitoring of respiratory function in asthma
  • compares current values to individual’s baseline values
  • safer to use in diagnosis of asthma than methacholine challenge
  • can be used by patients to help make medication decisions
    ○ ex. whether they are in the green, yellow, red zones
• Lung volumes: involves measuring lung capacity with patient inhaling specific volumes of gases that are measured by CXR
  • not frequently done
  • for use when you want to know about inspiratory and expiratory reserve volumes

• Maximal respiratory pressures:
• Forced inspiratory maneuvers:
• Cardiopulmonary stress testing: measures EKG, pulmonary gas exchange, and pulse oximetry while patient is on a treadmill or bicycle
  • used for evaluation of dyspnea, SOB, functional status determination in CHF, pre-op risk assessment, disability determination, measuring response to therapy, development of exercise prescriptions

18.8.3 Interpretation of PFT Results

• Spirometry
  • abnormal result is a decline in lung function more rapidly than expected from aging alone
  • variability between different spirometry sessions for the same individual in a year’s time should be no greater than 5%
  • possibly significant decline if decreased by 10-14% in a year
    ○ or 2-3% per year decline with 5 year monitoring
    ○ significant decline if decreased by 15% or more in a year
    ○ or 3% or more decline per year with 5 year monitoring
  • obstruction evidenced by low FEV1/FVC ratio
    ○ in late disease the vital capacity will be low as well
  • restriction evidenced by low vital capacity
18.8.4 Sleep Studies

- Normal sleep
  - stages occur in 90-120 minute cycles
    - REM sleep involves active/awake EEG pattern, atonic EMG, presence of rapid eye movements
    - non-REM sleep:
      - stage 1 involves light sleep, transition stage (2-5% of sleep time)
      - stage 2 involves intermediate sleep, slowing of EEG (40-50% of sleep time)
      - stages 3 & 4 involve deep/slow wave sleep (20% of sleep time)
    - first half of night: wakefulness 1 2 3 4 3 2 REM
    - second half of night: stage 2/REM alternate
  - Abnormalities of normal sleep architecture indicate sleep disorders
    - ex. narcolepsy
- Polysomnography: involves measurement of brain activity, eye movement, O2/CO2 levels, heart rate/rhythm, breathing rate/rhythm, air flow through nose and mouth, snoring, and body muscle/chest/belly movements
  - test results are then interpreted by a pulmonologist or neurologist
    - normal results:
      - brain waves appropriate for stages of sleep and awake time, no seizures
      - eye movement: slow movements present at start of sleep and become rapid during REM
      - muscle movement: no leg jerking or abnormal movements
      - blood O2 remains > 90%
      - normal HR and rhythm
      - breathing: reduced air flow or no air flow occurs < 5 times per hour
      - no abnormal chest or abdomen movements
      - no night terrors, sleepwalking, or sleeptalking
      - no excessive snoring or abnormal snoring patterns
      - air flow through nose and mouth is not blocked
  - when to do polysomnography
    - excessive daytime fatigue
    - excessive snoring
    - witnessed apnea
    - obesity/HTN/heart disease
  - active or violent nighttime behaviors
- parasomnias (nightmares)
- insomnia
- **Multiple sleep and latency test**: patient is given 4-5 opportunities to nap at 2 hour intervals during the day, with EEG, eye movements, and muscle tone tracked during naps
  - time from wakefulness to sleep onset is the “sleep latency”
    - should normally take 10-20 minutes
    - if it takes less than 5 minutes this indicates severe daytime sleepiness
    - if REM occurs during > 2 naps this indicate narcolepsy
- **Maintenance of wakefulness test**: patient reclines in a quiet, darkened room and tries to stay awake as long as possible
  - a more practical test to judge whether a person’s sleepiness is likely to impair work or driving

### 18.9 Obstructive Airway Disease and Pharmacologic Therapies

#### 18.9.1 Background
- **Obstructive airway disease**: when inflammation narrows airways → reduced airflow
  - can be proximal inflammation (asthma and bronchitis) or distal (emphysema)
  - proximal sections are cartilaginous, have smooth muscle and mucus glands to trap particles
  - distal sections are membranous and held open by the negative pressure of inspiration
- **chronic obstructive pulmonary disease (COPD)**: chronic bronchitis and/or emphysema that is progressive and where airflow limitation is not fully reversible
  - **chronic bronchitis**: recurrent excess mucus secretion into the bronchial tree → persistent cough and sputum production
  - **emphysema**: abnormal, permanent enlargement of the air spaces distal to the terminal bronchiole → bronchial wall destruction with chronic dyspnea
  - **asthma**: chronic inflammatory disease of the airways characterized by variable and recurring symptoms, reversible airflow obstruction, and bronchospasm
  - **COPD vs asthma**
    - differences: COPD has an older age of onset, antibiotics are used for exacerbations, inhaled corticosteroids give a poor response, and loss of function is progressive
    - similarities: both involve airway inflammation (although different kinds), ↓ FEV1, URI trigger, and an interaction between genetics and the environment
- **Determining obstructive vs restrictive pulmonary disease**
  - measure gas flow in the lung with a spirogram
    - normal VC should be ~ 5L and you should be able to get vital capacity out in < 6 seconds
    - obstruction measured by how much of your VC you can get out in 1 second (FEV1)
      - should be at least 70%
      - less than this = weak breathing muscles or airway obstruction
      - but if FEV1/VC is normal even when the VC and FEV1 by themselves are abnormally low, this indicates an airway restriction
        - ex. lung removal, large pneumonia, or stiff/fibrotic lung
- **Options for delivery of medication**
  - **nebulizers**: delivery of aerosol over a long period of time with slow velocity, tidal breathing
    - lower delivery → must use more drug
    - available for albuterol, ipratropium
    - useful for peds and the elderly
  - **metered dose inhaler**: delivers a measured amount of aerosol in a short burst that must be inhaled
    - should use spacer
    - requires patient hand-eye coordination
    - delivery ~40%
  - **dry power inhaler**: delivers medicine in the form of powder to be inhaled
    - easier to coordinate
    - delivery ~40%
- **Pulmonary rehab for treatment**
  - includes education, exercise, and psychosocial support
- won’t change the lung disease but will help with performance
- length of hospital stay decreased in rehab participants

18.9.2 Asthma

- Airways can become hyperreactive in response to:
  - allergens (IgE reaction): dust mites, pet dander, cockroaches, pollen, dust, mold
  - occupational or environmental exposures: smoke, temperature
  - viruses
  - exercise

- GERD
  - infection: sinusitis, rhinitis
  - stress/emotion
  - sulfites in wine and certain foods
  - medication: β-blockers

- Cells involved include mast cells, eosinophils, and CD4 T-cells

- Patient measures their expiratory flow using peak flow meters: detects fastest speed at which one can blow air out of the lungs
  - should be calibrated by measuring morning reading and a reading between noon-2 for 2-3 weeks to establish personal best, then every day thereafter

- Severity classifications:
  - also consider how much rescue inhaler is being used, severity of exacerbations, and interval between exacerbations

![Classification of Asthma Severity](image)

- Prevention: ages 19-64 who have asthma should be vaccinated for influenza and pneumococcus

- Presentation:
  - acute/episode: wheezing, SOB, reduced FEV1/FVC with increased residual volume
  - controlled: FEV1/FVC should be near normal

- Investigation:
  - not sure if it is asthma?
    - can do methacholine challenge to exacerbate symptoms and check for reduced FEV1/FVC

- Treatment involves a stepwise approach

  - overall goal is to prevent recurrent exacerbations!
  - want to maintain near normal pulmonary function and normal activity levels
  - treatment will include long-term control medications along with short-acting quick-relief meds
  - all patients will need a short-acting med PRN for exacerbations, including:
    - short-acting β2 agonists: for intermittent episodes of bronchospasm
- **albuterol**: longer half-life than levalbuterol
- **levalbuterol**:
- **pirbuterol**:
- good for prevention of exercise-induced bronchospasm (use 15 min before exercise)
- use of more than one canister per month indicates need to step up
  - anticholinergics: may have added benefit when use with β-agonist in severe exacerbation, otherwise no long-term benefit has been shown = only used when you can’t get a patient under control with other meds
    - ipratropium:
    - tiotropium:
- systemic corticosteroids
  - use for about 3-10 days until patient achieves 80% of baseline or until symptoms resolve
  - ex. prednisone, methylprednisolone, prednisolone
  - side effects: osteoporosis, glucose intolerance, fluid/electrolyte imbalance, weight gain, Cushing’s syndrome, peptic ulcers, ocular cataracts, behavioral disturbances
- **long-term control meds aim to decrease inflammation and include**:  
  - **inhaled corticosteroids**  
    - side effects: oral thrush, dysphonia, cough → use spacer with lowest effective dose, rinse mouth  
  - **long-acting inhaled β-agonists**: stimulate β-2 receptors in the airway to relax smooth muscle and decrease hyperresponsiveness
    - ***only prescribe in combination with ICS in patients with mod-severe persistent asthma!***
    - due to increased risk of death but we’re not sure why
    - use for shortest time needed to control symptoms
    - only use long-term for someone whose asthma is not adequately controlled on all other medications
    - salmeterol:
    - formoterol:
    - indacaterol:
    - make use of combination ICS/LABA inhalers to comply with guidelines:
      - fluticasone/salmeterol: ages 12+  
        - can use Advair Diskus for ages 4+
      - budesonide/formoterol: ages 12+  
      - mometasone/formoterol: ages 12+ → do not use for acute symptoms!
      - side effects: tachycardia, tremor, EKG changes with overdose
  - **leukotriene modifiers**: all oral; antagonize pro-inflammatory effects of leukotrienes
    - **montelukast**: 12 months and up
    - **zafirlukast**: 5 years and up, must be on empty stomach
    - **zileuton**: ages 12+, requires monitoring of LFTs → more rapid onset than ICS
    - rare side effect of elevated LFTs
    - good for exercise-induced asthma
  - **mast cell stabilizers**: inhibit inflammatory cell activation and mediator release, good for allergen-induced bronchoconstriction
    - **cromolyn**: takes 2 weeks for therapeutic response, effective for seasonal asthma and exercise-induced bronchospasms
  - **methylxanthine**  
    - **theophylline**: helps with bronchodilation, allergies, improved exercise tolerance
      - used as an adjuvant to ICS for management of nocturnal symptoms
      - problem: toxicities, requires serum monitoring = fallen out of favor
  - consider using the anti-IgE monoclonal antibody **omalizumab** for patients with severe allergic asthma
    - ideal patient has frequent exacerbations, already on high steroid dose, but still has poor pulmonary function
    - injected subcutaneously
- risk of anaphylaxis

- **bronchial thermoplasty**: procedure where the airway walls are heated to reduce smooth muscle mass and create a wider airway
  - approved for adults with severe persistent asthma that is not well controlled with ICS and LABAs
  - studies showed more symptom-free days but FEV1 did not change if step up if needed, and step down once asthma is well-controlled for at least 3 months
    - need to step up if any of the “rules of two” are being fulfilled:
      - short-acting β-agonist is being used 2+ times a week
      - nighttime awakenings are 2+ times per month
      - quick relief inhaler is being refilled 2+ times per year

- **Self-management of acute attack**
  - green zone: if baseline peak flow is lowered but still > 80% function, continue meds as prescribed
  - yellow zone: if only 50-80% baseline, increase β agonist, increase inhaled corticosteroid
  - red zone: if < 50% baseline, increase β agonist, increase ICS, and go the ED

- **Emergent treatment of an acute exacerbation**
  - if FEV1 is > 40%, use oxygen, inhaled SABA for up to 3 doses
    - then oral corticosteroids if no improvement
  - if FEV1 is < 40% use oxygen, high dose inhaled SABA + ipratropium every 20 mins, oral corticosteroids
  - if impending or actual respiratory arrest, intubate and ventilate with 100% O2, use nebulized SABA and ipratropium, IV corticosteroids

- **Prognosis**
  - childhood allergic asthma often dissipates as their immune system matures
  - acquired adult asthma may wax or wane with igniting factors, or may persist
    - increased risk of developing COPD in the future due to airway remodelling
  - can be fatal with either progressive worsening over 1-3 days or sudden death
    - risk factors: history of near fatal asthma +/- intubation, frequent hospital/ED visits, comorbidities, frequent use of meds needed, low socioeconomic status, psychiatric illness

18.9.3 **Chronic Obstructive Pulmonary Disease**

- Usually caused by inhaled toxins such as tobacco, wood smoke, occupational dusts, air pollution
  - toxins damage epithelial cells - CD8 killing and alveolar destruction
• irritation attracts alveolar macrophages, which attract neutrophils and release of proteases and further destruction with mucus hypersecretion

• Can also be caused by anti-protease deficiencies or airway remodelling in persistent asthma

• Exacerbations can be caused by environmental pollution and viral or bacterial pathogens

• Classifications:

<table>
<thead>
<tr>
<th>I: Mild</th>
<th>II: Moderate</th>
<th>III: Severe</th>
<th>IV: Very Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV1/FVC &lt; 70%</td>
<td>FEV1/FVC &lt; 70%</td>
<td>FEV1/FVC &lt; 70%</td>
<td>FEV1/FVC &lt; 70%</td>
</tr>
<tr>
<td>FEV1 ≥ 80%</td>
<td>FEV1 &lt; 80%</td>
<td>FEV1 &lt; 50%</td>
<td>FEV1 &lt; 30% or presence of chronic respiratory failure or right heart failure</td>
</tr>
<tr>
<td>With or without symptoms</td>
<td>With or without symptoms</td>
<td>With or without symptoms</td>
<td>With or without symptoms</td>
</tr>
</tbody>
</table>

- Presentation:
  - exacerbation: use of accessory respiratory muscles, paradoxical chest wall movements, worsening or new onset central cyanosis, peripheral edema, hemodynamic instability, signs of right heart failure, mental status change
  - takes a while for symptoms to appear because there is a large ventilatory reserve that is not used up until lung functioning gets down to 50-60%

- Disease location lies on a spectrum, and which side it ends up presenting as may be genetic
  - chronic bronchitis is proximal-predominant disease affects the large airways and involves overproduction of mucus with gland hypertrophy, reduced respiratory drive, and airway hyperreactivity
    - accessory muscles need to work extra hard, so hypoventilation occurs to reduce their workload, increased CO2 with decreased O2 = hypoxia
    - patients on this side of the spectrum are “blue bloaters”: productive cough, wheezing, rhonchi, hyperinflation of lungs, cor pulmonale (right heart failure)
  - emphysema is distal-predominant disease affects the smaller airways and alveoli and involves dyspnea (active respiratory drive), and reduced DLCO
    - respiratory centers in alveoli keep RR high = maintenance of tissue oxygenation
    - patients on this side of the spectrum are “pink puffers”: high RR, distant breath sounds, hyperinflation of lungs, late right heart failure

- COPD becomes a systemic disease as the chronic airway inflammation causes inflammatory cytokines to reach the circulation → CAD, renal insufficiency, neuromyopathy, osteoporosis, cachexia, debility, overall downward health spiral

- Investigation
  - for acute exacerbation, must rule out PE, CHF, pneumothorax
  - CT to rule out other causes
  - CXR showing enlarged retrosternal air space from barrel chest, flattened diaphragm

- Treatment
  - major goal is to reduce exacerbations requiring hospitalization
  - tobacco cessation
  - standard treatment is a stepwise approach
    - avoid risk factors and get influenza vaccination
    - add short-acting bronchodilator PRN:
      - β-2 agonist like albuterol
      - anticholinergic:
        - ipratropium: no mortality benefit, but has been shown to produce greater bronchodilation and fewer side effects than inhaled β-2 agonists in COPD pts
    - pulmonary rehab, add 1+ long-acting bronchodilators daily
      - salmeterol
      - formoterol
      - tiotropium: anticholinergic that may improve FEV1, no acute relief of bronchospasm
      - theophylline: use 2nd line when patients are inadequately controlled, no established benefit nor risk
  - certain factors/meds may increase or decrease metabolism
• risk of toxicity = need to do serum monitoring
  o add inhaled glucocorticosteroids if there are repeat exacerbations
    ▪ for stage 3 & 4
    ▪ use of oral corticosteroids is ??
  o add long-term oxygen, consider surgery
    ▪ transplant: lasts 5-10 years
    ▪ lung volume reduction involves removal of distended regions to allow more normal
      regions to expand □ return of diaphragm from being flattened
    ▪ endobronchial valve placement: utility is disputed
    ▪ biologically mediated scar formation
    ▪ new collateral channels for ventilation
• for acute exacerbations □ SABAs, systemic corticosteroids, oxygen, noninvasive positive pressure
  ventilation
• antibiotics if there is increased sputum purulence or volume or increased dyspnea
  o mild COPD □ Strep pneumo
  o moderate COPD □ Moraxella, H. flu
  o severe COPD □ Pseudomonas
• usually warrants a change in daily medications
• new drugs:
  o roflumilast: a selective phosphodiesterase 4 inhibitor indicated for severe COPD with
    chronic bronchitis and history of acute exacerbations
    ▪ questionable if it is better than an inhaled steroid
• not recommended: expectorants, antitussives (COPD cough is not centrally mediated), respiratory
  stimulants
• Prognosis depends on length of toxin exposure and susceptibility to toxin irritation
• lung is not capable of regenerating itself after damage, even if patient has quit smoking
• increased survival when those on oxygen therapy use it for > 18 hours a day

18.10 Interstitial Lung Disease/Diffuse Parenchymal Lung Disease

18.10.1 Background

• Parenchyma: although often used to refer solely to alveolar tissue, it describes any form of lung tissue
  including bronchioles, bronchi, blood vessels, interstitium, and alveoli
• A group of diseases (200+) affecting the air spaces between the alveoli and lung capillary beds
• involves infiltration of this space with inflammatory cells and collagen □ restriction of lung function and
  impaired gas exchange
• can also involve the cells bordering the air space, alveolar space, the small airways, vessels, and pleura
  □ why it is preferred to call it diffuse parenchymal lung disease
• all are diffuse, primarily affect the parenchyma, and involve variable amounts of inflammation and
  fibrosis
• Damage eventual leads to tissue remodeling
• causes restrictive disease due to reduced compliance
  □ stiff lungs with smaller air volumes
• interstitium becomes thickened
• capillaries are lost due to impaired gas exchange, hypoxia, and secondary pulmonary hypertension
• Causes include connective tissue disease, occupation or environmental exposure, iatrogenic (radiation
  or drugs), inherited, inflammatory bowel disease, idiopathic interstitial pneumonia, granulomatous
  diseases, amyloid, etc.
• Presentation
• acute/subacute: dyspnea, cough, rapid progression to respiratory failure, infiltrates, fever
• chronic: dyspnea on exertion, chronic cough, inspiratory rales, subtle interstitial infiltrates
• extrapulmonary manifestations caused by same disease that is affecting the lungs: acid reflux, muscle
  weakness, Raynaud’s, Sicca syndrome, rash, joint pain/swelling/deformity, GI symptoms, hematuria
• common mimics to be aware of: diffuse neoplasia (lymphoma, lymphangitic carcinomatosis, bronchoalveolar cell carcinoma), infections such as PCP, bronchiolitis, CHF, chronic aspiration
- clubbing of the extremities
- Investigation
  - good history:
    - certain ages and genders associated with certain diseases
    - family history
    - smoking history
    - medications associated with lung toxicity
    - hobbies/exposures: pigeons, parakeets, hot tubs, saunas, humidifiers, damp basements, woodworking, mining, sandblasting, welding, shipyard labor, pipefitting, electrical work, automotive mechanics, poultry work, aerospace, nuclear industry, computer, electronics, farming, animal husbandry/handling
- focused physical exam:
  - lungs: listen for rales
  - heart: S3 from pulmonary HTN (results in CHF), fixed split S2 with accentuated P2 from elevated pulmonary pressure
- labs to order:
  - CBC
  - renal and hepatic function
  - sedimentation rate
  - creatine kinase and aldolase (muscle tissue enzyme)
  - antinuclear antibody and rheumatoid factor
  - anti-Ro, anti-La, anti-RNP, anti-Jo1, anti-Scl70
  - anti-neutrophilic cytoplasmic antibodies
  - serum precipitins
- pulmonary function tests: look for diffusion impairment +/- restrictive pattern
- imaging:
  - certain radiographic features are distinctive of certain diseases, including lines, nodules, cysts, consolidation, and ground-glass opacity
    - upper-zone predominance of features is characteristic of sarcoidosis, hypersensitivity pneumonitis, silicosis, coal worker’s pneumoconiosis, berylliosis, PLCH, ankylosing spondylitis, eosinophilic pneumonia, nodular rheumatoid arthritis
    - lower-zone predominance of features is characteristic of IPF, NSIP, asbestosis, chronic hypersensitivity, connective tissue disease-related ILD
      - CXR is usually abnormal but subtle and nonspecific
      - CT has greater sensitivity
      - high res CT uses smaller slices and is more sensitive and specific with details to the level of the pulmonary lobe
  - surgical biopsy
    - bronchoscopic biopsy usually inadequate unless disease is sarcoid, eosinophilic pneumonia, infection, or alveolar proteinosis
    - may cause acute exacerbation
- Prognosis is often bleak
- most of these diseases are fatal and without treatment
- many people don’t know how to recognize these diseases and there is frequent misdiagnosis

18.10.2 Idiopathic Pulmonary Fibrosis
- fibrosis in the interstitium for no apparent reason
- Chronic and progressive disease that is usually fatal and follows a variable and unpredictable rate
- Most common form of pulmonary fibrosis
- Incidence increases with age, most are in 60-70s
- More common in men than women
- Associated with tobacco use
- Presentation:
  - initial presentation: subtle onset of dyspnea on exertion, intermittent dry cough, crackles, clubbing
    - frequently mistaken for heart disease
- acute exacerbation: subacute increase of symptoms
- Investigation
- characteristic patterns on surgical lung biopsy
  - usual interstitial pneumonia (UIP): includes patchwork patterns (heterogenous destruction) with areas of normal lung, active fibrosis, and end-stage “honeycomb” appearing fibrosis, as well as fibroblastic foci
    - appears on CT as rows of cysts lined up with each other (also known as honeycombing)
    - will also see traction bronchiectasis, architectural distortion
    - patients with honeycombing are poor surgical candidates
- CXR shows reticulations with honeycombing and traction
- bronchoalveolar lavages shows neutrophils
- if it is an acute exacerbation, need to rule out infectious cause
- Treatment
  - no proven therapy = get patient in a medical trial!
  - current medical trials for n-acetylcysteine therapy treat comorbidities such as GERD, CHF, pulmonary HTN (controversial to treat as vasodilation may shunt blood to dead areas of the lungs), sleep apnea smoking cessation, weight loss, pulmonary rehab, supplemental oxygen end-of-life planning
- lung transplant: requires early evaluation
- acute exacerbations may respond to steroids
- Prognosis: average survival from time of diagnosis is 3 years, but progression is unpredictable

### 18.10.3 Nonspecific Interstitial Pneumonia
- inflammation with or without fibrosis
- Usually associated with connective tissue diseases, may be caused by undifferentiated connective tissue
- Affects people in their 40-50s = younger than IPF
- No association with tobacco use
- Presentation: insidious onset of cough, dyspnea
- Investigation
  - screen for connective tissue diseases
    - labs: ESR, CRP, antibody and autoantibody labs
    - on PE look for dilated capillaries of the fingertips, shawl rash, or mechanic’s rash on hands
  - high res CT and biopsy
  - histological pattern also known as nonspecific interstitial pneumonia
    - homogenous and symmetric infiltration of the interstitium, with ground-glass appearance, consolidation, volume loss, and sub-pleural sparing
- bronchoalveolar lavage shows lymphocytes
- can have both UIP and NSIP
- Treatment: prednisone, azathioprine, mycophenolate show a good response in many cases
- requires monitoring of CBC, Cr, liver function
- these meds have toxicities = why you want to distinguish from IPF, where treatment will have no real benefit
- Prognosis: patients with features of NSIP fare much better than those with features of UIP, with < 10% mortality 5 years after diagnosis

### 18.10.4 Cryptogenic Organizing Pneumonia
- non-infectious inflammation of the bronchioles and surrounding lung tissue without apparent cause
- Typically affects males more than females
- Most are nonsmokers in their 60s
- Different from secondary organizing pneumonia, which has an identifiable cause such infection, toxin exposure, or inflammatory bowel disease
- Presentation:
  - mimics pneumonia with fever, cough, dyspnea, crackles
but fails to respond to multiple antibiotics

- no clubbing
- Investigation
- leukocytosis with elevated ESR
- CXR can have many different appearances, most commonly with patchy focal consolidations, ground glass, migratory appearance
- tissue histology:
  - Masson bodies: polyploid plugs of proliferating fibroblasts and myofibroblasts within alveolar ducts that can block the bronchioles
    - contained plugs are what make it “organized”
    - hard to differentiate from the fibroblastic foci of UIP = why you want a pulmonary pathologist to look at your biopsies
  - varying degrees of bronchiolar involvement
  - preserved lung architecture with no honeycombing
- bronchoalveolar lavage shows mixed lymphocytes and neutrophils
- Treatment: several different steroid strategies provide excellent response
- Prognosis: relapses are common

18.10.5 Sarcoidosis

- abnormal collections of chronic inflammatory cells (granulomas) form as nodules in multiple organs, including the lungs
- Affects young and middle-aged adults of African or northern European descent
- Staging is based on radiographic findings
  - 0 = no sarcoid manifestations in the lung
  - 1 = bilateral hilar lymphadenopathy
  - 2 = BHL + pulmonary infiltrate
  - 3 = pulmonary infiltrate alone
  - 4 = pulmonary fibrosis
- Presentation
  - common manifestations: bilateral hilar lymphadenopathy, pulmonary infiltrates, ocular lesions, skin lesions (erythema nodosum, lupus pernio)
  - possible syndrome presentations:
    - asymptomatic
    - chronic respiratory symptoms
    - Lofgren’s syndrome: fever, bilateral hilar lymphadenopathy, erythema nodosum, arthralgias
    - extrapulmonary symptoms: uveitis, hepatitis, hypercalcemia, skin lesions
- less common: liver, spleen, lymph nodes, salivary glands, heart, nervous system, muscles, bones
  - a frequent cause of sudden death in young athletes due to cardiac manifestations
- Investigation
  - need clinical and radiographic findings to be supported by histology:
    - bronchoscopic biopsy showing well-formed non-caseating epithelioid cell granulomas
      - must exclude local sarcoid-like reactions and known causes of granuloma such as tumor or fungal/mycobacterial infection
      - CXR showing bilateral hilar lymphadenopathy
      - high-res CT:
        - could show multiple patterns: ground glass opacity, nodules, fibrosis, mass, consolidation, cysts, bronchial wall thickening
        - upper lobe predominance of lesions with bronchocentric distribution
        - septum appears to have “beads on a string”
        - lesions appear like “candle wax drippings”
- Treatment is tailored to the setting
- begin treatment with onset of pulmonary symptoms: corticosteroids for 1-3 months
- if steroid side effects or disease progression, try methotrexate, chloroquine, pentoxifylline, or anti-TNF
- Prognosis: chance of spontaneous resolution decreases with progression to stage 4
18.11 Occupational Lung Disease

18.11.1 Common Occupational Lung Diseases

- Work-related asthma
- Hypersensitivity pneumoniitis
- Pneumoconioses: silicosis, coal worker’s pneumoconiosis, asbestosis
- Byssinosis (grain dust)
- Inhalation fevers
- Hard metal disease (ex. tungsten carbide)
- Berylliosis
- Acute inhalation injury: smoke (CO), silo-filler’s disease (NO2), chlorine, ammonia

18.11.2 Clinical Approach to Evaluation

- Must take a very thorough history
- job description
- potential hazards at home and at work: cleaning products
- use of protective devices
- environmental exposures: cooking fires, particulates from wildfire or disaster, sand storms
- history of exposure to respiratory irritants associated with asthma, COPD, bronchiolitis obliterans, acute lung injury/ARDS
- history of exposure to fibrogenic dusts associated with COPD, cancer, interstitial lung disease
- history of exposure to allergens and haptens associated with asthma and interstitial lung disease
- Soluble toxins affect upper airway while insoluble toxins affect the alveolar space
- Investigation
- pulmonary function tests
- methacholine challenge during and off work
- peak flow during and off work
- blood or skin tests for IgE or IgG
- imaging
- go over MSDS from patient’s work
- biopsy is rarely helpful

18.11.3 Coal Worker’s Pneumoconiosis

- inhaled coal dust progressively builds up in the lungs and is unable to be removed by the body
  - inflammation, fibrosis, and possibly necrosis

18.11.4 Silicosis (Potter’s Rot)

- inhaled dust ends up in alveoli
- macrophage attack and inflammation
- Historical epidemics occurred with tunnel workers, gold miners, Texas oil field sandblasters, and silica flour mill workers
- Associated industries: construction, mining, blast furnaces, iron/steelworkers, mineral and stone products, quarrying, machinery, agricultural products, crops, structural clay products, pottery and related products, clothing (jean sandblasters)
- Presentation: may be asymptomatic
- Investigation:
- CT shows diffuse tiny nodules
- Prognosis: lung function will continue to decline

18.11.5 Asbestosis

- parenchymal lung disease caused by inhalation and retention of asbestos fibers
- Many different kinds of asbestos
• Nonasbestos silicate dusts causing similar disease: clay minerals (kaolin, bentonite), talc, micas, glasswool, rock wool, slagwool, ceramic fiber, fiber glass
• Incidence is increasing!
• Presentation
• long latency period before disease presents = exposure history may be obscure
  o pleural effusion takes 10-20 years
  o pleural plaques and asbestosis take 20 years to develop
  o mesothelioma: a rare form of cancer that develops from transformed cells originating in the mesothelium (protective lining covering many internal organs of the body), usually caused by exposure to asbestos
    ▪ takes > 35 years to develop
    ▪ differentiate from pleural plaque by presence of chest pain
• Investigation:
  imaging may show benign asbestos pleurisy, pleural plaques, interstitial lung disease (asbestosis), mesothelioma, or lung cancer
  postmortem autopsy may show iron-coated asbestos fragments (ferruginous bodies) in the lung

18.11.6 Hypersensitivity Pneumonitis
• inflammation of the alveoli within the lung caused by hypersensitivity to inhaled organic dusts or low molecular weight chemical antigens [granulomatous or lymphocytic interstitial and bronchiolar lung disease
• Often related to farming, ventilation systems, or birds
• Antigenic chemicals can be found in paints, resins, polyurethane foams, plastics, electronics, dry cleaning agents, metal degreasers, dyes
• Many, many kinds!
  ex. hot tub lung, Miller’s disease, bird fancier’s lung
• Presentation: crackles, wheezing, or clubbing
• Investigation
  precipitin panels to evidence exposure
  PFTs showing restriction, reduced DLCO
  CXR may show small opacities in the upper lung regions
  Treatment: remove exposure, steroids

18.11.7 Occupational Asthma
• asthma due to causes and conditions attributable to a particular occupational environment and not stimuli encountered outside the workplace
• Potential causes: animal lab poop, grain molds or mites, flour dust, antibiotic dust, pine wood resin, wood dusts, isocyanate, acid anhydrides, polyamines, reactive dyes, metals
• Investigation:
  work-related changes in FEV1 or PEF
  work-related changes in bronchial responsiveness
  onset of asthma with clear association with a symptomatic exposure to an inhaled irritant in the workplace
  Treatment: treat as asthma
  Prognosis: if symptoms still present 2 years later, disease is likely to be permanent

18.11.8 Reactive Airways Dysfunction Syndrome
• an asthma-like syndrome developing after a single exposure to high levels of an irritating vapor, fume, or smoke
• Presentation: asthma symptoms minutes to hours (but less than 24 hours) after an exposure
• Investigation:
  positive methacholine challenge
  rule out other pulmonary disorders
18.11.9 Carbon Monoxide Poisoning

- Presentation depends on level of blood HbCO
  - 5-10% causes mild headache, SOB with exertion, decreased exercise tolerance, decreased angina threshold
  - 10-20% causes moderate headache, fatigue, dizziness, blurred vision, nausea, possible SOB at rest
  - 20-30% causes severe headache, confusion and impaired judgment, vomiting, SOB at rest, decreased cardiac arrhythmia threshold
  - 30-40% causes muscle weakness, incapacitation, cardiac arrhythmias, decreased seizure threshold
  - 40-50% causes seizures, syncope, and cardiac arrest
  - 50-60% is fatal

- Investigation:
  - measure HbCO by CO-oximetry
  - remember that an active smoker can be as high as 8-10% at baseline

- Treatment:
  - oxygen
  - hyperbaric chamber for any loss of consciousness, neurological signs, cardiovascular dysfunction, severe lactic acidosis, or HbCO levels > 20%

18.11.10 Silo Filler’s Disease

- an acute inhalation injury caused by exposure to NO2 (brown gas) created by bacteria breaking down silage
- Presentation:
  - acute phase (ranging from mild to high exposure): cough, dyspnea, fatigue, upper airway irritation, ocular irritation, cyanosis, vomiting, vertigo, loss of consciousness, ARDS, laryngeal spasm, bronchiolar spasm, reflex respiratory arrest, asphyxia
  - latent phase: mild cough and wheezing or asymptomatic
  - delayed phase: sudden onset of fever, chills, cough, dyspnea, and crackles
- Investigation
  - lung biopsy will show histology of cryptogenic organizing pneumonia

18.12 Venous Thromboembolism

18.12.1 Background

- Venous thromboembolism: refers to the life-threatening venous thromboses of deep vein thrombosis (clot formation in deep vein) and pulmonary embolism (clot blockage of the pulmonary artery)
- Risk factors for development: reduced blood flow, venous injury, hypercoagulability
  - includes previous VTE, malignancy, over 70 years old, obesity, prolonged bed rest, surgery, pregnancy & postpartum, nephrotic syndrome, severe medical illness, stroke, myocardial infarction, varicose veins, oral contraceptives, travel
  - inherited or acquired disorders causing hypercoagulability
  - Thrombi arise in veins that are richest in valves, usually in the venous valve pockets
  - begin as a conglomeration of leukocytes, platelets, and fibrin
  - can be a result of valve necrosis, less flexible cusp
  - typically in deep veins such as the femoral vein
  - usually several clots are thrown from the large clot
  - Clots can travel to the lungs (pulmonary embolism)
  - usually affects both lungs
  - results in a ventilation-perfusion mismatch: air gets in just fine but the clots are blocking the vessels so there is no perfusion
  - pressures in blocked pulmonary artery go up and transfer to the right ventricle of the heart □ heart must work harder to pump □ RV failure, BP drop, death
  - Clots can permanently damage the valves □ chronic venous insufficiency: inability of the veins to return blood back to the heart
can progress to stasis dermatitis, chronic edema and associated skin changes, and ulcers

18.12.2 Deep Vein Thrombosis

- **Prevention**
  - prophylaxis for at-risk patients: CHF, severe respiratory disease, bedrest + cancer/previous VTE/sepsis, acute neurologic disease, irritable bowel disease
    - LMWH, heparin, or fondaparinux for all medical patients unless risk for bleeding outweighs benefits
    - compression stockings
    - mechanical leg pumps: limited evidence for effectiveness = currently not recommended
      - only indicated for patients at high risk for bleeding (can’t give anticoagulants)
- **Presentation**: positive Homan’s sign, leg or arm pain/tenderness/swelling/warmth/erythema, sensation of muscle cramping
- symptoms are neither sensitive nor specific for DVT
- acute or subacute
- may not have any risk factors
- **Investigation**: must rule out postphlebitic syndrome, cellulitis, trauma/hematoma, muscle cramp, Baker’s cyst
  - **low suspicion**
    - D-dimer will likely be negative if it is not DVT
  - **high suspicion**
    - get imaging such as US (most common), contrast venography, MRI, or CT
      - US tries to compress leg veins, if an area won’t compress there is a clot

18.12.3 Pulmonary Embolism

- **Classifications**
  - massive if there is sustained hypotension, pulselessness, persistent bradycardia, or need for inotropic support
  - submassive if pt is normotensive but with RV dysfunction, myocardial necrosis
    - point at which you would see EKG changes, elevated BNP
  - minor/nonmassive if pt is normotensive with no RV dysfunction and no myocardial necrosis
- **Presentation**: dyspnea, pleuritic chest pain, cough, leg swelling/pain, hemoptysis, palpitations, syncope, wheezing, anginal chest pain
- symptoms do not have to be sudden!
- **physical exam signs**: tachycardia, tachypnea, crackles, loud P2 from pulmonary HTN, diaphoresis, hypotension, fever, wheezing, RV lift, + Homan’s sign, pleural rub, cyanosis
- **Investigation**: must rule out pneumonia, infection, obstructive lung disease, CHF, musculoskeletal disease, acute MI, anxiety, other cardiopulmonary diseases causing symptoms/signs
  - D-dimer
  - ABG to look for hypoxemia
  - troponin to look for RV damage (may have mini-infarction)
  - BNP will increase with LV or RV dilation (but will be increased at baseline for pts with CHF, etc)
  - EKG may show S1 Q3 T3 but this is not diagnostic nor specific for PE
  - CXR showing edema, cardiomegaly, full hilum, interstitial markings, prominent pulmonary vein, left sided pleural effusion
  - pulmonary arteriogram is the gold standard but requires R heart cath and is rarely done
    - invasive, expensive, requires experienced reader
  - ventilation/perfusion scan compares lungs for a mismatch
  - spiral CT is the most commonly performed imaging
  - compression US
  - MRI
  - Treatment
    - give heparin or direct thrombin inhibitor for HIT patients
      - do while waiting for outcomes of diagnostic tests
      - continue anticoagulation on warfarin for at least 3 months
• if repeat clots despite intervention or you can’t use anticoagulants, consider placing an IVC filter
• can remove clot via catheter embolectomy
• consider giving tPA or other thrombolytic for massive PE
• Prognosis
  • risk of death from RV failure if left untreated

18.12.4 Future DVT Therapies
• Oral direct thrombin inhibitors
• Oral anti-factor Xa inhibitors
• Biotinylated idraparinux (reversible)
• Aptamer therapy
• Atrial fibrillation stroke prevention/DVT prevention in total hip or knee replacement:
  • dabigatran will probably replace warfarin soon
  • rivaroxaban

18.13 Pulmonary Hypertension

18.13.1 Background
• Defined by a mean pulmonary artery pressure > 25 mm Hg at rest
• requires R heart cath to determine
• Multiple causes:
  • arteriolar narrowing in the lungs → build-up of pressure that is transferred to the right side of the heart
    • may be idiopathic, familial, or due to connective tissue disease (scleroderma), congenital
    • hunting, portal hypertension, HIV, schistosomiasis, drugs or toxins, chronic hemolytic anemia
  • left heart disease
    • systolic or diastolic dysfunction, valvular disease
  • lung disease or hypoxia
    • COPD, interstitial lung disease, sleep-disordered breathing, alveolar hyperventilation disorders, chronic exposure to high altitude, developmental abnormalities
  • chronic thrombotic or embolic diseases
  • other causes
    • splenectomy, sarcoidosis, histiocytosis X, lymphangioleiomyomatosis, compression of pulmonary vessels
• Results in vascular injury and potentially permanent vasoconstriction
• Prognosis
  • mortality predicted by higher pulmonary artery pressures, depressed cardiac index (cardiac output to body surface area), elevated right atrial pressure, lack of response to vasodilators during cath, poor functional status at diagnosis, poor 6 minute walk results

18.13.2 Presentation
• Dyspnea, fatigue, chest pain, palpitations, lower extremity swelling, abdominal swelling, lightheadedness/dizziness, syncope
• Other symptoms of underlying causes such as loud snoring, daytime hypersomnolence, etc.
• Exam findings: tachypnea, tachycardia, evidence of R heart failure (JVD, ascites, edema, RV lift), loud P2 from elevated pulmonic pressures slamming valve shut, tricuspid regurgitation murmur (can’t shut all the way due to dilation of muscle), pulmonic regurgitation murmur (high pressure), pulsatile liver

18.13.3 Investigation
• Need to determine cause, rule out chronic PE/sleep disorder, establish baseline, determine a prognosis
• Average time for correct diagnosis is 15 months because symptoms other than SOB may not be present and there is a lot to rule out!
• Initial “pivotal” tests:
• CXR: may see patchiness, huge retrosternal space due to lung hyperinflation (lateral view),
• EKG
• echo
• CT or VQ scan
• pulmonary function tests
• labs: HIV, ANA, BNP
• 6 minute walk to monitor oxygenation
• R heart cath: needed to begin treatment
• Then based on results, continue with “contingent” tests as needed:
  • TEE
  • exercise echo
  • pulmonary angiography
  • coag profile
  • ABG
  • polysymnography
  • further serologies

18.13.4 Treatment
• Survival
• Reduce symptoms and improve quality of life
• Initial regimen depends on severity of illness
• oral therapies if manageable
  • ex. epoprostenol, treprostinil, iloprost, bosentan, ambrisentan, tadalafil, sildenafil
• IV meds with hospitalization if severe
• Follow-up in 4-12 weeks with reassessment of symptoms, labs, 6 minute walk
• adjust FIO2, warfarin, diuretics, specific therapies as needed
• Repeat follow-up at least every 3 months
• Annual PFTs, ABG, CXR
• Repeat R heart cath as needed over the years

18.14 Lung Cancer and Pleural Disease
18.14.1 Lung Cancer
• Etiologies
• cigarette smoking: major carcinogen is benzopyrene
  • increases risk of lung cancer by 10-30x
    • risk increases with dose (ppd history)
• occupational exposures: asbestos, benzene, nickel, radiation
• environmental exposures: asbestos, radon
• genetic factors: oncogenes and tumor suppressor gene abnormalities
• Background on different types:
  • small cell carcinoma: a type of highly malignant cancer that most commonly arises within the lung, although it can occasionally arise in other body sites, such as the cervix and prostate
    • “small cell” because microscopically the cells don’t have much cytoplasm
    • accounts for 20% of cases
    • in the lung, it is derived from neuroendocrine cells in the hilum/mediastinum = tends to release hormones associated with paraneoplastic effects (ADH, etc)
      • paraneoplastic syndromes such as SIADH, Cushing syndrome, myopathies, neuropathies, CNS dysfunction
    • mets occur early
    • most chemotherapy-sensitive cell type
  • non-small cell carcinoma: any type of epithelial lung cancer other than small cell lung carcinoma, most are relatively insensitive to chemo
    • squamous: accounts for 20-30% of primary lung tumors
• most common form in males
• most are smokers
• originates in hilar/endobronchial region
• frequently causes cavitation
• may secrete PTH → hypercalcemia
• resectable if caught early
• radiosensitive but chemotherapy resistant
• histological hallmark is the creation of “keratin pearls” as the squamous cell behaves like a skin cell and produces a lot of keratin
  o adenocarcinoma: accounts for 30-40% of primary tumors
    • most common form in females
    • weak or no association with tobacco use, may be genetic?
    • usually originates peripherally
    • resectable if caught early
  o large cell: 12% of primary tumors
    • grows rapidly
    • usually originates peripherally
    • resectable if caught early
    • poorer prognosis
  o mixed: tissue of origin is unknown
    • mets from distant site: breast, gut, skin (melanoma), sarcoma, renal, head/neck tumors
    • others: carcinoid, bronchial gland tumor, carcinoma
      • generally unresectable
      • nodule usually presents peripherally
      • poor prognosis
• Role of preventative screening
  • CXR: study showed 80% of lung masses were detected by screening, but no mortality benefit
  • CT: study showed it is better than CXR in detecting lung cancer, with a 20% reduction in mortality
    • however there are a lot of false positives and screening is costly to implement
• Presentation
  • 10% of lung cancers may be found incidentally on routine imaging
  • 55% of the time local/regional symptoms are the precipitating factor for a doctor’s visit
    • primary tumor in central/endobronchial region: cough, SOB, hemoptysis (especially squamous cell), wheezing, stridor, post-obstructive pneumonia
    • primary tumor in lung periphery: chest wall pain, cough
    • nodal spread: tracheal or esophageal obstruction, hoarseness d/t impingement of recurrent laryngeal nerve, paralyzed diaphragm d/t phrenic nerve impingement, SVC syndrome
    • local spread: chest wall pain, pleural effusion, Horner’s syndrome from invasion of sympathetic nerves, brachial plexus neuropathy from invasion
  • 35% of the time there will be distant or paraneoplastic symptoms
    • weight loss, anorexia, fatigue, fever, neuropathy
    • brain mets: seizure, headache, aphasia, paresis, confusion
    • bony mets: pathologic fracture, spinal cord compression, bone marrow invasion
    • adrenal mets: Addison’s disease
    • squamous: hypercalcemia from PTH secretion
    • small cell: hyponatremia and SIADH, Eaton-Lambert syndrome (muscle weakness)
• Investigation
  • hilar or mediastinal mass (central)
    • imaging: CXR or CT
    • bronchoscopy: pretty sensitive but risk of bleeding, infection, respiratory failure, arrhythmia
    • transthoracic needle aspiration: usually not for central tumors, best for peripheral
      • sensitive, but can cause pneumothorax or hemorrhage
    • surgical resection rarely indicated, mediastinoscopy is preferred
  • solitary pulmonary nodule
    • can follow with serial CXRs if probability of cancer is < 5%
      • look at old films to rule out injury vs malignancy
      • when someone is young and from an area endemic for fungal pneumonias


- when lesions are < 1 cm
- when someone is not a candidate for resection or curative radiotherapy
  - CT scan
    - better information about shape of lesion and whether calcification pattern is benign or not
      - probably benign if lesion is round and well-bordered
      - lobulations, irregular border, or spiculations are more indicative of malignancy
      - eccentric or diffuse calcification patterns are probably malignant
    - good for looking for additional nodules
    - malignancy will have increased uptake of contrast while benign tumor will have decreased uptake
  - PET scan
    - not useful for differentiating infection vs malignancy
    - sensitive for lesions > 1 cm
      - potential for false negatives with slow-growing cancers like bronchoalveolar cell carcinoma, carcinoid tumors, or very small lesions
    - follow up with CXR
  - bronchoscopy: not sensitive (cancer or benign disease) but very specific
  - transthoracic needle aspiration: sensitive & specific for cancer, poor sensitivity for benign disease
  - surgical resection: for when there is > 50% probability of cancer or known diagnosis

### Staging
- non-small cell lung cancer follows the TNM system
- small cell lung cancer is nonsurgical because it will recur, but responds to chemo

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### 18.15 Acute Respiratory Distress Syndrome

#### 18.15.1 Background
- ARDS is a catch-all term for severe lung disease with a variety of causes that is characterized by parenchymal inflammation impaired gas exchange and systemic release of inflammatory mediators further inflammation, hypoxemia and frequently multiple organ failure
- term is criticized for being too vague and all-inclusive
  - does not take into account ventilator pressure
  - additional criteria including this have been added to make the Murray-UCSF score for evaluation of patients with suspected ARDS
- a less severe form of ARDS is known as acute lung injury (ALI)
- Potential causes:
  - primary: trauma, aspiration, inhalation of toxic gas, pneumonia, contusion
  - secondary/indirect: sepsis, pancreatitis, hypotension
- Greatest risk of developing ARDS is with septic patients
- Pathology due to permeability edema from injured/leaky pulmonary capillaries, collapsed alveoli from abnormal surfactant, capillary thrombi
- Clinical progression:
- stage I occurs with infiltration of neutrophils to the site of inflammation
  - CXR will be clear at this time
- stage II occurs over days 1-2, where edema and type I alveolar cell damage occurs
  - CXR will show patchiness
- stage III occurs over days 2-10 and results in exudate as well as proliferation of type II alveolar cells functioning as repair cells
  - CXR will show diffuse infiltration
- stage IV occurs after day 10, with involvement of lymphocytes and resulting in fibrosis
  - CXR will show diffuse infiltration

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### 18.15.2 Diagnosis and Treatment of ARDS
• Presentation: stiff lungs, muscle fatigue, hypoxia, pulmonary hypertension
• Diagnostic criteria: fraction of PaO2/FiO2 being < 200
• FiO2 = fraction of inspired oxygen in a gas mixture
• CXR shows bilateral infiltrates but definitive criteria for ARDS is vague
• vs unilateral that is more characteristic of pneumonia or aspirate
• no evidence of LA hypertension = infiltrate can’t be explained by CHF
• Treatment is to block events in ARDS cycle
  • block triggers with proper infection management and prevention measures
    o antibiotics
    o surgical drains
    o reduction of aspiration risks
    o minimize transfusions
  • block inflammation mediators? so far all attempts have failed
    o questionable use of steroids in preventing fibrosis
  • block manifestations
    o gentle ventilation
      ▪ keep balanced to prevent volutrauma (overdistension of alveoli) as well as atelectrauma (rapid opening/closing of alveoli)
      ▪ using smaller tidal volumes saves lives!
    o right components in delivered oxygen
    o keep lungs dry but balance fluid in and out
    o slow and steady fluid resuscitation
• Prognosis: mortality is 30-40%
• ARDS due to secondary cause carries worse outcome
• long term mortality depends on underlying health status

18.16 Cystic Fibrosis

18.16.1 Background
• An autosomal recessive genetic disease affecting most critically the lungs, and also the pancreas, liver, and intestine
• affected gene is the cystic fibrosis transmembrane regulator (CFTR) on chromosome 7
  o makes a protein product that functions as a chloride channel
  o also regulates bicarb and other ions
  o mutation causes protein misfolding and targets the CFTR for destruction
    ▪ 90% of CF patients have the mutation that blocks processing of this protein, called F508del
  o defective ion transport to the cell surface causes liquid depletion and defective mucociliary clearance
    o leads to mucus obstruction □ infection, inflammation, and fibrosis
• any organs with cilia are also affected: pancreas, vas deferens
• Most commonly affects Caucasians (historically may be due to cholera outbreaks in Europe’s past)

18.16.2 Diagnosis and Treatment
• Presentation:
  • recurrent pulmonary infections, poorly controlled asthma, failure to thrive, meconium ileus (obstruction of an infant’s first stool in the ileum), pancreatitis, growth failure due to vitamin deficiencies (no pancreatic enzymes to absorb fat-soluble enzymes) and poor absorption of meals, nasal polyps, sinusitis, fatty liver, clogging of liver vessels, liver failure due to fibrosis □ cirrhosis and portal hypertension, gallstones, jaundice, frequent fractures/osteoporosis/arthritis from vitamin D deficiency, rectal prolapse from thick stools, intestinal strictures, appendicitis, reflux disease, infertility, delayed puberty, widening of bronchioles, smooth muscle growth around bronchioles □ inhibition of gas diffusion, bronchiectasis (widening), pneumonia, hemoptysis, pneumothorax, asthma, chest pain, dyspnea, respiratory failure, diabetes, enlarged or dysfunctional spleen, infertility
• presentation is on a continuum depending on severity of mutation and percentage of normal CFTR functioning
  o with 50-100% functioning there is no known abnormality
  o with 10-49% functioning there is still no known abnormality
  o with < 10% functioning there is absence of the vas deferens
  o with < 5% functioning there is also a clinically demonstrable sweat abnormality
  o with < 4.5% functioning there is also a progressive pulmonary infection
  o in severe deficiency <1 % of the CFTR function normally and there is also pancreatic exocrine deficiency
• infections occur with more atypical bacteria
  o in infancy Staph predominates
  o in adults Pseudomonas predominates
• signs of an acute exacerbation: increased cough/sputum, sputum color change, dyspnea, fatigue, decreased exercise tolerance, poor appetite, new tachypnea/retractions/rhonchi/wheezes, weight loss, fever, new findings on CXR, decreased PFTs, hypoxia
  o remember that a CF exacerbation (bronchial disease) is different than pneumonia (a parenchymal infection)
• Investigation
• most cases diagnosed by age 12, with a median age of 6 months
• newborn screening for immunoreactive trypsinogen blood test is required in all 50 states
  o levels are elevated in CF patients with pancreatic insufficiency
• genetic screening of 23 most common mutations available
  o but will only identify CF in predominantly Caucasians, while missing more of the mutations that are more common in blacks and Hispanics = detection rates will vary by ethnicity!
• buccal swab DNA test for remaining mutations
• nasal testing also available to test functioning of CFTR channels
• confirmatory test is the sweat chloride test
  o less than 40 is normal
  o levels at 40-60 are inconclusive
  o greater than 60 is + for CF
• Treatment
• prevent exacerbations via:
  o dietary support: lung function increases as BMI goes up
    ▪ high caloric intake: lose a lot of nutrients in malabsorption
    ▪ salt supplements in newborns
    ▪ pancreatic lipase replacement at every meal
    ▪ AEDK supplements with minerals
  o promote mucus clearance
    ▪ percussion and chest compression vests
    ▪ upside-down coughing
    ▪ huff breathing
    ▪ oral oscillators
    ▪ exercise
    ▪ positive airway pressure like CPAP
    ▪ meds: rhDNase breaks down bacterial DNA, hypertonic saline or Mucomyst causes osmosis and wetting of airways so cilia can beat, albuterol increases ciliary beat frequency and dilates airways
  o control infections: goal is to decrease endobronchial burden of disease rather than total organism eradication
    ▪ on/off cycles of inhaled antibiotics against Pseudomonas
    ▪ intermittent IV antibiotics
  o slow lung function decline
    ▪ deterioration occurs at 2% per year
    ▪ speeds up with increasing exacerbations, as with each exacerbation you are unable to bring patient back up to their former baseline
• for exacerbation:
  o outpatient: targeted oral antibiotics for 2-3 weeks, up airway clearance treatments
- inpatient: targeted IV antibiotics for 2-3 weeks, 4x daily airway clearance treatments, nutritional monitoring, monitoring for hypoxia and respiratory failure
  - discharge with improvement to near-baseline of respiratory status, nutrition, and energy level
- future meds: gene therapy, CFTR modulation to open the gate back up
- Follow-up/monitoring
- frequent office visits with yearly evaluation of labs and CXR
  - PFTs, sputum culture, diabetes screen, bone, CBC, PT/PTT, UA, vitamin levels, LFTs, albumin
  - immunizations
- Prognosis: median survival is age 38, with primary cause of death being respiratory complications or failure
19  Rheumatology Exam Notes

19.1  Introduction to Rheumatic Diseases

19.1.1  Background

- Rheumatic disease
- diseases are on a spectrum, with most being inflammatory
  - there are 6 diffuse connective tissue diseases: scleroderma, dermatomyositis, rheumatoid arthritis, polymyositis, systemic lupus erythematosus, Sjogren’s syndrome
    - patients with signs and symptoms overlapping these categories are often given the diagnosis of undifferentiated connective tissue disease (UCTD)
    - patients with features of SLE, scleroderma, polymyositis, dermatomyositis are given the diagnosis of mixed connective tissue disease
    - one category of a disease can develop into another down the road
  - different from arthritis, which only refers to the joint
    - rheumatism includes inflammation of the bones, muscles, tendons, and ligaments
    - sometimes can involve organs such as the lungs, skin, heart, kidneys
- acute and chronic
- most prevalent in older adults and women
- higher incidence in Hispanics
- may have genetic predisposition with complex inheritance patterns
  - influenced by environmental factors such as geographical location, cigarette smoke, and female sex hormones
  - familial aggregation of disease varies with different disorders
  - identical twins have much higher relative risk if one twin is affected than if a sibling is affected
  - control of immune function regulated by genes in the major histocompatibility complex (MHC)
    - MHC I and II proteins bind antigens to present to T-cells
    - MHC III genes encode proteins to make TNF and complement
  - but, genes other than those located in the MHC are also associated with increased risk of rheumatic disease
- Non-rheumatologic illnesses causing arthritis and arthralgias include hepatitis, Celiac disease, IBD, hemochromatosis, hemophilia, plasma cell dyscrasias, sickle cell, amyloidosis, diabetes, thyroid disease, parathyroid disease, sarcoidosis, malignancy, systemic infection
- Total cases of all kinds of arthritis are increasing due to an increase in the aging population and the obesity epidemic
- but rheumatoid arthritis alone is decreasing in incidence
- Trends in arthritis imaging on radiographs:
  - involvement is DISTAL with OA (DIPs), psoriatic arthritis (DIPs), and Reiter’s syndrome (1st IP joint)
  - involvement is PROXIMAL with RA (carpals, MCPs), and pseudogout (MCPs)
19.1.2 Musculoskeletal Disease

- Mechanisms
  - metabolic
    - rare
  - degenerative: loss of articular cartilage
    - includes the rheumatologic diseases
    - may be crystal-induced, infectious, autoimmune, or idiopathic in nature
      - autoimmune: RA, lupus, spondyloarthropathies, scleroderma, inflammatory myopathies, vasculitis
        - a result of either autoantibodies or autoreactive T-cells
        - organ-specific (thyroid, MS) or systemic (most rheumatic diseases)
        - release of normally sequestered self antigens?
        - failure to anergize self-reactive T-cells?
        - microbial antigens similar to self antigens?
        - defective T-cell functioning?
  - degenerative: osteoarthritis
  - infectious: infectious arthritis
  - crystal-induced: gout, pseudogout

- traumatic
- overuse injuries
- Most common ailments are back pain and periarticular disease
- non-inflammatory illness usually affects the axial skeleton
- inflammatory illness usually affects the synovial joints of the extremities
  - may involve the joint itself (fibrous capsule and synovial membrane) as well as associated structures of articular cartilage, tendons, ligaments, bursae, muscles, and menisci
    - synovitis: inflammation of the synovial membrane
    - enthesitis: inflammation of a tendon or ligament at the insertion into bone
    - myositis: inflammation of skeletal muscle

19.1.3 Approach to the Patient with Rheumatic Disease

- Must differentiate:
  - articular vs non-articular disease
  - acute or chronic
  - localized or systemic
  - inflammatory vs non-inflammatory
  - Clues for establishing a rheumatic etiology
    - insidious onset
    - no recollection of a cause or source of insult
    - FH of similar symptoms
- joint swelling, effusion, redness, pain, stiffness, instability, deformity that is symmetric
  - PE: localized pain, joint-line tenderness, synovial thickening (bogginess), bony enlargement, crepitus
- extra-articular complaints such as IBD, psoriasis, uveitis
- inflammatory pain and stiffness is worsened with inactivity and is often worst in the morning
  - vs non-inflammatory pain that is relieved with rest and is worsened by activity
- preceding infection, especially GI or GU
- Rheumatologic ROS: fever, weight loss, fatigue, rash, weakness, paresthesias of extremities, GI symptoms, ocular symptoms
- imaging
  - plain x-rays of hands/feet, spine/sacroiliac joints, or other symptomatic joint
    - look for signs of osteopenia, erosions, joint space narrowing, soft tissue swelling, joint subluxations
  - CT or MRI for early changes in SI joints or axial disease
  - bone scan for detection of infection, stress injury, osteonecrosis
- functional assessments
  - social and emotional functioning
  - performance of ADLs
  - assessment of limitations
  - assessment of need for physical therapy
  - can make use of Health Assessment Questionnaire (HAQ): a comprehensive measure of health outcome based on measures of discomfort, drug toxicity, costs, disability, and death
    - performance of ADLs measured on a scale of 0-3, with 0 being no difficulty and 3 being unable to do
    - pain measured as present or absent over duration of a week
    - patient global scale measures quality of life
    - ***diagnosis is frequently delayed due to waxing/waning nature of rheumatic disease, shared clinical features and autoantibodies between diseases, and provider’s fear of delivering a life-altering diagnosis
- Referral needed when diagnosis is uncertain, there is an increase in disability or deformity, management of disease is uncertain, or if immunosuppressive therapy is needed

19.2 Common Rheumatological Lab Tests

1.) CBC: elevated WBCs with ↑ neutrophils, mild anemia from chronic disease, thrombocytosis

2.) Acute phase reactants: can include ESR, CRP, fibrinogen, haptoglobin, prothrombin, ferritin, C3, C4, antitypsin, plasminogen, Ig, or lipoprotein analysis
- ESR and CRP the most commonly used
- erythrocyte sedimentation rate: rate at which RBCs fall to the bottom of an anticoagulated column in a set period of time
  - faster, less expensive, but prognostic use is limited to RA, PMR, and temporal arteritis
  - neither sensitive nor specific
  - loose guidelines with no low end of normal
  - increased in anemia, inflammation, females, pregnancy, older age, high cholesterol
  - decreased in sickle cell, abnormalities of RBC size and shape
  - aspirin, NSAIDs, cachexia, recent meal, or high-dose steroid therapy will not affect results
- C-reactive protein: correlated to tissue necrosis or inflammation
  - rises 12-24 hours after inflammatory event
  - more sensitive but more expensive, takes longer, requires patient fasting, can be affected by meds
  - levels change faster than ESR (come down quickly with resolution of inflammation)
- caveats: acute phase reactants can also be elevated in cancers and they are not good for screening someone who is asymptomatic
- use for screening symptomatic patients of unknown etiology
3.) **Antinuclear antibodies (ANA):** measures antibodies to a variety of nucleoproteins
   - used as a screening test for connective tissue disorders; if + follow up with confirmatory testing of specific autoantibodies
   - used primarily to diagnose SLE but are also + in RA, scleroderma, Sjogren’s, polymyositis, and vasculitis
   - helps establish a diagnosis in a patient with clinical features suggestive of an autoimmune or connective tissue disorder, exclude certain diagnoses, or subclassify a patient with a known autoimmune or connective tissue disease
   - order with patients that have systemic disease suggestive of lupus and in patients with rash, polyarthritis, or renal disease not explained by other causes
   - can also be used to monitor disease activity
   - often uses fluorescence techniques, where the type of pattern visualized is suggestive of a particular disease
   - may be + but with low titer in a person with no autoimmune disease
   - healthy relatives of SLE patients are more likely to have a + ANA = genetic role?

4.) **Antiextractable nuclear antigens:** an autoantibody set of the most common anti-nuclear antibodies
   - order in patients with a positive ANA, those with strong clinical features of SLE, patients with skin manifestations of SLE, mothers of newborns with SLE
   - only need to be tested once as these antibodies will not change over time
   - anti-Sm: highly diagnostic of SLE, + in 25% of patients with SLE (and some with mixed connective tissue disease)
   - anti-ribonucleoprotein (anti-RNP): highly diagnostic of mixed connective tissue disease, + in ~100% of patients with MCTD (and 25% of those with SLE, discoid lupus, and scleroderma)

5.) **Autoantibodies as immunologic markers**
   - **rheumatoid factor (RF):** anti-IgM autoantibody measured in patients with inflammatory polyarthritis with joint swelling and stiffness after inactivity
   - positive in ¾ of RA cases but also positive in many other diseases (TB, syphilis, sarcoid, SBE, other viral and parasitic diseases)
     - can’t be used to screen the general population due to low positive predictive value
     - higher sensitivity when used in specific populations
     - may initially be negative in a patient with RA but can become + over course of disease
   - anti-cyclic citrullinated peptide (anti-CCP): a byproduct of arginine conversion that occurs during inflammation
   - more specific than RF, only found in serum of 80% of RA patients
     - also positive in other autoimmune diseases, TB, and some chronic lung diseases
   - a predictor of persistent, erosive RA that will change the course of treatment if positive

6.) **SLE autoantibodies**
   - **anti-DNA antibody:** diagnostic of SLE but many SLE patients lack this antibody
   - levels may change during course of disease
   - order in patients with + ANA and clinical presentation suggestive of SLE
   - if positive, is associated with development of lupus nephritis
   - anti-SS-A (anti-Ro): against a protein associated with RNA; found in 70% patients with primary Sjogren’s, SLE, others
   - anti-SS-B (anti-La): against a protein associated with RNA; found in patients with SLE and 60% of primary Sjogren’s patients
   - anti-Sm and anti-RNP

7.) **Other autoantibodies**
   - **myositis-associated antibodies:**
     - anti-Jo-1 (anti-synthetase):
     - anti-signal recognition peptide (anti-SRP): associated with acute, severe myositis
     - anti-Mi2: more specific for dermatomyositis
     - anti-SS-C: found in 75% of patients with RA or secondary Sjogren’s associated with RA
anti-centromere antibodies: found almost exclusive in scleroderma
anti-ScI-70 (anti-topoisomerase): anti-scleroderma antibody; diagnostic for scleroderma (present in 45% of patients with scleroderma)
also associated with increased frequency of interstitial lung disease
anti-RNAP: associated with diffuse scleroderma and increased risk of renal crisis
antineutrophil cytoplasmic antibodies (ANCA): includes cytoplasmic ANCA (more specific, useful in diagnosis of Wegener’s granulomatosis) and perinuclear ANCA (poorly specific but seen in many forms of vasculitis)
order in patients with renal disease of unknown etiology, patients with renal-pulmonary syndromes, systemic disease of unclear etiology

8.) Arthrocentesis & culture
used to evaluate monoarticular effusions or when joint disorder etiology is unknown
must be done for accurate diagnosis of crystal-induced and infectious arthropathies
heparinized, non-heparinized, and plain sterile specimens (culture & crystal analysis) are collected
complication: rice bodies (fibrin, debris, cells, calcium apatite) clogging needle
examination categorizes appearance, viscosity, cell count & differential, and crystal patterns of joint fluid
determines whether fluid is non-inflammatory, inflammatory, septic, or hemorrhagic
normal fluid is clear, straw-colored, viscosity of 4-5 cm, < 200 WBC/µL, < 2000 RBCS/µL, glucose content similar to plasma (within 10 mg/dL), and is sterile

9.) UA
10.) Other pertinent lab draws: thyroid function panel, renal & liver function test, Lyme titers, CPK, aldolase
serum protein electrophoresis to look for hypoalbuminemia

11.) Imaging studies
typically plain x-ray of symptomatic joint is all you need
can do CT or MRI for SI joint or axial disease
bone scan if concerned about infection, stress fracture, or osteonecrosis

19.3 Rheumatoid Arthritis

19.3.1 Background
RA is the most commonly diagnosed systemic inflammatory arthritis, with the synovial membrane the site of attack
pathology:
- triggering incident □ proliferation of macrophages and fibroblasts
- lymphocytic invasion of the perivascular space
local blood vessels become occluded
formation of a pannus (outpouching of synovial membrane)
pannus invades cartilage and bone
cytokines, proteases, and interleukins are released
further joint destruction

- major cells involved: T-cells, macrophages
- minor cells involved: fibroblasts, B-cells, endothelial cells, dendritic cells
- neutrophils seen in the synovial fluid

- More common in women than men (up to age 65)
- Peak incidence in ages 30-50, with total incidence on the decline
- Genetics play a strong role in susceptibility and disease severity
- HLA-DR1 and HLA-DR4 alleles have a strong association with RA
- Protective effects with estrogen, tea use, high vitamine D intake, silicate exposure, breastfeeding
- Increased risk with nulliparity, older age, FH, female sex, cigarette smoking, infection (Mycoplasma, Mycobacterium, enteric bacteria, rubella, parvovirus B19, EBV)

19.3.2 Presentation

- Classic manifestations:
  - slow, insidious onset with duration of symptoms over weeks to months
  - waxing and waning of symptoms with acute episodes
  - hallmark sign is morning stiffness for at least one hour
    - stiffness is worse also after prolonged periods of rest in the same position
  - fatigue, malaise, low-grade fever, weight loss
  - pain and stiffness in multiple or single joints (usually > 5)
    - small bones of the hands and feet most likely to be affected early on, wit
to larger joints
    - joints are swollen and/or warm
    - erythema is uncommon
    - muscles may atrophy around inflamed joints
- Less common manifestations:
  - palindromic rheumatism: involvement of 1-7 joints over days followed by months without symptoms
    - half of these patients will go on to develop RA
    - can use hydroxychloroquine to slow down or prevent progression
  - monoarthritis of a large joint followed by polyarthritis
  - extra-articular presentations:
    - skin: nodules (hard, calcified synovium that is nontender), fragility, vasculitis, pyoderma
gangrenosum
    - CV: pericarditis, premature atherosclerosis, vasculitis, valve disease, valvular nodules
    - pulm: pleural effusions, interstitial lung disease, bronchiolitis obliterans, rheumatoid
nODULES, vasculitis
    - eye: keratoconjunctivitis sicca (Sjogren’s), episcleritis, scleritis
    - neuro: cervical myelopathy, mononeuritis multiplex, peripheral neuropathy (carpal tunnel, trigeminal neuralgia)
    - hematologic: anemia, thrombocytosis, lymphadenopathy, Felty’s syndrome
    - renal: amyloidosis, vasculitis, nephrotic or nephritic syndrome
    - bone: osteopenia
- Established disease: articular manifestations
  - not seen as much today due to prevention of progression with aggressive treatment
  - hands: ulnar deviation, swan neck deformities, boutonniere deformities
  - feet: subluxation of MTP joints formation of characteristic callus
  - wrists: synovial proliferation median nerve compression, extensor tendon rupture
  - manifestations in TMJ, cricoarytenoid joint, sternoclavicular joint
  - manifestations in the atlantoaxial joint subluxation from ligamentous laxity, pain radiation to
occipital area, progressive quadriparetesis with decreased sensation in hands, upper extremity
paresis with head movements, transient episodes of vertebral artery compression
Differential: post-infectious sequelae (group A strep or virus), other systemic rheumatic disease, Lyme arthritis, fibromyalgia, psoriatic arthritis, IBD-associated arthritis

Definitive diagnosis of RA is currently based on a points system, where at least 6 points are needed
- involvement of joints, + RF/ACPA serology results, longer duration of symptoms, and abnormal CRP/ESR results all accrue points
- radiographic findings are not taken into account because these new criteria aim to treat people early on in disease

Labs
- acute phase reactants: ESR, CRP, thrombocytosis
- autoantibodies: + anti-RF, anti-CCP, ANAs if RF and CCP are negative
- CBC: anemia of chronic disease (inflammatory proteins inhibit body’s ability to process Fe for RBCs)
- synovial fluid analysis will show increased WBCs with a predominance of neutrophils

Imaging
- early radiographic findings: soft tissue swelling, osteopenia in periarticular space (visualized as abnormal lucency/darkness), marginal erosions, with bilateral symmetry
- late radiographic findings: joint space narrowing, diffuse osteopenia, deformities
- specific manifestations:
  - hand radiograph: affects the carpal bones and CMC joints  
    ▪ see ulnar deviation at the MCP joints, carpal crowding with joint space loss, marginal erosions
  - all symmetric bilaterally
  - hip radiograph: joint space loss that is axial (central) on the femoral head
  - atlantoaxial joint radiograph: instability due to destruction and laxity of the transverse ligament  
    ▪ increased movement on flexion visible on radiography
  - shoulder radiograph: joint space loss, high-riding shoulder from lax rotator cuff ligaments, osteoporosis
- MRI is only used to detect early changes not yet visible on radiograph
  - fatty bone marrow with low-signal dark areas of early RA

19.3.4 Treatment & Prognosis

- Goals are to prevent or control joint damage, prevent loss of function, decrease pain, control systemic complications, and maximize quality of life

- Analgesics:
  - NSAIDs:
    - can be used as initial treatment or as bridge therapy for pain reduction but should not be used alone because they do not alter disease course or prevent joint destruction
    - caution! RA patients are twice as likely to experience side effects as OA patients
  - glucocorticoids:
    - functional improvement within days of being administered
    - usually used long-term for RA
      ▪ side effects are more likely: osteoporosis, CV risk/CAD, hyperglycemia, skin fragility, GI bleed, cataracts, Cushing’s
        - give Ca and vit D (and maybe bisphosphonates) to augment osteoporotic effects
        - addition of a PPI or H2 blocker may prevent GI complications
      ▪ may modify course of disease

- DMARDs:
  - disease-modifying: reduce and prevent joint damage and preserve joint integrity and function
  - reduce total healthcare costs and maintain economic productivity of patient
  - should be started within 3 months of diagnosis
  - non-biological drugs:
    - methotrexate: inhibits difolate reductase which is involved in DNA synthesis, inhibits proliferation of lymphocytes by interfering with DNA synthesis, decreases accumulation of toxic compounds, increases anti-inflammatory adenosine
      ▪ teratogenic!
      ▪ first-line DMARD!
- slows radiologic damage
- may reduce mortality
- side effects: nausea, vomiting, diarrhea, anorexia, alopecia, rash, myelosuppression, liver or renal failure, hyperuricemia, oral ulcers, cough, SOB, infection from live vaccines □ monitor LFTs, CBC, SCr, liver biopsy every 1.5 g, CXR □ supplement with folate and avoid alcohol to reduce toxicity and GI effects
- interactions:
  - myelosuppression and GI tox with NSAIDs
  - liver tox and anemia with leflunomide
  - increased toxicity with penicillins
  - contraindications: pregnancy, severe renal or hepatic impairment
  - hydroxychloroquine: impairs complement-dependent antigen-antibody reactions, interferes with antigen presentation
    - takes 1-6 months to work
    - does not slow radiologic damage so should not be used alone
    - half-life of 30-60 days
    - side effects: nausea, vomiting, diarrhea, myopathy, headache, retinopathy, agranulocytosis, skin pigmentation □ monitor with eye exams, CBC, muscle strength
    - best tolerated DMARD
    - interactions:
      - increased activity with cimetidine
      - increased activity with digoxin
  - sulfasalazine: impairs lymphocyte transformation, suppress NK cells
    - takes 1-3 months to work
    - slows radiographic progression
    - side effects: headache, photosensitivity, rash, yellow-orange discoloration, nausea, vomiting, diarrhea, anorexia, myelosuppression, liver and kidney failure, oligospermia □ monitor CBC, LFTs, renal function
    - interactions:
      - hypoglycemia with sulfonlurea
      - bone marrow suppression with methotrexate
      - thrombocytopenia with thiazides
      - bleeding with warfarin
  - leflunomide: inhibits dihydroorotate dehydrogenase (pyrimidine synthesis) in lymphocytes, anti-
    - can be used alone or with methotrexate
    - metabolized in liver to undergo enterohepatic recirculation
    - teratogenic!
    - half-life of 14-15 days, with elimination taking up to 2 years = women and men who wish to conceive must undergo a cholestyramine washout to remove drug
    - side effects: diarrhea, weight loss, HTN, alopecia, rash, elevated LFTs, RTI □ monitor LFTs, SeCr, CBC, signs of infection, pregnancy tests
    - interactions:
      - decreased activity with bile acid sequestrants
      - myelosuppression and liver tox with methotrexate
      - bleeding with warfarin
      - increased activity with rifampin
  - contraindications: pregnant women, history of alcohol abuse, hepatitis
- older meds: azathioprine, gold salts, cyclosporine, minocycline
- biological drugs:
  - anti-TNF-α: etanercept, infliximab, adalimumab, certolizumab
    - work in 1-2 weeks
    - costly
    - used in combination with methotrexate and other DMARDs
    - get a TB skin test and make sure there are no active infections before starting
    - side effects: headache, infusion rxn, RTI, abdominal pain, vomiting, myelosuppression
      - infections if using abatacept or anakinra with a live vaccine
- malignancy with cyclophosphamide or etanercept
  - infliximab is contraindicated in heart failure and should not be used alone
- anti-TNF-α: golimumab
  - used if other agents have failed
  - administered in combination with methotrexate
  - infection in 28% of patients
- anakinra: IL-1 antagonist
  - used in those unable to tolerate anti-TNF-α agents
  - side effects: headache, injection site reaction, infection, neutropenia
    - infection in anti-TNF-α agents and live vaccines
    - monitor neutrophil counts
  - contraindicated in active infection
- abatacept: binds APCs to inhibit T-cell activation
  - side effects: nausea, headache, URI
  - infection in anti-TNF-α agents, anakinra, and live vaccines
  - TB test prior to initiating therapy
- rituximab: anti-CD-20, activates complement-dependent cytotoxicity
  - side effects: fever, chills, headache, pain, hypotension, rash, angioedema, abdominal pain, nausea, myelosuppression, cough
    - infection in biologics and live vaccines
    - monitor CBC, platelets, CV during infusion
  - interactions:
    - renal tox with cisplatin
    - hypotension with antihypertensives
- tocilizumab: anti-IL-6
  - side effects: injection site reaction, rash, hypertension, increased LDL/HDL/trig, abdominal pain, myelosuppression, increased LFTs
    - infection in biologics and live vaccines
    - monitor CBC< platelets, LFTs, lipids, for signs of demyelinating disorders
  - interactions:
    - hematologic tox in leflunomide
- alemtuzumab:
  - Follow algorithms based on disease progression, disease activity, and prognosis
  - DMARD + biological is more effective than either agent alone
  - don’t use biologics with each other
  - mild disease can be treated with less aggressive DMARDS
    - hydroxychloroquine
    - sulfasalazine
  - moderate-severe disease requires combination therapy
    - methotrexate
    - biologic
- Adjunct therapy: glucocorticoids, NSAIDs, analgesics, physical and occupational therapy
- Provide management for disability, medication side effects
- Survey for infections, malignancy, osteoporosis, and depression
- Work on cardiovascular risk reduction
- Prognosis:
  - will be a lifelong illness with 3-5 year reduction in life expectancy
  - spontaneous remissions can occur
  - complications:
    - immnosuppressive treatments may result in infection with unusual pathogens
    - Felty’s syndrome: addition of splenomegaly, neutropenia, and recurrent pulmonary infections to existing RA symptoms
      - may also see leg ulcers or vasculitis
    - Baker’s cyst from rupture of synovial fluid into the calf (looks like a DVT)
    - increased risk of malignancy, particularly lymphoma
  - poor with low function score, low socioeconomic status, increased ESR or CRP, early radiographic changes
19.4 Infectious Arthritis

19.4.1 Background

- Pathogen reaches joint via hematogenous spread or direct inoculation
- most commonly affects the knee, with tropism for larger joints
- usually a monoarticular condition
- 66% of cases are gonococcal as a sequelae of disseminated gonococcal infection
- nongonococcal agents: usually Staph aureus or Strep, also gram neg bacilli
  - prosthetic joints: Staph epidermidis if early infection, Staph aureus if late infection
  - uncommon: spirochetes, syphilis, Lyme, mycobacteria (reactivation)
- viruses: hep B, hep C, rubella, parvovirus
- fungi in immunocompromised patients: endemic dimorphs in gardeners or outdoorspeople, Candida
  - in patients with history of surgery or joint injections or IV drug users
  - uncommon: Aspergillus, Cryptococcus, Pseudallescheria, dematiaceous fungi
- Considered to be a medical emergency!
- can result in joint destruction and loss of function
- associated with high rates of morbidity and mortality
- More common in children and those > 50 years
- Women at greater risk than men, with increased risk during menses and pregnancy due to increased blood supply
- Increased risk of infection with underlying joint disease, prosthetic joints, diabetes, alcoholism, chronic renal failure, AIDS, TB, history of trauma to the area, recent joint injection or surgery, advanced age, immunosuppressive therapy, malignancy, exposure to animals, low socioeconomic status, and IV drug use

19.4.2 Gonococcal Arthritis

- Presentation: 1-4 days of migratory arthralgias followed by:
  - syndrome of rash, fever, chills, migratory tenosynovitis of knees, ankles, wrists, feet, hands
  - may have skin lesions that are papulovesicular hemorrhagic
- monoarticular arthritis of the knee, hip, wrist, or elbow
- Investigation:
  - synovial fluid examination and blood cultures have low yield
  - cervical, anal, or oropharyngeal culture may be +
  - WBCs are usually normal
- Treatment:
  - hospitalization with IV ceftriaxone
  - PO cefixime or cefpodoxime for at least one week

19.4.3 Nongonococcal Arthritis

- Presentation:
  - host is usually immunocompromised
  - moderate to severe pain surrounding the joint
  - effusion, spasm, warmth, or erythema
  - chills and fever
  - most cases are monoarticular and involve the small joints of the hands and feet
  - IV drug users: arthritis of the spine, sacroiliac joints, or sternoclavicular joints
  - congenital syphilis: arthritis of a long bone
  - secondary syphilis: generalized arthralgias
  - TB arthritis: usually a chronic monoarticular disease process
    - pain develops over months to years
    - affects knee and hip most commonly
  - Lyme arthritis: occurs in 70% of patients not treated for primary disease, with varying presentations
    - intermittent monoarticular or oligoarticular process involving the knee or other large joints
    - waxing/waning polyarthralgias
inflammatory synovitis with erosions and joint destruction
- fungal arthritis: slow course with history of trauma weeks to months before development of symptoms
- Investigation:
  - synovial fluid and blood cultures
    - AFB if suspecting mycobacteria
    - may be negative in fungal arthritis
- Lyme antibody titer
  - if suspecting fungal source: complement fixation, antigen assays, synovial biopsies
- imaging:
  - if infected prosthetic joint will have increased lucency around the prosthesis
- Treatment: alter as needed based on culture and sensitivity results
- Strep or Staph
  - IV drugs for 2 weeks
    - IV nafcillin or cefazolin
    - suspect MRSA
  - 1-4 weeks of PO antibiotics
- Gram negs (neutropenic patients, IV drug users, underlying joint damage)
  - ceftriaxone or ofloxacin
  - if needing to cover Pseudomonas: ceftazidime or piperacillin, gentamicin
- TB: same therapy as for pulmonary disease
- Lyme arthritis: oral doxycycline or amoxicillin for 1-2 months, or IV ceftriaxone for 2-4 weeks
- viral arthritis is usually self-limiting and nondestructive
- fungal arthritis: amphotericin B
- aggressive surgical debridement or removal with prosthetic joint

19.5 The Spondyloarthropathies

19.5.1 Background
- Spondyloarthropathies: a group of clinically, genetically, and pathologically related arthritides that involve the axial skeleton but do not test positive for rheumatoid factor
- characterized by enthesopathies: inflammations at a ligament or tendon’s site of attachment to bone
  - includes the Achilles, plantar fascia, pubic symphysis, ischium, iliac crest, greater trochanter, fingers, toes, anterolateral ribs
- involves the sacroiliac joints (bilaterally) and spine
  - bilateral sacroiliitis often mistaken for normal result of pregnancy
- may also involve peripheral arthritis
- extra-articular manifestations:
  - ocular: uveitis (inflammation of middle eye layer), conjunctivitis, sicca symptoms (dry eyes and mouth)
  - cardiac: aortic insufficiency, conduction delays
  - renal: IgA nephropathy, amyloidosis
  - neuro: cauda equina syndrome
  - msk: C-spine fractures or dislocations due to bamboo spine and osteoporosis
  - GI: colitis (may be asymptomatic)
  - skin manifestations in psoriatic arthritis and reactive arthritis
- occurs mostly in white males, but can happen outside of this population
- genetic association with HLA-B27
  - familial inheritance
  - disease presents at an earlier age with axial involvement along with ocular symptoms
- can also occur without HLA-B27, but has a different disease presentation
  - presents as peripheral arthritis, gut inflammation, and skin/nail problems
- Low back pain: inflammatory vs non-inflammatory?
• inflammatory pain has a slow onset, worsens with inactivity but improves with exercise, persists > 3 months, is associated with morning stiffness, often radiates to the buttoc k or thigh, no meds required to relieve pain (just activity)
  o but never goes beyond the thigh like sciatica
• non-inflammatory or mechanical pain is acute, worsens with activity but improves with rest, lasts 2-4 weeks, has no morning stiffness, and rarely radiates
• do FABER test to see if it is due to sacroiliitis
• Investigation of suspected spondyloarthropathy:
  • labs: ↑acute phase reactants, thrombocytosis, anemia, ↑IgA (host response to enteric pathogens?)
    o less common: ↑alkaline phosphatase, ↑creatine phosphokinase, ↑CSF protein content, ↑complement
  • European diagnostic criteria:
    o either inflammatory spinal pain OR synovitis (asymmetric, predominantly lower limb)
    o and one or more of these characteristics: FH, psoriasis, IBD, urethritis/cervicitis/acute diarrhea one month before onset of arthritis, alternating buttock pain, enthesopathies, sacroiliitis
  • Amor diagnostic criteria:
    o involves a list of symptoms with each getting 1-2 points, diagnosis with ≥ 6 points
    o includes all European criteria plus: lumbar pain/stiffness, asymmetric oligoarthritis (inflammation of ≤ 4 joints), dactylitis, prior psoriasis, HLA-B27+, iritis, + response to NSAIDS

19.5.2 Ankylosing Spondylitis
• chronic autoimmune inflammation of the spine and sacroiliac joint
• Background:
  • the “prototypical” spondyloarthritis (but not the most common)
  • usually begins in adolescence or early adulthood
  • strong association with HLA-B27
• Presentation:
  • initial presentation is usually inflammatory back pain > 3 month’s duration that is improved by exercise and worsened with rest
  • tenderness at areas of enthesopathy
  • involvement of hips, shoulders, and commonly the joints of the lower extremity
    o usually asymmetric
  • almost all patients will have bilateral sacroiliitis
  • decreased chest expansion due to arthritis at the sternoclavicular joints
  • loss of lumbar flexion (test with Schober maneuver, should gain at least 5cm of flexion)
  • extra-articular manifestations in the eye and heart
• Investigation:
  • x-ray:
    o spine: marginal symmetric syndesmophytes (bony growth inside a spinal ligament) bridging
      and fusion of vertebral bodies creation of a “bamboo spine” with limited mobility, vertebral body squaring
    o SI joints: bilateral symmetric sacroiliitis that is erosive, leading to scarring and fusion
  • CT can be used to detect sacroiliitis
• Prognosis:
  • indicators of poorer outcome: severe hip disease, early age of onset, persistent elevation of ESR
• Treatment:
  • indomethacin

19.5.3 Reactive Arthritis
• acute inflammatory arthritis following 1-4 weeks after an enteric or genitourinary infection, usually with Chlamydia
• Background:
- includes Reiter’s syndrome (triad of urethritis, arthritis, and conjunctivitis), posturethral reactive arthritis, and postdysenteric arthritis
- commonly affects the spine, SI joints, distal hands, distal feet
- posturethral arthritis more common in women
- moderate association with HLA-B27

**Presentation:** acute or chronic
- asymmetric oligoarthritis of the lower extremities (peripheral arthritis)
- may have sacroiliitis
- dactylitis or “sausage toes”
- enthesopathies
- extra-articular involvement of skin, eye, and mucous membranes: keratoderma blennorrhagicum, balanitis circinata

**Investigation:**
- x-ray:
  - spine: non-marginal asymmetric syndesmophytes
  - SI joints: unilateral or bilateral sacroiliitis
  - hands & feet imaging is identical to psoriatic arthritis but affects feet > hands
- CT can be used to detect sacroiliitis

**Treatment:** antibiotics if infection is still present, rest, NSAIDs, intra-articular steroid injections, DMARDs if disease becomes chronic

**Prognosis:** recovery is usually spontaneous with good outcome, but chronic cases do occur (more common with SI joint and axial disease)

### 19.5.4 Psoriatic Arthritis

- an inflammatory arthritis found in some patients with psoriasis
- **Background**
  - the most common spondyloarthropathy
  - psoriasis usually precedes joint disease by 20 years, then triggering incident brings on the arthritis (infection, trauma, etc.)
  - many patients don’t know they have psoriasis, as it can be on the scalp, underneath nails, or in other hidden areas
    - appears as large plaques with silvery scale
  - weak association with HLA-B27 but strong genetic predisposition

**Presentation:** there are 5 clinical symptom groups:
- predominantly DIP involvement
- symmetric polyarthritis that is clinically indistinguishable from RA
  - the most common presentation!
- asymmetric oligoarthritis of small joints with dactylitis
- arthritis mutilans (resorption of bones to the point of soft tissue collapse) with sacroiliitis
  - see “pencil-in-cup deformity” on x-ray
- ankylosing spondylitis-type with sacroiliitis and spondylitis may also see nail pitting but other extra-articular manifestations are rare

**Investigation:**
- x-ray:
  - spine: non-marginal asymmetric syndesmophytes
  - SI joint: unilateral or bilateral sclerosis
  - hands & feet: proliferative erosions at the DIPs (“pencil-in-cup”), soft-tissue swelling
- CT can be used to detect sacroiliitis

**Treatment:**
- NSAIDS +/- sulfasalazine
- add methotrexate if no improvement
- can use steroid injections for oligoarthritis form
- physical therapy

### 19.5.5 Enteropathic Arthritis
• an inflammatory arthritis associated with known IBD
• Background:
  • seen in both UC and Crohn’s, but is more common in Crohn’s
  • arthritis is the most common extra-intestinal manifestation of IBD, and may be axial or peripheral
  • relationship goes both ways: patients with spondyloarthropathies (especially if HLA-B27 neg) have a high prevalence of silent IBD
  • the course of the arthritis is temporally independent of the bowel disease and often precedes it
• Axial presentation: arthritis is temporally independent of bowel disease and frequently precedes it
  • sometimes there is sacroiliitis and/or spondylitis
  • can also have peripheral arthritis
  • weak association with HLA-B27
• Peripheral presentation: arthritis and IBD flares are temporally linked and often occur together
  • more common in Crohn’s
  • arthritis is oligoarticular and asymmetric and in the lower extremities
  • dactylitis and enthesopathies are common
  • Extra-articular manifestations may be seen in the eye

19.5.6 Undifferentiated Spondyloarthropathy
• Overlapping clinical features between several spondyloarthropathies

19.6 Idiopathic Inflammatory Myopathies

19.6.1 Background
• Idiopathic inflammatory myopathies: a group of rare disorders with overlapping clinical features, characterized by progressive, symmetric proximal weakness
  • a result of immune-mediated injury to muscle fibers
    • may be triggered by environmental factors such as UV light, infection, and drugs
  • more common in women (except for inclusion body myositis)
  • more common in children and those around age 50
  • frequently associated with malignancies, other connective tissue diseases, or autoimmune disease
• Presentation
  • involves the neck, pelvis, thighs, or shoulders
  • onset is usually subacute
  • can also be associated with interstitial lung disease
  • can cause characteristic rashes
• Investigation:
  • differential diagnoses: drug-induced myopathy, endocrine myopathy, polymyalgia rheumatica, infectious myositis, neurologic disorders, electrolyte disorders, exercise intolerance
    • labs:
      • increased muscle enzymes (total CKs of 4,000-10,000+ are not unheard of)
      • increased acute phase reactants
      • LDH, aldolase, and liver enzymes often elevated
      • CBC
      • presence of myositis-associated autoantibodies: ANA, anti-Jo, anti-PM-Scl, anti-Mi-2
    • EMG: abnormal fibrillations, decreased amplitude, spontaneous discharges
    • biopsy (definitive): histologic changes in muscle tissue with inflammatory infiltrate
    • MRI will show edema in affected muscles
    • ***and do a malignancy screen!
• Treatment:
  • glucocorticoids
    • also prevention of side effects of osteoporosis via vit D supplementation, bone density scans, bisphosphate therapy
  • other immunosuppressives: azathioprine, MTX, cyclophosphamide, mycophenolate mofetil
- immunomodulators: IV Ig, rituximab
- cardiovascular risk management: smoking cessation, BP, cholesterol management

19.6.2 Polymyositis
- a persistent inflammatory muscle disease that causes proximal weakness of the skeletal muscles
- Background:
  - caused by killer T-cells attacking muscle cells expressing MHC class I
  - the rarest inflammatory myopathy
- Presentation:
  - insidious onset with nonspecific symptoms = a diagnosis of exclusion
  - frequently co-occurs with another systemic autoimmune disease, another connective tissue disease, or bacterial or viral infection
  - can also occur as a result of certain drugs

19.6.3 Dermatomyositis
- a connective-tissue disease related to polymyositis and Bramaticosis that is characterized by inflammation of the muscles and the skin with characteristic rashes
- Background:
  - caused by perivascular B-cells and helper T-cells causing Ig and complement deposition in capillaries
- Presentation:
  - characteristic rash typically preceded by proximal muscle weakness, or rash can present alone without any sign of myositis
    - heliotrope: erythematous or purple rash of the eyelid(s), usually with edema
    - Gottron’s papules: slightly raised pink, dusky red, or purple papules over the dorsal sides of the MCP/PIP/DIP joints, or over the wrists, elbows, or knees
    - Gottron's sign: same as Gottron’s papules but without the… papules
    - V sign: macular photosensitivity rash over the anterior neck, face, or scalp
    - shawl sign: macular rash over the posterior shoulders or neck
- associated with certain malignancies: ovarian, breast, colorectal cancers, melanoma, non-Hodgkin's lymphoma
  - if patient doesn’t have an existing cancer, you need to look for one if you see this!
  - may also see mechanic's hands: rough, cracked skin at the tips and lateral aspects of the fingers, forming irregular dirty-appearing lines that resemble those seen in a laborer

19.6.4 Inclusion Body Myositis
- an inflammatory muscle disease, characterized by slowly progressive weakness and wasting of distal muscles, most apparent in the muscles of the arms and legs
- Background:
  - caused by killer T-cells improperly stimulated to invade muscle cells and deposit abnormal proteins intracellular vacuoles
  - usually occurs in men over age 50
- Presentation:
  - insidious but progressive, asymmetric weakness and atrophy of the calves, foot flexors, hand flexors
    - weak grip, foot drop, tripping/dropping
  - weak quadriceps muscles falls, impaired mobility
    - ask to see patient stand up without using arms of the chair
- Prognosis: response to immunosuppressive treatment is poor

19.6.5 Anti-Synthetase Syndrome
- comprises the association of polymyositis and/or dermatomyositis, interstitial pneumonitis, mechanic’s hands, Raynaud's phenomena, inflammatory polyarthritis and, at the biological level, antinuclear antibodies known as anti-synthetases
- Background:
• clinically resembles polymyositis but histologically more similar to dermatomyositis

• Presentation:
  • symmetric inflammatory arthritis with joint contractures
  • 40-60% of patients will have interstitial lung disease
  • exertional dyspnea
  • fever, malaise, weight loss
  • GI: esophageal/stomach/small bowel dysmotility, dysphagia
  • CV: cardiac conduction abnormalities and dilated cardiomyopathy
  • skin calcinosis □ nontender nodules

• Investigation:
  • labs: anti-tRNA synthetase antibodies such as Jo-1, PL-7, PL-12, EJ, OJ, KS, and Zo

19.7 Scleroderma

19.7.1 Background

• Scleroderma: a chronic systemic autoimmune disease, primarily of the skin, characterized by fibrosis, vascular alterations, and autoantibodies
  • a result of defective fibroblast metabolism
  • monocytes and T-cells congregate in affected skin and organs
  • can also involve the lungs, kidneys, heart, GI tract, tendon sheaths, and some endocrine organs
  • may be influenced by environmental factors such as viral infection, silica exposure, radiation, etc.
  • several clinical subsets:
    □ diffuse cutaneous scleroderma:
    □ limited cutaneous scleroderma: aka “CREST” syndrome
      ▪ C = calcinosis
      ▪ R = Raynaud’s phenomena
      ▪ E = esophageal dysmotility
      ▪ S = sclerosis
      ▪ T = telangiectasias
    □ systemic sclerosis sine scleroderma: no skin manifestations, internal organs only
      ▪ autoantibodies are +
    □ localized scleroderma:
      ▪ linear scleroderma: kids
      ▪ morphea: hypo or hyperpigmented lesions of the skin, no internal organ involvement
        ▪ adults
      □ scleroderma overlap syndrome: involves skin changes that are consistent with scleroderma, but also features presentations of other diseases such as SLE or inflammatory myopathies

• Increased incidence in women and black patients
• Usually occurs after age 30

19.7.2 Scleroderma Presentation

• Common:
  • vasculopathy:
    □ Raynaud’s phenomena: vasoconstriction with pallor, followed by reactive hyperemia with erythema
    □ digital ischemia
    □ infarction
  • facial skin changes: loss of normal lines of expression
  • swelling of hands that gives way to contractures
    □ sclerodactyly: thickening and tightness of the skin of the fingers and toes
  • pulmonary hypertension
  • GI: dysmotility, GERD
  • MSK: peripheral neuropathies such as carpal tunnel or trigeminal neuralgia, generalized arthralgias, tendon rubs
19.7.3 Scleroderma Workup

- Labs:
  - ANA is + in 95% of scleroderma patients
  - anti-Scl-70 more common in diffuse scleroderma
  - anti-centromere antibodies more common in limited scleroderma

19.7.4 Scleroderma Treatment and Prognosis

- Treatment: tailored to patient's symptoms
- GI: PPIs or H2 blockers, antibiotics, prokinetics, frequent small meals
- vasculopathies: smoking cessation, Ca channel blockers, topical nitroglycerin, losartan, prazosin
  - statins may delay progression
- CV/pulm: treatment of R-sided failure and pulmonary HTN
- Prognosis: increased mortality if anti-Scl-70 +

19.8 Crystal-Induced Arthritis

19.8.1 Gout

- a kind of arthritis that occurs when uric acid builds up in blood and causes joint inflammation
- Background:
  - usually a result of decreased renal clearance of uric acid, but can also be caused by increased renal production
  - precipitation of uric acid crystals in joints inflammatory response
  - xanthine oxidase is responsible for converting purines into uric acid, but humans do not have the enzyme that breaks down uric acid, so it must be eliminated by the kidneys
  - causes of overproduction: purine consumption, alcohol use, myeloproliferative disorders, polycythemia, leukemia, EBV, psoriasis, drugs
  - causes of underexcretion: alcohol, renal disease, low urine volume, HTN, diuretics, aspirin, vasopressin, lactic acidosis, myxedema, respiratory acidosis, pre-eclampsia, MI, renal insufficiency
  - also influenced by body type, diet, insulin resistance, CHF, and organ transplantation
- has 4 typical stages:
  - hyperuricemia: typically asymptomatic
    - also seen in conditions of HTN, metabolic syndrome, CAD, CKD
  - acute gout: development can take decades after onset of hyperuricemia
  - intercritical gout: period between attacks
  - chronic gout: resembles RA with chronic symmetric polyarthritis
    - attacks are less sudden and begin to involve multiple joints
    - slower to resolve
- incidence is increasing
- peak age of occurrence in males is 40-50 years, 65+ years for females
  - estrogen is protective, so gout is rarely seen in a premenopausal woman
- associated with genetic factors, obesity, and metabolic syndrome
- risk factors: infection, trauma, weight loss (especially extreme diets), hospitalization, dyslipidemia (especially high triglycerides)
- Presentation:
  - initial attack(s): sudden monoarticular inflammation, usually of the 1st MTP (podagra) warmth, swelling, dusky red appearance (looks just like a septic joint)
    - also common in the insole, heel, ankle, knee
- more frequently occurs in the lower extremities than upper
- usually manifests at night due to fluid shift and recirculation
- extremely painful
- systemic signs may be present
- subsequent/chronic attacks can lead to **chronic tophaceous gout**: an advanced form that develops anywhere from 3-42 years after initial attack
  - directly related to serum uric acid levels
  - a destructive, polyarticular disease that resembles RA and other arthropathies
  - multiple tophaceous deposits in the hands, feet, ear helices
  - no pain-free intercritical periods
- Investigation:
  - must differentiate from septic joint but there are no unique labs or imaging = need to do a joint aspirate to demonstrate presence of uric acid crystals
- imaging:
  - radiographic findings include well-defined erosions, overhanging edges of lesions on both sides, soft-tissue nodules (tophi), random distribution with no symmetry, no osteoporosis
    - foot: overhanging edges of lesions, well-defined bony erosions, involvement of 1st MTP, tophi (can calcify)
  - MRI is only used to detect early changes
- Rome diagnostic criteria (2/4 must be present):
  - serum uric acid > 7 mg/dL in men or > 6 mg/dL in women
  - tophus
  - urate crystals in synovial fluid or tissues
  - history of attacks of abrupt painful joint swelling with remission in 1-2 weeks
- New York diagnostic criteria:
  - urate crystals in synovial fluid or tissue
  - or at least 2 of the following:
    - history of at least 2 attacks of painful limb swelling with remission in 1-2 weeks
    - history of podagra
    - tophus
    - history of good response to colchicine
- ACR diagnostic criteria:
  - urate crystals in synovial fluid
  - or tophus
  - or presence of at least 6 of the following:
    - more than one attack of acute arthritis
    - max inflammation within 24 hours
    - monoarthritis attack
    - joint redness
    - painful 1st MTP
    - unilateral tarsal joint attack
    - tophus
    - hyperuricemia
    - asymmetric joint swelling on x-ray
    - negative joint fluid culture
- Treatment:
  - do not treat asymptomatic hyperuricemia!
  - acute attack:
    - continue taking any gout prophylaxis medications
    - treat the arthritis first, then the hyperuricemia, NEVER both at the same time
    - treating hyperuricemia first can further precipitate uric acid crystals in the joint
    - NSAIDS: work by inhibiting prostaglandin synthesis by blocking the cyclooxygenase enzyme
      - indomethacin, ibuprofen, naproxen, diclofenac, sulindac, nabumetone, piroxicam
      - start at onset of symptoms and taper 24 hours after resolution
      - all are similarly effective
- renal elimination
- best inhibitor of uric acid reabsorption is diflunisal but it is $$$
- side effects: GIB or ulceration, GI perforation, edema, HTN, diarrhea, constipation, renal tox, indigestion, nausea, dizziness, headache, somnolence
  - most pronounced in those over 65 or with CrCl < 50 mL
  - nabumetone has least GI effects
  - least renal toxicity with sulindac, nabumetone
- caution with CHF or hepatic dysfunction
- contraindicated in peptic ulcer disease or with anticoagulation
- interactions:
  - bleeding with warfarin, LMWH, SSRIs, corticosteroids
  - toxicity with methotrexate
  - increased BP with diuretics, ACEI, beta-blockers
  - hypoglycemia with sulfonylureas
  - seizures with fluoroquinolones = hard to use safely in old folks

- colchicine: reduces lactic acid production in leukocytes, reduces phagocytosis
  - no analgesic or anti-uric acid effects
  - elimination is biliary and renal
    - renal dosing needed
  - most benefit if started within 36 hours
  - side effects: GI, alopecia, anorexia, bone marrow suppression, myopathy, death
  - contraindications: mod-severe renal or hepatic disease, severe cardiac disease
  - interactions:
    - increased colchicine toxicity with macrolides
    - increased nephrotox with verapamil
    - rhabdomyolysis with statins and gemfibrozil

- Colcrys is the only FDA-approved form

- corticosteroids: decrease migration of leukocytes
  - for those need intra-articular injection for monoarticular involvement:
    - must to prior aspirate & culture
    - triamcinolone hexacetonide
    - triamcinolone acetonide
    - methylprednisolone
  - oral used only when NSAIDs and colchicine are not effective
    - prednisone: metabolized to active prednisolone by the liver
  - IM: triamcinolone acetonide, methylprednisolone
  - side effects: hyperglycemia, insomnia, restlessness, increased appetite, peptic ulcer or bleeding, osteoporosis, glaucoma, edema, impaired wound healing, myopathy, risk of infection with live vaccines
  - interactions:
    - aspirin and anticoagulants
    - antifungals inhibit steroid metabolism increased levels
    - NSAIDs: increased risk of bleeding
    - bupropion: decreased seizure threshold

- chronic tophaceous gout:
  - prevent with lifestyle modifications: limitation of offending foods (organ meats, mushrooms, shellfish, red meats, pork, canned sardines, foods with high yeast content, asparagus, cauliflower, spinach, high fructose corn syrup), limiting alcohol consumption, increase fluid intake, weight loss
  - discontinue provoking meds if possible: diuretics, aspirin, niacin
  - consider pharmacologic prophylaxis if > 2 attacks/year, erosions seen on x-ray, uric acid nephropathy or nephrolithiasis, or with chronic polyarticular gout
    - course lasts from 3-12 months, with d/c once patient has reached a uric acid goal (< 6 mg/dL)
should not be initiated during an acute attack, but 4-6 weeks after attack
get 24 hour urine sample to measure uric acid production before determining meds
possible meds:

- allopurinol: inhibits xanthine oxidase
  - metabolized to active alloxanthine in the liver, with a half life of 15-30 hours
  - requires renal dosing
  - side effects: skin rash (can be fatal if Stevens-Johnsons), acute gout, nausea, diarrhea, increased LFTs, renal failure, myelosuppression
  - interactions:
    - rash with ampicillin, amoxicillin, ACEI
    - bleeding with warfarin
    - toxicity with theophylline
- febuxostat: inhibits xanthine oxidase more selectively than allopurinol
  - eliminated hepatically and renally with no dose adjustments needed
  - interactions: azathioprine, didanosine, mercaptopurine, theophylline, ntacids
    - side effects: increased LFTs, acute gout, arthralgia, nausea, diarrhea, rash, CV  monitor LFTs, serum uric acid levels for effectiveness
- probenecid: inhibits tubular reabsorption of urate at the proximal convoluted tubule  increased excretion
  - for patients with recurrent gout attacks on allopurinol alone
  - always use + allopurinol
  - contraindications: kidney stones, CrCl < 50 mL
  - side effects: headache, nausea, vomiting, hypersensitivity, sore gums, myelosuppression, exacerbation of gout
  - interactions:
    - toxicity with methotrexate
    - increased levels with carbapenems, PCN, cephalosporins, NSAIDs
    - decreased effect when used with salicylates
  - colchicine can be used for 3-6 months while titrating urate-lowering therapy to avoid triggering a flare
  - fenofibrate and losartan have mild uricosuric effects
  - pegloticase: genetically engineered uricase, an enzyme that breaks down uric acid that humans don’t normally have
    - clears tophi
    - indicated for chronic, severe gout refractory to all other treatment
    - highly immunoreactive, must premedicate patient with antihistamine and corticosteroids
      - infusion reactions are as high as 40%: bruising, hives, erythema, itching
      - 7% incidence of anaphylaxis
    - other side effects: exacerbation of CHF
- biologic response modifiers:
  - Arcalyst: IL-1 blocker now being used in clinical trials for gout
  - canakinumab: another IL-1 blocker

19.8.2 Calcium Pyrophosphate Deposition Disease (CPPD)
- acute or recurrent arthritis of large joints due to the accumulation of crystals of calcium pyrophosphate dihydrate in the connective tissues
- Background:
  - instigating factor can be idiopathic or associated with a primary disorder such as hyperparathyroidism, hypothyroidism, hemochromatosis, or hypophosphatemia
  - associated with chondrocalcinosis
  - more common in women
• familial association
• risk factors: trauma, MI, CVA, infection, surgical procedure (especially knee arthroscopy), intra-articular hyaluronate injections?

• Presentation:
  • may be asymptomatic
  • symptomatic presentation varies:
    o sudden onset
    o mimics RA, OA, or gout of the MCPs, hips, shoulders, ankles, elbows
    ▪ or can worse pre-existing OA
    o can have post-traumatic hemarthrosis
    o systemic disease: fever, chills
    o axial disease, especially of the cervical spine

• Investigation:
  • labs: serum Ca, Mg, phosphorus, alkaline phosphatase, ferritin, iron, TIBC
  • joint aspiration and examination for calcium pyrophosphate crystals
  • imaging:
    o x-ray: chondrocalcinosis, associated osteoarthritis
      ▪ knee: chondrocalcinosis of the medial and lateral menisci (visualized as a faint white line)
      ▪ atypical OA of the hand: chondrocalcinosis of the triangular fibrocartilage, MCP OA (joint space loss, sclerosis, osteophytosis)
    o CT, MRI, and US can also detect CPPD

• Treatment:
  • treat underlying disorder
  • if idiopathic:
    o NSAIDS, celecoxib
    o corticosteroids: systemic or intra-articular
    o low dose colchicine
    o hydroxychloroquine
    o arthrocentesis

19.8.3 BCP Crystal Arthropathies

• Basic calcium phosphate: forms crystals associated with severe osteoarthritis and acute periarticular inflammation

• Presentation:
  • can affect the knee and hip but has a tropism for the shoulder  □ Milwaukee shoulder: inflammation leads to severe pain, decreased ROM, large effusion, and rapid destruction of the glenohumeral joint
    o typically in elderly women
    o aspiration of affected joint results in a bloody fluid
  • calcific tendonitis from deposits in rotator cuff
    o occurs in 40-50 year olds, especially diabetics
  • bursitis

• Investigation:
• Treatment: NSAIDs or short course prednisone, physical therapy
  • calcific tendonitis may resolve on its own

19.9 Sarcoidosis and Other Systemic Diseases with Rheumatic Manifestations

19.9.1 Background

• Sarcoidosis: a disease in which abnormal collections of chronic inflammatory cells (granulomas) form nodules in multiple organs
• Helper T-cells are triggered by local antigen-presenting cells
• Cause is unknown
may have predisposition based on ethnicity, hormones, age, immune complex formation, or environmental factors
  o involves some form of antigen
  o studies investigating connection with TB, pine pollen, tobacco, and hypersensitivity pneumonitis were inconclusive
  o more common in females, young adults, and those in their twenties and thirties
    ▪ but can have a chronic presentation in older population
  o higher incidence in black patients
  o cases are often geographically clustered

19.9.2 Sarcoidosis Presentation

- Most commonly involves lung symptoms similar to asthma: dyspnea, cough, chest pain
- Acute, chronic, or asymptomatic
  - acute (AKA Lofgren syndrome): erythema nodosum (red, hot, shiny, tender areas) or other skin lesions, fever, fatigue, polyarthritis in the ankles
  - chronic: insidious onset, plaque-like skin lesions, keloids, or lupus pernio (aka butterfly lesions = purple plaques with predilection for the nose, cheeks, and ears), pulmonary infiltrates, nephrocalcinosis, arthritis of the knees, ankles, wrists, or elbows, synovitis, bone resorption
    - May mimic RA
- Skin lesions are seen in 25% of all sarcoid patients:
  - lesions often overlie sites of musculoskeletal involvement
  - maculopapular lesions on the face, posterior hairline, and at previous sites of trauma
  - nodular lesions on the trunk and extremities
  - uncommon: ulcers, psoriatic lesions, follicular lesions
- Ocular signs are seen in 20% of sarcoid patients: uveitis with keratitic precipitates, retinal vasculitis with "candle wax drippings", keratoconjunctivitis (sicca if longstanding), extraorbital muscle and tissue lesions such as lacrimal granuloma, secondary glaucoma, cataracts, blindness
- Musculoskeletal symptoms occur in 10% of sarcoid patients:
  - gum hyperplasia and tooth loss from involvement of maxilla and mandible
  - swelling, tenderness, stiffness, arthritis
  - most often on the small bones of the hands and feet, rarely on the face
  - myopathies and myositis occur but are not common
  - phalangeal bone lesions occur in 3% of chronic sarcoid patients
    - permeative bone lesion: cortical tunneling of bone
    - lytic bone lesion: large, round, punched-out cysts involving cortex and medulla
    - destructive bone lesion: multiple fractures with demineralization of the cortex and sequestrum formation
- Neurologic symptoms occur in 5% of sarcoid patients:
  - commonly involves the hypothalamus, third ventricle, or pituitary gland
  - cranial nerve palsies
  - acute or chronic meningitis or encephalitis
  - granulomatous brain lesions □ seizures, encephalopathy, focal deficits
    - masses resemble meningiomas or lesions of MS
  - spinal lesions
  - neuroendocrine dysfunction: diabetes insipidus, insomnia, pituitary dysfunction
  - Cardiac: arrhythmias, conduction delays (from lesions causing heart block), pulmonary HTN, CHF, pericarditis, arrhythmias
  - cardiac manifestations indicate systemic sarcoid
- GI involvement in 10% of sarcoid patients:
  - stomach damage, crampy epigastric and periumbilical pain, diarrhea without blood or mucus
    - how you rule out UC, because it always causes a bloody diarrhea
  - esophageal involvement □ dysphagia, oral regurgitation, weight loss
- Liver involvement in 90% of cases:
  - jaundice, varices, pruritus, epithelioid granulomas, hepatomegaly, granulomatous hepatitis
Pancreas:
- abdominal pain with nausea and vomiting, anorexia, weight loss
- biliary obstruction, duodenal obstruction, liver nodules, pancreatic insufficiency
- Endocrine: hypercalcemia, hypercalciuria, goiter, thyroid nodules
- Renal: calculi, interstitial nephritis, renal failure

GU:
- men: epididymitis, testicle, prostate, erythematous induration of the penis, nodules and ulcerations
- female: uterus, abnormal uterine bleeding, necrotizing epithelioid granulomas of the myometrium

19.9.3 Sarcoid Workup
- Differential diagnoses: leukemia, multiple myeloma, amyloidosis, SCD, diabetes, thyroid disease, parathyroid disease, Crohn’s, UC, hemochromatosis; sarcoidosis is a diagnosis of exclusion!
- Ophthalmoscopic exam
- PFTs
- Serum chemistries
- Serum ACE: often elevated but not specific to sarcoidosis
- UA
- EKG
- Granuloma biopsy shows non-caseating histology: epithelioid cell, macrophage, and giant cell core surrounded by fibroblasts, lymphocytes, and connective tissue
- Can consider doing bronchoscopy or mediastinoscopy with lavage if biopsy is not feasible
- CXR to stage (BUT not all patients will have abnormal CXRs!)
- also takes into account PFT findings
  - 0 = clear CXR but PFTs may be abnormal
  - I = bilateral hilar lymphadenopathy (enlargement of mediastinal lymph nodes), PFTs may be abnormal (impaired DLCO)
  - II = bilateral hilar lymphadenopathy, parenchymal infiltration, miliary shadowing, cotton-wool patches, multiple “cannon balls”
  - III = diffuse pulmonary infiltration with fine or coarse reticulonodular interstitial pattern, bilateral involvement of entire lung except for apices and extreme bases
  - IV = irreversible fibrosis with hilar retraction, bronchiectasis, formation of bullae (looks like emphysema with severe airway obstruction), peaked/tented diaphragm, alveolitis sarcoid (interstitial lymphocytic infiltration), cysts, rarely cavitation or hemorrhage
- CT for detection of further abnormalities and final diagnosis
- PET scan

19.9.4 Sarcoidosis Treatment and Prognosis
- Treatment is aimed at site of disease activity
  - goals: decrease number of granulomas, decrease inflammation, prevent fibrosis
  - pulmonary symptoms: steroids, lung transplant in later stage of disease
  - arthropathy: steroids, NSAIDs, colchicine, hydroxychloroquine, anti-TNF inhibitor (pentoxifylline, tetracyclines, infliximab, etanercept, pentoxifylline, adalimumab, thalidomide)
  - other steroid sparing agents: methotrexate, cyclosporine, mycophenolate mofetil, azathioprine, cyclophosphamide
- Prognosis: acute presentation has a high chance of spontaneous resolution

19.9.5 Other Diseases with Rheumatologic Manifestations
- Malignancies:
  - leukemia: can cause bone pain, synovitis, asymmetric oligoarthritis of the large joints
  - lung cancer: can cause secondary hypertrophic osteoarthritis: arthritis, periositis, clubbing of digits and toes
  - breast, colon, lung, and lymphoproliferative malignancies can cause carcinogenic polyarthritis
- **Cryoglobulinemia**: presence of abnormal proteins in the blood that become insoluble at cold temperatures
- causes polyarthritis, fatigue, neuropathy, renal/pulmonary syndromes, Raynaud’s, positive RF
- occurs with viral syndromes such as hep C, lymphoproliferative disorders, and connective tissue disorders
- **Amyloidosis**: a group of disorders characterized by deposition of misfolded proteins in tissues and organs
  - most commonly occurs in the form of primary amyloidosis
  - can also occur as secondary amyloidosis, familial amyloidosis, and β-2 microglobulin-associated amyloidosis
  - causes symmetric, small joint polyarthritis that resembles RA
  - suspect in patients > 40 years old with unexplained CHF, idiopathic peripheral neuropathies, and nephritic syndromes
- **Whipple’s disease**: a rare systemic disease caused by bacterial infection
  - causes arthritis, abdominal pain, steatorrhea, weight loss, fever, lymphadenopathy
  - Primary biliary cirrhosis:
  - associated with asymmetric small joint arthritis
- **Hemochromatosis**: iron overload
  - commonly causes arthritis of the MCP, wrist, knee, and ankle joints
- Diabetes mellitus is associated with Charcot arthropathy, adhesive capsulitis, carpal tunnel, diabetic stiff hand syndrome ("prayer sign")
- Hypothyroidism is associated with musculoskeletal abnormalities, swelling, stiffness, laxity, and effusions of the large joints
- Hyperthyroidism is associated with shoulder arthritis, myopathy, acropathy, and osteoporosis
- Hyperparathyroidism is associated with CPPD, RA-like symptoms, renal osteodystrophy, and proximal muscle weakness
- Adrenal disorders secondary to steroid use are associated with osteonecrosis, osteoporosis, and steroid myopathy
- Sickle cell is associated with knee arthritis (and also hands, elbows, lumbosacral spine) during acute crises, and also dactylitis, gout, osteomyelitis, and osteonecrosis
- Hemophilia is associated with hemarthrosis, chronic arthropathy with persistent synovitis

### 19.10 Systemic Lupus Erythematosus

#### 19.10.1 Background

- **Systemic lupus erythematosus**: a systemic autoimmune disease that can affect any part of the body, where the immune system attacks the body's cells and tissue, resulting in inflammation and tissue damage
  - a type III hypersensitivity reaction caused by antibody- immune complex deposition and activation of complement
    - a result of abnormalities in apoptotic cell clearance with generation of autoantibodies to nuclear antigens, phospholipids in the cell membrane, and other cell surface proteins
    - immune complexes can get stuck in glomeruli inflammation and damage
  - hereditary predisposition based on MHC II polymorphisms (HLA-DR2 or HLA-DR3) or complement deficiencies
  - presumed to be triggered by an exposure in a genetically susceptible individual
    - ex. infection, UV light, drugs, stress
  - periods of flare and latency
  - Peak incidence is in women ages 15-40, and it is more common in women
  - Non-caucasian patients have a greater incidence of lupus with higher mortality rate
  - results in detectable serum titers of autoantibodies against specific nuclear components, hematopoietic stem cells, and other tissues

#### 19.10.2 SLE Presentation
• Onset can be acute and fulminant or can be an insidious and chronic onset
• Common signs & symptoms:
  • fatigue
  • low-grade fevers
  • skin:
    o malar rash: sun-sensitive butterfly rash, always spares the nasolabial fold (vs rosacea which predominates in the nasolabial fold)
      ▪ can also be present around the mouth and on the forehead
    o discoid rash: scarring rash that may cover face and scalp
      ▪ a result of immune complex deposition in the dermoepidermal junction
    o diffuse papulosquamous lesions with erythematous scaling papules and plaques (psoriasis-like)
    o annular polycyclic lesions with an erythematous, scaling border and central clearing
      ▪ leads to alopecia over areas of scarring
      ▪ more common in black patients
    o skin photosensitivity: raised red rash lasting several days
  • oral or nasal ulcers that are painless
  • musculoskeletal features: arthritis or arthralgia, tenosynovitis, tendon rupture, osteonecrosis, myositis, myalgias
    • arthritis is inflammatory (warmth, swelling, pain, morning stiffness) but not erosive like RA
      ▪ frequently affects the hands and feet, rarely the shoulder or hip
  • vasculitis occurs in 20% of SLE patients
    • painful if on the extremities, stays fixed for a few weeks after onset
    • may correlate to lupus activity
    • can occur in the brain and cause a CVA
  • serositis: inflammation around the heart or lung pleuritic chest pain, friction rub, peritonitis, GI syndrome, diffuse abdominal pain, anorexia, nausea and vomiting
  • nephritis from glomerular inflammation: edema of lower extremities, hypertension, “foamy” urine due to high protein content
  • neuropsychiatric features (“CNS lupus”):
    • most commonly seizures or psychosis
    • also: transverse myelitis (an emergency!), depression, peripheral neuropathy, optic neuritis, and
    • many more!
  • hematologic manifestations:
    • hemolytic anemia from autoimmunity
    • normal neutrophils but low lymphocytes and low thrombocytes
  • pulmonary features: pneumonitis, pulmonary hemorrhage, pulmonary HTN, shrinking lung syndrome
  • cardiac: myocarditis, Libman-Sacks endocarditis, CAD
  • GI: mesenteric vasculitis, IBD, pancreatitis, liver disease, lupoid hepatitis
  • lymphadenopathy and reactive nodes

19.10.3 SLE Workup
• Findings accumulate over time
• diagnosis may take years to make
• American College of Rheumatology SLE classification criteria (must have 4/11): malar rash, discoid rash, photosensitivity, oral ulcers, arthritis, serositis, renal disorder, neurologic disorder, hematologic disorder, immunologic disorder, ANA +
• Labs:
  • CBC: mild anemia and mild leukopenia
  • creatinine
  • elevated inflammatory markers
  • lowered C3, C4
  • elevated ANA titer (low titer = negative)
o don’t need to check it ever again after the first time! levels are not correlated with disease progression or severity

***up to 20% of healthy women will have an elevated ANA at some point in their lifetime, and most will ever go on to develop autoimmune disease

- positive anti-dsDNA, anti-Sm, anti-RNP, antiphospholipid, anti-Ro, and/or anti-La
- others: antiplatelets, anti-RBCs
- but, + autoantibodies are not present in all SLE patients

- Imaging:
  - x-ray:
    - Jaccoud’s arthropathy: radiographic findings of ulnar deviation, MCP subluxation, swan-neck deformities, and diffuse soft-tissue swelling
      - different from RA because there is no true joint space narrowing or erosion, rather it is caused by tendon laxity vs bony destruction
    - fluid around lung
  - CT: may see UBOs (unidentified bright objects): punctate white matter lesions from CNS lupus
  - UA: proteinuria and RBC casts
  - lupus nephritis is classified based on these findings (does not go in order of increasing severity):
    1 = minimal mesangial lupus glomerulonephritis: normal glomeruli but with immune deposits
    2 = mesangial proliferative lupus glomerulonephritis
    3 = focal lupus glomerulonephritis
    4 = diffuse lupus glomerulonephritis
    5 = membranous lupus glomerulonephritis: global immune deposits with protein spillage
    VI = advanced sclerotic lupus glomerulonephritis: at least 90% of glomeruli are sclerosed
    classes II, IV, and V are most likely to lead to glomerulonephritis
  - urine protein:creatinine ratio

19.11 SLE Treatment and Prognosis

- Treatment:
  - drugs:
    o aspirin
    o prednisone
    o hydroxychloroquine: immunomodulator that decreases flares, kidney & CNS symptoms, and death
      ▪ must be on it continuously
      ▪ “lupus life insurance”
      ▪ side effects: retinal toxicity, skin hyperpigmentation
    o azathioprine: a purine analog that inhibits nucleic acid synthesis
      ▪ patients with a TPMT gene mutation can’t metabolize the drug, so check for its presence before starting treatment
      ▪ side effects: infection, low blood counts, hepatotoxicity
      ▪ can be used during pregnancy
    o methotrexate
    o leflunomide
    o mycophenolate mofetil: inhibits purine synthesis
      ▪ side effects: GI, low blood counts, infection
      ▪ teratogenic!
    o cyclophosphamide: an alkylating agent that cross-links DNA and proteins
      ▪ side effects: low blood counts, infection (need prophylaxis to prevent PCP), ovarian or testicular failure, hemorrhagic cystitis and associated bladder cancer (less risk with monthly IV dose), lymphoma = don’t use this unless we have to
    o new drug: belimumab, an IV biologic that modifies the activity of B-cells
      ▪ SLE with no activity: prednisone + hydroxychloroquine
      ▪ SLE with mild activity: prednisone + hydroxychloroquine + methotrexate + leflunomide + azathioprine
SLE with moderate activity: prednisone + hydroxychloroquine + methotrexate + leflunomide + azathioprine + mycophenolate mofetil + belimumab
SLE with severe activity: prednisone + hydroxychloroquine + mycophenolate mofetil + cyclophosphamide

- non-drug treatments: sunscreen all the time (and vit D supplements as a result), sun avoidance, behavioral therapy for fatigue
- cardiovascular risk modification
- Prognosis: death can occur from the disease itself, from therapy, or from related causes such as increased cardiovascular disease

19.12 Miscellaneous Rheumatic Diseases

19.12.1 The Vasculitides

- a group of conditions characterized by inflammation of vessel walls
- Background:
  - can affect arteries, veins, or capillaries
  - idiopathic, or can be triggered by an infection or a new drug
  - many are autoimmune-mediated
- Large vessels: disease involves the aorta and major named vessels branching off of it
  - giant cell arteritis (temporal arteritis):
    - seen mostly in white patients over age 50
    - more common in females
    - presentation: headache that is new or different from before, scalp tenderness, tenderness over temporal artery, jaw claudication, weight loss, fevers, malaise
    - investigation: very high ESR/CRP, anemia, low albumin
    - treat immediately with prednisone if you suspect it!
    - then have ENT or ophtho do a biopsy of the temporal artery
    - prognosis: sudden, irreversible blindness if left untreated
  - polymyalgia rheumatica:
    - seen mostly in white patients over age 50
    - more common in females
    - presentation: pain and stiffness of the pelvic and shoulder girdles, severe morning stiffness
      - but no weakness
    - investigation: elevated ESR/CRP
    - treatment: prednisone
      - response is diagnostic of giant cell arteritis and polymyalgia rheumatica often co-exist
- Medium vessels: disease involves named vessels
  - polyarteritis nodosa:
  - Beurger’s disease:
- Small vessels: disease involves unnamed vessels, palpable purpura
  - granulomatosis with polyangiitis (Wegener’s granulomatosis):
    - presentation: severe sinus disease, epiglottic changes, lung nodules or hemorrhage, acute glomerulonephritis, “Saddle nose” deformity
    - investigation:
      - labs: + C-ANCA, high ESR/CRP, anemia
      - biopsy
    - treatment: corticosteroids, cyclophosphamide or rituximab
- Churg-Strauss syndrome: associated with asthma and allergies
- Henoch-Schonlein purpura: seen in kids after an infection
- hypersensitivity vasculitis: usually secondary to a medication
- Suspect in any patient with multi-system disease not explained by infection or malignancy, especially those with renal dysfunction, skin lesions, neurologic symptoms, and arthritis/arthralgias

19.12.2 Sjogren’s Syndrome
an inflammatory disorder of the exocrine glands

Different manifestations:
- **primary Sjogren’s**: when there is no other autoimmune disease
- **secondary Sjogren’s**: when there is another autoimmune disease such as RA or SLE

Presentation:
- sicca syndrome: dry eyes and mouth, can’t wear contacts, can’t eat crackers, etc.
  - measure tear production with Schirmer’s test (paper strip)
  - look at corneal damage with Rose-Bengal stain
- parotid gland enlargement
- fatigue, myalgias
- rarely, internal organ involvement
- Investigation:
  - salivary gland biopsy
  - labs: anti-Ro and anti-La

Treatment:
- artificial tears or punctal plugs for dry eyes
- fluids, Biotene mouthwash, cholinergic agonists for dry mouth
- for systemic symptoms: hydroxychloroquine, steroids, DMARDs if severe

Prognosis: more of an annoying disease than a dangerous disease, but also increases risk for later lymphoma

19.12.3 Anti-Phospholipid Syndrome

- antibody-mediated hypercoagulability
- Presentation: recurrent thrombosis, late pregnancy loss or 3 first-trimester miscarriages, early pre-eclampsia, livedo reticularis rash with ulceration
- Investigation:
  - labs:
    - anti-PL antibodies: anticardiolipin, anti-glycoprotein I, anti-lupus anticoagulant
    - false + syphilis test
- Treatment:
  - aspirin, heparin
- Prognosis: if untreated, women have a 90% chance of miscarrying any pregnancy, as well as increased risk of stroke and maternal thrombosis

19.12.4 Fibromyalgia: chronic pain syndrome of unknown etiology

- Background:
  - not autoimmune or inflammatory
  - may be due to loss of desensitization to chronic pain stimuli
  - more prevalent in women ages 20-50
  - can coexist with lupus
- Presentation: muscle tenderness to palpation, fatigue, disturbed sleep, stiffness
  - especially tender trigger points at the back of the head, upper and lower chest, upper back, low back, buttock, greater trochanter, medial knee, lateral epicondyle
- Investigation:
  - r/o rheumatic cause by lack of joint swelling or inflammation
- Treatment:
  - effective treatment has yet to be found
  - can try exercise, yoga, or meditation
  - sleep ease: treat sleep apnea or restless leg, prescribe tricyclics along with Flexeril, trazodone, or Ambien to help fall asleep
  - antidepressants: SSRIs, Cymbalta

19.12.5 Mixed Connective Tissue Disease
• an overlap syndrome of lupus and scleroderma
• Presentation: severe Raynaud’s, swollen hands, arthritis, nail capillary changes, any symptoms of SLE and scleroderma
• Investigation: + anti-RNP
• Treatment is targeted at symptoms

19.12.6 Undifferentiated Connective Tissue Disease
• Aka “lupus light”
• A few features of autoimmune disease but not enough to fulfill a diagnosis
• Majority of these patients will not progress to lupus

19.13 Osteoarthritis

19.13.1 Background
• Osteoarthritis: refers to a group of mechanical abnormalities involving degradation of joints, involving progressive loss of articular cartilage with subchondral bone remodelling
  • primary causes are those that are inherent: joint instability
  • secondary causes are those as a result of any kind of articular trauma: fracture or bone trauma, repetitive or overuse injury, metabolic diseases (hyperparathyroidism, hemochromatosis, ochronosis, metabolic syndrome), neurologic disorders such as tabes dorsalis (related to neurosyphilis), local inflammation from synovitis
• Risk factors for development: obesity, occupation, trauma, sports-related injuries, advancing age, females & black patients at increased risk, FH
• Articular cartilage structure:
  • hyaline layer is 1-5 mm thick and covers the surface of all articular joints (not the TMJ)
    o no blood vessels, no lymph, or nerves, with low cellular density □ poor healing
    o functions: distribute weight load over wider surface area, decrease contact stress and friction on joint surfaces
    o made up of:
      ▪ chondrocytes: make the organic matrix (collagen fibrils in proteoglycan mesh)
      ▪ lots of water to allow for diffusion of gases, nutrients, and waste between the chondrocytes and the synovial fluid
  • tangential layer is made of small collagen fibers woven in a parallel direction, accounts for 10-20% of thickness
  • middle transitional layer is made of randomly oriented but homogenously dispersed collagen fibers, accounts for 40-60% of thickness
  • deep zone is made of large, radially oriented collagen fibers that cross the tide mark (line between calcified and uncalcified cartilage)
• OA pathophysiology:
  • loosening of collagen network □ abnormal proteoglycan expansion and tissue swelling □ decreased cartilage stiffness and increased permeability □ altered cartilage function during joint motion □ fibrillation of the superficial articular cartilage □ deepening of fibrillations into the subchondral bone □ fragmentation of cartilage into the joint space □ matrix degradation □ complete cartilage loss
    o collagen fibers give tensile strength but offer little resistance to compression
    o proteoglycans are what resist compression forces
      ▪ composition changes with aging: loss of protein and chondroitin sulfate
    o wearing down of the cartilage occurs with:
      ▪ interfacial wear: when articular surfaces contact without sufficient lubricant
        • due to adhesions or abrasions
      ▪ fatigue wear: when repetitive stresses cause accumulation of microtraumas
    o there is limited capacity for regeneration or repair due to lack of blood flow in this area
    o once the load-carrying capacity of tissue is damaged it is mostly irreversible
• progression of cartilage failure is proportional to magnitude of imposed stress, total number of sustained stress peaks, changes in matrix structure, and changes in cartilage mechanical properties

19.13.2 Presentation

• Half of all OAs are asymptomatic
• Most characteristic is mechanical pain of the DIP joints (Heberden nodes), PIP joints (Bouchard nodes), CMC joint of the thumb, hip, knee, 1st MTP, cervical spine, or lumbar spine
• worsened with activity and weight-bearing and better with rest
• Stiffness after prolonged inactivity for < 30 minutes
• PE: crepitus with movement, joint deformity, joint laxity, joint-line tenderness, joint effusion or soft tissue swelling

19.13.3 Investigation

• Diagnosis is made by history, PE, and characteristic radiographic features
• ACR provides clinical classifications for OA that are joint specific
• Radiographic findings:
  • joint space narrowing from loss of cartilage, subchondral sclerosis from bone rubbing on bone, osteophytosis from bony overgrowth, and subchondral cysts
    • hand: 1st CMC joint, DIP joints, PIP joints
    • commonly seen women with symmetric involvement
    • knee: most commonly affects the medial compartment
    • hip: joint space loss that is more superior on the femoral head, brightness = sclerosis, osteophytosis
    • lumbar spine: loss of disc space, osteophytosis, sclerosis
    • ankle & foot: loss of joint space, sclerosis, osteophytosis
    • shoulder: joint space loss, sclerosis, osteophytosis, evidence of a geode (subchondral cyst)
• MRI may show some interesting morphological changes such as bone marrow lesions or muscle degeneration but is not routinely done for diagnosis

19.13.4 Osteoarthritis Treatment

• Non-inflammatory
• Goals are to reduce pain and swelling, maintain or improve mobility, and increase quality of life
• Nonpharmacologic therapies:
  • lifestyle modifications: evaluate occupation stress of patient’s job on their joints, encourage regular exercise like aerobics, strength training (promotes nutrient exchange to articular cartilage), ROM exercises, weight loss
    • exercise decreases pain, decreases disability, and preserves cartilage = write it on a prescription pad to make patients compliant!
- recommended exercises: walking, cycling, swimming, low-impact aerobics, yoga, tai chi, pilates, weight training, resistance bands, elliptical
  - not recommended: running, stair climber, rower, jumping
  - stop activity if it causes significant joint pain or delayed pain lasting more than 2 hours
- joint protection via cushioned shoes, orthotics, walking cane, wedge insoles to correct valgus/varum, unloader braces (data is ??), patellar taping, ergonomics
- alternative therapies: vit C/D/Ca supplementation, acupuncture
- Drugs:
  - acetaminophen: inhibits synthesis of prostaglandins in the CNS and peripheral pain impulse generation
    - first line for OA!
    - side effects: hepatotoxicity, renal toxicity, rash, GIB, myelosuppression
    - overdose effects: abdominal pain, nausea, vomiting, liver injury, encephalopathy, coma
    - interactions:
      - bleeding with warfarin
      - increased live: toxicity with alcohol use, phenytoin, and carbamazepine
  - topical capsaicin: depletes substance P
    - can be used alone or in combination with other treatments
    - side effects: burning, stinging, erythema, cough if inhaled
    - interactions: increased cough with ACEI
  - topical methylsalicylate:
    - interactions: increased bleeding with GIB
  - topical diclofenac:
    - side effects: skin irritation
    - interactions: NSAIDs
    - gel form is Voltaren
    - solution form is Pennsaid
  - NSAIDS: add to treatment if pain is not relieve with acetaminophen
    - use lowest dose for shortest duration possible
    - contraindications: 3rd trimester pregnancy, CABG
  - COX-2 inhibitors: celecoxib
    - GI protective unless pt is taking aspirin or warfarin
    - contraindicated: sulfonamide allergy
  - tramadol: binds mu opioid receptors in the CNS to inhibit pain transmission and to inhibit serotonin and norepinephrine reuptake
    - active metabolite (M1) is 6x more potent
    - half-life is increased in the elderly and with renally and hepatically impaired patients
    - side effects: flushing, dizziness, headache, insomnia, somnolence, itching, constipation, nausea, vomiting, GI upset, weakness, orthostatic hypotension, seizures, hallucinations
    - contraindications: concurrent selegiline or rasagiline use
    - interactions:
      - seizures with carbamazepine
      - seizures or serotonin syndrome with SSRIs, antidepressants, antipsychotics
      - increases effects of CNS depressants
  - opioids: bind to mu and kappa receptors in the CNS, spinal cord, and muscle to decrease pain transmission to the CNS
    - hydrocodone, codeine, oxycodone, hydromorphone, fentanyl, morphine
    - for those in severe pain or those unable to tolerate NSAIDs or tramadol
    - side effects: itching, rash, constipation (must always give a stimulant-based laxative with!), nausea, vomiting, urinary retention, respiratory depression
    - interactions:
      - increase activity of CNS depressants
      - urinary retention and ileus with anticholinergics
    - neuroleptics such as gabapentin
    - intra-articular injections:
      - for those with OA of the knee who have not responded to analgesic treatments and nonpharmacologic therapies
- **Hyaluronic Acid**: reacts with water to form a joint lubricant
  - several injections with results that last up to 6 months
  - side effects: respiratory infection
  - interactions: injection site bleeding with anticoagulants and antiplatelets

- **Glucocorticoids**:
  - triamcinolone hexacetonide, triamcinolone acetonide, methylprednisolone
  - last 4-8 weeks
  - max 4 injections per year

- **Natural Products**:
  - jury is still out on their effectiveness, so these should be tried for 6 months and then discontinued if no improvement
  - **Glucosamine**: naturally produced in humans to maintain elasticity and strength of cartilage in joints
    - contraindicated in shellfish allergies
    - side effects: edema, arrhythmia, GI upset, headache, sleep disturbance
    - interactions: increased bleeding with warfarin
  - **Chondroitin**: a natural component of cartilage that absorbs water and thickens the cartilage while inhibiting enzymes involved in cartilage destruction
    - limited oral absorption
    - interactions: increased bleeding with antiplatelets and anticoagulants

- **Methyl Sulfonyl Methane (MSM)**: an anti-inflammatory agent that inhibits pain along C-type nerve fibers
  - side effects: bloating, constipation, decline in concentration, fatigue, headache, indigestion, insomnia

- **Surgical Interventions**:
  - **Wedge Osteotomy**: take out a wedge of femur to correct genu valgus or varum
    - only helpful in patients with OA on one side of the knee
  - **Abrasion Chondroplasty**: arthroscopic debridement of abrasions, loose bodies, and torn meniscus
    - found to be no better than placebo unless patient is having symptoms of catching or locking
  - **Free-Floating Interpositional Devices**: for one-sided OA only
  - **Microfracture**: area of defect has holes drilled in it in an attempt to stimulate production of new cartilage
    - produces fibrocartilage vs articular cartilage, not as durable
  - **Carticel Procedure**: cartilage is harvested from an area of intact cartilage, grown in culture, and injected into the damaged site
    - no data for effectiveness yet
  - **OATS Procedure**: transfer of cartilage from a healthy part of the knee to a damaged part of the knee
  - **Total or Partial Arthroplasty**: for the hip, knee, ankle/foot, DIP, PIP, shoulder, elbow, lumbar spinal discs, and cervical spinal discs
    - indicated for patients ages 40-90
    - proven to relieve pain, decrease disability, and improve function
    - not first-line option because it is costly, long-term effectiveness is unknown (10-15 year estimate), and it is very invasive
20 Surgery Exam I Notes

20.1 Intro to the OR

20.1.1 Scrubbing

- First the fingernails, then the four surfaces of each finger, the palmar and dorsal hands and wrists, then the forearms
- Techniques:
  - **anatomic timed scrub**: 5 minutes total scrub time
    - 30 sec fingertips
    - 30 sec fingers
    - 1 min hand
    - 30 sec wrist
  - **counted stroke method**: specific number of bristle strokes for the fingers, hands, and arms
    - nails: 10 strokes, rinse, 20 strokes
    - each side of finger and webs spaces: 30 strokes each
    - palm and dorsum of hand: 20 strokes each
    - wrist to above elbow: 20 strokes each surface
- Hat, mask, and shoe covers, then wash hands, dry with sterile towel from hand to elbow, gown, then glove
  - grasp gown by neckline and drop from shoulder level
  - push both arms through at the same time and put gloves on using the sleeves (closed gloving)
  - your gown is only considered sterile from waist to shoulders and at the lower portion of sleeves because you can easily brush up on non-sterile areas with the other parts

20.1.2 Prepping the Patient

- Done after anesthesia and positioning on the OR table
- Procedure:
  - solution is chosen based on spectrum of activity, non-toxicity, patient allergies, location of surgical site, and skin condition
    - betadine scrub: removes dirt and oil, caution with allergies to seafood or iodine
    - alcohol: denatures microbial proteins
      - works well against TB, fungi, and viruses
      - removes soap
    - betadine solution: left on, caution in patients allergic to seafood and iodine
    - iodine 2%: oxidizer
      - must be rinsed with alcohol, contraindicated in iodine allergies
      - works well against TB, fungi, and viruses
    - chlorhexidine (Hibiclens): disrupts cell walls
      - poor action against TB
      - prevents staining, substituted for iodine allergic patients
      - can't be used on eyes or ears
    - benzalkonium chloride: nonstaining, usually for the face
    - hexachlorophene: disrupts cell walls
      - poor activity against Gram negs, TB, fungi, and viruses
      - caution: neurotoxicity
    - chloroxylenol: disrupts cell walls
      - intermediate action against TB, fungi, and viruses
      - prolonged skin contact increases risk of toxicity
    - triclosan: cell wall disruptor
      - poor activity against fungi
  - place drip pads (nonsterile) around prep site to catch solution
  - start at intended incision site and work out
• remove pads and allow site to air dry
• site is considered disinfected but not sterile

Specific preps:
• abdominal surgery: prep from nipple to 3 inches below pubic symphysis, and from bedline to bedline

20.1.3 Draping the Patient

• Creates a sterile field over the prepped area to prevent microbes from landing on the prepped area
• Drapes should be resistant to blood and fluid, lint free, tightly woven to reduce passage of airborne bacteria yet porous enough to prevent heat buildup, and should conform easily to contours
  • can be fabric or disposable
  • can have adhesive backing
• Make a cuff when laying the drape to protect the sterile field
• Don’t move drapes once placed

20.1.4 Misc.

• Emergency levels
  • Level I emergency = to the OR in < 1 hour
  • Level II = to OR within 4 hours
  • Level III = to OR within 12 hours
  • Level IV = to OR within 24 hours
  • Level V = not elective
• Surgical consents are good for 90 days
• H&P must be done within 7 days from date of surgery
• Surgical counts of equipment/supplies are done by the scrub assistant and circulating nurse many times during an operation

20.1.5 Incision Sites

• Upper abdominal midline: stomach, duodenum, pancreas
• Lower abdominal midline
• Left lower transverse
• Right lower paramedian
• McBurney: appendix
• Right horizontal flank or right flank
• Right upper oblique, right subcostal: gallbladder, biliary system
• Left upper paramedian
• Left lower oblique or left inguinal: hernia repair
• Pfannesteil, modified lower midline abdominal transverse, or bikini: uterus, ovaries, fallopian tubes

20.1.6 Surgical Instruments

• Critical items: must be sterile because they will be entering the bloodstream or a sterile body cavity
• Semicritical items: sterilization or high level disinfectant preferred, because items will come in contact with intact mucous membranes
  • ex. scopes, urology equipment, GI equipment, anesthesia fiberoptics and equipment
• Noncritical items: only need to be cleaned or decontaminated because they will touch only intact skin
  • ex. pads, pillows
• Decontamination: when contaminants are removed manually or mechanically with the help of solutions
  • begins in the OR with the scrub assistant
  • ends in handwashing by processing department
    o ultrasonic washing removes hidden blood or debris
      • works well for items having a lumen
    o washer-sterilizer mechanically agitates items in a bath with detergent, followed by several sterilization cycles
    o washer-disinfector uses higher pH detergent and less agitation
- better for delicate items
- Autoclave shortens the life of instruments
  - indicator organism is Bacillus stearothermophilus
- Gaseous processing is expensive and takes a long time
  - indicator organism is Bacillus subtilis
- Scopes are cleaned in peracetic acid
- Hydrogen peroxide can be used for moisture-sensitive items but is expensive
- Ionizing radiation via cobalt-60 is utilized by manufacturers for disposable items

20.1.7 Surgical Specimens
- Photograph specimens for evidence
- Don’t send with a counted sponge or the scrub nurse will kill you
- Solutions: 10% formalin, glutaraldehyde, fixative, or ringer’s
  - but always send a bullet or calculi dry

<table>
<thead>
<tr>
<th>Cutting Instrument</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>#3 handle</td>
<td>Short or long lengths for cutting heavy, deep, tough tissue. Short handle is the “skin knife.”</td>
</tr>
<tr>
<td>#10 blade</td>
<td>General purpose blade for larger skin incisions. Cutting surface is halfway between the tip of the blade and its attachment on the scalpel handle. Blade should be parallel to skin when cutting, and should NOT be held like a pencil.</td>
</tr>
<tr>
<td>#7 handle</td>
<td>Slender for delicate cutting.</td>
</tr>
<tr>
<td>15 blade</td>
<td>Small blade for delicate cutting where cutting surface is close to the tip. Should be held like a pencil when attached to a handle.</td>
</tr>
<tr>
<td>#11 blade “Stab blade”</td>
<td>A pointed, straight blade used for puncturing tissues, cysts, or abscesses.</td>
</tr>
<tr>
<td>#12 blade “Hook blade”</td>
<td>Often used to make the initial cut in the side of a vessel wall to avoid going all the way through the opposite wall.</td>
</tr>
<tr>
<td>Straight Mayo scissors</td>
<td>Have a heavy, blunt tip with a straight blade.</td>
</tr>
<tr>
<td>“Suture scissors”</td>
<td>Used for cutting surgical materials.</td>
</tr>
<tr>
<td>Curved Mayo scissors</td>
<td>Have a curved blade for cutting heavy, thick tissue.</td>
</tr>
<tr>
<td>Metzenbaum scissors</td>
<td>Finer, curved scissors used for cutting and dissecting delicate tissue. They are the all-purpose dissection scissors.</td>
</tr>
<tr>
<td>Chest scissors</td>
<td>Long scissors used for deep cutting and dissection.</td>
</tr>
<tr>
<td>Wire cutters</td>
<td>Blunt, angled scissors used to cut wire and other surgical material.</td>
</tr>
<tr>
<td>Hemostats</td>
<td>Close severed ends of bleeding vessels with minimal tissue damage.</td>
</tr>
<tr>
<td>Crile hemostat “Mosquito”</td>
<td>Fine, short, curved clamp for superficial vessels.</td>
</tr>
<tr>
<td>Kelly hemostat</td>
<td>Heavier curved clamp which varies in length. The all-purpose clamp.</td>
</tr>
<tr>
<td>Tonsil hemostat</td>
<td>Fine curved clamp with medium-sized length.</td>
</tr>
<tr>
<td></td>
<td>Most commonly used clamp for hemostasis.</td>
</tr>
<tr>
<td><strong>Mixter hemostat</strong></td>
<td>Clamp with a right angled tip and medium length.</td>
</tr>
<tr>
<td>----------------------</td>
<td>--------------------------------------------------</td>
</tr>
<tr>
<td><strong>“Right angle”</strong></td>
<td>Used to pass suture around an uncut vessel.</td>
</tr>
<tr>
<td><strong>Grasping Clamps</strong></td>
<td>Hold tissue for retraction. Varying length and thickness. +/- teeth.</td>
</tr>
<tr>
<td><strong>Allis clamp</strong></td>
<td>Has multiple short teeth that don’t damage tissue in its grasp. For use on delicate tissue.</td>
</tr>
<tr>
<td><strong>Babcock clamp</strong></td>
<td>Has curved, fenestrated blades without teeth to grip or enclose delicate structures such as intestines, ureters, and fallopian tubes.</td>
</tr>
<tr>
<td><strong>Kocher clamp</strong></td>
<td>Has a single, heavy-toothed tip for grasping tough tissue such as fascia, bone, and muscle.</td>
</tr>
<tr>
<td><strong>Sponge stick clamp</strong></td>
<td>Has ring-shaped jaws used to hold sponges and delicate tissue like the lung.</td>
</tr>
<tr>
<td><strong>Towel clips</strong></td>
<td>Has sharp, needle-like curved tips to secure drapes or hold tissue like bone.</td>
</tr>
<tr>
<td><strong>Forceps (Pickups)</strong></td>
<td>Used to grasp tissue. Available +/- teeth.</td>
</tr>
<tr>
<td><strong>Adson forceps</strong></td>
<td>Single-toothed fine short forceps use to hold skin.</td>
</tr>
<tr>
<td><strong>Bayonet forceps</strong></td>
<td>Heavier, longer forceps to hold thick tissue such as muscle and fascia.</td>
</tr>
<tr>
<td><strong>Debakey forceps</strong></td>
<td>Nontoothed forceps with variable length. The all-purpose forceps. Not to be used on skin.</td>
</tr>
<tr>
<td><strong>Ring forceps</strong></td>
<td>Has ring-shaped tips used to handle large but delicate structures that might be punctured using pointed forceps.</td>
</tr>
<tr>
<td><strong>Bayonet forceps “Cautery forceps”</strong></td>
<td>Angled forceps used commonly in neurosurgery for better visualization. Can also be used as an extension of the cautery on deep structures.</td>
</tr>
<tr>
<td><strong>Needle Holders</strong></td>
<td>Designed to grasp metal instead of tissue. Vary in size, style of tip, and design.</td>
</tr>
<tr>
<td><strong>Hand-Held Retractors</strong></td>
<td>Exposes operating site without traumatizing surrounding tissue. Blade is usually at a right angle to the shaft and blades may be smooth, raked, or hooked. Handles may be hooked, notched, or ring-shaped to give the holder a firm grip without tiring.</td>
</tr>
<tr>
<td><strong>Vein retractor</strong></td>
<td>Has a smooth, small blade which retracts tissue without puncturing.</td>
</tr>
<tr>
<td><strong>Skin rake retractor</strong></td>
<td>A toothed retractor used to grasp and pull back tissue such as skin.</td>
</tr>
<tr>
<td><strong>Army-Navy retractor</strong></td>
<td>A double-ended retractor.</td>
</tr>
<tr>
<td><strong>Appendiceal retractor</strong></td>
<td>Has a short, right-angled blade. Used on abdominal cases.</td>
</tr>
<tr>
<td><strong>Richardson retractor</strong></td>
<td>An abdominal retractor with varying blade size.</td>
</tr>
<tr>
<td><strong>Deaver retractor</strong></td>
<td>A curved abdominal retractor with varying blade width.</td>
</tr>
<tr>
<td><strong>Malleable retractor “Ribbon retractor”</strong></td>
<td>Is bendable and may be shaped by the surgeon at the operating site.</td>
</tr>
<tr>
<td><strong>Self-Retaining Retractors</strong></td>
<td>Exposes operating site without traumatizing surrounding tissue. Blades are applied to both edges of the wound and then spread. A locking mechanism holds the blades open.</td>
</tr>
<tr>
<td><strong>Weitlaner retractor “Self-retaining thyroid retractor”</strong></td>
<td>Ratchet-style, used for superficial areas.</td>
</tr>
</tbody>
</table>
Balfour retractor
Finochietto retractor
“Chest retractor”

An abdominal retractor to which a bladder blade may be added.

Suction

Used to remove blood and fluid at the operative site. Number and size of holes determine suction capacity.

Yankauer suction

The most commonly used suction.

“Chest or tonsil suction”

Baby chest suction

Similar to Yankauer, but with thinner shaft and smaller holes.

Frazier suction

“Abdominal suction”

Straight suction with multiple holes for rapid suctioning.

Poole suction “Neuro suction”

Right angled suction varying in shaft length and width.

Electrosurgical Devices

True electrosurgical apparatus

Patient must be grounded. Allows for cutting and coagulation. Cutting blade can’t be used for cutting through epidermis, but can be used for dermis, subcutaneous tissue fascia, and muscle.

20.1.8 Surgical Asepsis

- Surgery in the absence of infectious agents
- Increased risk of infection with:
  - malnutrition: altered inflammatory response
  - extremes of age
  - obesity: fat is mostly avascular
  - chronic disease
  - remote focus of infection
  - immunosuppression
  - stress
  - prolonged preoperative hospitalization
  - GI or GU operations
  - wounds of the abdomen, thighs, calves, or buttocks: increased fat tissue
  - presence of catheters and drains
  - indiscriminate use of antibiotics
  - breakdown of isolation techniques
  - Wounds and infection:
    - an uninfected wound will heal without discharge
    - an inflamed wound with no discharge may be infected
    - infected wounds always pus
    - Surgically-induced infection:
      - a clean procedure has an expected infection rate of 1-3% 
      - a clean-contaminated procedure has an expected infection rate of 8-11%
      - a contaminated procedure has an expected infection rate of 15-20%
      - Sources of contamination:
        - skin, especially the head, neck, axilla, hands, groin, legs, and feet
        - hair harbors staph
        - nasopharynx
        - fomites, especially the floor
        - air: keep doors closed, control traffic, and limit movement
20.2 Casting

20.2.1 Splints

- Can be as simple as a support wrapped in Ace bandage
- Other kinds:
  - thumb spica for thumb sprain, immobilization following laceration repair, ulnar or radial collateral ligament sprain, or scaphoid fracture
  - ulnar gutter splint is used for 4th or 5th metacarpal fracture
  - radial gutter splints are used for 2nd or 3rd metacarpal fracture
  - upper extremity posterior splints are used for biceps tendonitis, radial head fractures, stable distal humeral fractures, and following aspiration of the olecranon bursa
  - lower extremity posterior splints are used for stable ankle fractures
  - Best for immobilization while fracture is fresh because they allow for swelling
  - Used for 10-20 days before cast is applied
  - Can also be used for sprain or strain to immobilize joint

20.2.2 Types of Casts

- Plaster casts
  - cheaper
  - require 24 hours to cure
  - can be removed by soaking
  - best for fresh fractures
- Synthetic casts
  - more expensive
  - stronger
  - lighter
  - water resistant
  - durable
  - short curing period
  - need to saw off
  - best for open fractures
- Cast-braces: hold fracture bone immobile while allowing for joint motion above and below fracture site
  - very expensive
  - minimal muscle atrophy
  - lightweight
  - more rapid rehab
  - accelerated healing of fracture
  - short hospital stay
  - hard to apply

20.2.3 Technique for Cast Application

- Stockinette over the skin
- 3 in width for arms, 4 in for legs
- Cotton roll over stockinette to make 2-3 layers
- Plaster to make 4-6 layers
- Check when done to make sure there are adequate pulses, sensation, and cap refill

20.2.4 Cast Side Effects

- Disuse osteoporosis: reversible
- Joint stiffness
- Foreign body within cast causing ulceration
- Cast dermatitis due to poor ventilation or allergy to casting materials
- Sloughing of skin from loose cast
20.3 Sutures & Knots

20.3.1 Types of Suture Material

- Absorbable sutures: absorbed by body via an inflammatory reaction within 3-6 weeks
  - **plain gut**: made from hog intestine, unmodified will lose tensile strength in 1-2 weeks
    - complete reabsorption in 70 days
    - very reactive
  - **chromic gut**: made from hog intestine soaked in chromic acid salts strength retained for 2-3 weeks
    - complete reabsorption in 90 days
    - most reactive
    - **Dexon**: synthetic suture made from polyglycolic acid strength retained for 3 weeks
    - complete reabsorption in 80 days
  - **Vicryl**: synthetic suture made from polyglactin 910
    - complete reabsorption in 120 days
  - use when continued strength of the suture is not important, or where infection would make it desirable to have a suture that can be absorbed
  - generally for suturing subcutaneous tissue and mucosal layer of the intestine
- Nonabsorbable sutures
  - **silk and cotton**
    - silk is most widely used and is most inflammatory
  - braided synthetics: Dacron, Dacron + Teflon, Dacron + silicone, Dacron + polybutylate, nylon braid
    - less reactive than silk
    - less memory than monofilaments
    - Teflon acts as lubricant and makes it harder to tie but is thought to prevent bacterial infection
  - monofilament synthetics: polypropylene, nylon, polybutester
    - more difficult to handle, require more knots to keep in place
    - do not tend to shelter bacteria like other sutures
    - less resistance when passing through tissue than a braided
    - hold strength well over time
    - polybutester is uniquely stretchy
    - nylon and polypropylene are often preferred for suturing the skin (less reactive)
  - **wire**: made of stainless steel
    - available as monofilament or braided
    - may create holes for infection
    - hard to tie
    - good for suturing bone
    - the least reactive suture
  - use when tissue reaction needs to be minimal or where continued strength beyond 2-3 weeks is desirable generally for suturing skin and fascia

20.3.2 Suture Sizing

- Sizes 2-5 are for bone and tendon work
- Size 1 for fascial repair
- Sizes 4-0 through 0 are standard, with size 3-0 being most typical
  - fascia, skin
  - chromic catgut 0
  - small vessels
  - chromic catgut 3-0
  - gastrointestinal anastomosis
  - chromic catgut 3-0 or 4-0
- Sizes 5-0 through 7-0 are for delicate vascular anastomoses
- Sizes 8-0 through 10-0 are for microvascular work and eye surgery

20.3.3 Choice of Needle

- Eyed needles require making a hole larger than the suture
- Swaged needles only make a hole as large as the suture = required for suturing of the bowel, blood vessels, etc.
- Straight needles are manipulated by hand while curved needles use a needle driver
- curved needles easy for working in deep holes
- Point and cross sectional shape of the needle determine
  - soft tissue and fascia : round tapered needle
  - skin, periosteum, or perichondrium are tougher : cutting needle
    - even better : reverse cutting needle (hole created points away from pull of suture)
  - graft attachment : sharp ground point wire needle

### 20.3.4 Common Suture + Needle Choices

<table>
<thead>
<tr>
<th>Location</th>
<th>Suture Material</th>
<th>Possible Alternative</th>
<th>Needle Point</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin</td>
<td>Synthetic non-absorbable Absorbable monofilament</td>
<td>Coated braided synthetics</td>
<td>Conventional Cutting</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Premium Cutting</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Reverse Cutting</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>X-Cutting</td>
</tr>
<tr>
<td>Subcutaneous</td>
<td>Synthetic absorbable</td>
<td>Natural absorbable</td>
<td>Taper Point</td>
</tr>
<tr>
<td>Fascia</td>
<td>Synthetic absorbable Synthetic non-absorbable</td>
<td>Coated braided synthetic non-absorbable</td>
<td>Taper Point</td>
</tr>
<tr>
<td>GI-Mucosa</td>
<td>Coated synthetic absorbable</td>
<td></td>
<td>Taper Point</td>
</tr>
<tr>
<td>GI- Serosa</td>
<td>Synthetic absorbable</td>
<td></td>
<td>Taper Point</td>
</tr>
<tr>
<td>GYN- Uterus</td>
<td>Synthetic absorbable</td>
<td></td>
<td>Taper Point</td>
</tr>
<tr>
<td>GYN- Uterine tube</td>
<td>Coated synthetic absorbable</td>
<td></td>
<td>Taper Point</td>
</tr>
<tr>
<td>Vascular- grafts</td>
<td>Polypropylene PTFE</td>
<td>Braided polyester (valves only)</td>
<td>Taper Point</td>
</tr>
<tr>
<td>Ortho- Fibrous</td>
<td>Polypropylene Synthetic absorbables</td>
<td></td>
<td>Taper Cutting</td>
</tr>
<tr>
<td>capsule</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ortho- Tendon</td>
<td>Coated braided polyester Stainless Steel</td>
<td></td>
<td>Taper Cutting Cutting Taper Point</td>
</tr>
<tr>
<td>Suture</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### 20.3.5 Care of Lacerations

- Before suturing:
  - most important: irrigate and debride area
  - look for retained foreign material
  - remove jagged edges
  - determine wound orientation to Langer’s lines and try to suture parallel to in order to minimize scarring
  - Primary closure with tape or sutures is indicated if wound is clean and time elapsed from injury does not exceed 8 hours
  - may need to suture deeply at the subcutaneous layers to eliminate dead space and relieve tension on the skin above
  - Contaminated wounds, human bite wounds, or wounds that are > 6-8 hours old should be closed by delayed primary closure(3-4 days later) or should heal by secondary intention (ie naturally)
  - allows time for contamination or infection to subside
• Puncture wounds (small entrance and deep tract) need to be left open to drain to discourage anaerobic growth
  • may need to insert a wick to help drain
• Suture technique:
  • if using lidocaine:
    o NEVER use + epinephrine on tissue with poor circulation because it is a potent vasoconstrictor
    o watch for signs of toxicity
  • choose a suture that is the smallest possible to maintain closure, and is about the strength of the tissue needing to be closed
  • skin edges should be approximated but not too tight
    o approximate, don’t strangulate! remember to leave room for edema
    o want to prevent ischemia and overlapping wound edges
    o make sure first throw just barely brings edges of wound together
      ▪ minimize excess tension
        • use subcutaneous absorbable sutures
        • release dermis and superficial fascia from deeper attachments (“wound undermining”) if necessary
        • a larger number of small sutures rather than a few large sutures creates less scarring and less tension
  • use forceps as little as possible
    o toothed forceps for skin and smooth forceps for internal tissue
  • the farther away from the wound edge the needle is placed, the bigger the bite (tissue taken) of the needle
  • match skin layer to layer to prevent excessive scarring
  • avoid leaving open spaces behind that can accumulate fluid and breed infection
  • Topical adhesive may be used as an alternative to sutures
    o contraindications: allergy to cyanoacrylate or formaldehyde, wet wounds, wounds under tension
    o patient can shower after 48 hours, but can’t soak or swim
• Removal of sutures:
  • leave sutures in place until wound heals
    o timeframe depends on would location, age of patient, immune status, and general health of patient
    o typically:
      ▪ face or neck = 3-5 days
      ▪ trunk = 7-10 days
      ▪ upper extremities = 10-12 days
      ▪ lower extremities = 12-16 days
  • too long □ scarring and infection
  • should be painless
  • procedure: swab wound with alcohol to remove dried exudate, grasp knot or loose ends with forceps and slightly pull up, then cut suture just before it enters the skin to prevent pulling contaminated suture through the tract

### 20.3.6 Types of Suture Closures

<table>
<thead>
<tr>
<th>Closure Style</th>
<th>Information &amp; Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simple interrupted</td>
<td>Most useful and most commonly used.</td>
</tr>
<tr>
<td>Continuous</td>
<td>Fast but risk of strand breakage □ wound dehiscence.</td>
</tr>
</tbody>
</table>
### Vertical mattress
Good for creating everted wound edges. Most effective in accurate skin approximation with minimal wound edge tension and distortion. Can act as a deep as well as a superficial closure all in one suture.

### Horizontal mattress
Good for creating everted wound edges.

### Subcuticular (continuous intracutaneous)
Excellent for cosmetic purposes, eliminates crosshatching caused by suture marks. Can only be used for straight lacerations < 2-3 inches long.

### Deep dermal
Done at end of suturing. Reduces wound tension by bringing dermis close together before suture closure. Knot is “buried” so as to not interfere with epidermal healing.

### 20.3.7 Types of Knots
- Square knot is the strongest kind, having 80-90% of the tensile strength of the uninterrupted strand
- Surgeon’s knot is a square knot with a double first throw better knot security with less slippage of suture
- Holds wound edges in place while performing subsequent throws

### 20.3.8 Suture-Related Complications
- Causes of infection:
  - too tight sutures ischemia and proliferation of bacteria
  - too many sutures placed large amount of ischemia
  - multifilament braided suture material crevices for bacteria to grow and evade phagocytosis
- Causes of wound dehiscence:
  - insufficient suture strength
  - insecure knots
  - premature loss of strength
  - premature suture removal
  - too tight sutures
  - wound infection
  - weak tissue layers
- compromised health
- delayed wound healing
- tearing of tissue
- excess force placed on wound post-op
- obesity
- compromised vascularity of wound edges

20.4 Bandaging

20.4.1 Dressings

- Non-adherent:
  - used over raw wounds
- Dry dressings:
  - used for wounds with intact skin or closely approximated wound edges
  - allows for circulation
  - should be changed once soiled or wet, and not every day unless it is needed
  - collodion spray is good for small lacerations and is sprayed over a gauze dressing
- Wet dressings:
  - used for infected wounds that are being left open and regularly irrigated
  - wet compresses can’t be used more than 24 hours to prevent skin breakdown
  - Wounds needing repeated dressing changes over time can make use of Montgomery straps

20.4.2 Methods

- Circular bandage: for tubular structures
- Figure-eight: for over joints like the elbows and knees
- Recurrent: for distal stumps
- Reversed spiral: for tubular structures of changing diameter like the forearm
- Spice: to cover two parts of unequal size like the shoulder + chest, or thumb + hand, or thigh + groin
- Head dressing

20.4.3 Drains

- Penrose drain: for small wounds
- Sump drain: attach to suction; for large abscess, the peritoneal cavity, or biliary fistulas

20.5 Pre & Post-Op Considerations

20.5.1 Pre-Op Evaluation for All Surgical Patients

1.) H&P
- HPI
- med review: look for use of anticoagulants, steroids, or diabetic medications
- PMH including ROS
- PE: complete!
2.) Routine tests: CBC, Chem 7, clotting studies, UA, type & screen (or cross-match), EKG
   - CXR in all patients over 40 or with risk factors
3.) Special tests: varies by patient and operation
4.) Explanation, questions, and consent
   - phone consents require a 2nd person to witness
   - confused or demented patient needs consent from next of kin (spouse, then adult child)
   - Point of all this is to prepare the patient and family mentally for the operation, to assess the patient’s clinical condition and needs, to optimize physiologic status for the procedure, to promote patient safety and minimize surprises during the surgery, and to prevent post-op complications

20.5.2 Anesthesia
   - Kinds:
     - local injection
     - IV sedation + local anesthetic (monitored anesthesia care or MAC)
     - regional injection into a nerve (nerve block)
       - can cause vasodilation with loss of BP
     - general anesthesia: requires intubation
   - PE: be sure to look at mouth and neck and make sure intubation is feasible

20.5.3 Cardiac Pre-Op Evaluation and Surgical Complications
   - Pre-op H&P:
   - ROS: especially ask about dyspnea, exercise tolerance, PND or orthopnea, peripheral edema, irregular heart beat, or chest pain
   - PMH: especially ask about congenital heart disease, rheumatic fever, atherosclerosis, pacemaker, angina, past MI, HTN, diabetes, previous cardiac surgery
   - Med review: especially ask about diuretics, digoxin, antianginals, antihypertensives, antiarrhythmics
   - PE: pulse, orthostatic BPs, cyanosis, clubbing, JVD, rales, wheezes, PMI palpation, bruits, liver palpation
   - CXR: look for cardiac enlargement, pulmonary vessel distension, lung infiltrates, tortuous aorta, and calcification of arteries and veins
   - EKG: look for arrhythmias, conduction deficits, ischemia or previous MI, hypertrophy, hyperkalemia, digoxin tox
   - ***Remember the 9 significant risk factors for a cardiac complication after surgery: S3 gallop or JVD, MI in last 6 months, abnormal rhythm or PACs, > 5 PVCs/min documented at any time pre-operatively, intraperitoneal, intrathoracic, or aortic operations, age > 70 years, significant aortic stenosis, emergent nature of operation, poor medical condition (abnormal ABG, K, bicarb, BUN, Cr, liver enzymes, or bedridden from non-cardiac disease)
     - patients deemed to be a high risk cardiac case are given an arterial line to monitor BP, a central line to assess volume, and possibly a pulmonary artery catheter to follow oxygen consumption and cardiac output
   - Potential intraoperative complications:
     - myocardial depression from anesthesia decreased contractility and lowered cardiac output
     - fluid shifts, anemia, and hypothermia
   - Potential postoperative complications:
     - arrhythmias: PVCs are common but must be worked up if numerous
     - MIs usually occur 2nd or 3rd day post-op, when fluids given during surgery are mobilized from the soft tissues and interstitium back into the vascular space increased workload on the heart
     - CHF

20.5.4 Pulmonary Pre-Op Evaluation and Surgical Complications
   - Pre-op H&P:
   - ROS: especially ask about dyspnea +/- exertion, wheezing, chest pain, cough, sputum, hemoptysis
PMH: especially ask about tobacco use, occupation exposures, TB, pneumonia, asthma, pulmonary medications (including inhalers) and steroids

Med review: especially ask about diuretics, digoxin, antianginals, antihypertensives, antiarrhythmics

PE: cyanosis, clubbing, adventitious lung sounds, lung hyperresonance, pain, tenderness

CXR: look for infiltrate, granulomas, atelectasis, hyperlucency, pneumothorax, vascular abnormalities, masses

Pre-op labs: ABC, PFTs

Potential postoperative complications:
- atelectasis (the number one cause of fever in the immediate post-op period)
  - prevent with coughing, turning, deep breathing (incentive spirometry helps), early ambulation
- pneumonia
- pain control
- poor wound healing in smokers
- COPD: pneumonia, mental status changes from hypoxia, pulmonary edema

20.5.5 Renal/Genitourinary Pre-Op Evaluation and Surgical Complications

Pre-op H&P:

ROS: especially ask about urinary frequency, dysuria, poor stream, incontinence, hematuria, sexual dysfunction

PMH: especially ask about renal disease, calculi, HTN, diabetes, diuretics, exposure to nephrotoxins

PE: edema, state of hydration, friction rubs

Labs: UA, BUN, Cr

Potential postoperative complications:
- urine retention: nerve injury, pain medication, or enlarged prostate
- UTI
- low urine output
  - prerenal cause: hypovolemia as fluid shifts from vascular spaces into the tissues
  - renal cause: tubular dysfunction from nephrotoxins, trauma, loss of blood supply
  - postrenal cause: obstruction of flow at the ureter, bladder, or urethra due to trauma, tumor growth, enlarged prostate, or blocked catheter
  - what to do?
    - assess, and if no cardiac disease or stress □ IVF bolus
    - if low urine output continues or there is tachycardia or hypotension, get CBC to rule out bleeding and chemistries to evaluate BUN and Cr

20.5.6 Other Considerations

Adrenal functioning

- normally adrenal glands secrete increased amounts of cortisone and aldosterone to maintain homeostasis in times of physiologic stress
- patients on steroids or in other states of immunosuppression may have hypoadrenal response to stress □ hypotension and tachycardia that is unresponsive to fluids and pressors = need to place these patients on exogenous stress-dose steroids to prevent
- can do ACTH response stress if recent steroid use is uncertain

Diabetic patients

- hyperglycemia inhibits wound healing and promotes infection
- post-op glucose goal is 100-200 mg/dL
- if coming in for same-day surgery and won’t need IVF overnight, don’t give insulin or oral meds
- if IVF are given, give half the usual insulin dose but no oral meds
- start oral meds once patient is taking food

Development of postoperative fever (4 W’s):
- wind: atelectasis and other pulmonary problems develop in first 48 hours
- wound: infection or dehiscence occurs in 5-7 days post-op
- water: UTIs occur 5-8 days post-op
• walk: DVT occurs 7-14 days post-op

• IV fluids:
  • crystalloid: aqueous solutions of mineral salts or other water-soluble molecules
    o tend to dilute blood and thus reduce osmotic pressure
    o NS, LR are both crystalloids
  • colloid: contains larger insoluble molecules, such as gelatin
    o maintain high osmotic pressure
    o blood is a colloid
  • standard pre-op and maintenance fluid is D5 + ¼ NS + 20 mEq/L KCl @ 75 mL/hour (the “house wine”)
    o but don’t add KCl in renal patients
    o always keep the D5 in diabetics to prevent hypoglycemia
    o not needed if patient is having thoracic or cardiac surgery (want them dry)
  • standard post-op fluid for the first 24 hours is LR +/- D5 @ 125 mL/hour

20.6 Shock & Transfusions

20.6.1 Hemodynamic Parameters

A.) Mean arterial pressure = DBP + 1/3 (pulse pressure) = CO x SV
  • normally > 65

B.) Stroke volume

C.) Ejection fraction: normally > 55%

D.) Cardiac output: normally 4-8 L/min
  • can increase with HR up to 120-150 but beyond that ends up decreasing due to decreased diastolic filling time of the heart
  • kidney gets 25% of cardiac output, brain gets 15%, and heart gets 5%

E.) Cardiac index (CO/body surface area): normally 2.5-4 L/min/m$^2$

F.) Systemic vascular resistance

G.) Pulmonary capillary wedge pressure: normally 20/6 to 30/15 mm Hg

H.) Mean pulmonary artery pressure: normally 10-17 mm Hg

I.) Mixed venous oxygen saturation: normally 65-75%
  • Can measure these noninvasively or invasively:
    o Swan-Ganz catheter can be put in pulmonary artery
    o arterial line catheter can be placed in aorta or peripheral artery and measures beat-to-beat blood pressure
  • Shock: any condition in which there is inadequate delivery of oxygen and nutrients to the tissues sufficient to meet metabolic demands
    o signs and symptoms are related to poor tissue perfusion: mental status changes, acidosis, oliguria, cool/pale skin

• Causes of shock:
  • failure of the pump (heart):
    o cardiac compressive shock: when extrinsic compression of the heart or great veins slowed blood return to the heart
      ▪ ex. pericardial tamponade, tension pneumothorax, diaphragmatic rupture, positive pressure ventilation
      ▪ PE: hypotension, JVD, rales, Kussmaul’s sign, pulsus paradoxus
      ▪ treatment is to resuscitate with fluids and correct mechanical abnormality
        • ex. pericardiocentesis
    o cardiogenic shock: a result of failure of the heart muscle, arrhythmia, valvular or septal defects, or excessive afterload (systemic or pulmonary HTN)
      ▪ PE: JVD, rales, extra heart sounds, peripheral edema
- treatment is to optimize volume status (balance fluid or diuretics), reduce afterload (vasodilators), optimize heart rate and rhythm (beta-blockers, anti-arrhythmics, pacemaker), improve pump function (inotropes like epinephrine or intra-aortic balloon pump or ventricular assist device)

- failure of the oxygen carrier (blood)
  - hypovolemic shock: due to inadequate circulating volume from blood loss or unreplaced fluid loss (vomiting, sweat, 3rd spacing) □ decreased venous return to the heart and decreased cardiac output
    - mild hypovolemia (< 20% loss): decreased pulse pressure, postural hypotension, cutaneous vasoconstriction, collapsed neck veins, concentrated urine, concentrated blood
    - moderate hypovolemia (20-40% loss): thirst, tachycardia, moderate hypotension, oliguria
    - severe hypovolemia (> 40% loss): mental status changes, arrhythmias, ischemic EKG changes, profound hypotension □ treatment: large-bore peripheral IVs with crystalloid bolus (2 L LR or NS), may need blood products

- failure of the conduit to the cells (vessels)
  - loss of venous tone □ venous pooling with decreased return to the heart and decreased cardiac output
    - neurogenic shock: failure of the autonomic nervous system (spinal cord injury or regional anesthetics) □ loss of sympathetic tone and adrenergic stimulation (if above level of T4)
      - PE: warm, flushed skin and bradycardia, venous pooling
      - treatment: IVF, peripheral vasoconstrictors (phenylephrine, vasopressin), turn off epidural
  - loss of arterial tone □ decreased systemic vascular resistance and hypotension
    - septic shock: usually due to overwhelming Gram neg infection □ systemic inflammatory response with arterial vasodilation and organ dysfunction
      - sepsis: SIRS + documented infection
      - severe sepsis: SIRS + infection + organ dysfunction
      - septic shock: SIRS + infection + hemodynamic instability
      - early signs: tachycardia, increased cardiac output, hypotension, fever, chills, bounding pulses, warm/flushed skin, hyperglycemia, confusion, hyperventilation, respiratory alkalosis
      - late signs: bradycardia, decreased cardiac output, hypothermia, coagulopathy, pulmonary failure, renal failure
      - treatment: antibiotics, surgical debridement or resection, volume replacement, mechanical ventilation, vasopressors, inotropes □ oxygen delivery = [Hb] x (decimal arterial O2 sat) x (1.39) x (cardiac output)x (10)

<table>
<thead>
<tr>
<th>Causes</th>
<th>Cardiac Output</th>
<th>Heart Rate</th>
<th>LV Filling Pressures</th>
<th>Systemic Resistance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart</td>
<td>Compressive</td>
<td>↓</td>
<td>↑↑↑</td>
<td>⇔/↑</td>
</tr>
<tr>
<td></td>
<td>Cardiogenic</td>
<td>↓↓</td>
<td>↓/⇔/↑↑↑</td>
<td>↑</td>
</tr>
<tr>
<td>Blood</td>
<td>Hypovolemic</td>
<td>↓</td>
<td>↓↓</td>
<td>↑</td>
</tr>
<tr>
<td>Vessels</td>
<td>Neurogenic</td>
<td>↓⇔</td>
<td>↓/⇔</td>
<td>↓/⇔</td>
</tr>
<tr>
<td></td>
<td>Septic (early)</td>
<td>↑</td>
<td>↑</td>
<td>↑/⇔</td>
</tr>
</tbody>
</table>
20.6.2 Transfusions and Blood Products

- Threshold for transfusion is based on clinical judgment
- Indications:
  - restoration or maintenance of normal blood volume
  - correction of severe anemia
  - correction of bleeding and coagulation disorders
- Potential reactions:
  - hemolysis (up to 1/500 incidence of minor hemolysis): symptoms of apprehension, headache, fever, chills, flank or chest pain, hematuria, hypotension
  - febrile nonhemolytic reactions due to attack against donor WBCs
  - d/c transfusion
  - anaphylaxis (usually host IgG vs transfusion IgA)
  - graft vs host (TRALI): due to donor antibodies against host WBCs
  - disease transmission: most commonly CMV (50%) or hep C
- Other considerations:
  - hypocalcemia may be induced by sodium citrate preservative
  - large amounts of IV fluids can dilute coagulation factors = why many trauma patients have a prolonged PT/PTT
  - acidosis can affect pH-sensitive coagulation factors
  - hypothermia slows coagulation cascade
  - dilutional coagulopathy with multiple units of RBCs
  - some cells will hemolyze during transport → delivery of extra K load to the patient

<table>
<thead>
<tr>
<th>Product</th>
<th>Volume</th>
<th>Therapeutic Effect/ Unit</th>
<th>Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRBC’s</td>
<td>~300 cc</td>
<td>↑↑ Hct by 3%</td>
<td>hypovolemia + anemia</td>
</tr>
<tr>
<td>Platelets</td>
<td>~250 cc</td>
<td>↑↑ Plts by ~40,000</td>
<td>Plts &lt;50,000 (bleeding)</td>
</tr>
<tr>
<td>FFP</td>
<td>~200 cc</td>
<td>Variable</td>
<td>Correction of vit K dependent clotting factors</td>
</tr>
<tr>
<td>Cryoprecipitate</td>
<td>~25 cc</td>
<td>↑↑ Fibrinogen by 3%</td>
<td>Fibrinogen &lt;100 mg/dL</td>
</tr>
</tbody>
</table>

20.7 Gastrointestinal Surgery I

20.7.1 Appendicitis

- Anatomy
  - locate the appendix opening by finding the confluence of the cecal teniae
  - appendix can be in several different orientations, but usually it is retrocecal
    - pregnancy will push the appendix superiorly and the tip medially
    - physical findings will change with location of the appendix
- Pathophysiology
  - obstruction of appendix opening → bacterial overgrowth within → increased wall pressure & production of mucus → mucosal ischemia → gangrene and necrosis
- Presentation: vague periumbilical pain, anorexia, nausea, RLQ pain
PE: low-grade fever, focal abdominal tenderness (usually at McBurney’s point), Dunphy’s sign (pain with coughing), Rovsing’s sign (pain in RLQ during palpation of LLQ), obturator sign with pelvic appendix (pain on internal rotation of hip), iliopsoas sign with retrocecal appendix (pain on extension of the right hip)

Investigation:
- labs: CBC mild WBC elevation with simple appendicitis or high WBCs with complicated appendicitis (gangrene or perforated)
- imaging:
  - US to look for thick-walled, non-compressible appendix: best for peds and pregnancy
  - CT + contrast to look for distended appendix, periappendiceal fat stranding, edema, peritoneal fluid, phlegmon, periappendiceal abscess

Treatment:
- if there is an appendiceal abscess, don’t operate!
  - high mortality with operation
  - use antibiotics like Cipro or Zosyn
  - drain
  - 3-4 weeks after resolution, do an appendectomy on kids or a colonoscopy on adults (colon cancer can manifest as appendiceal abscess)
  - if colonoscopy is clear, consider appendectomy in adults

20.7.2 Gallbladder Disease

Anatomy & physiology
- cystic duct comes off of the gallbladder to join the hepatic duct from the liver formation of common bile duct to empty into small intestine (control via Sphincter of Oddi)
- blood supply to the gallbladder is via the cystic artery (comes off of right hepatic artery)
- functions of bile: absorption and digestion of fats, absorption of fat-soluble vitamins, elimination of cholesterol and bilirubin
- cholesterol gallstones occur when gallbladder epithelium reabsorbs water and electrolytes present in bile concentrated bile with increased cholesterol and calcium
- Risk factors for developing disease: obesity, bariatric surgery or rapid weight loss, multiparity, female sex, FH, certain drugs including TPN, Native American or Scandinavian, ileal disease, increasing age
- the “4 F’s” are Fat, Female, Forty, and Fertile
- Diseases are on a spectrum
  - asymptomatic disease
  - biliary colic (symptomatic cholelithiasis): gallbladder is contracting against an obstruction in the cystic duct
    - presentation: RUQ or epigastric pain for 1-5 hours (until gallbladder manages to squeeze stone through), nausea or vomiting
      - triggered by fatty foods
    - labs are normal
    - US to look for hyperechoic stones
- can also do CT
- treatment: elective cholecystectomy if complications or symptoms are severe enough
  - **acute cholecystitis:** when persistent obstruction of cystic duct by stone → gallbladder distension, inflammation, and edema → necrosis
    - presentation: RUQ pain/rigidity/guarding, **Murphy’s sign** (inspiratory arrest with palpation of RUQ)
      - referred pain to shoulder not frequently seen
    - labs: elevated WBCs, mild elevations in LFTs
    - US: detects gallbladder wall thickening, pericholecystic fluid, can do US Murphy’s sign
    - hepatobiliary iminodiacetic acid (HIDA) scan: a nuclear medicine test that detects inability of gallbladder to fill with radiotracer
    - treatment: IV antibiotics, IV fluids, analgesia, cholecystectomy in 2-3 days
  - **cholangitis:** when gallstone travels to the common bile duct (now it is considered cholelithiasis) and creates a blockage → bacterial infection
    - presentation: Charcot's triad (RUQ pain, jaundice from no bile to excrete bilirubin, fever), or Reynold’s pentad (RUQ pain, jaundice, fever, shock, mental status changes)
    - labs: elevated WBCs, increased bilirubin and alk phos
    - treatment: IV antibiotics, biliary decompression via ERCP
  - gallstone pancreatitis

### 20.7.3 Hernia

- Types of hernias:
  - **reducible hernia:** when contents of hernia can manually be returned to their correct anatomic location
  - **incarcerated hernia:** when contents can’t be reduced
    - associated with high morbidity and mortality
  - **strangulated hernia:** when hernia contents have compromised blood supply
    - most serious type of hernia, potentially fatal
- Anatomy
  - inguinal canal: contains spermatic cord or round ligament of the uterus
  - borders:
    - superficial = external oblique
    - floor/posterior = transversalis fascia
    - superior = internal oblique + transverse abdominal
    - inferior/running underneath = inguinal ligament
  - Hesselbach’s (inguinal) triangle:
    - borders:
      - medial border = rectus sheath
      - superior border = inferior epigastric vessels
      - inferior border = inguinal ligament
    - significance:
      - a direct inguinal hernia will lie within Hesselbach’s triangle (a result of plowing through weak muscle) and an indirect inguinal hernia will be lateral to it (a result of it slipping through the inguinal canal opening)
- More about hernias:
  - direct inguinal hernias: plowing through weak tissue
    - less common
    - mechanism: increased intra-abdominal pressure (coughing, constipation, urinary retention, ascites), weakening of tissue due to age or smoking
  - indirect inguinal hernias: slipping through an abnormally open canal
    - more common
    - mechanism: a result of a patent processus vaginalis
      - common in kids
  - a femoral hernia occurs via the femoral canal and will appear as a bulge BELOW the inguinal ligament
    - occur mostly in women, and many become incarcerated or strangulated = repair early!
- a ventral hernia occurs by protrusion through the abdominal wall
- umbilical hernia:
  - congenital in infants and most close spontaneously
    - repair at 5 years if hernia persists
  - acquired in adults
    - repair if symptomatic or incarcerated
- Presentation: bulge in groin area, mild pain or discomfort
  - usually not painful unless incarcerated or strangulated
  - suspect an incarcerated hernia if there are signs of sepsis, tachycardia, skin changes, fever, etc.
- PE: examine supine and standing, have pt cough or strain (and repeat with finger pressing in inguinal canal)
- Investigation:
  - differential: hydrocele, inguinal adenitis, varicocele, ectopic testis, lipoma, hematoma, sebaceous cyst, hidradenitis, psoas abscess, lymphoma, metastatic neoplasm, epididymitis, testicular torsion, femoral hernia, femoral adenitis, femoral aneurysm or pseudoaneurysm
- Treatment for inguinal hernia:
  - if mild symptoms or asymptomatic □ consider watchful waiting
  - if symptomatic □ surgical hernia repair
    - laparoscopic vs open?
      - usually surgeon preference determines
      - bilateral or recurrent hernias are always done laparoscopically to avoid making multiple incisions/scars
      - open if patient can’t go under general anesthesia
      - more intraoperative complications and recurrent hernias with lap
      - more neuralgia or pain with open repair
- Treatment for incarcerated hernia:
  - OR if any signs of strangulation
  - if no signs of strangulation, attempt reduction

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<th>Table 1 Nyhus Classification System for Groin Hernias</th>
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20.8 Gastrointestinal Surgery II

20.8.1 Colon Anatomy & Physiology

- **Anatomy**
  - colonic flexures susceptible to ischemia: splenic flexure (Griffith’s point), rectosigmoid junction (Sudak’s point)
  - colonic wall innervation:
    - submucosa (inner) by Meissner’s plexus
    - myenteric (outer) by Auerbach’s plexus
    - sympathetic: lumbar, splanchnic, and hypogastric nerves
      - inhibit motility and secretion and increase sphincter tone
    - parasympathetic: vagus
      - increase motility and secretions while relaxing the sphincter
  - Colon functions: absorption of water, electrolytes, carbs, and some bile salts, storage, digestion
  - ascending colon mixes and absorbs
  - descending colon stores

20.8.2 Diverticular Disease

- **True diverticula**: outpouchings of colon wall that contain all layers of the wall
  - congenital, solitary, and rare
- **Pseudodiverticula**: herniation of the mucosa and submucosa through circular muscle at the level of penetrating arterial supply
- **Diverticulosis**: presence of multiple penetrating diverticula
  - present in most people older than 70
  - usually sigmoid diverticulosis
  - asymptomatic or may have lower GI bleed
- **Diverticulitis**: inflammation or microperforation of diverticula
  - severity varies from mild inflammation to severe (free perforation with free air, abscess)
  - presentation: fever, LLQ pain
    - bleeding is uncommon
  - investigation:
    - CT with contrast to look for free air, free fluid, abscess
  - treatment depends on severity
    - mild: NPO with IV fluids and IV antibiotics
    - percutaneous draining of abscess
    - peritonitis, obstruction, fistula, recurrence, or intractable disease requires surgery
      - may need to remove diseased part of colon
      - may need to make temporary colostomy (Hartmann’s procedure)
  - follow-up with colonoscopy 3-6 months after treatment to evaluate healing and extent of diverticulosis complications:
    - abscess
    - obstruction
    - fistula: present with symptoms of fecaluria and pneumaturia
      - colovesicular in men (colon-to-bladder)
      - colovaginal in women

20.8.3 Sigmoid Volvulus

- torsion of floppy or extra-long sigmoid colon
- Can lead to ischemia and necrosis
- Presentation: abdominal pain or distension, nausea, vomiting
  - classic: elderly patient with history of chronic constipation
- Investigation:
  - KUB: see huge dilated colonic loop
  - contrast enema: see “bird’s beak”
• Treatment:
  • if peritonitis → laparotomy
  • if stable → colonic decompression via rectal tube placement, then surgical resection with placement of a primary anastomosis (otherwise volvulus will almost always recur)

20.8.4 Hematochezia
• bright red blood per rectum
• Not melena, which is dark red blood
• Causes: upper GI bleed, lower GI bleed (diverticulosis, cancer, arteriovenous malformation, polyp, hemorrhoid, fissure, ischemic colitis, IBD)
• Investigation:
  • draw blood for CBC, electrolytes, type and cross-match
  • insert NG tube and Foley catheter to measure outputs
  • proctoscopy & colonoscopy
  • tagged RBC scan for bleeding > 0.1 mL/min
  • angiography for bleeding > 0.5 mL/min
• Treatment of massive lower GIB:
  • treat hypovolemia with 2 large bore IVs and 1-2L LR bolus
  • transfuse for anemia or inadequate response to IVF
  • embolization of bleeding vessel
  • segmental resection
  • total abdominal colectomy if no response to resuscitation and no source is identified

20.8.5 Inflammatory Bowel Disease
A.) Crohn’s: a type of inflammatory bowel disease that may affect any part of the gastrointestinal tract from mouth to anus, causing a wide variety of symptoms
• unknown etiology
• mucosal inflammation is full-thickness
• presentation: abdominal pain, frequent BM or diarrhea, abdominal distension, nausea, vomiting, weight loss
• investigation: cobblestoning histology, non-caseating granulomas in submucosa
• treatment: sulfasalazine, steroids, other immunosuppressants, monoclonal antibodies, metronidazole
• surgery is not curative because it affects the entire GI tract!
  • can do a strictureplasty to open up stenotic bowel areas
  • for refractory segmental disease → segmental resection with anastomosis
  • for pancolonic disease or toxic megacolon → proctocolectomy with end ileostomy
  • keep procedures as conservative as possible as pt will likely require multiple operations during their lifetime
  • indicated for obstruction, perforation, fistula, cancer, perianal disease, failure of medical therapy, or failure to thrive
• complications: formation of fistula or stricture
B.) Ulcerative colitis: a superficial inflammatory process restricted to the colon that involves the colonic mucosa and submucosa
• begins with the rectum and moves proximally
• associated with HLA-B27
• clinical course fluctuates with exacerbations and remissions
• presentation: abdominal pain, weight loss, dehydration, bloody stool, primary cholangitis, ankylosing spondylitis, uveitis
• investigation: histology shows crypt abscesses and inflammatory pseudopolyps
• treatment is similar to Crohn’s
• surgery indicated for symptoms refractory to medical therapy, colon cancer or dysplasia, toxic megacolon, disease > 10 years
  • total proctocolectomy with end ileostomy or Koch pouch
• total colectomy and rectal mucosectomy with ileal pouch anal anastomosis

20.8.6 Ischemic Colitis
• inflammation and injury of the large intestine result from inadequate blood supply
• Presentation:
  • acute: bloody diarrhea
  • chronic: episodic LLQ pain
  o occurs in low blood flow states such as CAD, CHF, etc.
• Treatment:
  • supplemental oxygen, maximize cardiac output, withdraw vasopressors, bowel rest, TPN
  • surgery if complicated (perforation, peritonitis, progression, or persistence of symptoms)

20.8.7 Colorectal Cancer
• Types of polyps:
  • hyperplastic: most common and incurs no cancer risk
  • hamartomatous: Peutz-Jegher's syndrome
  • adenomatous: premalignant
    o tubular (best prognosis), villous (highest risk of cancer), or tubulovillous
• Risk factors: FH, FAP or HNPCC, IBD, obesity, excess fat or alcohol intake, sedentary lifestyle = a disease of Western industrialized countries
• Presentation: change in stool habits or caliber (“pencil thin stools”), rectal bleeding, obstruction, perforation, abscess, fistula, abdominal pain, weight loss, jaundice (with mets to the liver)
• Investigation:
  • initial colonscopy, barium enema
    o bowel preps:
      ▪ golytely safe for renal failure
      ▪ mag citrate requires smaller vol but is not safe for renal failure
      ▪ Fleet’s phosphosoda is smallest vol but is not safe for renal failure
  • abdominal CT for liver mets and nodal involvement
  • CXR for lung mets
  • endorectal US for rectal cancer
  • CEA levels?
• Treatment:
  • total or partial colectomy depending on tumor location

20.8.8 Anorectal Anatomy
• Pelvic floor muscles include the iliococcygeus, pubococcygeus, puborectalis
  • puborectalis is the most important
    o dysfunction is associated with fecal incontinence

20.8.9 Benign Anorectal Disease
• Hemorrhoids: painful, swollen veins in the lower portion of the rectum or anus as a result from increased pressure in the veins of the anus
  • kinds:
    o external hemorrhoids: are below the dentate line and are covered in squamous epithelium
      ▪ sensate
      ▪ more common in women due to enlargement from pregnancy
      ▪ may thrombose
    o internal hemorrhoids: occur above the dentate line and are covered by columnar epithelium
      ▪ insensate
      ▪ may prolapse, bleed, or thrombose
        • classified by degree of prolapse (determines treatment)
          ▪ painless bleeding with BM= 1st degree
protrusion through anal canal but are spontaneously reducible = 2nd degree
- protrusion with pressure but are manually reducible = 3rd degree
- permanent prolapse = 4th degree

- occurs when anal cushions slide downward: disintegration of supporting tissue above the normal position of the hemorrhoids, distal migration of hemorrhoids
- increased risk with age, gravity, shearing forces, and increased abdominal pressure
- treatment: only if symptomatic!
  - usually only treat internal hemorrhoids (treat external if thrombosed)
  - grades 1-3 are treated nonsurgically
    - sitz baths, psyllium for bulking, lots of water, diaper rash ointments, topical hydrocortisone
      - can treat acute thrombosis with hydrocortisone if there is no necrosis or bleeding
  - grade 4 or with persistent bleeding needs surgery
    - contraindications: bleeding diathesis, portal HTN, pregnancy
    - banding for internal hemorrhoids without significant external disease
      - causes necrosis and sloughing of hemorrhoid tissue
    - resection for large mixed hemorrhoids or with other benign anorectal disease present
  - patients over age 40 should also get a colonoscopy

- Anal fissure: elliptical tear or ulcer in anal canal
- occurs during defecation
- usually posterior to anal canal
  - lateral location in IBD, viral ulcers, or squamous cell carcinoma
- treatment: stool softeners, sitz baths

- Anorectal abscess: when obstruction of anal crypts leads to bacterial overgrowth in the anal glands
  - more common in males
  - presentation: pain, swelling, fever, purulent anal discharge
  - investigation: localize abscess via CT
    - may spread downward into the perianal area (most commonly), laterally through the external sphincter to make an ischiorectal abscess, through the internal sphincter to form a submucosal abscess, or upward above the levator ani to form a supralevator abscess (rare)
  - treatment: antibiotics, I&D
  - prognosis:
    - many patients will still develop a fistula or have a recurrent abscess

- Perianal fistula: an abnormal connection between the epithelial surface of the anal canal and another surface
  - occur in same sites as abscess, usually on the perianal skin
  - investigation:
    - determine position of tract via Goodsall’s rule: draw an imaginary line through the anus, if the fistula is above this line (towards the cheeks), the tract curves toward midline, if it is below, the tract courses straight towards the anal canal
  - treatment:
    - surgical fistulotomy
      - should not be performed when sphincter involved is > 1 cm thick
    - stick in a seton (device that keeps tract from closing) to promote drainage
    - treatment of an anterior midline fistula is associated with increased risk of incontinence

- Fecal incontinence
  - usually caused by damage to the pudendal nerve during childbirth
  - treatment: dietary modification, antimotility agents, surgical creation of a new sphincter

20.9 Fluids, Electrolytes, and Acid-Base Regulation

20.9.1 Body Water and Fluid Compartments
- Total body water
  - measured in kg
  - younger males have 60% of their total weight being water
  - males over 60 50%
  - younger females have 50% of their total weight being water
  - females over 60 40%
- Fluid compartments: water passes freely between these compartments to maintain osmotic equilibrium
  - intracellular fluid: all fluid inside of cells, makes up 60% of body water
    - dehydration causes fluid loss here to keep up the BP
    - high in K⁺, Mg²⁺, PO₄⁻, proteins
  - extracellular fluid: all fluid outside of cells, makes up 40% of body water
    - this is where loss causing hypovolemia occurs
    - 20% of this is the intravascular fluid (within vessel walls)
    - 80% of this is interstitial fluid or "third space" (surrounding vessels and at tissue interfaces)
      - does not contribute to circulation or cell volume!
    - high in Na⁺, Cl⁻, HCO₃⁻
  - circulating volume and fluid loss
    - sources of loss: urine, intestines, sweat, skin, lungs, fever, 3rd spacing, drains, tubes, vomit, fistulas
      - hyponatremia because there is less drawing of water into the vessels
      - heart failure because pooling of blood in the oversized heart causes a loss of fluid to the interstitium
      - each degree body temp increases, insensible fluid losses increase by 10%
- Fluid movement between compartments
  - molality: the number of moles of a solute per kilogram of solvent in a solution
  - molarity: the number of moles of solute per litre of solution
  - osmolarity: the total concentration of solutes (including ions) in a solution
    - takes into account the total concentration of penetrating solutes and non-penetrating solutes
    - does not depend on whether the solutes can cross the cell membranes or not
  - tonicity: relates to the osmotic gradient created by solutes that affects a semi-permeable membrane
    - only solutes that can’t freely cross the membrane contribute to this effect
    - example: high BUN makes the blood serum hyperosmotic (more solutes) but it can cross cell membranes to equalize its concentration between the serum and cell, so it has no ability to generate oncotic pressure and draw water out of cells = serum remains isotonic to the body cells
    - example: hyperglycemia makes the blood serum hyperosmotic as well as hypertonic because glucose can’t freely diffuse into the cells (requires transporters) = water leaves cells to equilibrate glucose concentrations between the cells and blood
- Plasma osmolality calculation:
  - plasma osmolality = 2(Na) + glucose/18 + BUN/2.8

20.9.2 H&P Assessing Volume Status

- Significant history:
  - volume overload: fluid retention, weight gain, heart failure symptoms
  - volume deficit: prolonged fever, profuse sweating, vomiting, diarrhea, thirst, decreased fluid intake, weight loss, weakness, confusion, lethargy, seizures, coma, third spacing of fluids, use of diuretics, adrenal insufficiency or Addison's disease, ketonuria
- PE:
  - volume overload: pulmonary edema, peripheral edema, ascites, S3, JVD, rales
  - volume deficit: tachycardia, orthostatic hypotension, decreased turgor, dry mucosal membranes, oliguria

20.9.3 IV Fluids

- normal blood serum is 290-310 mOsM
Med Surg Quick Notes

- Fluids will re-distribute in body fluid compartments like water distributes

A.) 5% Dextrose in Water (D5W)
- 252 mOsm = slightly hypotonic in relation to the body
- Shift of water into cell until osmolarity equilibrates across all compartments = good for rehydration of intracellular fluid
- Dextrose is rapidly metabolized by the liver, so you are essentially just giving the patient water
- pH = 3.5-6.5

B.) 0.9% NaCl (normal saline or NS)
- 308 mOsm = isotonic in relation to the body
  - No fluid shifts, no change in osmolarity, just restoration of intravascular volume
  - Eventually results in ADH being turned off with excretion of excess water
- pH = 4.5-7
  - Good for maintenance fluid
C.) Lactated Ringer’s solution
- 273 mOsm = iso-tonic in relation to the body
- Contains Na, K, Ca, Cl, and lactate
- Most commonly used resuscitation fluid, especially for trauma
- Used in the first 24 hours post-op, then replaced with NS because the lactate can cause metabolic alkalosis if used for too long

D.) ½ NS
E.) ¼ NS
F.) 3.0% NaCl
- For initial treatment of severe hyponatremia

20.9.4 Replacement of Fluid Losses
- First, replace deficit
  - Intraoperative blood loss can usually be tolerated unreplaced up to 500 mL
    - Calculate fluid deficit:
      - \[ \text{deficit} = \text{IVF} - 3(\text{expected blood loss}) - \text{urine output} \]
      - Each 1 mL of estimated blood loss must be replaced by 3 mL of isotonic IVF
        - Because 2/3 of the fluid will leave the vascular space
        - An acute rise in Cr in an otherwise healthy post-op patient is due to underresuscitation!
  - Then, fulfill daily maintenance requirements
    - Calculate need:
      - 100 mL/kg/day for the first 10 kg
      - 50 mL/kg/day for the next 10 kg
      - 20 mL/kg/day for every kg over 20 then divide by 24 for hourly rate
    - Common maintenance fluids:
      - Adults: D5 + ½ NS + 20 mEq KCl/L
      - Kids: D10 + ¼ NS + 10 mEq KCl/L
  - Lastly, replace any ongoing losses

***Correct all abnormalities at approximately the rate at which they developed!***

20.9.5 Hyponatremia
- Normal serum Na mOsm is 280-295; low if < 280
- Treatment of hyponatremia
  - Depends on whether patient is symptomatic and if it is acute or chronic
    - Chronic asymptomatic mild-moderate hyponatremia may not need any treatment
    - Correct to magic number 125

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• severe symptoms □ 1.5-2 mEq/L/hour for first 2-4 hours
• don’t exceed 12 mEq/L/day
• asymptomatic patients □ < 0.5 mEq/L/hour
• definitive treatment based on underlying cause of impaired renal water excretion

20.9.6 Hypernatremia

• When serum Na mOsM > 145
• Usually from loss of water with failure to adequately replace water loss
  • extrarenal water losses: sweat, fever, severe burns
  • renal losses:
    • osmotic diuresis,
    • diabetes insipidus (central or nephrogenic): deficiency of ADH or insensitivity to ADH
      • treat with slight volume depletion to increase water absorption at the proximal
        tubule, low salt diet, thiazide diuretic
      • don’t use loop diuretics or NSAIDs
    • iatrogenic: administration of hypertonic NaCl)
• Presentation: lethargy, weakness (brain cell shrinkage), irritability, twitching, seizures, coma, focal
  intracerebral and subarachnoid hemorrhages (due to vessel attachment to shrinking cells)
• Treatment fluid tips:
  • D5W will replace water without adding Na
    • caution: not good at restoring ECF in hypovolemic patients, can develop
      hyperglycemia or glucosuria, can aggravate the hypernatremia by causing an
      osmotic diuresis?
  • 1/2 NS will replace water and Na
    • less efficient than D5W but ok to use when patient is both hypernatremic and
      hyperglycemic
    • can be used to restore ECF in hypovolemic patients

20.9.7 Hyperkalemia

• When serum [K+] > 5.5
  • usually K+ balance is maintained until GFR < 10
  • prevent by avoid K-sparing diuretics and cautious use of ACEIs and ARBs in later stage CKD
  • causes:
    • acidosis, which causes K+ to shift out of cells and into the ECF
  • investigation: peaked T waves on EKG
  • treatment depends on EKG findings
    • EKG changes □ concern for arrhythmias
      • IV calcium chloride or calcium gluconate to modify myocardial excitability
      • onset in 1-3 min with duration of 30-60 min
      • repeat every 30-60 minutes until EKG normalizes
      • won’t lower the hyperkalemia!
    • use a K+ binder to lower total body potassium
      • sodium polystyrene sulfonate exchanges Na+ for K+ in the colon
        • takes 2-3 hours to work
    • dialysis to remove excess potassium
    • get K+ back into cells
      • glucose (or not if hyperglycemic) and insulin to increase intracellular uptake of K+
        • onset in 5-10 min with duration of 2 hours
      • sodium bicarb IV over 5 minutes if acidosis is present
      • albuterol to increase intracellular uptake of K+ (stimulates β-cells in pancreas to
        make insulin)
        • onset of 30-40 min with duration of 2-6 hours
        • may not work in 20% of people

20.9.8 Hypokalemia
- **Causes:**
  - decreased K+ intake
  - increased entry into cells: alkaline pH, insulin, stress, β-agonists, increased RBC production, hypothermia, chloroquine toxicity
  - increased GI losses: vomiting, diarrhea, tube drainage, laxative abuse
  - increased urinary losses: diuretics, mineralocorticoid excess, loss of gastric secretions, nonreabsorbable anions, metabolic acidosis, hypomagnesemia, amphotericin B, salt-wasting nephropathies, polyuria
    - increased sweat losses
    - dialysis
    - plasmapheresis
  - investigation
    - EKG flattening of T waves into U waves
  - treatment

20.10 Venipuncture and IV’s

- **Catheter placement:**
  - best place is the cephalic vein on the dorsal hand
  - other choices: digital veins (last resort), metacarpal veins (can’t be used with irritants), basilic veins, antecubital veins
  - avoid lower extremities whenever possible to avoid increased risk of thrombosis or PE
  - needle goes in bevel up
- **Layers of the vein:**
  - innermost is the **tunica intima**: elastic endothelial sheet with immunologic properties to recognize foreign bodies within the vein
  - in the middle is the **tunica media**: thick muscle and elastic tissue that forms the bulk of the vein, contains nerves for vasodilation/constriction and muscle tone
    - where vasospasm occurs
  - outermost layer is the **tunica adventitia**: connective tissue for support and nutrient supply
- **Types of access**
  - **peripheral IV**: can be used with isotonic or hypotonic solutions, good for 5 days
    - first try placement in a metacarpal vein
    - new access should be placed proximal to previous site of access
  - **peripherally inserted central catheter (PICC)**: can be used with any solution for short or long-term therapy
    - dressing change once a week
  - **triple lumen catheter**: nontunneled catheter for use with any solution short-term
    - can draw blood from
    - increased risk of complications
  - **Hickman or Groshong catheters**: tunneled catheters for use with any solution long-term
    - can draw blood from
    - placed in vascular radiology or surgery
    - requires dressing changes
  - **port**: catheter implanted under the skin and tunneled into a vein for long-term therapy with any solution
    - single or dual
    - can draw blood from
    - placed in vascular radiology or surgery
    - needle must be changed once a week
    - must be flushed with heparin once a month when not in use
- **Complications of IV therapy**
  - **infiltration**: extravasation of IV fluid caused by a dislodged cannula or hole
    - most common
    - signs: burning, blanching, edema, coolness, solution leakage
  - **phlebitis**: intimal inflammation
20.11 Principles of Surgical Infections

20.11.1 Common Surgical Infections

- Within 48 hours of surgery, usually *Clostridium* or group B strep
- Within 5-10 days post-op, skin flora
- Post-op fever: “the 4 W’s”
  - wind = atelectasis (most common)
  - wound infection
  - water = UTI
  - wonder drug = fever caused by medication
- Necrotizing fasciitis is caused by *Clostridium perfringens*, group B strep, or mixed Gram negs
- Fournier’s gangrene is a necrotizing soft tissue infection of the perineum
- Diabetics and obese patients most at risk

20.11.2 Process of Wound Healing

- First 10 days are inflammation: platelets, neutrophils, macrophages, fibroblasts, then lymphocytes

20.11.3 Surgical Wound Classification

- **Clean**: an uninfected operative wound in which no inflammation is encountered and the respiratory, alimentary, genital, or urinary tract is not entered
  - primary closure indicated
- **Clean-contaminated**: an operative wound in which the respiratory, alimentary, genital, or urinary tracts were entered under controlled conditions and without unusual contamination
- **Contaminated**:
  - open, fresh, accidental wounds
  - operative wound with major breaks in sterile technique or gross spillage from intestinal tract
  - incisions in which acute, nonpurulent inflammation was encountered
- **Dirty**:
  - old traumatic wound with retained devitalized tissue
  - wound involving existing clinical infection
  - perforated viscera

20.11.4 Antibiotics

- Perioperative antibiotics are given 1 hour prior to skin incision in order to maintain adequate tissue concentration during period of potential contamination
- choice of antibiotics depends on site of surgery
20.12 Surgical Nutrition

20.12.1 Background

- 15-50% of hospitalized patients suffer from some degree of malnutrition
- Normal weight individuals carry a 60-day supply of energy stored as fat
- Lean body mass (skeletal muscle, RBCs, connective tissue, organs) makes up 40% of total body weight and is critical
  - depletion is a severe insult and defines patient morbidity and mortality
  - estimate skeletal muscle mass by 24 hour urine Cr, 3-methyl histidine
- Malnutrition syndromes:
  - cachexia: loss of weight, loss of appetite, muscle atrophy, and weakness in someone not trying to lose weight
  - kwashiorkor: acute visceral protein depletion from chronic protein insufficiency 
    - edema, pigmentation, pot belly
  - marasmus: simple starvation from chronic caloric insufficiency
    - loss of lean body mass, fat, and visceral proteins
- Process of simple starvation
  - glycogen stores in liver and muscle last 24 hours
  - after that proteolysis is dominant
  - in later starvation, the body adapts to conserve protein and fat becomes the major energy source
  - brain begins to use ketone bodies vs glucose
  - minimization of urinary N loss
- Stressed starvation: a neuroendocrine-mediated response
  - hyperglycemia from increased cortisol
  - brain and peripheral tissues fail to ketoadapt and continue preference for glucose
  - protein catabolism for gluconeogenesis
- Best measure to assess recent nutritional status is serum prealbumin

20.12.2 Vitamin Deficiencies

- Vitamin A: night blindness
- Vitamin D: rickets, osteomalacia
- Vitamin K: coagulopathy
- Vitamin E: nephropathy
- Vitamin B12: anemia, beefy tongue, peripheral edema
  - causes: gastrectomy, intrinsic factor deficiency
- Folate: anemia, beefy tongue
  - causes: IBD, malabsorption
- Niacin: pellagra (diarrhea, dermatitis, dementia)
  - causes: alcohol abuse, lack of protein
- Chromium: hyperglycemia
  - causes: TPN without trace elements added

***Physical signs are usually not pathognomonic and have overlap

20.12.3 Feeding Tubes

- Contraindications: gastroparesis, intestinal obstruction, ileus, high-output fistula, short bowel syndrome
- Kinds:
  - nasogastric (NG tube)
    - for short-term, less than 30 days
    - must have gag reflex
  - nasointestinal (Dobhoff)
    - for short-term
    - for aspiration risk patients
    - should cross the spine twice when properly positioned
• gastrostomy: skin to stomach
  o adequate gastric emptying required
  o can’t use in obtunded patients
  o three kinds:
    ▪ Stamm: temporary
    ▪ Glassman/Janeway: permanent
    ▪ PEG

• jejunostomy: stomach to jejunum
  o for obtunded patients or those with high GI fistule or obstruction
  o must be infused continually

• combined GJ tube:

20.12.4 TPN
• Elemental formula only used for patients not tolerating standard formulation
• Should be considered for any patient not having a function GI tract for 5-7 days
• Complications: sepsis, pneumothorax, hemothorax, hydrothorax, subclavian vein injury, cardiac arrhythmia, embolism, cardiac perforation, cholecystitis, cirrhosis
21 Surgery Exam II Notes

21.1 Peripheral Vascular Disease and Other Atherosclerosis

21.1.1 Background

- Atherosclerosis involves diseases of large and medium-sized arteries
- CAD, carotid (cerebrovascular) artery disease, renal artery disease, lower extremity PVD, visceral ischemic disease, aortic aneurysms
  - especially at bifurcations!
- raises risk of ischemia, thrombosis, downstream embolization, and also inflicts end-organ damage to the brain (CVAs) and kidneys (ESRD)
- Pathophysiology:
  - cycle of atherosclerosis:
    - LDL accumulation inside vessel
    - LDL molecules become susceptible to oxidation by free radicals and become toxic to the cells
    - triggers a cascade of immune responses
    - macrophages and T-cells summoned to absorb the oxidized-LDL
    - formation of growing foam cells that are not able to process the oxidized LDL
    - foam cells ultimately rupture, depositing a greater amount of oxidized cholesterol into the artery wall in the form of plaques
    - summation of more WBCs
    - cycle continues and artery becomes inflamed
    - plaques cause the muscle cells to enlarge and form a hard cover over the affected area
  - arterial narrowing
- fatty streaks made of cholesterol-filled macrophages and smooth muscle cells start developing as early as 5 years old
- advancement to fibrous plaques
- advancement to complex plaques (intimal damage or bleeding)
- Risk factors: smoking, diabetes, HTN, hypercholesterolemia, age, FH, male, obesity
- Investigation:
  - arterial biopsy grades level of stenosis histologically

21.1.2 Peripheral Vascular Disease

- systemic atherosclerosis distal to the aortic arch
- A result of atherosclerosis in the descending aorta, external iliac arteries, or lower extremity arteries
- At risk: smokers, diabetics, those with HTN, hyperlipidemia, or those with obesity
- Presentation: symptoms depend on the degree of occlusion and the location of the plaques
- diminished peripheral pulses
  - femoral bruits
  - cool skin or abnormal skin color
  - poor hair growth (look for those shiny hairless toes!)
- intermittent pain and claudication as a result of muscle tissue ischemia that is reproducible
  - will occur in area BELOW the level of disease
  - usually worsens with activity and goes away with rest
  - can also have resting pain, especially at night, when baseline demand for oxygen is greater than inflow
- ulcers and gangrene from lack of blood flow
  - mostly in diabetics
- Investigation:
  - differential: Baker cyst, compartment syndrome, arthritis, nerve root compression, spinal stenosis, and venous claudication
  - doppler/PE for pulses at each level and evaluation of ischemia
    - determines velocity of blood flow
      - loss of triphasic velocity to bi- or monophasic indicates severity of occlusion
  - ankle/brachial index: compares arm to ankle BP; take BP measurements all along legs and compare to both arm BPs to determine if there is variation in pressures
should be done serially for proper evaluation
- normally ankle SBP should be 10-15 mm Hg higher than arm SBP
- ratio of 1.0 to 1.2 is normal
- **caveat:** diabetics will often have ABIs >1 due to calcified, noncompressible vessels, so ABI measurements in this population are invalid for diagnosis of PVD!
- if ratio is <0.9 — mild PVD
- if ratio is <0.7 — moderate PVD
- if ratio is <0.4 — severe PVD with pain at rest
- if ratio is <0.2 — impending tissue necrosis

- **arteriography**
  - test of choice if intervention is needed
  - invasive, involves injection of radiopaque dye into vessels to illuminate the lumen
  - gives information about inflow and distal targets
  - determines angioplasty vs. endovascular procedure

- **CT/MR arteriography**
  - not as accurate as traditional arteriography but not invasive

**Treatment**
- primary treatment is behavioral!
  - risk factor modification, smoking cessation, walking program
- antiplatelet therapy to prevent thrombi from the sluggish blood flow
- revascularization if necessary via open surgery or stent
- indications: tissue loss (nonhealing ulcers, etc), rest pain, lifestyle-limiting claudication
- options:
  - surgical bypass: vein conduit is always better than synthetic
  - angioplasty
  - stenting
  - atherectomy

- amputation is necessary in cases of critical ischemia or gangrene
  - BKA always preferred to allow possibility of patient walking again, also has lower mortality than AKA
    - however has a lower healing rate than AKA (70% vs 95%)
  - these patients will be at high risk of death from an MI

- Follow-up with yearly non-invasive arteriography

### 21.1.3 Cerebrovascular Disease

- **Background:**
  - most strokes are due to atherosclerotic disease at the carotic bifurcation
  - risk of stroke depends on degree of stenosis and presence of symptoms
    - symptomatic disease incurs 2-year stroke risk of 26%

- **Presentation:**
  - carotid bruits: not always a reliable sign
    - many patients with a bruit don’t have true carotid stenosis, and vice versa
  - TIAs due to emboli originating from carotid plaque
    - contralateral motor and sensory deficits, aphasia
    - ipsilateral amaurosis fugax (retinal artery embolization) = transient monocular blindness
  - RIND (reversible ischemic neurologic deficit) = focal neuro deficit that lasts > 24 hours but is reversible
  - CVA = focal neuro deficit > 24 hours that is NOT reversible
    - symptoms depend on vessels affected:
      - internal carotid artery = contralateral motor and/or sensory loss, expressive or receptive aphasia, ipsilateral monocular blindness
      - vertebrobasilar artery = diplopia, syncope, vertigo, dizziness = posterior neuro symptoms related to cerebellum that do NOT occur with carotid artery disease

- **Investigation:**
  - **duplex scan**: US + Doppler
    - test of choice for carotid artery disease
o determines velocity and direction of flow, detects wall defects, assesses severity of stenosis
  - follow-up for carotid bruits
- brain CT establishes baseline of cerebral cortex prior to operative intervention
- four-vessel arteriography: examines aortic arch, carotid arteries, vertebral arteries, and intracranial arteries
  - gold standard for diagnosis of lesions of in these areas
  - incurs procedural risk of stroke
  - alternative: CT/MR angiography
- Treatment:
  - when to repair:
    - asymptomatic with > 70% stenosis
    - symptomatic with > 50% stenosis
  - options:
    - carotid artery stenting: associated with higher risk of procedural stroke than endarterectomy, but also associated with fewer heart attacks
    - carotid endarterectomy: greatest complication is heart attack, also stroke, postoperative bleeding, damage to recurrent laryngeal, hypoglossal, or greater auricular nerves
- Follow-up all CVD patients with yearly carotid US

21.1.4 Abdominal Aortic Aneurysm

- Background
  - normally the aorta is ~ 2cm, it becomes aneurysmal when > 3 cm
  - more common in men
  - more commonly rupture in COPD patients
  - vs pseudoaneurysm: a collection of blood and connective tissue located outside of the vessel wall
  - caused by atherosclerosis and inflammation, with genetic/environmental influence
  - categorized based on morphology: saccular, fusiform (most common)
  - causes disruption of blood flow and prothrombotic state
  - rupture of the aneurysm most commonly occurs into the retroperitoneal space but is more deadly when it occurs in the peritoneal space
    - 80% mortality with rupture
  - risk factors for development: tobacco use, age, HTN, hyperlipidemia, atherosclerosis, male, familial predisposition
    - diabetes is protective!
  - risk factors for rupture: rapid progression, female, FH, uncontrolled HTN, smoking, COPD
- Prevention:
  - USPSTF recommends an US screen in all men age 65-75 who have ever smoked
  - Vascular Consensus Statement: screen all men 60-85, all women 60-85 if they have a cardio risk factor, and both sexes > 50 years old with FH of AAA
  - Presentation: usually discovered on accident during physical exam, otherwise may have pain in abdomen or back
  - if ruptured: severe pain, palpable abdominal mass, hypotension
- Investigation
• abdominal US
• CT if US is not informative or pre-op
• Treatment: surgical repair generally indicated when > 5 cm
  • endovascular repair: stent is placed to relieve pressure in aneurysm
    o considered elective in males at 5.5 cm and females at 4.5 cm
    ▪ consider doing earlier if there is rapid expansion
    o indicated for higher risk patients with conducive anatomy (when stent can make it through the groin)
      ▪ unfavorable anatomy may require open surgical repair
  • open surgical repair: aneurysm replaced with graft
  • if not that big, keep watching it and reimage, work on risk factor modification
    o don’t want to surgically intervene too early because the surgery has significant morbidity/mortality
• Post-op complications:
  • most common is MI
  • absent lower extremity pulses from arterial occlusion by dislodged emboli = “trash foot”
  • ARF from being clamped during surgery (ischemia)
  • colon ischemia: suspect if there is bloody stool in the first 24-72 hours
  • spinal cord ischemia: monitor for with neuromuscular exams (leg strength, sphincter function)

21.1.5 Acute Arterial Occlusion
• Caused by embolism or thrombosis
• Usually only occurs in an already-diseased vessel
• Presentation:
  • 5 P’s: pain, pallor, pulselessness, poikilothermia, paresthesias/paralysis
• Treatment: this is a surgical emergency that must be addressed within 6 hours of symptom onset or amputation will be necessary
  • thrombectomy or bypass

21.2 Suturing Techniques
21.2.1 Types of Suture Closures

<table>
<thead>
<tr>
<th>Closure Style</th>
<th>Information &amp; Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simple interrupted</td>
<td>Most useful and most commonly used.</td>
</tr>
<tr>
<td>Continuous</td>
<td>Fast but risk of strand breakage and wound dehiscence.</td>
</tr>
<tr>
<td>Vertical mattress</td>
<td>Good for creating everted wound edges. Most effective in accurate skin approximation with minimal wound edge tension and distortion. Can act as a deep as well as a superficial closure all in one suture.</td>
</tr>
<tr>
<td>Horizontal mattress</td>
<td>Good for creating everted wound edges.</td>
</tr>
<tr>
<td>Subcuticular (continuous intracutaneous)</td>
<td>Excellent for cosmetic purposes, eliminates crosshatching caused by suture marks. Can only be used for straight lacerations &lt; 2-3 inches long. Non-absorbable suture is recommended.</td>
</tr>
<tr>
<td>Procedure</td>
<td>Description</td>
</tr>
<tr>
<td>-----------------</td>
<td>---------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Deep dermal</td>
<td>Done at end of suturing. Reduces wound tension by bringing dermis close together before suture closure. Knot is “buried” so as to not interfere with epidermal healing.</td>
</tr>
<tr>
<td>Stellate</td>
<td>For closure of irregular wounds.</td>
</tr>
<tr>
<td>Ellipse method</td>
<td>For closure of wounds with a non-viable flap or circular wound. An ellipse is cut out.</td>
</tr>
</tbody>
</table>

### 21.3 Trauma and Care of the Acutely Injured Patient
- what is a flail chest, triage of trauma patients, Glasgow coma scale

#### 21.3.1 Trauma Background
- Death due to trauma occurs in three time periods:
  - seconds to minutes: patients will die regardless of intervention
  - minutes to hours: patients will die due to loss of airway or blood
    - reversible with early care
  - days to weeks: patients die as a result of infection, organ failure, or other causes
    - damage can be mitigated by appropriate pre-hospital care
- Advanced trauma/life support (ATLS) system focuses on traumas where death will occur within minutes to hours if there is no intervention
  - goal is to standardize care of the acutely injured patient
    - first step should be primary survey and resuscitation: ABCDE’s
      - airway: assess patency and ability to maintain patency
        - chin lift/jaw thrust temporarily opens airway
        - low intubation threshold for patients with impaired consciousness, compromised airway, or ventilatory problems
        - last resort is a cricothyroidotomy: 1 cm incision through cricothyroid membrane with subsequent placement of breathing tube
          - this is different than tracheostomy, which is placed lower and in a surgical setting
      - breathing: evaluate breath sounds and percuss lung fields
        - administer oxygen if needed
        - intubate if needed
        - treat pneumothorax, hemothorax, flail chest
      - circulation: pulse, BP, skin color
        - control severe external hemorrhage
        - obtain large-bore IV access and administer IVF as needed
        - EKG monitoring
        - treat arrhythmias
        - treat cardiac tamponade
      - disability: assess neurologic status, level of consciousness, motor functioning, pupils
      - exposure: remove all clothing while taking measures to prevent hypothermia
    - secondary survey (“fingers and tubes in every orifice”):
      - history from patient, family, and EMTs: allergies, meds, PMH, last meal, events related to injury
      - complete physical exam
        - head: lacerations, fx, rhinorrhea, otorrhea
- ears: hemotympanum
- eyes: visual acuity, pupils
- neck: tracheal deviation, spinal tenderness, stepoffs
- maintain midline immobilization during exam
- chest: breath sounds, symmetric chest rise, rib and sternal fx, heart sounds
- back: spinal tenderness, stepoffs, ecchymoses
- Abd: bowel sounds, distension, tenderness, contusions
- msk: pelvic instability
- rectal: sphincter tone, high-riding prostate
- GU: blood at urethral meatus
- neuro: Glasgow score
  - 13 = mild brain injury
  - 9-12 = moderate brain injury
  - ≤ 8 = severe brain injury
- place NG tube (or orogastric if concern for facial fx)
- place Foley
- radiology “triple trauma” studies - cross-table C-spine, portable CXR, pelvic x-ray
- labs: CBC, chem. 7, ABG, T&S, +/- chem. GI

- Level I trauma centers have 24-hour care by in-house surgeons, specialty care by on-call surgeons, and research and teaching
- Level II trauma centers are similar to level I but have no research/teaching component
- Level II trauma centers provide prompt assessment, stabilization, and resuscitation followed by surgical treatment or referral to a level I or II center

21.3.2 Common Life-Threatening Injuries

A.) Closed head injuries
- Concussion: temporary neurologic deficit without radiologic abnormality
- Contusion: focal brain bruise
- Intracranial hemorrhage:
  - epidural hematoma: usually an arterial bleed (middle meningeal artery) between the skull and dura mater, associated with skull fx, “lucid interval” following loss of consciousness
    - requires immediate surgical intervention
    - CT: biconvex, lenticular, limited by sutures
  - subdural hematoma: usually a venous bleed (tear of bridging veins) in potential space between the dura and arachnoid mater
    - may require surgical evacuation depending on severity
    - associated with underlying brain injury
    - acute, subacute, or acute-on-chronic
    - CT: crescent-shaped, crosses sutures
  - intracerebral hematoma: occurs within the parenchyma and is often associated with other injuries
  - subarachnoid hemorrhage: bleeding into the space between the brain and arachnoid mater, into the CSF space
    - usually due to trauma
    - can also be due to hemorrhage
      - Fisher grade: classifies appearance of hemorrhage on scan
        - 1 = no hemorrhage evident
        - 4 = hemorrhage with ventricular or parenchymal extension
      - Hunt Hess scale: classifies severity of symptoms
        - 1 = mild headache, slight nuchal rigidity, 70% survival
        - 6 = instant death
    - frequently missed on CT
    - rarely requires immediate treatment
    - may block arachnoid villi and cause hydrocephalus
Diffuse axonal injury: neurologic deficit resulting from prolonged global ischemia
- usually a result of traumatic deceleration injury to the white matter
- cerebral edema and raised ICP
- a microscopic shear injury that is usually not apparent on CT
- poor prognosis
  - consider head CT for all patients with altered consciousness, neurologic abnormalities, loss of consciousness > 5 minutes, or evidence of skull fx
  - treatment of all serious closed head injuries involves minimizing intracranial HTN and risk of herniation = intubation with hyperventilation (↓ CO2), careful fluid resuscitation, diuresis with mannitol?
  - use of steroids is not indicated

B.) Skull fractures: can be seen alone or in combination with brain injury
- non-depressed fx: rarely requires specific treatment
- depressed fx: may need surgical elevation to minimize damage to underlying brain
- open fx: requires early surgical intervention to reduce risk of infection
- basal fx: presents with CSF rhinorrhea, otorrhea, hemotympanum, raccoon eyes
- treatment is observation with antibiotics

C.) Spine trauma: injury to the spinal cord and/or vertebral column
- should be assumed in all significant trauma patients until the spine can be cleared clinically and radiographically
- immobilization in semi-rigid collar, spine board, logroll only
- central cord syndrome: when hyperflexion or hyperextension of the neck " loss of blood flow to spinal arteries " loss of neuro fcn in upper extremities with preservation of LE fcn
  - can be transient and improve with time
- Brown-Sequard syndrome: when partial transection of the cord " split in motor and sensory deficits
  - ipsilateral motor function deficit
  - contralateral sensory deficit
  - treatment:
    - steroids may be indicated in incomplete spinal cord injuries if started within a few hours of injury
    - preserve remaining function by preventing further ischemic injury to spinal cord
    - surgery for unstable injuries

D.) Pneumothorax: air in the pleural space usually resulting from mechanical ventilation or blunt lung trauma
- tension pneumothorax: air enters but does not leave the lung (closed space still under negative pressure) " mechanical compression of the heart and great veins
  - presentation: tracheal deviation away from side of pneumothorax, ↑JVD, ↓breath sounds, tympany to percussion, hypotension
  - investigation: diagnosis is clinical!
  - treatment: needle thoracostomy @ 2nd intercostal space in the midclavicular line, followed by chest tube placement @ 4th intercostal space in the midaxillary line
- open pneumothorax: penetrating trauma opens intrathoracic space to external environment " equilibration to atmospheric pressure and inability to expand lung
  - treatment: place one-way “flutter valve” dressing
E.) **Hemothorax**: blood in pleural space
- presentation: similar to pneumothorax with dullness to percussion
- treatment: chest tube

F.) **Flail chest**: when multiple consecutive rib fx produce a segment of chest wall with paradoxical movement during breathing
- treatment: intubation with mechanical ventilation

G.) **Cardiac tamponade**: acute accumulation of fluid in the pericardium
- can occur with blunt or penetrating trauma
- presentation: “Beck’s triad” of increased JVD, muffled heart sounds, hypotension
- investigation: US
- treatment: immediate pericardiocentesis +/- surgery

H.) **Intra-abdominal hemorrhage**: must be ruled out in every patient with significant trauma
- investigation:
  - stable patients without drugs or head injury → observation only with serial exams
  - unexplained hypotension or unreliable/equivocal exam → diagnostic peritoneal lavage
    - positive with aspiration of gross blood
  - stable patient but unreliable/equivocal exam → abdominal CT better than DPL because the retroperitoneum can be evaluated
  - US to detect free intraperitoneal fluid
  - unstable patient with evidence of abdominal injury or penetrating trauma → immediate exploratory laparotomy

I.) **Pelvic fractures**: can cause significant blood loss
- requires emergent external fixation
- pelvic angiography followed by embolization for continued bleeding

J.) **Extremity fractures**: can also cause blood loss

K.) **Coagulopathy**
- may patients arrive in trauma bay with prolonged clotting times, and IVF resuscitation further dilutes clotting factors
- hypothermia can also slow coagulation reactions
- acidosis affects pH-sensitive clotting factors

L.) **Hypovolemic shock**

M.) **Neck wounds**: neck is divided into 3 zones to help analyze wounds
- **zone I**: damage here → CT, bronchoscopy, esophagogram if stable
- **zone II**: damage here → immediate surgical exploration
- **zone III**: damage here → CT, bronchoscopy, esophagogram if stable

N.) **Pulmonary contusion**: from blunt trauma to the lungs
- suspect with overlying rib fx

O.) **Diaphragmatic injuries**
- can be caused by penetrating trauma
• investigation: CT, DPL, thoracoscopy, laparoscopy

P.) Small bowel ischemia

Q.) Splenic laceration or hematoma
• treatment: try to avoid operation to avoid post-splenectomy infection

21.3.3 Focused Abdominal Sonogram for Trauma (FAST)
• evaluates four anatomic areas
• Examines right upper abdomen, left upper abdomen, suprapubic region, and subxiphoid region

21.4 Congenital Heart Disease

21.4.1 Background
• Bicuspid aortic valve not included in this category, as the problem does not surface until adulthood
• Half require treatment within first year of life, although many are asymptomatic
• Fetal heart circulation:
  • blood carried in from placenta via umbilical vein □ liver □ bypass most of the liver via ductus venosus into the IVC □ right atrium
  • blood in right atrium:
    o can bypass right ventricle and enter left atrium via foramen ovale shunt
    o or can enter right ventricle □ pulmonary artery
      ▪ bypasses lungs via ductus arteriosus to empty instead into aortic arch
        • problem if ductus arteriosus remains patent after birth!
  • 2 right-to-left shunts: foramen ovale (RA to LA), ductus arteriosus (pulmonary artery to aorta)
• Classification of defects:
  • by clinical presentation: acyanotic, cyanotic, or valvular/aortic
  • by physiology: L to R shunts, R to L shunts, other
    o L to R shunts are acyanotic because the oxygenated blood from the L side of the heart is just flowing back through the lungs again
    o R to L shunts are cyanotic because the deoxygenated R sided blood is skipping the pulmonary circulation and instead going directly into systemic circulation
• Congenital defect presentations:
  • angina pectoris
  • dyspnea or tachypnea
  • syncope
  • poor feeding
  • irritability
  • cyanosis
  • failure to thrive
  • edema
  • ascites
  • palpitations
• Investigation:
  • most cases are diagnosed prenatally by US screening
  • CXR
  • functional or anatomic studies:
    o echo: main diagnostic tool for congenital heart disease, identifies most defects
    o MRI: similar utility to echo, better assessment of end-diastolic volumes
      ▪ currently not very useful in kids
      ▪ not the best for defining anatomy
    o cardiac cath: not routine, but commonly performed
21.4.2 Left to Right Shunts

- Causes:
  - atrial septal defects: can occur in the sinus venosus, ostium secundum, ostium primum
    - presentation: R heart failure, pulmonary edema, increased pulmonary vasculature
  - ventricular septal defect: the most commonly diagnosed congenital cardiac defect
    - presentation: holosystolic murmur, heart failure, Down’s syndrome association, increased pulmonary vasculature
  - atroventricular septal defect: entire septum between atria and ventricle is disrupted
    - endocardial cushion defect
    - associated with Down’s syndrome
    - presentation: R sided congestion, hepatomegaly
  - patent ductus arteriosus: persistent shunt between aorta and pulmonary artery
    - presentation: harsh continuous machine murmur
    - treatment: meds to make ductal tissue regress, surgical repair
  - Presentation: pulmonary congestion, Eisenmenger’s syndrome (phenomenon occurring with longstanding L to R shunts where increasing peripheral vascular resistance from pulmonary congestion will result in shunt reversal to a R to L shunt)

21.4.3 Right to Left Shunts

- Very unusual, as L sided pressures are usually much higher than the R side = most often occurs with transposition of the great arteries
- Causes:
  - transposition of the great arteries: aorta and pulmonary trunk switched so that deoxygenated blood gets pumped through the aorta to systemic circulation while the oxygenated blood gets pumped through the pulmonary artery back through the lungs
    - cyanotic
    - treatment: requires intracardiac/great vessel shunt for life outside uterus, and reparative arterial switch for long-term survival
  - truncus arteriosus: when aorta and pulmonary trunk get merged into one single trunk to supply both systemic and pulmonary circulation with mixed blood
    - presentation: cyanosis, systolic thrill, prominent apical pulse
    - treatment: must be repaired before age 2, 10% operative mortality
  - total anomalous pulmonary venous drainage: all four pulmonary veins are malpositioned and drain into the RA, SVC, or IVC
    - PFO or atrial septal defect must also be present for life to continue
    - must be repaired before 1st birthday, or risk 80-90% mortality
  - tetralogy of Fallot: pulmonary stenosis, overriding aorta, RV hypertrophy, and ventricular septal defect
    - most common cyanotic heart defect
    - results in decreased pulmonary blood flow
    - presentation: cyanotic “tet spells” where child turns blue, squats to valsalva and increase blood flow, harsh systolic precordial murmur
    - treatment: palliative shunt or curative surgical repair
  - tricuspid atresia: absence of tricuspid valve = no connection of RA to RV
    - ASD and VSD (or patent ductus arteriosus) must also be concomitantly present for life to be sustained

21.4.4 Systemic-Pulmonary Shunts

- Blalock-Taussig shunt: subclavian or carotid artery is abnormally connected to the pulmonary artery = increased pulmonary circulation
- surgical repair needed
21.4.5 Hypoplastic Ventricle
- Results in poor-performing ventricle
- For LV hypoplasia, surgical repair is done in 3 stages for a final result where the RV pumps to lungs and body all at once
- Prognosis: high operative mortality, CHF by 30s, heart transplant needed soon after

21.4.6 Obstructing Lesions
- Most commonly pulmonary stenosis
- Also aortic stenosis, aortic coarctation (narrowing of aorta distal to L subclavian artery), vascular rings

21.5 Acquired Heart Disease
21.5.1 Ischemic Heart Disease
- Background
  - stable angina: chest pain with activity or stress that can be controlled with medication alone
    - unchanged in pattern for 4-6 weeks
  - unstable angina: chest pain at rest that requires hospitalization and IV meds to control
- Investigation:
  - imaging available:
    - radionuclide angiography (MUGA) evaluates EF
    - perfusion scanning is used to detect ischemia
    - echoes
      - TEE allows for better visualization of valvular anatomy
- Treatment:
  - surgical: CABG or PCI (stenting)
  - CABG:
    - indicated for patients with L main coronary artery disease > 50%, coronary disease of 3+ vessels, failed medical management, complicated disease, and diabetics
    - preferred vessel is the internal mammary artery because its 10-year patency is > 90% (radial artery and great saphenous vein have lower lifespan)
  - meds:
    - survival benefit with beta blockers, ACEIs, statins
    - no survival benefit shown with aspirin, Ca channel blockers
- Complications:
  - post-MI complications: VSD, acute mitral regurg, LV aneurysm
  - post-CABG complications: stroke, MI, wound, afib

21.5.2 Valvular Heart Disease
- valve choices for valvuloplasty: mechanical, porcine, homograft, autograft
- mechanical valves are more durable, have lower reoperation rates, but have higher risk of thromboembolism
- tissue valves have lower clot risk and may be safer in older/debilitated patients but don’t last as long

A.) Aortic valve stenosis: obstruction □ increased pressure in LV □ LVH □ eventual heart failure □ systolic dysfunction □ progression of heart failure & irreversible LV injury
- from calcification:
  - associated with 50% increase in risk of cardiovascular death and MI
  - a result of inflammation, lipid accumulation, upreg of ACE, infiltration of tissue with macrophages and T-cells
  - development has same risk factors as for CAD: HTN, hyperlipidemia, DM, smoking, metabolic syndrome
  - senile aortic stenosis: age-related calcific build-up on a normal tricuspid valve
    - occurs by age 60-80
• **bicuspid aortic stenosis**: congenital abnormality that accelerates calcific build-up = stenosis occurs 10 years sooner than normal age-related stenosis  
  • treatment: statins  
  • rheumatic fever-related aortic stenosis: causes adhesion and fusion of cusps  
  • can also cause aortic regurgitation and mitral valve disease  
  • classification:  
    • normal valve is 3-4 cm²  
    • mild stenosis is < 1.5 cm² with pressure < 25 mm Hg  
    • moderate stenosis is 1-1.5 cm² with pressure 25-40 mm Hg  
    • severe stenosis is < 1 cm² with pressure > 40 mm Hg  
  • presentation: classic triad of angina, syncope, and CHF  
  • if early, may be asymptomatic with murmur  
    • systolic ejection: harsh, heard at aortic with potential radiation to neck  
      • S4 from the HTN  
  • late: DOE, SOB, angina (end-stage), syncope, CHF, paroxysmal nocturnal dyspnea, orthopnea, presyncope  
  • exam: pulsus parvus et tardus (pulse is slow in relation to contraction, and weak), hyperdynamic displaced apical impulse  
  • investigation: EKG for LVH, CXR for cardiomegaly, echo for valvular morphology/gradient/LV function (or cardiac cath to assess for all this plus concomitant CAD)  
  • treatment:  
    • no proven benefit with drugs other than statins  
    • valve replacement if severe  
    • aortic balloon valvotomy as bridge to surgery or palliative  

B.) **Hypertrophic cardiomyopathy**: a result of inappropriate hypertrophy of the septum with disorganized muscle bundles  
  • hypercontractility of LV with reduced ventricular volume, fibrosis of tissue  
  • background:  
    • hypertrophy unrelated to valvular disease or HTN  
    • can be asymmetric or global enlargement of the septum (or apex if Japanese)  
    • abnormal thickness and arrangement of wall muscle puts pt at risk for electrical dysfunction  
    • in many HCM patients there is obstruction to outflow of blood from LV (dynamic outflow obstruction)  
      • usually due to abnormal changing of pressure gradient during systole due to systolic anterior motion of the mitral valve (SAM, a kind of backwards mitral prolapse)  
      • LV must build up more pressure to overcome the regurg + increased O2 demand with increased filling pressures  
    • most commonly in men ages 30-50  
    • can be familial  
    • risk of sudden death is higher in <30-35 year olds due to arrhythmias  
    • can progress to dilated cardiomyopathy  
  • presentation: clinical deterioration is slow, most are asymptomatic or only mildly symptomatic  
  • dyspnea, angina, fatigue, syncope, afib  
  • patients without gradient will have minimal findings: LV lift, S4  
  • patients with established outflow obstruction: forceful/displaced apical impulse from thickened muscle, systolic thrill, S4, harsh crescendo systolic murmur +/- mitral regurg murmur  
  • investigation:  
    • must distinguish from aortic stenosis!  
      • valsalva will increase the murmur of HCM while it will decrease the murmur of AS  
      • carotid pulses will be brisk with mid-systolic decline in HCM while they are always sluggish in AS (parvus et tardus)  
    • EKG □ LVH, ST/T changes, giant T wave inversion (Japanese apical), Q waves  
    • echo □ LVH, asymmetric septal hypertrophy, outflow obstruction with SAM/dynamic pressure gradient  
    • cardiac cath to evaluate gradient  
  • treatment: manage symptoms  
    • beta blockers for angina, dyspnea, pre-syncope
- reduce outflow obstruction during exercise
- reduce O2 demand

- Ca channel blockers to reduce contractility, decrease outflow gradient, improve diastolic relaxation, and increase exercise capacity
- treat tachyarrhythmias: pacemaker or AICD
- surgical strategies: myectomy or mitral valve surgery, percutaneous ethanol ablation (inject alcohol into thickened septum to kill it)
- transplant for those with LV dilation

C.) Aortic valve regurgitation: causes increased end-diastolic vol in LV dilation of LV to accommodate increased end-diastolic pressure in LV backup into pulmonary circulation
- from aortic cusp or valve disease
- congenital: bicuspid or unicuspid
- infectious: rheumatic fever, infective endocarditis
- inflammatory: SLE, RA
- anorexic drugs
- from disease of aortic root: unhealthy tissue of cusp, annulus, or valve
- ex. Marfan syndrome, syphilis, ankylosing spondylitis, cystic medial necrosis, aortic dissection, trauma

- presentation
  - if acute: bacterial endocarditis, prosthetic valve dysfunction, aortic dissection
    - since there is no time for LV compensation, there will be flash pulmonary edema
    - classic physical findings will be absent
    - treatment: nitroprusside and surgery
  - if chronic:
    - symptoms of left-sided heart failure
    - increased pulse pressure
    - diastolic murmur: soft, blowing decrescendo at 1st and 2nd pulmonic due to regurgitant spray hitting the bicuspid
      - can cause premature closure of the bicuspid
    - S3 gallop: high pitched at 1st and 2nd pulmonic from changed ventricular compliance
    - Austin Flint murmur: mid-diastolic, low frequency murmur at the apex from regurgitant flow competing with inflow from the left atrium = functional mitral stenosis
    - DeMusset sign: head bob with each heartbeat
    - water hammer (Corrigan pulse): radial and carotid pulses are abrupt/distensive with fast collapse
    - Traube sign (pistol shot femoral): booming systolic and diastolic sounds heart over femoral artery
    - Muller sign: systolic pulsations of the uvula
    - Duroziez sign: systolic murmur heard over the femoral artery when compressed proximally, diastolic murmur heard when compressed distally
    - Quincke sign: capillary pulsations seen in fingernails or lips
    - Hill sign: when the SBP in the popliteal space is > 20 mm Hg higher than brachial SBP

- investigation: same as for aortic stenosis
- treatment:
  - meds: vasodilators (ACE or ARB or hydralazine + nitrates) reduce afterload, endocarditis prophylaxis in certain patients
  - aortic valve replacement if having symptoms of CHF, if acute with hemodynamic compromise, or if ejection fraction is < 55%

D.) Mitral regurgitation: causes increased end-diastolic vol in LA dilation of LA to accommodate increased end-diastolic pressure in LA backup into pulmonary circulation
- background:
  - most commonly due to pathological weakening of connective tissue or mitral valve prolapse
  - other causes: ischemic LV dysfunction post MI, dilated cardiomyopathy, rheumatic fever, ventricular dilation, papillary muscle dysfunction, mitral annulus calcification, congenital abnormality, bacterial endocarditis, anorexic drugs
presentation:
- acute: flash pulmonary edema, cardiogenic shock, new murmur
  - from bacterial endocarditis or other infection, papillary muscle rupture, chordae rupture, necrosis
- chronic: asymptomatic for years, then progressive L heart failure, afib
- holosystolic murmur at apex with radiation to axilla
  - severity of leakage correlated with duration of murmur rather than intensity
  - exaggerate with valsalva
  - decrease with squatting
- soft S1
- S3 often present
- JVD
- laterally displaced apical impulse
- investigation: EKG for LVH, echo, cath to grade severity
- treatment:
  - ACEI to reduce afterload
  - diuretics
  - digoxin
  - endocarditis prophylaxis
  - if acute surgery for valve reconstruction (vs replacement)
  - other indications for surgical repair: symptoms, LA enlargement + afib, LV dilation, decreased LV function

E.) Mitral valve stenosis: elevated LA pressure □ LA hypertrophy □ transmission of high pressures to pulmonary vasculature □ pulmonary edema

background:
- most commonly due to rheumatic heart disease (occurs 10-20 years after fever)
  - rarely due to congenital malformation or connective tissue disease
- mostly in women
- cardiac output is reduced
- can progress to right-sided heart failure
- hypertrophy of tissue makes it unhappy and prone to electrical problems like afib
- worsens with pregnancy because there is more demand for cardiac output □ increased HR
  - valve size is usually < 1.5 cm²
- presentation: fatigue, dyspnea, orthopnea, hemoptysis, peripheral edema, palpitations, afib (or associated embolic events)
  - S1 will be loud and palpable
  - opening snap of mitral stenosis after S2
  - low pitched diastolic rumble at apex (best heard in LLD or accentuate with exercise)
  - accentuated P2
  - RV heave if it has progressed to pulmonary HTN
- investigation
  - use echo to classify stage
    - normal if valve is 4-6 cm² with pressure gradient of 0 mm Hg
    - mild if valve is 2-4 cm² with pressure < 8 mm Hg
    - moderate if valve is 1-2 cm² with pressure of 8-12 mm Hg
    - severe if valve is < 1 cm² with pressure > 12 mm Hg
- treatment
  - if asymptomatic, may only need prophylaxis for endocarditis
  - initially try:
    - HTN management: diuretics & salt restriction to reduce blood volume, nitrates
    - afib management: antiocoagulation for high embolic risk
    - beta-blockers: control HR to prevent pulmonary edema (greater HR = greater disparity between what is pumped out and what the lungs are returning)
  - if patient remains symptomatic after meds or has episodes of pulmonary edema, decline in exercise capacity, or evidence of pulmonary HTN:
o mitral valve replacement
o balloon valvuloplasty

F.) Tricuspid stenosis: causes diastolic pressure gradient between RA and RV
- background:
  - uncommon in adults
  - affects more females
  - most frequently a result of rheumatic disease
  - rarely an isolated disease = other mitral/aortic defects usually coexist
  - presentation: symptoms related to elevated RA pressures such as edema, hepatosplenomegaly, ascites, fatigue, weakness
  - diastolic murmur is soft, high-pitched, and brief at left sternal border
    - increases with inspiration
  - JVD with giant venous A waves (whatever that means)
    - palpate liver to accentuate
  - treatment: if symptomatic with mean valve gradient is > 5 mm Hg ☐ balloon valvuloplasty or valve replacement

G.) Tricuspid regurgitation: failure of the tricuspid valve to close properly during systole ☐ leakage into the right atrium
- background
  - can be present in small degrees and be normal
  - causes of mod-severe regurg: Ebstein’s anomaly (displacement of valve towards apex), rheumatic disease, carcinoid, endocarditis, trauma from previous surgery
  - presentation: symptoms of RV failure
  - anasarca (woody looking edema)
  - JVD with c-waves & hepatojugular reflux
  - pulsatile liver
  - holosystolic murmur at left sternal border
    - increases with inspiration
  - afib
  - treatment: only if severe
    - diuretics for R-sided heart failure, digoxin for arrythmias, treatment for pulmonary HTN
    - surgery: repair is better than replacement
  - prognosis: not good if pulmonary HTN is present

21.5.3 Aortic Disease

A.) Thoracic aortic aneurysm: further classified as ascending, descending, or arch
- background
  - much less common than AAA
  - could be ascending or descending thoracic aorta, or arch
    - most to least common: aortic root or ascending aorta, descending aorta, arch
  - spontaneous rupture less common than AAA
  - symptomatic patients have greater chance of rupture
  - ascending thoracic aortic aneurysm: usually due to cystic medial necrosis (elastin degeneration) ☐ weakening of aortic wall ☐ formation of fusiform aneurysm
    - often involves aortic root as well ☐ aortic valve insufficiency?
    - cystic medial necrosis may be a normal result of aging but is accelerated by HTN, connective tissue disorders, RA, and bicuspid aortic valve
    - causes other than cystic medial necrosis: vasculitis, syphilis, atherosclerosis
  - aortic arch aneurysm: can be an extension of ascending or descending aneurysm
    - seen with history of trauma or deceleration injury (MVA, hockey, etc)
• **descending thoracic aorta aneurysm**: primarily caused by atherosclerosis
• presentation: most patients asymptomatic at diagnosis
• potential vascular symptoms: aortic insufficiency, CHF, thromboembolic event
• potential mass effect symptoms: SVC syndrome (compression from enlargement of aorta), tracheal deviation, cough, hemoptysis, dysphagia, hoarseness
• steady, deep, severe substernal/back/neck pain
  o excruciating pain if ruptured
    ▪ hematemesis if ruptured into the esophagus
• investigation:
  - CXR □ widened mediastinum, enlarged aortic knob, tracheal displacement
  - MRI or CT if negative
  - echo
• treatment:
  - surgeries are much more complicated than for AAA with greater risks, rarely done
  - weigh risk of rupture (increased for Marfan’s or bicuspid aortic valve)
  - when surgery is indicated (gender is not considered in these kinds of aneurysms):
    o ascending aortic aneurysm □ 5.5 cm
      ▪ aortic root replacement: Bentall or David procedure (David more common)
    o Marfan’s or bicuspid valve □ 5 cm
    o aortic valve replacement □ 4 cm
    o descending aortic aneurysm □ 6 cm

B.) **Aortic dissection**: a tear in the inner wall of the aorta causes blood to flow between the layers of the wall of the aorta, tearing the layers apart and creating a false lumen
• background
  - can be acute or chronic
  - predisposition to tearing with connective tissue disorder, bicuspid aortic valve, or coarctation of the aorta
  - more common in men 60-70 years old
    o but for females there is an increased risk in pregnancy in last trimester
  - often preceded by medial wall degeneration or cystic medial necrosis
  - tear usually goes in direction of blood flow but can go backwards
  - most occur in the ascending or descending aorta, just past aortic valve or at ligamentum arteriosum
  - usually a result of poorly controlled HTN
• presentation
  - acute: sudden, excruciating, “ripping” pain in chest, hyper or normotensive, shock, pulse discrepancy, syncope, acute aortic regurg, focal neuro deficits or CVA due to nonperfusion of brain
• investigation
  - CXR □ widened mediastinum, left sided pleural effusion, or could look normal
  - EKG for LVH or signs looking like inferior MI (cusps associated with dissections are in the same region)
  - TEE is the best screening test
• treatment
  - all pts need aggressive BP control
  - may be based on classification
  o **Debakey classification**: takes into account origin of dissection
    ▪ Debakey I = ascending aorta with extension to the arch and maybe beyond that
    ▪ Debakey II = ascending aorta only
    ▪ Debakey III = descending aorta only
  o **Stanford classification**: more commonly used, doesn’t care about the origin
    ▪ Stanford A = any involvement of ascending aorta
      ▪ go directly to surgery
Stanford B = not involving ascending aorta
- may be medically managed unless there are symptoms of rupture, ischemia, ongoing pain, uncontrolled HTN, or aortic regurg
- higher mortality procedure
- chronic or asymptomatic drugs + yearly re-imaging
- prognosis: > 20% intraoperative mortality, with only 50% 10-year survival for all hospital survivors

C.) Aortic transsection: tear or rupture of the aorta due to trauma
- 80% of victims die at the scene
- investigation: CXR, TEE, CT scan, angiography
- treatment: emergency operation
- prognosis: high rate of paraplegia post-op due to spinal cord ischemia

21.5.4 Cardiac Tumors
- 75% are benign but still need to be removed to prevent emboli or obstruction
- most arise in the left atrium mitral stenosis like symptoms
- diagnose with echo
- Malignant tumors include angiosarcomas and mets from the lung, breast, or melanoma
- create bloody effusion around heart

21.5.5 Acute Pericarditis
- acute inflammation of the pericardium
- background:
  - idiopathic or viral
  - can be caused by MI, any kind of heart surgery, TB, neoplasm, or trauma
  - tissue has increased vascularity with fibrous adhesions and exudate
- presentation:
  - chest pain: pleuritic, hard to distinguish from ischemia, aggravated by laying down
  - pericardial friction rub: pre-systolic, ventricular systolic, and early diastolic
  - dyspnea from chest pain
  - symptoms of underlying illness
- investigation:
  - serial EKGs diffuse ST elevation with inverted T waves, then return of ST to baseline with flat T waves, then T wave inversion, then normal T waves
  - labs: inflammatory markers, myocardial markers
  - echo for effusion
  - pericardiocentesis for patients with tamponade
  - biopsy?
- treatment: treat underlying cause
  - watch for development of tamponade
  - pain relief: bed rest, NSAIDs, aspirin, corticosteroids, colchicine
  - antibiotics +/- drainage
  - IV anticoagulants
  - prognosis: usually self-limiting, some can have recurrent symptoms (give chronic colchicine therapy)

21.5.6 Cardiac Transplantation
- Indications: NYHA class IV, age < 65, good psychosocial functioning
- Contraindications: portal HTN, poor medical management, infection, malignancy
- Complications: rejection, infection
- Prognosis: 5-year survival of 78%

21.6 Wound Healing, Sutures, and Wound Closures
21.6.1 Background

- Cells are high in K, so when they lyse patients can have hyperkalemia
- Types of wound closures:
  - primary closure: prompt suture (or graft or flap) closure after irrigation, heals rapidly with best scar
    - for wound with low risk of infection
  - secondary intention: wound is left open to granulate, involves debridement, irrigation, and frequent dressing changes
    - for contaminated wounds at high risk of infection
    - slower healing but strength is adequate
  - delayed primary closure (tertiary intention): wound is cleaned, debrided, irrigated, and closed 3-5 days later
    - allows for reduced bacterial counts before closure
  - tissue transposition: flaps and grafts used for wounds that are too large to close with adequate cosmetic and functional results
- Layers of the skin
  - epidermis: stratified squamous epithelium
  - dermis: papillary and reticular; contains collagen, elastin, matrix
- Key factors in wound healing: platelet-derived growth factor, histamine, prostacyclin, TGF-B
- Epithelium should cover wound within 48 hours, don’t need to protect from water after this
  - but no baths for 6 weeks

21.6.2 Steps in Wound Healing

1.) Coagulation: release of thromboxane → vasoconstriction and platelet recruitment → mast cell histamine release → extravasation of WBCs, fluid, electrolytes, macromolecules

2.) Inflammation/proliferation:
- neutrophils arrive within 2 minutes to phagocytose and release cytokines
- neutrophils are not essential for wound healing, but macrophages are
  - die in 24-48 hours → release of lysozymes to digest necrotic debris
  - release proteases, IL-1, TNF
  - attract fibroblasts, which appear after the first 24 hours
  - fibroblasts predominate by day 10
- macrophages also arrive around time of neutrophils and predominate after the 3rd day

3.) Proliferation: rapid cell growth and turnover of epithelium and fibroblasts, formation of granulation tissue
- marginal basal cells migrate along fibrin mesh and usually close the wound within 48 hours
- endothelial cells produce TPA to lyse the fibrin mesh and allow growth of new capillaries
- ground substance produces collagen
  - cofactors required: vit C, vit E, Fe, oxygen, protein, galactose, glucose, manganese

4.) Maturation: lasts months to years
- wound shrinking, thinning, and paling
- fibroblasts change to myofibroblasts to form actin-myosin complexes for wound contraction
- cross-linking of collagen to give tensile strength
- provided by fascia and dermis, not fat
- dissolution of poorly organized collagen by collagenase
- strength of wounded area will only be 80% of its original strength
- strength plateaus 1 year after injury

21.6.3 Factors Putting Patients at Risk for Poor Wound Healing

- Vasoconstriction in smokers → stop smoking
- Diabetics → tight control of blood sugars
- HTN → prompt pain control and antihypertensives
- infection → dilute pathogens, give preoperative antibiotics
- hypoperfusion → maintain adequate blood vol, BP, and hct
• hypoxia □ maintain constant oxygen sats, incentive spirometry, coughing, deep breathing
• pain □ analgesia
• hypothermia □ warm OR and post-op blankets
• poor nutrition □ augment preop nutrition and postop
• albumin, vit C, vit A, zinc
• steroids □ give vit A and wean off steroids ASAP
• immunosuppression □ give vit A
• foreign bodies □ remove and debride surrounding tissue
• significant anemia □ transfusions PRN
• obesity □ encourage preop weight loss whenever possible
• osteogenesis imperfecta (type I collagen deficiency with blue sclera)
• Ehlers-Danlos syndrome
• ionization radiation
• aging & loss of collagen
• drugs: doxorubicin, tamoxifen, antiestrogens, glucocorticosteroids

***Chronically inflamed wounds that do not proceed to closure are at risk for developing squamous cell carcinoma
• derangements in levels of cytokines, growth factors, or proteases
• can occur with foreign body

21.6.4 Scars
• Occur with excessive collagen deposition vs degradation
• Keloids: scars that grow beyond the border of original wound and rarely regress with time
• Hypertrophic scars: raised scars within confines of original wound that frequently regress spontaneously

21.6.5 Surgical Wound Classification
• **Clean**: an uninfected, nontraumatic operative wound in which no inflammation is encountered and the respiratory, alimentary, genital, or urinary tract is not entered
  • primary closure indicated
  • infection rate < 5%
• **Clean-contaminated**: an operative wound in which the respiratory, alimentary, genital, or urinary tracts were entered under controlled conditions and without unusual contamination
  • can use primary closure
  • infection rate < 10%
• **Contaminated**:
  • open, fresh, accidental wounds
  • operative wound with major breaks in sterile technique or gross spillage from intestinal tract
  • incisions in which acute, nonpurulent inflammation was encountered
  • infection rate < 15%
• **Dirty**:
  • old traumatic wound with retained devitalized tissue
  • wound involving existing clinical infection
  • perforated viscera
  • infection rate 30%

21.6.6 Tetanus and Wounds
• Previously immunized patients:
  • if last booster was 10+ years ago, give another booster (tetanus toxoid)
  • if last booster was 5+ years ago, give another booster except for wounds that are very clean
  • if last booster was < 5 years ago, no further action needed
• Non-immunized patients:
  • give tetanus booster and 250 U of tetanus Ig
21.6.7 Wound Dressings
- Open contaminated wound with wet-to-dry saline soaked dressing (intermittent debridement) or wound vac (continuous debridement = better option)

21.7 Neurosurgery

21.7.1 Brain Anatomy
1.) Cerebrum
- frontal lobe: higher functions, consciousness, stimuli response, motor coordination
- parietal lobe: vision and touch, coordination of sensory input, writing, math, language, body position, drawing, handling objects, verbal and nonverbal memory
- temporal lobe:
  - left: hearing, understanding, visual and auditory memory, word recognition, personality, behavior, sex
  - right: hearing, understanding, organizing, concentration, recognition of musical tones, personality, behavior, sexual behavior
- occipital lobe: vision, interpretation of visual images, object recognition, reading, writing, finding objects, color identification

2.) Cerebellum: balance, posture, motor control, some memory for reflex movements
3.) Brain stem: breathing, HR, digestion, alertness, sleep, balance

21.7.2 Intracranial Tumors
- Benign tumors have distinct boundaries, don’t metastasize, surgery alone may be curative
- Malignant tumors metastasize and require adjunct therapy to surgery
  - but mets seldom occur outside of the CNS
- Mets to the brain often come from lung and renal cancers, also breast, colon, melanoma
  - usually go the cerebrum
  - show up as ring-enhancing lesions, usually between white and gray matter
- Tentorium is an important dividing line, with lesions above and below having different characteristics
  - supratentorial masses:
    - lateral: in the lobes
      - presentation: epilepsy/seizures, dysphasia, parietal spatial disorders, sensorimotor hemiplegia
    - central: anterior III ventricle (in the basal ganglia, corpus callosum, foramen of Monro), sellar, parasellar
      - more likely to cause hydrocephalus due to proximity to the ventricles
      - anterior II ventricle presentation: Parkinsonism, hemiplegia, capsular hemianopia, precocious puberty, endocrine imbalance with obesity or wasting
      - sellar & parasellar mass presentation: chiasmal compression, endocrine abnormalities
  - infratentorial masses:
    - infants: prominent sutures, tight fontanelles, large head, vomiting, headache, squint
    - lateral: cerebellar hemisphere, cerebello pontine angle
      - presentation: ataxia, intention tremor, rotational or vertical nystagmus, dysphagia, dysarthria, CN palsies
    - central: vermis, IV ventricle, foramen magnum
      - presentation: vomiting, facial palsy, respiratory abnormalities
  - transtentorial masses:
    - lateral: attached to tentorium, through hiatus
    - central: midbrain, posterior III ventricle
  - Investigation:
    - MRI is the study of choice
    - pan CT of chest, abdomen, pelvis
    - biopsy or resection to confirm pathology
21.7.3 Epilepsy

- Surgery in appropriate candidates offers an 85% cure rate
  - e.g., medication failure, uncontrolled epilepsy
- Resection
- Palliative vagal nerve stimulator reduces seizures by 30-60%
- Choose treatment by location of seizure

21.7.4 Functional Neurosurgery

- For movement disorders, Parkinson’s, essential tremor, dystonia, pain
- Procedures available: deep brain stimulator, motor cortex stimulator, epidural stimulator, baclofen pump placement, selective dorsal rhizotomy
  - dyskinesia/rigidity □ target subthalamic nucleus or globus pallidum
  - tremor □ target thalamus
  - pain in body □ target sensory thalamus
  - pain in limbs or back without structural lesion □ epidural stimulator
  - spasticity □ baclofen pump or selective dorsal rhizotomy
  - cancer pain □ morphine intrathecal pump

21.7.5 Traumatic Brain Injury

- May involve skull fx, epidural hematoma, subdural hematoma, subarachnoid hemorrhage, diffuse axonal injury, contusions
- See trauma lecture
- Craniosynostosis: a condition in which one or more of the fibrous sutures in an infant skull prematurely fuses by ossification □ change in the growth pattern of the skull
- Causes: metabolic, mucopolysaccharidoses, mucolipidoses, hematologic disorders, teratogens, malformations
- Can occur in syndromes, with Crouzon and Apert being the most common
- Crouzon = skull deformity, facial deformity, exophthalmos
  - frequently occurs with hydrocephalus
- Apert = high brachycephalic head and severe syndactyly of the limbs
  - frequently seen with cleft palate, mental retardation
- Surgery indicated with increased intracranial pressure, ocular dysmorphia, aesthetic concerns

21.7.6 Myelomeningocele

- Most severe form of spinal bifida where the unfused portion of the spinal column allows the spinal cord to protrude through an opening in the external skin
- Associated with genetic inheritance, trisomy of 13/18, decreased folic acid intake, teratogens
- Usually occurs in lumbar or sacral region and leaves infant with disability even with surgical closure
- Screening:
  - maternal serum AFP at weeks 16-18
  - US: lemon sign or banana sign
  - amniocentesis + US has highest sensitivity
- Treatment:
- planned C-section with emergency closure of defect within 24 hours, antibiotics
- Complication: tethered cord (abnormally low conus medullaris)
- presentation: scoliosis, gait disturbance, motor and sensory deficits, bladder and bowel dysfunction
- treat with surgical laminectomy and cord untethering, other supportive surgeries

21.7.7 Hydrocephalus
- abnormal accumulation of CSF in ventricles
- Two kinds:
  - communicating hydrocephalus
  - noncommunicating (obstructive) hydrocephalus
- Causes: meningitis, hemorrhage, myelomeningocele, choroid plexus papilloma, Chiari malformation, aqueductal stenosis, tumors
- Presentation: cranial enlargement, facial growth, irritability, nausea, vomiting, poor head control, enlarged/bulging fontanelle, upward gaze palsy, hyperactive reflexes, irregular respirations with apneic spells, bradycardia
- Treatment:
  - taps
  - shunts in adults: lumboperitoneal is best option
  - Follow-up with CT shunt flow study to ensure functioning

21.8 Common Office Procedures
21.8.1 Common Complaints
1.) Lacerations
- primary closure for clean wounds < 6-8 hours old
- dry dressing for 2-3 days during epithelialization
- sutures removed and replaced with steri strips in 3-10 days
- secondary intention closure for dirty wounds or those > 8 hours old
- debridement
- dressing for 1-3 days to absorb secretions
- subsequent wet-to-dry dressings for 3-5 days
- closure with sutures are steri-strips after appearance of granulation tissue

2.) Puncture wounds: gunshot, stab, etc.
- always dirty
- irrigation and debridement
- packing with gauze changed every 1-2 days
- foreign body removal if needed

3.) Abscesses: includes boils, furuncles, carbuncles
- not on finger:
  - drain and culture pus
  - pack initially with dry gauze and then wet-to-dry dressings
- on finger:
  - paronychia: infection of nail base
    - raise nail to express pus
    - warm moist compresses for 24 hours followed by dry dressings for 3-4 days
  - felon: infection of finger pad
    - lance and drain
    - pack with petroleum gauze for 2-3 days then dry dressings
  - if due to ingrown nail, remove ingrown portion of nail

4.) Subungual hematoma: collection of blood under nail due to blunt trauma
- remove pressure by making a small hole in nail
5.) Animal bites
   - always leave open initially
   - give broad-spectrum antibiotics
   - risk of hemolysis with snake and venomous reptile bites

6.) Pigmented lesions
   - suspicion for melanoma with asymmetry, irregular borders, variegated color, increasing diameter
   - always punch biopsy any pigmented lesions
   - lesions that can be shaved: skin tags, basal cell carcinoma, molluscum contagiosum, nevi, papilloma, warts, others

7.) Skin and soft tissue lesions
   - lipomas: only excise if symptomatic
   - epidermal inclusion cysts: arise from obstructed follicles; contain disgusting stuff
   - frequently recur
   - I&D with removal of the cyst lining
   - seborrheic keratosis: curettage after slight freezing
   - actinic keratosis: skin biopsy, liquid nitrogen, topical creams
   - skin cancers: excise with a margin

8.) Traumatic wounds
   - irrigate
   - control bleeding
   - closure vs leaving open
   - leave open: pack with soaked strips, cover with dressing, change daily
   - closure: anesthetic, suture
     - small suture (5-0 or 6-0) if on the face
     - absorbable if below the skin, inside mouth, or in difficult area
     - usually non-absorbable
     - staples for scalp, trunk, some extremities

21.8.2 Office Anesthesia

Types:
   - **local anesthesia**: topical or intradermal injection at the wound site
     - work by blocking Na influx = voltage gated Na channels can’t work
     - loss of pain, then temp, then touch, then motor function
     - acidic (infected) tissues have reduced penetration of anesthetics
     - be aware of risk of toxicity: CNS symptoms first, then cardiovascular
     - most common is lidocaine
       - most rapid
       - can be combined with epinephrine for local vasoconstriction
         - don’t use on digits, ears, nose, penis due to risk of ischemia
       - mepivocaine: takes 20-30 min
       - bupivicaine: takes 30-45 min
   - **field block**: infiltration of local anesthetics all around the wound site
     - for irregular wounds or in areas of thin or difficult to handle skin
   - **peripheral nerve block**: injection of local anesthetics adjacent to appropriate peripheral nerve
     - good for procedures on the digits
   - Pre-medication with analgesics or anxiolytics if needed
   - Injection technique:
     - gentle cleaning of wound
     - warm lidocaine to room temperature
     - buffer anesthetic solution with sodium bicarb to minimize sting, increase onset, neutralize pH
     - use small-gauge needle
     - minimize pain: have pt keep eyes open, distraction techniques, leg lifts, vibrate or pinch skin as you inject
• aspirate before injecting to make sure you’re not in a blood vessel
• test adequacy of anesthesia before beginning procedure

21.9 Chest Tube Placement

21.9.1 Chest Tube Insertion

• Indications: pneumothorax, fluid in the chest, prophylaxis for high risk patients (rib fx, penetrating trauma, positive pressure ventilation)
• Technique:
  • place the patient in the supine position
  • prep the skin with providine-iodine solution and drape operative site
  • measure the chest tube from the desired entrance site to the apex of the chest.
  • anesthetize the skin with lidocaine using a 25-gauge needle. Anesthetize the deeper tissues with a 20-gauge needle. The pleura should be infiltrated with lidocaine.
  • incise the skin one interspace below the desired site of insertion.
  • create a subcutaneous tunnel with a Kelly clamp over the rib above the incision.
  • enter the pleural space immediately above this rib with the tip of the clamp and open the clamp, spreading the pleura
  • insert a finger into the hole and confirm that the space is free of adhesions
  • grasp the tip of the thoracostomy tube with the Kelly clamp and insert both into the pleural space
  • direct the tube superiorly and posteriorly for drainage of hemothorax or hydrothorax and anterior for pneumothorax
  • ensure that the last hole in the tube is within the thoracic cavity and secure the tube to the skin with a suture.
  • cover with a sterile dressing and connect to the drainage system
• Complications: hemorrhage, infection, lung laceration, cardiac injury, subcutaneous placement, pulmonary edema, intraperitoneal tube placement

21.10 Intubation

21.10.1 Tracheal Intubation

• Indications:
  • airway protection
    • compromised airways in facial fx, neck trauma, decreased level of consciousness (drugs or head injury), laryngospasm, extrinsic compression, foreign body
      • signs: agitation, tachypnea, stridor, gurgling, hoarseness
    • tongue can obstruct airway
  • inadequate ventilation or oxygenation
    • compromised in head injury, shock, general anesthesia, spinal cord injury, neuromuscular paralysis, COPD, rib fx, pneumonia, PE, secretions
• Relative contraindications: awake patient, severe airway trauma and obstruction, C-spine injury
• Options:
  • first choice is orotracheal intubation
  • 2nd choice is nasotracheal intubation because it is a blind technique
    • good for cervical spine injuries, other spine injuries, clenched teeth, jaw fx, obesity, arthritic neck
    • contraindicated in apnea, severe midface fractures, basilar skull fx, coagulopathy
  • last resort is surgical airway: cricothyroidotomy or tracheostomy
• Technique:
  • preoxygenate for 5 minutes in controlled setting
  • use an uncuffed ET tube in kids < 8
  • use a curved laryngoscope (Mac) blade in adults and a straight one (Miller) in kids
  • always hold laryngoscope in left hand
  • insert laryngoscope on right side and advance while sweeping to the left
• external pressure on cricoid cartilage can help visualize vocal cords
• don’t take more than 30 secs before ventilating with bag/mask
• confirm tube placement
• Complications: hypoxia, respiratory acidosis, HTN, arrhythmias, elevated ICP, aspiration, bronchospasm, trauma to teeth, oropharynx, C-spine, eyes
  • long-term: accidental extubation, ventilator-associated pneumonia, vocal cord paralysis, tracheal ischemia, sinus infections

21.10.2 New Techniques
• Laryngeal mask airway
• Esophageal tracheal Combitube

21.10.3 Orogastric and Nasogastric Tubes
• NG tubes
• tolerated by awake patients
• can speak
• Orogastric tubes
• usually in unresponsive patients
• safe in facial trauma

21.11 Orthopedic Surgery
• rotator cuff tears, injuries that need to be referred to ortho right away, when to give post-op antibiotics, indications for pre-op antibiotics

21.11.1 Anesthesia
• Local + sedation for knee scopes, smaller cases
• Blocks + sedation for axillary, interscalene, spinal, ankle, rotator cuff surgeries, ACL reconstruction
• General for when blocks are contraindicated

21.11.2 Knee Injuries
• Meniscal tears
• MOI: twisting, deep flexion
  • presentation: swelling, pain with weight bearing, twisting, or squatting, joint-line tenderness, mechanical symptoms
  • treatment:
    o conservative if symptoms are not significant
    o surgical: arthroscopy with resection or repair
      • bucket-type tear needs surgery right away to fix it
• ACL tear
  • MOI: twisting on planted foot, hyperextension, collision, cutting sports
  • commonly associated with bone bruising and meniscal tear
  • treatment: evaluated case by case as it is a major surgery that you won’t want to do in everyone
    o initial: weight-bearing activity, NSAIDs, ice, aspiration, PT, gradual return to activity
    o arthroscopic reconstruction: autograft vs cadaver
      • followed by PT and 6 months rest from cutting sports
• Knee osteoarthritis
  • presentation: pain (initially with activity only), stiffness and loss of ROM
  • treatment:
    o conservative: activity modification, PT, weight loss, acetaminophen, steroid injections, viscous supplementation
    o surgical: total knee arthroplasty
21.11.3 Hip Osteoarthritis

- **Presentation:** pain increased by walking, painful limp, decreased ROM
- **At risk:** > 60 years old, avascular necrosis from prolonged steroid use
- **Treatment:**
  - conservative: intra-articular steroid injections, PT
  - surgical: total hip arthroplasty or resurfacing
  - only if steroid injections do not adequately control symptoms

21.11.4 Shoulder Injuries

- **Impingement syndrome:** shoulder pain commonly caused by impingement of the acromion, coracoacromial ligament, AC joint, and coracoid process on the underlying subacromial bursa, rotator cuff, and biceps tendon
  - disease occurs on a continuum, from chronic bursitis/tendonitis to complete rotator cuff tear
    - rotator cuff tear:
      - rare in a person under age 40
      - presentation: weakness and pain with resisted flexion and external rotation
      - treatment:
        - conservative: PT, NSAIDs, subacromial cortisone injection
        - surgical (after 8-16 weeks):
          - arthroscopy with subacromial decompression
            - indicated for patients with fatty infiltration of muscle, presence of GHJ arthritis
          - shoulder reverse replacement for irreparable tear
  - Adhesive capsulitis
    - higher incidence in diabetics
    - treatment:
      - conservative (first 6 months): injections, PT
      - surgical: arthroscopy for lysis of adhesions
  - Shoulder dislocations
    - most commonly anterior
    - associated with bony Bankart fx and rotator cuff tear in the elderly
    - Labral tear
    - SLAP tears
      - presentation: + O'Brien's and Speed's tests, clicking, popping, pain with activity
      - treatment: arthroscopic repair

21.12 Non-Small Cell Lung Cancer

21.12.1 Lecture Highlights:

- **Majority of lecture:**
  - lung cancer is more deadly in women than any other cancer so therefore we should spend more money researching it than we do on breast cancer and HIV research
  - it's always lung cancer
  - tell the insurance companies "it's XYZ until proven otherwise" any time you want imaging done that they won't cover
  - Most deaths are due to distant mets
  - Small cell lung cancer:
    - less than 20% of new cases
    - not surgically treated, rather treated with chemo and radiation
    - low survival rate for extensive disease
    - likes to metastasize
    - NSCLC:
• most lung cancer cases
• includes squamous cell carcinoma, adenocarcinoma, carcinoid, large cell cancer, others
  o adenocarcinoma is located more peripherally
• Most cases present symptomatically at stage III or IV
• stage I findings are usually incidental

Imaging:
• CXR is first step for lung ca suspicion
• CT provides additional information about lymph nodes
• PET for metastatic survey
  o requires concomitant CT and lesions > 8 mm
• MRI used for evaluation of mediastinal or chest wall invasion
• brain CT for abnormal PET or clinical suspicion

Further investigation:
• bronchoscopy
• transthoracic needle aspiration
  o risk of pneumothorax, lots of false negatives
• cervical mediastinoscopy
  o needed for lymph node status
  o last step in determining staging
  o alternative: endobronchial US
  f. anterior mediastinoscopy
    o only for patients with aortopulmonary adenopathy
• Treatment:
  • evaluation of pulmonary functioning
  • complete surgical resection
    o thoracoscopy
  • adjuvant chemo +/- radiation (before surgery if stage III)

21.13 Esophageal Cancer

21.13.1 Lecture Highlights

• Background
  • more frequent in men and blacks
  • highest incidence in northern China and Japan
  • squamous cell tumors are most common, but incidence of adenocarcinoma is increasing
    o may be due to increased GERD □ Barrett’s esophagus
  • low 5-year survival
  • risk factors: heavy alcohol use, heavy smoking, FH, poor nutrition, Fe deficiency anemia, Barrett’s esophagus, reflux esophagitis, longstanding reflux, hot beverages, caustic injuries, underconsumption of nutritious foods
• Presentation:
  • usually advance disease if symptomatic: dysphagia, weight loss, pain, anemia, hoarseness, tracheoesophageal fistula, bronchitis, lung abscess, cardiac arrhythmias
  • proximal and middle tumors are usually squamous cell carcinoma
  • distal tumors are usually adenocarcinoma
• Investigation:
  • barium swallow confirms need for EGD
  • EGD for biopsy
  • chest and abdominal CT
  • esophageal US for staging
  • PET for metastatic survey
  • bronchoscopy if suspected bronchial involvement
• Treatment:
  • advanced disease is not resectable
o palliative measures: gastrostomy feeding tube, laser ablation or photodynamic therapy, stent placement
- if T3N1 or better, surgical resection is best
  o preoperative induction chemo + radiation + platinum
  o esophagectomy, removal of part of stomach, lymph nodes
- Complications: malnutrition, aspiration pneumonia, hemorrhage, sepsis, tracheoesophageal fistula, dumping syndrome, reflux, Anastomosis leakage

21.14 Transplantation

21.14.1 Lecture Highlights:
- Best 5-year survival in kidney and kidney-pancreas transplants
- Recent trend in increased deceased donors vs living donors, although total transplant demand is going up
- Types of transplants:
  - isograft/autograft = identical twin or self graft
  - allograft = same species
  - xenograft: different species
- Transplant immunology:
  - matching transplants:
    o crossmatching is a more specific test that determines tissue compatibility between donor and recipient
    o panel reactive antibody testing is a more general test where recipient’s blood is tested for antibodies against a panel of foreign antigens
- tolerance means there is no immune reaction against an antigen
- MHC I is found on all nucleated cells in the body
- MHC II is found in APCs like B-cells, macrophages, dendritic cells
- transplant rejection:
  o methods:
    ▪ direct pathway: killing by CD8 cells
    ▪ indirect pathway: activation of CD4 cells by APCs holding foreign protein from donor
  o types of rejection:
    ▪ hyperacute: immediate rejection by a type I hypersensitivity reaction
      • requires previous exposure to the antigen and preformed antibodies ready and waiting
      • occurs with transplantation of organs of wrong blood type or in a patient who has had multiple past blood transfusions
    ▪ acute: rejection 5-90 days after transplant
      • T-cell mediated
    ▪ chronic: graft vasculopathy that occurs in every transplant patient unless organ came from an identical twin
      • macrophage mediated
- Preventing rejection:
  - induction immunosuppression: given before or at time of transplant
    o involves use of anti-lymphocyte antibodies, antimetabolites (azathioprine, mycophenolate mofetil)
    o used to bridge therapy until maintenance suppression is at target level
  - maintenance therapy: long term therapy that makes use of 2-3 drugs
    o uses a specified parameter of drugs that works in 95% of the population
    o antimetabolites
    o calcineurin inhibitors (cyclosporine or tacrolimus)
    o mTOR inhibitors (sirolimus, everolimus)
- treatment of acute rejection: steroid and antilymphocyte preparation given for several days
  o can use horse anti-human lymphocyte antibodies in steroid-resistant cases
    • risk of serum sickness and anaphylaxis
• anti IL-2 antibodies (daclizumab, basiliximab)
  • tacrolimus
• complications of immunosuppression include infection and increased cancer risk (esp squamous cell skin cancer)
• Mechanics of transplantation
  • keeping the organs cold reduces metabolic demand
  • preservation solution to reduce free radicals and nourish organ with glucose
  • hearts: 6 hours
  • lungs: 8 hours
  • pancreas: 24 hours
  • liver: 2 days
  • kidneys: 3 days
• Renal transplant
  • superior to dialysis
  • contraindicated in active malignancy, infection, end stage vascular disease, age
• Liver transplant
  • contraindications: acute sepsis, extrahepatic malignancy, HIV, advanced cardiopulmonary disease, inability to comply with medication regimen, poor MELD score
• Pancreas transplant
  • indicated in DM1, usually along with kidney transplant
• Small bowel transplant
  • limited success due to highly immunogenic nature of small bowel
  • indicated in short gut syndrome dependent on TPN
• Heart transplant
  • indicated in end stage idiopathic cardiomyopathy, ischemic heart disease, congenital disease, malignant arrhythmia
  • high operative mortality
  • acute rejection associated with tachycardia
• Lung transplant
  • indicated for lung disease with life expectancy < 2 years
  • late mortality is due to bronchiolitis obliterans from chronic rejection and associated acid reflux. All lung tx pts are given a Nissen fundoplication to prevent reflux