FM/ IM Cheat Sheet

Mere's slides

Online med ed sheets

Dr. High Yield

Divine intervention Bible

https://divineinterventionpodcasts.com/category/cardiovascular-usmle-step-2/

Mere's Step 1 study guide

USPSTF Screening Recommendations

https://www.boardsbeyond.com/dashboard

https://www.picmonic.com/home

https://cramfighter.blueprintprep.com/schedule/tasks/

PRACTICE WORKSHEETS for COMLEX/COMAT- Coming soon!

Level 3

Dimension 1: Competency Domains		Minimum % Level 3
1	Osteopathic Principles, Practice, and Manipulative Treatment	10%
2	Osteopathic Patient Care and Procedural Skills	40%
3	Application of Knowledge for Osteopathic Medical Practice	15%
	3.1 Foundational Biomedical Sciences Knowledge Base	10%
4	Practice-Based Learning and Improvement in Osteopathic Medical Practice	8%
5	Interpersonal and Communication Skills in the Practice of Osteopathic Medicine	5%
6	Professionalism in the Practice of Osteopathic Medicine	6%
7	Systems-Based Practice in Osteopathic Medicine	6%

Dimension 2 consists of 10 clinical presentations, which represent the manner in which a particular patient, group of patients, or community present for osteopathic medical care.

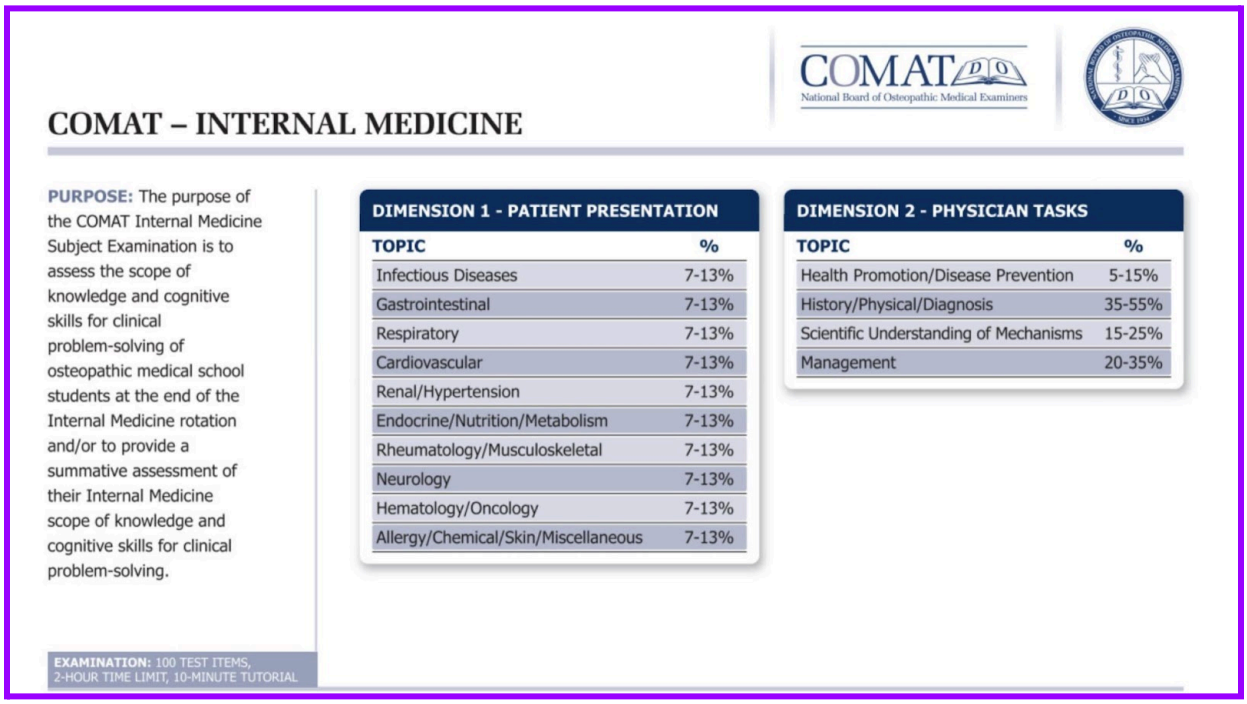
Dimension 2: Clinical Presentations		Minimum % Level 3
1	Community Health and Patient Presentations Related to Wellness	12%
2	Human Development, Reproduction, and Sexuality	5%
3	Endocrine System and Metabolism	5%
4	Nervous System and Mental Health	10%
5	Musculoskeletal System	13%
6	Genitourinary/Renal System and Breasts	5%
7	Gastrointestinal System and Nutritional Health	10%
8	Circulatory and Hematologic Systems	10%
9	Respiratory System	10%
10	Integumentary System	5%

IM Exam Blue Print

NBME medicine self-assessment

https://youtu.be/8DTYbxtV7Tk

https://quizlet.com/90745909/internal-medicine-comat-review-flash-cards/



COMAT – INTERNAL MEDICINE

COMAT
National Board of Osteopathic Medical Examiners

PURPOSE: The purpose of the COMAT Internal Medicine Subject Examination is to assess the scope of knowledge and cognitive skills for clinical problem-solving of osteopathic medical school students at the end of the Internal Medicine rotation and/or to provide a summative assessment of their Internal Medicine scope of knowledge and cognitive skills for clinical problem-solving.

EXAMINATION: 100 TEST ITEMS, 2-HOUR TIME LIMIT, 10-MINUTE TUTORIAL

DIMENSION 1 - PATIENT PRESENTATION

TOPIC	%
Infectious Diseases	7-13%
Gastrointestinal	7-13%
Respiratory	7-13%
Cardiovascular	7-13%
Renal/Hypertension	7-13%
Endocrine/Nutrition/Metabolism	7-13%
Rheumatology/Musculoskeletal	7-13%
Neurology	7-13%
Hematology/Oncology	7-13%
Allergy/Chemical/Skin/Miscellaneous	7-13%

DIMENSION 2 - PHYSICIAN TASKS

TOPIC	%
Health Promotion/Disease Prevention	5-15%
History/Physical/Diagnosis	35-55%
Scientific Understanding of Mechanisms	15-25%
Management	20-35%

OMM

- [OMM cheat sheet]

General: USPSTF recommendations

- **In general**
  - **Initial therapy → most conservative**
- **High yield case presentations**
  - 50 yoM annual physical: screen for CVD with lipid panel & blood pressure; cancer screening with fecal blood or colonoscopy. NO PSA! Immunizations: Tdap, acellular pertussis booster, influenza
  - Smoker with COPD needs vaccination: Tdap, pneumococcal, influenza
  - Sedentary dude asks about exercise: counseling on exercise is not effective
  - Adolescent: HIV, G&C and sexual health and safety, depression screen, **lipids**
    - Screening: HIV Ag-Ab → immunoassay (confirmatory)
  - Patient with HTN → screen for DM, fasting blood glucose, HbA1c, serum chemistry
- **Health maintenance examination**
  - **Primary prevention:** prevent disease
  - **Secondary prevention**: early detection of disease so prompt tx can get started
  - **Tertiary prevention:** therapeutic and rehabilitative measure once dz is dx
  - There is no such thing as a routine blood test or routine xray.
- **Cancer**
  - **Breast**: mammogram every other year from 50-74 yo
  - **Colonoscopy**: Fecal blood and colonoscopy at **45 yo**, 50-75 yo. Don't screen > 85.
    - Colonoscopy every 10 years if normal or hyper plastic polyps
    - Annual fecal occult blood
    - If colectomy, repeat colonoscopy 1 year → every 3-5 years

        - Flexible sigmoidoscopy every 5 years w/ or w/o stool testing every 3 years
        - Family history < 60 → screen 10 years before family member dx with colon cancer
        -

Colon cancer screening	
Patients at average risk	• Start at age 45: ◦ Colonoscopy every 10 years ◦ gFOBT **or** FIT every year ◦ FIT-DNA every 1-3 years ◦ CT colonography every 5 years ◦ Flexible sigmoidoscopy every 5 years (or every 10 years with annual FIT)
Patients with FDR with CRC or high-risk adenomatous polyp*	• Colonoscopy at age 40 (or 10 years prior to age of diagnosis in FDR, whichever comes first) • Repeat every 5 years (every 10 years if FDR diagnosed at age >60)
Patients with ulcerative colitis	• Start screening 8-10 years after diagnosis • Colonoscopy every 1-3 years

    - **Lung cancer**: 55-80 annually with low dose CT if > 30 pack year history and current smoker. Stop if > 15 years since smoking
    - **Cervical**: PAP smear every 3 years 21-65 yo
        - PAP plus HPV test for 30-65 yo
    - **Prostate**: PSA antigen not recommended
    - No routing screening for ovarian, testicular, pancreas
    - Screening not recommended if mortality is < 5 years due to time to benefit
- **Osteoporosis screening**
    - > 65 yo females via DEXA scan
    - Calcium recommended > 50 yo women and > 70 yo men
    - Corticosteroids: give Calcium and Vit D
- **pregnancy screening**
    - gestational diabetes with Oral glucose tolerance test
        - increased risk of T2DM, screen 12 weeks postpartum

- **AAA**: 65-75yo guy who smoked/ history of smoking→ Abdominal ultrasound q6-12 months
- **Anemia:** check CBC in pregnancy
- Aspirin for cardiovascular dis/colorectal ca prophylactic in 50-60 yo with high risk (level B rec)
- **Aspirin** preggo if previous preeclampsia, >12w, Men 45-79 daily aspirin
- **Bacteriuria** preggo 12-16w (screen to treat, then recheck)
- Blood Glc 40-70yo obese
- Breast Ca: Mammogr 50-74yo/ 2y
- Breast Ca in family: familial risk ass tool -> Tamox/raloxifene/genetics..
- **Cervical Ca :**
    - 21-29: PAP 3y, 30-65: 3 years with cotesting
    - PAP 3y or PAP/co-testing q 5y.
    - Also preggo gets PAP, don't forget!
    - HPV vaccine: 9-26 yo guys and girls

- Colorectal Ca 45-75y (choose your screening method, but colo every 10y, FOBT/Immunotest yearly, etc.)
- Caries screen >5yo (most common Strep mutans-was a question on nbme)
- Depression screen 12-18yo, esp with positive PHQ2 → screen for Suicidal ideartion
- **Diabetes**: 35-70 yo with BMI > 25 (serum glucose, HbA1c, serum chemistry)

  There are four ways to diagnose diabetes: 1.) Hemoglobin A1C of 6.5 percent or greater, 2.) Fasting serum glucose over 126 mg/dL, 3.) Serum glucose over 200 mg/dL two hours after 75 g of oral glucose, and 4.) Random serum glucose over 200 mg/dL with classic diabetic symptoms
-
- Falls prevention 75yo
- **Folic Acid/Iron/Vitamins** give in preggo
- **Gestat Diabetes** >24w with 50g 1h test first, cutoff 140
- Healthy diet and physical activ in any
- Hearing test in 2yo (this is not USPSTF)
- **Hep B and HIV** in preggo
- **HCV** test in any 18-79yo
- Hep A: liver cirrhosis, travel to endemic areas
- Hep B: liver cirrhosis, Men sex with men,
- HIV test in any 13-64yo (this is CDC recommendation, not USPSTF)
- **Hypertension** screen (office BP measurement) in **>18yo**. women > 45 with risk factors should be screened with lipid panel.
- Intimate partner violence: all reproductive age women
- Influenza vaccine- health maintenance for Fall
- Lipid screen starts ~40yo (men 35 / women 45). Start at 20yo if risk factors present (Diabetes etc)
- Lung Ca: Low dose CT 50-80yo, >20y smoker, not if <15y last smoke
- Ocular gonorrhea prophylaxis newborn (erythr/tet)
- Osteoporosis DXA scan: >65y female, or FRAX>10%, or high risk pplTx: 1200 mg calcium, weight-bearing exercise, 600 U Vit D
- **Peripartum** Depression screen
- **Pneumococcal vaccine**: < 65 (liver disease, lung disease, smoke, heart disease, DM), everyone > 65
- PrEP in high risk (gay with recent/ongoing contact, drug users..): Truvada for some time
- **Preeclampsia**: measure BP in preggo
- **RhD** in preggo. Never give RhoGAM in Rh neg preggo who already has antibodies (too late), otherwise 28w+within 72h after birth
- **STD**: Chlamydia/gonorrhea in women <24yo sexual active
- **STD+** in preggo: Chlamydia, syphilis, HIV, Hep B, rubella (varicella)
- Syphilis in all high risk people
- Statins: give in 40-75 yo with risk: Diabetes, HTN etc.. Dyslipidemia, Smoker, LDL>190, 10y CVD risk >10%, LDL>190...
- Screen all for Ethanol, Smoking, Drug use
- TB screen: risk groups (immigrants, prisoners etc)
- **Tdap**: every 10 years
- Vision screen once in 3-5yo (amblyopia?)
- Weight loss program if BMI >30
- **Prevention PST = PST.** primary secondary tertiary = prevent screen treat. BP measurement at a local health fare?- secondary (screen for disease that already is there but was undetected)
    - Statin in a person with high LDL?- primary (prevent development of disease with statin)

    - ACE inhibitor in a person with MI?- tertiary (treat..)
    - Of course, all vaccinations are primary.
- **Vaccinations**
    -

Recommended vaccines for patients with chronic liver disease	
Tetanus	Every 10 years
Influenza	Annually
Pneumococcal	At diagnosis & at age 65
Hepatitis A	Initiate series if not immune
Hepatitis B	Initiate series if not immune

    - **Meningococcal vaccination**
        - Primary vaccination 11-18 yo
        - Booster vaccine: 16 yo, travel to endemic areas
    - **Yellow fever**
        - Travel to endemic areas (africa)
            - Contraindicated in egg allergy, AIDS, immunosuppressive
            - Counsel on mosquito protection
- **Lifestyle**: tobacco cessation and alcohol misuse; exercise 30 min/ day. Healthy diet. Safe sexual practices, seat belts

Pediatrics

- **Mer's Cheat Sheet**
- **Molly's study guide**

Adults

- **Signs**
    - **Chvostek sign**: hypocalcemia, positive with tapping on facial nerve causes contraction of ipsilateral facial muscles
    - **Courvoisier sign**: palpable gallbladder carcinoma
    - **Cullen sign:** blue discoloration of periumbilical area in early pregnancy
    - **Grey turner sign**: blue discoloration of flank area in early pregnancy or pancreatic necrosis
    - **Russell sign**: callus on back of fingers from self-induced vomiting
    - **Murphy sign**: acute cholecystitis
    - **McBurney point**: acute appendicitis
    - **Chandelier sign**: pelvic inflammatory disease
    - **Kernig**: knee towards head, meningitis
    - **Brudzinski**: bend head, meningitis

Sign	Physical-Examination Finding	Differential Diagnosis
Murphy sign	Abrupt cessation of inspiration with right-upper-quadrant palpation	Cholecystitis
Kehr sign	Left-shoulder-tip pain while lying supine, caused by referred pain due to diaphragmatic irritation	Ruptured spleen; ruptured ectopic pregnancy
McBurney point	Point tenderness two-thirds the distance from the navel and the anterior superior iliac spine	Appendicitis
Rovsing sign	Paradoxical right-lower-quadrant pain with palpation in the left-lower quadrant	Appendicitis
Obturator sign	Abdominal pain with flexion and internal rotation of the right hip	Appendicitis
Psoas sign	Right-lower-quadrant pain with extension of the right hip while the patient lies on the left side	Appendicitis
Pulsatile mass	Pulsatile mass upon abdominal palpation	Aortic aneurysm
Grey-Turner sign	Flank ecchymosis	Hemorrhagic pancreatitis, retroperitoneal hemorrhage
Cullen's sign	Periumbilical ecchymosis	Hemorrhagic pancreatitis, retroperitoneal hemorrhage
Courvoisier sign	Smooth, nontender, right-upper-quadrant mass	Pancreatic cancer, cholangiocarcinoma

- Immunizations
  - Prevention
  - Reportable events:
    - Anaphylaxis or shock < 7 days of any vaccine
    - Encephalitis, seizures
    - Any sequelae or serious, unusual event
    - Vaccine side effects listed as contraindications
- Drugs
  - Cocaine
    - ST depression, T wave inversion, psychomotor agitation, dilated pupils, atrophic nasal mucosa, HTN
      - Do not give beta blocker
      - Tx: IV benzos (diazepam)
- Alcohol abuse
  - **acamprosate**: glutamate modulator, used with naloxone
  - disulfiram: causes vomiting with alcohol use
  - fomepizole: ethanol glycol poisoning
  - naloxone: opiate use
- Pharmacology
  - CYP inducer= St john wart → decreased drug concentration
  - CYP inhibitor= grapefruit juice → increased drug concentration

Geriatrics

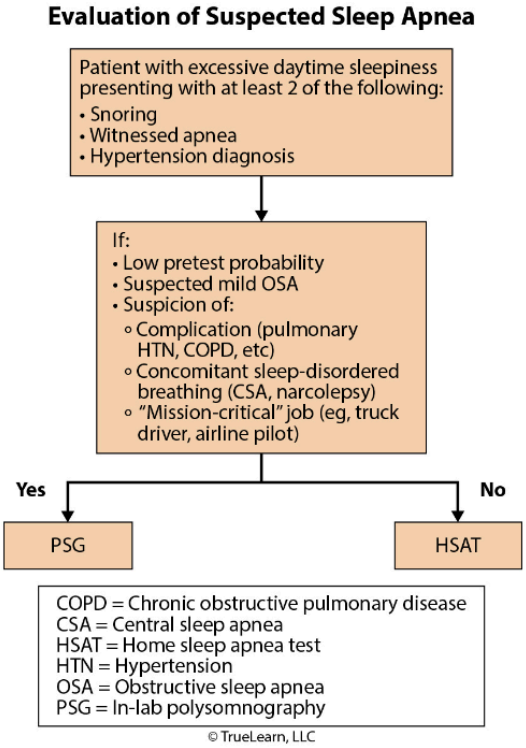
- Falls

    - Increase supervision, patient sitter
    - Supervised toileting
    - Lights during day, dark at night (reduces delirium)
    - Remove objects that could cause a fall
    - Avoid restraints/ rails (patients will fall, fight)
- 65 yo Female patient
    - Mammogram (50-74 yo)
    - Influenza vaccine
    - Tdap booster
    - Pneumococcal vaccine 13 → PV 23 at least one year later
    - Fasting cholesterol levels
    - PAP test
        - Cytology : 3 years
        - High risk HPV: 5 years
        - Co-testing: 5 years
        - Tdap booster every 10 years
        - Colon cancer screening > 45 yo
            - After removal, screen at 1 year, then 3-5 years
        - Fasting blood glucose
        - Zoster vaccine
    - **Iron deficiency anemia** → get colonoscopy (most common cause is GI bleed)
        - Negative Fecal occult test does not exclude colon cancer
- **New medications → new symptoms**
    -

Relative Anticholinergic Properties of Common Medication Classes			
Medication Class	**High-Potency Medications**	**Low-Potency Medications**	**Uses**
TCAs	All TCAs are high potency	N/A	Depression, IBS, fibromyalgia
SSRIs	Paroxetine may be moderate to high potency	All other SSRIs are low potency	Depression, anxiety
Muscle relaxers	Tizanidine and cyclobenzaprine are moderate potency	Methocarbamol, baclofen	Muscle spasms, low back pain
Antimuscarinics	Oxybutynin, solifenacin, dicyclomine, hyoscyamine, atropine	N/A	Overactive bladder, antispasmodic
Antiparkinsons	Benztropine	Amantadine, bromocriptine	Parkinsonism
Antihistamines	1st generation H1 blockers: diphenhydramine, doxepin, hydroxyzine, meclizine	2nd generation H1 blockers: fexofenadine, cetirizine, loratadine	Seasonal allergies, allergic reactions
Antipsychotics	Chlorpromazine, fluphenazine, clozapine	Olanzapine, quetiapine, risperidone	Schizophrenia, bipolar disorder
IBS = irritable bowel syndrome; SSRIs = selective serotonin reuptake inhibitors; TCAs = tricyclic antidepressants.			

Common Treatments for Sleep-Onset and Sleep-Maintenance Insomnias			
Medication	**Mechanism of Action**	**Usual Dosage**	**Indication**
Benzodiazepines (estazolam, flurazepam, lorazepam, temazepam, triazolam)	Binds to stereospecific benzodiazepine receptors on the postsynaptic gamma-aminobutyric acid neuron	Varies	Sleep onset and sleep maintenance (triazolam is only for sleep onset)
Doxepin	Histamine H1 receptor antagonist	3 to 6 mg	Sleep maintenance
Eszopiclone	May interact with gamma-aminobutyric acid-receptor complexes at binding domains	1 to 3 mg	Sleep onset and sleep maintenance
Ramelteon	Melatonin receptor agonist	8 mg	Sleep onset
Trazodone	5-hydroxytryptamine-2, alpha-1 adrenergic, and histamine H1 receptor antagonists	25 to 100 mg	Sleep onset and sleep maintenance
Zolpidem	Enhances the activity of gamma-aminobutyric acid via selective agonism at the benzodiazepine-1 receptor	5 to 10 mg	Sleep onset and sleep maintenance

- **Sleep**
  - Sleep apnea= Cheyne stokes respirations (crescendo-decrescendo)
  - Biot respirations= regular uniform deep respirations (hyperpnea) with periods of apnea
  - Next step: home sleep test (low risk, no high profile work)
  - In lab polysomnography: risk factors, works as a pilot or other profession



- **Driving**

- Old guy with comorbidities getting into minor car accidents: driving test for complex cases
- Getting lost driving and Alzheimer's: local trips
- Severe cognitive impair: driving restrictions

- **Osteoporosis**
  - 50% post-menopausal women have osteoporosis related fractures in their lifetime
  - Defined as fragility (fractures) or T score -2.5
  - **DXA** screening best predictor of hip fracture
    - **< -2.5 = osteoporosis**
  - Prevention:
    - Estrogen
    - Calcitonin inhibits osteoclast (rarely used)
    - Calcium and vitamin D

Common Bone Mineralization Disorders and Laboratory Results				
Disorder	**Calcium**	**Phosphate**	**Alkaline Phosphatase**	**Parathyroid Hormone**
Osteoporosis	Normal	Normal	Normal	Normal
Osteopetrosis	Normal	Normal	Elevated	Normal
Vitamin D_3 deficiency/rickets	Normal/decreased	Normal/decreased	Elevated	Elevated
Osteitis fibrosa cystica/hyperparathyroidism	Elevated	Decreased	Elevated	Elevated
Paget disease	Normal	Normal	Elevated	Normal

  - Tx:
    - #1 calcium and Vit D tx and **prevention**
    - Weight bearing exercises
    - teriparatide (recombinant PTH), bisphosphonates (alendronate) taken in AM on empty stomach
    - **bisphosphonates**: prevents further bone mass loss, inhibits osteoclasts, decrease bone resorption and turnover
      - treats osteoporosis, osteitis deformans (pagets)
      - Indications: osteopenia (T score -1 to -2.5) have 10 year probability for hip fracture of > 3% using FRAX tool
      - Contraindicated: CKD, esophageal dysmotility, gastric bypass
    - Risedronate: can cause atypical bone fractures
    - **Hydrochlorothiazide**: osteoporosis with HTN

Drugs for Osteoporosis			
Drugs	**Mechanism of Action**	**Use**	**Adverse Effects**
Bisphosphonates • Alendronate • Risedronate • Ibandronate • Zoledronic acid (IV)	Decrease osteoclast activity	• First-line for osteoporosis • Paget's disease • Hypercalcemia (zoledronic acid)	• Esophageal irritation (do not lie down for at least 30 minutes) • Low bioavailability (take on an empty stomach) • Osteonecrosis of the jaw • Avoid in patients with reduced renal function
Denosumab (monoclonal antibody)	Binds to RANKL, blocks the interaction between RANKL and RANK (a receptor located on osteoclast surfaces), and decreases osteoclast formation	• Osteoporosis not responsive to bisphosphonates • Patients with impaired renal function	• Fatigue • Diarrhea • Hypersensitivity
Selective-estrogen receptor modulator (SERM) • Raloxifene	Acts like an estrogen agonist in the bone to prevent bone loss	Post-menopausal females with osteoporosis and breast cancer	• Thromboembolism • Hot flashes
Parathyroid hormone • Teriparatide	• Recombinant PTH • Stimulates osteoblast function, increases gastrointestinal calcium absorption, and increases renal tubular reabsorption of calcium	• Osteoporosis intolerant to other therapies • Decreases fracture risk	Hypercalcemia

RANKL inhibitor	Osteoporosis with impaired renal function or difficulty with bisphosphonates	Binds to RANKL and inhibits interaction with RANKL and decreases osteoclast production	Denosumab	• Hypersensitivity • Pregnancy • Hypocalcemia	• Hypocalcemia • Increased serious infections • Osteonecrosis of the jaw

- **Psych**
  - avoid antipsychotics, anticholinergics (TCAs), and benzodiazepines
    - anticholinergics: sedating, orthostatic hypotension, syncope, vagotonic effect slowing SA and AV node (prolonged PR interval)
  - best antidepressant: Escitalopram (lexapro)
  - depression: screen with PHQ-9
  - alcohol: screen with CAGE questionnaire
- **Neurocognitive disorders**
  - **Parkinsons**
    - Tremor
    - Rigidity
    - Akinesia/ bradykinesia
    - Postural instability
    - Amantadine : NMDA antagonist and dopaminergic antagonist
    - Parkinsons hallucinations ⇒ quetiapine
    -
  - **Alzheimers**
    - Cholinesterase inhibitors: donepezil, rivastigmine, galantamine improve functioning
    - Memantamine: NMDA antagonist used on moderate AD
    - Findings 5 A's
      - Agnosia: cannot recognize objects
      - Anomia: cannot remember names of things
      - Aphasia: difficulty speaking
      - Apraxia: difficulty carrying out tasks
      - Amnesia: memory loss
    - Tx: donepezil, galantamine, rivastigmine
  - **Frontotemporal dementia**

        - Early personality changes
        - Apathy, disinhibition, compulsive
        - FTD atrophy
    - **Lewy body dementia**
        - Visual hallucinations, parkinsonism, fluctuating cognition
        - REM behavior disorder, sun-downing
    - **Pseudodementia**
        - Due to depression
        - Fluoxetine
        - Make sure they meet criteria for MDD
    - **Normal pressure hydrocephalus**
        - Wet, wobbly, wacky
        - Ventriculomegaly
        - Evans ratio

Evans Index	
Variable	**Size**
Normal ventricle size	0.20–0.25
Early/questionable ventricular enlargement	0.25–0.30
Definite ventricular enlargement	**> 0.30**

    - **Prion disease**
        - Behavioral changes, rapid progressive decline
        - Myoclonus, seizure
- **Sleep**
    - Increased night time awakenings
    - Sleepy in early evening and early morning awakenings
    - Increased somnolence (napping)
- **Hospice care**
    - Maximize comfort vs extending length of life
    - Terminal illness requiring morphine (doctrine of double effect)
        - Adjust the dose q 8 hours
        -

Hospice model
• Focus on quality of life, not cure or life prolongation • Symptom control (eg, pain, nausea, dyspnea, agitation, anxiety, depression) • Interdisciplinary team (eg, medical, nursing, psychosocial, spiritual, bereavement care) • Services provided at home, assisted-living facility, or dedicated facility • Requires survival prognosis of ≤6 months

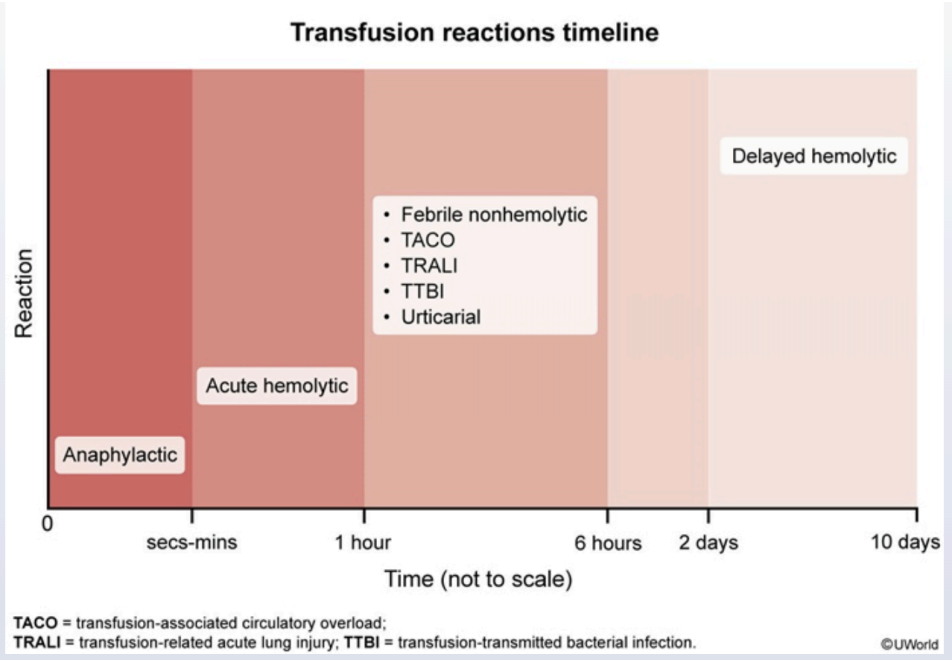
- **Advanced directives**
    - patients need capacity to make decision
        - inconsistent answers to questions
- **Erectile dysfunction**
    - ED drug increases cGMP- sildenafil
- **Elder abuse**
    - Atypical abstractions, fractures, contusions
    - Pain not consistent with reported etiology
    - Inadequate nutrition, limited access to medications, missed appointments, unpaid expenses

Heme-Onc

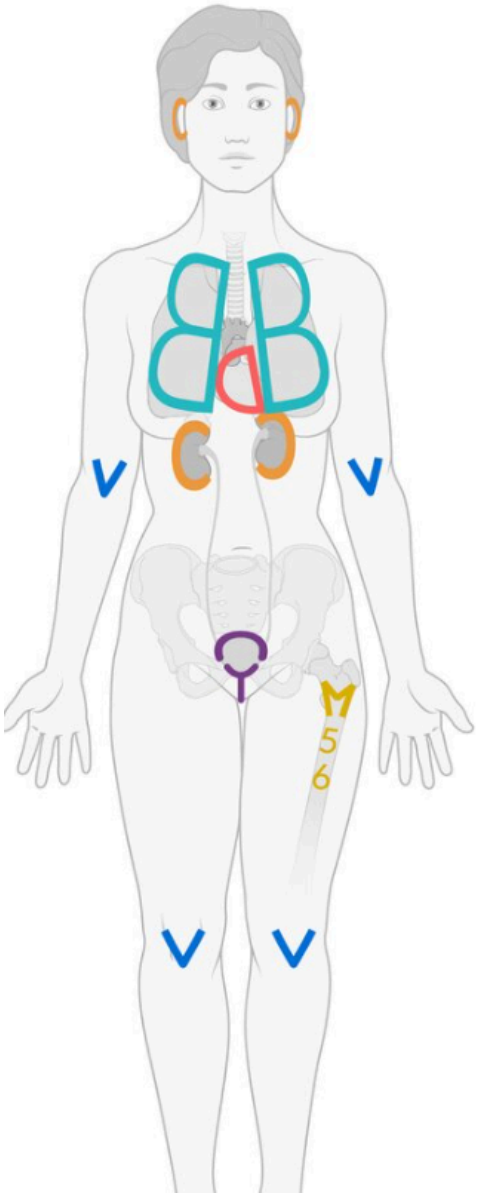
- **Next step**
  - Bone marrow biopsy= figure out cause of cytopenias
  - Flow (blood or BM)= classify type of leukemia
    CT abdomen/ pelvis with contrast= teratoma + NMDA encephalopathy
  - Enlarged lymph
    - Need excision to evaluate LN architecture (FNA is not sufficient)
    - PET/ CT for staging in Ann Arbor system
  - **Colonoscopy**
    - Iron deficiency in old patient, MOST COMMON is GI bleed
  - Most resistant to radiation therapy → bone (low cell turnover)
  - **orchiectomy**= testicular neoplasm → chemotherapy and low-dose radiation
  - Pulmonary nodules
    - Next step if malignant→ **image-guided and endoscopic biopsy** techniques
    - **Transbronchial needle aspiration** → small central tumor, LN, large tumors
    - **Bronchoscopy** → central pulmonary nodules
    - **Serial CT scan** → nodules 4-8 mm
  - Kid with mediastinal mass → ALL
  - Atypical lymphocytes= CMV (IgM CMV) or EBV (heterophile Ab)
  - vwF disease= ristocetin low-dose ristocetin-induced platelet aggregation, assists in further sub-classifying VWD.
  - hemophilia= plasma mixing studies
  - Immunosuppressed/chronic Abx → bleeding → give Vitamin K

Most Common Causes of New Cancer Cases in Men and Women	Most Common Causes of Cancer Deaths in Men and Women
1. Female breast	1. Lung and bronchus
2. Prostate	2. Female breast
3. Lung and bronchus	3. Prostate
4. Colon and rectum	4. Colon and rectum
5. Corpus and uterus	5. Pancreas
6. Melanomas of the skin	6. Ovary
7. Urinary bladder	7. Liver and intrahepatic bile duct
8. Non-Hodgkin lymphoma	8. Leukemias
9. Kidney and renal pelvis	9. Non-Hodgkin lymphoma
10. Thyroid	10. Corpus and uterus

Indications for specialized RBC treatments	
Irradiated	• Bone marrow transplant (BMT) recipients • Acquired or congenital cellular immunodeficiency. • Blood components donated by first or second degree relatives
Leukoreduced	• Chronically transfused patients • CMV seronegative at-risk patients (e.g., AIDS, transplant patients) • Potential transplant recipients • Previous febrile nonhemolytic transfusion reaction
Washed	• IgA deficiency • Complement-dependent autoimmune hemolytic anemia • Continued allergic reactions (e.g., hives) with red cell transfusion despite antihistamine treatment



Warfarin Reversal Agents			
Medication	**Fresh Frozen Plasma**	**4-Factor Prothrombin Complex Concentrate**	**Vitamin K**
Mechanism	• All coagulation factors present at normal plasma concentration	• Factors II, IX, and X, and variable amounts of factor VII, concentrated to 25x plasma concentration	• Required for vitamin K epoxide reductase, the enzyme responsible for the addition of glutamate residues to the vitamin K-dependent clotting factors (mainly II, VII, IX, and X) • This enzyme is competitively inhibited by warfarin, so sufficient levels of vitamin K can overcome this inhibition
Drawbacks	• Large volumes and slow infusion required	• Expensive	• Slow ◦ Requires time to synthesize new clotting factors (many hours to days)
Indications	• Warfarin reversal in non-life-threatening but more urgent scenarios ◦ An example is moderate-risk surgical interventions	• Life-threatening hemorrhage on warfarin	• Need for long-term anticoagulation reversal or normalization of INR in vitamin K deficiency



Cisplatin/Carboplatin	*Acoustic nerve damage*
Bleomycin, Busulfan	*Pulmonary fibrosis*
Doxorubicin	*Cardiotoxicity*
Cisplatin/Carboplatin	*Nephrotoxic damage*
Vincristine	*Peripheral neuropathy*
CYclophosphamide	*Hemorrhagic cystitis*
Methotrexate 5-FU/6-MP	*Myelosuppression*

- **Emma holliday**
  - Anticardiolipin Ab= thrombosis, livedo reticularis, miscarriages
  - Antithrombin 3 deficiency
  - Fibrinogen abnormality
  - **Antiphospholipid syndrome** → SLE, low PTT, miscarriages. Hypercoagulable, no OPCs with progesterone
  - **Thrombocytopenia**: give 1:1 ration of blood to platelets → oozing from IV sites
  - thrombocytosis
  - Sickle cell with sudden drop in Hct= aplastic crisis, due to hypoxia, dehydration, acidosis → tx: opioids for pain crisis
    - Pain crisis → fluids, morphine, oxygen
    - Prophylactic → hydrea and penicillin
      - Increase fetal hemoglobin
  - Cyanosis of fingers, ears, nose and recent mycoplasma infection= **cold agglutinin**s

        - Destruction occurs in liver, IgM
    - Sudden onset after PCN, ceph, sulfa, rifampin or cancer= **warm agglutinins**
        - Tx: steroids, splenectomy
    - Splenomegaly, FMhx, bilirubin gallstones, high MCHC= **hereditary spherocytosis**
        - AD loss of spectrin
        - Tx: splenectomy
    - **Paroxysmal nocturnal hemoglobinuria**
        - Dark urine in morning, associated with thrombosis and budd-chiari syndrome
        - Defect in PigA lysis by complement
    - G6PD deficiency: heinz bodies, bite cells, avoid oxidant stress, heinz bodies, bite cells. Avoid oxidant stress
        - Give pRBCs
        - Acute disease leads to false negatiev
    - **Hemophilia**: hemarthrosis, increased PTT corrected with mixing studies
        - Tx: DDAVP, replace factors
    - **HLH**: Fever, hepatosplenomegaly, elevated liver enzymes, pancytopenia
    - Recurrent infections
        - Immunodeficiency → check serum IG, HIV
    - BM biopsy → bone marrow disease expective
    - CML → Imatinib = TRK inhibitor
    - Microcytic anemia

	Iron Deficiency	Anaemia of Chronic Disease	Acute Phase Reaction	Iron Overload
Serum Iron	↓	↓	↓	↑
Transferrin / TIBC	↑	↓	↓	N / ↓
Transferrin Saturation	↓	↓	↓	↑
Ferritin	↓	Normal	↑	↑
Soluble Transferrin Receptor	↑	Normal	Normal	↓

        -
    - **Macrocytic anemia**
        - High homocysteine= folate deficiency
        - High homocysteine + MMA= B12 deficiency
    - Sickle cell kid with sudden drop in Hct → **aplastic crisis** due to hypoxemia, dehydration or acidosis
        - Low reticulocyte count, no splenomegaly, severe anemia
        - Due to parvovirus B19
    - Cyanosis of acral body parts with recent mycoplasma infection → **cold agglutinins, IgM**
    - Sudden onset after PCN, ceph, sulfas, rifampin, cancer → **warm agglutinins, Ig**G

        - Tx: steroids → splenectomy
    - **Paroxysmal nocturnal hemoglobinuria** → dark urine in AM, budd-chiari syndrome
        - Defect in PIG-A. Lysis by complement, decreased CD55 and CD59
        - Increased risk of venous thrombosis, budd-chiari syndrome
    - Tumor markers
        -

Tumor Markers	
Serum Markers	**Associated Cancer**
PSA	Prostate
CEA	Colon
CA 19-9	Pancreatic
CA 125	Ovarian
AFP	Hepatocellular or germ cell
Calcitonin	Medullary thyroid

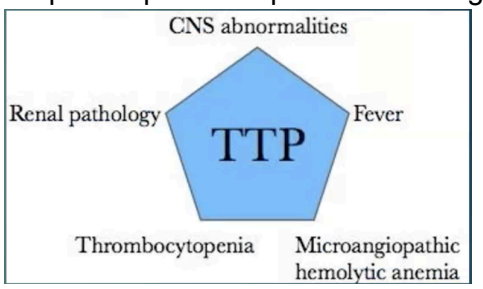
- **immunodeficiency syndrome**
    - Albino, lysosomal disorder, neuropathy → recurent infections of stap/ strep = **chediak higashi**
    - **DiGeorgo**= T cell deficiency, infected with everything. Lymphopenia
    - **Leukocyte adhesion deficiency** → leukocytosis and neutrophilia, cold abscess
    - **MPO deficiency**= candida infections
    - **Wiskott-aldrich syndrome**= leukocyte and platelet defect → atopic dermatitis, recurrent infections, bruising
    - hyper-IgE syndrome = atopic dermatitis, recurrent infections (sinopulmonary, noninflammatory abscesses), eosinophila
- **Transfusion reaction**
    - **Acute febrile transfusion reaction**
        - Most common transfusion reaction
        - Performed cytokines in transfused blood
        - Not related to cross match typing
        - Tx: acetaminophen + fluids
    - **Urticarial transfusion reaction**
        - Patients with IgA deficiency seconds- minutes after receiving blood products
    - **Hemolytic transfusion reaction**
        - Positive coombs test, free Hgb in serum
        - Minutes to hours after ABO incompatible blood transfusion
        - HTN, tachycardia, fever, flank pain, myoglobinuria → DIC
    - Anaphylactic transfusion reaction
        - IgA deficiency, anti-IgA ab with transfused blood
        - RDS, hypotension
- **Heparin induced thrombocytopenia**
    - LMWH → subQ → necrotic skin lesions
    - Antibody induced platelet aggregation (platelet factor 4)
    - **> 50% reduction in platelets**, thrombosis, necrotic skin lesions, anaphylactoid

reactions after heparin administration
    - HIT1= not immune-mediated
    - HIT2= antibody induced thrombocytopenia
    - Tx: switch to direct thrombin inhibitor, argatroban, bivalirudin
- **DVT**
    - Unilateral leg swelling, pain, post-operative, malignancy
    - COMMON FEMORAL (veins above knee)
    - Low platelets, antiplatelet factor 4 antibodies→ **heparin induced thrombocytopenia***
    - Dx: lower extremity ultrasound
    - Stop heparin products and switch to direct thrombin inhibitor (gatran)
        - Tx: SubQ enoxaparin
        - heparin induced thrombocytopenia: 4-7 days after initiation of heparin and is antibody induced
        - manifestation as thrombosis with platelets ~50% baseline
        - HIT tx: Bivalirudin
        - Switch to warfarin once platelets 150K. Lowers protein C → increased risk of thrombus
            - **Protein C deficiency** → warfarin and purpuric lesions (warfarin-induced skin necrosis)
            - Transient hypercoagulable state with warfarin → bridge with heparin
    - Start heparin 5 days (inr 2-3) and warfarin. Bridging therapy prevents necrosis
    - Complications: valvular insufficiency due to residual dysfunction
        - Skin changes and swelling of ankles, varicose veins
        - **Postthrombotic syndrome:** DVT → chronic venous insufficiency → leg pain, edema, fatigue, superficial venous dilation, ulcer.
            - Tx: exercise, compression
    - Obstructed lymph channels→ nonpitting edema
    -

Congenital Hypercoagulable States	
Etiology	**Comments**
Factor V Leiden	Most common: 5% of the general population
Prothrombin gene mutation	Second most common; caused by a prothrombin G20210A mutation
Hyperhomocysteinemia	Typically due to an *MTHFR* gene mutation or deficiencies of folate, vitamin B6, or vitamin B12
Antithrombin III deficiency	Heparin should not be used
Protein C or protein S deficiency	Uncommon; characterized by reduced levels of these 2 natural anticoagulants
Plasminogen or fibrinolysis disorders	Rare

- **Anemia**
    - dyspnea on exertion, fatigue, dizziness, palpitations, pallor (hgb < 9)
        - 1 unit packed RBCs increases Hgb by 1 g/dL and Hct by 3%
        - transfusion threshold is < 7
    - Classified as macrocytic, microcytic or normocytic
    - Causes
        - **B12 deficiency:** neuropathy, unsteady gait, marocytic anemia

        - nitrous oxide/ whippet use
- **geriatrics**: think gastrointestinal (if post-menopausal), NSAID use
    - order FERRITIN (low= IDA)
    - CBC, ECG, PTT, PT, serial cardiac enzymes
    - EGD and colonoscopy
        - microcytic anemia = **iron deficiency** (polyps, nutritional)
            - low iron, low ferritin, high TIBC
            - **B12 deficiency** presents in 3-5 years after diet change, pernicious anemia, intrinsic factor antibody. Normal MMA r/o B12. check for neurologic symptoms
            - Bone marrow biopsy is gold standard
        - **Anemia of chronic disease**
            - Low everything
        - normocytic anemia= Anemia of chronic inflammation, renal insufficiency
            - iron stores normal, decrease ability to use iron
    - tx: ferrous sulfate 325 mg for 3x/ day
        - B12 1000ug IM for 7 days, then weekly for 4 weeks
    - treat underlying condition
    - alcohol abuse causes folate deficiency and B12 deficiency
- **Sideroblastic anemia (x-linked)**
    - Ring sideroblasts in bone marrow, iron laden granules
    - Pappenheimer bodies are iron-containing inclusion bodies in mature RBCs
        - Low TIBC, high transferrin saturation
    - Acquired: lead toxicity, isoniazid, alcohol, chloramphenicol
- **Alpha-thalassemia**
    - Target cells, micro Uric high rbc, asymptomatic
    - Normal iron and ferritin, low/ normal MCV, normal RDW
- **Sickle cell disease**
    - Exchange transfusion therapy for sickle cell infarct (remove sickls and replace with allogeneic blood)
    - Don't give tpa in patients < 18 yo
    - Vaccinations: meningococcal at 2 months and pneumococcal polysaccharide (PPSV23) at 2 years
    - osteomyelitis= staph or salmonella
- **Hereditary spherocytosis**
    - defect in RBC membranes —> hepatosplenomegaly. RBCs lack central pallor
    - Microcytic
- **Aplastic anemia**
    - Pancytopenia, hypocellular BM
- **Pure red cell aplasia**
    - Acquired, profound anemia, absence of reticulocytes and erythroid precursors
- **Paroxysmal nocturnal hemoglobinuria**
    - Pancytopenia, intravascular hemolysis (high indirect bili, low haptoglobin, high LDH)
    - Absence of CD55 and CD59
- **Iron deficiency in infants**

        - > 6 months exclusively breastfeeding/ cows milk, premature
        - Developmentally normal
    - **Lead toxicity**
        - Neurologic abnormality, behavioural changes
        - Normal iron, ferritin, etc
    - **Hemolytic anemias**
        - **Hemolytic anemia**
            - Low Hct, low Hct
            - Normal MCV
            - Low haptoglobin
        - **TTP** (thrombotic, thrombocytopenic purpura)
            - **Pentad: MAHA, fever, thrombocytopenia, CNS abnormalities, renal pathology**
            - Tx: plasmapheresis/ plasma exchange
            - 

- **Asplenic**
    - N. meningitidis, H. flu, strep pneumonia
    - sickle cell disease:
        - all kids 2-16 yo should be screened with transcranial doppler US
- **Splenic abscess**
    - Staph, strep, salmonella
    - Fever, leukocytosis, LUQ pain
    - Left sided pleuritic chest pain/ effusion seen
    - Infective endocarditis with septic emboli
- **Platelet abnormalities**
    - **DIC**
        - Increased PT and PTT
        - Decreased D-dimer and fibrin split products
    - **Von Willebrand disease**
        - Young woman with recurrent epistaxis, heavy menses, petechiae, normal platelets, increased bleeding time and PTT
        - Dx: ristocetin test looks for platelet agglutination
        - Tx: **desmopressin** → releases vwf from endothelium → TXA
        - Tx: Factor VIII concentrate, tranexamic acid (antifibrinolytic)
        - Acute blood loss, iron deficiency, FMHx

Treatment of Bleeding in von Willebrand Disease		
Treatment	**Mechanism**	**Use**
• DDAVP	• Releases stored vWF and factor VIII	• Minor bleeding, before minor procedures
• vWF concentrate	• Exogenous addition of vWF	• Minor bleeding (if DDAVP is ineffective) • Major bleeding, before major surgery
• Factor VIII	• Exogenous addition of factor VIII	• Major bleeding • Emergent major procedures
• Tranexamic acid	• Displaces plasminogen from fibrin to inhibit fibrinolysis	• Minor or major bleeding, especially of mucosal tissue
• Platelet transfusion	• Increases platelet levels	• Bleeding with thrombocytopenia or platelet dysfunction
DDAVP = desmopressin; vWF = von Willebrand factor.		

- **TTP**
  - Normocytic anemia, thrombocytopenia, renal dysfunction
  - Pentad of MAHA, Thrombocytopenic purpura, neurologic (more severe) changes, fever, renal disease
  - ADAMTS-13 assay
  - Tx: plasmapheresis
- **HUS**
  - Similar to TTP but more common in children
  - In setting of shiga toxin from E coli infection
- **ITP**
  - Young woman with recurrent epistaxis, heavy menses, petechiae, isolated thrombocytopenia (less severe and not life threatening)
  - isolated Thrombocytopenia and increased bleeding time in the setting of recent URI infection. Platelets are NOT defective.
  - Bleeding, petechiae (red, non-blanching skin macules)
  - Increased megakaryocytes in bone marrow biopsy, **isolated thrombocytopenia**
  - Anti GP2b/ 3a antibodies, follow viral infection (HIV) with complicated bruising and epistaxis **(IgG AutoAb** on platelet surface)
    - Primary ITP= autoimmune
    - Secondary ITP= infection or systemic disorder that disrupts homeostasis

- AVOID ALL ANTI-Platelet drugs (NSAIDS, Ibuprofen, etc)
- Dx: HIV Ab
- Tx: IV methyprednisolone, **glucocorticoids** plt < 30K, IVIG if < 10K and rituximab → prednisone taper
- 2nd line: T**PO agonists** and **splenectomy**
- IV RhoD helps raise platelets
- IVIG is platelets are very LOW

■ **Heparin-induced thrombocytopenia**
- antibody mediated thrombocytopenia and thrombosis 4-7 days after heparin tx. Tx is direct thrombin inhibitors

○ **Plasma cell dyscrasias**

■ **Multiple myeloma**
- Rouleaux formation RBCs, congo red apple green birefringence, primary light chains → damage to kidneys, SOB, pathologic fractures of bone
- Back pain is common complaint
- Anemia, elevated Cr, hypercalcemia
- Imaging: lytic lesions in cranium, long bones, ribs, etc.
- Workup: SPEP and UPEP (M-spike) → bone marrow biopsy (> 10% clonal plasma cells)
- 

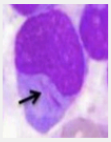
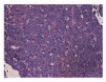
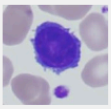
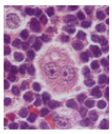
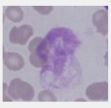
■ **MGUS**
- Asymptomatic
- Serum M protein < 3, bone marrow < 10% monoclonal plasma cells, end organ damage
- Incidental finding
- Small risk of progression to premalignant stages

■ **Waldenstrom macroglobulinemia**
- IgM production
- ~ presentation to MM, hyperviscosity, neuropathy, IgM spikes

○ **Cancer staging systems**
- Rai system, Binet system= CLL
- Ann arbor system= lymphoma
- revised international prognostic index= diffuse large B cell lymphoma

○ **Lymphomas**

Histology Images and Associated Malignancies

Disease/Notes	Image
Acute Promyelocytic Leukemia • Subclass of AML • Arrow pointing to classic Auer rod • Translocation t(15;17) • Associated with disseminated intravascular coagulation • Treatment: Emergent all-trans retinoic acid (Pubmed/Subashchandrabose, Madanagopaal, Rao)	
Burkitt Lymphoma • Classic "starry-sky" appearance with sheets of atypical lymphoid cells (sky) with evenly dispersed normal macrophages (stars) • Translocation t(8;14) c-myc • Jaw or abdomen tumors • Aggressive non-Hodgkin lymphoma (Pubmed/Magrath)	
Hairy Cell Leukemia • Rare B cell lymphoma (< 2%) • Tartrate-resistant acid phosphatase stain positive • Dry bone marrow aspiration • Hair-like protrusions from cell (Pubmed/Pilichowska, Shariftabrizi, Mukand-Cerro, Miller)	
Hodgkin Lymphoma • Reed Sternberg cells, a giant cell with a multinucleated or bilobed nucleus resembling owl's eyes • Pain with alcohol ingestion • Cyclical fevers (Pubmed/Knecht, Righold, Mai)	
Chronic Lymphocytic Leukemia • Smudge cell lacking identifiable cytoplasm or nuclear structure • Indolent leukemia, often found incidentally • Affects older individuals	

-
- **Burkitt lymphom**
  - CD20 B cells —> tx: rituximab
  - types: endemic (africa), sporadic
  - t (18;14) of c-myc gene
  - starry sky sheets of atypical cells and normally dispersed macrophages
  - tx also include prophylaxis for tumor lysis syndrome
- **Hodgkin lymphoma**
  - Granulomatous that increases Vit D → increases 1-alpha hydroxylase
  - Fever, weight loss, fatigue, painless LN= B symptoms
  - Anterior mediastinal mass
  - Eosinophilia and elevated LDH, reed-sternberg cells on biopsy
  - Bimodal age distribution
  - PET scan with 18-FDG uptake, mediastinal mass with distant

metastases
        - Increased risk of solid organ malignancy and cardiovascular disease
        - Most common subtype: nodular sclerosing
    - **Non-hodgkin lymphoma**
        - Chronic autoimmune disease with B symptoms (painless LN, fever, weight loss)
        - Elevated LDH
        - Dx: LN biopsy
    - **Mantle cell lymphoma**
        - t(11;14) BCL-1 → overexpression of cyclinD1
    - **EBV**
        - URI cold, fever, lethargy. Can cause hepatitis
        - atypical lymphocytosis, positive heterophile antibody test
        - increased risk of splenic rupture

Hodgkin Lymphoma Subtypes			
HL Type	**HL Subtype**	**Peak Age (years)**	**Prognosis**
Classic[a]	**Nodular sclerosis CHL**	15-35	• CHL curable in >85% of cases **Risk factors include:** • Bulky mediastinal mass • Extranodal disease • Elevated erythrocyte sedimentation rate • Involvement of 3 or more nodal areas
	Lymphocyte-rich CHL	30-50	
	Mixed cellularity CHL	20-50	
	Lymphocyte-depleted CHL	Bimodal; 20-30 and 40-50	
Non-classic[b]	**Nodular lymphocyte-predominant HL**	30-50	• Frequently relapses, but remains responsive to therapy • Stage I or II 10-year survival rate >80%

- **Leukemia & myeloproliferative disorders**
    - Concerning signs of leukemia= pancytopenia (pallor, easy bruising)
    - Bone marrow involvement, leg pain
    - Involvement of CSF is poor prognostic indicator (ALL)

Chromosomal Translocations		
Disease	**Translocation**	**Affected Gene/Product**
Burkitt Lymphoma	t(8;14)	c-Myc oncogene
Chronic Myelogenous Leukemia	t(9;22)	Philadelphia chromosome: BCR-ABL
Mantle Cell Lymphoma	t(11;14)	BCL-1; Overexpression of cyclin D1
Follicular Lymphoma	t(14;18)	BCL-2
Acute Promyelocytic Leukemia	t(15;17)	PML-RAR
Ewing's Sarcoma	t(11;22)	EWS-FLI-1

- **AML**
  - Downs syndrome increased risk
  - Dx: Bone marrow biopsy
- **APML**
  - t(15;17)
  - DIC
- **ALL**
  - Downs syndrome increased risk
- **CML**
  - BCR-ABL 9;22 translocation
  - Also triggered by radiation exposure
  - basophilia with granulocytosis, myeloblasts, left shift, leukocytosis (50k- 100k)
  - splenomegaly
  - hydroxyurea slows down cellular production
  - can progress to chronic —> progressive —> tumor lysis syndrome
  - Tx: imatinib (TKI) → causes edema, nausea, myalgia
- **CLL**
  - B lymphocytes
  - most common > 50 yo men, asymptomatic, granulocytopenia
  - mature, small lymphocytes, smudge cells
  - Very high WBC > 100K
  - **Risks: Autoimmune hemolytic anemia**
    - Hemolysis by IgG warm agglutinins
  - Dx: flow cytometry on serum → LN biopsy
  - **Richter transformation to DLBCL >> Hodgkins lymphoma**
- **Essential thrombocytosis**
  - nonreactive chronic MPD with platelets > 600K
  - r/o infection or inflammation
  - thrombotic events, bleeding
- **Polycythemia vera/ PCV***
  - JAK2 mutation —> xs RBC production → Low EPO
  - severe pruritis after hot shower, hyperviscosity and elevated blood

volume
        - Episodic pain and red-blue discoloration due to blood clot formation
        - DVT, stroke, MI common, bleeding
        - Hct > 50%, hgb high
        - Dx: bone marrow biopsy
        - Tx: phlebotomy
    - **Myelodysplastic syndrome**
        - hypercellular bone marrow with pancytopenia
    - **Hairy cell leukemia**
        - Splenomegaly, pancytopenia, filamentous cells
        - Minimal live and LN involvement
        - Dry tap bone marrow
        - Arises from mature B cells, BRAF V600E mutation
    - **Tumor lysis syndrome**
        - Massive release of intracellular products
            - Hyperkalemia
            - Hyperphosphatemia
            - Hypocalcemia
            - Hyperuricemia
                - AKI
        - Prophylaxis: IV fluid, allopurinol, rasburicase, febuxostat
    - **Neutropenic fever**
        - Most common source of infection in neutropenic fever with chemotherapy port= Staphe, enterococci, coagulase-negative staph

Children's Oncology Group and National Cancer Institute Risk Stratification

Risk Group	Features	Therapy	Projected 5-Year Event-Free Survival
Low	1. Initial WBC < 50,000/uL **AND** age 1 to 13 years **AND** lesser risk cytogenetics (trisomies 4 and 10, *ETV-RUNX1* fusion) **AND** rapid response to therapy	Conventional antimetabolite-based therapy	>95%
Average	1. Initial WBC < 50,000/uL **AND** age 1 to 13 years **AND r**apid response to therapy **OR** 2. Initial WBC < 50,000/uL **AND** age 1 to 13 years **AND** lesser risk cytogenetics (trisomies 4 and 10, *ETV RUNX1* fusion) **AND** slow response to therapy	Intensified antimetabolite-based therapy	90%-95%
High	1. Initial WBC ≥50,000/uL **OR** age >13 years **AND** rapid response to therapy **OR** 2. Initial WBC < 50,000/uL **AND** age 1 to 13 years **AND** slow response to therapy **OR** 3. CSF-positive leukemia **OR** 4. Testicular leukemia	Intensive multi-agent chemotherapy	88%-90%
Very high	1. Positive mean residual disease **OR** 2. Induction therapy failure **OR** 3. MLL rearrangements **OR** iAMP21 amplification **OR** 4. Age < 1 year **OR** age >13 years	Intensive multi-agent chemotherapy and consider allogeneic hematopoietic cell transplant in first remission (except in infants aged < 1 year)	< 80%
Special circumstances	1. T-cell ALL **OR** 2. t(9;22)	Intensive multi-agent chemotherapy; combine with tyrosine kinase inhibitory if t(9;22) is present	66%-80% T-cell ALL; 70% t(9;22)

- **Pancytopenia**

Causes of pancytopenia	
Bone marrow aplasia	• Aplastic anemia • Infection (eg, parvovirus, HIV, viral hepatitis) • Nutritional deficiency (eg, vitamin B_{12}/folate) • Medications (eg, hydroxyurea)
Bone marrow infiltration	• Cancer (eg, hematologic, metastatic) • Myelofibrosis • Infection (eg, tuberculosis, fungal infection)
Mature blood cell destruction	• Intravascular (eg, DIC, TTP) • Extravascular (eg, hypersplenism)

    -
    - Pancytopenia hepatosplenomegaly= myelofibrosis
    - Idiopathic, viral, autoimmune: acquired deficiency of HSCs
- **Graft vs Host disease**
    - Immune mediated, multisystem inflammatory condition
        - Acute GVHD: donor cytotoxic T cells attack the host with in 100 days.
            - Maculopapular rash, water diarrhea, liver inflammation
            - Tx: **methylprednisolone** (topical < 50% BSA; systemic if more severe)
        - Post-transplant lymphoproliferative disorder: years after transplant with extranodal and CNS lesions
        - **Methotrexate**: folic acid antagonist prevents GVHD. can cause renal insufficiency and hyperbilirubinemia
            - Giving leucovorin reduces MTX side effects
        - **Cyclosporine**: immunosuppressant for allogeneic kidney, liver and heart transplant
        - **Sirolimus** (rapamycin): prevents rejection after renal transplant and treat lymphangioleiomyomatosis. Binds FK bp-12
        - **Mycophenolate**: cytopenia, GI disturbance
        - **Calcineurin inhibitors** (tacrolimus): AKI

Graft Versus Host Disease (GVHD)		
Characteristic	**Acute GVHD**	**Chronic GVHD**
Timing	Classically presents in the early post-transplantation period (first 100 days)	Classically presents > 100 days after transplantation
Findings	• Skin: maculopapular rash, generalized erythroderma • GI: diarrhea, abdominal pain, anorexia, nausea/vomiting • Liver: abnormal liver function tests, cholestasis, hyperbilirubinemia • Lungs: interstitial pneumonitis • Kidneys: nephritis or nephrotic syndrome (membranous nephropathy) • Ocular symptoms: photophobia, conjunctivitis, lagophthalmos • Hematologic: cytopenias	• Skin: classically a lichen planus-like or sclerotic rash; other rashes are possible (eg, poikiloderma, morphea-like rash) • Eyes: dry eyes, cataracts, corneal staining, chemosis, conjunctival hyperemia • GI: dry mouth, oral ulcerations, dysphagia/esophagitis • Liver: similar to acute GVHD • Lungs: bronchiolitis obliterans, other obstructive or restrictive changes • Hematologic: thrombocytopenia, eosinophilia, IgA deficiency

    -

- **Acute transplant rejection**
  - Occurs in 3 months
  - Fever, lethargy, LFT abnormalities
  - Dx: liver biopsy, endotheliitis (subendothelial lymphocytes), mixed portal tract inflammation, nonsuppurative cholangitis
- **Osler-Weber-Rendu syndrome**
  - Telangiectasis (blanchable papules), epistaxis , AVMs (AV shunting)
  - Reactive polycythemia
- Other tumors
  - **Osteosarcoma:** periosteal elevation, sunburst, METAPHYSIS, LONG BONES
    - Kids & young adults
    - Dx: biopsy mass
    - Metastasizes to LUNGS
    - Tx: neoadjuvant chemotherapy, surgical excision, maintenance chemotherapy
  - Langerhan cell histiocytosis
    - Lytic lesion in DIAPHYSIS + eczematous rash
  - **Ewing sarcoma**: periosteal elevation, onion skinning/ concentric
    - Small round cells with hyperchromatic nuclei
  - **Rhabdomyosarcoma**: arises from mesenchymal cells. Occur in head and neck region (retro-orbital, middle ear, nasopharynx)
  - **Lynch syndrome**: AD HNPCC, DNA mismatch repair gene microsatellite instability. Increased risk of colorectal and endometrial cancer→ screen annually
    - Increased risk of ascending colon cancer
  - Neuroblastoma
    - Most common intra-abdominal malignancy of childhood, crosses midline
    - Retrobulbar metastasis is common
    - Opsoclonus-myoclonus (dancing eyes and feet)
    - Dx: US, open biopsy, elevated serum or urinary catecholamines (VMA, HVA)
  - Hepatoblastoma
    - Childhood tumor of liver
    - Elevated AFP
    - Tx: resection
  - Rhabdomyosarcoma
    - Mesenchymal cell tumors, can occur anywhere
  - Wilm's tumors
    - Renal parenchymal tumor, rarely crosses midline
    - HTN, hematuria

Genitourinary

- **Knee jerks**
  - **Apple green birefringence= amyloid**
  - **Linear anti-GBM= goodpastures**
  - **Spike and dome C3= membranous nephropathy**
  - **Tram-track= MGGN**
  - **Membrane splitting= alport**

- **cryoglobulinemia=** meltzer triad (purpura, althragia, weakness)
- 

Genitourinary Chapman Points		
Organ	**Anterior**	**Posterior**
Adrenals	1 inch lateral and 2 inches superior to the umbilicus (ipsilateral)	T11–T12 (ipsilateral)
Kidneys	1 inch lateral and 1 inch superior to the umbilicus (ipsilateral)	T12–L1 (ipsilateral)
Bladder	Periumbilical area	L2 TP bilaterally
Ovaries/testes	Superior pubic ramus, 2 cm lateral to the symphysis	T9–T11 (ipsilateral)
Urethra	Pubic symphysis	L2 TP bilaterally
Prostate	Outer femur (posterior iliotibial band)	Lateral sacral base bilaterally
Uterus	Inferior pubic rami	L5 TP bilaterally, medial to the PSIS
TP = transverse process.		

- **Emma holliday**
  - Numbness, chvostek or trousseau, prolonged QT= **hypocalcemia**
  - Stones, bones, groans, psych overtones, short QT= **hypercalcemia**
  - Paralysis, ileus, ST depression, U wave= **hypokalemia**
  - Peaked T waves, prolonged PR and WRS, sine waves= **hyperkalemia**
    - Tx: ca-gluconate, insulin + glucose, kayexalate, albuterol and sodium bicarb
    - Last resort= dialysis
  - CT scan of abdomen indicated when hematuria, hemodynamic instability, active bleeding
  - **Renal biopsy**
    - Fusion of podocytes on EM= minimal change disease (kids, nephrotic)
    - Linear IgG deposits along BM= Goodpasture disease (hemoptysis and nephritic)
    - Lymphocytic infiltration in interstitium, WBC casts= allergic interstitial nephritis, new med (cefazolin)
    - Mesangial deposition of IgA on EM= Bergers disease (days after URI)
    - Scattered electron-dense subepithelial deposits= membranous nephropathy
  - Proteinuria
    - 1-2 g/ 24 hours (0.05-0.08 g/ 24 hour)
    - > 5 g/ 24 hour= severe nephrotic disease
  - Erectile dysfunction
    - Fibrosis of tunica albuginea= peyronies
    - Depression
    - Atherosclerosis = decreased pelvic blood flow

- Electrolyte abnormality syndromes
  - Low serum Na, K, Cl and high urine Na and K= diuretic abuse
  - Laxative abuse = low electrolytes in urine
  - Vomiting = hyponatremia, hypokalemia, low urine electrolytes
- Renal diseases
  - Bartter syndrome
    - Defective Na/K/2Cl in ascending loop of henle
  - RTA 1= sjogren syndrome
  - RTA 2= fanconi syndrome, multiple myeloma
-

	Type 1	Type 2	Type 4
Location	Distal tubules	Proximal tubules	Adrenals
Acidemia	Present	Present	Present, but mild
Potassium	Low	Low	High
Pathophysiology	Failure to secrete H+ and absorb K+	Failure to reabsorb bicarbonate	Aldosterone deficiency or resistance

Commonly Tested Nephritic Syndromes						
Henoch-Schönlein Purpura	**IgA Nephropathy**	**Post-Infectious Glomerulonephritis**	**Anti-Glomerular Basement Membrane Antibody Disease**	**Hereditary Nephritis**	**Vasculitis**	**Allergic Interstitial Nephritis**
• Typically young adults and children • Abdominal pain, joint pain, and vasculitic rash	• After viral upper respiratory tract or gastrointestinal infection	• After streptococcal infection (commonly tonsillitis or skin infection)	• Also called Goodpasture Syndrome • Antibodies to type IV collagen • Often pulmonary symptoms, such as hemoptysis	• Also called Alport Syndrome • Hearing loss • Visual changes	• Systemic signs of vasculitis • Granulomatosis with polyangiitis, microscopic polyangiitis, and eosinophilic granulomatosis with polyangiitis	• After antibiotics or drugs (commonly NSAIDs, penicillins, or cephalosporins)

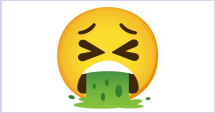
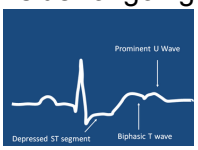
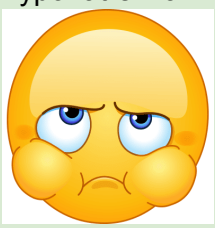
- **Next best step**
  - **Calciphylaxis** → wound care, end stage renal disease
  - **Urine protein electrophoresis** → multiple myeloma, MGUS, amyloidosis
  - **Urine culture** → + dipstick and symptoms for UTI
    - Tx: nitrofurantoin
    - TMP-SMX, cephalexin, fluoroquinolone
  - **Cystoscopy** → microscopic hematuria consistent with malignancy
  - **Renal biopsy** → elevated Cr, renal functions, and hematuria; suspect glomerulopathy or interstitial renal disease for dx
  - **oxybutynin=** urge incontinence
  - **Overflow incontinence=** intermittent self-catheterization
  - **Sacral nerve stimulation** ⇒ bladder and bowel incontinence
  - **Sling procedure=** stress incontinence
  - **Catheterization** → urinary retention in BPHto prevent acute complications of

obstruction
- **Abx** → only for symptomatic UTI
- **MRA of renal arteries**→ renal artery stenosis
- **Plasma renin, urine catecholamines** → pheochromocytoma
- **Renal biopsy** → definitive diagnosis of primary renal pathology, persistent nephrotic syndrome
- **Prostate biopsy** → peripheral nodule, prostate cancer
- **Voiding cystourethrogram:** vesicoureteral reflux, frequent UTIs
- **Retrograde urethrogram**: urethral injury
- **Cystoscopy**: direct visualization of bladder
- **Abdominal CT and US** → renal cancer with hematuria
- **Ischemic priapism < 4 hours=** intracavernosal injection of phenylephrine
- **Ischemic priapism > 4 hours=** aspiration blood from corpus cavernosum and irrigation of corpora cavernosa
- **Corticosteroid**s → Minimal change disease, protein losing disease in kids
- **Renal biopsy** → MCD in adults
- Orchiopexy → procedure to descend testicle, improves fertility, reduce risk of seminoma
- Pyelonephritis → ceftriaxone/levofloxacin 5-7 days

Types of Diuretics

Diuretic Class	Mechanism of Action	Side Effects
Thiazide	• Acts in the distal convoluted tubule	• Hypokalemia • Hyponatremia • Hyperglycemia • Hyperlipidemia • Hypomagnesemia • Hypercalcemia
Loop	• Acts on the Na-K-2Cl cotransporter in the thick ascending limb of the loop of Henle	• Hypokalemia • Hypocalcemia • Hypomagnesemia • Alkalosis • Ototoxicity
Potassium-sparing	• Acts on the principal cells in the distal nephron along the connecting tubule and collecting duct	• Hyperkalemia • Kidney stones
Carbonic-anhydrase inhibitors	• Block carbonic anhydrase in the proximal convoluted tubule	• Metabolic acidosis • Hypokalemia
Osmotic	• Inhibits sodium and water reabsorption in the proximal tubule and loop of Henle through the use of nonreabsorbable sugars (mannitol)	• Increases plasma osmolality • Hypernatremia

Hyperkalemia	Peaked T waves + wide QRS Low aldosterone, AceI or ARB, K sparing, ESRD, CKD Lisinopril ACEEEEinhibitors	**Calcium gluconate=** EKG changes present (stabilize membrane) **Insulin + glucose =** most cases **Albuterol=** severe hyperkalemia and EKG changes **Remove K=** stool (polystyrene), urine, hemodialysis

		Bicarbonate= hyperkalemia and metabolic acidosis
Hypokalemia < 3.5 	**FurOOOsemide** Fatigue, weakness, ST depression, flat, biphasic or inverted T waves or **flattened t waves** v4-6, U waves ST segment depression, QT prolongation These factors often cause hypokalemia: • Diarrhea • Dehydration • Insulin exposure • Hyperglycemia (which stimulates endogenous insulin secretion from the pancreas in normal conditions) • Hyperosmolality • Hyperthyroidism • Bartter syndrome • Metabolic alkalosis • Beta-2 adrenergic agonists	IV K+ If not corrected, consider ongoing hypomagnesemia 
Hypernatremia	> 145 Due to hypovolemia from free water loss Lethargy, irritability	Hyper/ Euvolemic no symptoms= free water to water down saltiness Hypovolemic w/o symptoms= D5 half normal saline Hypovolemic w/ symptoms= normal saline
Hyponatremia 	Hypovolemic, euvolemic, hypervolemic Nausea, fatigue, HA, confusion Iatrogenic osmotic demyelination if too quick **Answer E:** Hyponatremia is typically defined as serum sodium of < 135 mmol/L. The differential for hyponatremia is broad. These factors commonly cause hyponatremia: • Pseudohyponatremia (secondary to hyperglycemia) • Congestive heart failure • Nephrotic syndrome • Renal insufficiency • Burns • Diuretic use • Angiotensin-converting enzyme inhibitor use • Adrenal insufficiency • Excessive sweating (especially in patients with cystic fibrosis)	Hyper/ Euvolemic no symptoms= water restriction Hypovolemic w/o symptoms= normal saline Hypovolemic w/ symptoms= hypertonic saline
Hypercalcemia	AMS Decreased/shortened QT interval	IV fluids + calcitonin Bisphosphonates NO THIAZIDES If multiple myeloma, get bone marrow biopsy after stabilization
Hypocalcemia	Blood transfusion (citrate) Post-thyroidectomy **QT prolongation** Pseudohyperparathyroidism HYPOMAGNESEMIA	Weakness, perioral tingling, trousseau sign, chvostek sign, prolonged QT Worsened with respiratory alkalosis

		Answer C: Hypocalcemia is typically defined as serum total calcium < 8.4 mg/dL. These factors commonly cause hypocalcemia: • Renal failure • Hypoparathyroidism • Vitamin D deficiency • Hypomagnesemia • Pancreatitis
Hypermagnesemia	Loss of DTRs, weakness, respiratory failure, hypocalcemia **Answer A:** Hypermagnesemia is typically defined as serum magnesium > 2.6 mg/dL. Common causes include increased magnesium ingestion (from antacids, laxatives, or dietary supplements) and renal insufficiency. Patients typically present with bradycardia and decreased deep tendon reflexes with ECG findings of PR, QRS, and QTc prolongation, along with possible heart block. Given this patient's history of 4 days of diarrhea and vomiting, muscle pain, and flattened T waves on ECG, hypokalemia is much more likely than hypermagnesemia.	IV calcium gluconate (stabilize cardiac membranes)
hypomagnesemia	Weakness (promotes loss of K in renal) Associated with malnutrition, ostomy	IV magnesium sulfate Watch for hypokalemia
Hyperphosphatemia		**Answer B:** Hyperphosphatemia is typically defined as serum phosphorus > 4.5 mg/dL. These factors commonly cause hyperphosphatemia: • Acute phosphate ingestion • Hyperparathyroidism • Vitamin D toxicity • Renal failure • Rhabdomyolysis • Tumor lysis syndrome

- **Urology**
  - VAP (vein, artery, pelvis)
  - Left gonadal v drains into left renal vein
  - Renal stones: UVJ, over iliac vessels
    - Indication to treat (laser, remove, stent): NVD, SKI, sepsis
  - Stent: stone
  - Percutaneous nephrostomy tube: severely septic, large stones > 1.5cm
  - Stones: use non-contrast CT
    - Radiolucent stones: uric acid (not seen on xray), indinavir (not seen on CT)
    - Uric acid stones seen with crohn's disease/ chronic diarrhea and loss of HCO3
- **Common renal disease**

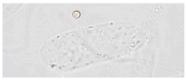
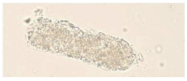
Commonly Tested Renal Pathology	
Renal Condition	**Biopsy Findings**
Minimal Change Disease	• Effacement of the podocytes (foot processes) on electron microscopy
IgA Nephropathy	• Dominant or co-dominant deposition of IgA, as seen with immunofluorescence
Postinfectious Glomerulonephritis	• "Lumpy bumpy" deposits of IgG and complement C3b on the renal basement membrane
Anti–Glomerular Basement Membrane Antibody Disease	• Bright linear deposits of IgG and complement C3 on the glomerular basement membrane
Hereditary Nephritis	• Longitudinal splitting of the lamina densa of the glomerular basement membrane on electron microscopy
Membranous Nephropathy	• "Spike and dome" subepithelial deposits on electron microscopy
Membranoproliferative Glomerulonephritis	• Subepithelial deposits and subendothelial deposits in the mesangium and subendothelial space
Focal Segmental Glomerulosclerosis	• Segmental scarring on light microscopy
Vasculitis	• Mild focal and segmental glomerulonephritis to a diffuse necrotizing and crescentic glomerulonephritis, usually without immune deposits (pauci-immune)
Amyloidosis	• Apple-green birefringence and amyloid deposits in the mesangium, as seen with polarized light

Acute interstitial nephritis	WBCs casts, proteinuria **FEAR: fever, eosinophils, azotemia, rash + took Aspirin, ABx, diuretics**	Legionella or new Abx TMP-SMX 1-2 weeks ago Stop offending agent, add **steroids** if no improvement Definitive dx: renal biopsy
Acute pyelonephritis	Pyuria, bacteria, nitrites, LE Perinephric stranding	CVA tenderness
Acute Glomerulonephritis	Hematuria, proteinuria	End stage renal disease, nephritic and nephrotic disease

Nephrolithiasis	Stone in Urinary tract with hydronephrosis	Kids: kidney US Adult: noncontrast CT
Renal infarction	Wedge-shaped renal defect	A fib, renal artery trauma, hypercoagulability, infectious endocarditis
Acute tubular necrosis*	Muddy brown casts, patient with ampho, AG, cisplatin or ischemia Arises from surgery, trauma, sepsis. Dx once pre-renal and post-renal causes are r/o	Tx: fluids, avoid nephrotoxic, add steroids if no improvement
Rhabdomyolysis *	High CPK, blood on dipstick Check K or EKG	Tx: bicarb, alkalinize urine
Ethylene glycol toxicity	Envelope shaped crystals	Tx: dialysis, NaHCO3 if ph < 7.2
Contrast-induced nephropathy**	48-72 hours after cardiac cath or CT scan	Hydrate before the procedure* with 0.9% saline Give bicarb or NAC
Obstructive uropathy	Urinary retention and hydronephrosis Dx: renal US	
Renal tubular necrosis	Anion gap: MUDPILES Non-AG: diarrhea, RTAs	1: H+ (not excreted → acidotic); stONE 2: BI= can't absorb Bicarb 4: ALDO= hypoaldo (hypoNa, hyperK)
Allergic interstitial nephritis	Hypersensitivity Penicillin, diuretics, sulfonamides Eosinophilic pyuria	SLE
Interstitial cystitis (bladder pain syndrome)	Urinary frequency/ urgency Relieved with voiding, dyspareunia Psych + IBS, fibromyalgia	Normal UA
Glomerulosclerosis	Fibrosis of glomeruli FSGS, diabetic nephropathy	HIV, opioid abuse, sickle cell
Post strep glomerulonephritis	Swelling, brown urine post URI and treatment for strep	Supportive care only Dx: streptozyme

- **Acute Kidney Injury (AKI)**
  - acute reduction in glomerular filtration rate (GFR)
    - > 25% or 0.5 rise in Cr
    - Work-up: BUN/Cr → > 20:1= prerenal
    - Check urine Na and Cr → if FeNA < 1%= prerenal

        - If pt on diuretic check FENurea → < 35%= prerenal
    - Tx:
        - Prerenal causes= anything keeping kidney from being perfused
        - **Fluids** and underlying illness
        - Discontinue causative medications: metformin, nsaids, nephrotoxic drugs
    - Due to:
        - hypertension
        - chronic kidney disease
        - dehydration and volume depletion
        - diabetes
        - chronic liver or lung disease
        - Uremia
            - Nausea, asterixis, encephalopathy, platelet dysfunction, pericarditis
    - **Pre-renal AKI**
        - #1 Decreased renal perfusion (listed above)
            - True volume depletion (dehydration)
            - Decreased arterial blood volume (cirrhosis, HF)
            - Displaced intravascular fluids (sepsis, pancreatitis)
            - Renal artery stenosis
            - Afferent arteriole vasoconstriction (NSAIDS)
        - Prerenal azotemia
            - Presentation: increased Serum Cr above baseline (> 50%), decreased urine output, BUN/Cr > 20:1, FEna < 1%, bland urine sediment
            - Tubules become ischemic and necrotic
            - Tx: aggressive hydration
    -

Differentiating between: Prerenal Disease and Acute Tubular Necrosis (ATN)		
Characteristics	**Prerenal disease**	**ATN**
Urine microscopy (casts)	Hyaline casts (nonspecific) or bland	Muddy brown granular casts
Casts pictures		
Ability to concentrate urine?	Preserved	Decreased
Serum BUN:Cr ratio	>20:1	< 15:1
Urine sodium	< 20 mEq/L	>40 mEq/L
FeNa[1]	< 1%	>2%
FeUrea	< 35%	>40%
Urine osmolality (Osm)	>500 mOsm/kg	< 350 mOsm/kg
Fluid responsiveness[2]	Return to baseline creatinine w/in 72 hours once euvolemic	Persistent elevation of creatinine >72 hours once euvolemic
Causes	Volume depletion, hypotension, and edematous states (cirrhosis or CHF)	Severe prerenal disease, particularly severe hypotension, sepsis or shock, and nephrotoxins

    -

Disease	Diagnosis	Treatment
Primary kidney disease	UA, BUN/creatinine, renal US	Treat underlying renal issue; BP control with an ACE inhibitor
RAS: FMD	Duplex Doppler renal US, CTA or MRA	Revascularization and BP control
RAS: Atherosclerosis	Duplex Doppler renal US, CTA or MRA	BP control (ACE inhibitor or ARB + diuretic); revascularization only if complications
Primary aldosteronism	Elevated aldosterone: renin ratio; aldosterone >20 ng/dL; hypokalemia	Mineralocorticoid receptor antagonist (e.g., spironolactone)
Obstructive sleep apnea	Polysomnography	CPAP machine
Medication-induced	Stop medication and monitor for improvements	Discontinue suspected medication
Pheochromocytoma	24-hour urine metanephrine levels	Surgical removal under the cover of an alpha antagonist, which prevents a hypertensive crisis
Cushing syndrome	24-hour urine cortisol, dexamethasone suppression test, late-night salivary cortisol swab	Surgical removal of the ACTH-secreting pituitary or ectopic tumor or removal of cortisol-secreting adrenal tumors
Coarctation of the aorta	CTA; rib notching often seen on chest radiograph	Surgical intervention

- **Contrast induced nephropathy***
  - Muddy brown granular and epithelial cell casts
  - Resolves 3-5 days
  - Pretreatment with saline / hydration **

Risk Factors for Contrast-Induced Nephropathy	
Major risk factors	**Preventative measures**
Chronic kidney disease (decreased glomerular filtration rate)	Avoid volume depletion (increases renal vasoconstriction)
Poorly-controlled diabetes	Avoid NSAIDs (increases renal vasoconstriction)
Contrast dose > 125 mL	Low doses of contrast (< 125 mL)
Ionic and hyperosmolar contrast agents	Iso-osmolar or non-ionic low-osmolar agents
Proteinuria and Hyperglycemia	Administer isotonic saline prior to the procedure

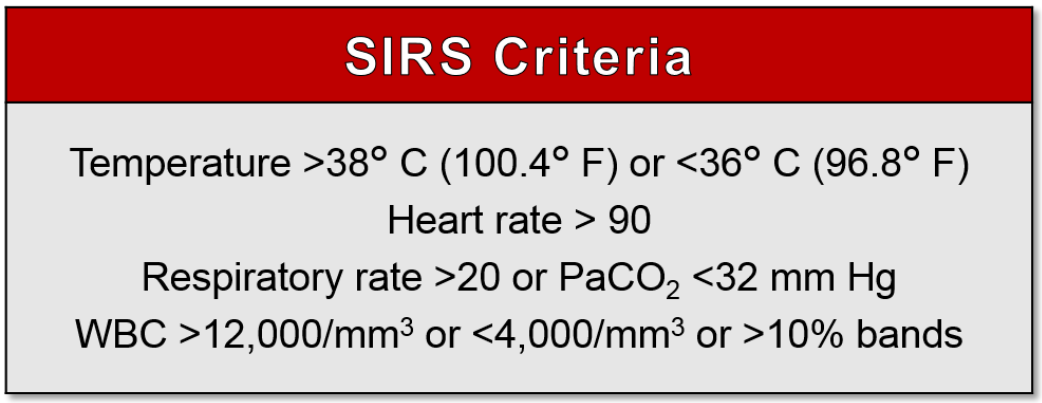
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- **Renal tubular acidosis**
  - Non-anion gap metabolic acidosis (check bicarb, AG)
    - Type 1= lithium, hypOkalemia, give bicarb
      - Most common causes: analgesic nephropathy, obstructed urinary tract anomalies, amphotericin, autoimmune
    - Type II= myeloma, hypOkalemia
    - Type IV= DM, hypERkalemia, fludrocortisone
    - Note: salicylate intoxication results in respiratory alkalosis with hyperventilation and delay AG metabolic acidosis

	Cause	Presentation/Dx	Treatment
Type I *Distal*	**Lithium**/Ampho B analgesics SLE, Sjogrens, sickle cell, hepatitis	Urine pH > 5.4 **HypoK**, Kidney stones Problem? Cannot excrete H+	Replete K **Oral bicarb**
Type II *Proximal*	*Fanconi's syndrome **Myeloma**, amyloid, vitD def, autoimmune dz	**HypoK**, Osteomalacia Problem? Cannot reabsorb HCO3.	Replete K Mild diuretic **Bicarb won't help**
Type IV *Hyperrenin Hypoaldo*	>50% caused by **diabetes!** Addisons, sickle cell, any cause of aldo def.	**HyperK** HyperCl High urine [Na] even w/ salt restriction	**Fludrocortisone**

Renal Tubular Acidosis				
Type of RTA	**Urine pH**	**Serum Potassium**	**Physiologic Defect**	**Urine Anion Gap**
Type I (Distal)	>5.5	Low	Impaired distal acid secretion	Positive
Type II (Proximal)	< 5.5	Low	Impaired proximal bicarbonate reabsorption	Negative
Type IV	< 5.5	High	Hypoaldosteronism or aldosterone resistance	Positive

	Type 1	Type 2	Type 4
Location	Distal tubules	Proximal tubules	Adrenals
Acidemia	Present	Present	Present, but mild
Potassium	Low	Low	High
Pathophysiology	Failure to secrete H+ and absorb K+	Failure to reabsorb bicarbonate	Aldosterone deficiency or resistance

- **Chronic kidney disease**
  - #1 cause: DM >> HTN
  - #1 cause of death: cardiovascular disease → target LDL < 100
  - Complications
    - HTN → increased aldosterone, fluid retention→ CHF
    - Normochromic normocytic anemia → loss of EPO
    - ↑K, ↑PO4, ↓Ca (leads to 2ndary hyperPTH)
      - Decreased active Vit D (1,25), less vit D synthesis, less Ca uptake and reabsorption
    - ↑PO4 leads to precip of Ca into tissues → renal osteodystrophy and **calciphylaxis** (skin necrosis)
      - Due to ESRD, hyperphosphatemia
      - Painful soft tissue calcifications and ulcerations
      - Hospice vs dialysis
    - Uremia confusion, pericarditis, itchiness, increased bleeding 2/2 platelet

dysfxn
        - ASTERIXIS
        - Tx: dialysis
    - **Dialysis**
        - Dialysis related amyloidosis → high beta-2-microglobulin
        - Causes arthritis in shoulders, carpal tunnel, bone cysts
        - Affinity for osteoarticular structures
- **Cholesterol embolization**
    - Acute renal failure, skin manifestations, ischemia, hollenhorst plaques after arteriography and cardiac catheterization
    - Livedo reticularis, acute renal failure, eosinophilia
- Septic Shock
    - 

- **Renovascular hypertension**
    - Renal artery stenosis= periumbilical bruit
    - Resistant hypertension due to atherosclerosis
    - Elevated serum Cr > 30% after starting ACEi or ARB, flash pulmonary edema, asymmetric kidney, abdominal bruit
- **Polycystic kidney disease**
    - First line: antihypertensive (ARBs, ACEi)
        - Supportive, vasopressin-2 antagonists (tolvaptan)
    - CT head if berry aneurysm rupture/ symptoms
    - Risk of: cerebral aneurysms, hepatic/ pancreatic cysts, cardiac valve disease, colonic diverticula
    - AD= shows later in life
    - AR= shows early in life
- **Cardiorenal syndrome**
    - HF and low CO → decreased renal perfusion → RAAS → vasoconstriction and volume retention, increases load on LV and reduces renal perfusion
    - Elevated CVP → reduces glomerular capillary filtration gradient
    - Tx: diuretics to restore filtration gradient and improves GFR
- **Hepatorenal syndrome**
    - Liver cirrhosis → NO in splanchnic circulation due to portal hypertension
    - Systemic vasodilation → renal hypoperfusion → AKI
    - Labs show prerenal azotemia (elevated Cr, low urine Na, FeNa < 1%), bland urine
    - Caused by dehydration, xs diuretics, GI bleed, NSAIDS, sepsis
    - Tx: octreotide, splanchnic vasoconstriction

Hepatorenal syndrome	
Risk factors	• Advanced cirrhosis with portal hypertension & edema
Precipitating factors	• Reduced renal perfusion • GI bleed, vomiting, sepsis, excessive diuretic use, SBP • Reduced glomerular pressure & GFR ◦ NSAID use (constricts afferent arterioles)
Diagnosis	• Renal hypoperfusion • FeNa <1% (or urine Na <10 mEq/L) • Absence of tubular injury • No RBC, protein, or granular casts in urine • No improvement in renal function with fluids
Treatment	• Address precipitating factors (eg, hypovolemia, anemia, infection) • Splanchnic vasoconstrictors (midodrine, octreotide, norepinephrine) • Liver transplantation

- **Nephropathy****
  - Features:
    - proteinuria > 3.5 g/day
    - generalized edema
    - hypoalbuminemia
    - Hyperlipidemia
  - Best first test: **repeat protein** (albumin/ creatinine), then quantify w/ 24 hour urine
  - Renal vein thrombosis in nephrotic syndrome? Pee out coag factors, protein C and S. Do CT or US stat.
  - **Minimal change disease**
    - Podocyte foot process disease
    - Tx: steroids
  - **Focal segmental glomerulosclerosis (FSGS):** common cause of nephrotic syndrome in HIV
    - tx: HAART, ACEi to reduce virus and proteinuria
  - **Acute tubular necrosis**
    - Intrinsic acute end-stage renal disease due to ischemic or nephrotoxic insults —> oliguric → uremic, hyperkalemic, metabolic acidosis → polyuria recovery phase
    - ischemia, low BP, sepsis, contrast dye
    - Most common AKI
    - nephrotoxic: aminoglycosides, cisplatin, amphoB
  - **IgA nephropathy**: hematuria, proteinuria, increased Creatinine
  - **Membranous nephropathy**: idiopathic, caused by SLE, HBV, syphilis, malignancy
  - **MPGN**
    - Tram-track BM w/ subendo deposits
    - Chronic hepatitis and low complement, Hep C
  - **HIV nephropathy**
    - Advanced HIV → edema, AKI and proteinuria
    - APOL1 gene variant in AA of sub-saharan descent
    - Bx: collapsing focal segmental glomerulosclerosis
    - Bad prognosis

- **Goodpasture syndrome** (anti-GBM)—> linear IgG deposits on GBM. nephritis (red casts) and hemoptysis
  - New onset pulmonary and renal issues
  - tx: plasma exchange, immunosuppression with corticosteroids and cyclophosphamide
- **Wegener granulomatosis/ granulomatosis with polyangiitis**: vasculitis with saddle nose deformity, C-ANCA (in blood)
  - Kidney, lung involvement
  - Most accurate test is biopsy
  - Cough, pulmonary infiltrates, hemoptysis, renal involvement
  - Hx of chronic rhinosinusitis, ulceration and tracheal narrowing, hemoptysis
  - Dx: lung nodules with cavitation, opacities, necrotizing granulomas, pauci-immune glomerulonephritis (negative IF) crescentic nephritis, RPGN
  - Anemia of chronic disease
  - Tx: steroids, cyclophosphamide
- **Churg strauss/ eosinophilic vasculitis**
  - Best test is lung biopsy
  - p-ANCA, renal failure, asthma, eosinophilia
  - Tx: cyclophosphamide
- **Polyarteritis nodosa**
  - P-anca, no lung involvement, Hep B
  - small/ medium arteries of every organ except lung
  - Microaneurysms → tissue ischemia
  - Dx: mesenteric angiography. Gold standard= biopsy
  - Tx: cyclophosphamide

Renal Diseases with Extrarenal Manifestations		
Disease	**Biopsy/Laboratory Findings**	**Clinical Features**
Alport syndrome	Thickening of the GBM; no immune deposits	Sensorineural hearing loss; ocular abnormalities (eg, cataracts)
IgA nephropathy	Mesangial IgA deposits; normal serum complement levels	Develops concurrently or days after an upper respiratory infection (URI)
Goodpasture syndrome	Anti-GBM antibodies; linear IgG deposits on the GBM	Progressive glomerulonephritis; hemoptysis
Postinfectious glomerulonephritis	Decreased serum complement levels; serum antistreptolysin O antibodies	Develops weeks after a group A beta-hemolytic streptococcal infection (skin or upper respiratory tract)
Granulomatosis with polyangiitis	c-ANCA (anti-proteinase 3 antibodies)	Involves the upper and lower airways; progressive glomerulonephritis; skin lesions

- **Nephritic syndromes**
  - Proteinuria < 2g, hematuria, edema, azotemia
  - 1-2 days after runny nose, sore throat, cough= Bergers disease (IgA neph)
  - **Henoch-schonlien purpura**
    - IgA, kid s/p viral URI → renal failure, abdominal pain, arthralgia, and purpura
    - Tx: steroids

- **HUS**
  - E. coli or shigella
  - Kiddo s/p hamburger and diarrhea, renal failure, MAHA and petechiae
- **TTP**
  - Tx: plasmapheresis
  - Cardiac patient s/p ticlopidine with renal failure, MAHA, low platelets, fever and AMS

- **Metabolic alkalosis**
  - Tx: 0.9% saline IV fluid bolus, give back potassium
    - also anything to stop vomiting, replenish K+, supportive therapy
  - repeated vomit/ dehydration —> contraction alkalosis
  - Acetazolamide best in hypervolemia w/ metabolic alkalosis

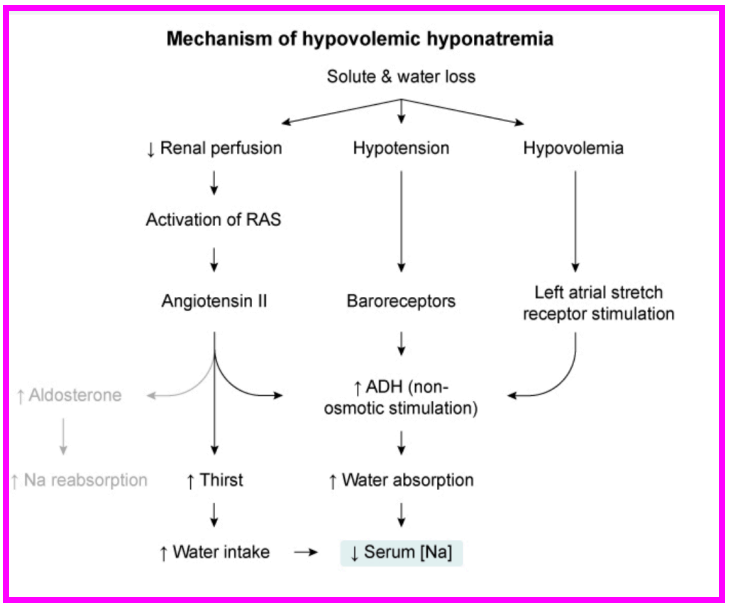
Metabolic Alkalosis Physiology	
Type/Cause	**Mechanism**
Gastric acid loss (nasogastric tube suctioning, vomiting)	Loss of hydrogen ions leads to hypochloremic, hypokalemic metabolic alkalosis
Contraction alkalosis	Overdiuresis leads to the loss of large volumes of sodium-rich, bicarbonate-low fluid, resulting in an increased serum bicarbonate concentration. Concomitant increase in aldosterone production (secondary hyperaldosteronism) and decrease in glomerular filtration rate also contribute.
Hypertensive types (Conn syndrome, secondary hyperaldosteronism)	Increased aldosterone/mineralocorticoids increase Na+/K+ pump activity, leading to hypokalemia. This activates H+/K+ exchangers to increase H+ secretion. Mineralocorticoids also directly stimulate the secretory H-ATPase pump in the kidneys.

- **Metabolic acidosis**
  - Nonanion gap: due to loss of HCO3
    - Type 1 RTA: impaired H excretion , hypokalemia, pH > 5.5
    - Type 2 RTA: impaired HCO3 reabsorption in PTA, hypokalemia
    - Type 4 RTA: reduced aldosterone secretion, impaired H/ K excretion in collecting duct, pH < 5.5
  - Tx:
- **Hypernatremia**
  - Increase Na= loss of water
  - **Central diabetes insipidus** (decreased ADH from pituitary)
  - High sodium, high serum osm > urine Osm
  - Replace water with D5W or other hypotonic solution
  - Don't correct faster than 12-24/ day= cerebral edema
  - Tx: Hypernatremia
    - Hyper/ Euvolemic no symptoms= free water to water down saltiness
    - Hypovolemic w/o symptoms= D5 half normal saline
    - Hypovolemic w/ symptoms= normal saline
- **Hyponatremia (Na+ < 135)**
  - H2O retention: CHF, SIADH, thiazides (salt wasting)
  - hyperglycemia (osmotic hyponatremia)
  - high fluid intake
  - **#1: check serum osmolarity**
    - Low?—> check UNa (see chart below)
    - Normal? —> hyperlipidemia, multiple myeloma (**pseudohyponatremia**)
    - high? —> **hyperglycemia** or mannitol

- Check Osm → **then check volume status**
  - **hypervolemic**= high BP, edema, crackles in lungs
  - **hypovolemic**= dry mucous membranes
  - **euvolemic**= normal vitals and PE
  - Correct with normal saline in hypovolemic
  - 3% if seizures or Na < 120
  - Fluids + diuretics
  - Don't correct 12-24/ day= central pontine myelinolysis
- **Check urine Na**
  - High: **SIADH (**urine osm > serum osm)
  - Low: psychogenic
- **Tx: Hyponatremia**
  - Hyper/ Euvolemic no symptoms= water restriction → tolvaptan
  - Hypovolemic w/o symptoms= normal saline
  - Hypovolemic w/ symptoms= hypertonic saline

	Hypovolemic	Euvolemic	Hypervolemic
Urina Na+ < 10 - Problem elsewhere	GI fluid loss, skin fluid loss (burn), 3rd spacing	psychogenic polydipsia	nephrosis, cirrhosis, CHF
Urine Na+ > 20 - Intrinsic kidney disease	thiazides	SIADH (pulling in water, Na higher in urine), adrenal insufficiency, hypothyroidism, pregnancy, MDMA	renal failure / CKD/ AKI/ ATN

Hyponatremia						
	Hypovolemic		**Euvolemic**		**Hypervolemic**	
	Renal Losses	**Extrarenal Losses**	**SIADH**	**Polydipsia**	**Congestive Heart Failure/Cirrhosis**	**Renal Failure**
Urine sodium	> 20	< 10	> 20	—	< 10	> 20
Urine osmolality	—	> 200	> 200	< 100	> 200	—
SIADH = syndrome of inappropriate antidiuretic hormone.						



- **SIADH**
  - xs release of ADH —> euvolemic, hypoosmolar hyponatremia (high Na in urine)
  - caused by CNS pathology, head trauma, psych causes, paraneoplastic syndromes (SCLL), HIV, surgery, pneumonia, pulmonary inflammation
    - AMS, lethargy, seizures
    - **Euvolemic, hypoosmolar hyponatremia**
  - Tx: fluid restriction, loops, hypertonic saline
  - Demeclocycline: inhibits ADH mediated insertion into collecting tubules
  - Tolvaptan: V2 vasopressin receptor antagonist causes selective water loss in kidney without affecting Na and K → used if standard therapy does not work
  -

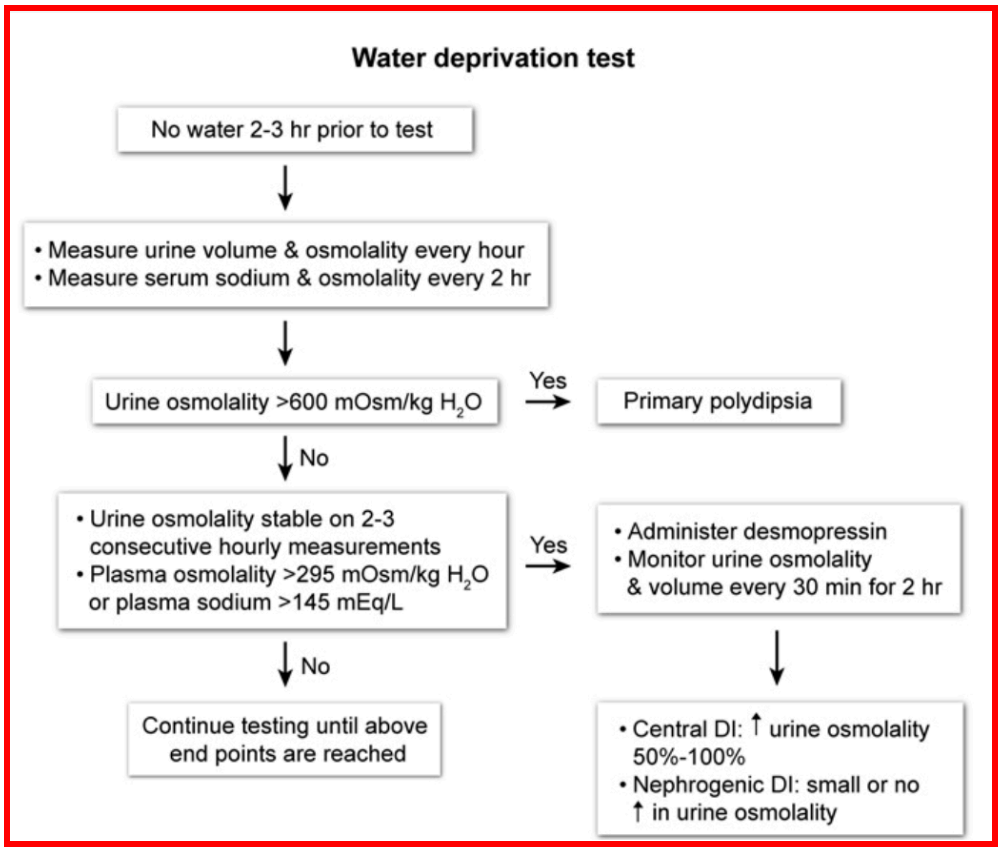
Syndrome of inappropriate antidiuretic hormone	
Etiologies	• CNS disturbance (eg, stroke, hemorrhage, trauma) • Medications (eg, carbamazepine, SSRIs, NSAIDs) • Lung disease (eg, pneumonia) • Ectopic ADH secretion (eg, small cell lung cancer) • Pain &/or nausea
Clinical features	• Mild/moderate hyponatremia: nausea, forgetfulness • Severe hyponatremia: seizures, coma • Euvolemia (eg, moist mucous membranes, no edema, no JVD)
Laboratory findings	• Hyponatremia • Serum osmolality <275 mOsm/kg H_2O (hypotonic) • Urine osmolality >100 mOsm/kg H_2O • Urine sodium >40 mEq/L
Management	• Fluid restriction ± salt tablets • Hypertonic (3%) saline for severe hyponatremia

- **Diabetes insipidus**
  - Central: failure of posterior pituitary to secrete ADH
    - tx: desmopressin (ADH analogs)
    - low urine osm, hypernatremia

        - Polyuria, polydipsia
    - nephrogenic: kidneys do not respond to ADH
        - tx: salt restriction, increased H2O intake, thiazides, treat underlying disease
        - Hx of lithium
        - Tx: amiloride
    - **Hypernatremia, low urine osmolality < serum osmolality with large urine volume**
    - dx: water deprivation test —> ADH administration
        - increased urine osmol: central DI
        - no increased urine osmol: nephrogenic DI

Causes of polyuria & dilute urine			
	Primary polydipsia	**Central DI**	**Nephrogenic DI**
Cause	• ADH independent (excessive water intake)	• ADH deficiency (CNS pathology)	• ADH resistance (renal disease)
Etiology	• Antipsychotics (dry mouth) • Psychiatric conditions	• Idiopathic • Trauma • Pituitary surgery • Ischemic encephalopathy	• Chronic lithium use • Hypercalcemia • Hereditary (*AVPR2* & aquaporin 2 mutations)
Results of water deprivation	• High urine osmolality	• Low urine osmolality	• Low urine osmolality
Response to desmopressin	• No change	• Increased urine osmolality	• No change

- **Polyuria**

- 

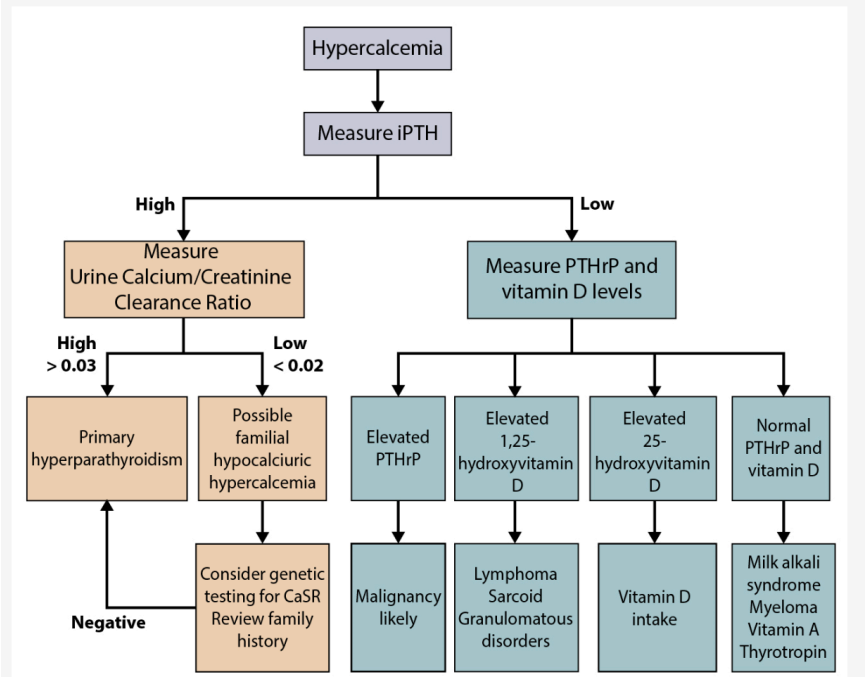
- **Causes of Polydipsia and Polyuria with Dilute Urine**

Diagnosis	Etiology	Causes	Diagnostics	Treatment
Primary polydipsia	Increase in water intake	Psychiatric disease, hypothalamic infiltration (sarcoidosis)	Low serum sodium (< 137 mEq/L) with dilute urine (less than 1/2 the plasma osmolality)	Restrict drugs that cause dry mouth, restrict water
Central DI	Pituitary gland fails to make antidiuretic hormone	Head trauma, neurosurgery, infection	• High-normal plasma sodium concentration (> 142 mEq/L) • Urine osmolality less than plasma osmolality (U_{osm}/P_{osm} < 0.7) • Desmopressin challenge: U_{osm} increases by at least 50%	Desmopressin
Nephrogenic DI	Kidneys are unresponsive to antidiuretic hormone	Renal failure, hypercalcemia, demeclocycline, lithium, sickle-cell anemia	• High-normal plasma sodium concentration (> 142 mEq/L) • Urine osmolality less than plasma osmolality (U_{osm}/P_{osm} < 0.7) • Desmopressin challenge: U_{osm} does not increase	Low-sodium diet and thiazide diuretics

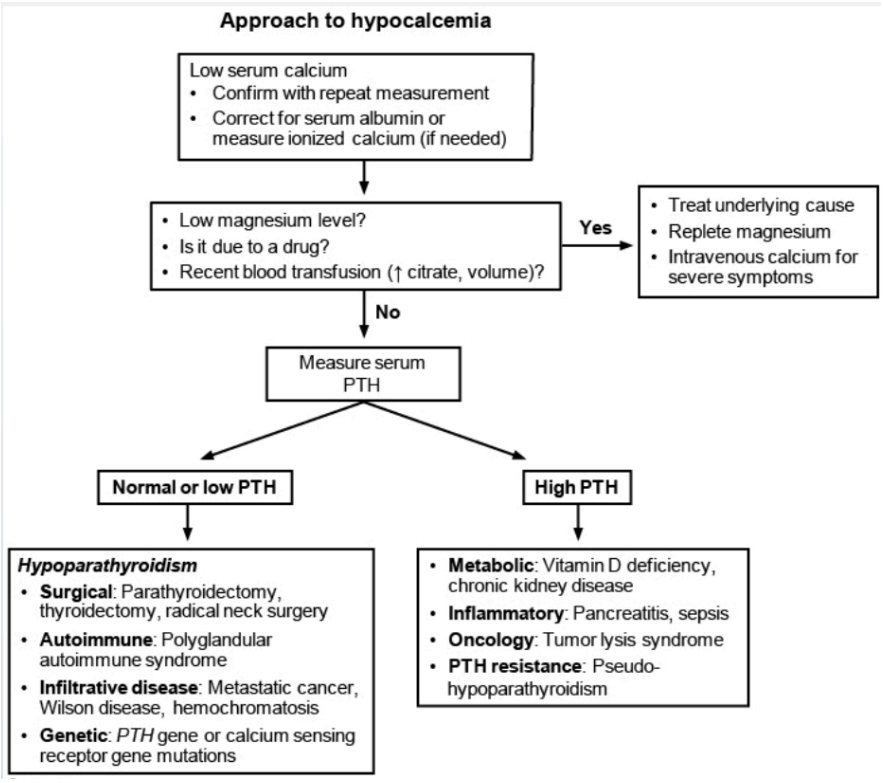
- **Renal artery stenosis***
  - Abdominal bruit + <u>secondary hypertension</u> despite HTN medication management
  - High renin, aldosterone, Angiotensin
    - Hyperaldosteronism has HTN with metabolic derangements
  - Young patient: fibromuscular dysplasia
  - Older patient: atherosclerosis
- **UTI**
  - Increased urinary frequency, burning
  - Common cause of delirium / seizure in <u>elderly</u>
  - Risk factors: young women, contraception, anal sex
    - GNR: E coli, Klebsiella, Proteus

    - Work-up: U/A, Urine culture, CT scan (non-pregnant), US (pregnancy)
        - UA: positive WBC, nitrates, LE + symptoms
        - NAAT of first-catch urine
    - **Complicated**: Penis, plastic, procedure, pyelonephritis, pregnant
        - Tx: 7 days
    - **Uncomplicated**: non-pregnant
        - Tx: 3 days
    - **Urethritis**
        - Gonorrhea, chlamydia, mycoplasma, trichomonas
        - Dx: urine PCR, negative gram stain
        - Tx: ceftriaxone + azithromycin x 1 or doxycycline 7 days
        - HIV screen
    - **Asymptomatic Bacteriuria**
        - GNR, GBS...don't treat unless Pregnancy or urologic procedure
        - Tx: amoxicillin or nitrofurantoin
    - **Cystitis**
        - GNR
        - Urgency, frequency, dysuria
        - Work-up: UA
        - Tx: TMP-SMX, nitrofurantoin, fosfomycin
    - **Pyelonephritis**
        - CVA tenderness, fever, chills, sepsis
        - UA: WBC casts
        - Urine culture
        - IV ceftriaxone (hospitalized), Ciprofloxacin (ambulatory)
        - Tx: give quinolones first → wait until 48 hours improvement → switch to ceftriaxone
    - **Perinephric abscess**
        - Pyelo without improvement in 72 hours
        - Dx: CT or US
        - Tx: incision and drainage, Abx for 14 days
- **PSA + Prostate cancer**
    - ~ 4 is cut-off, used to monitor for disease recurrence
        - Tx: leuprolide: GnRH agonist
    - Screening > 50, 40 if family history
    - Dx: spine xray, DRE, transrectal US
    - Prostate cancer dx: 12 core biopsies
        - Gleason 6: watch
        - Gleason 7: radiation, radical prostatectomy
    - Tx that reduces invasive prostate cancer
        - finasteride= BPH
        - Saw pimento = similar action to finasteride as 5-alpha reductase inhibitor
        - Radiation = metastatic cancer, not candidate for surgery
- **Bladder cancer**
    - Risk factors: smoking
    - Found on cystoscopy for hematuria work-up
        - Muscle invasive= bladder resection
        - non-invasive= scraped out
- **Renal cancer**
    - Flank pain, mass, hematuria
    - Renal cell carcinoma most common → secretes EPO → secondary polycythemia

    - Invades from renal vein → IVC → atrium
    - < 3cm = good prognosis
    - > 3 cm= bad prognosis
- **Hypercalcemia**
    - Stones, bones, and psychiatric overtones
        - Renal: stones, distal RTA, polyuria, nephrogenic DI, renal insufficiency
        - GI: anorexia, N/V, pancreatitis, PUD
        - MSK: weakness, bone pain, osteopenia, osteoporosis
        - Neuro: AMS, confusion, fatigue, coma
        - Cardio: short QT, bradycardia, HTN
    - consider hyperPTH, bone mets, Vit D toxicity
    - Check for PTHrp (paraneoplastic syndrome)
    - tx: calcitonin, bisphosphonate if volume expansion does not lower serum Calcium < 14
        - **IV fluid** (can cause dilution)
        - loop diuretics (maintain euvolemia)
        - Intranasal calcitonin: increases renal Ca excretion , decrease bone resorption
        - Bisphosphonate
- **Milk-alkali syndrome**
    - Acute renal failure from hypercalcemia → afferent arteriole vasoconstriction → oliguria
    - Too many tums



- **Hypocalcemia***
    - Paresthesias
    - Transfusion products contain citrate (calcium chelator). Hyperkalemia occurs as well
    - Caused by hypomagnesemia and hypophosphatemia
        - Common in hospitalized alcoholics

        - Hypomagnesemia causes hypocalcemia due to inducing resistance to PTH
    - Tx: **calcium gluconate IV**
    - 

- **Hyperkalemia***
    - K+ > 5
    - due to impaired excretion, CKD, increased K intake, shift from intracellular to extracellular space
        - beta blockers, statins, metabolic acidosis, rhabdomyolysis
    - symptoms: MSK weakness, cardiac arrhythmias (peaked T waves), recent use of Bactrim
    - tx:
        - Stabilization of cardiac membrane with **calcium chloride or gluconate***
        - Temporize**:** shift potassium intracellularly w/ **insulin and glucose**;
        - promote K secretion thru diuretics, na, polystyrene sulfonate or dialysis.

Emergent Treatment of Hyperkalemia (CIGAR-B)			
Treatment	**Function**	**Indications**	**Administration**
Calcium	Protects the myocardium until potassium improves (Does not change potassium levels)	If EKG changes are present	• Calcium gluconate: given through peripheral IV • Calcium chloride: Must be given through a central line. Irritating to vessels. Extravasation can cause necrosis
Insulin	Activates sodium/potassium ATPase, shifting potassium into the cells	Most cases of hyperkalemia	Give 10-20 units of regular insulin IV in combination with glucose (prevents hypoglycemia)
Glucose	Prevents hypoglycemia from insulin administration	Most cases of hyperkalemia	1 amp D50. May forego if blood glucose is > 250 mg/dL
Albuterol	Similar to insulin; activates sodium/potassium ATPase, shifting potassium into the cells	Severe hyperkalemia with EKG changes	Give with insulin and glucose for a synergistic effect. Nebulized 10-20 mg over 10 minutes
Remove	While other modalities shift potassium into cells, potassium must ultimately be removed from the body	Stool: Severe hyperkalemia Urine: Good renal function Hemodialysis: ESRD or refractory	• Stool: Gastrointestinal cation exchangers. Patiromer (preferred) or sodium polystyrene sulfonate (can cause bowel necrosis) • Urine: Furosemide (Lasix) 40 mg IV + saline to maintain euvolemia • Hemodialysis: Only if refractory to medicine or if ESRD
Bicarbonate	Sodium bicarbonate causes an alkalotic environment. Acid shifts out of cells to neutralize the pH. When acid moves out, potassium moves in to keep cell neutrality	Patients with metabolic acidosis	Controversial: 1 amp boluses (50 mEq) were previously used. A bicarbonate drip may be more effective

- **Hypokalemia**
  - Paralysis, weakness
  - Next step: recheck potassium → do EKG
  - Tx: IV or oral potassium with cardiac monitoring
    - Agressive tx if K is < 4.0 due to life-threatening arrhythmias
    - PO > IV
      - 10mEq= 0.1 increase in K
      - Replace Mg
  - Genetic
    - barters= loops
    - gitelman's= thiazides
- **Hypomagnesemia**
  - Mg < 1.5
  - renal (diuretics, amphotericin, EtOH, DM, hypercalcemia) or GI loss (diarrhea)
  - symptoms: prolonged QT
  - Common in alcohol use disorder
  - Hyperreflexia and tremor, **twitching**, muscle cramps
  - **Hypokalemia** occurs, **Hypocalcemia** can occur too
  - **Hypoparathyroidism** due to low Mg impairs PTH release
  - Hyperglycemia
- **Altitude sickness → respiratory alkalosis, noncardiogenic pulmonary edema**
  - Symptoms: HA, light-headedness, lethargy, lack of appetite, N/V, HYPERVENTILATION, pulmonary edema, cerebral edema
  - Tx: acidify urine with acetazolamide (CA inhibitor in proximal tubule)
    - Increase urinary excretion of HCO3
    - cerebral/ pulmonary edema= hyperbaric O2, dexamethasone, thermal regulation
- **Hyperventilation syndrome**
  - Respiratory alkalosis
  - Hypocalcemia (perioral tingling)
- **BPH (benign prostatic hyperplasia)**
  - enlargement of the prostate —> difficulty urinating, nocturia, hesitancy/ incomplete emptying, dribbling
  - Increased cell # in central/ transitional zones
  - Work-up: PSA for baseline, UA to r/o infection

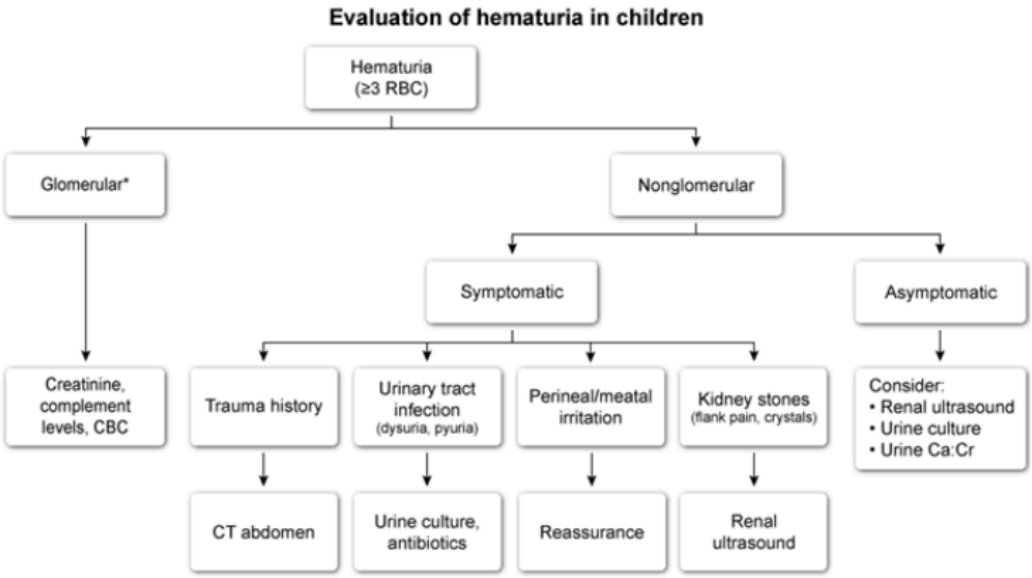
- tx:
  - #1: alpha adrenergic antagonist (-osin), tamsulosin (flomax)
    - hypotension/ dizziness, retrograde ejaculation
  - 5alpha reductase inhibitor if PSA > 1.5 ng/mL (finasteride)
    - 3-6 months to take effect
    - Suppresses PSA artificially in ½
  - Anticholinergic
  - B3 agonist Mirgabetron
  - PDE-5 inhibitor
- Work-up:
  - TURP
  - Prostatectomy
  - Laser prostatectomy

- **Prostate**
  - Peripheral, transitional, central zones
  - Storage symptoms: urgency, frequency, nocturia, incontinence
  - Voiding symptoms: dribbling, dysuria, weak stream
  - Post-micturition: post void dribbling, sensation of incomplete emptying
  - **Prostate cancer**
    - risk factors: age, AA, BRCA2
    - Pathology: gleason score
    - PSA is not a regular screening tool
  - **Prostatitis**: TMP-SMX (e coli)
    - Dysuria, low back pain, fever
    - Indurated and tender prostate
  - **Acute bacterial prostatitis:**
    - Urinary retention with prostate swelling
    - Dx: suprapubic catheter, UA and culture → E.coli from intraprostatic urinary reflux
    - Tx: levofloxacin
- **Erectile dysfunction**
  - PDE5 inhibitors
  - Contraindicated with alpha blockers and CCB
- **Infectious urethritis in men**
  - Due to gonorrhea, chlamydia, mycoplasma, trichomonas
  - Tx:
    - G&C= ceftriaxone + doxycycline
    - Chlamydia/ myco: azithromycin
    - Trich: metronidazole
- Balanitis & balanoposthitis
  - Inflammation of glands and foreskin due to poor hygiene
  - Dx: KOH if on skin, G&C if in urethra
- **Testicular diseases**
  - **Epididymitis**
    - < 35 yo= **Gonorrhea & chlamydia**
    - > 35 yo= bladder outlet obstruction, coliform bacteria, **E.coli**
    - U/L posterior testicular pain, improved with elevation, febrile, leukocytosis, swelling, erythema
    - Pain improved with elevation
    - Tx: Abx (ceftriaxone + doxycycline < 35 yo) or levofloxacin alone > 35 yo
  - **Testicular torsion**

        - Urgent surgery, B/L orchiopexy
        - Severe pain and negative cremasteric reflex, affected testicle high-riding than the other
        - Pain worsened with elevated scrotum
        - Spermatic cord twisted in the tunica vaginalis → ischemia
    - **Testicular hydrocele**
        - Fluid between parietal and visceral layers of tunica vaginalis
        - Painless swelling over weeks- months
    - Testicular appendage
        - Blue dot sign
        - Causes a testicular torsion picture, but less severe.
    - **Testicular cancer**
        - Painless nodule on testicle
        - Screen with AFP, hcg, LDH
        - Dx: **ultrasound**
        - Tx: orchiectomy (needle biopsy contraindicated due to tumor seeding)→ pathology for dx →
            - Look for mets to the retroperitoneal lymph nodes

Causes of Testicular Swelling	
Etiology	**Finding**
Hydrocele	• Scrotal fluid collection • Transilluminates
Tumors	• Does not transilluminate • Slow enlargement • May be accompanied by B-type symptoms[1]
Varicocele	• Dilated veins in pampiniform plexus • Most common cause of scrotal enlargement • Does not transilluminate • Can lead to infertility
Torsion	• Rotation of testicle around the spermatic cord • Acute, severe pain, high-riding testis • Absent cremasteric reflex
Epididymitis	• Inflammation (often infectious) of the epididymis • Improved pain with testicular elevation • Often a STI in younger patients (< 35 years old)

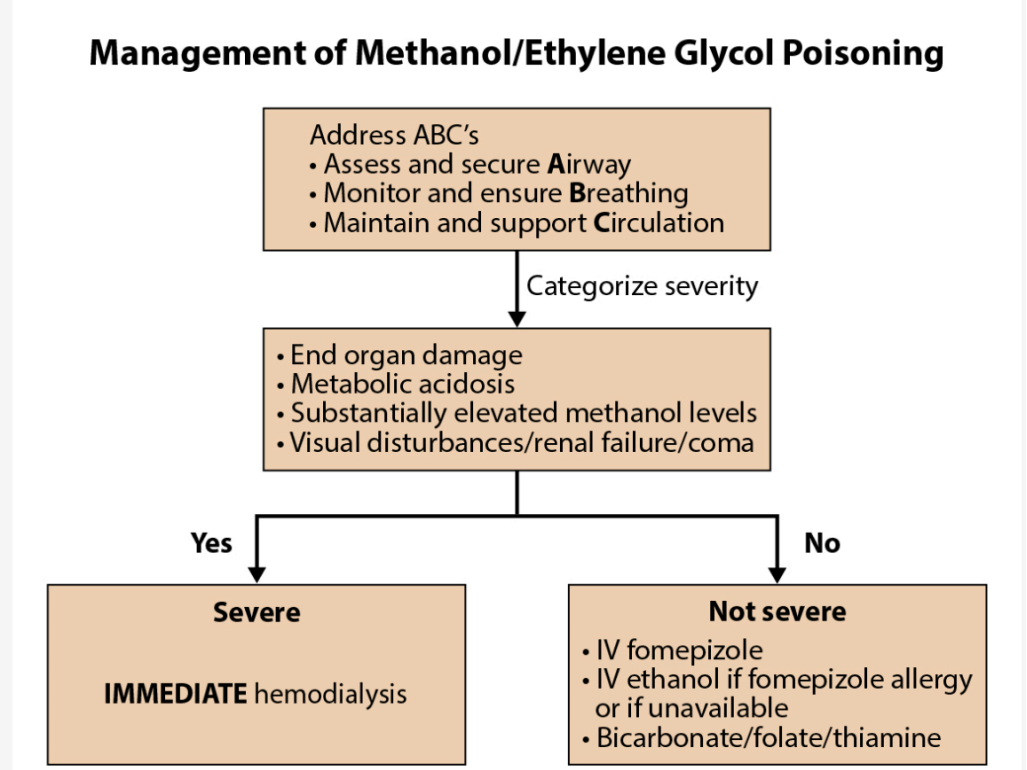
    -
- **Nephrotic syndrome**
    - proteinuria 24 hour urine —> spot protein/ creatinine ratio first morning void
    - r/o exercise or stress-induced functional proteinuria
- **Hematuria**



-
- UTI, exercise, procedure, renal disease (Renal cell carcinoma), bladder transitional cell carcinoma—> needs thorough work up
  - **#1 UA**
  - **CT** if radiating flank pain + hematuria
  - Abdominal mass → nephrectomy
  - Bladder mass → cystoscopy
  - Trauma → CT
  - UTI → urine culture + empiric Abc
- Causes of **hematuria**:
  - **Painless hematuria**= renal/ bladder cancer (RCC, transitional cell carcinoma)
  - Terminal hematuria with tiny clots= bladder cancer, hemorr cystitis (cyclophosphamide)
  - Dysmorphic RBCs/ casts= glomerular source
  - Nephritic syndrome= proteinuria, hematuria, edema, azotemia
  - 1-2 days after runny nose, sore throat, cough= nergers disease (IgA nephropathy)
  - 1-2 weeks after sore throat or skin infection= PSGN, cola urine
    - ASO titer, subepithelial IgG humps
  - Hematuria + hemoptysis= **goodpasture syndrome**
    - Abs to type IV collagen → anti-GBM ab linear
  - Hematuria + deafness= **alport syndrome**
    - XR mutation in type IV collagen → splitting of basement membrane
    - Cant see, cant pee, cant hear a bee
  - **Membranoproliferative nephropathy**
    - Tram track appearance
    - Nephrotic syndrome
  - **Membranous nephropathy**
    - Spike and dome appearance
    - IgG and C3 deposits
  - menses (resolves)
  - exercise (resolves)

        - UTI (+ WBC, +/-nitrates, pyuria)
        - Unilateral flank pain —> calculus, malignancy, IgA nephropathy
            - Work up: non contrast CT (size and location of stone)
        - African american
        - no cause? —> CT w/o contrast
        - AKI/ glomerular bleed/ risk of malignancy —> CTU, cystoscopy
        - pregnant? —> bladder/ kidney US
    - **microscopic** hematuria: 3 RBCs per HPF
        - further work up
    - **macroscopic**: overtly red urine, acute kidney injury
        - grossly, color of blood does not indicate amount of blood less. mostly clots will be present
        - urine dipstick —> urine sediment to r/o myoglobinuria
        - dx: CT urography, CT to rule out stone, cystoscopy to r/o bladder neoplasia
- **Hypogonadism**
    - testosterone deficiency: decreased libido, ED
        - test FSH, LH for primary causes
            - karyotyping (klinefelters)
        - test prolactin and serum iron, TIBC for secondary causes
        - MRI of pituitary gland
        - Nonfunctioning pituitary adenoma= secretes alpha subunit, mass effect, low LH and FSH.
            - Normal thyroids
            - Elevated prolactin
- **Urine analysis** “urine is the window into the soul”
    - Whiff: sulfa= cystine, ammonia= urinary retention, fruity= DKA, pungent= UTI
    - RTA 1= distal, cannot secrete protons
    - RTA2= proximal, cannot reabsorb HCO3
    - Alkaline Urine: urease splitting (pseudomonas, proteus (struvite), klebsiella , morganella, corynebacterium)
    - Hematuria: > 3 RBCs / hpf in 2 of 3 samples
        - IgA nephropathy is most common cause
    - Crystals:
        - **Coffin lid**= struvite
        - **envelope**= calcium oxalate, antifreeze (ethylene glycol)
        - **square**= uric acid
        - **needles**= bilirubin
        - **hexagon**= cysteine
            - Rotten egg smell
            - Defective renal amino acid transport
    - Kidney stones
        - Most common= **calcium oxalate** (enveloped)
            - Conditions: hyperparathyroidism, type 1 RTA, sarcoidosis, high protein, bariatric surgery, crohn's disease (Ca binds to fatty acids)
            - Tx: normal calcium diet, low fat, low salt diet, increased fluids
        - Kid with fmhx of stones= cystinuria (can resorb AA)
        - **Uric acid (rhomboid)**
            - Low urine pH, gout
            - **Chondrocalcinosis**
            - Tx: alkalinize urine, xanthine oxidase inhibitor (allopurinol)

        - Chronic foley with alkaline pee
            - Struvite (magnesium ammonium phosphate)= coffin lid
            - Proteus, staph, pseudomonas, klebsiella
        - s/p bowel resection for volvulus
            - Oxalate stone
            - Ca cannot be reabsorbed in gut
        - Stones < 5mm= pass, hydrate
        - Stones > 2 cm= open or endoscopic removal
        - Stones 5mm-2cm= extracorporeal shock wave lithotripsy
    - Sterile pyuria
        - Chlamydia, ureaplasma, TB, virus, cyclophosphamide
    - https://microbiologyinfo.com/
- **Emergent hemodialysis**
    - A- **Acidosis**
    - E- **Electrolyte imbalance** particularly high K > 6.5
    - I-**Intoxication** (MALE)
        - **Methanol → fomepizole**
        - **Aspirin**
            - **Hypokalemia**
            - **Sodium bicarb**
        - **Lithium**
        - **ethylene glycol**
    - O- **Overload** of volume sxs of CHF or pulmonary edema
    - U- **Uremia** pericarditis, altered mental status
        - Uremia: hemolytic HUS, uremic pericarditis, platelet dysfunction
    - NOT for high creatinine or oliguria alone!



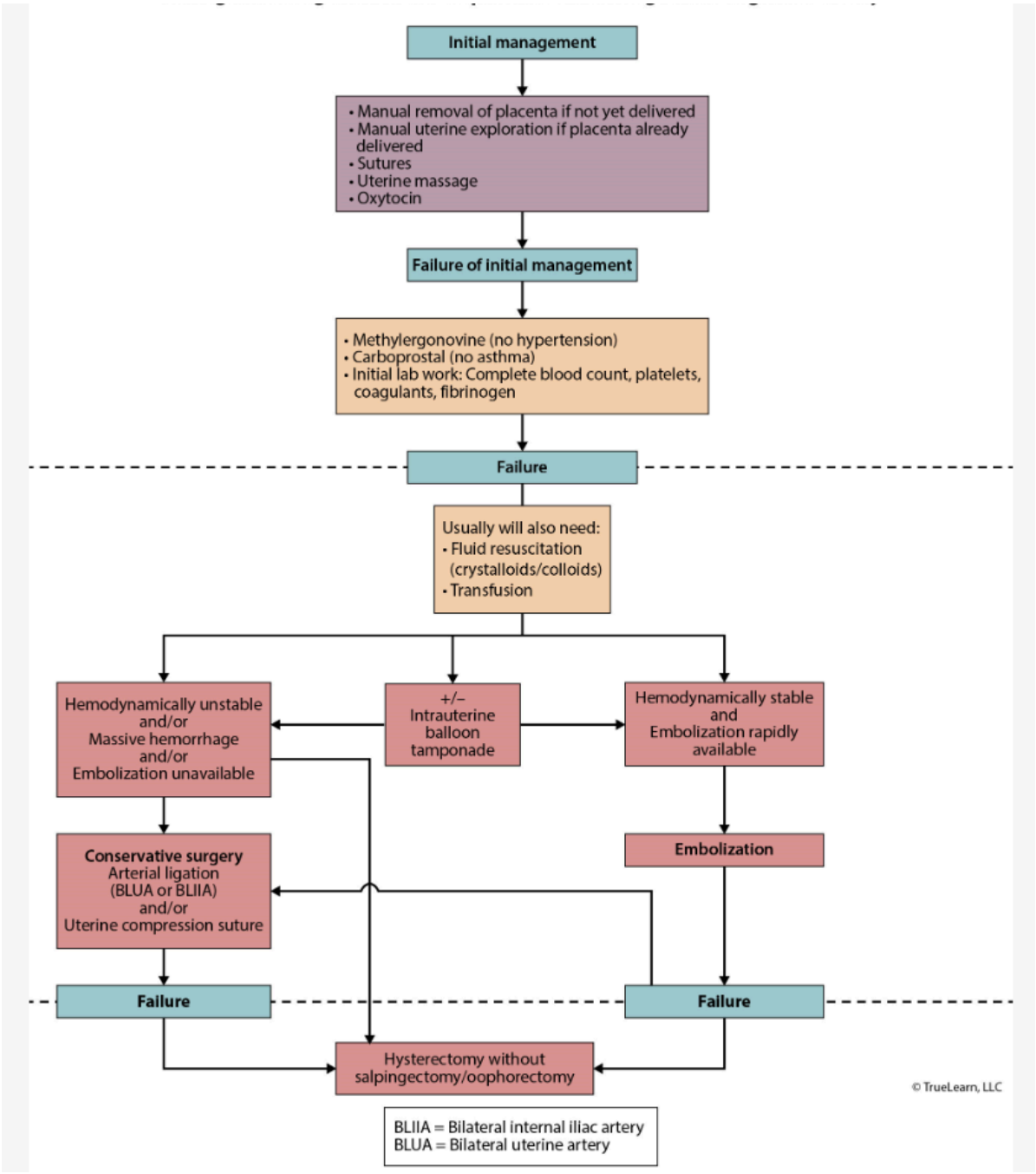
- **Diuretics**

Mechanisms of Action of Diuretics		
Class of Medications	**Examples**	**Mechanism of Action on the Nephron**
Thiazide diuretics	Hydrochlorothiazide and Chlorthalidone	Inhibits resorption of sodium and chloride at the distal convoluted tubule
Loop diuretics	Furosemide, Bumetanide, and Torsemide	Inhibits sodium and chloride resorption at the loop of Henle, and proximal and distal convoluted tubule
Potassium-sparing diuretics	Spironolactone and Eplerenone	Antagonizes aldosterone-specific mineralocorticoid receptors (primarily in the distal convoluted tubule), decreasing sodium and water reabsorption and increasing potassium retention

Gynecologic/Obstetric

- **See Mer's OBGYN cheat sheet**

Antihypertensive Therapy During Pregnancy	
First-line	• β-blockers (**labetalol**) • Calcium channel blockers (extended-release nifedipine) • Hydralazine • Methyldopa
Second-line*	• Clonidine • Thiazide diuretics
Contraindicated	• Angiotensin-converting enzyme inhibitors • Angiotensin II receptor blockers • Direct renin inhibitors • Mineralocorticoid receptor antagonists (spironolactone) • Nitroprusside


Initial management
• Manual removal of placenta if not yet delivered
• Manual uterine exploration if placenta already delivered
• Sutures
• Uterine massage
• Oxytocin
Failure of initial management
• Methylergonovine (no hypertension)
• Carboprostal (no asthma)
• Initial lab work: Complete blood count, platelets, coagulants, fibrinogen
Failure
Usually will also need:
• Fluid resuscitation (crystalloids/colloids)
• Transfusion
Hemodynamically unstable and/or Massive hemorrhage and/or Embolization unavailable
+/– Intrauterine balloon tamponade
Hemodynamically stable and Embolization rapidly available
Conservative surgery
Arterial ligation (BLUA or BLIIA) and/or Uterine compression suture
Embolization
Failure
Failure
Hysterectomy without salpingectomy/oophorectomy
© TrueLearn, LLC
BLIIA = Bilateral internal iliac artery
BLUA = Bilateral uterine artery

Types of Spontaneous Abortion*		
Type	**Clinical Features**	**Notes**
Complete	• Resolution of cramping and vaginal bleeding • No visualization of intrauterine pregnancy • Closed (usually) or open cervical os	Usually no treatment is necessary after establishing the diagnosis.
Incomplete	• Vaginal bleeding • Cramping • Partial expulsion of POC • Dilated cervical os	More specific wording is preferred, such as "persistent empty gestational sac despite the initial diagnosis of nonviability (insert the number of weeks) weeks ago."
Inevitable	• Vaginal bleeding • Lower abdominal pain • Dilated cervical os • No expulsion of POC	As it can be difficult to differentiate between an open external or internal cervical os, the term "vaginal bleeding in early pregnancy" (regardless of cervical os dilation) is preferred.
Missed	• Often asymptomatic, ± mild bleeding or cramping • Loss of previous pregnancy-related symptoms (eg, nausea/vomiting) • Intrauterine pregnancy with no fetal heart activity • Closed cervical os	"Asymptomatic pregnancy loss" is the current terminology.
Septic	• Vaginal bleeding • Cramping • Purulent discharge, fever • ± retained POC or intrauterine pregnancy • Open or closed cervical os	"Septic" is the current terminology.
Threatened*	• Vaginal bleeding or spotting • Intrauterine pregnancy with fetal heart activity • Closed cervical os	As it can be difficult to differentiate between an open external or internal cervical os, the term "vaginal bleeding in early pregnancy" (regardless of cervical os dilation) is preferred.
POC = products of conception		

Treatment Options for Pregnancy Complications or Termination			
Treatment	**Ectopic Pregnancy**	**Miscarriage**	**Termination of Pregnancy**
Mifepristone	Not used	Can be given 24 hours before misoprostol to improve the efficacy in managing early pregnancy loss	Given with misoprostol for medical termination of pregnancy up to 10 weeks' gestation
Methotrexate	Can be given as a single-dose, 2-dose, or multi-dose regimen	Not used	Less frequently used (less effective than mifepristone; significant risk of teratogenicity if the pregnancy proceeds)
Misoprostol	Not used	Can be given as a single dose or 2 doses (if the first dose is ineffective)	Used 24 hours after mifepristone as part of a medical management regimen
Dilation and curettage	Can be used to help identify chorionic villi if the location of the pregnancy is unknown	Can be performed in the office or operating room	Surgical option for termination

Gastroenterology

- **Labs**
  - Alcoholic hepatitis: Scotch > Tonic (AST > ALT)
  - Viral hepatitis: ALT > AST in 1000s
  - AST and ALT in 1000s after trauma = ischemic hepatitis
  - Elevated direct bilirubin= obstructive (stone/ cancer), Dubin Johnson, Rotor
  - Elevated indirect bilirubin= hemolysis, Gilberts, Crigler Najjar
  - Elevated ALP and GGT= bile duct disease
  - Elevated ALP, normal GGT and Ca= Paget's disease (increased hat size, hearing loss, HA. Tx: Bisphosphonates)
  - AMA ab= PBC, Tx with bile resins
  - ANA and anti-smooth muscle Ab= autoimmune hepatitis. Tx: steroids
  - High Fe, low ferritin, low Fe TIBC= hemochromatosis (hepatitis, DM, bronze skin)
    - Tx: phlebotomy
  - Low ceruloplasmin, high urine Cu= wilsons (hepatitis, psych from Cu deposits in basal ganglia , corneal Kyser flescher) → zinc
  - Transferrin → Hereditary hemochromatosis
  - CT abdomen: inflammation, diverticulitis, malignancy, chronic pancreatitis
  - Colonoscopy: IBD or malignancy
  - HIDA scan= gallbladder evaluation when inflamed or obstructed
  - Stool analysis= WBC inflammatory
  - Normotensive + diarrhea= oral rehydration therapy (glucose + salt)
  - Hypotensive + diarrhea= IV fluids
  - Stool ova & parasite analysis = chronic diarrhea
  - EGD= H pylori
  - Urea breath test= H pylori
  - Tissue transglutaminase Ab= celiac disease
  - Hydrogen breath test= lactose intolerance
  - CCK: released in duodenum in presence of fat

- Gastrin : zollinger ellison syndrome → ulcers
- Pepsin: produced by chief cells in stomach
- Somatostatin: inhibitory to histamine and gastrin, treats ZES
- Glucose challenge test: Dumping syndrome in acutely ill post-op roux-en-y

- **Heavy metal poisoning**
  - Mercury: fearfulness, personality change (mad hatter) from fluorescent lab
  - Lead: neuropathy, burton lines in gums
    - Tx: EDTA and dimercaperol
  - Arsenic: QT prolong, respiratory distress, garlic odor breath
    - Tx: Sodium 2,3-dimercapto-1-propane sulfate

Bugs

- **Campylobacter**: bloody diarrhea
  - GBS → cytoalbumin dissociation
- **Salmonella**: bloody diarrhea, high fever
- **Shigella**: bloody diarrhea
- **Shiga toxin producing E coli=** self limited bloody diarrhea, HUS, AKI, anemia and thrombocytopenia
- **Clostridium difficile**: opportunistic, abdominal pain, watery diarrhea → vancomycin → metronidazole
- **Giardia**: > 1 week after exposure → watery diarrhea
- **Rotavirus**: severe watery diarrhea in unimmunized kids, self-limited

- **Next best step**
  - **Barium enema/CXR:** pneumoperitoneum and assess free air under the diaphragm → perforated gastric ulcer
  - **Contrast-enhanced CT of abdomen**: acute infection / inflammation , neoplasm, diverticulitis
  - **Abdominal x ray**: bowel perforation
  - **Incision and drainage:** abscess due to bacterial drainage, pseudocyst > 5cm
  - Immediate groin exploration: inguinal hernia that symptoms
  - **FNA**: lymphadenopathy
  - **Frequent colonoscopy**: kid with FAP is watched; total proctocolectomy in late teens and twenties
  - **ERCP**: choledocholithiasis, symptomatic persistent gallstones and biliary obstruction and get stone out, cannulization. Can be therapeutic if there's an obstruction. Gets TISSUE BIOPSY
  - **MRCP:** choledocholithiasis, diagnostic uncertainty (no bile duct seen on US)
  - **Cholecystectomy**: acute pancreatitis due to gallstones
  - **HIDA (scintography) scan**: diagnose acute cholecystitis with stones
  - **EGD**: symptomatic GERD, dysphagia, PUD
  - **Mesenteric angiography:** mesenteric ischemia, obstruction in setting of Gi bleed
  - **Air contrast enema:** intussusception
  - **Abdominal xray**: intestinal obstruction or malrotation
  - **Abdominal US:** AAA
  - **Stool culture:** infectious gastroenteritis
  - **manometry=** achalasia, spasm, scleroderma
  - **Fundoplication** = treatment for achalasia
  - **N-AC** = tylenol ID, elevated liver enzymes > 10K, hepatic failure ~ 72 hours
  - **Liver transplant=** acute liver failure with decompensation (asterixis, high enzymes, worsening condition)
  - **Ursodeoxycholic acid=** PBC

- **Hydrogen breath test=** lactose intolerance
- **Urine test for reducing substances=**glucosuria, galactosuria
- **Stool pH** = lactose deficiency
- **Spironolactone and furosemide**= cirrhosis management

Tests Used to Diagnose Gastrointestinal Disorders			
Test	**Uses**	**Indications**	**Additional Comments**
Colonoscopy	• Direct visualization and tissue sampling of the rectum, colon, and distal small intestine	• Colon cancer screening • Evaluation of abdominal pain, changes in bowel habits, and/or GI bleeding • IBD surveillance	• Invasive: may result in bowel perforation or persistent bleeding from the biopsy site
Fecal leukocytes	• Detection of nonspecific bowel inflammation or infection	• Provide ancillary information in the evaluation of diarrhea suspicious for an infectious or inflammatory etiology	• Variable sensitivity and specificity (as low as 20%)
Hydrogen breath test	• Diagnosis of lactose intolerance	• Used to establish a definitive diagnosis of lactose intolerance in the evaluation of a patient with diarrhea	• Antibiotics can result in a false-negative test and should be avoided for ~ 1 month before testing
Stool culture	• Identification of the source of GI symptoms	• Evaluation of patients with persistent diarrhea, fever, and/or abdominal bloating • Suspected bacterial or parasite infection	• Results may be obscured by bismuth, antibiotics, or mineral oil
Tissue transglutaminase IgA	• Diagnosis and detection of disease activity in celiac disease	• Screening for celiac disease in patients with unexplained diarrhea, dermatitis herpetiformis, and/or evidence of malabsorption	• IgA deficiency can result in a false-negative test

- **High yield**

  Aspirin use → gastritis, NSAID induced
  - **Alcoholic liver disease:** AST> ALT x2 (scotch > tonic)
  - **Nonalcoholic fatty liver disease:** obese, asymptomatic
  - **Autoimmune hepatitis:** AST and ALT in thousands, arthralgias, fatigue
  - **PBC**: high ALP, pruritus, fatigue
  - **Statin induced liver injury:** STATINs (rate limiting enzyme of HMG-CoA reductase)
  - **Hepatitis**: ALT > AST x2
  - **Ascending cholangitis:** dilated intrahepatic ducts,Pentad, E coli
  - **Hemochromatosis**: hyperpigmentation, arthralgia, fatigue, older women
  - **Eosinophilic esophagitis**: cannot tolerate liquids, food impaction, young person with heartburn
  - **Mesenteric thrombosis/ ischemia:** pain out of proportion to exam
  - **PUD**: bloody vomit and poop
  - **Diverticulitis**: painless bleeding, large volume bleeding

- **Angiodysplasia**: painless low-volume bleeding, less common
- **Budd-chiari**: RUQ pain, ascites, hepatosplenomegaly, jaundice → get doppler US
- **Stress induced ulcer:** sick ICU patients
- Pain WORSE with food= **gastric ulcer**
- Pain BETTER with food= **duodenal ulcer**
- Weight loss= **cancer, gastric ulcer**
- **GERD: worse with laying down, spicy food, coffee, chest burn → dietary modifications and PPI**
- tenderness= **pancreatitis**
- Bad taste, cough, hoarse= **GERD**
- DM, bloating= **gastroparesis**
- No history= **non-ulcer dyspepsia**
- Gas in Gallbladder wall= **emphysematous cholecystitis**
- Microscopic colitis → **budesonide**
- Pancreatic enzyme replacement → **pancreatic insufficiency**
- Ulcerative colitis → **sulfasalazine**
- Peutz-Jeghers= pigmented mucosa, hamartomas
- Turcot syndrome= FAP variant, medulloblastoma
- FAP= AD, millions of polyps, risk of cancer adenocarcinoma
- Whipple= Whipple disease is a systemic, Gram-positive bacterial infection that should be considered in all patients presenting with arthralgia, abdominal pain, diarrhea, and weight loss.
- Cullen sign→ pancreatitis = periumbilical bruising
- Grey Turner sign→ pancreatitis = flank bruising
- Cope sign/obturator sign = appendicitis

- **Nutrition**
  - **Vegan diet**
    - Vit B12, Vit D and calcium deficiency >> iron, zinc, iodine
    - Sufficiency folate and essential amino acids
  - B1 deficiency: thiamine,
    - wet beriberi (high output heart failure, dilated cardiomyopathy)
    - dry beriberi: distal peripheral neuropathy
    - **Hepatic encephalopathy**
      - High serum ammonia
      - Tx: underlying precipitant (infection, sedative, GI bleed) & lower serum ammonia
        - Lactulose, lactitol (acidifies GI tract → formation of ammonium, reduce ammonia)
        - rifaximin : give if lactulose fails to improve ammonia. Reduces GI bugs

Hepatic encephalopathy	
Precipitating factors	• Drugs (eg, sedatives, narcotics) • Hypovolemia (eg, diarrhea) • Electrolyte changes (eg, hypokalemia) • ↑ Nitrogen load (eg, GI bleeding) • Infection (eg, pneumonia, UTI, SBP) • Portosystemic shunting (eg, TIPS)
Clinical presentation	• Sleep pattern changes • Altered mental status • Ataxia • Asterixis
Treatment	• Correct precipitating causes (eg, fluids, antibiotics) • ↓ Blood ammonia concentration (eg, lactulose, rifaximin)

- **wernicke encephalopathy:**
  - **triad of ataxia, confusion, ophthalmoplegia (nystagmus)**
  - heart chambers enlarge
  - COAT
- **Korsakoff syndrome:**
  - later stage with chronic, irreversible with wernicke + confabulation
  - RACK= retrograde and anterograde amnesia, confabulation, korsakoff psychosis

Dietary Trace Elements					
Element	**Dietary Sources**	**Metabolism**	**Deficiency Symptoms**	**Toxicity Symptoms**	**Genetic Diseases**
Chromium	• Grains, fruits, vegetables, processed meats	• Absorbed in the small intestine • Bound in the blood to albumin and transferrin	• Usually seen in hospitalized patients with malnutrition or short gut and increased catabolism • Results in increased insulin needs due to insulin resistance	• Poor bioavailability, no toxicity reported for most oral forms • Industrial chromium is carcinogenic if inhaled and causes skin ulceration and contact dermatitis	• None
Copper	• Vegetables, grains, legumes mostly, some in meat and fish	• Absorbed in the small intestine and stomach • Bound to ceruloplasmin	• Triad of subacute combined degeneration, microcytic anemia, and leukopenia (often neutropenia) • Excessive zinc intake blocks copper absorption	• Acute: abdominal pain, diarrhea, vomiting, renal failure, and hemolysis with hepatic necrosis and encephalopathy • Chronic: cirrhosis, heart failure, diabetes, and encephalopathy with neurologic decline	• Wilson disease: disorder of copper excretion • Menkes disease: disorder of copper uptake
Fluoride	• Groundwater, toothpaste	• Absorbed in the stomach and small intestine, usually bound in bone once absorbed	• Dental caries	• Acute: abdominal pain, nausea, vomiting, and diarrhea; if severe, renal and cardiac failure coma, and death • Chronic: dental fluorosis (mottled teeth) and skeletal fluorosis (dense but brittle bones)	• None
Iodine	• Fish, water, vegetables • Salt and dairy fortified in developed countries	• Absorbed in the small intestines and primarily absorbed in the thyroid gland	• Goiter, hypothyroidism, intellectual disability	• Rare, even with large ingestion, rarely causes issues, may sometimes exacerbate hypo- or hyperthyroidism	• None
Iron	• Meat, fish, vegetables, fruit (cereal and bread often fortified)	• Absorbed in the duodenum, increased by vitamin C, bound to transferrin, and stored in ferritin	• Microcytic, hypochromic anemia, possible developmental delay in children	• Acute: abdominal pain, vomiting, diarrhea, metabolic acidosis, shock, coagulopathy, liver failure, cardiac failure, renal failure • Chronic: cirrhosis, cardiomyopathy, diabetes, arthritis	• Hemochromatosis: a disorder of absorption (too much absorbed)
Manganese	• Grains, fruits, vegetables, nuts • Can have high levels in certain well water supplies	• Absorbed in the small intestine	• Very rare, only reported in those with extremely restricted diets • Scaly dermatitis and dyslipidemia	• Parkinson's-like syndrome, headache, vomiting, confusion, hepatic toxicity (associated with well water and welding/steel industry)	• None
Selenium	• Seafood and meat mostly	• Absorbed in the small intestine	• Keshan disease: cardiomyopathy • Other symptoms: mood disorders, macrocytosis, white nail beds	• Diarrhea, nausea, hair loss, peripheral neuropathy	• None
Zinc	• Meat, nuts, lentils (cereal often fortified)	• Absorbed in the small intestine	• Growth failure and dwarfism in children, hypogonadism, alopecia, dysgeusia, impaired wound healing, skin lesions (vesiculobullous and pustular lesions)	• Acute: abdominal pain, diarrhea, nausea, vomiting (rare, high zinc intake well tolerated) • Chronic: usually causes copper deficiency symptoms as zinc competes with copper for absorption	• Acrodermatitis enteropathica: impaired zinc absorption

Digging Deeper:

As mentioned above, Wernicke-Korsakoff syndrome is a combination of two different conditions that result from thiamine deficiency. There is a helpful mnemonic to differentiate the features and tie in the etiology of the disease. Wernicke encephalopathy, which develops first, can be remembered through the **COAT** mnemonic. This stands for **C**onfusion, **O**phthalmoplegia, **A**taxic gait, and **T**hiamine deficiency. The ophthalmoplegia is demonstrated by the presence of nystagmus (vertical and horizontal), lateral rectus weakness leading to double vision, and conjugate gaze palsy. The patient's ataxic gait is slow, wide-based, and composed of short steps.

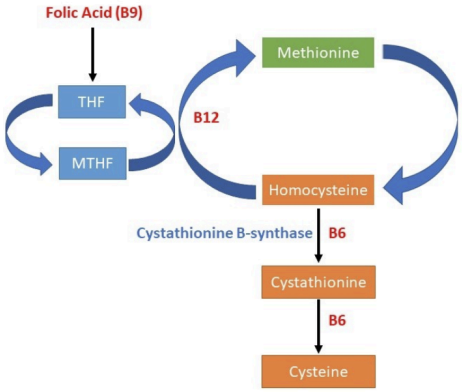
Now getting to Korsakoff psychosis, we can utilize the **RACK** mnemonic. This represents **R**etrograde and **A**nterograde amnesia, **C**onfabulations, and **K**orsakoff psychosis. These patients are unable to learn new things as well as recall past events. Confabulation is in the form of a patient incorrectly filling in gaps of their recall of events since the onset of their disease with distorted or made up memories. Destruction of the anterior thalamus is thought to contribute to the memory impairment. These patients are also not aware of their illness.

We now have a combination mnemonic of **COAT-RACK** to remember the most common features of Wernicke-Korsakoff syndrome. Whereas Wernicke encephalopathy is treatable with thiamine replacement, the memory loss seen in Korsakoff psychosis is irreversible.

- **Cerebellar degeneration**
  - Most common cause of ataxia, secondary to alcohol use and thiamine deficiency
  - Cannot stand with feet together, coarse tremor
- **Delirium tremens**: 48-96 hours after alcohol cessation, delirium, hallucinations, autonomic instability

Wernicke Encephalopathy Triad	
Encephalopathy	This is the most common presenting symptom, which is characterized by inattentiveness, significant disorientation, and apathy.
Oculomotor dysfunction	Various ocular findings may be present, with the most common being horizontal nystagmus and sluggish or nonreactive pupils. Occular findings seldom occur alone, but most often are seen in conjunction with encephalopathy or ataxia.
Gait ataxia	Stance and gait abnormalities range from findings seen only on tandem gait, all the way to severe impairment with inability to walk.

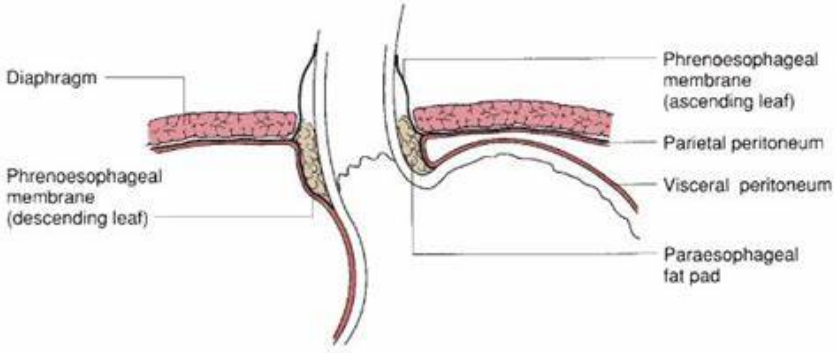
- B2 riboflavin
  - cofactor in fatty acid oxidation
  - causes **Cheilosis** and corneal revascularization , seborrheic dermatitis
- B3 niacin
  - pellagra, diarrhea, dermatitis, dementia
  - Derived from tryptophan
  - Isoniazid use can interfere
- B6 pyridoxine
  - drugs like isoniazid cause this
  - sideroblastic anemia, neuropathy
  - Treatment with folate normalizes homocysteine levels



- B9 folate
  - Absorbed in jejunum
  - Alcohol interferes with folate absorption
- **B12 cobalamin**
  - megaloblastic anemia, peripheral neuropathy, glossitis → absorbed in the terminal ileum
  - elevated MMA, homocysteine
  - Schilling test is old method to dx megaloblastic anemia
  - Long-term PPI use → B12 deficiency due to achlorhydria
  - Impaired MVP (proprioception, vibration)

Vitamin B Deficiencies			
B Number	**Common Name of Vitamin**	**Deficiency Conditions**	**Sources**
B1	Thiamine	• Wernicke encephalopathy • Korsakoff • Beriberi (wet and dry)	Yeast, legumes, pork, whole grains
B2	Riboflavin	Sore throat, cheilitis, stomatitis, glossitis	Milk, eggs, meats, fish, green vegetables
B3	Niacin	Pellagra (dermatitis, diarrhea, dementia, death)	Meats, grains, legumes
B5	Pantothenic acid	Rare; parasthesias in feet	Egg yolk, milk, broccoli
B6	Pyridoxine	Peripheral neuropathy, microcytic anemia, glossitis	Plants, meats, grains, vegetables, nuts
B7	Biotin	Dermatitis around eyes, nose, and mouth; conjunctivitis Note: Raw egg whites bind and cause deficiency	Liver, egg yolk, yeast, soybeans
B9	Folate	Macrocytic anemia without significant neurologic findings, mouth ulcers	Dark green leafy vegetables, fruits, nuts, beans, seafood, eggs, meat, poultry, grains
B12	Cyanocobalamin	Subacute combined degeneration, macrocytic anemia; psychosis; glossitis	Fish, meat, poultry, eggs, milk

- **Hiatal hernia**
  - Initial work up: CBC, BMP, LFTS
  - Imaging: EGD/barium swallow, esophageal manometry
  - Tx: Laparoscopic fundoplication
    - Type 1: gastric cardia slides into the chest. Most common
    - Type 2: gastric fundic herniates through the phrenoesophageal membrane
    - Type 4: Other organs herniate through the membrane

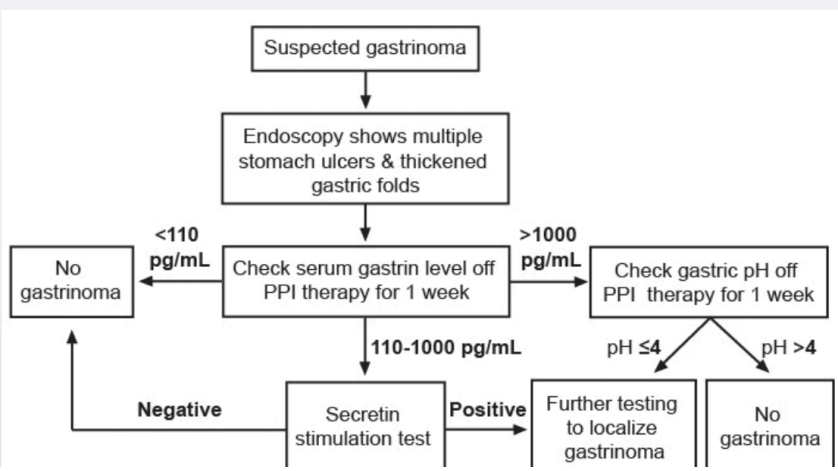


- **GERD/ acid reflux**
  - Tx: PPI/ omeprazole/ famotidine → upper endoscopy
    - risks: hop, wrist and spine fractures; C difficile, hypomagnesemia, vitamin absorption
- **Esophageal perforation (Boerhaave syndrome)**
  - Forced vomiting, tear in esophagus
  - Elevated amylase
  - work-up: water soluble esophagram/ gastrografin swallow study
- **Mallory-Weiss syndrome**
  - Non-transmural tear/ partial thickness laceration at GE junction
  - Painful hematemesis, self-revolving after vomiting
  - Too Much Whisky (MW)
- **Boerhaave syndrome**
  - spontaneous perforation of the esophagus that results from a sudden increase in intraesophageal pressure combined with negative intrathoracic pressure
  - Crepitus
- **Eosinophilic esophagitis**
  - Intermittent dysphagia, chest/ epigastric pain, reflux/ vomiting, food impaction, atopy. Asthma
  - Trachealization of esophagus
  - Dx: esophageal biopsy > 15 eos
  - Allergen avoidance, elimination diet, PPI, topical glucocorticoids
- **Pill induced esophagitis**
  - Mucosal injury due to acid effect, osmotic tissue injury, NSAIDs
  - Sudden onset odynophagia and retrosternal pain
  - Tx: stop offending medication
Medication-induced esophagitis	
Drug class	**Drug**
Antibiotics	Tetracyclines
Anti-inflammatory agents	Aspirin & many nonsteroidal anti-inflammatory drugs
Bisphosphonates	Alendronate, risedronate
Others	Potassium chloride, iron
- **Achalasia**

- Degeneration of myenteric plexus → presents lower esophageal sphincter to relax
- Dysphagia to solids and liquids

- **Ulcers**
  - **Duodenal ulcers**: pain relieved by food, weight gain
  - **Gastric ulcers**: pain worse by food, weight loss
    - Alcohol use, NSAID use
    - Fluids, pRBCs if hgb < 7, PPI
  - H. Pylori
    - Complication: **Gastric outlet obstruction** **
      - Malignancy most common
      - Recurrent vomiting → hypokalemic hypochloremic metabolic alkalosis
    - Tx:

Treatment Regimens for *Helicobacter pylori*	
Triple therapy	• Clarithromycin + amoxicillin + PPI • Metronidazole can be substituted for amoxicillin in cases of allergies to penicillin
Quadruple therapy	• Bismuth subsalicylate + metronidazole + tetracycline + PPI

- **Gastrinomas**
  - Zollinger ellison syndrome
  - Prominent gastric folds and multiple peptic ulcers
  - Dx: fasting serum gastrin > 1000
  - 

- **Esophageal varices**
  - Cirrhosis, portal hypertension
  - Tx: non-selective beta blocker (propranolol)= non-bleeding, slows progression, alpha mediated vasoconstriction
  - 2 large IV catheters → IV octreotide (stops active bleeding)
    - Urgent endoscopic therapy
      - No further bleeding= beta blocker and band ligation 1-2 weeks later
      - Continued bleeding= balloon tamponade → TIPS/ shunt therapy
      - Early rebleeding → repeat endoscopy tx → TIPS/ shunt therapy
    - If Hgb < 9 → transfusion
  - Most appropriate management→ endoscopy with igation

Abdominal Pain

Etiology of Abdominal Pain After Eating		
Disorder	**Presentation**	**Confirmatory Testing**
Celiac disease	• Abdominal pain and diarrhea after consuming gluten • Dermatitis herpetiformis • Associated with IgA deficiency	• Tissue transglutaminase antibody • EGD with biopsy
Lactose intolerance	• Bloating, flatulence, and diarrhea after consuming dairy products	• **Hydrogen breath test**
Helicobacter pylori	• Upper GI tract symptoms related to peptic ulcer disease or gastritis • Iron deficiency if chronic bleeding	• Urea breath test • EGD • Stool antigen
Peptic ulcer disease	• Usually a gnawing epigastric pain • Variable pain relationship to food intake ◦ Gastric ulcers: pain precipitated by food ◦ Duodenal ulcers: pain improves with food	• EGD
Biliary colic	• RUQ pain radiating to the right shoulder • Associated with fatty food consumption • Pain, nausea, and vomiting persisting for ~ 1–4 hours	• RUQ ultrasound

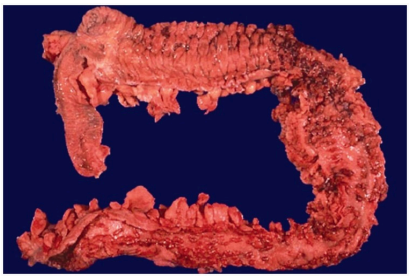
- **Celiac disease**
  - IgA anti ttg, IgG DPG, anti-gliadin, anti-endomysial (autoimmune response to gluten proteins)
  - bloating, dermatitis herpetiformis,osteopenia, Vit D deficiency, Vit ADEK, steatorrhea
  - dermatitis herpetiformis (IgA deposits in upper dermis)
  - villous atrophy —> nutrient malabsorption → iron deficiency anemia
  - Risk of enteropathy associated T cell lymphoma
  - Malabsorption → low Ca, low P, high PTH → low ADEK absorption → BONE FRACTURE
  - Dx: D-xylose absorbed passively by proximal small intestine → reduced= malabsorption
  - tx: gluten avoidance, supplements, azathioprine (immunosuppressants), dapsone (abx and steroid for dermatitis herpataformis)
- **Lactose intolerance**
  - lactose breath hydrogen test, tx: lactose avoidance
  - stool osmotic gap > 125 mOsm/kg
- **Inflammatory diarrhea**
  - Campylobacter, EHEC, Salmonella, Shigella, Yersinia
  - Tx: supportive care
    - Abx if young, immunosuppressed, elderly
    - NO antidiarrheals= traps bacteria. Must excrete it out
    - EHEC + fluoroquinolone= HUS (anemia, renal failure) → dialysis
- **IBS**
  - Recurrent abdominal pain relieved by defecation with changes in stool frequency and form.
    - Constipation predominant
    - Diarrhea predominant
      - Screen for celiac disease

- Young women with psych comorbidities
- types: constipation, diarrhea, mixed
- association with patients with psych history (abuse, stress, PTSD, anxiety), hypersensitization of visceral afferent nerves
- chronic abdominal pain relieved with defecation
- lifestyle modifications
- Dx: histology normal
  - **ROME criteria:** recurrent ab pain > 3 days/ month for 3 months with symptoms improved with defecation, change in stool frequency and form
- tx: antispasmodic, prozac
- Constipation IBS= guanylate Cyclase agonist -> increased secretion of bicarbonate and chloride -> BM
  - Linaclotide, polyethylene glycol
- Diarrhea IBS
  - Loperamide
- Abdominal cramping
  - Dicyclomine, TCA
- work -up: labs to rule out alarm features. Trial of fiber supplementation / anti-diarrheal
-

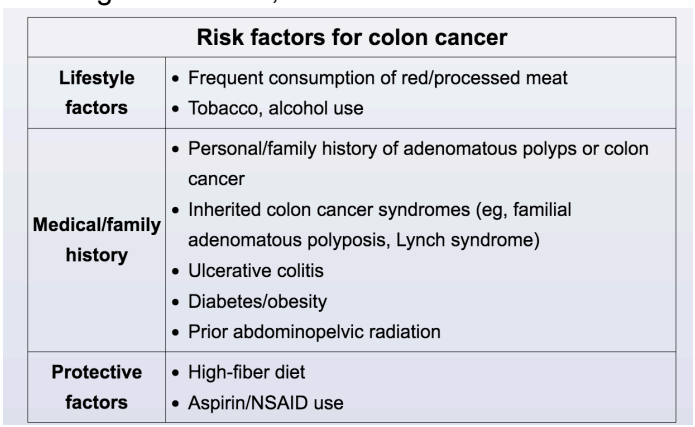
Clinical features of irritable bowel syndrome	
Rome IV diagnostic criteria	Recurrent **abdominal pain**/discomfort ≥1 day/week for past 3 months & ≥2 of the following: • Related to defecation (improves or worsens) • Change in stool frequency • Change in stool form
Alarm features	• Older age of onset (≥50) • Gastrointestinal bleeding • Nocturnal diarrhea • Worsening pain • Unintended weight loss • Iron deficiency anemia • Elevated C-reactive protein • Positive fecal lactoferrin or calprotectin • Family history of early colon cancer or IBD

- **IBD**
  - **Crohn's disease**
    - Th1 mediate inflammation of entire GI tract
    - erythema nodosum, pyoderma gangrenosum, aphthous stomatitis
    - cobblestone mucosa, skip lesions, bowel wall thickening, ulcers and fissure, **Fistula** → **give metronidazole**
    - Involves terminal ilium, can mimic appendicitis
    - Smokers have high risk of crohns
    - Iron deficiency anemia
    - Biopsy: granulomas, transmural inflammation
    - Dx: string sign on imaging, colonoscopy

- tx:
  - 5-ASA, infliximab
  - Abx (metronidazole, cipro) for any ulcer or abscess
  - loperamide (anti-diarrhea)
  - Azathioprine, 6MP and MTX for severe disease
- 

- **Ulcerative colitis**
  - autoimmune inflammation of colon- **rectum**
  - **continuous** lesions —> blood and mucus diarrhea, tenesmus, joint pain
  - bimodal age distribution
  - Increased risk of primary sclerosing cholangitis
  - extraintestinal manifestations
    - PSC, sacroiliitis, uveitis, pyoderma gangrenosum (not infectious)
    - **erythema nodosum (t**ender, non itchy violaceous nodules)- delayed type 4 hypersensitivity
    - Pyoderma gangrenosum caused by pathergy (local trauma)
    - Complications: Dx: barium enema (lead pipe appearance), **pANCA**, ESR (chronic inflammation), colonoscopy
  - Tx:
    - **5-ASA** (sulfasalazine, mesalamine) for < 4 BMs/ day, maintains remission → TNF-a inhibitor for > 6 BMs/ day and hematochezia;
    - **Prednisone** to induce remission during flare
    - total colectomy for severe, cured by **colectomy** → high risk of colorectal CA
  - complications:
    - toxic megacolon (severe systemic toxicity, abdominal distension, cessation of diarrhea)
    - Perforation (rebound tenderness)
    - colorectal cancer, severe bleeding, colitis, colonic perforation, Clostridium difficile
  - Gross: ulcerations, pseudopolyps
  - 

- **Colon cancer**
  - Risk factors: obesity, FmHx, Inherited syndromes, ulcerative colitis, diabetes

- Smoking and alcohol, red meat
- 

Risk factors for colon cancer	
Lifestyle factors	• Frequent consumption of red/processed meat • Tobacco, alcohol use
Medical/family history	• Personal/family history of adenomatous polyps or colon cancer • Inherited colon cancer syndromes (eg, familial adenomatous polyposis, Lynch syndrome) • Ulcerative colitis • Diabetes/obesity • Prior abdominopelvic radiation
Protective factors	• High-fiber diet • Aspirin/NSAID use

- **Intussusception**
  - Palpable purpura
  - Kid with abdominal pain
- **Toxic megacolon**
  - need SIRS criteria, dilated colon on xray
  - chagas disease —> bloody diarrhea, systemic toxicity, SEPSIS, dehydration
- **Obstruction of small bowel**
  - Blockage of small bowel lumen, due to adhesions and hernias
  - Abdominal pain, distension, tympanic percussion, borborygmi (high pitched bowel sounds)
  - Complication of rupture and necrosis
  - Xray: multi air fluid levels with dilated bowel loops
  - Hx of abdominal surgery / adhesions
  - Dx: water-soluble contrast challenge (can be curative, stimulates the gut)
    - GI consult if active crohns
  - Tx: NG tube placement, rest and hydration
- **Small intestinal bacterial overgrowth**
  - low B12, serum folate, carbohydrate breath test, jejunal aspirate with > 10^5
  - Impaired peristalsis → loss of peristaltic propulsion → malabsorption, diarrhea, bloating, pain
  - Dx: hydrogen breath test
  - tx: rifaximin, neomycin, metronidazole
  - correct blind loop
- **Blind loop syndrome**
  - Gastric roux-en-y procedure → anion gap metabolic acidosis
- **Cecal / sigmoid volvulus**
  - Twisting of cecal/ sigmoid mesentery
  - Sigmoid > cecal volvulus → coffee bean appearance on xray
  - Most common cause: constipation
- **Pseudo-obstruction**
  - Ogilvie syndrome – dilation of large bowel w/o mechanical obstruction
  - Elederly with comorbidities and electrolyte imbalance
- **Ileus**
  - Intestinal hypomobility w/o mechanical obstruction. Follow surgery or electrolyte disturbances
- **Melanosis Coli**
  - Pigmented colon due to senna/ anthraquinone laxatives

- Factitious disorder/ elder abuse

- **Spontaneous bacterial peritonitis****
  - Abdominal discomfort, mental status changes, fever, leukocytosis
  - History of abdominal surgery (appendectomy), due to E coli or klebsiella
  - Work-up: paracentesis (> 250 PMNs) with cell count/ differential (new-onset ascites)
  - SAAG > 1.1
  - Tx: third generation cephalosporins
    - Cytology = malignancy suspected
    - Glucose + LDH= infection, malignancy, perforation
  -

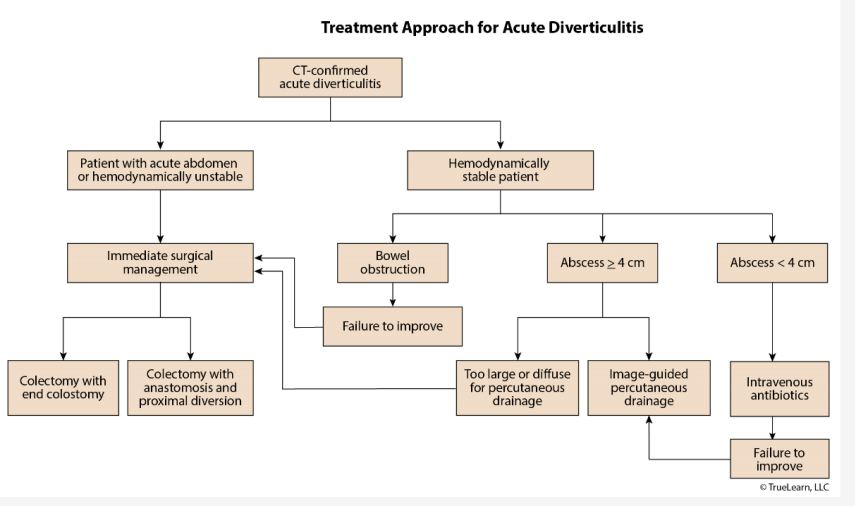
Spontaneous bacterial peritonitis	
Clinical presentation	• Temperature ≥37.8 C (100 F) • Abdominal pain/tenderness • Altered mental status (abnormal connect-the-numbers test) • Hypotension, hypothermia, paralytic ileus with severe infection
Diagnosis from ascitic fluid	• PMNs ≥250/mm^3 • Positive culture, often gram-negative organisms (eg, *Escherichia coli*, *Klebsiella*) • Protein <1 g/dL • SAAG ≥1.1 g/dL
Treatment	• Empiric antibiotics - third-generation cephalosporins (eg, cefotaxime) • Fluoroquinolones for SBP prophylaxis

- **Acute diarrhea**
  - < 2 weeks= acute; most common cause: acute gastroenteritis, self-limited
    - most treatment is oral electrolyte and fluid replacement
    - Rotavirus= winter, watery diarrhea
    - C. difficile= hospitalized, anyone taking antibiotics
      - dx: toxin immunoassay
      - tx: metronidazole
  - > 4 weeks= chronic diarrhea
  - 2-4 weeks= subacute diarrhea
    - volume depletion/ dry mucous membranes
    - 90% due to infectious etiology, recent travel history, sick contacts
      - **watery= non-invasive**
        - < 6 hours: Staph aureus (picnics, parties)
        - 8-12 hours: Clostridium perfringens
        - 12-14 hours: E coli
        - chicken: salmonella, shigella
        - sea food: vibrio, salmonella, hep A
        - daycare: rotavirus, shigella, giardia
        - nursing home: C difficile
        - camping= giardia
      - bloody= invasive
      - pathophysiology: PMNs and lactoferrin released
    - next steps: fecal leukocyte, fecal lactoferrin, rehydration (oral or IV)
  - **traveler's diarrhea= E coli**
    - avoid contaminated food and water

        - fluoroquinolones for prophylaxis, bismuth subsalicylate
            - ciprofloxacin 500mg bid x 3 days
            - azithromycin 1000mg
            - rifaximin 200mg TID
- **Constipation**
    - **functional constipation**: several months of a few BM/ week
        - tx: stool softeners
            - polyethylene glycol > lactulose, senna or magnesium hydroxide
            - fiber not recommended
            - milk of molasses enema
            - Opioid use? Give naltrexone
        - Stepwise treatment: 1) education, 2) increase fiber
            - Bulk forming laxatives (psyllium, methyl cellulose)
            - Osmotic (lac tulles), surfactant (docusate), stimulant (bisacodyl)
            - Suppositories if severe
    - **Dose-dependent constipation:**
        - CCB (verapamil)
        - **Dehydration**: Dry mucosa, hypotension
    - **Hemorrhoids**
        - Causes painless bleeding (internal), or painful bleeding (external)
        - #1: lifestyle modification (fiber, water)
        - Next steps: rubber band ligation → hemorrhoidectomy
    - **Angiodysplasia**
        - Dilated submucosal veins, AVMs, discolored lesions with dilated, thin-walled and without smooth muscle
        - Recurrent painless GI bleeding/ melena
        - Dx: colonoscopy
        - No treatment
    - **Hernias**
        - Femoral hernia: common in elderly women
        - Can cause strangulation of bowel → SBO
        - Xray: air-fluid levels
    - **Small bowel adhesions and strictures**
        - Crohn disease, intra abdominal surgery
    - **Small bowel intussusception**
        - More common in children, hematochezia, intermittent abdominal pain
        - Recurrent telescoping of bowel
    - **Superior mesenteric artery occlusion/ mesenteric ischemia**
        - Emboli → severe periumbilical pain, N/V
        - Sudden onset abdominal pain with bleeding in 24 hours
    - **Watershed bowel hypoperfusion**
        - Chronic mesenteric ischemia, affects splenic flexure and rectosigmoid junction
        - Hypotension and atherosclerosis
    - **Diverticular disease**
        - outpouchings of colonic mucosa and submucosa —> common in sigmoid colon
            - Diverticulosis → most common cause of massive lower GI bleeding
        - can get inflamed and perforate → do not scope while acutely infected
            - Diverticulitis

- LLQ pain, tenderness, fever, N/V
- Next step if stable and small abscess → IV antibiotics
  - METRONIDAZOLE + cipro/levo/tmp-smx
- Unstable and large abscess → drainage
- Perforation → remove that segment

■ Colonoscopy screening 6-8 weeks after resolution of uncomplicated diverticulitis



- **Hemorrhoids**
  - Initial management: increase hydration and fiber
  - WASH regimen
    - Warm water soaks
    - Analgesics (not opioids)
    - Stool softeners
    - High fiber
  - Thrombosed hemorrhoid
    - Firm and painful → surgery
  - Complications
    - Anal fissure
    - Perianal abscess (fever, leukocytosis) → amoxicillin clavulanic acid

	PAIN	BLEEDING	MASS
CANCER	+/-	+/-	+
ANAL FISSURE	++	+	-
THROMBOSED EXTERNAL HEMORRHOIDS	++	+	+
PROLAPSED INTERNAL HEMORRHOIDS	-	+	+
EXTERNAL HEMORRHOIDS	-	+/-	+

Key Clinical Features of Anal Fissures, Hemorrhoids, and Perianal Abscesses				
Evaluation	**Anal Fissure**	**Nonthrombosed Hemorrhoid**	**Thrombosed Hemorrhoid**	**Perianal Abscess**
History	• Severe pain with bowel movements • Bleeding usually confined to the toilet paper or coating the stool • No constitutional symptoms • No mass	• Painless • Bleeding usually confined to the toilet paper or coating the stool • May or may not be palpable • No constitutional symptoms • Associated with anorectal pruritus or stool leakage (if large and prolapsed)	• Severe, constant pain • Bleeding usually confined to the toilet paper or coating the stool • No constitutional symptoms • Palpable mass	• Progressive, severe, constant pain • Symptoms of systemic infection (eg, fever, malaise) are very common • Does not bleed
Physical examination	• Tear in the anal mucosa • Very painful • Can cause anal sphincter spasm	• Visible externally if external hemorrhoids or prolapsed internal hemorrhoids (otherwise, visualization requires anoscopy) • Not usually painful	• Tender, blue/red mass at the anal canal	• Erythematous, fluctuant bulge (if external) adjacent to the anus, often extending into the gluteal skin • If deep to the anal opening, may only be apparent as a fluctuant mass on rectal examination

- **Liver disease**
  - **Non-alcoholic steatohepatitis/ NAFLD**
    - Obesity, male, T2DM, hyperlipidemia, hepatomegaly→ **insulin resistance → increased peripheral lipolysis, TRIG synthesis, hepatic uptake of fatty acids**
      - Can occur in pregnancy
      - Associated with insulin resistance → increased peripheral lipolysis , TRIG and FFA synthesis. Causes increased oxidative stress and production of proinflammatory cytokines
    - Asymptomatic, fatty liver, metabolic syndrome, hyperechoic texture on US
    - r/o hepatitis, alcoholic liver
    - AST/ ALT < 1
    - Tx: lifestyle modification, weight loss, exercise

Nonalcoholic fatty liver disease	
Definition	• Hepatic steatosis on imaging or biopsy • Exclusion of significant alcohol use • Exclusion of other causes of fatty liver
Clinical features	• Mostly asymptomatic • Metabolic syndrome • ± Steatohepatitis (AST/ALT ratio <1) • Hyperechoic texture on ultrasound
Treatment	• Diet & exercise • Consider bariatric surgery if BMI ≥35

- **Alcoholic liver disease**
  - Fatty liver → alcoholic hepatitis → alcoholic cirrhosis
  - Hepatitis C increases rate of alcohol injury
  - Fatigue, weight loss, portal hypertension, GI bleed, ascitis, hepatic encephalopathy
  - AST / ALT > 2 (Scotch and Tonic)
- **Cirrhosis**
  - Portal hypertension, transudative ascites (> 1.1)
  - Loss of coagulation factors, loss of Protein C/S
  - Portal hypertension
    - NO → splanchnic vasodilation, decreased SVR, increased CO, hyperdynamic circulation, 3rd spacing, hypervolemia (loss of proteins, fluid in interstitium)
    - RAAS activated → Na and H2O retention , renal hyperperfusion
  - **Hepatic encephalopathy**
    - Hepatic cirrhosis, hyperammonemia → reduce catabolism of lactulose by colonic bacteria (reduce intraluminal pH)
    - Tx: lactulose and rifaximin
- **Decompensated alcoholic cirrhosis**
  - Abstinence from alcohol → reduced portal pressure and inflammation
  - Cirrhosis hx develops ascites
  - Baclofen decreases alcohol cravings
  - Tx: ETOH restriction, sodium restriction, spironolactone, furosemide → weekly drainage
- **Autoimmune hepatitis**
  - AST and ALT in the hundreds/ thousands, elevated bilirubin
  - associated with arthralgias, anorexia, fatigue
- **Hepatitis**
  - Work up: PT, albumin, HIV, Viral hepatitis A, B, C, RUQ US
    - Hep A: shellfish
    - HepB: blood and body fluids
      - Only dsDNA hep virus

- **Susceptible:** negative HBsAg, anti-HBc, anti-HBs
- **Immune (infected then recovered):** HBsAg (−), anti-Hbc (+), anti-HBs (+)
- **Immune (vaccinated):** HBsAg (−), anti-Hbc (−), anti-HBs (+)
- **Acute infection:** HBsAg (+), anti-HBc (+), IgM anti-HBc anti-HBs (−), HBeAg (+)
- **Chronic infection:** HBsAg (+), anti-Hbc (+), IgM anti-HBc (−), anti-HBs (−)

        - Hep C: IVDA, chronic infection, vertical transmission, HCC
            - Coats itself with LDL or VLDL, binds CD81
            - Cryoglobulinemia, lymphoma, MPGN, autoimmune thyroiditis, DM, porphyria cornea tarda
        - HepD: incomplete virus that coexists with HepB
        - HepE: mortality and poor fetal outcomes, fulminant hepatic failure
    - **Hepatitis C**
        - Elevated liver enzymes
        - False positive RF and ANA
        - Portal triad lymphocytic inflammation, fibrosis, cirrhosis
        - Usually asymptomatic or nonspecific symptoms
        - Mixed cryoglobulinemia, ITP and hemolytic anemia, MPGN
        - Can cause porphyria cutanea tarda, lichen planus
        - 
    - **Primary biliary cholangitis (PBC)**
        - **Autoimmune** disorder of intrahepatic bile ducts → cholestasis **+AMA**, xanthelasma, RUQ pain, pruritus, painless jaundice
            - More isolated ALP
            - 30-65 yo women
            - granulomatous destruction of small/ medium bile ducts —> chronic cholestasis
            - Increase ALP, GGT, conjugated hyperbilirubinemia
            - Order: AMA, ALP, Cholesterol (high in 50%), MRCP/ ERCP
            - Complication: bone disease, HCC, malabsorption
        - Anterior 6th ICS nodule
        - Tx: ursodeoxycholic acid (improve bile excretion), liver transplant
    - **Primary sclerosing cholangitis**
        - Common in men
        - p-ANCA +
        - Elevated ALP and GGT
        - Strictures and segmental dilations, intrahepatic and multifocal narrowing
        - Asymptomatic
        - Screen: colonoscopy → IBD
        - Bx: onion skinning
    - **Autoimmune hepatitis**
        - anti-LKM1, anti-smooth muscle, ANA, hypergammaglobulinemia
        - Elevated AST, ALT, ALP
        - Nausea, fatigue, pruritis, jaundice

        - Tx: prednisone +/- azathioprine
    - **Dubin-johnson**
        - Hereditary hyperbilirubinemia
        - Intermittent scleral icterus and conjugated hyperbili
        - Normal liver tests
        - Impaired excretion of conjugated bilirubin
        - Darker granular pigments in hepatocytes

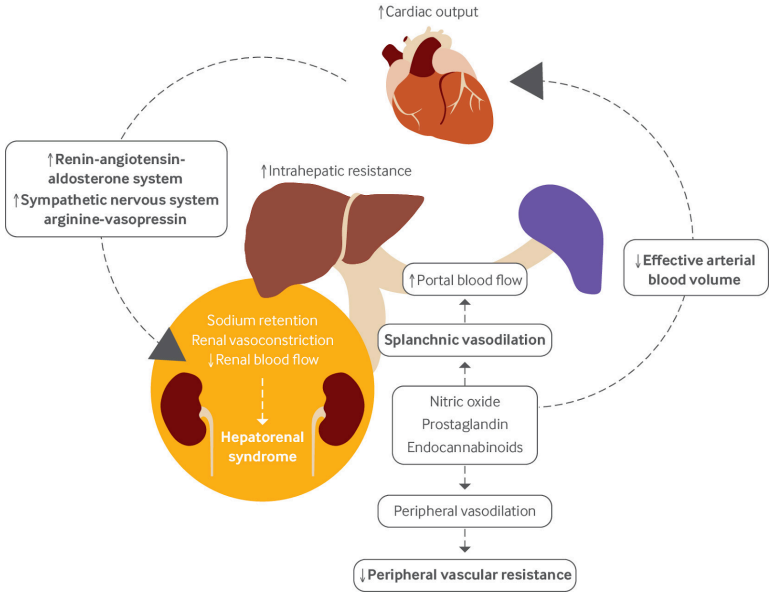
Disease	Pattern of Hyperbilirubinemia	Pathophysiology	Presentation	Distinguishing Feature	
Crigler-Najjar	Unconjugated	Type I = complete absence of UDPGT Type II = reduced UDPGT (0-10% of normal)	Type I = severe jaundice, kernicterus, death in infancy or childhood without liver transplant Type II = less severe jaundice, can live into adulthood	In type II, UDPGT activity can be induced by phenobarbital reducing bilirubin by >25%	
Gilbert's	Unconjugated	Reduced UDPGT (10-30% of normal) leads to decreased ability to conjugate bilirubin	Mild, episodic jaundice particularly during times of stress/illness	More common and less severe than Crigler-Najjar. UDPGT can be induced by phenobarbital and return bilirubin levels to normal	
Dubin Johnson	Conjugated	Lack of canalicular protein multidrug-resistant protein 2 (MRP2) leads to impaired transport of bilirubinglucuronides.	Benign jaundice	Liver appears grossly black	Note: Distinguishing between these two conditions has no clinical significance
Rotor	Conjugated	Defect in hepatic storage of bilirubin	Benign jaundice	Liver appears grossly normal	

    - **Gilbert disease**:
        - genetic disorder of conjugation of bilirubin, causes increase in unconjugated bilirubin. Elevated Bili with stress or acute illness
        - Decreased glucuronidation
        - Normal urinalysis
        -

Gilbert syndrome	
Epidemiology	• Most common inherited disorder of bilirubin metabolism
Pathogenesis	• ↓ Hepatic UDP glucuronosyltransferase activity → ↓ conjugation of bilirubin
Clinical findings	• Recurrent episodes of mild jaundice • Provoked by stress (eg, febrile illness, fasting, dehydration, vigorous exercise, menstruation, surgery)
Diagnosis	• ↑ Unconjugated bilirubin (ie, indirect hyperbilirubinemia) • Normal CBC, blood smear, reticulocyte count • Normal AST, ALT, alkaline phosphatase
Treatment	• Benign; no treatment required

    - **Hemolytic anemia**
        - Increased reticulocytes, unconjugated bilirubin, low Hgb
    - **Alpha-1 antitrypsin deficiency**:

        - emphysema and liver disease,
    - **Hemochromatosis**:
        - iron deposits in tissues. HFE gene defect or due to alcoholism.
        - High ferritin, transferrin > 45%, high iron, decreased serum transferrin, <u>normal hemoglobin</u>
        - Elevated AST. ALT
        - Arthropathy hereditary hemochromatosis
            - Chronic pain, bony swelling
            - 2nd & 3rd MCP joints
        - Tx: analgesics (NSAID, acetaminophen); phlebotomy
            - Avoid Vitamin C
            - Initiate therapeutic phlebotomy (even if asymptomatic)
    - **Hepatorenal syndrome**
        - Portal HTN → splanchnic vasodilation → decreased circulatory volume → RAAS -- renal sodium uptake, renal vasoconstriction
        - Rare form of AKI
        - Tx: IV albumin, midodrine, octreotide to reduce splanchnic vasodilation, liver transplant



Diagnostic criteria
1) Diagnosis of cirrhosis and ascites
2) Diagnosis of AKI according to ICA-AKI criteria
3) No response after 2 consecutive days of diuretic withdrawal and plasma volume expansion with albumin (1 g/kg body weight)
4) Absence of shock
5) No current or recent use of nephrotoxic drugs (NSAIDs, aminoglycosides, iodinated contrast media, etc.)
6) No macroscopic signs of structural kidney injury, defined as: - Absence of proteinuria (>500 mg/day) - Absence of microhematuria (>50 RBCs per high-power field) - Normal findings on renal ultrasonography
        - AKI, acute kidney injury; ICA-AKI, International Club of Ascites-Acute Kidney Injury; NSAIDs, non-steroidal anti-inflammatory drugs; RBCs, red blood cells.
    - **Wilson disease**:
        - Hepatolenticular degeneration → <u>impaired biliary copper excretion</u>, liver and neuropsychiatric changes (hepatolenticular degeneration)
        - Liver disease (jaundice, ascites, increased bilirubin, AST, decreased albumin)
        - Hemolytic anemia
        - behavior/ neurologic changes (tramor, seizure, behavior changes)

        - Kayser-fleischer rings (copper deposits)
        - Tx: zinc supplements(zinc chelates copper)
            - D-penicillamine, trientine
    - **Autoimmune**
        - Type 1: ANA and anti-SMC antibody
        - Type 2: anti-LKM, anti-LC
        - Tx: prednisone, azathioprine, liver transplant
    - **Intrahepatic cholestasis**
        - High ALP
        - Drug associated cholestasis

> **COMBANK Insight**
> Drugs associated with cholestasis include:
> - Antibiotics (eg, penicillins, sulfonamides, fluoroquinolones, tetracyclines)
> - Antifungals (eg, terbinafine, ketoconazole, itraconazole)
> - Antiretrovirals (eg, stavudine, didanosine, nevirapine)
> - NSAIDs (eg, diclofenac, ibuprofen)
> - Psychotropics (eg, tricyclic antidepressants, risperidone, duloxetine, benzodiazepines

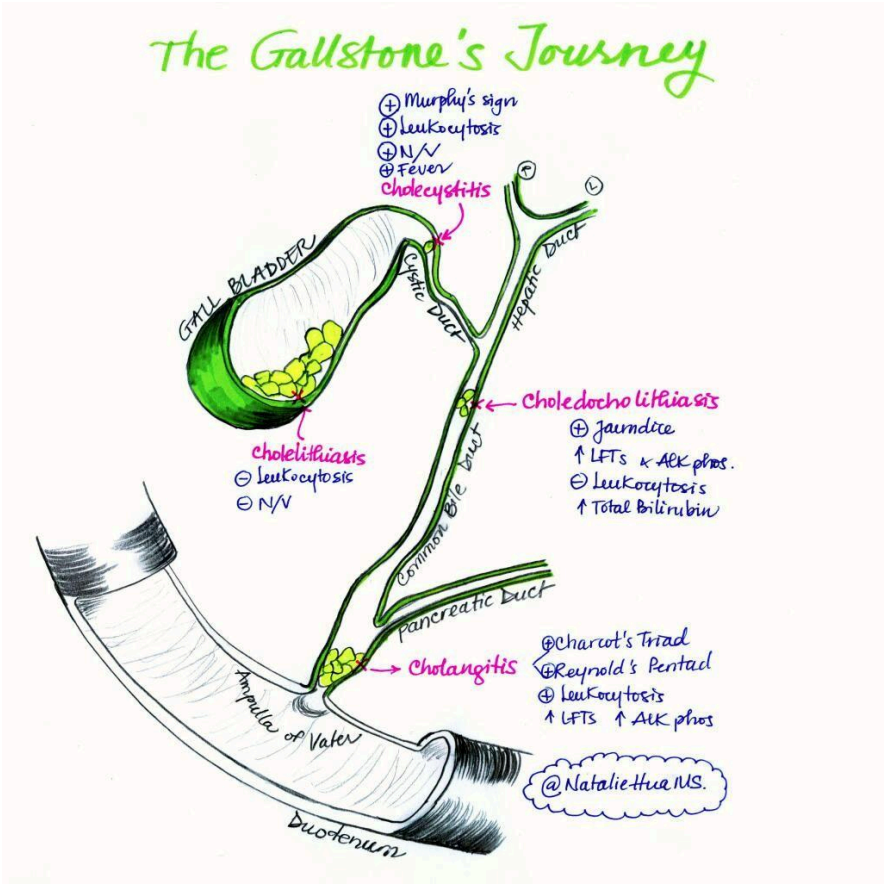
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    - **Budd chiari syndrome**
        - Hypercoagulable patients with hepatomegaly and ascites, myeloproliferative disorder, pregnancy, OCPs, 2 months post delivery
        - Abdominal pain, jaundice, ascites
        - Dx: abdominal doppler US (no CT in pregnancy, MRI better) >> venography (gold standard, but invasive)
        - Tx: anticoagulation with UFH bridge to warfarin
        - Surgery
            - Transjgular intrahepatic portosystemic procedure : best for acute liver failure
- **Liver abscess**
    - single abscess < 5 cm: needle aspiration and drainage
    - single abscess > 5cm: percutaneous drainage with catheter
    - surgery: abscess with thick wall, rupture, peritonitis, multiple large abscess, failed drainage procedure
    - multiloculated abscess: drain, aspiration
    - **pyogenic=** E coli (worldwide), klebsiella (SE asia)
    - hemorrhagic abscess= **entamoeba**
    - Well-circumscribed, hemorrhagic +/- calcification, fluid/ rupture, woman taking OCPs= **hepatic adenoma**
    - abx: combination of 3rd generation cephalosporins, metronidazole, piperacillin-tazobactam

Solid liver masses	
Focal nodular hyperplasia	• Associated with anomalous arteries • Arterial flow & central scar on imaging
Hepatic adenoma	• Women on long-term oral contraceptives • Possible hemorrhage or malignant transformation
Regenerative nodules	• Acute or chronic liver injury (eg, cirrhosis)
Hepatocellular carcinoma	• Systemic symptoms • Chronic hepatitis or cirrhosis • Elevated α fetoprotein
Liver metastasis	• Single/multiple lesions • Known extrahepatic malignancy

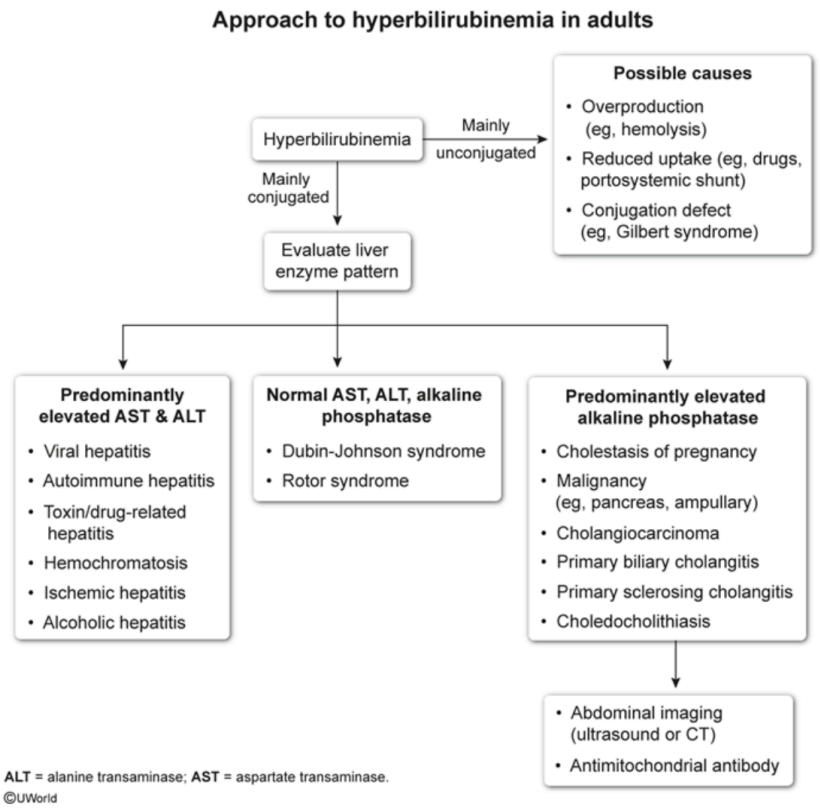
- **Gallbladder ****
  - Dx: US (suspect stones) → HIDA scan (visualize bile tract)
  - **Cholelithiasis**
    - asymptomatic
  - **Cholecystitis**
    - Most sensitive dx is the pericholecystic fluids
    - Abdominal pain, RUQ, fever, n/v, leukocytosis
    - Due to gallstone stuck in cystic duct → stasis, inflammation and infection
    - Dx: US
  - **Cholodocolithiasis**
    - Gallstones stuck in common duct
  - **Cholangitis**
    - Charcot triad: RUQ pain, fever, jaundice
    - Reynolds pentad: RUQ pain, fever,, jaundice, AMS, hypotension
    - DILATION of INTRAHEPATIC AND COMMON BILE DUCTS
    - Next steps: blood cultures, liver enzymes, lactic acid, CT abdomen
    - Tx: percutaneous transhepatic cholangiography, pipercillin-tazobactam
    - Ddx: acute viral hepatitis

Treatment of Acute Cholangitis	
Regimen	**Organism Susceptibility**
Piperacillin-tazobactam	• Effective against: Gram-positive cocci, Gram-negative rods, anaerobes, enterococci, *Pseudomonas, Acinetobacter, Serratia*
Ticarcillin-clavulanate	• Effective against: Gram-positive cocci, Gram-negative rods, anaerobes, enterococci, *Pseudomonas, Acinetobacter, Serratia*
Ampicillin-sulbactam	• Effective against: Gram-positive cocci, Gram-negative rods, anaerobes, enterococci
Ceftriaxone + metronidazole	• Effective against: some Gram-positive cocci, mostly Gram-negative rods, anaerobes (metronidazole) • Not reliably effective against *Enterococcus***
Ciprofloxacin + metronidazole*	• Effective against: some Gram-positive cocci, mostly Gram-negative rods, anaerobes (metronidazole) • Not reliably effective against *Enterococcus***
Gentamicin + metronidazole*	• Effective against: some Gram-positive cocci, mostly Gram-negative rods, anaerobes (metronidazole) • Not reliably effective against *Enterococcus***
Carbapenems*	• Effective against: Gram-positive cocci, Gram-negative rods, anaerobes • Not reliably effective against *Enterococcus***

- Malignancy
  - Asymmetric GB wall thickening with porta hepatitis Lymphadenopathy
  - Elevated ALP > AST/ ALT, elevated bilirubin
  - Weight loss, fatigue



- **MRCP**: MRI to image biliary and pancreatic ductal systems. determines if stones are lodged in the ducts. evaluated patients with suspected cholangitis or choledocolithiasis



- **Pancreatitis****
  - epigastric tenderness; history of cholelithiasis, alcohol intake, medications: thiazides, azathioprine, tetracyclines, mercaptopurine, statins, GLP-1 inhibitors
  - Mumps, scorpion sting, diuretics, IBS meds, azathioprine, HIV meds, Abx
  - more clinical signs & abnormal labs= higher mortality
  - workup: lipase, amylase, AST, ALT, CBC diff, CRP
  - Predicted severity of pancreatitis (ransons criteria)
    - 11 factors, 5 measured at admission, 6 at 48 hours
    - Serum calcium concentration
    - Amylase is not a risk factor
  - Tx: fluids and supportive care ONLY

At Presentation	
Age	>55
Leukocyte count	>16,000/mm^3
Glucose	>200 mg/dL (11.1 mmol/L)
Lactate dehydrogenase	>350 U/L
AST	>250 U/L
At 48 hours	
Hematocrit	Decrease by ≥10 percent
Urea nitrogen	Increase by ≥5 mg/dL (1.8 mmol/L) despite fluid resuscitation
Ca^{2+}	<8 mg/dL (2 mmol/L)
po_2	<60 mmHg
Base deficit	>4 MEq/L
Fluid sequestration	>6000 mL

Score	Mortality
0 - 2	0 - 3%
3 - 4	15%
5 - 6	40%
7 - 11	Almost 100%

        -
    - Hypertriglyceridemia
        - 1st line: fenofibrate + Statin
        - Ezetimibe: lowers LDL and cholesterol
        - Cholestyramine: lowers cholesterol
        - Niacin: nasty side-effects, last resort in poorly controlled familial hyperlipidemia

Potential Drug Therapies and their Expected Effects			
Drug Class	**Serum LDL-C (% change)**	**Serum HDL-C (% change)**	**Serum Triglycerides (% change)**
Statins	20-60 decrease	5-10 increase	10-33 decrease
Cholesterol absorption inhibitors	17 decrease	1 increase	7-8 decrease
Gemfibrozil/fenofibrate	10-15 decrease	5-20 increase	35-50 decrease
Nicotinic acid (niacin)	10-25 decrease	15-35 increase	25-30 decrease
Omega-3 fatty acid	Variable	5-9 increase	23-45 decrease
PCSK9 inhibitors	38-72 decrease	4-9 increase	2-23 decrease
HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol.			

        -
- **Pancreatic adenocarcinoma**
    - Head of pancreas. Ab discomfort, weight loss, obstruction and dilation (double-duct sign), weight loss, jaundice, atypical diabetes
    - Migratory thrombophlebitis (trousseau sign)
    - Monitor CA 19-9 or CEA
    - Risk factors: smoking, obesity
- **Other pancreatic cancers**
    - **VIPoma**
        - Tea colored stool, flushing
    - **Glucagonoma**
        - Hyperglycemia
        - Necrolytic migratory erythema

        - 7th intercostal space on right
        -
    - **Insulinoma**
        - Hypoglycemia unawareness until severe hunger
        - Tumor of beta cells → measure insulin, proinsulin and C-peptide
        - CT abdomen → tumor in pancreas → surgery
        - Symptomatic treatment: IV/Oral dextrose
        - Non-surgical treatment: Octreotide
- **Mesenteric ischemia**
    - Acute onset abdominal pain
    - Seen with polyarteritis nodosa
    - Mesenteric angiography

Endocrine

- **Next step****
    - Isolated thyroid nodule (benign or malignant) → **US**, **TSH** and Free T4 levels → FNA → surgical resection
        - Most likely papillary carcinoma > follicular > medullary
        - MEN2A or 2B= medullary
    - lobectomy —> follicular thyroid cancer (benign)
    - thyroidectomy
    - radioactive therapy
    - external beam radiation
    - Thyroid scintigraphy
    - CT neck
    - CT chest → Lambert eaton syndrome
    - Dexamethasone suppression test → cushing syndrome
    - Plasma free metanephrine → pheochromocytoma
    - Surgical treatment of pheochromocytoma → phenoxybenzamine and propranolol → resection
    - Ratio plasma aldosterone to plasma renin – primary hyperaldosteronism
    - Restart corticosteroids → someone on steroids, undergoes surgery, then becomes really sick and unstable
    - DKA: increased urination and respiratory symptoms → admit, give IV fluid and IV insulin
    - Reassurance → gynecomastia in teen males
- **Knee jerks**
    - **11-beta hydroxylase**= congenital adrenal hyperplasia
    - **21-hydroxylase**= classic congenital adrenal hyperplasia
    - **McCune albright syndrome**= somatic mutation in Gcpr for hormonal FSH/LH signaling
    - Failed GnRH migration= **Kallman syndrome**
    - Diabetes mellitus dx= HbA1c > 6.5% and fasting blood glucose > 126
    - Glucose control goal= Hgb < 7%
- **Metabolic syndrome**
    - HDL < 40 (men), < 50 (women)
    - TRIGS > 150
    - Fasting plasma glucose > 100
    - Abdominal obesity > 40 (men), >35 (women)
    - Blood pressure >130/85
- **Nonketotic hyperosmolar state**
    - Severe hyperglycemia and increased serum osmolality → dehydration

- Occurs in T2DM, infection
- Lethargy, thirst, polyuria, AMS, coma and death
- Hyperglycemia, increased osmolality, no acidosis/ no ketones
- Tx: aggressive fluids, insulin

- **Diabetes**
  - **Type 1**= juvenile onset, insulin dependent, autoimmune loss of B-islet cells
    - Once started on insulin, check blood glucose multiple times a day
      - If exercising, decrease dose of insulin to avoid **exercise-induced hypoglycemia**
    - **DKA**: low insulin, high glucagon —> degradation of TRIGs into FA —> high anion gap metabolic acidosis
      - Hyperglycemia, ketosis, metabolic acidosis
      - Nausea/ vomiting
      - Kussmaul breathing (rapid and deep)
      - Psychosis
      - Fruity breath
      - K related to amount of H+ due to action of Na/K pump → hyperkalemia
        - Insulin/ inhaled beta agonists draws K back into the cells
      - Labs: anion gap metabolic acidosis, ph < 7.3, low serum bicarb < 18, + ketones, hyperkalemia
      - Tx: **IV n/s, regular insulin drip, potassium** as needed, treat underlying cause
        - Monitor bicarb, Mg, Phos, glucose
        - Monitor serum anion gap
        - Avoid Bicarb in kids due to cerebral edema

Diabetic ketoacidosis	
Patient characteristics	• Young age • Brittle type 1 diabetes mellitus • May be initial manifestation of diabetes
Clinical symptoms	• Acute to subacute onset ◦ **Initial:** polydipsia/polyuria, blurred vision, weight loss ◦ **Later:** altered mentation, hyperventilation, abdominal pain
Diagnosis	• ↑ **Glucose (typically 300-800 mg/dL)** • Metabolic acidosis (bicarbonate <18 mEq/L) • ↑ Anion gap • Positive serum ketones
Treatment	• High-flow IV fluids (normal saline) • IV insulin • Follow & replace potassium

Management of diabetic ketoacidosis	
IV fluids	• Rapid infusion of 0.9% normal saline • Add dextrose 5% when serum glucose is ≤200 mg/dL
Insulin	• Start continuous **IV** insulin infusion; hold if K <3.3 mEq/L • Switch to **SQ** (basal bolus) insulin for the following: able to eat, glucose <200 mg/dL, anion gap <12 mEq/L & serum HCO_3^- ≥15 mEq/L • Overlap SQ & IV insulin by 1-2 hr
Potassium	• Add IV K if serum K^+ <5.3 mEq/L; hold if ≥5.3 mEq/L • Nearly all patients' K^+ depleted, even with hyperkalemia
Bicarbonate	• Consider for patients with pH ≤6.9
Phosphate	• Consider for serum phosphate <1.0 mg/dL, cardiac dysfunction, or respiratory depression • Monitor serum calcium frequently

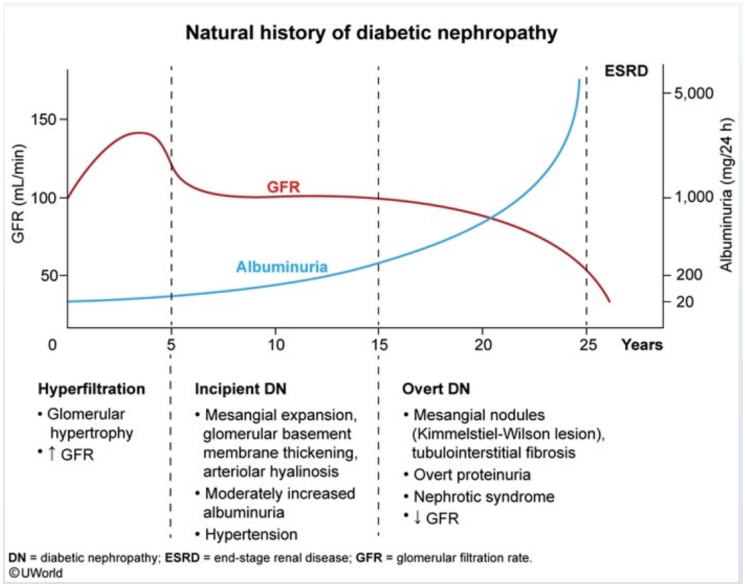
- **Type 2=** acquired, tissue acquired resistance to insulin, non-insulin dependent diabetes
  - HHS (Hyperosmolar hyperglycemic state): hyperglycemia with dehydration
    - Poorly Controlled Diabetes: Pseudomonas ear infection, Mucor and candida
- Diagnosis: ADA criteria
  - HbA1C > **6.5%-8%**
  - Fasting glucose > **126** on 2 occasions (no caloric intake for 8 hours)
  - Random glucose > **200** with symptoms: polydipsia, polyphagia, polyuria, weight loss
  - 2 hour oral glucose tolerance test > **200**

Take Home Message:

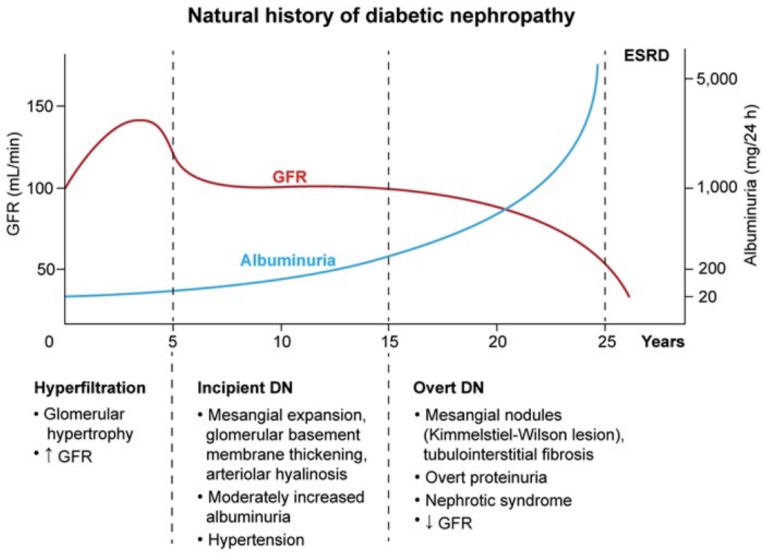
Impaired insulin resistance is an intermediate category between normal and diabetic. Patients will have a fasting blood sugar between 100 and 125 mg/dL on two separate occasions or a hemoglobin A1C of 5.7% to 6.4%. Recommend dietary changes, weight loss, exercise, and smoking cessation to patients whose fasting plasma glucose is between 100 and 125 mg/dL.

- **Goals**
  - HbA1c < 7 (<9 for geriatrics, **6.5-8%** depending on patient comorbidities)- measure every **3 months**
    - Slows progression of **microvascular** issues (retinopathy, neuropathy, nephropathy)
  - BP < 140/90
  - LDL < 100
  - Smoking cessation, aspirin, foot and eye exam yearly, urine microalbumin yearly
    - Non Nutritive sweeteners are acceptable for use
  - Weight loss → calorie-reduced diet
  - Dietary protein restriction to 0.6 g/kg daily
- **Screening**
  - Yearly dilated retinal exam, foot exam, microalbuminuria
- **Treatment**:
  - #1= **Metformin** (biguanide)

        - Contraindications in renal disease and CHF → metabolic (lactic) acidosis
    - #2 **insulin**
        - Better control of T2DM
        - Regular insulin: onset 30 minutes, duration 4-8 hours
        - Rapid acting: lispro (humolog), aspart, glulisine “take something quick before eating”
        - Intermediate: NPH
        - long acting: glargine (lantus), detemir
    - #3 **GLP-1 receptor agonists (liraglutide, exenatide, dulaglutide)**
        - lowered risk of cardiovascular events
        - nausea, satiety, weight loss
    - **SLGT2 inhibitors (flozins)**
        - risk of yeast vaginitis, UTIs
    - **DDP-4 inhibitors**
        - few side effects, minimal effect on weight
    - **Sulfonylureas** (glipizide)
        - weight gain, hypoglycemia
    - TZDs
        - Pioglitazones
        - Weight gain, fluid retention, increased risk of heart failure
- Associated symptoms (especially if uncontrolled)
    - **Gastroparesis** (chronic N/V, weight loss)
        - Dx: gastric scintigraphy
    - **GERD, chronic diarrhea**
    - **Peripheral neuropathy,** ischemic (osmotic), cranial nerve
    - **Autonomic neuropathy**: syncope
    - **Diabetic retinopathy** (nonenzymatic glycation)
    - **Large vessel disease** (DM is the new heart disease)
    - **Diabetic nephropathy**
        - Most sensitive test is urine albumin: creatinine ratio
        - > 30 mg/g for > 3 months
        - Blood pressure control is most important (add ACE inhibitors, ARBS) to reduce progression of nephropathy
            - Glycosylation of GBM and efferent arterioles → increased GFR → microalbuminuria



- **Diabetic foot infections**
  - Polymicrobial infections and osteomyelitis due to contiguous spread
  - Dx: foot xray to r/o osteomyelitis



- **Addison's disease**
  - Autoimmune destruction of the adrenal cortex —> adrenal insufficiency → decreased glucocorticoids, mineralocorticoids, adrenal androgens
  - skin hyperpigmentation (non-velvety) in palmar creases (ACTH—> POMC and MSH, decreased aldosterone
  - Hyponatremia, hyperkalemia, hyperchloremia, metabolic acidosis, hypoglycemia
  - **Adisonian crisis**
    - Gastrointestinal symptoms: N/V/pain
    - Excessive weight loss
    - Myalgias
    - Hyperpigmentation of sun exposed areas exposed to chronic friction (axilla, perineum, areola, palmar creases)

    - Due to high POMC → MSH and ACTH
- Posterior chapman point **T11**
- Volume depletion and decreased vascular tone
- Hyponatremia, hyperkalemia, hypercalcemia, low plasma cortisol

Hormone Deficiency Finding in Addison Disease		
Deficient Hormone	**Symptoms**	**Laboratory Findings**
Aldosterone	• Hypotension • Salt craving	• Hyponatremia • Hyperkalemia • Non-gap metabolic acidosis
Cortisol	• Anorexia and weight loss • Fatigue, lethargy, and weakness • Nausea, vomiting, and diarrhea • Orthostatic hypotension	• Hyponatremia • Hypoglycemia
Androgens	• Loss of libido • Lower sperm count (men) • Loss of axillary and/or pubic hair	Lower DHEA-S

-
- Angiotensinogen: from liver, inactive
- Renin: from JXG in afferent renal arterioles
- AGI: inactive, converted by ACE
- AGII: active, increases BP, vasoconstriction, stimulates aldosterone
- Aldosterone: secreted by adrenal gland, acts in DCT and Collecting ducts, increase Na reabsorption in and potassium excretion

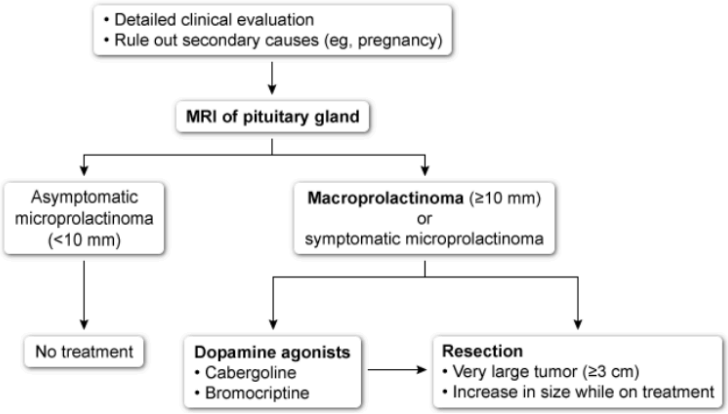
Primary adrenal insufficiency	
Etiology	• **Autoimmune adrenalitis** (most common) • Infection (eg, tuberculosis) • Metastatic infiltration
Clinical features	• Fatigue, weakness, anorexia/weight loss • Nausea, vomiting, abdominal pain • Salt craving, postural hypotension • Hyperpigmentation • **Acute adrenal crisis:** confusion, hypotension/shock
Laboratory findings	• Hyponatremia, hyperkalemia, eosinophilia • Low morning cortisol, high ACTH
Treatment	• Glucocorticoids (eg, hydrocortisone, prednisone) • Mineralocorticoids (eg, fludrocortisone)

-

Primary versus secondary adrenal insufficiency		
	Primary	**Secondary**
Mechanism	• Destruction of bilateral adrenal cortex	• Disruption of hypothalamic-pituitary axis
Possible etiologies	• Autoimmune adrenalitis • Infection, malignancy	• Chronic glucocorticoid therapy • Infiltrative disease
Cortisol	↓	↓
Aldosterone	↓	Normal
ACTH	↑	↓
Clinical features	• More severe symptoms • Hypovolemia • Hyperkalemia, hyponatremia • Hyperpigmentation	• Less severe symptoms • Euvolemia • Minimal electrolyte disturbance • No hyperpigmentation

- **Cushing's syndrome****
    - **Hypercortisolism****
        - Binds mineralocorticoid → acts as aldosterone → hypokalemia
        - T wave flattening
        - Leukocytosis (margination)
        - Secondary amenorrhea, weight gain, hirsutism, striae
    - **Paraneoplastic cushings****
        - Small cell carcinoma of lung
        - Weight loss, hyperpigmentation, fatigue, weakness, muscle waiting
        - HTN, hyperglyvemia, edema, hypokalemia
        - Ectopic ACTH secretion
    - **Work-up**
        - #1 urine free cortisol concentration in 24 hour specimen
        - Late night salivary cortisol
        - Inadequate oppression on **1 mg dexamethasone**
    - Dx: non-suppression of cortisol in overnight dexamethasone suppression test
        - Pituitary adenoma
        - Adrenal tumor
            - DHEA-S elevated
            - CT scan abdomen
        - Ectopic / paraneoplastic
- **Adrenal insufficiency**
    - Primary= addisons with skin pigmentation and electrolyte changes/ hypotension
    - central/ sheehan= low ACTH, RAAS unaffected
- **Pituitary adenoma**
    - Homonymous hemianopia, headache, decrease in pituitary secretion
    - Dopaminergic agonists (cabergoline) inhibit prolactin secretion
    - prolactinoma= bromocriptine or cabergoline → resection

- **Management of hyperprolactinemia in premenopausal women**

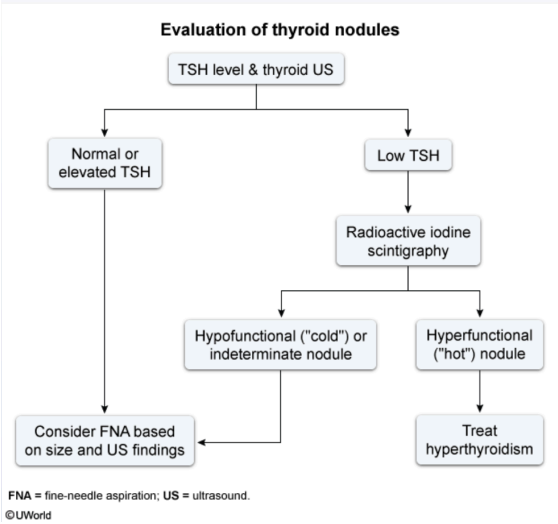


Common causes of hypogonadism in men	
Primary (testicular)	• Congenital (eg, Klinefelter syndrome, cryptorchidism) • Drugs (eg, alkylating agents, ketoconazole) • Orchitis (eg, mumps), trauma, torsion • Chronic kidney disease
Secondary (pituitary/hypothalamic)	• **Gonadotroph damage**: Tumor, cranial trauma, infiltrative diseases (eg, hemochromatosis), apoplexy • **Gonadotropin suppression**: Exogenous androgens, hyperprolactinemia, diabetes mellitus, morbid obesity
Combined (primary & secondary)	• Hypercortisolism • Cirrhosis

Thyroid

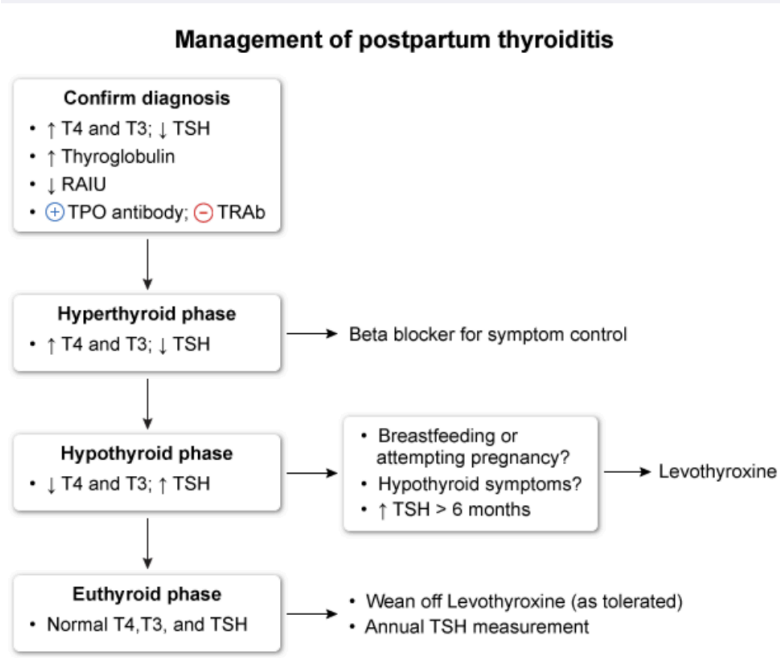
Laboratory and Imaging Results in Hyperthyroidism						
Endocrine Axis	**Condition**	**Enlarged Thyroid**	**RAI Uptake and Scan**	**Serum TSH**	**Serum T3**	**Serum Free T4**
Normal hypothalamic-pituitary function	**Euthyroid**	No	Normal	Normal	Normal	Normal
	Adenoma or multinodular goiter	Yes	Increased in specific areas	Low	High	High
	Graves' disease	Yes	Increased	Low	High	High
	Exogenous hyperthyroidism	No	Decreased	Low	High	High
	Struma ovarii	No	Decreased	Low	High	High
	Subclinical hyperthyroidism	No	Depends on cause	Low	Normal	Normal
	Thyroiditis	Yes	Decreased	Low	High	High
	T3 toxicosis	No	Decreased	Low	High	Normal/low
Abnormal hypothalamic-pituitary function	**Pituitary-mediated hyperthyroidism**	Yes	Increased	High	High	High
	Euthyroid sick syndrome	No	Decreased	Low	Low/normal	Low/normal
RAI = radioactive iodine uptake; T3 = triiodothyronine; T4 = thyroxine.						

- **Thyroid nodule****
  - Palpable neck mass confirmed by US needs an FNA to rule out malignancy
    - #1 get **TSH** level → thyroid US
    - #2 get FNA, radionucleotide scan, antibodies indicated by clinical picture
    - Benign nodules= no malignancy, cystic with well-defined walls
    - Spongiform nodules, biopsy > 2 cm
    - isoechoic/ hypoechoic, biopsy if > 1.5cm
    - Hypoechoic with walls (intermediate suspicion) , biopsy if > 1 cm
    - Solid, hypoechoic, calcification, irregular margins, extension, LN, biopsy if > 1 cm
    - Disease recurrence:
      - **thyroglobulin** (follicular, papillary) - secreted by thyroid gland
      - **calcitonin** and CEA (medullary)
    - Thyroidectomy: toxic adenoma, debulk goiter, follicular nodules differentiation
      - **Recurrent laryngeal nerve injury= posterior cricoarytenoid muscle**
      - Cricothyroid muscle inn by superior laryngeal nerve, less likely to be injured

- 

  - Work-up
Thyroid Evaluation Modalities		
Tool	**Use**	**Common Findings**
Hormone levels	Confirm hypo/hyperthyroidism; identify thyroid versus pituitary disease	In primary (thyroid) disease, TSH and free T4 change in opposite directions: • High TSH, low T4 = primary hypothyroidism • Low TSH, high T4 = primary hyperthyroidism/thyrotoxicosis In secondary (pituitary) disease, TSH and T4 change in the same direction: • Low TSH, low TSH = secondary hypothyroidism • High TSH, high T4 = secondary hyperthyroidism
Thyroid ultrasound	Confirm the presence of a nodule and stratify the risk of carcinoma	Higher cancer risk: solid, large (>2 cm) nodules with calcifications Lower cancer risk: cystic and small nodules
Thyroid uptake scan	In hyperthyroidism, to evaluate specific foci of activity versus diffuse disease (thyroid cells take up iodine to produce T4/T3)	Demonstrates patterns of update: • Specific focus of increased uptake: "hot" autonomously functioning nodule • Diffusely increased uptake: Graves disease (gland activated by stimulating thyrotropin receptor antibodies) or secondary (pituitary) hyperthyroidism • Diffusely low uptake in the setting of thyrotoxicosis (high T4, low TSH): subacute thyroiditis (T4 is released by damaged cells, not by increased production) • Diffusely low uptake: hypothyroidism
Fine needle aspiration biopsy	Evaluate suspicious nodules for carcinoma; usually performed after an ultrasound	Demonstrates hyperplasia of particular cell types (papillary, follicular), presence of dysplastic cells (malignancy), or presence of immune cells (thyroiditis)
Thyroid-related antibodies	Evaluate the etiology of primary thyroid disease	Autoantibodies are interpreted in the context of hypo/hyperthyroidism: • Hypothyroidism: Elevated anti-thyroid peroxidase (anti-TPO), anti-thyroglobulin (anti-TG), or blocking/inhibiting thyrotropin receptor antibodies (thyroid-blocking immunoglobulins) • Hyperthyroidism: Elevated stimulating thyrotropin receptor antibodies (thyroid-stimulating immunoglobulins)

- **Hyperthyroidism**
  - subclinical hyperthyroidism: low TH normal T4/ T3
  - **Pregnancy**
    - < 1st trimester (13 weeks)= PTU
    - > 1st trimester = methimazole
  - **Postpartum thyroiditis**
    - Self-limited, propranolol for symptoms only.
    - Brief hyperthyroidism → hypothyroid – euthyroid
    - Due to **Anti-TPO > anti-TG**



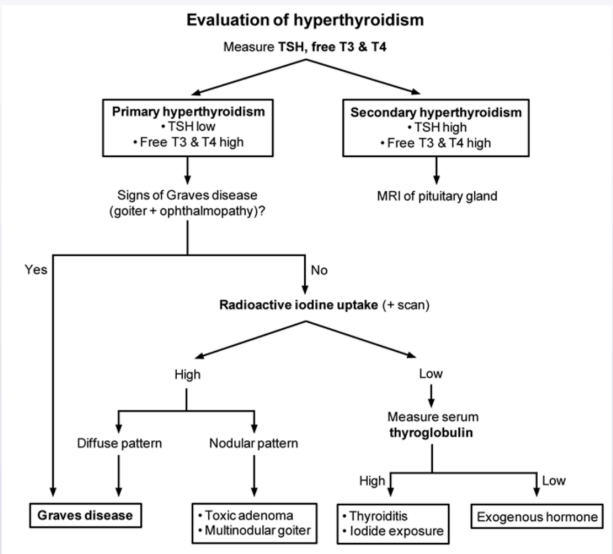
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Thyrotoxicosis with normal or ↑ RAIU	Thyrotoxicosis with ↓ RAIU
• **Graves disease** • Toxic multinodular goiter • Toxic nodule	• **Painless (silent) thyroiditis** • **Subacute (de Quervain) thyroiditis** • Amiodarone-induced thyroiditis • Excessive dose (or surreptitious intake) of levothyroxine • Struma ovarii • Iodine-induced • Extensive thyroid cancer metastasis
RAIU = radioactive iodine uptake.	

-

Findings in Hyperthyroidism				
Condition	**TSH**	**Free T4**	**Total T3**	**Clinical Features**
Graves disease	↓	↑	↑	• Orbitopathy • Thyrotoxicosis symptoms* • Diffuse thyroid enlargement
Postpartum thyroiditis	↓	↑	↑	• Recent pregnancy • Thyrotoxicosis symptoms*
Subacute thyroiditis	↓	Normal	↓	• Painful thyroid • Recent illness
Subclinical hyperthyroidism	↓	Normal	Normal	• Asymptomatic
Toxic adenoma	Normal or ↓	↑	↑	• Discrete thyroid nodule

-
- Graves disease, thyroid adenoma, multinodular toxic goiter
    - **Graves**: TSH ab → global enlargement of thyroid
    - **Toxic adenoma:** single nodule
        - TSH independent thyroid hormone discretion
        - Tx: beta blocker
        - Complications if untreated: osteoporosis

        - **Toxic multinodular goiter:** multiple nodules
        - **Riedel thyroiditis:** fibrosis of gland. Hyperthyroid → hypothyroid
        - **De Quervains thyroiditis:** give ibuprofen, subacute granulomatous thyroiditis, common in women following URI illness
    - tx indicated for pt > 65 yo, TSH < 0.1
        - Propranolol controls symptoms
        - Methimazole decreases thyroid function
        - Prednisone for subacute de quervain's thyroiditis, amiodarone-induced thyrotoxicosis
        - Propylthiouracil, methimazole → drug-induced neutropenia
    - check DEXA, US study screen
    - Overproduction of thyroid hormone: graves, toxic multinodular goiter
    - Release of hormone: painless thyroiditis, subacute thyroiditis
    - Estrogen OCPs increases T4
    - 

Conditions that alter TBG concentration	
Increased TBG	**Decreased TBG**
• **Estrogens** (eg, pregnancy, OCs, HRT) & estrogenic medications (eg, tamoxifen) • Acute hepatitis	• Androgenic hormones • High-dose glucocorticoids/hypercortisolism • Hypoproteinemia (eg, nephrotic syndrome, starvation) • Chronic liver disease
    -
- **Thyrotoxicosis**

Mechanisms of Thyrotoxicosis in Various Conditions	
Condition	**Mechanism**
Graves disease	Thyroid-stimulating immunoglobulins activate thyroid cells, causing the production of thyroid hormone independent of TSH
Autonomous "hot" (toxic) nodule	Thyroid cells become unregulated, undergoing hyperplasia (forming nodule[s]) and producing thyroid hormone independent of TSH
Toxic multinodular goiter	
Subacute thyroiditis	Inflammation of the thyroid gland (usually after a viral upper respiratory infection) causes damage to thyroid follicles, with the unregulated release of thyroid hormone
"Hashitoxicosis"	At the onset of Hashimoto thyroiditis, high levels of antibodies (often anti-TPO or anti-TG) directed against thyroid cells cause unregulated release of thyroid hormone from damaged cells in some patients, resulting in a transient thyrotoxic state before the appearance of hypothyroidism
Silent (painless) thyroiditis	Anti-thyroid antibodies (often anti-TPO or anti-TG) cause transient inflammation, with unregulated release of thyroid hormone; transient hypothyroidism can occur before full recovery
Postpartum thyroiditis	Similar to painless thyroiditis but occurs postpartum; may be related to pregnancy-related changes in immune regulation
Palpation thyroiditis	Physical manipulation of the thyroid gland causes the unregulated release of thyroid hormone (this may occur, for example, when an individual concerned about a palpable nodule frequently feels or manipulates it)
Exogenous thyroid hormone	Usually the result of excessive treatment of hypothyroidism; may occur when thyroid hormone is used as a weight loss supplement (desiccated bovine or porcine thyroid, for example, is available without a prescription in capsule form); occasionally appears as a factitious disorder (intentional self-induced hyperthyroidism)

Thyrotoxicosis with normal or ↑ RAIU	Thyrotoxicosis with ↓ RAIU
• **Graves disease** • Toxic multinodular goiter • Toxic nodule	• **Painless (silent) thyroiditis** • **Subacute (de Quervain) thyroiditis** • Amiodarone-induced thyroiditis • Excessive dose (or surreptitious intake) of levothyroxine • Struma ovarii • Iodine-induced • Extensive thyroid cancer metastasis
RAIU = radioactive iodine uptake.	

- **Thyroid storm**
  - Extreme thyrotoxicosis: tachycardia, hypotension/ hypertension
  - Tx: fluids, hydrocortisone, propranolol, PTU
- **Hypothyroidism**
  - **Work up:** TSH level at 6 weeks
  - **Congenital hypothyroidism**
    - Prolonged jaundice, lethargy, poor feeding
    - Enlarged fontanelle & protruding tongue
    - Constipation, poor weight gain
    - Differential: cystic fibrosis (does not have large fontanelle and hypotonia)
  - **hashimoto's thyroiditis**
    - anti-TPO
    - thyroid replacement —> monitor TSH 6-8 weeks later. T3 not necessary
  - **Subacute thyroiditis (de Quervain's thyroiditis)**
    - Thyrotoxicosis → Transient hypothyroidism post URI
    - Tenderness to palpation
  - **Myxedema coma**
    - Order TSH, T4, cortisol
    - Severe hypothyroidism → hypothermia, non pitting edema, altered mental status

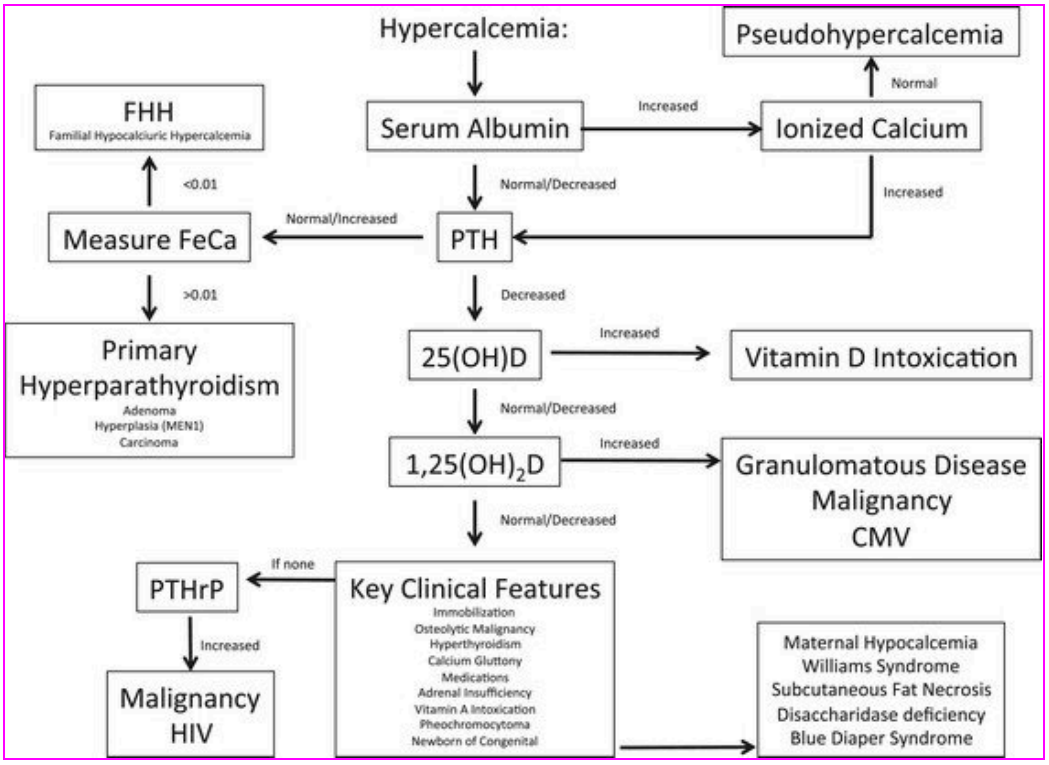
        - Tx: noninvasive rewarming, intravenous (IV) levothyroxine (T4) and IV hydrocortisone until adrenal insufficiency has been ruled out. Consideration for the addition of IV liothyronine (T3) is often based on the preference of the treating physician. Additionally, the precipitating cause of myxedema coma (eg, urinary tract infection, drug overdose, myocardial infarction) should be treated if possible.

Myxedema Coma		
Etiology	**Presenting Symptoms**	**Laboratory Evaluation**
• ↓ production (or inadequate replacement) of thyroid hormone • Often occurs in the setting of a physiological stressor (eg, infection)	• Altered mentation • Bradycardia • Hypoglycemia • Hyponatremia • Hypotension • Hypothermia • Hypoventilation • Nonpitting edema	• **TSH** • **Free T4** • Free T3 • **Serum cortisol**
T3 = triiodothyronine; T4 = thyroxine; TSH = thyroid-stimulating hormone.		

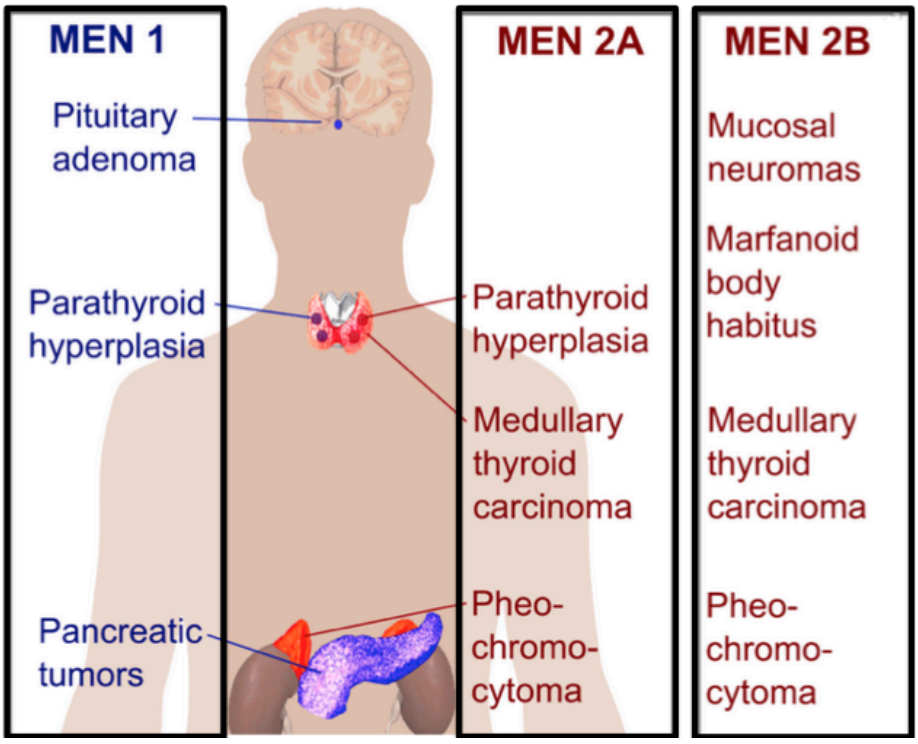
- **Euthyroid sick syndrome**
    - Decreased T3-T4 by 5' monodeiodinase
        - What decreases conversion? Caloric deprivation, inflammation, elevated free fatty acids
        - Mild transient central hypothyroid state -- minimizes maladaptive catabolism in disease
        - Low T3, normal T4 and TSH
        - Tx: conservative, just watch return to baseline
- Graves disease
    - tachycardia and/or palpitations
        - thyroid hormone increases heart rate and contractility and decreases systemic vascular resistance
    - hyperactivity and/or tremulousness
    - diarrhea
    - warm moist skin and sweating
    - heat intolerance
    - eye pain and/or double vision
    - fatigue and muscle weakness
    - weight loss

Complications of Graves disease treatment	
Treatment	**Adverse effects**
Antithyroid drugs (thionamides)	• **Agranulocytosis** • Methimazole: 1st-trimester teratogen, cholestasis • Propylthiouracil: **Hepatic failure**, ANCA-associated vasculitis
Radioiodine ablation	• Permanent hypothyroidism • Worsening of ophthalmopathy • Possible radiation side effects
Surgery	• Permanent hypothyroidism • Risk of recurrent laryngeal nerve damage • Risk of hypoparathyroidism

- **Hyperparathyroidism****
  - **Brown tumors**: osteocystica ?
    - Due to hyperparathyroidism → hypercalcemia
  - **Primary hyperparathyroidism** due to parathyroid adenoma→ increased PTH (MEN1, 2a)
    - Measure serum Ca, urine Ca, PTH
      - Hypercalcemia, hypophosphatemia
        - Stones, bones, psych overtones
        - Renal resistance to ADH → nephrogenic DI
    - PTHrp is indicative of malignancy (decreases PTH, increase Ca)
      - Vit D and Ca negative feedback
    - PTH actions
      - Bones to release Ca and P
      - Kidneys to increase Ca absorption, P excretion
      - Convert calcidiol to calcitriol → increase Ca and P absorption in gut
    - Tx: **parathyroidectomy**
      - If poor surgical candidates → cinacalcet (inhibits PTH)
  - **Secondary hyperparathyroidism**
    - Kidney disease → decreased Vit D and inadequate P excretion → PTH secretion
    - High phosphorus, low Calcium
  - **Tertiary hyperparathyroidism**
    - Poorly controlled secondary hyperPTH in ESRD → PTH secretion unresponsive to calcium levels. **PTH high, Ca is low, P is high**
    - Bone cysts
- **Hypercalcemia**
  - **cancer-associated hypercalcemia:** Gallium nitrate
  - Dialysis for severe hypercalcemia, last resort

- 

- **Hypocalcemia**
  - Common cause: Hypoparathyroidism (low Ca, high P, normal everything else)
  - chvostek sign, trousseau, tetany (neuromuscular irritability) ionized Ca < 4.3, total Ca < 7-7.5
  - Prolonged QT
  - Causes: post-thyroidectomy, autoimmune, digeorge, defective Calcium-sensing receptors, non-autoimmune destruction
  - Tx: oral or IV calcium gluconate
    - IV calcium gluconate better if symptomatic
- **Vitamin D deficiency**
  - High PTH, low Ca, low P due to low Vit D3
  - Cannot absorb calcium from kidney and gut
- **Pheochromocytoma**
  - T8-11, adrenal gland tumor
  - Hypertension, tachycardia not responsive to treatment
- **MEN syndromes**



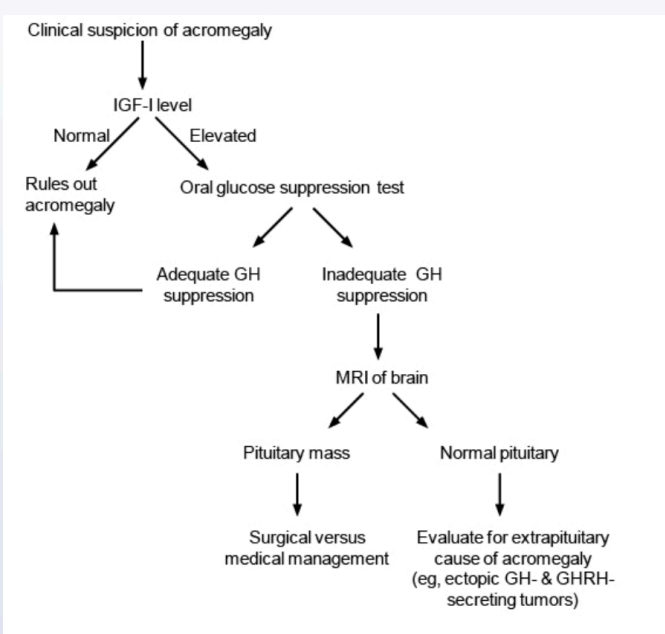
- **MEN1**: Pituitary adenoma, pancreatic tumor, PTH hyperplasia (3Ps)
  - Hyperparathyroidism, gastrinomas, insulinomas, prolactinomas, acromegaly
- **MEN2A**: PTH hyperplasia, Medullary thyroid carcinoma, Pheochromocytoma (2Ps)
  - flushing, diarrhea and pruritus are first signs of the disease
  - MTC: calcitonin elevated, calcitonin can cause amyloid deposition
  - vs. hyperparathyroidism treated with cinacalcet
  - vs. papillary thyroid carcinoma has psammoma bodies
- **MEN2B**: Mucosal neuromas, marfanoid, Medullary thyroid carcinoma, Pheochromocytoma

- NF vs. VHL vs. TSC

COMMON NEUROCUTANEOUS SYNDROMES (NF1, NF2, TS & VHL) - MNEMONIC
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	NEUROFOBROMATOSIS TYPE 1	NEUROFOBROMATOSIS TYPE 2	TUBEROUS SCLEROSIS	VON HIPPEL-LINDAU
INHERITANCE	AD	AD	AD	AD
CHROMOSOME	17q11.2	22q12.2	9q34.3	3p26-p25
GENE	NF1	NF2	TSC1, TSC2	VHL
PROTEIN	Neurofibromin	Merlin, Schwannomin	Hamartin, Tuberin	pVHL
MNEMONIC	***NEUROFIBROMA*** **N**eurofibroma **E**ye -Lisch Nodule **U**nder arm freckle **R**enal Artery Stenosis **O** d**O**minant (AD) **F** neuro**F**ibromin **I**ntellectual Disability **B**one Abnormality **R**enal Artery Stenosis **O**ptic Nerve Glioma **M**acrocephaly **A**strocytoma	***Rule of "2"*** **2** (B/L) Schwannoma **2** (B/L) Cataract **2** of the following: Meningioma Ependymoma	***HAMARTOMAS*** **H**amartomas **A**denoma sebaceum **M**itral regurgitation **A**sh Leaf Spot **R**habdomyomas **T**S1,TS2 gene **O** -d**O**minant (AD) **M**ental Disability **A**strocytomas, GBM. **S**hagreen Patch, seizures	***HIPPLE*** **H**emangioblastomas **I**nfertility (Reproductive organ tumors) **P**heochromocytomas **P**ancreatic tumor **L**oss of hearing **E**ndolymphatic sac tumor WWW.OPENMED.CO.IN

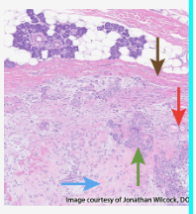
- **Acromegaly**
  - Work-up: **IGF-1** → OGST → MRI

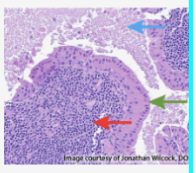
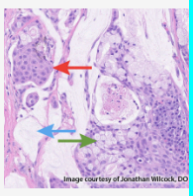
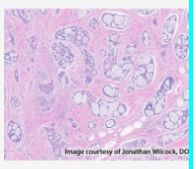


- **Waterhouse-friderichsen**
  - B/L hemorrhagic necrosis and infarction
  - meningococcemia
  - shock, hyponatremia, hyperkalemia
  - abdominal pain
  - confusion and disorientation
  - coagulopathy
  - high renin levels due to low aldosterone
    - vs. cullen sign (periumbilical bruising) in pancreatitis

- **Carcinoid syndrome**
  - 5HIAA test (serotonin metabolite)
  - mets of carcinoid tumors (⅓ in small intestine, ⅓ multiple, ⅓ have second malignancy, ⅓ mets
  - diarrhea, flushing, wheezing, cardiac abnormalities (diastolic decrescendo murmur)
  - dx: 24 hour urinary 5 HIAA test
  - tx: IFN-a
  - Niacin and tryptophan deficiency
- **Sjogren syndrome**
  - Dry eyes, dry mouth, Patients in 50s
  - Autoimmune salivary glands
  - Increase risk of non-hodgkin's lymphoma
  - Labs: anti-Ro/La, SSA
  - Dx: biopsy showing infiltrates, schirmer test
- Salivary gland tumors
  - Acute parotitis
  - Warthin tumor
    - Must have history of smoking
  - Pleomorphic adenoma
    - Most common benign salivary gland tumor
  - Adenoid cystic carcinoma
  - Mucoepidermoid carcinoma

Salivary Gland Tumors			
Tumor	**Clinical Features**	**Pathology**	**Image**

Pleomorphic adenoma	• Benign
	• Malignant transformation possible
	• Most common salivary tumor
	• Parotid
	• Recurs
		• Capsule (brown arrow)
		• Triphasic:
		  ◦ Ducts (red arrow)
		  ◦ Myoepithelial cells (green arrow)
		  ◦ Stroma (blue arrow)
			

Warthin tumor	• Benign • Bilateral is common • "Motor oil" fluid • Parotid • Found in smokers	• Double-layered epithelium (green arrow) • Lymphoid stroma (red arrow) • Proteinaceous debris (blue arrow)	
Mucoepidermoid carcinoma	• Good prognosis • Malignant • Most common salivary cancer • Found in the parotid and palate	• Epidermoid cells (red arrow) • Extracellular mucin (blue arrow) • Mucous cells (green arrow)	
Adenoid cystic carcinoma	• Locally recurs, has distant metastasis • Malignant • Parotid and minor salivary glands • Poor prognosis	• Nerve invasion is common • Prominent cribriform architecture	

MSK, Rheumatology

- **Next steps:**
  - Xray: ottawa rile (> 55 yo, tenderness to palpation at head of fibula, patellar pain, cannot flex knee, unable to bear weight)
  - MRI knee: meniscus tears “knee catches”
  - MRI shoulder: rotator cuff tendinopathy & tear, pain with abduction & external rotation, subacromial tenderness, impingement test, wea
  - CT: traumatic injuries to bone
  - Joint aspiration: effusion w/o history of injury, suspicion for infection
  - DEXA: osteoporosis
  - Spencer techniques: improve shoulder range of motion, no shoulder pathology
  - Braggards test= sciatic pain
  - Patricks test= FABERE
  - Scheuremann disease: degenerative kyphosis → OMT/PT
  - Fasciotomy for compartment syndrome → Ps → Pain, pulseless, paresthesia

,paralysis, pallor, poikilothermia
    - Bracing for scoliosis → slows curve progression
    - Closed reduction using hyperpronation → radial head subluxation
    - Club feet → reposition and serial casting
- **High yield:**
    - Pain out of proportion = compartment syndrome
    - Golgi tendon organ = muscle energy
    - Muscle spindle proprioceptors= counterstain
    - midline/ spinal bone tenderness= fracture
    - Compression fracture= anterior wedge deformity
    - Straight-leg raise test= herniated disc
    - Lumbosacral strain= paraspinal tenderness
    - Back pain worse with extension= lumbar spinal stenosis
    - Cord compression= cancer and neurologic symptoms
    - RA tx: sulfasalazine + NSAID
    - Fibromyalgia + anxiety/depression → ESR
    - Drugs that increase osteoporosis: phenytoin
    - Hoffman sign → Hoffmann sign is elicited by flicking the nail of the middle finger of the hand down. It is positive if there is an involuntary contraction of the contralateral thumb and index finger. If the sign is negative, no contraction or change occurs. Hoffmann sign or Hoffmann reflex is most commonly indicative of cervical myelopathy and is considered an **upper motor neuron sign**
    - Dupuytren's contracture= ring finger
    - Baker cyst= observe, not palpable in flexion
- **Autoimmune**
    - Antibodies

Disease	Antibodies
Systemic lupus erythematosis	ANA, anti-dsDNA, anti-Smith antibody
Drug-induced lupus	Antihistone antibody
Polymyositis/Dermatomyositis	Anti-Jo-1 antibody
CREST syndrome	Anticentromere antibody
Systemic sclerosis	Scl-70 antibody (anti-DNA topoisomerase I antibody)
Rheumatoid arthritis	Rheumatoid factor Anticyclic citrullinated peptide
Mixed connective tissue disease	Anti-U1 ribonucleoprotein antibody
Sjogren syndrome	SSB/La antibody SSA/Ro antibody

Diseases and HLA Associations	
Disease	**Associated HLA**
Subacute cutaneous lupus erythematosus	HLA-DR3, HLA-B8
Psoriasis	HLA-Cw6
Dermatitis herpetiformis	HLA-DQ2, HLA-DQ8
• Ankylosing spondylitis • Reactive arthritis • Psoriatic arthritis • Inflammatory bowel disease-related arthritides	HLA-B27
Behcet disease	HLA-B51

Commonly Tested Rheumatic Conditions		
Condition	**Associated Autoantibody**	**Symptoms and Findings**
Sjögren Syndrome	• Anti-Ro (SSA) and anti-La (SSB)	• Xerophthalmia, xerostomia, arthritis, parotid swelling
SLE	• Anti-dsDNA, anti-Smith	• Malar rash, mucositis, serositis, arthritis, nephropathy, and cytopenias
Drug-Induced Lupus	• Anti-histone	• Similar to SLE, but correlated with medication use
Polymyositis	• Anti-Jo-1, anti-Mi-2	• Progressive proximal muscle weakness and pain
Dermatomyositis	• Anti-Jo-1, anti-Mi-2	• Progressive proximal muscle weakness and pain associated with heliotrope rash
CREST Syndrome	• Anticentromere	• Calcinosis, Raynaud phenomenon, esophageal dysmotility, sclerodactyly, and telangiectasia
Systemic Scleroderma	• Anti-Scl-70 (anti-topoisomerase)	• Diffuse symptoms of CREST, which may involve skin and viscera throughout the body
Primary Biliary Cirrhosis	• Antimitochondrial	• Xerophthalmia, xerosis, pruritus, may progress to cirrhosis with associated symptoms
CREST = calcinosis, Raynaud phenomenon, esophageal dysmotility, sclerodactyly, and telangiectasia; SLE = systemic lupus erythematosus.		

- **HLA**

MHC Subtypes Associated With Diseases			
Class I Haplotype	**Diseases**	**Class II Haplotype**	**Diseases**
A3	• Hemochromatosis	DQ2/DQ8	• Celiac disease
B8	• Addison disease • Myasthenia gravis • Graves disease	DR2	• Multiple sclerosis • Hay fever • Systemic lupus erythematosis • Goodpasture syndrome
B27	• Psoriatic arthritis • Ankylosing spondylitis • Inflammatory bowel disease • Reactive arthritis	DR3	• Diabetes melliutus type I • Systemic lupus erythematosis • Graves disease • Hashimoto thyroiditis • Addison disease
-	-	DR4	• Rheumatoid arthritis • Diabetes mellitus type 1 • Addison disease
-	-	DR5	• Pernicious anemia • Hashimoto thyroiditis

- **Scleroderma**
  - Limited scleroderma= CREST
  - Diffuse: more severe lung and joint involvement

Scleroderma			
Variable	**Limited Cutaneous Scleroderma**	**Diffuse Cutaneous Scleroderma**	**Scleroderma Sine Scleroderma**
Raynaud phenomenon	• Present for years before diagnosis (often 10+), often with telangiectasias	• Presents close to skin changes and diagnosis (within 1 year)	• May be present
Skin changes	• Hands, proximal forearms, feet, face only	• Also often has truncal and skin involvement	• None
Organ involvement	• Minimal • Some dysphagia or heartburn	• Early renal, lung, gastrointestinal, and myocardial disease	• Early renal, lung, gastrointestinal, and myocardial disease
Autoantibodies	• Anticentromere antibody in 50–60% of cases	• Anti-Scl-70 and anti-RNA polymerase antibodies	• Any antinuclear antibody pattern may be present (anti-Scl-70, anti-centromere antibody, or anti-RNA polymerase)

Systemic sclerosis subtype characteristics	
Limited cutaneous	**Diffuse cutaneous**

• Scleroderma on head & distal UE
• Prominent vascular manifestations
  ◦ Raynaud phenomenon
  ◦ Cutaneous telangiectasia
  ◦ Pulmonary arterial hypertension
• CREST syndrome
• Anticentromere antibodies
• Better prognosis
	• Scleroderma on trunk & UE
	• Prominent internal organ involvement
	  ◦ Scleroderma renal crisis
	  ◦ Myocardial ischemia & fibrosis
	  ◦ Interstitial lung disease
	• Anti-Scl-70 (topoisomerase-1) antibodies
	• Anti-RNA polymerase III antibodies
	• Worse prognosis

-
- **CREST syndrome (+ anti centromere)**
  - Calcinosis
  - Raynaud's phenomenon
  - Esophageal dysmotility
  - Sclerodactyly
  - Telangiectasia
- Raynaud's phenomenon
  - associated with cold weather exposure
  - Symmetric
  - classic color pattern beginning with white and subsequently changing to blue, then deep red before returning to normal.
  - Vascular imaging (eg, arterial duplex ultrasonography, CT angiography) to look for arterial thrombosis and/or additional investigations to identify secondary causes of Raynaud phenomenon should be considered in some situations.
    - presence of asymmetric findings, persistent pallor or cyanosis after rewarming, a reduced or absent pulse, findings of chronic ischemia, or change in pattern of pre-existing Raynaud phenomenon.
- **Marfan syndrome**
  - Acute aortic dissection, root dilation → chronic **aortic regurgitation → early diastolic murmur**
  - Mitral valve prolapse= midsystolic click
  - Fibrillin-1 mutation

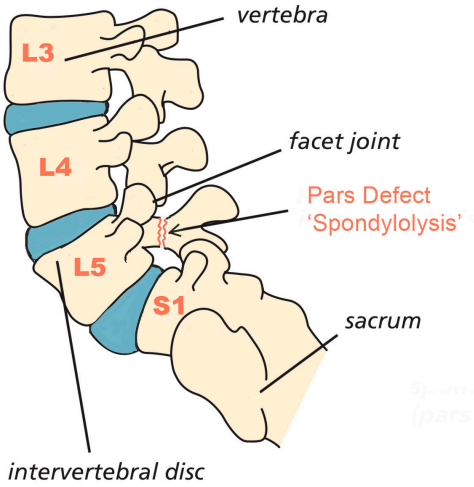
Clinical features of Marfan syndrome	
Skeletal	• Arachnodactyly • ↓ Upper-to-lower body segment ratio, ↑ arm-to-height ratio • Pectus deformity, scoliosis, or kyphosis • Joint hypermobility
Ocular	• Ectopia lentis
Cardiovascular	• Aortic dilation, regurgitation, or dissection • Mitral valve prolapse
Pulmonary	• Spontaneous pneumothorax from apical blebs
Skin	• Recurrent or incisional hernia • Skin striae

- **Misc Syndromes**
  - **Antiphospholipid syndrome**: thrombotic event or pregnancy, positive AutoAb to phospholipids (anticardiolipin, bet2gp, lupus anticoagulant)
    - Fatigue, thrombocytopenia, SLE + thrombotic event
    - Dx: Increased PT(anti-cardiolipin inhibits coagulation cascade)
    - Tx: warfarin
  - **Restless leg syndrome**
    - Discomfort in legs at night
    - Next step: iron studies
- **Myopathy**

Common causes of myopathy	
Connective tissue diseases	• Polymyositis/dermatomyositis • Inclusion body myositis • Vasculitis • Overlap syndrome (mixed connective tissue disease)
Endocrine/ metabolic	• Hypothyroidism, thyrotoxicosis • Cushing syndrome • Electrolytes (↓ potassium, calcium, phosphorus)
Drugs/toxins	• Corticosteroids, statins • Zidovudine, colchicine • Alcohol, cocaine, heroin
Miscellaneous	• Infections, trauma, hyperthermia

  - **Hypothyroid myopathy:** proximal weakness with delayed DTRs, elevated CK. Check TSH and free T4.
  - **Polymyositis**: symmetric proximal muscle weakness. ESR and CK are elevated. Confirm with muscle biopsy.
  - **Dermatomyositis**
    - Proximal muscle weakness
    - anti-M2, aldolase,elevated CK
    - Tx: corticosteroids
- **Pain syndromes**
  - **Chronic pain syndrome**
    - Stage 1: burning, throbbing to touch or cold, edema, vasomotor changes

        - Stage 2: progression of edema, thickened skin, muscle wasting
        - Stage 3: decreased ROM, contractures, waxy trophic changes, brittle nails
    - **Scoliosis**
        - Lateral curvature of spine in coronal plane
        - Incidental diagnosis
        - Adams forward bend test= screen
    - **Fibromyalgia**:
        - middle-aged women, widespread pain in > 11 spots, normal labs
        - b/l shoulder pain and stiffness
        - Tx: Exercise helps with pain , **TCAs**
            - Watch for anticholinergic symptoms (dry mouth, constipation, urinary retention_
            - Histamine effects → lethargy
            - Alpha-adrenergic receptors→ orthostatic hypotension
    - **Polymyalgia rheumatica:**
        - older women, stiffness in proximal shoulder joints, elevated ESR and CRP
        - Worse in morning
        - BILATERAL
        - Cross between arthritis and MS, but other symptoms are subjective
        - Tx: oral corticosteroids
    - **Fibromuscular dysplasia**
        - Young woman, renal artery stenosis, **bruit (carotid stenosis), hypertension, pulsatile tinnitus**
        - Doppler renal US, CTA
        - Do a depression screen
    - **Spondylolisthesis**
        - Grades
        - Anterior slipping of vertebral body due to defect in pars interarticularis
        - Pain worse with activity, relieved by rest
        - Stork test = pain worse (stand on one leg, hyperextend back)
    - **Spondylolysis**
        - Fracture of Pars articularis



- **Spondylosis**
  - Degenerative Change in vertebra
  - Leads to spinal stenosis
  - Neurogenic claudication
  - Shopping cart sign → leaning forward relieves pressure
- **Spondylolisthesis**
  - L5-S1 slippage, step down depression of spinous process
  - Tx: home exercise program or PT to strengthen abdominal muscles, decrease lumbar extension and increase flexibility
  - Surgery indicated when patient shows neuro deficits
    - Grade 1: < 25% slippage
    - Grade 2: 25 -50%
    - Grade 3: 50-75%
    - Grade 4: 75-100
- **Seronegative spondyloarthropathies**
  - **Ankylosing spondylitis**: young, ESR and CRP elevated
    - Bone loss due to osteoclast activity from chronic inflammation → ossification of spinal ligaments
    - Pain worse with rest, improved with activity
    - Seronegative inflammatory arthritis
    - associated with aortic regurgitation
    - Ethestisis : heel pain
    - AXIAL skeleton fusion, SI joint involvement B/L
      - Forward stooped posture with increased thoracic kyphosis and loss of lumbar lordosis
      - Schober test positive: ROM of lower spine measures forward flexion
    - Tx: indomethacin → etanercept (TNF inhibitors) → sulfasalazine
    - Surgery: total hip arthroplasty, cervical fusion, wedge osteotomy
    - Complications: vertebral fractures

Symptoms/signs of ankylosing spondylitis
• Low back pain (onset age <40, insidious onset, improves with exercise but not with rest, pain at night) • Hip & buttock pain • Limited chest expansion & spinal mobility • Enthesitis (inflammation at the site of insertion of a tendon to the bone) • Systemic symptoms (eg, fever, chills, fatigue, weight loss) • Acute anterior uveitis (unilateral pain, photophobia, blurry vision)

- **Psoriatic arthritis**:
  - distal / small joints. Psoriasis with pitting nails.
  - Sausage digits
  - Psoriasis
  - Painful in morning for several hours
  - Symmetric polyarthritis
- **Reactive arthritis**

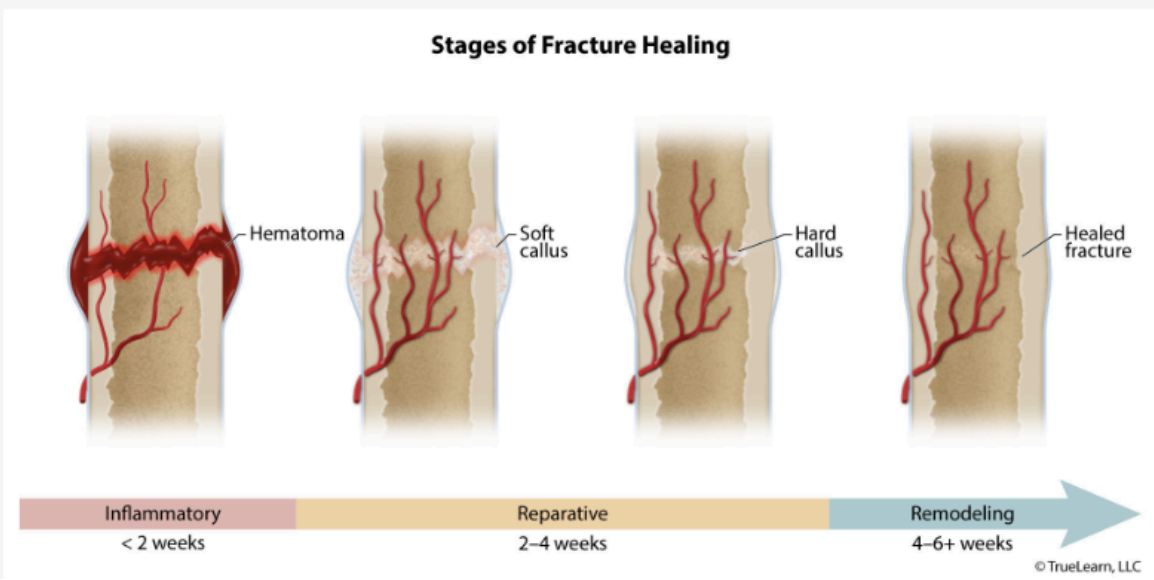
Distinguishing features of fibromyalgia, polymyositis & polymyalgia rheumatica		
	Clinical features	**Diagnosis**
Fibromyalgia	• Young to middle-aged women • Chronic **widespread pain** • Fatigue, impaired concentration • Tenderness at trigger points (eg, midtrapezius, costochondral junction)	• ≥3 months of symptoms with **widespread pain index** or **symptom severity score** • **Normal** laboratory studies
Polymyositis	• Proximal muscle **weakness** (eg, increasing difficulty climbing stairs) • Pain mild/absent	• **Elevated muscle enzymes** (eg, creatine kinase, aldolase, AST) • Autoantibodies (anti–Jo-1, ANA) • Biopsy: endomysial infiltrate, patchy necrosis
Polymyalgia rheumatica	• **Age >50** • Systemic signs & symptoms • **Stiffness** > pain in shoulders, hip girdle, neck • Association with giant cell (temporal) arteritis	• **Elevated ESR, C-reactive protein** • Rapid improvement with glucocorticoids

- **Osteoporosis**

T-score	Interpretation
+1 to -1	Normal bone density
-1 to -2.5	Osteopenia
< -2.5	Osteoporosis

- T score < -2.5= **osteoporosis**
  - 2.5-1 BMD measurement= low bone mass, osteopenia
  - Common in postmenopausal women, increased morbidity and mortality 20%
  - Due to estrogen deficiency → increased resorption, osteoclasts , increased fracture risk

        - Calcium and vitamin D insufficiency , decreased Ca reabsorption
        - weight bearing and muscle strengthening exercises, avoid smoking, avoid alcohol > 3 drinks/ day
        - Secondary hyperparathyroidism (low Vit D, increased PTH, stimulates osteoclasts)
        - Also caused by glucocorticoids, MTX, PPIs, aromatase inhibitors, SSRI, antiretroviral
        - Primary osteoporosis= age-related
    - Secondary osteoporosis= result of disease or medication
        - Bone loss with anemia, renal insufficiency and anemia= Multiple myeloma
    - Management: measure Vit D, bone density scan > 65 yo
    - Treatment:
        - **#1 Bisphosphonates**: decrease mortality post-hip fracture, increased BMD, decreased vertebral fractures → assess DEXA in 2 years
            - Side effects: osteonecrosis of jaw, femur fractures, can't use in achalasia or dilated esophagus
            - Contraindications to ORAL bisphosphonates: GI issues → Give IV
        - SERMs: Raloxifene exacerbates hot flashes and vaginal dryness. Estrogen agonist in bone and heart, estrogen antagonist in breast and uterine tissue. Increased DVT
        - RANKL inhibitors: denosumab, monitor for hypocalcemia
            - Use it renal damage
        - Teriparatide : PTH analog, anabolic
        - Nasal Calcitonin: decrease calcium
- **Bone diseases**
- **Stages of bone repair**



	Serum Calcium	Serum Phosphate	Alkaline Phosphate	Parathyroid Hormone	Radiographic Findings
Osteomalacia	↓	↓	↑	↑	Pseudofractures
Rickets	↓	↓	↑	↑	Genu varum; rachitic rosary
Osteopetrosis	↔/↓	↔	↔	↔	Uniformly sclerotic and dense bone
Osteoporosis	↔	↔	↔	↔	Compression fracture
Paget Disease of Bone	↔	↔	↑	↔	Mosaic pattern
Primary Hyperparathyroidism	↑	↓	↑	↑	"Salt and pepper" sign in skull; subperiosteal bone resorption
Secondary Hyperparathyroidism	↓	↑	↑	↑	Subperiosteal bone resorption

- **Osteopetrosis**
  - Marble bone disease, failure of bone resorption → thick, dense bones prone to fracture
  - Abnormal osteoclasts
  - Xray: erlenmeyer flask deformity
- **Osteomalacia/ Rickets (kids)**
  - Vitamin D deficiency → bone mineralization/ calcification of osteoid
  - High PTH, low Vit D
  - Pseudofractures, accumulation of radiolucent bands
  - Tx: Vit D (poor Calcium and Phosphorus uptake due to CKD)
- **Blounts disease**
  - Varus deformity in obese african american males
  - Can progress ot metaphyseal braking and increased angle
- **Pagets disease of bone**
  - Increased bone turnover, Xs resorption and xs bone formation → MOSAIC lamellar bone pattern
  - Asymptomatic, aching bone and joint pain, deformities like enlarged head, hearing changes
  - TART changes T11-L2, radiotracer uptake
  - Increased ALP
  - Risk of hearing loss due to cranial bone involvement, frontal bossing, HA, cranial nerve involvement
  - Tx: bisphosphonates and calcitonin slow osteoclastic bone resorption

Laboratory Abnormalities in Select Bone Disorders				
Etiology	**Serum Phosphate**	**Serum Calcium**	**Serum Alkaline Phosphatase**	**Parathyroid Hormone**
Osteomalacia/rickets	• Decreased	• Decreased	• Increased	• Increased
Osteoporosis	• Normal	• Normal	• Normal	• Normal
Osteopetrosis	• Normal	• Normal or decreased	• Normal	• Normal
Paget disease of the bone	• Normal	• Normal	• Elevated	• Normal
Osteitis fibrosa cystica	• Primary hyperparathyroidism ○ decreased • Secondary hyperparathyroidism ○ increased	• Primary hyperparathyroidism ○ increased • Secondary hyperparathyroidism ○ decreased	• Primary and secondary hyperparathyroidism ○ increased	• Primary and secondary hyperparathyroidism ○ increased
Hypervitaminosis D	• Increased	• Increased	• Normal	• Decreased

- **Legg-calve-perthes disease**
  - UL hip pain → idiopathic avascular osteonecrosis of femoral epiphysis
  - IT band dysfunction= positive Ober test
  - Fmhx, low birth weight**, short stature**, HIV, low SES, second hand smoke, down syndrome, young kids
  - More insidious onset
  - PE: limited abduction and INTERNAL rotation
  - Tx: supportive, surgical femoral osteotomy
- **Avascular necrosis**
  - Associated with Sickle cell disease
  - Very painful hip and limited ROM
  - Next step: MRI
- **Slipped capital femoral epiphysis**
  - Growth spurts → displacement of femoral neck
  - Kids 10-15 yo, obesity
  - PE: frog leg, short and EXTERNAL rotation
  - Tx: surgery, internal fixation with single cannulated screw
- **Scoliosis**
  - **Adolescent idiopathic scoliosis:**
    - > 10 yo, prominence on forward bend test (adams test), short leg syndrome, rib deformities
    - < 10 years old = bracing
    - Cobb > 10 degrees= scoliosis
    - **10-20 degrees** curve in kids= brace, home exercise, observation, serial xrays q6-12 months
    - **20-45 degree** curve in kids= brace and serial radiographs
    - **> 45 degree** curve= surgical fusion
    - > 60 degree= PFTs baseline

- > 100 degrees= risk of death with core pulmonale, cadiac failure
- Risk factors: Female (3-10x risk of progression), premenarche, < 12, cobb > 25

- Treatment
  - < 50: OMT and PT
  - 50-70 degrees: back brace and radiograph
  - > 75 degrees: surgical fusion

- **Joint Pain**
  - Most common cause of a stiff or painful joint following a sprain is inadequate rehabilitation
    - < 2 weeks: NSAID, immobilize
    - > 2 weeks: regain range of motion
  - Monoarticular: trauma, infection, crystals
  - polyarticular: RA, SLE, autoimmune causes, wear and tear
  - **Septic arthritis**
    - ANY JOINTS. Monoarticular, limited ROM, joint effusion, fever, warmth, erythema
    - Mechanism: direct inoculation, hematogenous spread, extension from infected joint
    - Risk factors: alcoholism, malignancy, diabetes, hemodialysis, HIV, chronic medical conditions
    - #1 is staph aureus > Staph epi (if IVDA or abrasions)
      - widened joint space due to inflammation, increased WBCs
      - blood inoculation, contiguous infection, direct inoculation from trauma or surgery
      - Chronic septic arthritis, consider fungal
      - HIV: salmonella, H flu
      - IVDA: strep, staph, GNR, pseudomonas
    - tx: IV antimicrobials, cefazolin, drain joint space
      - Ceftriaxone and vancomycin (gram positive and gram negative coverage)
      - Vanco for MRSA
      - **Drug Therapy for Septic Arthritis**

Drug	Mechanism of Action	Spectrum of Coverage	Adverse Effects
Staphylococcus Penicillins • Oxacillin • Nafcillin	• Inhibition of transpeptidase • Cell wall autolytic enzymes destroy bacteria.	*S. aureus*	• Hypersensitivity • Acute interstitial nephritis • Resistance is through alterations of penicillin-binding proteins.
Vancomycin	Binding of d-alanine subunit	• MRSA • Used in patients with penicillin allergy	• Redman syndrome • Nephrotoxicity • Ototoxicity
Third-generation cephalosporins • Ceftriaxone • Ceftazidime • Cefotaxime • Cefepime (Fourth-generation)	• Inhibition of transpeptidase • Cell wall autolytic enzymes destroy bacteria.	• Lipophilic and broad-spectrum • Gram-negative organisms • Ceftazidime and cefepime can also treat *Pseudomonas* infections.	• Hypersensitivity (cross-reaction with penicillins) • Give aztreonam to patients with penicillin allergies
Antipseudomonal penicillins • Piperacillin-tazobactam • Ticarcillin-clavulanate • Ceftazidime and cefepime can treat *Pseudomonas* infections.	• Inhibition of transpeptidase • Cell wall autolytic enzymes destroy bacteria. • Beta-lactamase inhibitors reduce resistance.	*Pseudomonas*	• Hypersensitivity (cross-reaction with penicillins) • Give aztreonam to patients with penicillin allergies

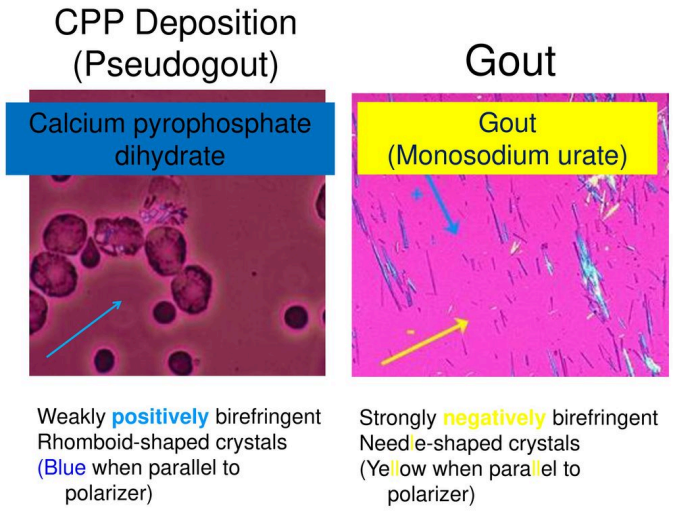
      -
    - **Lymes disease:**
      - Acute monoarticular arthritis
      - Due to borrelia burgdorferi

Stage	Lyme disease clinical features
Early localized (days to 1 month)	• Erythema migrans • Fatigue, headache • Myalgias, arthralgias
Early disseminated (weeks to months)	• Multiple erythema migrans • Unilateral/bilateral CN palsy (eg, CN VII) • Meningitis • Carditis (eg, AV block) • Migratory arthralgias
Late (months to years)	• Arthritis • Encephalitis • Peripheral neuropathy

- **Gonococcal septic arthritis:** disseminated gonococcal infection
  - Primary infection usually silent (may not have discharge)
    - N gonorrhoeae (adolescent)
    - H flu, Strep pneumo (unvaccinated kids)
  - Young, sexually active women with Migratory polyarthritis, tenosynovitis, dermatitis
  - Detect N gonorrhoeae in urine, cervical or urethral sample
  - Blood culture not as sensitive, synovial culture may be negative
  - Synovial fluid may be purulent (high WBCs < 50K)
  - Tx: ceftriaxone and azithromycin
- **Non-gonococcal septic arthritis:**
  - common in underlying joint disease, diabetes, immune suppression, IVDA
- **Reactive arthritis**
  - 1-4 weeks after GI infection or chlamydia infection. Typically occurs with urethritis and conjunctivitis/ uveitis
- **Transient synovitis**
  - Self-limited, reactive arthritis after URI
  - Common in young kids < 10

- **Gout**:
  - monoarticular (podagra or knee), affects metatarsophalangeal joint
  - men 30-50 yo, women 50-70 yo
  - precipitated by deli meats, nitrites, alcohol, hyperuricemia, thiazide diuretics
  - swollen, red, painful toe or other joints.
  - **next steps**: **joint aspiration** for crystals and r/o infection on any red, swollen joint
    - **Pseudogout**= CPPD: rhomboid, weekly positive birefringence, knee, chondrocalcinosis
    - Gout= needle-shaped crystals with negative birefringence
    - **calcium oxalate**: positive birefringence, End stage renal disease
    - **Calcium hydroxyapatite**: seen on EM, cytoplasmic inclusions non birefringent
    - **MSU** needle crystals: gouty arthritis
    - increased WBCs 90% neutrophils
    - Acute= INTRACELLULAR negative bi-refringent needle shaped crystals

- Prior= extracellular



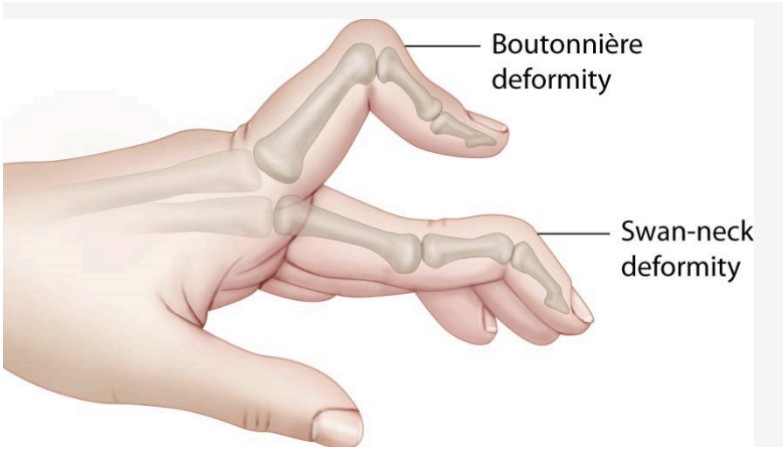
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  - Ddx: crystal gout, infectious arthritis, osteoarthritis, rheumatoid arthritis
  - tx:
    - NSAID (indomethacin), analgesics
      - Careful of NSAIDs in elderly, heart failure, PUD, liver or renal disease
    - **acute** treatment: colchicine, NSAIDs, intra articular glucocorticoids
    - Stop thiazides and chlorthalidone
    - **Chronic** treatment/ prevention: **probenecid** (increases excretion of uric acid), **allopurinol** (reduces production of uric acid)
    - If kidney disease, intra-articular steroid injection

Joint Aspirate Findings of Various Joint Pathologies

Condition	Color	Clarity	Viscosity	WBC count (cells/mm^3)	Neutrophil Percentage	Gram Stain	Crystals
Normal	Colorless	Translucent	Increased	< 200	< 25%	Negative	Negative
Non-inflammatory arthropathy	Yellow/straw-like	Translucent	Increased	200-2,000	< 25%	Negative	Negative
Inflammatory arthropathy	Yellow	Cloudy	Decreased	2,000-50,000	> 50%	Negative	• Negatively birefringent needle-shaped (gout) • Positively birefringent rhomboid-shaped (pseudogout)
Septic arthritis	Yellow/green	Cloudy/opaque	Decreased	> 50,000	> 75%	Positive	Negative
Hemarthrosis	Red	Bloody	Variable	200-2,000	< 25%	Negative	Negative

- **Septic gout**
  - Tender swollen joint, cannot bear weight, fever and leukocytosis
  - Next step: arthrocentesis
    - > 90% PMNs
  - Tx: Abx
- **Tophaceous gout**

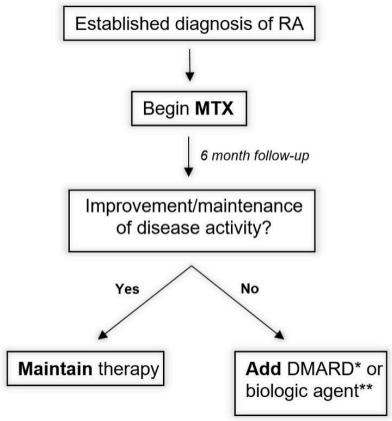
        - Chalky white appearance in skin → painful joints
    - **Calcinosis cutis:** calcium and phosphorus deposits in skin. Scattered white papules, plaques, nodules.
    - **Avascular necrosis**
        - prednisone/ steroids for hip pain
        - Lucency of femoral head seen on MRI
    - **Osteoarthritis**
        - > 65 yo, obesity associated with trauma, repetitive joint injury, obesity
        - dull, deep ache, gradual onset, worse with activity at end of day.
        - Morning stiffness < 10 minutes
        - PIPs (bouchards) and DIPs (heberdens) deformity, affects thumb
        - Xray normal at first —> bone sclerosis, cysts and osteophytes, looks like hazy crap
        - Prevention: smoking cessation, swimming and walking
        - Tx: *weight loss*, topical NSAIDs (diclofenac)(if no cardiac, CKD or ulcers), **acetaminophen**
            - **quadriceps strengthening exercises** stabilize knee and reduce pain
            - Intraarticular injection of hyaluronic acid derivatives (has risks with it)
            - Smoking is a risk factor, but quitting has less effect on bone mineral density
            - Estrogen does not prevent osteoarthritis
        - Hand osteoarthritis
            - Bony enlargement of proximal and distal ICPs
            - Heberden & bouchard nodes
            - Tx: topical or oral NSAIDS diclofenac
                - More advanced disease: duloxetine, tramadol, low-dose opioids
    - **Rheumatoid arthritis**
        - 33-55 yo women (3:1)
        - Morning stiffness > 30 minutes
        - MCPs and PIPs= Swan neck deformity, **Boutonniere's** deformity



        - TNF and IL-6 destroys cartilage, **+ anti-ccp** (most specific), RF (most sensitive), crp, ESR
            - Tx: Etanercept (TNFa inhibitor, safe in pregnancy)
            - Methotrexate

- OA instability → when intubated can cause compression of spinal cord
- **Table 3–1 • ACR/EULAR CRITERIA FOR DIAGNOSIS OF RHEUMATOID ARTHRITIS**

  1. Synovitis (swelling) is present in at least 1 joint
  2. All other diagnoses for clinical synovitis are excluded
  3. Individual score ≥6 points is reached based on the following criteria:
     a. Joint involvement: 1 large[a] joint (no points), 2-10 large joints (1 point), 1-3 small[b] joints +/– large joint (2 points), 4-10 small joints +/– large joints (3 points), >10 joints (5 points)
     b. Serology: Negative RF **and** anti-CCP (no points), low positive RF **or** anti-CCP (2 points), high positive RF **or** anti-CCP (3 points)
     c. Acute-phase reactants: normal CRP **and** normal ESR (no points), abnormal CRP **or** abnormal ESR (1 point)
     d. Duration of symptoms: <6 weeks (no point), >6 weeks (1 point)
- tx: **MTX monotherapy for 3 months —> 6 month follow up —> other DMARDs if no improvement**, sulfasalazine, leflunomide, hydroxychloroquine (, NSAIDS, glucocorticoids, anti cytokines, analgesics
  - MOA: inhibits DHFR
  - Infliximab
  - Etanercept



- **Felty syndrome**
  - Seropositive RA
  - Triad: RA, splenomegaly, granulocytopenia
  - RF and anti-CCP + neutropenia

Felty syndrome	
Clinical features	• Rheumatoid arthritis ◦ Severe erosive joint disease & deformity ◦ Rheumatoid nodules ◦ Vasculitis (mononeuritis multiplex, necrotizing skin lesions) • Neutropenia (ANC <2000/μL) • Splenomegaly
Diagnosis	• Anti-CCP & RF are positive in >90% of patients • Markedly elevated ESR, often >85 mm/hr • Peripheral smear & bone marrow biopsy to rule out other causes of neutropenia

- **Caplan syndrome**
  - RA with pneumoconiosis, pulmonary nodules

- **Polymyalgia rheumatica**
  - Worse in the morning, improves through the day. Abrupt onset of symptoms (few weeks vs. RA takes longer)
  - Shoulders and Hips
  - Tx steroids
- **Disease modifying antirheumatic drugs**

Disease-modifying antirheumatic drugs		
Agent	**Mechanism**	**Adverse effects**
Methotrexate	• Folate antimetabolite	• Hepatotoxicity • Stomatitis • Cytopenias
Leflunomide	• Pyrimidine synthesis inhibitor	• Hepatotoxicity • Cytopenias
Hydroxychloroquine	• TNF & IL-1 suppressor	• Retinopathy
Sulfasalazine	• TNF & IL-1 suppressor	• Hepatotoxicity • Stomatitis • Hemolytic anemia
TNF inhibitors (eg, adalimumab, certolizumab, etanercept, golimumab, infliximab)		• Infection • Demyelination • Congestive heart failure • Malignancy

  -
- **Psoas abscess**
  - Diabetics, pain with passive extension
  - r/o UTI, renal abnormalities

- **Non Traumatic joint pain**

Commonly Tested Finger Pathology	
Dupuytren contracture	Painless and nodular lesions typically evident in the palmar fascia, loss of full extension of the affected finger or fingers at the MCP joint
Diabetic cheiroarthropathy	Painless, limited ability to fully flex or extend the MCP joints and/or interphalangeal joints; generally affects all fingers symmetrically
MCP joint sprain	Tenderness on either side of the MCP joint associated with loss of full flexion
Infection	Severe pain and tenderness of the flexor tendon in the hand, particularly in the setting of a preceding puncture or bite wound involving the finger or hand
Calcific peritendinitis or periarthritis	Significant pain and erythema so severe that it simulates infection; locking or triggering of the finger is also not observed
Noninfectious tenosynovitis	Tenosynovitis often leads to swelling and pain along the long axis of the affected tendon, joints, or finger, resulting in limited or painful extension of the involved digit

  - **Trigger finger**
    - Splint/stretch → corticosteroids → release of A1 pulley
  - **Osgood-schlatter disease**

- Apophysitis/ chronic avulsion of the tibial tuberosity
  - Boys 12-15yo; girls 8-12 yo during a growth spurt → traction of the apophysis → avulsion, patellar tendon insertion separate from tibial tubercle
  - Ossification of proximal tibial tuberosity and calcification with in the patellar tendon
  - Knee pain, enlarged tibial tubercle
  - Testing: ask patient to squat, which will cause pain
  - 

- **Systemic juvenile idiopathic arthritis**
  - Daily > 2 weeks fever (quotidian fever), chronic fixed arthritis > 6 weeks and rash that worsens with fever
  - Leukocytosis, thrombocytosis, elevated ESR, anemia
  - Oligoarthritis, polyarthritis, systemic-onset of small joints in hands and feet
- **Knee injury**
  - triad : MCL, ACL, meniscus
- **Paget's disease**
  - Elevated ALP, Bone turnover from rapid resorption and xs bone formation → disordered **osteoclastic bone resorption** and sclerotic bone
  - Mosaic bone pattern
  - Bowing long bones, arthritis, bone pain, frontal bossing, HA, cranial nerve dysfunction
  - Tx: bisphosphonates >> calcitonin
    - Bisphosphonates inhibit osteoclasts and suppress bone turnover
    - Calcitonin inhibits osteoclasts and reduces disease activity
  -

Paget disease of bone	
Clinical features	• Most patients are asymptomatic • Bone pain & deformity ◦ **Skull:** headache, hearing loss ◦ **Spine:** spinal stenosis, radiculopathy ◦ **Long bones:** bowing, fracture, arthritis of adjacent joints • Giant cell tumor, osteosarcoma
Pathogenesis	• Osteoclast dysfunction • Increased bone turnover
Laboratory testing	• Elevated **alkaline phosphatase** • Elevated bone turnover markers (eg, PINP, urine hydroxyproline) • Calcium & phosphorus are usually normal
Imaging	• X-ray: osteolytic or mixed lytic/sclerotic lesions • **Bone scan:** focal increase in uptake
Treatment	• **Bisphosphonates**

- **Osteomyelitis**
  - inflammation of bone, disseminated, hematogenous or contiguous spread
    - bright T2, subperiosteal abscess
  - IVDA: staph and pseudomonas
  - tx: surgical debridement and irrigation, IV Abs for 4-6 weeks
  - common at metaphyseal blood supply from hematogenous seeding
    - Xray —> MRI
      - Early, acute osteomyelitis can have normal imaging
    - CRP
    - Blood culture
    - Bone biopsy and culture
- **Complex regional pain syndrome**
  - Patchy demineralization
  -

Complex regional pain syndrome	
Triggers	• Trauma: fracture, sprain • Surgery
Clinical features	• Pain: severe, regional (not dermatomal), burning/stinging • Edema, abnormal sweating • Vasomotor changes, altered skin temperature • Trophic skin, hair & nail changes
Diagnosis	• Primarily based on clinical features • X-ray: patchy demineralization • Bone scintigraphy: ↑ uptake in affected limb
Management	• Physical & occupational therapy, exercise • Medications: NSAIDs, antineuropathic medications (eg, pregabalin, TCAs)

- **Sports Medicine**
  - Sports Medicine Patient Advisor, pierre rouzier
  - https://stanfordmedicine25.stanford.edu/the25/knee.html (stanford medicine PE techniques)
  - look for hitory of repetitive movements (overhead), history of labral tears or shoulder injury
  - xray is initial imaging modality for painful joints —> MRI for ligaments
  - **Stress fracture**= normal X-ray and point tenderness
  - Muscle strain= muscle pain and pain with ROM
  - Tx: NSAIDS, immobilize, PT to regain muscle strength and improve range of motion

ROTATOR CUFF	<table><tr><th>Muscle</th><th>Supraspinatus</th><th>Infraspinatus</th><th>Teres Minor</th><th>Subscapularis</th></tr><tr><td>Action</td><td>Initiates abduction of the humeral head against the upward pull of the deltoid</td><td>Externally rotate the humerus</td><td>Externally rotate the humerus</td><td>Internally rotate the humerus</td></tr><tr><td>Test</td><td>Empty/full can tests (Jobe and Neer)</td><td>External rotation test</td><td>External rotation test</td><td>Lift off test</td></tr></table>	
Empty can test/ jobs	**supraspinatus** Suprascapular nerve subacromial bursitis	rotator cuff injury
External rotation	infraspinatus, teres minor	rotator cuff injury

lift-off test (touch your shoulder blade)/ internal rotation	subscapularis	rotator cuff injury
Hawkins impingement	subacromial impingement of supraspinatus tendon	rotator cuff injury
Drop-arm rotator cuff	Supraspinatus tear	larger rotator cuff injury
Speed test	Biceps tendinopathy	Patient flex arm past 90 degrees against resistance with forearm extended and supinated “Pop-eye” arm
Yergason test	Bicep tendon instability	Supinate and extent forearm, patient resists rotating forarm
Military posture test/ costoclavicular syndrome	Compression of brachial plexus, subclavian bw clavicle and first rib	Diminish radial pulse when arm extended and depressed. Thoracic outlet syndrome
Adson test	Scalene triangle (anterior & middle scalene and rib 1 Towards tested arm= **rib 1** Away from arm= **scalene** Thoracic outlet syndrome	Muscle hypertrophy, narrowed space with shoulder extension, ex rotation, slight abduction, hold breath and look to side being tested. Compression of brachial plexus/ subclavian vessels
anterior drawer	ATFL	ATFL injury
inversion stress test	calcaneofibular ligament	click of talus on tibia or excessive translation suggests ligament tear
squeeze test	syndesmosis	high ankle injury
lachman test	ACL	Anterior laxity of tibia
McMurray test	Meniscus tear	Audible click as torn fragment grinds over femoral condyle Varus force + internal rotation
anterior drawer test	ACL	
valgus stress	MCL	
Varus stress	LCL	
obriens test (cross arm and press down against resistance)	superior labral tear	

SLAP test (lift up at elbow)	labral tear	
Neer's impingement	Impinged rotator cuff tendon against coracoacromial arch Rotator cuff inflammation Subacromial bursitis	patients arm is relaxed as you flex it
Hawkins test	Similar to neers Rotator cuff inflammation	Abduct shoulder and elbow to 90, drive into internal rotation
Winged scapula	Serratus anterior **Long thoracic nerve injury**	Press arm against wall, see scapula pop out
Spinal accessory nerve CNXI injury	Weakness in SB the neck and rotating, SCM and trapezius weakness	Depression of right shoulder
Hoover test	Determine lower extremity weakness	Positive: lift affected leg, no downward pressure from opposite leg due to lack of true effort. Negative: lift affected leg, downward pressure from opposite heel
Apley scratch test	Shoulder mobility	
apprehension/ relocation test	Anterior release	Arm flat abducted, external rotated. Apply pressure
Froment's sign	Ulnar nerve entrapment Cubital tunnel syndrome	Pinch piece of paper with thumb and index finger, then pull paper out
Ok sign	Median nerve entrapment	
Neers sign		
Talar tilt test	Calcaneofibular ligament	
Thessaly test	Meniscal tear, stand on one leg and bend knee	
Patrick test	Faber, make figure four and flex leg	
Thomas test		Hip flexor tightness, bend one knee and extend the other leg off the table
Thompson test	DVT	
Stinchfield test	Interarticular joint dysfunction	arthritis

FADIR	Hip impingement	
Craig test	Femoral anteversion	

Tests For Thoracic Outlet Syndrome		
Location of Compression	**Name of Test**	**Description of Test**
Between the anterior and middle scalene or a cervical rib	• Adson test	• Patient extends the elbow and shoulder, externally rotates the arm and slightly abducts • Patient turns head towards the ipsilateral arm • Positive test = a decrease or absence of radial pulse
Between the clavicle and first rib	• Military posture test	• Physician depresses and extends the patient's shoulder • Positive test = a decrease or absence of radial pulse
Between the pectoralis minor and the ribs	• Wright test (arm hyperextension test)	• Patient hyperabducts the arm above the head and then extends • Positive test = is a decrease or absence of radial pulse

Lower Extremity Provocative Tests		
Test	**Structure/Pathology Evaluated**	**Technique**
Homan	Deep vein thrombosis	With the patient supine and relaxed, the calf muscle is squeezed.
Ober	Tensor fasciae latae and iliotibial band	With the patient in the lateral position and the tested side up, the lower extremity is abducted and extended at the hip. The extremity is then allowed to slowly fall toward the table.
Patrick	Sacroiliac disease	With the patient supine, the hip joint is moved into flexion, abduction, and external rotation.
Thomas	Iliopsoas muscle	With the patient supine, the examiner flexes both knees maximally toward the chest. The tested leg is then released and allowed to extend and fall toward the table.
Thompson	**Achilles tendon**	With the patient prone, the examiner squeezes the calf muscle.

Muscle contractions

Explanations of the Types of Muscle Contractions		
Type of Contraction	**What Happens**	**Example Exercise**
Concentric	Muscle shortens while generating force, thus overcoming resistance	• Biceps curl on the way up
Eccentric	Muscle lengthens while still generating force	• Biceps curl on the way down
Isokinetic	Constant speed of muscle, despite a varying amount of force	• Requires a special machine • Often used by physical therapists
Isometric	Muscle remains the same length while generating force	• External rotation of the arm against a wall
Isotonic	Muscle changes in length, but there is constant tension on the muscle (may be concentric or eccentric)	• Lifting a weight
Plyometric	Muscle exerts maximum force in short intervals of time, with the goal of increasing power	• Box jump

- **Hip injury/ pathology**
  - **Hip dislocation**
    - Anterior = externally rotated
    - posterior= internally rotated, adduction, shorter leg
    - most common hip disorder in adolescents (8-15yo) is **slipped capital femoral epiphysis**
      - common in boys > girls; obesity
      - unexplained pain in hip, grouin, thigh, knee
      - limited internal rotation of hip
  - **Hip fracture**
    - Flexed, externally rotated, abducted
    - Closer reductions → follow closely
    - Common in elderly (poor balance, vision), young (trauma)
      - Femoral head fractures: rare, due to high energy trauma
      - Femoral neck fractures and intertrochanteric fractures common
    - Work up: Xray → surgical correction
  - **Meralgia paresthetica**
    - Lateral femoral cutaneous neuropathy
    - Tight pants, cant put wallet in front pocket
  - **Trochanteric bursitis**
    - Lateral hip pain
    - Next steps: Xray, US
    - Tx: NSAID → local corticosteroid injection

- **Knee injury/ pathology**
  - **ACL/ PCL tear**
    - Common with non-contact twisting motions
    - POP
  - MCL/ LCL tear
  - **Posterior fibular head**
    - Plantarflexion (supination)
    - Common fibular nerve compression
    - Inversion ankle sprains
  - **Anterior fibular head**
    - Dorsiflexion (pronation)
  - **Meniscal tear**
    - pain with squatting, knee gives out
  - **pes anserine bursitis**
    - medial knee pain below the joint line
    - MEDIAL pain
  - **Patellofemoral syndrome**
    - Due to vastus medial oblique weakness/ overuse
    - Pain worse with weight bearing with knee flexed (squat, stairs, run or sit long time)
    - ANTERIOR KNEE PAIN
    - Pain worse with isometric contraction of quadriceps, pain with sitting, pain with grinding, squatting and walking up stairs
    - Patellar compression test (patella pushed into trochlear groove) reproduces pain, pain with isometric contraction
    - Tx: **exercise and physical therapy**, activity modification, stretch, strengthen quadriceps

Common Causes of Patella-Related Pain	

Patellofemoral pain syndrome	• Aching in the anterior knee that worsens with activity
	• Worsened by stair climbing, jumping, and prolonged sitting
	• Contributing factors may include:
	  ◦ Increased Q angle at the knee
	  ◦ Tight hamstrings
	  ◦ Weak gluteus muscles
	  ◦ Weak quadriceps

Patellar instability	• Transient displacement of the patella (usually laterally) • Can cause acute or chronic patellar pain

Patellofemoral arthritis	• Arthritis of the patellofemoral joint
	• Radiographic findings:
	  ◦ Spurring on the patella (lateral view)
	  ◦ Decreased joint space (sunrise view)

Patellar tendinosis/tendinopathy	• Chronic wear of the patellar tendon • Focal patellar tendon tenderness
Synovial plica syndrome	• Inflammation in a redundant fold of synovial lining, which can become painful and fibrotic • Usually occurs at the medial border of the patella • Can occasionally "catch," worsening the pain

Causes of Knee Pain by Location	
Location	**Differential Diagnosis**
Medial	• Medial compartment arthritis • Medial collateral ligament sprain • Meniscus injury • Pes anserinus pain syndrome
Lateral	• Iliotibial band syndrome • Lateral compartment arthritis • Lateral collateral ligament sprain • Meniscus injury
Focal anterior	• Osgood-Schlatter • Patellar or quadriceps tendinitis • Prepatellar or infrapatellar bursitis • Synovial plica
Vague anterior	• Avascular necrosis • Chondromalacia patellae • Chronic patellar dislocation/subluxation • Osteoarthritis exacerbation • Patellar stress fracture • Patellofemoral pain • Referred pain from the hip
Posterior	• Gastrocnemius strain • Hamstring strain • Popliteal artery aneurysm or entrapment • Popliteal cyst (eg, Baker cyst)

- Iliotibial band syndrome
  - LATERAL knee pain
  - Tenderness proximal to joint line
  - Pressure over IT band
- **Prepatellar septic bursitis ****
  - Common to patients who kneel a lot
  - Fever, good ROM, tenderness on anterior aspect
- **Baker cyst**
  - Popliteal fossa
- **Q angle**
  -

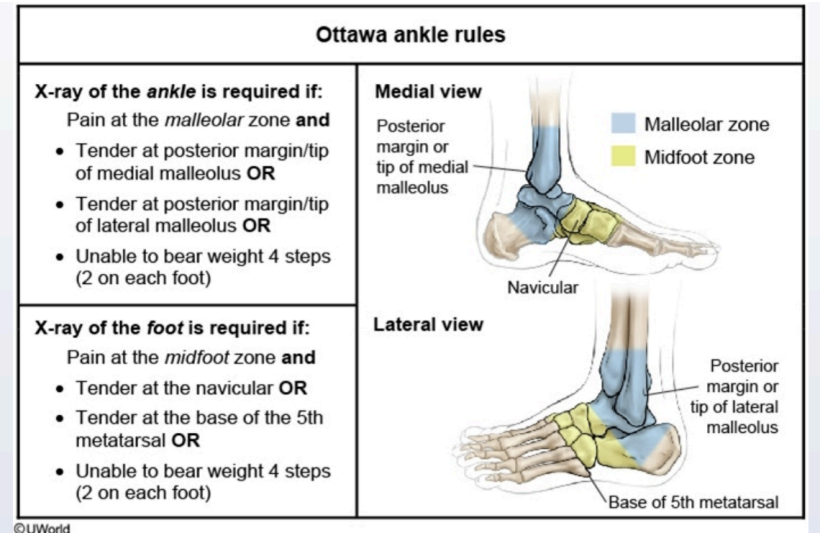
Genu valgum	Q > 17 degrees	Women, knock-kneed Weak vastus medialis → lateral tracking of patella with quadriceps firing
Genu varum	< 14 degrees	bowlegged

Genu recurvatum	Extension > 0 degrees	Postural hyperextension of a joint

-
- **Ankle injury**
  -
    - Work-up: Xray → bracing, corticosteroids, bracing
  - Type 1: ATFL
  - Type 2: + calcaneofibular
  - Type 3: posterior talofibular
  - **ATFL sprain**
    - ATFL sprain more common. PTFL
    - tx: PRICE (protest, rest, ice, compression, elevation)
      - aimed at decreasing pain and swelling, protecting against recurrence, provide support, increase ROM
      - surgery is last resort
  - **Tendonitis**
  - **Anterior tarsal tunnel syndrome**
    - Inferior extensor retinaculum, dorsum of foot and first dorsal webspace
  - **Posterior tarsal tunnel syndrome**
    - Medial malleolus with overlying flexor retinaculum
    - Not on plantar surface of foot
  - **Calcaneal stress fracture**
    - Repetitive microtrauma (abrupt increase running)
    - Medial lateral squeeze test
  - **Plantar fasciitis**
    - pain on the ball and arch, anteromedial heel of feet, worse when waking up.
    - PT
    - Tx: over the counter heel inserts
  - **Charcot Marie Tooth: polyneuropathy**
    - Repetitive bone/ joint trauma due to impaired sensation
      - Due to DM or posterior column disease (B12 def, tabes dorsalis)
    - Acute → chronic with bone deformities, neuropathic ulcers, etc.
    - Xray shows reactive bone and necrosis
    - Tx: surgical realignment, orthotic footwear infection management
  - **Achilles tendinopathy**
    - eccentric calf-strengthening exercises (calf and toe raises)
    - finding: nodular appearance at site of insertion at posterior calcaneus, 2-6 cm proximal
    - Common in young athletes
    - Risk: fluoroquinolones
  - **Calcaneal apophysitis (sever disease)**
    - Posterior heel tenderness
    - Children and adolescents in running/ jumping sports
  - **Enthesitis**
    - Inflammation and swelling at insertion of tendon or ligament
    - Associated with ankylosing spondylitis, back pain and stiffness
  - **Subcutaneous calcaneal bursitis**

- Pain and tenderness at calcaneal prominence

- **Ankle fracture**
  - **Ottawa ankle rules**
    - Unable to bear weight or tender malleolus= X RAY
    - 100% sensitive to r/o significant malleolar and midfoot fractures
    - Must have at least pain in the **malleolar "lateral" zone OR pain in the midfoot**



  - sPrain= ligament stretch/ tear
  - sTrain= muscle/ tendon stretching or tear
  - Xray needed if pain in malleolar region, navicular or 5th metatarsal bone, inability to bear weight on ankle

- **Foot injury**
  - **metatarsal stress fracture**
    - no weight bearing activity for a few days, walking boot for 4-6 weeks; NSAIDS, ice, stretching.
    - Risks: high impact sports, sharp localized pain
    - Female athlete triad: xs exercise, oligomenorrhea, inadequate nutritional intake, osteopenia
  - **Plantar fasciitis**
    - Plantar aponeurosis inserts on calcaneus, worse with overuse and prolonged standing
    - POINT TENDERNESS, worse with first few steps in the morning
    - Tx: NSAID, heel insert, myofascial release
  - **Morton neuroma**
    - Clicking sensation, pain reproduced, interspace compression (mulder sign)
    - Neuropathic degeneration of interdigital nerves → numbness, aching, burning
    - Seen in runners. Worse with walking on hard surfaces
    - Dx: clinically
  - **Tarsal tunnel syndrome**
    - Compression of tibia nerve thru ankle → **burning**, numbness, aching
    - Tinel sign reproduces pain

Overview of running injuries of the foot & ankle	
Injury	**Clinical features**
Stress fracture	• Insidious onset • Focal pain in navicular or metatarsals • **Risk factors:** abrupt increase in intensity of training, poor running mechanics, female with eating disorder
Plantar fasciitis	• Plantar surface of the heel • Worse when initiating running or first steps of the day
Achilles tendinopathy	• Burning pain or stiffness 2-6 cm above the posterior calcaneus
Morton neuroma	• Numbness or pain between the 3rd & 4th toes • Clicking sensation when palpating space between 3rd & 4th toes while squeezing the metatarsal joints
Tarsal tunnel syndrome	• Compression of the tibial nerve at the ankle • Burning, numbness & aching of the distal plantar surface of the foot/toes

- **Neck pain**
  - Work up: xray
  - Physical exam
    - **spurling**: rotation and compression for 30 seconds → numbness and tingling
    - **Compression**: neutral and compression for 30 seconds
    - **Adson**: thoracic outlet syndrome
    - **Hoffmann** test: flick nails, ~ babinski for each cervical spinal level of CST
    - **L'hermitte's sign:** electrical shock with flexing neck
    - **Naffzinger sign**: hold jugulars, let go, and pain goes down nerve root
  - Nerve roots
    - Cervical spine: ABOVE vertebra
      - C8 goes below C7
    - Thoracic and lumbar spine: BELOW vertebra
  - Bulging disc
    - Annular rings intact
  - Herniated disc
    - Annular rings broken postero-laterally
- **Shoulder injury**
  - **AC joint sprain**
    - Pain over AC joint, pain with passive adduction
  - **Subacromial impingement & rotator cuff tendonitis**
    - Most common cause of shoulder pain
  - **shoulder impingement:** pain with raising arm against resistance
  - Acute glenohumeral dislocation

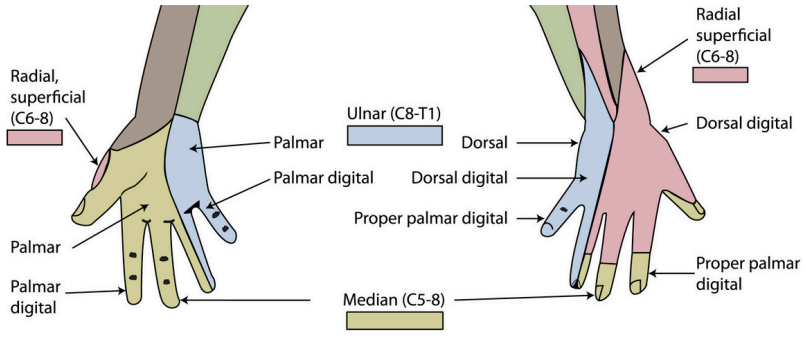
        - Anterior dislocation: abduction / external rotation
        - Posterior dislocation: adduction/ internal rotation
        - Tx: closed reduction, surgical repair, immobilize, progressive rehabilitation
        - Complications: recurrent dislocation
    - **Adhesive capsulitis:**
        - **"Frozen shoulder"** responds to lidocaine, worse with cold, inability to move shoulder
        - DIABETES
        - UNILATERAL!
        - Decreased ROM active/ passive, muscle atrophy, pain and stiffness
        - Shoulder injuries should not be immobilized bc of risk of adhesive capsulitis
        - Tx: spencer techniques , passive range of motion treatment exercises
        - Next step: range of motion exercises
    - **Bursitis**: pain with most shoulder movements
        - 

    - **Labral tear:** acute, painful; shoulder "catches" and crepitus
        - Glenohumeral joint worsened with overhead activities
        - Reduced active and passive ROM
    - **Subluxation**: traction test, jobs test restriction
    - **Rotator cuff**: cracking with movement
        - Work up: xray (doesnt show much, r/o fracture) → MRI (most sensitive)
        - Tx: PT, NSAIDs
        - SITS
            - subscapularis & teres minor- external rotation
            - suprascapular & deltoid= abduction
            - Supraspinatus
                - Tendonitis, subacromial bursitis
            - Infraspinatus
            - Teres minor
            - Subscapularis
        - **Rotator cuff tendinopathy**: symptoms based on specific muscle irritation from repeated trauma, impingement between humerus and acromion → fibrotic changes (tendinopathy)
            - Painful motion, but ROM is preserved
            - Can increase risk of rotator cuff tear with weakness
            - Tx: NSAIDS, PT, OMT (thoracic muscle energy)

- **Rotator cuff tear**
    - Acute: young athletes (hyperadduction, external rotation)
    - Chronic: degenerative, SIT tear, subacromial impingement and bursitis
- **Bicipital tendonitis**: inflammation of LH biceps tendon
    - Anterior shoulder pain, painful flexion and supination
    - Biceps rupture= cannot flex arm
    - MRI confirms diagnosis
    - Surgical repair in 2-3 weeks
- **SLAP lesions**
    - Superior labrum from A to P
        - Obriens test, compression-rotation, snyders biceps tendon test
- **Hill sachs defect**
    - Chondral impact injury on posterosuperior humeral head
- **Bankart lesion=** avulsion of anterior labrum and anterior band of labrum, fracture on inferior glenoid capsule w/ labral tear
-

- **Elbow injury**
    - **radial head subluxation/ nursemaid elbow → attempt closed reduction**
        - very common in 1-4 yo. pulling kid by the arm
        - arm pronated, extended, adducted
    - **Radial tunnel syndrome**
        - Radial nerve entrapment on lateral epicondyle → wrist drop
        - Pain with resisted supination
    - **Lateral epicondylitis (tennis elbow)**
        - Pain with supination and passive flexion, resisted extension of the wrist
        - Overuse of extensor tendons with extension and supination
        - Tx: PT, nsaids → glucocorticoids, surgery if no relief with conservative measures
    - **Medial epicondylitis (golfer elbow)**
        - FOOSH (fall on outstretched hand) → radial head injury
        - Pain with resisted wrist flexion, passive extension
    - **Ulnar nerve entrapment**
        - Cubital tunnel syndrome
        - Medial epicondyle, prolonged muscle flexion
    - **Median nerve entrapment**
        - Pain with pronation, cramping in fingers
        - Tinel's sign over elbow or wrist (if carpal tunnel)
    - **Anterior interosseous syndrome**
        - Cast pressure or trauma
        - No sensory symptoms, OK sign patient unable to resist, due to weak flexion of index finger DIP
    - Bursitis
        - Due to overuse, trauma, septic
        - Swelling
        - Tx: Rest, ice, NSAIDS, padding
            - Septic: anti-staph Abx, drainage

- **Hand injury**
  - FOOSH= scaphoid > triquetrum
  - Pain at base of thumb= OA, tenosynovitis, skier thumb
  - **Dequervain's tenosynovitis**
    - (thumb swelling, pain with passive motion radiating to forearm)= abductor pollicis longus
    - Tx: splinting, corticosteroids injection, then surgical release
  - **Scaphoid fracture**
    - FOOSH
    - Tx:
      - Immobilization= non-displaced pole (4-6 weeks), nondisplaced waist (10-12 weeks), nondisplaced proximal fracture (12-20 weeks)
      - Percutaneous screw fixation: minimally displaced fracture w/o angulation and proximal pole fractures
      - Open reduction= significantly displaced/ comminuted fractures, perilunate dislocation
      - Bone grafting and fixation: non-union fracture
      - Ice and ibuprofen for short-term symptomatic releif
  - **Cubital tunnel syndrome**
    - Ulnar nerve entrapment at elbow
    - More involvement of the ulnar-innervated forearm muscles (flexor digitorum profundus, flexor carpi ulnaris)
    - Cannot flex 4th-5th MCPs and IPs
  - **Guyon canal syndrome**
    - Hypothenar atrophy and difficulty abducting 4th-5th digits
      - Medial 1.5 digits
    - Ulnar compression through guyon canal. Contains motor and sensory fibers. Motor branch more commonly affected
    - ~ to carpal tunnel syndrome but fingertips are spared
  - **Carpal tunnel syndrome**
    - Median nerve entrapment at flexor retinaculum
      - Palmar lateral 3.5 digits and THENAR eminence
    - Cannot oppose thumb and index finger
    - Atrophy of thenar eminence
    - Work-up: Tinel test → Nerve conduction studies and EMG
      - US used to guide steroid injections
      - Next: wrist splinting
      - Last resort: surgical correction



        - Tx: splinting/ brace & OMM -> glucocorticoid injection -> surgical decompress
    - **Posterior interosseous nerve syndrome**
        - Compression of PIN in proximal forearm
        - Loss of finger extension bc of dysfunction of extensor muscles in forearm
    - **Radial nerve compression**
        - Dorsal aspect of lateral ⅗ digits and anatomical snuff box
    - **Dupuytren's contracture**: unable to extend finger, fibrous band and palmar nodule.
        - Abductor pollicis longus , thickened palmar fascia and contracture, nodule in palm of hand
        - Tx: surgery to release of contracture
            - Collagenase injection: symptomatic treatment to correct deformities

Test	Disease	Maneuver	Treatment
Finkelstein test	De Quervain tenosynovitis (ABductor pollicis longus, extensor pollicis brevis	Thumb inside fist, ulnar deviation. Pain over radius	Splint, modify activity, oral steroids, steroid injection
Allen test	Occlusion of radial and ulnar arteries with pumping of the fist	Delay in blood return to palm → compromised flow	
Phalen test	Carpal tunnel	Maximum flexion of both wrists → reproduce pain	
Tinel test	Carpal tunnel	Tapping volar wrist → numbness	
Watson test	Scapulolunate ligament injury	Push scaphoid AP with wrist in radial or ulnar deviation	

- **Back pain**
    - **acute-subacute nonspecific low back pain**
        - tx: NSAID and muscle relaxant
        - screen for red flags! Fever, defecation, sensory loss and muscle weakness, tenderness to percussion, straight leg test → **MRI**
    - **Chronic nonspecific back pain**
        - > 12 weeks, no known etiology
        - Maintain activity, stretch & strengthen, heat, CBT
        - Tx: NSAID, acetaminophen, TCA, non benzo muscle relaxants
            - Back braces discouraged bc limit movement

        - Physical therapy if > 4 weeks and those with chronic pain disorders (poor functional status and psych comorbidity)
    - Chronic radicular pain
        - Herniated disk
        - Tx: conservative → epidural corticosteroid
    - **Scoliosis**
        - Cobb angle > 20 degrees is a high risk
    - **Muscle strain**
        - Paraspinal tenderness, normal neuro exam
    - **Radiculopathy**
        - Herniated disc → radiation below the knee, positive straight leg raise, neurologic deficits
    - **Spinal stenosis**
        - Pseudoclaudication, relief with leaning forward
    - **Spondyloarthropathy**
        - Worse with rest, better with activity
        - Sacroiliitis
        - Affect site of ligamentous insertion (enthesitis) → destroy articular cartilage
    - **Ligamentous sprains**
        - Hx of injury, pain with movement.
        - Symptoms resolve with in days- weeks
    - **Metastatic cancer**
        - > 50 yo, worse at night, not relieved with rest
    - Work-up:
        - Red flag signs: neurologic deficits, urine issue → MRI
        - Infectious cause: MRI, xray and ESR/ CRP
        - Suspected malignancy/ recurrence, risk factors → MRI + ESR/ CRP
        - Uncomplicated back pain: no imaging
- **Rhabdomyolysis**
    - Patient found unconscious for unknown amount of time
    - Hyperkalemia, hyperphosphatemia
    - Hypocalcemia (dystrophic calcium deposition)
    - Elevated **AST, ALT, CK**
    - Increased risk of Acute kidney injury (AKI)
    - Prolonged immobilization with ischemic compression of skeletal muscles → decreased renal perfusion (volume depletion from shifting fluid) → direct renal tubular toxicity of heme pigments
    - Tx: hydration

Rhabdomyolysis	
Etiology	Skeletal muscle lysis/necrosis due to: • Crush injury or prolonged immobilization • Intense muscle activity (eg, seizure, exertion) • Drug/medication toxicity (eg, statins)
Clinical features	• Muscle pain & weakness • Dark urine (myoglobinuria/pigmenturia) • + Blood on urinalysis & no RBCs on microscopy • ↑ Serum K & PO_4, ↓ serum Ca, ↑ AST > ALT • Acute kidney injury
Diagnosis	• Serum creatine kinase >1,000 U/L • Consistent clinical features
Management	• Aggressive intravenous fluid resuscitation • Sodium bicarbonate in some cases

■

Dermatology

- High yield
  - **Lyme disease**: erythema migrans, tx: doxycycline
  - **Tinea capitis**: oral griseofulvin/terbinafine + topical ketoconazole shampoo (reduce spread)
  - **Tinea corporis**: annular lesions with central clearing (tx: terbinafine, griseofulvin)
  - **Tinea versicolor** tx: selenium sulfide
  - **Tinea pedis**= miconazole cream
  - **Lymphangitis=** Acute: strep pyogenes, MSSA (tx: cephalexin); chronic: sporotrichosis (itraconazole)
  - **Cat scratch disease=** bartonella henselae, tx: azithromycin
  - **Molloscum contagiosum=** cell mediated immunodeficiency, fleshy papules with central umbilication
  - **Basal cell carcinoma** → pearly, telangiectasias, on face above lip → Mohs surgery (on face), excision on body
  - **Squamous cell carcinoma** → scaly, ulcerated → mohs (face), excision on body
  - Keloid → intralesional corticosteroid
  - Alopecia → intralesional corticosteroid
  - Limited scleroderma= hands and face only
  - Diffuse scleroderma= skin and organs involved
  - morphea = skin thickening

Common Forms of Hair Loss		
Type of Hair Loss	**Characteristics**	**Treatment**
Female pattern	• Thinning hair mainly on the top and crown of the head, with the front intact	• Topical minoxidil • Oral spironolactone
Male pattern	• Thinning in the "M" pattern at the hairline with additional progression at the vertex	• Topical minoxidil • Oral finasteride
Alopecia areata	• Smooth, well-circumscribed, discrete areas of hair loss that appear suddenly without scarring	• Intralesional steroid injection in less severe cases
Tinea capitis	• Patchy, scaly scalp that presents with pruritus and erythema	• Topical antifungal cream or shampoo
Traction alopecia	• Hair thinning in the frontal and temporal regions • Typically associated with hair practices that involve pulling/traction	• Counseling and education on less damaging hair practices

- Next steps
  - **Shave biopsy** = superficial lesions (BCC)
  - Punch biopsy= large lesions or if small lesion can be removed
  - **Cryoablation**- warts and actinic keratosis
  - **Wide local excisio**n= definitive removal of biopsy proven lesion
- **Nails**
  - **Mees lines-** transverse leukonychia or leukonychia striae, is a type of true leukonychia characterized by a whitening discoloration that appears in striated bands running parallel to the base of the nail, as shown in the photograph below. Causes of Mees lines are varied and may include repetitive trauma, systemic illness, drugs (eg, retinoids or taxanes), or arsenic or thallium toxicity.
  - Muehrcke lines- leukonychia typically characterized by 2 transverse white bands running parallel to the base of the nail for the entire width of the nail, as shown in the photograph below. Muehrcke lines may be seen more commonly in patients with renal disease or hypoalbuminemia but may also be associated with systemic causes, such as liver disease or chemotherapy.
  - leukonychia punctate- type of true leukonychia, is the most common from of leukonychia overall. Leukonychia punctate typically involves small white spots in the nail that progress distally as the nail grows, as shown in the photograph below. This nail disorder most frequently occurs secondary to trauma to the nail and thus is often seen in children.
  - idiopathic leukonychia totalis- Idiopathic leukonychia totalis is a rare, inherited nail disorder caused by a mutation in the gene *PLCD1*. The disorder is characterized by all nails becoming a milky, porcelain white

color, as shown in the photograph below. Patients typically are otherwise asymptomatic.
    - Terry nails
- **<u>Rashes & Dermatoses</u>**
    - **Acne**

Treatment For Acne			
Treatments	**Mild** (Comedonal or few inflammatory lesions)	**Moderate** (Comedonal and inflammatory lesions, no nodules or scarring)	**Severe** (Widespread comedones, inflammatory lesions, or nodulocystic acne with potential for or signs of scarring)
1st line treatment	• Benzoyl peroxide (BPO) or • Topical retinoid or • Topical combination therapy (BPO + topical retinoid + topical antibiotic)	• Topical combination therapy or • Oral antibiotic and topical retinoid or • Oral antibiotic and topical combination therapy	• Oral antibiotic and topical combination therapy or • Oral isotretinoin
Alternatives	• Add topical retinoid or BPO (if not already on) or • Switch topical retinoid or • Add topical dapsone	• Alternate combination therapy or • Consider change in oral antibiotic or • Add combined oral contraceptive (OCP) or spironolactone (females) or • Oral isotretinoin	• Consider changing oral antibiotic or • Add spironolactone or OCP (females) or • Oral isotretinoin

        -
        - Tx: Benzoyl peroxide + tretinoin + clindamycin
            - Side effects of tretinoin: xs drying and peeling, lighten/ darken
            - Children: avoid tetracycline (doxycycline)
    - **Contact dermatitis**
        - T cell mediated cytotoxicity
        - Chronic irritant with scaling, lichenification, fissuring
        - Tx: emollients, topical steroids and irritant avoidance
        - Suspect if only one body part affected (hands)
        - Allergen patch testing might be useful
    - **Atopic dermatitis/ eczema**
        - IgE, associated with other allergies (asthma, celiac); due to mutation in filaggrin gene
        - “Itch that rashes” → acute patches and papules
            - Infant: flexor surfaces
            - Adults: EXTENSOR surfaces
        - Topical emollients and steroid cream #1, topical calcineurin inhibitors
    - **Hypersensitivity reactions**

Hypersensitivity Reactions		
Types	**Mechanisms**	**Examples**
I (Immediate; Anaphylactic/Atopic)	IgE-mediated triggering of presensitized mast cells and basophils	• Anaphylaxis
II (Cytotoxic)	Mediated by antibodies (which bind to cell-surface antigens) via 2 possible mechanisms: • The cells are opsonized, leading to phagocytosis or antibody-dependent cytotoxicity • Antibodies bind to and block the normal function of cells	• Autoimmune hemolytic anemia, transfusion reactions, hemolytic disease of the newborn • Myasthenia gravis, Graves disease
III (Immune complex)	Immune complexes (antigen, antibody, and complement) activate complement-mediated inflammation, leading to vasculitis and systemic effects	• Systemic lupus erythematosus, polyarteritis nodosa, poststreptococcal glomerulonephritis, serum sickness
IV (Delayed)	Mediated by T lymphocytes via 2 possible mechanisms: • Direct cell destruction via CD8+ cytotoxic T cells • Sensitized CD4+ helper T cells release cytokines in response to antigen recognition No antibodies are involved	• Contact dermatitis (poison ivy/oak, nickel), type 1 diabetes mellitus, graft-versus-host disease

-
- **Rosacea**
  - Papulopustular, phymatous, ocular
  - Facial erythema, flushing and telangiectasis
  - Involves nasolabial folds
- **Melasma**
  - Acquired hyperpigmentation on sun-exposed face (spares nasal folds)
  - Associated with pregnancy
  - Give sunscreen
- **Psoriasis**
  - Extensor surfaces, scalp, nail plates
  - Can have nail pitting, conjunctivitis, uveitis, arthritis
  - Tx: high potency glucocorticoids, Vit D analog, tar, retinoids, calcineurin inhibitors, tazarotene.
  - Systemic: MTX, apremilast, biologics
- **Seborrheic dermatitis**
  - “Greasy scale”
  - Tx: Mineral oil
  - Common inflammatory eruption in infancy on scalp, face, intertriginous areas
  - In adults, associated with HIV infection/ AIDS
- **Pityriasis rosea**
  - Herald patch → outbreak of macules and papules on trunk
  - Adolescents, resolves 4-6 weeks
  - herald patch followed by multiple smaller patches in Christmas tree pattern
  - increased risk of spontaneous abortion in 15 weeks of gestation
- **Erythrasma**
  - Corynebacterium infection

        - Common in DM and obesity, seen in intertriginous areas
        - Fine scaling lesion. Coral-red fluorescence on wood-lamp
            - Tinea is blue
    - **Erythema migrans**
    - **Erythema multiforme**
    - **Erythema nodosum**
        - Ulcerative colitis
    - **Lichen planus**
        - Pruritic, purple papules
        - Apparently associated with Hep C
        -

Lichen planus	
Clinical findings	• 5 "Ps": pruritic, purple/pink, polygonal papules & plaques • Lacy, white network of lines (Wickham striae)
Disease associations	• Hepatitis C • Medications: ACE inhibitors, thiazide diuretics
Natural history	• Chronic symptoms • Formation of lesions at sites of trauma (Köbner reaction) • Spontaneous resolution within 2 years
Treatment	• Topical high-potency glucocorticoids (eg, betamethasone) • Widespread lesions: systemic glucocorticoids, phototherapy

- **Inflammatory & Blistering Skin conditions**
    - **Hypersensitivity reactions**
        - Type 1: allergic, IgE, mast cells
        - Type 2: Antibody mediated
        - Type 3:
        - Type 4: delayed type inflammation with memory T helper cells
            - Contact dermatitis
    - **SJS/ TEN vs. Staph scalded skin syndrome**
        - SSS: no mucosal involvement
        - SJS: mucosal + < 10% BSA
        - TEN: Mucosal + > 30% BSA
        -

Stevens-Johnson syndrome & toxic epidermal necrolysis	
Nomenclature	<10% of BSA: SJS 10%-30%: SJS/TEN overlap >30%: TEN
Clinical features	• 4-28 days after exposure to trigger (2 days after repeat exposure) • Acute influenza-like **prodrome** • Rapid-onset erythematous macules, vesicles, bullae • Necrosis & **sloughing of epidermis** • **Mucosal involvement**
Common triggers	**Drugs** • Allopurinol • Antibiotics (eg, sulfonamides) • Anticonvulsants (eg, carbamazepine, lamotrigine, phenytoin) • NSAIDs (eg, piroxicam) • Sulfasalazine **Other** • *Mycoplasma pneumoniae* • Vaccination • Graft-vs-host disease

Serious Conditions Presenting with Cutaneous Findings				
Condition	**SSSS**	**SJS**	**TEN**	**EM**
Age	< 6 years-old	Any age	Any age	20-40 years-old
Targetoid lesions	No	Yes	Yes	Yes
Nikolsky sign	Positive	Positive	Positive	Negative
Mucosal involvement	No	Yes	Yes	Present in EM major only

- **Epidermolysis bullosa**
  - Bullae, erosions, ulcers, friction-induced blisters on palms and soles
  - Oral blisters
- **Pemphigus vulgaris**
  - Painful erosions and flaccid bullae on skin and oral mucosa
  - Tx: oral corticosteroids

Pemphigus vulgaris vs bullous pemphigoid		
	Pemphigus vulgaris	**Bullous pemphigoid**
Age of onset	• 40-60	• >60
Clinical features	• Painful • Flaccid bullae → erosions • Mucosal involvement common	• Pruritic • Tense bullae • Mucosal involvement rare
Histology	• Intraepidermal cleavage	• Subepidermal cleavage
Immunofluorescence	• Net-like intercellular IgG against desmosomes	• Linear IgG against hemidesmosomes along basement membrane

- **Bullous pemphigoid**
  - High-potency topical corticosteroids
    - Side effects: skin atrophy, striae, folliculitis
  - BM antibody → separation of epidermis from dermis

Treatment Options for Bullous Pemphigoid	
Treatment	**Side Effects**
High-potency topical corticosteroids	Skin atrophy/fragility, purple striae/purpura, folliculitis, telangiectasias
Systemic corticosteroids	Hypertension, hyperlipidemia, hyperglycemia, osteoporosis, infection susceptibility
Methotrexate	Nausea, vomiting, fatigue, hepatic transaminitis, mucosal ulcers, thrombocytopenia, photosensitivity
Cyclophosphamide	Diarrhea, fatigue, hemorrhagic cystitis, leukopenia

- **Lupus erythematosus**
  - Discoid SLE, widespread lesions, concurrent arthralgia/ arthritis
  - Sun-exposed “sun burns easily”, dermal atrophy, scarring, alopecia
  - CNS findings: seizures, lymphocytes in CSF
  - Best indicator of acute exacerbation = low complement
  - Renal involvement – lupus nephritis

        - Low C3 and C4
        - RBC casts
        - High BUN and Cr
    - **Photosensitivity**

Common drugs associated with photosensitivity reactions	
Antibiotics	Tetracyclines (eg, doxycycline)
Antipsychotics	Chlorpromazine, prochlorperazine
Diuretics	Furosemide, hydrochlorothiazide
Others	Amiodarone, promethazine, piroxicam

        -
- **Ulcerative & granulomatous lesions**
    - **Pyoderma gangrenosum**
        - Irregular ulcers, PMN dermatosis in association with IBD and inflammatory arthritis. Seen in LE
        - Ulcerative colitis
        - Pathergy (small trauma → new lesions)
        - Tx: oral corticosteroids, mycophenolate mofetil, cyclosporine infliximab
    - **Necrobiosis lipoidica**
        - Chronic granulomatous skin disorder
        - Seen in DM
        - Brown plaque → telangiectasias and ulceration
        - Confluent annular lesions with yellow-brown hye, dilated vessels, epidermal atrophy
        - Most common in diabetes mellitus
    - **Pyogenic granuloma**
        - Benign vascular lesion on skin or mucosa
        - Small papule that enlarges quickly
    - **Fournier gangrene**
        - Necrotizing fasciitis → sepsis and death
        - Polymicrobial infection
        - Crepitus, fever, hypotension, leukocytosis, acidemia, renal insufficiency
        - Tx: surgical exploration and debridement
- **Skin infections & Friends**
    - **Hidradenitis suppurativa**
        - Fistulas with progressive symptoms and exacerbations
        - Risk factors: Smoking, obesity, OBD
        - Tx:
            - Skin cleansing (pHisoHex and water), weight loss,
            - oral ABx: topical clindamycin, tetracycline, TNFalpha
            - surgical removal
    - **MRSA**
        - suppurative skin and soft-tissue infection
        - tx: vancomycin
    - **Erysipelas**
        - Superficial skin infection that is demarcated
    - **Folliculitis**
        - Inflamed hair follicle → acute, red pustular eruption
    - **Cellulitis**

        - Deeper skin infection. Resembles erysipelas. Management same as erysipelas
        - acute onset of skin inflammation, fever, redness
        - hx of trauma, surgery
    - **Necrotizing fasciitis**
        - Crepitus, purple discoloration, rapid and progressive infection despite Abx
        - Due to staph aureus, clostridium perfringens, strep pyogenes
        - “Undermining of the skin surrounding the wound”
        - Tx: clindamycin + penicillin G
    - **Scabies**
        - Intertrigous scaling lesions, web spaces or wrist
    - **Bed bugs**
        - Linear bites
    - **Tinea corporis**
        - Tx: terbinafine
- **Wood lamp**
    - pale blue= pseudomonas
    - yellow= tinea
    - pink= erythema sma / corynebacterium
    - white= vitiligo
    - lime green= normal
- **Benign skin lesions**
    - Dermatofibroma
    - **Keratoacanthoma**:
        - grows and resolves rapidly (might progress to SCC)
    - **Keratosis pilaris**
        - Painless papules on posterior surface of arm
        - associated with colder weather
        - Tx: emollients
    - Miliaria (heat rash)
        - Blocked eccrine sweat glands
        - Common in kids
    - Pseudofolliculitis
        - Ingrown hair shaft
    - Pseudomonal folliciulitis
        - Hottub → red pimples → conservative management
    - Ichthyosis vulgaris
        - Impaired epidermal barrier → reduced skin moisture→ fish scale dry skin
        - Tx: long baths, moisturization, keratolytics (alpha-hydroxy acid, salicylic acid)
        - Palmar hyperlinearity
- **Melanoma**
    - determine malignancy ASAP. Compare photos of moles over time
        - melanoma in situ: localized to epidermis
        - superficial spreading melanoma: most common
        - lentigo maligna: elderly, 70s; hawaii
        - amelanotic melanoma: nonpigmented
        - acral lentiginous melanoma: nails, soles of feet, palms; flat, irregular dark brown -black lesions
        - nodular melanoma: invasive at dx, most aggressive, 2nd most common melanoma

    - ABCDS: asymmetric, irregular border, abnormal color, large/ growing diameter
    - risk factors: UV radiation, FMHx
    - Work-up: full thickness biopsy
    - Tx: excision with 2-3cm margins, if cancer make 5 cm margins
        - melanoma < 1mm has a low rate of metastasis
    - Screening: whole body skin screen with risk factors; if otherwise healthy, counsel on avoiding tanning booths and wearing sunscreen
- **Misc skin conditions**
    - **Alopecia areata**
        - Painless hair loss due to autoimmune attack on hair bulb
        - Tx: topical/ intralesional corticosteroids; topical immunotherapy, oral corticosteroids (triamcinolone)

Alopecia Areata		
Main Types	**Hair Loss Pattern**	**Treatment**
Patchy alopecia areata	Smooth, discrete patches of hair loss on < 50% of the scalp	• Topical glucocorticoids • Intralesional glucocorticoid injections
Diffuse alopecia areata	Smooth, discrete patches of hair loss on > 50% of the scalp	• Oral JAK inhibitors • Topical immunotherapy
Alopecia totalis	Complete loss of hair on the scalp only (eg, not the eyebrows)	• Oral JAK inhibitors • Topical immunotherapy
Alopecia universalis	Complete loss of hair on the scalp and body	• Oral JAK inhibitors • Topical immunotherapy
JAK = Janus kinase.		

    - **Porphyria cutanea tarda**
        - Uroporphyrinogen decarboxylase defect, acquired
        - Onycholysis (nail plate separation), chronic skin lesions of sun exposued areas (blisters, erosions, hyperpigmentation, hypertrichosis, milia)
        - Alcohol and tobacco are risk factors for PCT
        - 

-

Psychiatry

- [Mer's Psych cheat sheet]

Toxin	Antidote
Acetaminophen	N-acetyl cysteine
Anticholinergic	Physostigmine, neostigmine
Arsenic	Dimercaprol, succimer
Benzodiazepine	Flumazenil
Beta-blocker	Glucagon
Calcium channel blocker	Calcium chloride, glucagon
Carbamate	Atropine
Cyanide	Hydroxycobalamin, thiosulfate, nitrate
Digoxin	Digoxin immune fab (Digibind/DigiFab)
Dopamine	Phentolamine
Ethylene glycol	Ethanol, fomepizole
Heparin	Protamine
Iron	Deferoxamine
Isoniazid	Pyridoxine (vitamin B6)
Lead	Ethylenediaminetetraacetic acid, dimercaprol
Methanol	Ethanol, fomepizole
Methemoglobinemia	Methylene blue, vitamin C
Opioid	Naloxone/naltrexone
Organophosphate	Pralidoxime, atropine
Salicylate/trichloroacetic acid	Sodium bicarbonate
Snake venom	CroFab
Warfarin	Vitamin K, fresh frozen plasma, prothrombin complex concentrate

Common Drugs of Abuse	
Drug	**Intoxication Signs and Symptoms**
Benzodiazepines	Disinhibition, mood lability, respiratory depression, confusion, hypotension, drowsiness, slurred speech, incoordination, ataxia
Barbiturates	Nystagmus, respiratory depression, confusion, hypotension, drowsiness, slurred speech, incoordination, ataxia
Opioids	Central nervous system and respiratory depression, pupil constriction, constipation, drowsiness, nausea/vomiting
Cocaine	Psychomotor agitation, euphoria, aggressiveness, pupil dilation, tactile & visual hallucinations, hypertension, tachycardia
Methamphetamines	Euphoria, dilated pupils, perspiration, tachycardia, tactile hallucinations, tooth decay, paranoid delusions, hypertension
Phenylcyclohexyl piperidine	Nystagmus (vertical/horizontal/rotatory), psychomotor agitation, aggression, tactile & visual hallucinations, hypertension, tachycardia
Lysergic acid diethylamide	Altered perceptual states (hallucinations, delusions, body image distortions), elevated mood, flashbacks, "bad trips" (panic reaction)
Cannabis	Euphoria, anxiety, perceptual disturbances (sensation of slowed time), dry mouth, increased appetite, conjunctival injection

Neurology

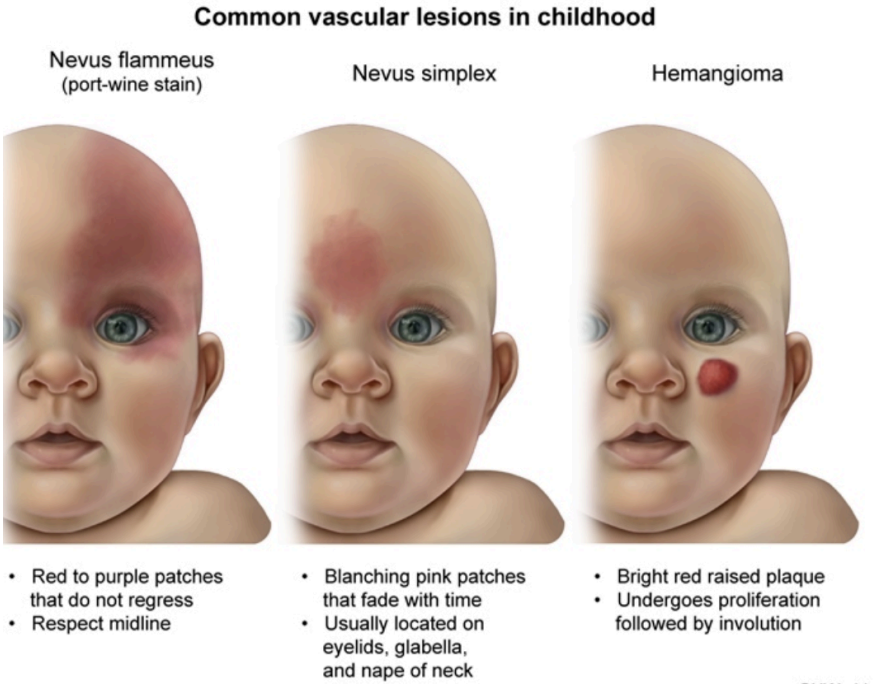
- **Next steps**
  - **New changing headache → non contrast head CT**
  - **Neurosurgery**: subdural hematoma with progressive worsening mental status

- **Mannitol**: elevated ICP
- **MRI spine**: spinal cord injury
- **CT w/o contrast**: potential fall and head injury
- TPA: ischemic CVA in 3-4.5 hours between symptom onset and presentation
- **Pyridostigmine** → prednisone→ myasthenia gravis
- **Plasmapheresis** + Ig → acute myasthenic crisis
- **Thymectomy** → thymoma (common > 40 yo)
- **MRI spine** → red flags
- **Immediate neurosurgery** → cauda equina syndrome
- **Carotid US** → amaurosis fugax, hullenburg crystals
- **Intramuscular botox** → spasticity
- TIA

ABCD^2 Score for Stroke Risk After Transient Ischemic Attack		
Age	≥ 60 years	1 point
	< 60 years	0 points
Blood pressure	Systolic ≥ 140 mmHg or diastolic ≥ 90 mmHg	1 point
	Systolic < 140 mmHg and diastolic < 90 mmHg	0 points
Clinical features	Unilateral weakness	2 points
	Isolated speech disturbance	1 point
	Other	0 points
Duration of symptoms	≥ 60 minutes	2 points
	10 to 59 minutes	1 point
	< 10 minutes	0 points
Diabetes	Present	1 point
	Absent	0 points
The tally of the ABCD^2 score is related to stroke risk over the next 48 hours since the last known normal: • Score 0 to 3: Low 2-day stroke risk (1%) • Score 4 to 5: Moderate 2-day stroke risk (4%) • Score 6 to 7: High 2-day stroke risk (8%)		

Evaluation of Transient Monocular Vision Loss	
Diagnostic Test	**Purpose**
MRI brain scan	Rule out infarction
Carotid ultrasound/CT angiogram of head and neck	Evaluation of the extra/intracranial vessels
Erythrocyte sedimentation rate and C-reactive protein	Evaluate for giant-cell arteritis (patients > 50 years of age)
Ophthalmologic evaluation	Evaluate for ocular etiology of transient vision loss
ECG/telemetry monitoring	Evaluate for arrhythmia as a cause of emboli (eg, atrial fibrillation)
Echocardiogram	Evaluate for structural cardiac etiology as a cause of emboli/evaluate for left ventricular thrombus
Hypercoagulable workup	Rule out hypercoagulable state as cause of thrombus (only if it fits the clinical picture)

- **High yield**
  - Hummingbird sign= supranuclear palsy
  - Trendelenburg= superior gluteal nerve
  - Gluteus maximus= inferior gluteal nerve
  - Tau → alzheimer's disease
  - Amyloid precursor protein (APP) → Trisomy 21
  - Diffuse axonal injury → coma, CT normal, punctate hemorrhages in the white

matter
- Downward displacement of cerebellar tonsils → brain herniation
- Blood in basal cisterns → SAH
- Epidural hematoma → middle meningeal artery, pterion fracture, biconvex, lucid interval→ emergency surgical intervention
  - If small epidural hematoma → observe closely
- SAH → worst headache of life, sudden onset
- Hypertensive vasculopathy → BASAL GANGLIA → herniation
- Subdural hematoma → older adult on blood thinners, insidious onset, lucid interval
- Neurocutaneous disorders
  - NF1= AD, seizures, neurofibromas, axillary freckles, cafe au lait, lisch nodules in iris
  - NF2= AD, B/L vestibular schwannomas, cataracts, cutaneous plaques/ tumors
  - **Tuberous sclerosis**= seizures, ash-leaf spots, angiofibromas (malar erythematous papules), shagreen patches (flesh colored plaque on back)
  - **Sturge weber**= capillary malformation/ port-wine stain along CNV, seizures, visual defects, leptomeningeal capillary-venous malformations, nevus flammeus
- Triphasic periodic sharpwaves, hyperreflexia, babinski, signal hyperintensity in basal ganglia and temporal/ frontal cortices= CJD → tx Supportive care
- 

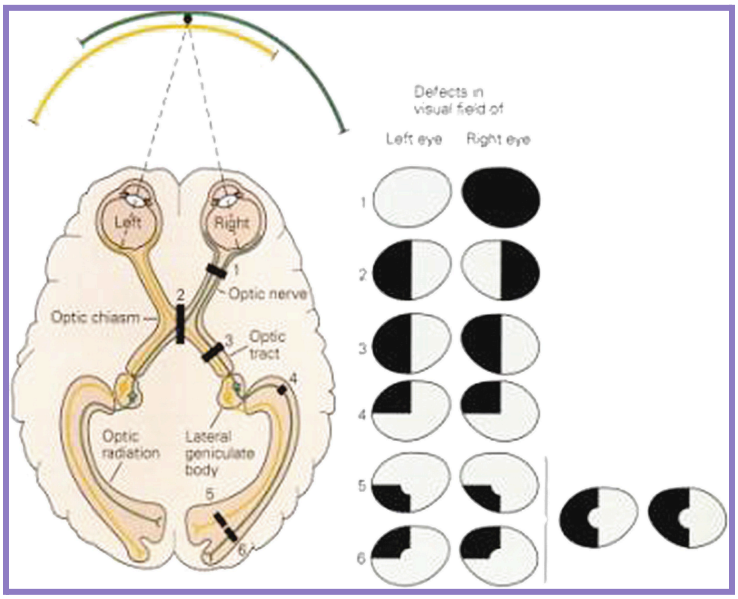
Diagnoses Associated with Brady/Akinesia			
Disease	**Main Signs/Symptoms**	**Additional Examination Findings**	**Imaging Findings**
Corticobasal degeneration	• Severe rigidity • Focal myoclonus • Dystonia • Akinesia	• Marked unilateral involvement • Alien limb phenomenon	• Asymmetric cortical atrophy
Drug-induced parkinsonism	• Resting tremor • Rigidity • Gait disturbances	• Brady/akinesia	• No specific findings
Lewy body dementia	• Dementia • Visual hallucinations • Brady/akinesia	• REM sleep behavior disorder • Autonomic dysfunction	• No specific findings
Multiple system atrophy	• Profound autonomic dysfunction • Akinetic-rigid parkinsonism • Cerebellar ataxia	• Orthostatic hypotension • Erectile dysfunction • Urinary frequency • Cognition is generally preserved	• "Hot cross bun" sign (seen on axial MRI at the level of the pons)
Normal pressure hydrocephalus	• Incontinence • Encephalopathy • "Magnetic" gait	• Brady/akinesia	• Disproportionately enlarged subarachnoid space • Enlarged lateral ventricles
Parkinson disease	• Tremor • Rigidity • Brady/akinesia • Postural instability	• Resting, pill-rolling tremor • Appendicular > axial rigidity • En bloc turns	• No specific findings
Progressive supranuclear palsy	• Restricted vertical gaze • Brady/akinesia • Postural instability	• Axial > appendicular rigidity • Trunk extension	• "Hummingbird" sign (seen on midsagittal MRI)
Wilson disease	• Psychiatric overlay • Tremor • Brady/akinesia	• Kayser-Fleischer rings • Rigidity	• "Face of the giant panda" sign (seen on axial MRI of the midbrain)

- Hypothalamic hamartoma → gelastic seizures, mental delay, precocious puberty
- Arnold-Chiari malformation → syringomyelia

    - ■ 

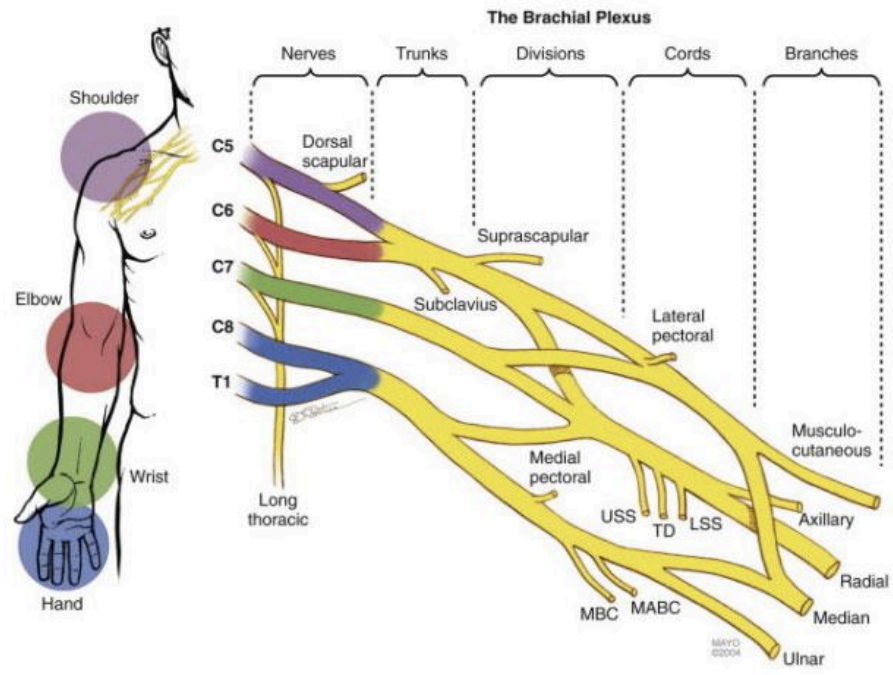
    - Hummingbird sign= supranuclear palsy
    - ■ 
    - Multiple system atrophy = hot cross buns
    - ■ 

- Physical Exam
    - mental status
    - gait
    - motor
    - sensory
    - DTR
    - cranial nerves
    - NIHSS stroke scale
    - TOAST criteria
    - RoPE score + PFO

    - ABCD2 stroke risk
    - CHADS-Vasc
- **Cranial nerves**
    - Location
        - 3 & 4: midbrain
        - 5, 6, 7, 8: Pons
        - 9, 10, 11, 12: medulla
    - **CN II= optic nerve**
        - 

        - **RAPD**
            - Pupils equal at rest, abnormal contraction in one eye with light
        - **Optic neuritis**
            - Painful loss of COLOR vision > acuity
            - red/green less than orange/ blue
            - First signs of multiple sclerosis
            - Tx: steroids
    - **CN III: oculomotor**
        - Pupil involved: mass effect, compressive
        - Pupil not involved: microvascular/ ischemia (even with ptosis and down & out= complete 3rd palsy)--> 6-26 week improvement, “spared with vascular lesions”
            - Partial third
            - CTA
        - CN III and VI= cavernous sinus
        - Posterior communicating artery aneurysm → CNIII palsy (Down, Out, and Blown out)
    - **CN IV**: trochlear nerve
        - Head tilts away from affected side
        - Eye is up and IN
    - **CN VIII**
        - Sensorineural hearing loss
        - Conductive hearing loss
        - Aminoglycoside poisoning
- **Neuropathy**

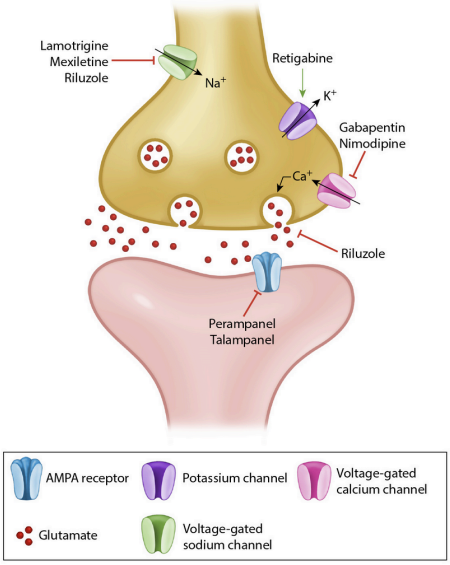
- **Radial nerve palsy**
- **Ulnar nerve**
  - Compression → weakness and muscle atrophy of medial aspect of hand
- **Median nerve**
- **Brachial plexus**
  - **Superior trunk**
    - Erbs-duchenne palsy- waiters tip hand. Adducted, medially rotated, hand pronated
  - **Inferior trunk**
    - Weakness of flexor and extensor muscles → weak hand grip/ extension → claw hand
  - **Middle trunk**
    - rare



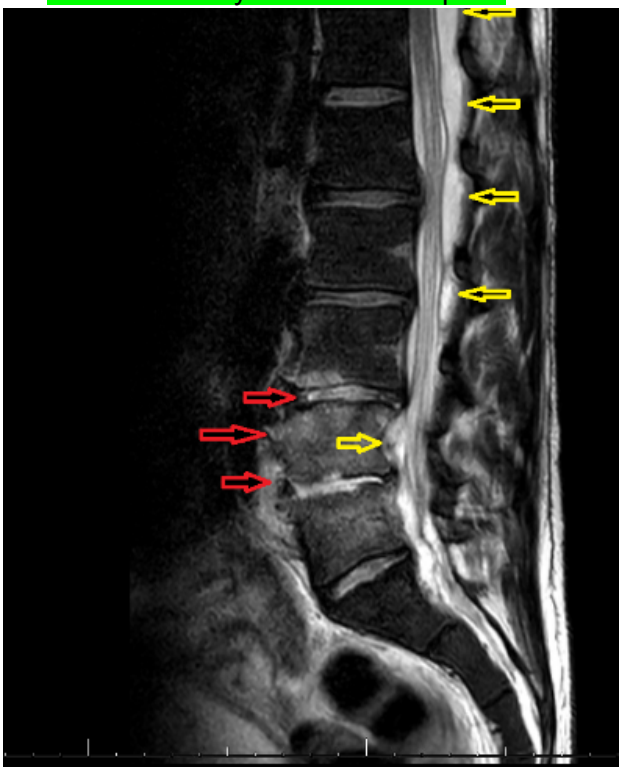
- **UMN vs LMN**
  - Pronator drift= UMN****
    - Pyramidal tract lesion → down going
    - Cerebellar dysfunction → up going
  - Romberg= proprioception

	UMN	LMN
Function	Inhibitory effect on muscle stretch reflex	Motor component of muscle reflex
Type of paralysis	Spastic	Flacid
DTR	Hyperreflexia	Hyporreflexia
Muscle Tone	Hypertonic ▪ Decorticate rigidity: lesion above midbrain ▪ Decerebrate rigidity: below midbrain	Hypotonic
Muscle Mass	Disuse atrophy	Wasting atrophy
Fasciculations	*Nope*	*PRESENT*
Babinski sign	*POSITIVE*	*Nope*
Other reflexes	Abdominal & Cremasteric LOST	-----
Voluntary movement	Decreased speed	Lost =(
Area of body involved	Large area	Small area

- **ALS (Amyotrophic lateral sclerosis)**
  - most common motor neuron disease with bulbar involvement, UMN and LMN dysfunction
  - respiratory dysfunction —> noninvasive positive pressure ventilation
  - Young guy with mixed UMN and LMN findings
  - **EMG**: active and chronic denervation, fibrillation potentials and positive sharp waves
  - tx: riluzole (glutamate antagonist) or edaravone (antioxidant)



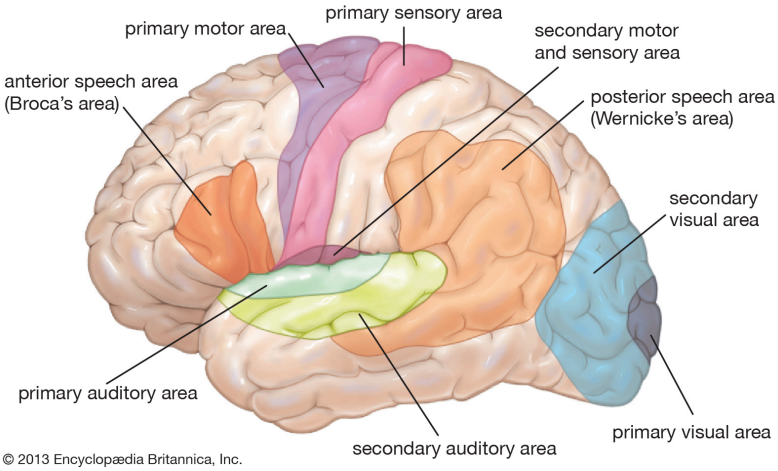
- **Multiple sclerosis**
  - Immune mediated disease of CNS → inflammatory plaques
  - T cells attack myelin, white matter → UMN findings
  - Females in 30s
  - Medial longitudinal fasciculus (MLF) → loss of coordinated horizontal movement of eyes
  - Sensory, motor, bladder/ bowel dysfunction
  - Hyperreflexia
  - Lhermitte sign: electrical sensation in limbs/ back
  - Uhthoff phenomenon: worsening symptoms with heat/ summer

    - Dx: oligoclonal IgG bands on Csf
    - Tx: IV corticosteroids → beta-interferon
- **Guillain barre syndrome**
    - GI illness (campylobacter)→ progressive ascending paralysis
    - Paresthesia and hyporeflexia
    - Workup: if respiratory concerns → CXR, pulse ox, ABG, CPKinase
    - Dx: albuminocytologic dissociation in CSF & **EMG**
    - Tx: Plasmapheresis
        - Steroids do not improve outcomes
- **Posterior columns lesion**
    - Loss of MVP
- **Spinal abscess**
    - Dx: MRI spine with contrast
    - Next step: consult neurosurgery for decompression and abscess drainage
    - Tx: intravenous drug abuse and epidural abscess are present, empiric antibiotic treatment should be given. This method will treat both methicillin-resistant Staphylococcus aureus and Pseudomonas until blood or tissue cultures have revealed the causative organism.
        - IV vancomycin and IV cefepime
    - 
- **Osmotic demyelination syndrome**
    - serum Na should not be increased > 8 in 24 hours
    - affects pons, brain due to sudden osmotic shifts
    - dx: MRI of the brain —> repeat MRI at later time
    - takes ~ 4 weeks for MRI to appear normal
- **Axonopathy**
    - Large nerve fiber injury = negative symptoms
    - Small nerve fiber injury = positive symptoms (allodynia, paresthesias)

Distal sensory peripheral neuropathy in diabetes mellitus		
	Large fiber neuropathy*	**Small fiber neuropathy***
Sensory function	• Pressure, proprioception & balance	• Pain & temperature
Major symptoms	• Numbness & poor balance	• Burning & stabbing pain
Examination findings	• Diminished/absent ankle reflexes • Reduced/absent vibration, light touch & proprioception	• Reduced pinprick sensation • Ankle reflexes possibly preserved

- **Pontine hemorrhage**
  - pinpoint pupils, CN V, VI, VII, VIII affected
  - bilateral paralysis
  - dysarthria
- **Cerebellar lesion**
  - Loss of balance, coordination
- **Wallenberg syndrome**
  - Lateral medullary syndrome
  - Ipsilateral vertebral artery pr PICA occlusion
    - Vertigo, nystagmus, diplopia, N/V
    - Loss of sensation of ipsilateral face
    - Contralateral loss of pain and temperature (pinprick)
- **<u>Definitions</u>**
  - **tremor**
    - **resting tremor**: uncontrolled movement of appendages, alleviated by intentional movement (occurs at rest, pill-rolling/ parkinson's @ rest)
    - **essential tremor**: high frequency tremor w/ sustained posture (outstretched hand), worse with movement, better with distraction
  - **dystonia**: sustained muscle contraction
  - **myoclonus**: sudden, brief uncontrolled muscle CXN, twitching is not rhythmic
  - **clonus:** rhythmic regular contraction of muscle or group of muscles
- **<u>Neuroanatomy</u>**
  - Broadmann's area 41&42 (superior temporal gyrus) —> lesion = B/L partial deafness
  - **Area 22** (around 41&42) —> auditory agnosia
    - left area 22= auditory verbal agnosia
    - right area 22= auditory nonverbal agnosia
  - **Broca's (nonfluent) aphasia**= can comprehend, cannot repeat, difficulty producing speech "telegraphic speech"
    - BROCA is BROKEN
    - How to test that?
      - Assess comprehension: which is bigger? Orange or grapefruit?
  - **wernicke's (fluent) aphasia**= cannot comprehend language with intact, nonsensical language production; cannot repeat

        - Wernicke is Wordy



    - **arcuate fasciculus**
        - per-sylvian area. Fluent speech, comprehension intact, cannot repeat.
    - **tactile agnosia**= lesions to R/L superior parietal lobe
        - cannot recognize objects felt through skin
        - astereognosis: cannot feel 3-D
    - **Visual agnosia**
        - impaired recognition of objects, intact visual and language
        - visual anosognosia= cortical blindness, confabulation, bilateral occipital cortex lesions
        - prosopagnosia: inability to recognize faces- can name or describe parts of a face
        - autoprosopagnosia: inability to recognize one's own face= lesion to right or bilateral lesions of lingual and fusiform gyri
    - **Anomia**
        - inability to name items in certain categories
    - **Alexia**
        - phonemes, morphemes and graphemes are elements of language that
        - alexia w/ agraphia: letter blindness
        - alexia w/o agraphia: word blindness "pure alexia", can read letters, letter-by-letter
    - **Apraxia**
        - Inability to perform purposeful movements
    - **gerstmann's syndrome**
        - R-L disorientation, acalculia, agraphia, finger agnosia, left angular gyrus lesion
- **Neuromuscular disorders**
    - **Myasthenia Gravis**
        - nicotinic **AChR Ab,** NMJ autoimmune disorder in women < 40yo, men > 50
        - type II hypersensitivity
        - associated with **thymoma**, thymic hyperplasia (chest mass)
        - fluctuating muscle weakness (worse at end of day); ptosis and diplopia, dysphagia, dysarthria, facial and prox muscle weakness, Kogan's twitch (look down then up)
        - Symptoms worse with repetitive use

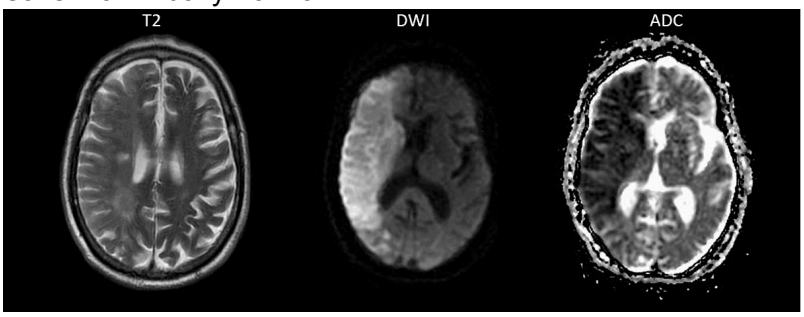
                - Fluctuating and fatigable weakness
                - Diplopia
                - Ptosis
                - Dysarthria, dysphagia
                - Respiratory insufficiency
            - Dx: #1 step is Ach Antibody test
                - ice-pack test (cold= improves)
                - edrophonium chloride (tensilon test) for ocular symptoms, AcheE inhibitor increases Ach in cleft
                - EMG: decremental decrease in the compound muscle action potential (CMAP)
                - CT: look for thymoma
                - dx: serum Ach receptor Ab —> follow up Tensilon/ edrophonium
            - Tx: 1st line is **AchE inhibitors** (**pyridostigmine**); chronic tx is corticosteroids' myasthenic crisis tx is IVIG, plasmapheresis; thymectomy= increased remission
                - myasthenic crisis: respiratory weakness due to MG → **plasmapheresis, Ig**
    - **Lambert-Eaton myasthenic syndrome (LEMS)**
        - presynaptic voltage-gated calcium channel —> decrease release of Ach
        - proximal muscle weakness improves with use, autonomic instability, associated with paraneoplastic syndrome (small cell lung cancer)
        - EMG: post-exercise increase in muscle action potential
        - Tx: chemotherapy
    - **Muscular dystrophy**
        - Calf pseudoatrophy
    - **Huntington disease**
        - CAG
    - **Myotonic dystrophy**
        - CTG
    - **Friedreich's ataxia**
        - GAA
    - **Statin-induced myopathy**
        - Necrotizing myopathy → non-specific muscle weakness after starting new statin drug
        - Bulbar and respiratory muscles rarely affected
        - Increases LDL receptors by inhibiting cholesterol formation
        - Elevated CK and liver enzymes, decrease CoQ10 synthesis → Check urine!
        - DDx: myopathy, rhabdomyolysis
        - Labs: CBC diff, BMP, LFT, Urinalysis, rune drug screen (check for renal damage or drugs causing myopathy)
        - Tx: stop simvastatin and gemfibrozil, drink fluids
- **Neurodegenerative**
    - **Huntington disease**: trinucleotide repeat, atrophy of caudate nuclei
        - Chorea, dystonia, slowed eye movements
        - Hyperreflexia, irritable, anxiety or paranoia
        - Disinhibition, depression
        - Loss of insight, memory loss, depression
        - Weight loss and cachexia
- **TRAUMATIC brain injury (**external force injures the brain)

- Brain trauma foundation (useful website/ resource for patients)
- post traumatic amnesia, LOC, HA, N/V
  - accelerating/ decelerating motion —> shearing forces to white axons, impaired neuron interconnection at junction of grey and white matter
- work up: noncontrast CT, perfusion (CPP)
- Glasgow coma scale:
  - E (eye) to Pain= 4
  - V (verbal) confused= 5
  - M (motor) localized= 6
    - lowest score is 3
    - best score is 15
    - mild TBI: 13-15
    - severe TBI: < 8 → intubate patient
- causes if TBI in kids (trauma), adults (MVA), geriatrics (falls)
- Tx: hemicraniectomy (increased risk of herniation/ stroke), CSF drainage (straw in 3rd ventricle)
- Blood pressure (SBP) kept above 100 to maintain perfusion pressure

- **Concussion**
  - loss of consciousness, headache, dazed
  - complete physical and cognitive rest for a couple days, individualized return to play until symptoms free
  - Due to neuronal functional disturbance
  - Tx: rest for a few days and gradually return to play
- **Anoxic brain injury**

	Brain death	Coma	Vegetative state	Minimally conscious state	Emergence from minimally conscious state
Eye opening	none	none	occasional	Occasional but inconsistent	present
Visual fixation or pursuit	none	none	none	Occasional but inconsistent	present
Spontaneous movement	none	none	nonpurposeful	present	purposeful
Response to noxious stimuli	none	none, flexion or extension	variable	variable	variable
Verbalization	none	none	none	Occasional but inconsistent	present
Functional communication	none	none	none	Occasional but inconsistent	consistent

  - **Brain death**
    - Loss of brainstem function: Lose corneal reflex, no pupillary reaction, respiratory effort, withdrawal from painful stimuli, no oculocephalic reflexes, no spontaneous respiration at $PaCO_2$= 60
    - DTRs persist (involve spinal cord)
    - Things that involve brain and brainstem stop
- **Stroke**
  - Risk factors: **HTN** >> Smoking
  - altered cerebral blood flow —-> acute focal neurologic deficits (ISCHEMIC > hemorrhagic)

        - modifiable risk factors vs non modifiable factors
            - **HTH**, DM, hyperlipidemia, prior stroke, MI, A fib.
                - > 140/90 increases risk of stroke
                - Decreased smoking, alcohol, low-fat diet
        - NIHSS stroke scale
    - Next steps: CT head w/o contrast
        - hemorrhagic= bright
        - ischemic= initially normal
        - 

    - **Pediatric stroke**
        - Non-localizing symptoms, HA, focal or generalized seizure and AMS (lethargy)
        - Dx: MRI with MR angiography
    - **Bell's Palsy**
        - **UMN lesion** → unilateral facial muscle paralysis (cannot blink, wrinkle forward, likely viral (HSV vs idiopathic)
            - tx: valacyclovir and glucocorticoids / prednisone
        - **CN VII LMN lesion/ brainstem** → unilateral facial paralysis W/ forehead sparing, loss of taste anterior ⅔ tongue
            - idiopathic facial nerve deficit
                - ptosis, loss of nasolabial fold, droop mouth, loss of tearing, hyperacusis, loss of taste on anterior ⅔ tongue
                - LMN lesion: involves forehead
                - UMN lesion: spares forehead (dual innervation)
            - commonly due to HSV1, sarcoidosis, lyme dz, etc.
            - r/o stroke, MS, myasthenia gravis
    - **Horner's syndrome**
        - Ptosis, miosis (blurry vision), anhidrosis
        - Carotid artery dissection, pancoast tumor, wallenberg syndrome
    - **Weber syndrome**
        - Unilateral weakness, ipsilateral ptosis and fixed dilated pupil
        - AICA infarct
    - **Facial colliculus**
        - lower motor neuron facial nerve palsy proximal to geniculate ganglion hence including loss of sensation of the taste in anterior two-thirds of the tongue and hyperacusis
        - diplopia
        - horizontal conjugate gaze palsy (including internuclear ophthalmoplegia)
    - **Lenticulostriate**
        - MOTOR ONLY defect
    - **Thalamic stroke**
        - Intracranial hemorrhage with thalamic hemorrhage → urine toxicology

        - COCAINE, young, no risk factors
- **Subarachnoid hemorrhage**
    - thunder-clap HA, aneurysm rupture
        - dx: CT w/o contrast, LP, 4 vessel angiography
        - tx: neurosurgery, coiling to stabilize aneurysm , BP management
        - Give nimodipine after aneurysm is clipper
    - Warfarin bleeding (FFP does work, but 4-factor PT complex concentrate (Factor II, VII-inactive, IX, X; protein S and C) works better and faster)
        - 4-factor complex: urgent reversal of acquired coagulation factor deficiency
        - IV vitamin K
- **Intracerebral hemorrhage**
    - diffusion restriction “all that glitters is not gold.”- Blood, abscess
    - most common cause: HTN
- **Subdural hematoma**
    - **accelerating/ decelerating trauma to subdural Bridging veins** —> crescent-shaped, concave hyperdensity
        - acute= hyperdense
        - subacute= isodense
        - chronic= hypodense
    - Presents as headache, personality change, seizures, confusion, hemiparesis
    - **Tx**: emergency neurosurgical emergency
- **Epidural hematoma**
    - head trauma to middle meningeal artery
    - LOC —> **lucid interval**
    - lens-shaped, biconvex hyperdense
- **Idiopathic intracranial hypertension**
    - Fat, fertile, females taking Vit A, OCPs or danazol
    - Holocephalic HA and blurry vision
- **Pituitary apoplexy**
    - Thunderclap headache, rapid-onset, hypotension, visual field defects, ophthalmoplegia
    - Papilledema
- **Ischemic stroke:**
    - ESUS
    - **TIA**
        - If presenting to the hospital give ASA, dipyridamole or clopidogrel
        - Carotid artery scan → endarterectomy if > 71%
    - **Carotid atherosclerosis**
        - Can lead to TIAs < 24 hours.
        - Risk factors: HTN, obesity, smoking, hypercholesterolemia
        - Dx: CT scan, carotid duplex sonography
        - tx: carotid endarterectomy, subclavian to carotid bypass
    - **subclavian steal:** arm requires more oxygen, vertebral artery steals blood from brain
    - tPa (tissue plasminogen activator)- hydrolyzes plasminogen to plasmin —-> fibrin degradation
        - use < 3-4.5 hours
        - BP < 185/ 110
        - contraindications
            - hx of stroke/ head trauma/ MI in 3 months

                - TIA in < 6 months
                - anticoagulation with INR > 1.7
                - prior intracranial hemorrhage
                - platelets < 100K
                - GI or GU bleed in < 21 days
                - Glucose < 50 or > 400
                - Seizures w/ stroke
            - complications: hemorrhage, rash (histamine release), angioedema; tx: methylprednisolone, ranitidine, fluid bolus
            - tx: cryoprecipitate > tranexamic acid
- **TIA (transient ischemic attack)**
    - History of smoking, poorly controlled diabetes, alcohol use
        - r/o migrain, seizure, hypoglycemia, tumor
    - Initial lab work: CBC and BMP
    - Initial imaging: CT/MRI brain
    - Additional labs/imaging: Lipids, HbA1c. Angiography/US, Echocardiogram, EKG
    - Tx: Carotid endarterectomy
    - Interventions: Smoking cessation, start atorvastatin, go on diabetic diet
- **Heat Stroke**
    - Hyperthermia, AMS, neurologic deficits
    - Tachycardia, hypotension, warm flushed skin
    - Rhabdomyolysis can occur, renal failure
- **Headache**
    - **Treatment:**
        - Acetazolamide, lumbar puncture, weight loss → pseudotumor cerebri
        - Carbamazepine → trigeminal neuralgia (side effects: hyponatremia)
        - Ergotamine → abort acute cluster HA after 100% O2
        - Glucocorticoids → temporal arteritis
        - Topiramate → migraine prophylaxis
        - Orbital massage → retinal artery occlusion
    - **cavernous sinus thrombosis**
        - Infection spreads from face to sinuses
        - Valveless ophthalmic venous system → proptosis and ophthalmoplegia
    - **Hypertensive headache**
        - HA, N/V
        - > 180/120
    - **Migraines**
        - POUNDS criteria: pulsatile, one day, unilateral nausea, debilitating
        - +/- aura, photophobia, phonophobia
        - Work up: CBC/BMP
        - Tx: Acetaminophen, Ibuprofen, propranolol (HTN headache), sumatriptan (abortive), venlafaxine
            - If it worsens → brain MRI, CBC and BMP → lifestyle modification, SNRI, topiramate
    - **Tension headache**
        - Last up to 1 week
        - Band-like pattern B/L
        - Dull, tight, persistent
        - Muscle tenderness in head, neck, shoulders
        - Tx: NSAIDs → prophylactic amitriptyline
    - **Cluster headache**

        - Young males with watery eyes, runny nose, pain behind the eye

	Types of headache		
	Migraine	**Cluster**	**Tension**
Sex predilection	Female > male	Male > female	Female > male
Family history	Often present	No	No
Onset	Variable	During sleep	Under stress
Location	Often unilateral	Behind one eye	Band-like pattern around the head (bilateral)
Character	Pulsatile & throbbing	Excruciating, sharp & steady	Dull, tight & persistent
Duration	4-72 hours	15-90 minutes	30 minutes to 7 days
Associated symptoms	Auras, photophobia, phonophobia & nausea	Sweating, facial flushing, nasal congestion, lacrimation & pupillary changes	Muscle tenderness in the head, neck, or shoulders

- **Syncope**
    - Abrupt and self-limited loss of consciousness
        - Acute global impairment of cerebral blood flow
        - Presyncope: dizzy, lightheadedness, weakness, visual/ auditory disturbances
        - Symptoms: pallor, sweating, hypotensive, altered, myoclonic jerking
        - Tx: treat underlying cause
    - Causes
        - Reflex syncope: vasovagal, stress/ emotional overtures, prolonged standing, severe pain, coughing, micturition/ defecation
            - Reciprocating factor, younger
            - Emotional stress → prodrome → PNS activation and cardioinhibitory response
            - Work-up: EKG → sinus bradycardia and cardiac arrest
        - Cardiogenic: chf, arrhythmia (V tach), orthostatic, bradycardia (too much CCB, BB), mechanical (aortic stenosis, HOCM), massive PE
            - Admission, Echo and ECG
            - FMHx of sudden cardiac death
        - Orthostatic: decreased flow, loss of vascular tone
            - Systolic drop > 2o, or diastolic drop > 10 on standing
            - Volume depletion (dehydration, CHF), autonomic dysfunction
            - Triggered by moving from sit to stand, many meds (nitrates, autonomic dysfunction, impaired baroreceptor sensitivity
        - Mimics: seizures, vertebrobasilar insufficiency, hypoglycemia, alcohol blackout, medication side effects, psychogenic pseudosyncope
        - **Narcolepsy**
            - Xs daytime sleepiness, cataplexy, hypnagogic hallucinations and sleep paralysis
            - Tx: modafinil (stimulant), sodium oxybate
    - Duration of LOC
        - > 5 min: meds, alcohol/ drug intox, concussion, narcolepsy
        - Seizures: tonic clonic movement, bowel/bladder incontinence, post-ictal

state
- **Febrile seizure**: young sick kids
- **Arrhythmic cause**s: sudden onset syncope in adults

Clues to etiology of syncope		
Reflex syncope	**Vasovagal**	• Trigger (eg, emotional stress, prolonged standing) • Prodrome (eg, nausea, sweating, warmth)
	Situational	• Occurs with micturition, defecation, swallow, or cough
	Carotid hypersensitivity	• Tactile stimulation of carotid sinus while standing • Advanced age, carotid atherosclerosis
Orthostatic syncope	**Medications**	• Vasodilators (eg, alpha-1 blockers, antihypertensives) • Inotropic/chronotropic blockade (eg, beta blockers)
	Hypovolemia	• History consistent with volume loss
	Autonomic dysfunction	• Advanced age • Predisposing disease (eg, DM, Parkinson)
Cardiac syncope	**LV outflow obstruction**	• Syncope with exertion • Systolic ejection murmur
	Ventricular tachycardia	• No warning symptoms • Cardiomyopathy or ischemic HD (monomorphic) • QT-interval prolongation (polymorphic)
	Conduction impairment*	• Preceding fatigue or light-headedness • ECG abnormalities (eg, sinus pauses, dropped QRS)

- **Real seizure vs. Psychogenic Seizure**

Distinguishing Seizures and Psychogenic Nonepileptic Seizures	
Seizure	**Psychogenic Nonepileptic Seizure**
Sudden onset	Gradual onset
Prodrome may consist of auditory, gustatory, olfactory, sensory, and/or visual aura	Prodrome may consist of behavioral, cognitive, and/or emotional changes
Eyes opened	Eyes closed
Ictal cry	Stuttering during event
Semiology follows physiological norms	Atypical movements such as hip thrusting, side-to-side head turning, and bicycling of legs
Rhythmic jerking of both sides of upper and/or lower extremities	Asynchronous jerking between left and right extremities
Typical seizure lasts < 2 minutes	Typical event lasts > 2 minutes

- **CNS infection**

Top Causes of Bacterial Meningitis in Pediatrics Based on Age	
Age	**Organisms**
Birth to 1 month (neonate)	• Group B *Streptococcus* • *Escherichia coli* • *Listeria monocytogenes*
1–3 months	• Group B *Streptococcus* • *Escherichia coli* • *Listeria monocytogenes* • *Streptococcus pneumoniae* • *Neisseria meningitidis*
3 months to 3 years	• ***Streptococcus pneumoniae*** • *Neisseria meningitidis* • Group B *Streptococcus* • *Escherichia coli*
3–10 years	• *Streptococcus pneumoniae* • *Neisseria meningitidis*
10+ years	• *Neisseria meningitidis*

-
    - **meningitis** (CSF infection)***fever, HA, increased ICP, photosensitivity, neck stiffness
        - acute= bacterial
            - increased protein, decreased glucose, increased **PMNs**/ Mono
            - neonate= listeria
            - kids= anything else
                - TB if went to other country
        - aseptic= viral (acute/ chronic)
            - nl/ decreased glucose, lower protein, increased **Lymphs**
        - cryptococcus
            - immunocompromised (cancer, HIV, transplant patients)
            - virchow-robins cleft
            - Normal MRI, high ICP and HA
            - Dx: crypto Ag on CSF
              Tx: amphotericin B and flucytosine, maintenance **fluconazole**

Meningitis			
Neonate	GNR + GBS Listeria	Ampicillin cefotaxime	Vaginal organisms common
1-23 mo	Strep pneumo N. meningitides Hib	Cefotaxime (ceftriaxone) + vancomycin	Hib less common due to vaccine
2-18y	N meningitides Strep pneumo Hib	Ampicillin + vancomycin +/- ceftriaxone	College kid= neisseria
19-59yo	Strep pneumo N. meningitides	Cefotaxime (ceftriaxone) + vancomycin	

	Hib		
60+	Strep pneumo Listeria GBS	Ampicillin + vancomycin + ceftriaxone	Listeria more common (that's why ampicillin is added)

- **encephalitis- myelitis** (bug infects cells)
  - polio= myelitis
  - HSV encephalitis= temporal lobe, tx: acyclovir
- **cerebritis/ abscess** (bacterial, fungal, parasitic)
  - One ring enhancing lesion= bacterial
  - Multiple ring enhancing= toxo

Brain abscess	
Microbiology	• *Staphylococcus aureus* • Viridans streptococci • Anaerobes
Pathogenesis	• Direct spread (eg, otitis media, mastoiditis, sinusitis) • Hematogenous spread (eg, endocarditis)
Clinical findings	• Headache, vomiting • Fever • Focal neurologic deficits, seizure • Ring-enhancing lesion on neuroimaging (CT, MRI)
Treatment	• Aspiration/surgical drainage • Prolonged antibiotic therapy

  -
- **Guillain barre syndrome**
  - Immune mediated demyelinating polyneuropathy, radicular shock-like sensations, bladder function/ ANS deficits
  - After URI or GI infection
  - Various neurologic deficits, normal MRI

- **Spinal Cord lesions**
  - **Cervical spine fracture**
    - tenderness of cervical spine, asymmetrical
    - deficits depend on level of lesion
      - 3, 4, 5 keeps the diaphragm alive
      - tx: spinal immobilization, ABCs
  - **Syringomyelia**
    - whiplash injury in MVA. months- years later, reduced motor and sensation "cape-like" due to cystic space in spinal cord
    - Loss of heat and cold sensation in hands B/L
    - Dx: PE and MRI
    - tx: steroids (acutely), self-resolves
  - **Cauda Equina syndrome**
    - Asymmetric multi radicular pain, leg weakness, bladder and rectal sphincter paralysis, sensory loss, unilateral saddle anesthesia, apraxic

gait

- **Conus medullaris**
  - Sphincter dysfunction, flaccid paralysis, importance, saddle anesthesia B/L
- **Guillain barre syndrome**
  - Inflammatory demyelinating polyneuropathy
  - Progressive ascending paralysis, AIDP, miller-fisher syndrome
  - Starts with sensory loss, eye muscles causing difficulty moving the eyes; impaired limb coordination and unsteadiness; and absent tendon reflexes.
  - Tx: IVIG/ plasmapheresis
- **CIPD**
  - https://step2.medbullets.com/neurology/120319/guillain-barre-syndrome
- **Transverse myelitis**
  - Progressive B/L motor and sensory deficits that occurred anywhere in spinal cord
  - T2 hyperintensity, spinal cord edema
  - Rapidly progressive myelopathy
  - Tx: IV glucocorticoids
    - Plasmapheresis if severe
    - Persistent deficits are common

- **Spinal cord compression**
  - Damage to nerve roots → UMN and LMN deficits
    - Lhermitte sign= **electric shock-like sensatio**n
    - malignant spinal cord compression is oncologic emergency —> urgent MRI
    - tumor compresses dural sac, associate with breast cancer
    - Progressively worsening back pain worse lying down
    - B/L lower extremity weakness
    - Work-up: if UMN symptoms cannot be explained, order **MRI** of spine
    - Tx: surgical decompression
    -

Spinal cord compression	
Causes	• Mechanical (eg, disc herniation, spinal stenosis) • Malignancy (eg, lung, breast, prostate cancers) • Infection (eg, epidural abscess)
Symptoms	• Gradually worsening, severe back pain • Pain worse in recumbent position/at night
Physical examination	• Early signs ◦ Symmetric extremity weakness ◦ ↓ Deep tendon reflexes • Late signs ◦ ↓ Rectal tone ◦ ↑ Deep tendon reflexes, bilateral Babinski reflex ◦ Paralysis
Management	• Emergency MRI of the spine • Emergency surgical ± radiation oncology consultation • Intravenous glucocorticoids (eg, malignancy) or antibiotics (eg, infection)

        - **Lumbar spine stenosis**
            - Low back pain + sensory loss/ weakness in LE
            - Worse with walking/ standing, alleviated with sitting
            - No UMN signs
    - **wallenberg syndrome**
    - **locked in syndrome**
    - **anterior cord syndrome**
        - ASA infarction —> weakness, P&T.
        - posterior columns spared.
    - **Brown sequard syndrome**
        - **ipsilateral weakness**
            - LMN @ level
            - UMN below level of lesion
        - **ipsilateral loss of MVP**
        - **contralateral loss of P&T** 1-2 levels below lesion
        - Findings of Brown-Sequard syndrome include:
            - Ipsilateral UMN signs below the level of the lesion (corticospinal tract)
            - Ipsilateral loss of vibration and proprioception below the level of lesion (dorsal column)
            - Contralateral loss of pain and temperature 2 levels below the level of the lesion (spinothalamic tract)
            - Ipsilateral loss of all sensation at the level of the lesion
            - Ipsilateral LMN signs (flaccid paralysis) at the level of the lesion
    - **Posterior cord syndrome**
        - tabes dorsalis, Friedreich ataxia, subacute combined degeneration
            - loss of MVP due to syphilis
    - **Conus medullaris**
        - sphincter dysfunction, flaccid paralysis of bladder/ rectum, B/L saddle anesthesia S3-5
    - **Cauda equina syndrome**
        - asymmetric multi radicular pain, leg weakness, bladder/ sphincter paralysis, sensory loss, unilateral saddle anesthesia
    - **spinal cord injury**
        - Reflexes are the key: HYPERreflexia
- **Tremor**
    - Psychogenic tremor: abrupt onset, changing characteristics, extinction with distraction
- **BPPV**:
    - posterior semicircular canal dislodgement of otolith
    - episodic vertigo and nystagmus triggered by changing head position in space (sit to stand; left to right), lasts < 1 minute
    - NO HEADACHE (r/o stroke)
    - dix-hallpike maneuver: upright to supine with head turned at 45 degrees and neck extended 20 degrees with affected ear down.
    - torsional, upbeating nystagmus with vertigo
    - Test of skew
    - epley maneuver: treatment for BPPV, extended version of Dix-Hallpike

- **Vertigo**

Common causes of vertigo	
Ménière disease	• Recurrent episodes lasting 20 minutes to several hours • Sensorineural **hearing loss** • **Tinnitus** &/or feeling of fullness in the ear
BPPV	• Brief episodes triggered by **head movement** • Dix-Hallpike maneuver causes nystagmus
Vestibular neuritis	• Acute, **single episode** that can last days • Often follows viral syndrome • Abnormal head thrust test
Migraine	• Vertigo associated with headache or other migrainous phenomenon (eg, visual aura) • Symptoms resolve completely between episodes
Brainstem/ cerebellar stroke	• Sudden-onset, persistent vertigo • Usually other neurologic symptoms

- **Acute onset dizziness**
  - stroke/ hemorrhage to cerebellum
  - **Central vertigo**
    - Nystagmus is not fatigable, not inhibited by fixation of gaze
    - Next step: CT w/o contrast
  - Peripheral vertigo
    - BPPV
    - Meniere disease
    - Vestibular neuritis

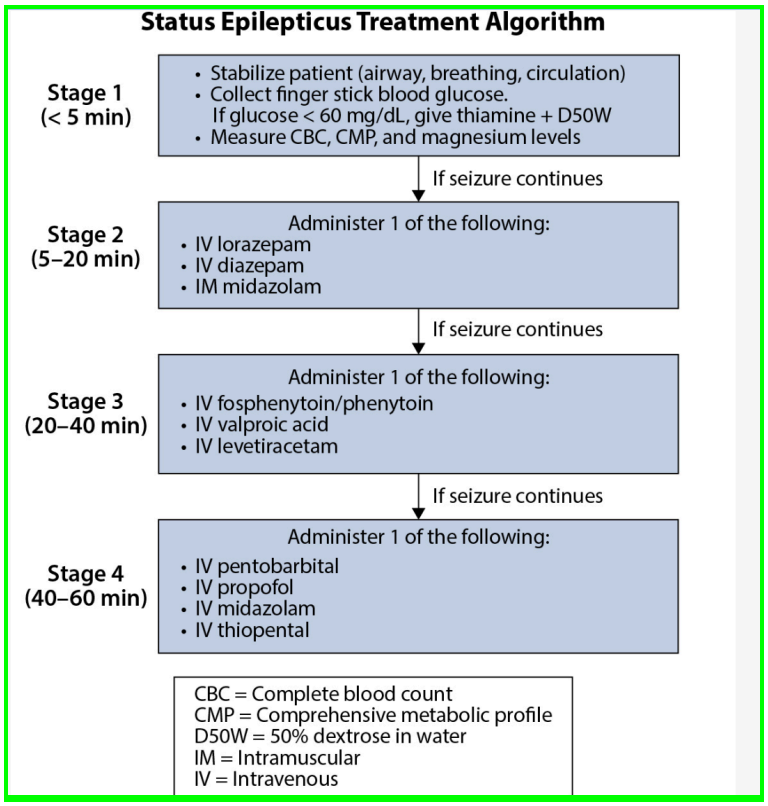
- **Neuro-metabolic syndromes**
  - **Acute intermittent porphyria**
    - Disorder of heme synthesis pathway → reduced porphobilinogen deaminase
    - Young patient with Attacks of abdominal pain, neuropathy and proximal muscle weakness, neuropsych manifestations, autonomic dysfunction
    - Normal labs, but urobilinogen is elevated in blood in urine
    - Red tinged urine that darkens when exposed to air or light
  - **Lead poisoning**
    - Abdominal pain and neuropsych in patient with history exposure to lead paint
    - ALA dehydrogenase → incomplete heme synthesis → basophilic stippling
    - In adults (battery factory)
      - Occupational exposure
      - GI: abdominal pain, constipation, anorexia
      - Neurologic: cognitive defect, peripheral neuropathy
      - Hematologic: anemia (microscytic?)
      - Elevated serum zinc protoporhyrin
  - **B12 deficiency**
    - elevated homocysteine (B12 and folate deficiency)
  - **Diabetic polyneuropathy**
    - B/L symmetrical sensory loss

        - DTR are diminished or absent
- **Altered mental status**
    - **Acute encephalopathy:** rapid AMS in < 4 weeks
        - check CBC, CMP, Glucose, Meds
        - Stroke
    - **Delirium**:
        - acute confusional state, fluctuates. Hallucinations
        - Acute onset of cognitive impairment and altered consciousness
        - Caused by meds (opioids, benzo), surgery, trauma, fluid/ electrolyte disturbances
            - Substance induced psychotic disorder r/o if it occurs during delirium
        - Tx: haloperidol
            - Modify environment to be more calming, sleep hygiene, avoid restraints

Characteristics of Delirium vs Dementia

	Delirium	**Dementia**
Onset	Acute	Insidious
Consciousness	Fluctuating	Generally preserved in early stages
Prognosis	Reversible if treated early	Progressive decline
Common causes	Multifactorial, medication induced, infection, physiologic derangements, substance withdrawal, central nervous system lesion	Neurodegenerative, vascular, infection, traumatic brain injury, alcoholism

- **Seizures**
    - **Cataplexy**
        - Sudden loss of muscle tone, brief paralysis
        - Strong emotion, consciousness is maintained
    - **petite mal**
    - **status epilepticus**
        - > 5 minutes of continuous seizures or > 2 seizures without complete recovery of consciousness
        - tx:IV lorazepam x2—> repeat dose in 3-5 minutes
        - after 2 doses of lorazepam —> try phenytoin, fosphenytoin, valproic acid, levetiracetam → phenobarbital, propofol → infusion of midazolam



- Absence
- Myoclonic
  - Focal
  - Generalized
- **Generalized Tonic clonic**
  - Abrupt loss of consciousness → stiff muscles through body, rhythmic jerking of extremities
  - Eyes open during ictal state, postictal confusion
- **Psychogenic seizures/ functional seizures (PNES)**
  - Psych/ PTSD → Brain → physical manifestation
  - take arm and drop it over face, they will stop it, “shakes”, forced eye closure, side to side head or body movements, lack of postictal state/ confusion
  - Conversion disorder
- Epilepsy
  - Electrical discharge → Brain → physical manifestation
- Juvenile epilepsy
  - An EEG reveals intermittent, bilateral polyspike and wave discharges consistent with a diagnosis of juvenile myoclonic epilepsy. The most appropriate antiseizure medication to initiate is
  - Juvenile myoclonic epilepsy is typically associated with myoclonic, absence, and generalized tonic-clonic seizures. The first-line treatment, unless contraindicated, is valproic acid.

Childhood Epilepsy Syndromes			
Syndrome	**Age at Onset (Years)**	**Semiology**	**First-Line Therapy**
Infantile spasms	0–1	Brief spasms either of the whole body or just the arms and legs	Corticotropin (ACTH)
Lennox-Gastaux syndrome	3–5	Multiple seizure types	Valproic acid
BECTS	3–10	Drooling and hemifacial clonic seizures (typically at night)	N/A
Absence	4–10	Unresponsiveness and amnestic symptoms, usually lasting a few seconds	Ethosuximide
Panyotopolous syndrome	7–9	Autonomic seizures (such as those leading to emesis), typically followed by GTC seizures	Levetiracetam (if treatment is required)
Juvenile myoclonic epilepsy	12–18	Absence, GTC, and myoclonic seizures	**Valproic acid**
ACTH = adrenocorticotropic hormone; BECTS = benign epilepsy with centrotemporal spikes; GTC = generalized tonic-clonic; N/A = not applicable.			

- **Neuropathology**
    - Congenital disorders of glycosylation
        - **Carbohydrate-deficient GP syndromes**
            - Neonatal hypotonia, Failure to thrive, stroke-like episodes
                - Cerebellar atrophy, liver cirrhosis
                - Hepatic steatosis, pontocerebellar atrophy, demyelination
        - Walker-walburg syndrome
            - Elevated CK, altered alpha-dystroglycan
    - Cerebral hypoxia
        - Pyknosis, red neurons
    - Paraneoplastic encephalitis syndromes

Paraneoplastic Encephalitis Syndromes		
Syndrome	**Manifestations**	**Associated Tumors**
Brainstem encephalitis	• Deafness • Dysarthria • Dysphagia • Hypoventilation • Opsoclonus (rhythmic, conjugate saccades) • Nystagmus • Vertigo	• Hodgkin lymphoma • Small-cell lung cancer • Teratoma • Testicular cancer • Thymoma
Encephalomyelitis	• Ataxia • Autonomic dysregulation • Sensory neuronopathy	• Small-cell lung cancer
Limbic encephalitis	• Memory deficits • Psychiatric disturbances • Seizures	• Hodgkin lymphoma • Small-cell lung cancer • Teratoma • Testicular cancer • Thymoma
Opsoclonus-myoclonus	• Children • Cognitive defects • Myoclonus • Opsoclonus • Truncal ataxia	• Neuroblastoma (children) • Small-cell lung cancer • Breast cancer • Ovarian cancer
Stiff-person	• Rigidity • Spasms • Worsened by stimuli	• Breast cancer • Small-cell lung cancer

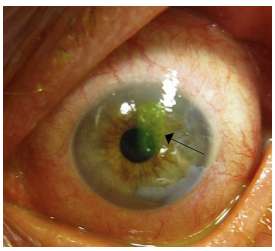
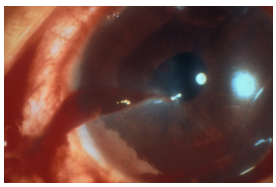
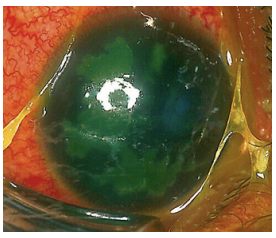
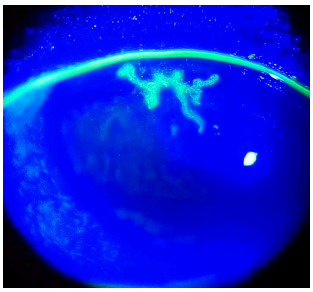
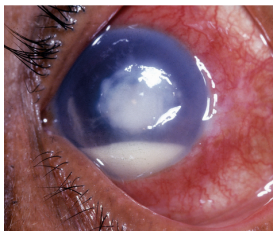
- **Ophthalmology**
  - **Next steps**
    - **Emergent optho consult** → ulcer, anterior chamber pyema, globe rupture
    - **Acetazolamide** → glaucoma
    - Work up for malignancy → ocular mucocutaneous membrane blisters
    - **Abx eye drops** → corneal abrasion

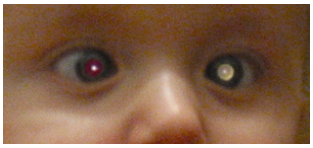
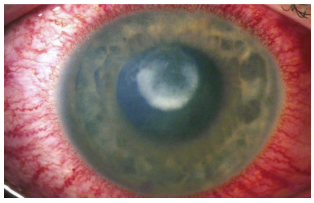
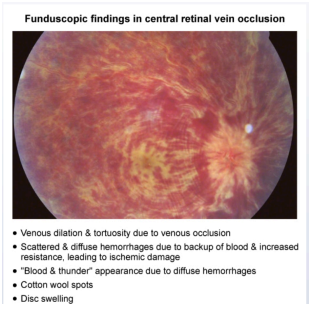
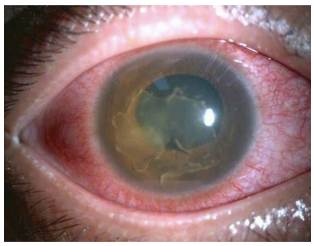
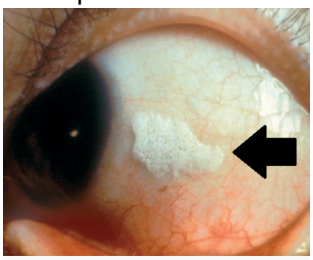
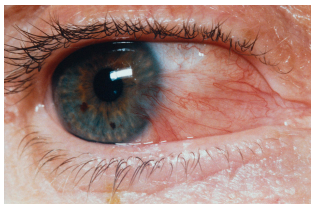
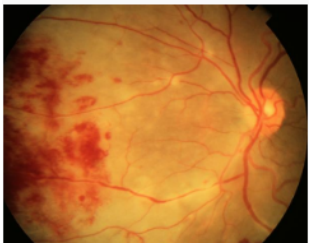
Commonly Tested Differential Diagnosis of Eye Pain					
Conjunctivitis	**Scleritis**	**Keratitis**	**Dry Eye**	**Acute Angle-Closure Glaucoma**	**Uveitis**
- Red eye - Bacterial: associated with purulent discharge, acute presentation - Viral: associated with watery discharge - Pain is usually quite mild	- Red eye - Severe, boring pain - Worse with movement - Decreased visual acuity - Associated with rheumatologic disease	- Red eye - Discharge - Photophobia - Decreased visual acuity	- Burning - Dry, foreign body sensation - Excess tearing - Usually bilateral and chronic	- Headache - Nausea and vomiting - Ciliary flush sign - Fixed mydriasis - Shallow anterior chamber	- Photophobia - Miosis - Ciliary flush sign - Hypopyon

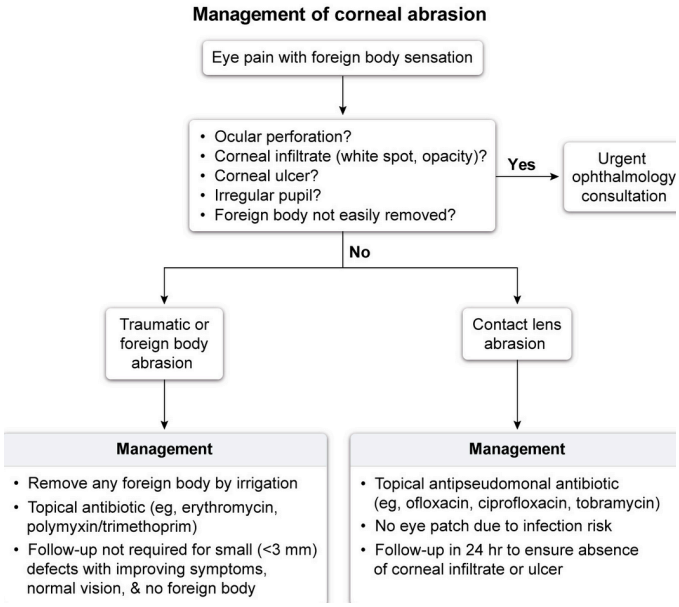
- **Papilledema**
  - Enlarged physiologic blind spot
  - Transient vision loss with head positioning
- **Acute angle-closure glaucoma:** emergency
  - Tonometry → Increased IOP, can manifest with abdominal pain & OMM dysfunction. Nonreactive and mild dilated pupil, redness and opacification
  - Occurs after cycloplegic drops → increased IOP, corneal hazing, N/V
  - Increased cupping (cup/disc ratio), increased IOP, Insidious onset and slow progression
  - Triggered by pupillary dilation (low ambient light), decongestants, anticholinergics
  - Tx: ACETAZOLAMIDE
  - URGENT OPHTHO= ACUTE…fluid cant get out
- **Open angle glaucoma**
  - Elevated IOP, cupping, loss of **peripheral vision → loss of retinal nerve layer**
  - Triggered by glucocorticoid drops (tx for uveitis)--> vision loss, worsened glares
  - Complains of blurry vision and glare with night time driving
  - Dx: tonometry
  - Tx: topical agents (PROSTAGLANDIN, bimatoprost) to decrease volume and pressure of aqueous humor, increase drainage of aqueous humor through uveoscleral pathway. → beta blocker (timolol)- avoid in comorbid asthma
  - CHRONIC= OPEN
- **Afferent pupillary defect**
  - Tx: CT orbits
- **Retinal detachment**
  - DM, trauma, degeneration
  - Vision loss, photopsia, floaters
  - Elevated retina with folds/ tear
- **Diabetic retinopathy**
  - Asymptomatic

        - Proliferative DR occurs with vitreous hemorrhage
    - **Vitreous hemorrhage**
        - DM with sudden onset vision loss, floaters, hemorrhage
    - **Central retinal vein occlusion**
        - Painless vision loss
        - HTN
        - Disk swelling, venous dilation, cotton wool spots, retinal hemorrhage
        - “Blood and thunder”
    - **Amaurosis fugax**
        - Atheroemboli from carotid arteries → vision loss like a curtain coming down
    - **Optic neuritis**
        - Acute, monocular vision loss and pain with EOM, optic disc edema. Young women with MS
        - Immune-mediated demyelination of optic nerve → RAPD
    - **Bitemporal hemianopsia**
        - Mass effect on optic chiasm → peripheral loss of vision
    - **Hypertensive retinopathy**
        - Blurred vision, AV nicking, copper wiring, flame hemorrhage, cotton wool spots, optic disc edema
        - Hypertensive and diabetic retinopathy can have similar fundoscopic findings. Hypertensive retinopathy causes <u>arteriovenous nicking and copper wiring.</u>
          Diabetic retinopathy can cause <u>neovascularization</u>.
    - **Nonarteritic anterior ischemic optic neuropathy**
        - Ischemia in optic nerve head → painless monocular vision loss
        - Optic disc edema and RAPD
    - **infectious conjunctivitis**: mucopurulent drainage from eye
        - Photophobia= infectious keratitis or iritis
    - Viral conjunctivitis
        - Similar to bacterial (caused by adenovirus)
        - Purulent discharge that is stuck on eyelashes
        - Mucoid discharge
        - Always see
        - edema, inflammation of tarsal conjunctiva, follicular appearance
        - Allergic shiners
    - **Blepharitis**:
        - chronic inflammation of eyelid margins due to blockage of follicles
        - meibomian gland dysfunction; r/o sjogren's syndrome, preseptal cellulitis, conjunctivitis
        - Tx: lid hygiene with warm compress and mild shampoo; topical Abx if more severe
    - **subconjunctival hemorrhage**: blood under conjunctiva
    - **Cavernous sinus thrombosis**
        - Life-threatening
        - Fever, HA, periorbital edema, lid erythema, chemosis, painful eye movements
    - **Acute ethmoiditis**
        - MOST COMMON rhinosinusitis → periorbital/ orbital cellulitis
        - Facial pain
    - **Sympathetic ophthalmia**

        - Ocular trauma → autoimmune response by T cell sensitization to self-antigens
        - Type 4 delayed hypersensitivity → decreased visual acuity, conjunctival erythema
        - Can also be seen in testicles → autoimmune orchitis (isolated immune system)
    - **Keratitis**
        - Infectious: pseudomonas/ Staph & contact lenses
            - Tx: moxifloxacin
    - **Episcleritis**
        - Common cause of red eye
        - Seen with RA, autoimmune
        - Self limited
    - **Bacterial endophthalmitis**
        - Infection of aqueous humor
        - Eye discomfort, blurry, hypopyon
        - Post-operative cataract surgery
- **Corneal injury**

Corneal abrasion Fluorescein staining → abx (esp if wears contact lenses, erythromycin ointment or amoxicillin drops)	Corneal laceration Erythromycin eye drops	HSV *immunosuppressed/cancer patients	Hypopyon
		 	
Leukocoria	Bacterial keratitis	Central retinal vein occlusion	Anterior uveitis

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<td>
U/L- retinoblastoma
B/L- congenital rubella syndrome</td>
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<tr>
<td>Vitamin A deficiency</td>
<td>pterygium</td>
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<td>Bitot spot
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tx: ganciclovir</td>
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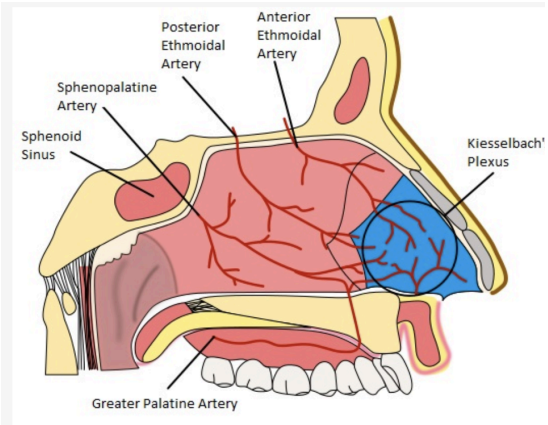
- **Argyll robinson**
  - accommodates but does not react
  - adie's pupil, parinaud, dementias
- **Lens dislocation**
  - Acute vision loss after trauma
  - No RAPD present
- **Internuclear ophthalmoplegia**
  - Disorder of conjugate horizontal gaze

        - Damage to medial longitudinal fasciculus
            - Unilateral lesions: lacunar stroke, pontine artery
            - B/L: MS
    - **Edinger-Westphal nucleus**
        - Ipsilateral fixed, dilated pupil nonreactive to light or accommodation
    - **Paramedian pontine reticular formation (PPRF)**
        - Lesion results in conjugate movement of both eyes away from side of lesion
        - Left lesion= right gaze deviation
    - **Medial longitudinal fasciculus (MLF)**
        - Communication bw right abducens nerve nucleus and left oculomotor nerve nucleus
        - Ipsilateral impaired adduction during movement to contralateral side
    - **Age-related macular degeneration**
        - Dry AMD= drusen
        - Wet AMD= subretinal fluid and hemorrhage
    - **Retinal detachment**
        - Separation bw neurosensory and retinal pigment epithelium
        - Full-thickness retinal tear or hole
        - Seen in older age, associated with myopia & cataract surgery
        - Black curtain falling over vision
    - **Retinal vein occlusion**
        - Sudden onset painless loss of vision
        - Thrombus formation
        - Scattered retinal hemorrhage
    - **Vitreous hemorrhage**
        - Floaters, decreased visual acuity
        - Hemorrhage with obscuration of fundal details
    - **Orbital vs periorbital cellulitis**

Periorbital vs Orbital Cellulitis		
Characteristics	**Periorbital Cellulitis**	**Orbital Cellulitis**
Eyelid swelling +/- erythema	Present	Present
Eye pain/tenderness	+/-	Present
Painful eye movement	Absent	Present
Proptosis	Absent	Likely present
Vision impairment	Absent	May be present
Chemosis (edema of conjunctiva)	Absent	May be present
Fever or leukocytosis	+/-	May be present

- **Imaging/ testing**
    - CT w/o contrast = best for blood (bright); dark= ischemia
        - hypoattenuating brain tissue= irreversible brain damage
    - MRI= most sensitive
    - EMG
        - Action potentials with muscle contraction

- ENT
  - **Nose bleed**
    - **anterior= Keisselbach**
    - **posterior= sphenopalatine**
  - **Gingival abscess**
    - Treatment → amox/clav
  - **Chronic rhinosinusitis and nasal polyposis**
    - Tx: intranasal saline → intranasal corticosteroids → oral corticosteroids → Abx/ sinus surgery, biologics, montelukast
  - **Patulous dysfunction**
    - Eustachian tube dysfunction during exercise → autophony (amplified voice and breathing)
      - Tx: nasal saline
  - Nose bleeds
    - Anterior= Kiesselbach plexus
    - Posterior= sphenopalatine artery
  - Nasal polyposis
    - Next step: intranasal corticosteroids and saline (treating allergies) → surgical resection if it does not shrink/go away



Epistaxis	Anterior	Posterior
Common source	Kiesselbach plexus	**Sphenopalatine artery**
Common causes	Trauma, dry air, rhinitis, foreign bodies	Typically spontaneous causes such as anticoagulant use, atherosclerosis, or bleeding disorders
Typical age range	Children and young adults	> 40 years of age
Examination findings	A bleeding site may be found on examination of the nasal vestibule or use of a nasal speculum	No bleeding site may be seen on examination of the nasal cavity
Severity and treatment	Typically mild bleeding can be stopped with the use of a topical vasoconstrictor, packing, or pressure	Higher likelihood of more significant bleeding; treatment involves posterior packing or use of balloon/foley catheter to achieve tamponade; urgent ENT evaluation and hospitalization should be considered

- EARS
  - **Next steps:**
    - **Audiogram**: evaluate hearing loss
    - **Flexible laryngopharyngoscopy**: malignancy that refers to ear pain
    - **MR brain:** acoustic neuroma
    - **Tympanometry**: eustachian tube dysfunction
    - **Tympanostomy** tube placement: recurrent otitis media
    - Weber lateralizes to conductive hearing loss
    - Rinne louder on bone with conductive hearing loss

Interpretation of Rinne & Weber tests		
	Rinne result	**Weber result**
Normal	AC > BC in **both** ears	Midline
Conductive hearing loss	BC > AC in **affected** ear, AC > BC in **unaffected** ear	Lateralizes to **affected** ear
Sensorineural hearing loss	AC > BC in **both** ears	Lateralizes to **unaffected** ear, **away** from affected ear
Mixed hearing loss	BC > AC in **affected** ear, AC > BC in **unaffected** ear	Lateralizes to **unaffected** ear, **away** from affected ear

    - **Weber:** lateralizes to good ear; **Rinne**: AC> BC in normal ear
- **Cerumen impaction**
    - Reversible conductive hearing loss
- **Cholesteatoma**
    - Epithelialized expansive lesion in temporal bone, occur from ™ injury
    - Unilateral conductive hearing loss (rinne lateralizes to affected ear)
- **Osteosclerosis**
    - Young people
    - B/L Conductive hearing loss when inner ear bones are sclerosed
    - Rinne negative in both ears. Weber lateralizes to the ear with the greatest hearing loss
- **Presbycusis**
    - Old patient with gradual sensorineural hearing loss
    - Degeneration of organ or corti
- **Acute mastoiditis**
    - Tenderness posterior to ear can spread to brain
- **Acute otitis media**
    - Kids, viral or bacterial
    - **SMOKE exposure**
    - Ear pain, fever, red ™, pus or middle ear infection
    - Tx: start with oral amoxicillin → amoxicillin/ clavulanic acid
    - If recurrent, add a pneumococcal polysaccharide vaccine
    - Tympanocentesis: AOM with failed Abx, immunocompromised, septic
- **Chronic otitis media**
    - Retrotympanic effusion
- **Fungal otitis media**
    - Common AFTER tx of acute otitis externa
    - Hearing aids, warm humid climates
    - Tx: debridement, topical azoles, oral fluconazole
- **Otitis externa/ swimmer's ear**
    - Mild external ear pain, watery discharge, swelling, redness
    - Due to trauma, foreign material, dermatologic conditions
    - Micro: PSEUDOMONAS or STAPH AUREUS (fluoroquinolones- floxacin)
    - Tx: clean ear, acidify canal, ear drops of fluoroquinolone
        - TMP-SMX and clindamycin empiric tx
        - ciprofloxacin/ hydrocortisone
- **Necrotizing otitis externa**
    - Pseudomonas or enterobacter
    - Poorly controlled DM, immunocompromised

        - Purulent discharge, granulation tissue
        - Tx: IV Abx
    - **Herpes zoster oticus/ ramsay hunt syndrome**
        - Severe ear pain, ipsilateral facial paralysis, vesicular rash in EAC
    - **Barotrauma**
        - Rupture of tympanic membrane (in setting of upper respiratory tract infection)--> persistent hearing loss
        - Tx: reassurance (heals on own)
        - Prevention: oxymetazoline
    - **Meniere disease**
        - Episodic vertigo, tinnitus, sensorineural hearing loss
        - Tx: restrict sodium, coffee, nicotine, alcohol, acetazolamide
    - **Sensorineural hearing loss**
        - Weber lateralizes to unaffected ear
        - Causes: **acoustic neuroma, loss of cochlear hair cells**
        - Older age
    - **Conductive hearing loss**
        - Otosclerosis, abnormal bone deposition
        - Younger patients
        - Improved speech understanding in background noise
    - **Osteosclerosis**
        - conductive hearing loss
            - Weber test lateralizes to affected ear
            - Rinne negative
    - **Labyrinthitis**
        - Vertigo, hearing loss, tinnitus for a few days- weeks
        - Tx: meclizine (antihistamine used to treat n/v and vertigo)
    - **Vestibular neuritis**
        - URI → Inflammation of CNVIII, vertigo for days, normal hearing
        - Tx: meclizine
    - **Ramsay Hunt syndrome**
        - HSV, shingles rash, ear pain, hearing loss, tinnitus, vertigo may occur
        - Tx: acyclovir
    - **Vestibular schwannoma**
        - Persistent and progressive imbalance and tinnitus, facial numbness due to CN V & VII compression
        - Usually unilateral, seen in 50 yo
        - MRI of internal auditory canal
        - Dx: audiogram, MRI
        - Tx: observation if small, surgery, radiation

Common causes of vertigo	
Ménière disease	• Recurrent episodes lasting 20 minutes to several hours • Sensorineural **hearing loss** • **Tinnitus** &/or feeling of fullness in the ear
BPPV	• Brief episodes triggered by **head movement** • Dix-Hallpike maneuver causes nystagmus
Vestibular neuritis	• Acute, **single episode** that can last days • Often follows viral syndrome • Abnormal head thrust test
Migraine	• Vertigo associated with headache or other migrainous phenomenon (eg, visual aura) • Symptoms resolve completely between episodes
Brainstem/ cerebellar stroke	• Sudden-onset, persistent vertigo • Usually other neurologic symptoms

Oncology

- Ovarian mass (not generally biopsied)
  - Simple cyst →
    - > 1 cm = follow up
    - > 7 cm = MRI or surgical evaluation
  - Complex cyst (thick septa)/ metastases/omental caking
    - Gyn-onc referral
- Rectal cancer
  - Chemo and radiation (nigro criteria) → SCC
  - Low anterior resection → upper-med ⅓ of rectum

Cardiovascular

- **Emma Holliday**
  - First time chest pain → ECG
  - Dyspnea, JVD and pitting edema= **cor pulmonale**
  - hypotension, muffled heart sounds, elevated JVD (Becks triad)= **cardiac tamponade**
  - Extra heart sound= **S3 (HTN), S4 (dilated cardiomyopathy)**
    - Patient with chest pain?
    - Best first test: # 1 EKG → troponins
      - **STEMI**= no enzymes needed. 1 mm ST elevation in > 2 leads, new LBBB with chest pain → straight to cath lab
      - **NSTEMI**= serial troponins and serial EKGs to see if evolving/ changing
        - Tx: ASA +PGY12 blocker (clopidogrel)- early on 24 hours
        - Heparin - 48 hours
        - Outpatient: beta blockers, statins, ACE/ ARBs, aldosterone antagonists
    - Work up: stress test (physically or chemically w/ dobutamine or adenosine) or MUGA

- If normal with daily activities, no further work up needed.
- STEMI → T wave inversion → Q waves old infarct
- Thrombolytics < 6 hours
  - Contraindicated: hemorrhagic stroke, recent ischemic stroke, recent head trauma
- Right ventricular infarct → give fluid to increase preload, nitro is Bad.

■ Rule out acute coronary syndrome: Unstable angina, NSTEMI, STEMI

■ **Post-MI**

- Common cause of death: arrhythmia, V fib
- New systolic murmur w/in (2-3 days - 1 week): **papillary muscle rupture****
- Acute severe hypotension/ shock, higher O2 in right heart: **ventricular free wall rupture**
- Persistent ST elevation: ventricular wall aneurysm
- Cannon A waves (JVP): AV dissociation in V fib or 3rd degree heart block
- 2-10 weeks later pleuritic pain: Dressler syndrome, tx ASA

■ Heart failure exacerbation → give **diuretics** (metoprolol can worsen, use later to improve mortality)

■ Egg on a string= transposition of great arteries

■ Boot shaped heart= tetralogy of fallot

■ Diabetic pregnancy with cyanotic newborn= D transposition of great arteries

■ **Prolonged QT: TCA, antibiotics, haloperidol**

○ **Treatment**

■ Atorvastatin → high intensity statin for cardiovascular disease, also use rosuvastatin

■ Adenosine → AV nodal reentrant tachycardia

■ Amiodarone → A fib and monomorphic ventricular tachycardia

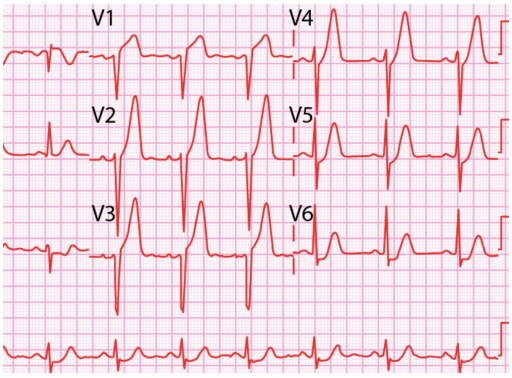
■ Anticoagulation → A fibrillation, heparin infusion to decrease risk of thromboembolism

■ Beta blockers → improved mortality

■ Metoprolol → rate control

■ IV magnesium sulfate → torsade de pointes

■ **Calcium gluconate** → sinusoidal pattern and hypocalemia (not eating/ drinking), HYPERKALEMIA (no matter what the history is)

- 

■ Cardioversion → acute conversion

■ CABG→ 3 vessel disease, proximal LAD disease

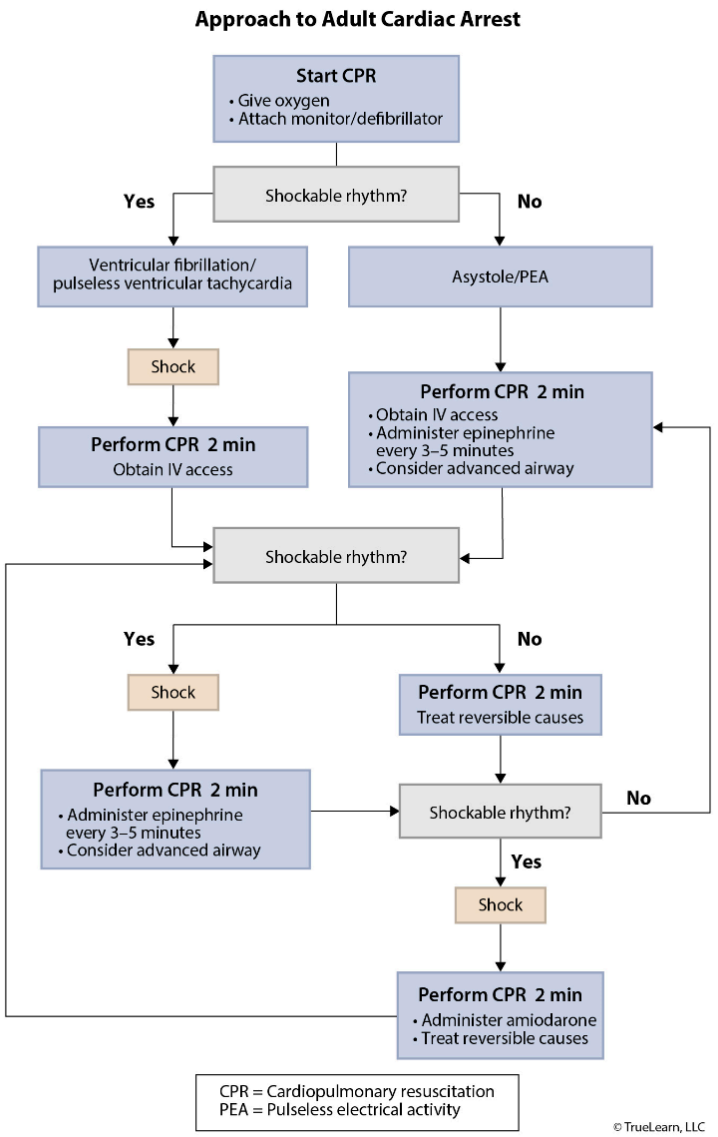
■ Carotid sinus massage → slow SVT

- Cardiac percutaneous pacing → 3rd degree heart block
- Clopidogrel → secondary prevention of stroke if ASA, claudication
- Direct current countershock → synchronized cardioversion and non-synchronized. Used in unstable tachyarrhythmia
- Flecainide → prevent recurrence of AVNRT
- IV Labetalol → Aortic dissection type B (after ligamentum arteriosum)
- Emergent cardiothoracic surgery → type A aortic dissection
- TPA → treats ischemic stroke
- Verapamil → SVT, A fib and A flutter
- Verapamil/Diltiazem → variant angina in young guy with coronary vasospasm
- Propafenone → wolff-parkinson white syndrome
- Propranolol → long QT syndrome
- **Pericardiocentesis** → pericardial effusion, cardiac tamponade!
- External pacing → refractory or unstable bradycardia
- Normal saline bolus → hypotensive shock
- Radiofrequency ablation → treats types of tachyarrhythmias, AVRT, WPW
- SA/ AV blocking meds (ABCD)= adenosine, beta blockers, CCB, digoxin
- Synchronized cardioversion → paroxysmal SVT (narrow regular QRS, tachycardia, buried P waves)
- Carotid sinus massage → unstable patients with paroxysmal SVT

Sinoatrial/Atrioventricular Nodal Blocking Medications (Memory Aid: ABCD)

Medication	Examples	Notes
Adenosine	NA	Half life of only 10 seconds. Used to abort supraventricular tachycardia and used in pharmacologic stress tests.
Beta blockers	Metoprolol, carvedilol, labetalol, propranolol, atenolol, bisoprolol, esmolol	Beta 1 specific medications have stronger heart rate affect (eg., metoprolol)
Calcium channel blockers	Nondihydropyridine only: verapamil and diltiazem	Dihydropyridines affect blood pressure, but not heart rate.
Digoxin	NA	Used for atrial fibrillation in the setting of heart failure with reduced ejection fraction.

Condition	Treatment Choice
Angina pectoris	Beta blocker or a calcium-channel blocker
Atrial fibrillation or flutter with uncontrolled rates	Beta blocker or nondihydropyridine calcium-channel blocker
Benign prostatic hyperplasia	Alpha blocker
Chronic kidney disease	ACE inhibitor or ARB
Diabetes mellitus	ACE inhibitor or ARB
Essential tremor	Beta blocker (non-cardio-selective)
Heart failure with reduced ejection fraction	ACE inhibitor or ARB or beta blocker or diuretic or aldosterone antagonist
Migraine	Beta blocker or calcium-channel blocker
Osteoporosis	Thiazide diuretic
Postmyocardial infarction	ACE inhibitor or ARB or beta blocker or aldosterone antagonist
Pregnancy	Beta blocker or calcium-channel blocker or methyldopa
Raynaud phenomenon	Dihydropyridine calcium-channel blocker



- **Next best step**
  - **Carotid endarterectomy:** >70% with TIA
  - **Carotid artery angioplasty:** symptomatic carotid stenosis w/ CHF or pulmonary disease
  - **EKG**: chest pain that hasn't been worked up
  - **ECHO**: murmur on auscultation, cardiac morphology, motion, ejection fraction, valvular function
  - **Transthoracic Echo (TTE)**: also dx valvular vegetations, thrombus, **best initial (least invasive)**
  - **TEE**: best to see infective endocarditis (plaques on valve and staph + culture), better sensitivity/ specificity, or aortic dissection, PFO, heart anomalies
  - **Stress test:** chest pain/ SOB with exertion, coronary artery disease
  - **Ambulatory ECG monitoring**: syncope, heart failure, atrial fibrillation, symptoms pointing to a heart problem)
  - 24 hour ECG: paroxysmal arrhythmias
  - Carotid doppler: carotid stenosis

- Tilt table test: orthostatic or vasovagal syncope
- CT: thoracic pathology
- Pre-op: **treadmill Stress test** (if mobile), nucleotide perfusion test if other contraindications to stress test
- **V/Q scan**
- **Calcium chloride, sodium bicarb, insulin, glucose:** hyperkalemia
- **Neck venography**= superior vena cava syndrome
- Anticoagulants

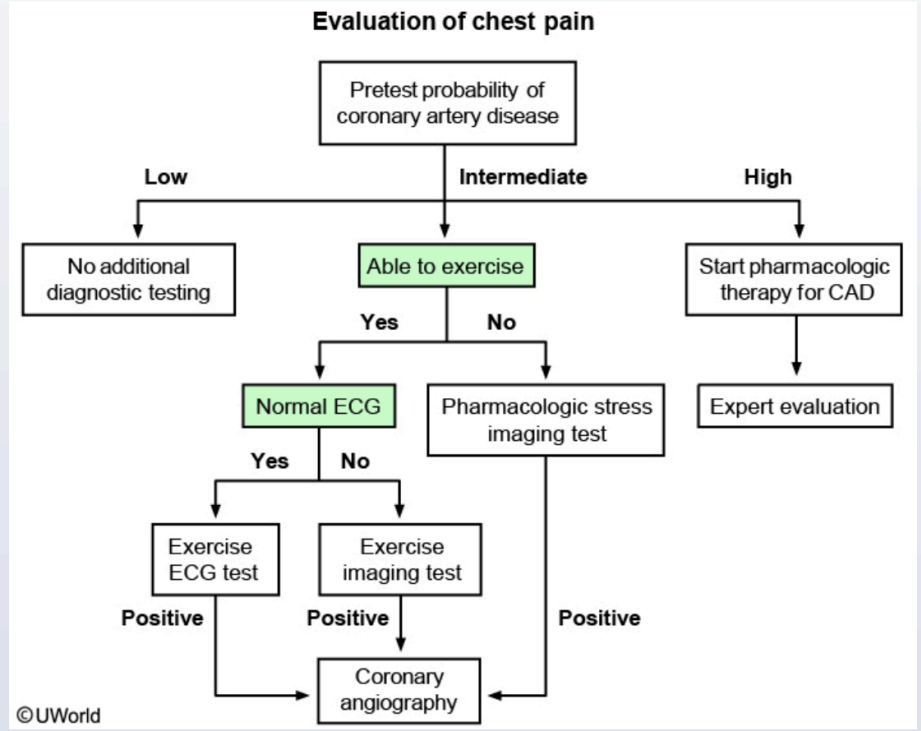
Exceptions to the Use of DOACs for Anticoagulation	
Condition	**Preferred Anticoagulants**
Antiphospholipid syndrome	**Warfarin**, unfractionated heparin, LMWH
Mechanical heart valve	Warfarin, unfractionated heparin, LMWH
Atrial fibrillation due to mitral stenosis	Warfarin, unfractionated heparin, LMWH
Severe renal or liver disease (ESRD or ESLD)*	Warfarin, unfractionated heparin, LMWH**
Pregnancy	LMWH, unfractionated heparin
Cancer	Recent data have shown that DOACs are equivalent to LMWH, but LMWH should be selected over a DOAC if this choice is offered.
DOACs = direct oral anticoagulants; ESLD = end-stage liver disease; ESRD = end-stage renal disease; LMWH = low–molecular-weight heparin. * Although some physicians use DOACs in patients with ESRD and ESLD, data supporting their use in these settings remain sparse. It is probably best to avoid using DOACs in these settings on exam questions at present. ** Use of LMWH is contraindicated in renal failure but acceptable in liver failure if the risk of bleeding is considered low.	

- **Heart murmurs and maneuvers**

Cardiac Murmurs and Changes in Intensity				
Murmur	**Venous Return/Preload**		**Afterload**	
	Increased (Leg raise/Squatting)	**Decreased (Valsalva/Standing)**	**Increased (Handgrip)**	**Decreased (Amyl Nitrate)**
Hypertrophic cardiomyopathy	↓	↑	↓	↑
Mitral/aortic regurgitation	↑	↓	↑	↓
Mitral/aortic stenosis	↑	↓	↓	↑
Mitral valve prolapse	↓	↑	*↑/↓	↓
Ventricular septal defect	↑	↓	↑	↓
↑ = increased intensity; ↓ = decreased intensity.				
* Isometric handgrip leads to an increase in left ventricular afterload, which delays left ventricular emptying. This delay results in a late onset of both the murmur and the click with a shorter murmur duration. Dependent upon the severity of prolapse and the patient's heart rate, the murmur can either increase in intensity or be diminished.				

-
    - **Supravalvular stenosis (rare)** → williams disease
    - Bicuspid aorta = coarctation of aorta
- **CHADVasc**
    - **C**: CHF/ LV dysfunction
    - H: HTN
      A2: Age > 75
    - D: DM
    - S2: stroke, TIA, thromboembolism
    - V: vascular disease
    - A: Age 65-72
    - Sex:
        - Score > 2: treat with warfarin
        - Score < 2: aspirin or heparin
- **Anticoagulation**
    - Warfarin
        - Best for non-valvular atrial fibrillation
        - Goal > 2 INR
        - If blood in urine → cystoscopy
    - LMWH
        - Inhibit Xa, SubQ but reduced dose if CKD
    - UFH
        - Binds ATIII to increase rate of ATIII inactivation of thrombin and factor Xa, IV
    - GpIIb/ IIIa inhibitors
    - Herbals
        - Ginkgo biloba increases bleeding
        - St. Johns wort decreases effectiveness of anticoagulants
- **ASCVD**
    - Gender, race, systolic BP, diabetes, age, total cholesterol, HDL, HTN, smoker

- Use to <u>determine guideline recommendations to start Statin</u>
- ***Lipid profile alone is not used to determine CVD***
- #1 tx: STATIN in > 7/5-10% risk
  - High intensity statin = muscle aches side effect → switch to moderate intensity
  - Decreases LDL
  - Extremely important for diabetics
- #2: fibrates= reduce TRIG
- Fenofibrates do not lower risk of atherosclerotic events. Best for high TRIG
- Ezetimibe is not as effective as statins
- PCSK9 inhibitors (alirocumab) is better option
- Apixaban reduces risk of clots

- **Cardiac chest pain**
  - always order ECG w/in 10 minutes
  - risk factors (smoking, obesity, older man)
  - order in conjunction with troponin
  - 

- **Work-up**
  - ECG: first best test to determine baseline
  - Exercise stress testing / perfusion imaging for risk stratification with intermediate risk features
  - TTE: segmental wall motion abnormalities during episode of chest pain
    - Can help dx Takotsuba (older women with broken heart)
  - Venous ultrasonography= DVT
  - Exercise myocardial perfusion imaging
- Cardiac maneuver

Effect of Physical Maneuvers on Murmur Intensity			
Parameter	**Squatting**	**Standing**	**Valsalva**
Hypertrophic cardiomyopathy	Decrease	Increase	Increase
Mitral valve prolapse	Decrease	Increase	Increase
Aortic stenosis	Increase	Decrease/no change	Decrease/no change
Aortic regurgitation	Increase	Decrease/no change	Decrease/no change
Mitral stenosis	Increase	Decrease/no change	Decrease/no change
Mitral regurgitation	Increase	Decrease/no change	Decrease/no change
Flow murmur	Increase	Decrease/no change	Decrease/no change

- **Shock**
  - Systemic hypoperfusion → inadequate perfusion of tissues
    - Vasoconstricted: cold shock, output problem
      - Cardiogenic, hypovolemic, obstructive
    - Vasodilated: warm shock, disruptive problem
      - Sepsis, anaphylaxis, neurogenic (spinal), adrenal
      - Tx: vasopressin, Ag II
      - IM epinephrine
  - **Hypovolemic/ Hemorrhagic shock**
    - Decreased preload/ intravascular volume, empty tank, decreased intravascular volume
    - Hemorrhagic trauma, fluid loss via skin (burn), renal, GI (vomit/ diarrhea), 3rd space loss
    - Decreased CO and decreased wedge pressure
    - Symptoms: hypotension (decreased 20%, elderly may have normal BP), tachycardia, dry membranes and cold skin, reduced skin turgor
      - Look at BP, Cr, Glasgow coma scale, IO's
      - MAP < 65 (tissue damage starts)
    - Tx: volume resuscitation, large bore **IVs, fluids** (only helpful with increasing preload)
      - Need 2 decent peripheral IVs (large radius, short length)
      - Mass transfusion: 1:1:1 plasma: platelets: pRBCs
        - Goal: keep SBP > 90

Class of haemorrhagic shock				
	I	II	III	IV
Blood loss (mL)	Up to 750	750–1500	1500–2000	> 2000
Blood loss (% blood volume)	Up to 15	15–30	30–40	> 40
Pulse rate (per minute)	< 100	100–120	120–140	> 140
Blood pressure	Normal	Normal	Decreased	Decreased
Pulse pressure (mm Hg)	Normal or increased	Decreased	Decreased	Decreased
Respiratory rate (per minute)	14–20	20–30	30–40	> 35
Urine output (mL/hour)	> 30	20–30	5–15	Negligible
Central nervous system/ mental status	Slightly anxious	Mildly anxious	Anxious, confused	Confused, lethargic

- **Septic (distributive) shock**
  - O2 delivery intact, problem with mitochondria, tissues cannot extract O2
  - Have suspicion for this when the patient meets SIRS criteria. Takes a couple days to brew.
  - high CO, **low PVR**, low PCWP
  - Early septic shock causes hyperdynamic cardiovascular state → peripheral vasodilation and leaks, intravascular hypovolemia – increased SV, HR, PP, bounding pulses
  - Vasopressors (increase SVR) with fluids → vasoconstriction, decreased perfusion, necrosis
- **Cardiogenic shock**
  - Pump problem, not enough Cardiac output
    - MI, cardiomyopathy, arrhythmias, trauma/ mechanical problem
  - Symptoms: hypotension, tachycardia, pulmonary edema (crackles, JVD), cool extremities, reduced urine volume
  - **Increased PCWP,** increased SVR, **decreased CO**
  - Work-up: ECHO, TEE, PAC
  - Tx: **EPI**, milrinone, dopamine > dobutamine, NE
  - **Cardiogenic pulmonary edema**
    - S3, crackles, hypoxemia
    - Tx: Positive pressure ventilation → decrease LV preload, increases intrathoracic pressure, decreases RV preload, increases RV afterload → reduced blood volume to left atrium to improve systolic ejection and stroke volume
- **Obstructive**
  - Blocked pump, extracardiac causes (PE, Pulmonary HTN, PTX, pericardial tamponade, constrictive pericarditis)
    - Spontaneous PTX: young, thin smoker with sudden hypoxia
  - Decreased CO and **increased SVR, increased PVR**
  - Symptoms: hypotension, tachycardia, JVD, cold and clammy skin
  - PCWP (variable depending on cause)
    - High in cardiac tamponade
    - Low is more common
  - **Tx: underlying cause**
- **Distributive**
  - Decreased SVR, floppy vessels from peripheral vasodilation →

compensatory increased CO
        - Septic shock
        - Non-septic: SIRS, neurogenic, anaphylactic (IgE), toxins (snake bite), endocrine
    - Decreased PCWP, decreased SVR
    - Tx: IV fluid, vasopressors
        - NE first, then add others
- **Neurogenic shock**
    - Hypotension, bradycardia, warm skin, motor/ sensory defects. High spinal cord injury C1-3
    - Tx: alpha-1 agonist (phenylephrine)
- **Anaphylactic shock**

Different Types of Shock				
Shock Type	**Skin**	**Wedge Pressure (PCWP) (Preload)**	**Systemic Vascular Resistance (SVR) (Afterload)**	**Cardiac Output**
Hypovolemic	Cold and clammy skin	↓↓	↑	↓
Cardiogenic		↑	↑	↓
Obstructive		↑ or ↓	↑	↔ or ↓↓
Distributive	Warm or dry skin	↔ or ↓	↓↓	↓ or ↑

- **Hypertension**
2017 ACC/AHA Updated BP Terminology and BP Ranges			
New Terminology	**New BP Range (mmHg)**	**Old Terminology**	**Old BP Range (mmHg)**
Normal	< 120/80	Normal	< 120/80 (same)
Elevated	120-129/80	Prehypertension	120-139/80-89
Stage 1 hypertension	130-139/80-89	Stage 1 hypertension	140-159/90-99
Stage 2 hypertension	≥ 140/90	Stage 2 hypertension	≥ 160/100
    - **Essential Hypertension** (95% most common) - no known cause
        - > 140/90 on 2 occasions
        - Check other causes of HTN- check lipids, chemistry panel, UA, Hgb, atherosclerosis, DM
    - Due to decreased vascular compliance
        - Proteinuria: lisinopril delays onset of kidney disease
        - r/o hypertensive emergency: re-evaluation/ repeat BP after 30 min rest period
        - if end organ damage: hospitalize
        - short acting antihypertensives if mild symptoms
    - Workup: CMP, CBC, TSH, UA, ECG
        - Screen for risk factors
    - Treatment goal:
        - < 60 yo: < 140/ 90

        - > 60 yo: < 150/90
        - DM or CKD: < 140/90
    - Secondary causes of hypertension
        - <u>OSA most common</u>
        - Think hyperaldo if low potassium or if potassium drops a lot on initiation of a thiazide diuretic
        - If 3 medications do not control BP, look for secondary causes
        -

Disease	Characteristics
Primary kidney disease	Elevated serum creatinine, abnormal urinalysis, or both
RAS: FMD	Younger females, "string of beads" appearance on imaging
RAS: Atherosclerosis	• Increase in creatinine >50% after starting an ACE inhibitor if bilateral • Older adult with other cardiovascular diseases • Recurrent flash pulmonary edema
Primary aldosteronism	Hypokalemia with metabolic alkalosis
Obstructive sleep apnea	Obese individuals who snore loudly with apnea
Medication-induced	On oral contraceptives, androgens, steroids, and NSAIDs
Pheochromocytoma	Paroxysmal elevated blood pressure, headaches, palpitations, and sweating
Cushing syndrome	Cushingoid facies, central obesity, proximal muscle weakness, and stria (>1 cm)
Coarctation of the aorta	Hypertension in upper extremities, decreased pulses in lower extremities

    - **Treatments**
        - **Non-pharmacologic:**
            - DASH diet >>weight loss < 25 BMI, aerobic exercise, dietary sodium, alcohol limitation
            - Smoking has minimal role in controlling hypertension
        - **ACE inhibitors:**
            - when starting lisinopril, Cr will increase normally. Best at preventing progression of CKD
            - Most commonly prescribed medication. Used for everyone, DM, HTN, microalbuminuria
            - side effects: cough, gag reflex issues due to kinin accumulation, increased production of PGs, activated arachidonic acid pathway, increased TXA → bronchoconstriction
            - First line in AA only if CKD present
        - Change **oral contraceptives** → alternative method
        - **ARBS**- sartans
        - **CCBs**: african americans, renal disease
        - African americans: CCB, Thiazides
        - NSAIDS stimulate renal sodium retention

Blood Pressure goals: JNC-8 vs ACC/AHA			
JNC-8 HTN Guidelines		**ACC/AHA 2017 HTN Guidelines**	
140/90 mmHg	**150/90 mmHg**	**130/80 mmHg**	**140/90 mmHg**
CKD/proteinuria, diabetes, or those age < 60 without comorbidities	Age ≥ 60 without DM or CKD	High risk patients: CKD, CAD, ASCVD ≥ 10% and relatively healthy adults age ≥ 65	Age < 65 without high risk cardiovascular risk
Both recommend ACEI/ARB as first line in CKD or proteinuria			

Choice of antihypertensive drug for comorbid conditions	
Coronary atherosclerosis	• Angina pectoris: β-blocker, CCB • Post–myocardial infarction: ACE inhibitor or ARB, β-blocker
Heart failure with reduced ejection fraction	• ACE inhibitor or ARB, β-blocker, diuretic, aldosterone antagonist
Atrial fibrillation or flutter	• β-Blocker, nondihydropyridine CCB
Chronic kidney disease	• ACE inhibitor or ARB
Gout	• Losartan, other ARB, CCB (avoid diuretics)
Osteoporosis	• Thiazide diuretic
Migraine	• β-Blocker, CCB

- **Hyperlipidemia**
  - High LDL, low HDL, high cholesterol
    - Pts with high risk: Atorvastatin (40-80mg/day), rosuvastatin (20-40mg/day)
    - Monotherapy with non-statins does not reduce CV morbidity and mortality.
  - Start on high intensity statin (side effects: muscle pain) —> moderate-intensity statin + ezetimibe
  - statins, aspirin, angiotensin inhibitors, lisinopril and beta blockers (metoprolol have increase survival in acute coronary artery events
  - Niacin → causes flushing, aspirin treats side effects. Prostaglandin related reaction
- **Peripheral vascular disease**
  - occlusion of peripheral blood (legs, claudication) due to atherosclerosis —> asymmetric ankle-brachial index < 0.9
  - Vasculopathy → demand-related ischemia → claudication
  - Tx: aspirin, statin, antiplatelets → exercise program → percutaneous and surgical stenting, bypass graft

        - #1 PDE3 inhibitor: cilostazol
        - #2 clopidogrel (ADP inhibitor on platelets, used for prevention)
- **Buerger disease/ thromboangiitis obliterans**
    - Small vessel vasculitis in heavy smokers. Ulcers on fingers
    - #1 varenicline decrease smoking cessation
    - Aspirin, high intensity statins
    - No vasodilator, anti-inflammatory, lipid-lowering, anticoagulants, revascularization can improve symptoms
- **Atherosclerosis**
    - Tx: catheterization
        - Atheroembolic phenomenon → abdominal pain, AKI, acute pancreatitis, dermatologic disease (livedo reticularis, cyanotic toes), stroke
    - Revascularization if symptomatic and 70+% stenosis
    - Due to decreased diameter vascular lumen
        -
- **70%-99% stenosis**: Revascularization with **carotid endarterectomy** (CEA) is generally **recommended**.
- 50%-69% stenosis: Revascularization is likely beneficial for men; its benefit has not been proven in women, so medical management alone is recommended for women.
- <50% stenosis: CEA has no proven benefit and is not recommended.
- **Varicosities**
    - venous valve insufficiency —> tortuous veins
    - asymptomatic, fatigue, restless legs, edema and ulceration
    - compression socks above the knee, exercise, removal of veins via sclerotherapy
- **Chronic venous insufficiency**
    - Venous duplex ultrasound used to identify cause
        - Ankle brachial index used for arterial insufficiency
    -

Chronic venous stasis	
Risk factors	• Obesity • Advanced age • Varicose veins • History of DVT
Clinical features	• Leg pain (achy, heavy) • Edema • Venous dilation (varicosities, telangiectasias) • **Dermatitis:** erythema, pruritus, scaling, weeping • Chronic woody induration and brown discoloration • Ulcers
Management	• Elevation • Compression stockings

- **Heart failure**

Left heart failure	Right heart failure
Pulmonary edema, crackles	JVD, peripheral edema Hepatojugular reflux: sustained elevation in JVP > 3 cm and highly specific for elevated right-sided cardiac pressure and RV failure

	(blood from IVC enters RV, it cannot handle the venous return, so it backs up into JVP)

- **Systolic heart failure** (can't squeeze)
  - Ischemic, dilated
  - Viral, EtOH, cocaine, Chagas, idiopathic
  - Alcoholic dilated CM is reversible if you stop booze
- **Diastolic heart failure** (can't fill)
  - HTN, amyloidosis, hemochromatosis
    - Hemochrom is reversible with phlebotomy
- **Acute decompensated heart failure**
  - Hx of radiation, doxorubicin, chemotherapy
  - ABCs
    - Give oxygen for respiratory failure
    - Inotropic agents for cardiogenic shock
    - Reduce preload with Nitro
    - Figure out underlying cause
    - Diuresis to remove excess fluids
- Work-up:
  - CXR (not diagnostic)
  - ECG
  - TEE → look for valvular pathologies
  - BNP
  - ECHO → ejection fraction, diastolic
    - Normal EF ~ 55%
      - Reduced EF= systolic failure/ can't squeeze
      - elevated= diastolic dysfunction/ can't relax
  - Left heart catheter
    - Determines if ischemic or not
- Treatment
  - **#1 manage HTN → diuresis + nitroglycerin**
  - ACE inhibitor or beta blocker for HfREF
  - Spironolactone if class III or IV on max dose
  - Classes
    - Class I: no symptoms
      - Tx: beta blocker, ACE/ ARB, Statin
      - Smoking cessation, < 2L fluid, Nacl < 2 g
    - Class II: no symptoms with ADLs
      - Same as 1 + loop diuretics
    - Class III: symptoms with ADLs
      - Same as 1+ 2, Hydralazine, spironolactone
      - Automatic cardiac defibrillator, EF < 35%
    - Class IV: symptoms all the time
      - Die in < 1 year. Inotropes (milrinone), transplant

Classification and Staging of Congestive Heart Failure			
NYHA Classification		**ACC/AHA Staging**	
Class I	No shortness of breath with exertion No limitation of physical activity	Stage A	At risk for heart failure (HF) No structural disease or symptoms[1]
Class II	Shortness of breath with moderate exertion Slight limitations of physical activity	Stage B	Structural heart disease No symptoms of heart failure
Class III	Shortness of breath with minimal exertion Marked limitation of physical activity	Stage C	Structural heart disease Symptoms of heart failure
Class IV	Shortness of breath at rest Inability to perform physical activity	Stage D	Refractory HF End-stage heart failure

- Which meds decrease mortality: ACE, ARB, Beta blocker, aldosterone antagonists, SGLT2 inhibitors
  - Aldosterone antagonists block cardiac remodeling, especially after MI

Pharmacotherapy for chronic heart failure with reduced ejection fraction	
Agent	**Mortality benefit**
Angiotensin receptor–neprilysin inhibitor (eg, sacubitril-valsartan) OR **ACE inhibitor** (eg, lisinopril) OR **Angiotensin II receptor blocker** (eg, losartan)	Yes
Beta blocker (eg, metoprolol, carvedilol)	Yes
Mineralocorticoid receptor antagonist (eg, spironolactone, eplerenone)	Yes
Sodium-glucose cotransporter 2 inhibitor (eg, dapagliflozin, empagliflozin)	Yes
Diuretics (eg, furosemide, metolazone)	No*
Digoxin	No**

- **Digoxin toxicity**
  - Antidote: Digoxin Fab
  - Blocks Na/K ATPase → increased contractility, suppress AV node
  - Toxicity
    - N/V/pain
    - Confusion
    - Yellow halos
    - Cardiac arrhythmias: PVCs, literally everything
    - Hyperkalemia

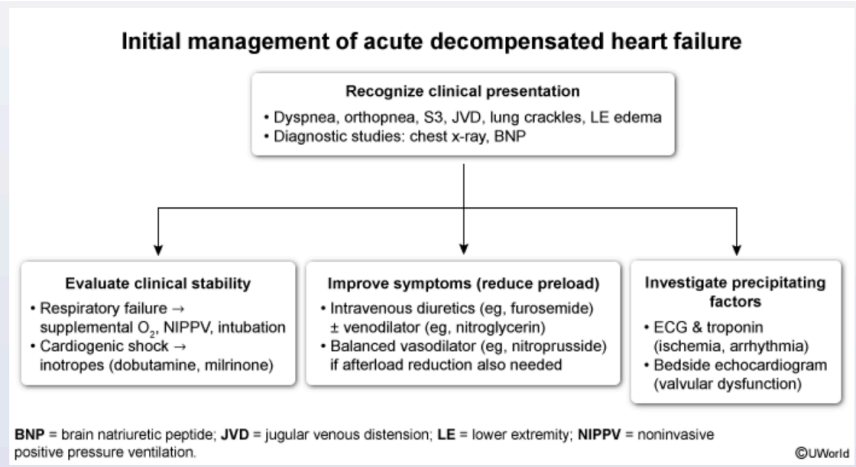
COMBANK Insight

Conditions Increasing Digoxin Toxicity	
Condition	**Effect**
Chronic renal failure	↓ renal excretion, which is the primary route of digoxin elimination
Hypercalcemia	↑ intracellular calcium, which is already ↑ by digoxin
Hyperkalemia	↑ cardiac conduction delay (eg, at the atrioventricular node)
Hypokalemia	↓ activity of the Na^+/K^+ ATPase pump
Hypomagnesemia	↑ digoxin uptake by the myocardium

- ○ **Cor pulmonale**: JVD, LE edema, increased Right atrial pressure
  - shortness of breath, orthopnea, swelling, medication compliance (esp diuretics), urine output, chest pain, ideal weight (> 4 lbs in 1 day, take more meds)
  - **COPD → right sided heart failure**
- ○ **constrictive pericarditis vs restrictive (amyloidosis)**
  - elevated JVP, prominent x and y descents, hepatojugular reflux, kussmaul's sign (change in JVP on inspiration), pericardial knock
  - calcifications= TB
  -

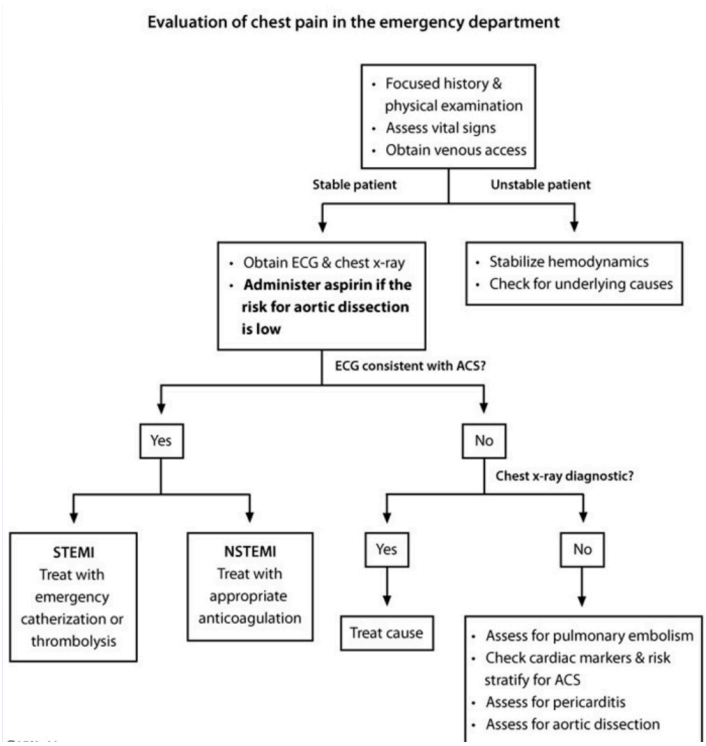
	Constrictive Pericarditis	Restrictive cardiomyopathy
Pericardium	Usually thickened	Normal
Atrial enlargement	Mild	Severe
MV and TV resp E variation	>25%	<15%
Ventricular septal motion	Abrupt early diastolic motion	Normal
PW TDI MV	Em pronounced	Em reduced
LVEF	→	↓

- ○ **Cardiac tamponade**
  - Beck triad: hypotension, JVD, muffled heart sounds
  - Pulsus paradoxus → DECREASED 10 mmHg
  - ECG: low voltage
  - CXR: enlarged cardiac silhouette
  - Common causes: aortic dissection, free wall rupture post MI, trauma, viral pericarditis
  - Increased fluid in pericardial sac → decreased venous return to heart → low CO, increased Central venous pressure, increases SNS activity, systemic vasoconstriction , elevated PCWP
  - Next step: call cardiology, vasopressors, **pericardiocentesis**
- ○ **CHF exacerbation ****
  - Acute worsening in heart failure
    - Evaluate stability
      - Respiratory failure→ ventilatory support
      - Cardiogenic shock hypotension → inotropes (dobutamine, milrinone)
    - Improve symptoms: diuretics, venodilator +/- vasodilator (nitroprusside)
    - Investigate precipitating factors: ECG, troponin, Echo
  - ACE inhibitors, beta blockers, Spironolactone decrease mortality
    - Tx: NO LIP

        - Nitrates
        - O2 (NIPPV)
        - Loops/ furosemide
        - Inotropes
        - Positioning
    - 

- CXR, ECG, BNP, Trop
    - STEMI= MONA BASH, Cath
    - CHF exacerbation= LMNOP
        - Lasix
        - Morphine
        - Nitrates
        - O2
        - Position sitting up
- Tx: ACE inhibitor, beta blocker, spironolactone decrease mortality in CHF

- **Coronary artery disease**

- 

- Hx: substernal, worse with exertion, improved with Nitro
- Associated with dyspnea, diaphoresis and Pre-syncope
- Risk factors:
  - Modifiable: Age, men > 45, women > 55, FmHx
  - Nonmodifiable: DM, smoking, HTN, HLD, obesity, vasculopathy
    - SMOKING is the biggest risk factor
- Physical: nonpleuritic, non-tender
- Work-up:
  - 12 lead → STEMI or LBBB→ cath lab < 90 minutes
    - Cath lab: wire placed in femoral artery
    - > 3 vessels affected → CABG
    - 1-2 vessels → STENT
  - Serial Troponins → elevated → Cath lab
  - **Stress test → positive → cath lab**
    - Treadmill
    - Pharmacological
    - EKG
    - Echo (bad EKG)
    - Nuclear (Bad Echo)
      - Pharmacologic test if obese/ unhealthy, contraindications
      - Adenosine or dipyridamole
  - Angiography = definitive diagnosis
- **MONA BASH-C**
  - **Morphine** (last intervention)- acute pain
  - **Oxygen** (can create ROS, do not over-oxygenate. Put on nasal cannula)
  - **Nitro** (best for angina, careful bc ventricle is preload dependent)- alleviates MI chest pain by reducing preload
  - **#1 Aspirin** (reduces mortality)
  - **Beta Blocker**

        - **ACE inhibitor**
        - **Statin**
        - **Heparin**
        - **Clopidogrel**
    - Meds: beta blockers + ACE inhibitor
        - DAPT: aspirin, clopidogrel
        - TPAL transport time to PCI is > 60 min

	Asx CAD	Stable angina	Unstable angina	NSTEMI	STEMI
Pain	-	Exertion, relieved with rest, nitro	Worsening, pain with exertion, relieved at rest	Pain at rest	At rest
Troponin T	-	-	-	Elevated	+/-
ST	-	-	-	-	ST elevation
Pathology	Stenosis < 70%	Stenosis > 70%	Thrombosis < 100%	Thrombosis < 100% Partial ischemia	100% thrombosis Transmural ischemia
Further work up		Stress test EKG ECHO Nuclear perfusion	Exercise stress test - stop CCB and Beta blockers Dobutamine or adenosine MUGA- perfusion study Unstable despite tx → cardiac cath	Cath lab	Serial troponins

- **Myocardial infarction**
    - **Prevention:** ASA (antiplatelet), beta blockers, smoking cessation, lipids, diabetes modification
    - Associated complications: **ventricular arrhythmias** (PVC, Vtach, Vfib) occur with acute MI → sudden cardiac arrest
    - **Acute MI**
        - dx: chest pain > 30 minutes,
        - Next best step
            - #1: ECG findings,
            - #2: elevated cardiac enzymes

Myoglobin	Rises 1st	Peaks in 2hrs, nl by 24
CKMB	Rise 4-8hrs	Peaks 24 hrs, nl by 72hs
Troponin I	Rise 3-5hrs	Peaks 24-48hrs, nl by 7-10days

            - #3: coronary angiography w/in 48 hours
                - PCI w/ stenting is standard
                - CABG if > 3 vessel, 2 vessels in diabetic, LAD main
                    - Graft arteries used from subclavian artery > internal

mammary arteries, saphenous viein
    - Send home on ASA, clopidogrel, ACE, beta blocker, STATIN
    - Indications

CABG is performed in patients with CAD to improve quality of life and reduce cardiac-related mortality. The main indications are:

- 3 or more-vessel CAD with hemodynamically significant lesions (traditionally greater than 70% stenosis)
- Left main CAD with greater than 50% stenosis
- 2-vessel CAD in patients with diabetes mellitus

- **STEMI**
    - Timeline
        - hyperacute T wave in ischemic vascular territory —> ST elevation in > 2 leads , new LBBB + chest pain —> hours to days later T wave inversion —> diminished R waves or Q waves
    - Transmural infarction: ST elevation
    - subendocardial infarction: ST depression
    - tx: aspirin, beta blockers, assess if candidate for rapid reperfusion (thrombolytics or **percutaneous coronary intervention**)
        - TPA: no access to PCI center
        - Nitrates: venodilator, less preload, dilates coronary arteries
    - **Cardioversion**: synchronized occurs during QRS if shock hits during the T wave.
    - **Defibrillation**: Vfib, V Tach, pulseless rhythm, shock not synchronized. Start with low Joules, then increase to higher Joules.
    - Inferior wall MI: give fluids
        - MI to RCA (II, III, AvF) can cause cardiogenic shock → give atropine (dobutamine for everything else)
            - Don't give nitrates, exacerbates the hypotension
        - Aspirin, beta blockers, ACE inhibitors decreases mortality
        - GIVE FLUIDS
        - Injury to SA node → give atropine
- **NSTEMI**
    - ST depression or T wave inversion
    - incomplete vessel occlusion, transient
    - Tx: MONA BASH
    - No troponin elevation
- **Acute MI mimics**: acute pericarditis, aortic dissection
    - Cocaine intoxication
        - Give benzodiazepine, morphine, oxygen, diltiazem
        - Percutaneous coronary intervention (restore blood flow)
- **Peri-infarction pericarditis**
    - Local inflammation due to myocardial necrosis 2-4 days after MI
    - Coronary reperfusion necessary
    - Dx: ECHO
    - Tx: NSAID, colchicine (apparently prevents recurrence?)
- **Dressler syndrome**: autoimmune pericarditis 2 weeks post-MI
    - Fever + leukocytosis + pericarditis symptoms
    - Tx: aspirin

- **Cardiac tamponade**
  - Becks triad: hypotension, JVD, muffled heart sounds
  - Pulsus paradoxus: inspire → IV bows over to left → decreases LV preload → stroke volume, systolic decreases by > 10 with inspiration
  - Electrical alternans: reduced EKG amplitude, low voltage QRS alternates
  - Tx: pericardiocentesis
  - 
  - Kussmaul sign: JVD increased with inhalation

Mechanical complications of acute myocardial infarction

Complication	Time course	Involved coronary artery	Clinical findings	Echocardiogram findings
Right ventricular failure	Acute	RCA	• Hypotension • Clear lungs • Kussmaul sign	• Hypokinetic RV
Papillary muscle rupture	Acute or within 3-5 days	RCA	• Severe pulmonary edema • New holosystolic murmur	• Severe mitral regurgitation with flail leaflet
Interventricular septum rupture	Acute or within 3-5 days	LAD (apical septal) or RCA (basal septal)	• Chest pain • New holosystolic murmur • Biventricular failure • Shock	• Left-to-right ventricular shunt • ↑ O_2 level from RA to RV
Free wall rupture	Within 5 days* to 2 weeks	LAD	• Chest pain • Shock • Distant heart sounds	• Pericardial effusion with tamponade
Left ventricular aneurysm	Up to several months	LAD	• Subacute heart failure • Stable angina	• Thin & dyskinetic myocardial wall

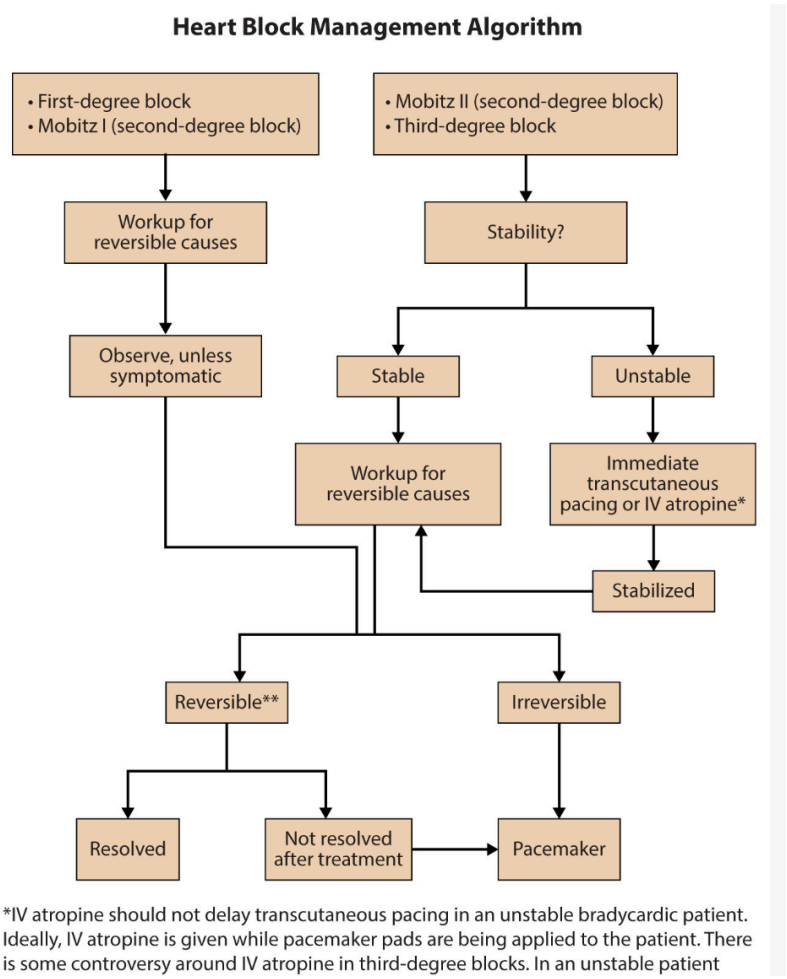
- **Acute coronary syndrome**
  - range of dz unstable angina pectoris to acute MI
    - vasospasm of arteries/ in situ thrombosis at ruptured atherosclerosis plaque
    - **Stable angina**: > 30 minutes that resolves with rest
      - **nitroglycerine**= direct relaxation of coronary vascular SMCs, reduce LV systolic wall stress
        - venodilator= decreased preload, left ventricular end-diastolic volume, reduce wall stress, decrease myocardial oxygen demand

        - unstable angina: does not resolve with rest
- **Prinzmetal's angina**
    - Vasospasm → intermittent chest pain relieved by nitro
    - Dx: ergonovine stimulation test
    - Tx: CCB (diltiazem), nitrates
- **EKG**:
    - inferior: 2, 3, avF
    - anterior: V2-V4
    - lateral: I, Av

Anterior	LAD	V1-V4
Lateral	Circumflex	I, avL, V4-V6
Inferior	RCA	II, III and aVF
R ventricular	RCA	V4 on R-sided EKG is 100% specific

      L, V5-V6
    -
- **Heart block**
    - **1st degree/ Type 1**: prolong PR→ no treatment (AV node problem)
    - **2nd degree Type 2:** tx → pacemaker (His-Purkinje)
        - **Wenckebach Mobitz 1-** progressively prolonged PR with a drop QRS (dont confuse with 3rd degree) 1, 2, 3…wenckebach
        - 

"Progressive, prolongation of the PR interval followed by a dropped beat"
        - **Wenckebach Mobitz 2-** no change in PR, dropped QRS -- tx with pacemaker
    - **3rd degree/ Type 3**: complete heart block → transcutaneous pacing
        - P waves do not relate to QRS
        - Cardiac pacing
        - RCA blockage – AV node damage → inappropriate pacing



- **Bundle branch block**
  - Turn signal method for wide QRS
    - Left = down= LBBB
    - Right= UP= RBBB
    - Sgarbossa's criteria for BBB with STEMI

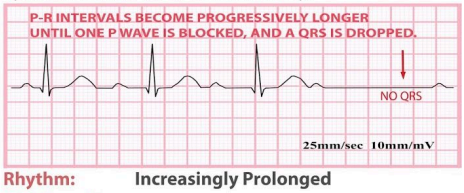
ECG Basics - Heart Blocks

First Degree AV Block



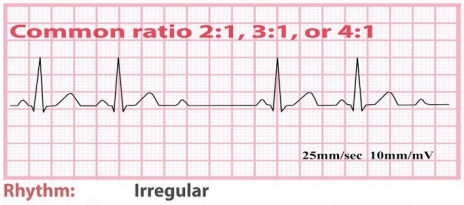
Rhythm:	Regular
PR interval:	Prolonged >0.20 sec
P Wave:	Normal
QRS:	<0.11 sec

Second Degree AV Block - Type 1 (aka Mobitz 1, Wenckebach):



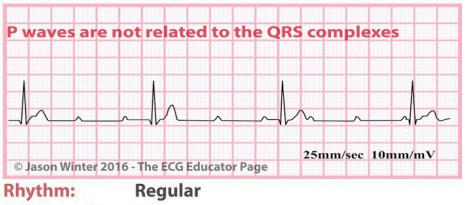
Rhythm:	Increasingly Prolonged
PR interval:	Irregular
P Wave:	Normal
QRS:	<0.11

Second Degree AV Block - Mobitz Type 2



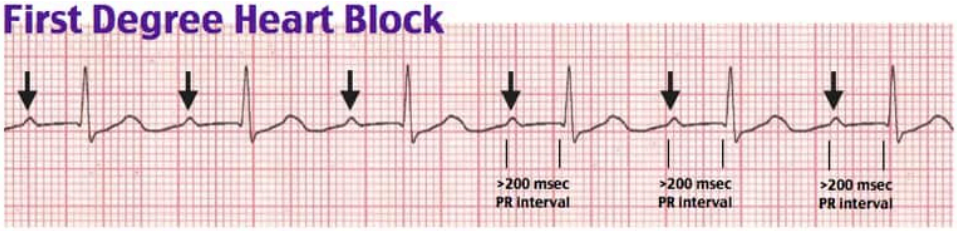
Rhythm:	Irregular
PR interval:	Normal (more P waves then QRS)
P Wave:	Normal
QRS:	Usually wide >0.10

3rd Degree AV Block

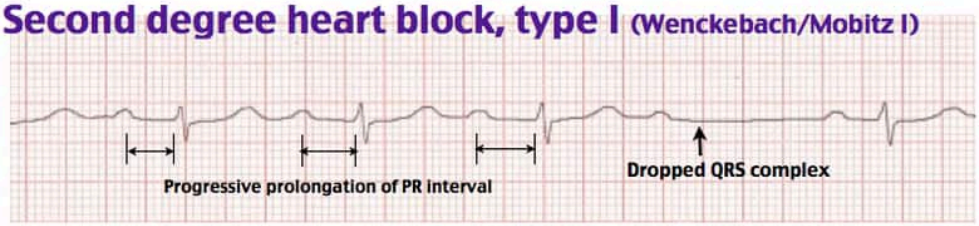


Rhythm:	Regular
PR interval:	None
P Wave:	Normal does not relate to QRS
QRS:	Normal or wide

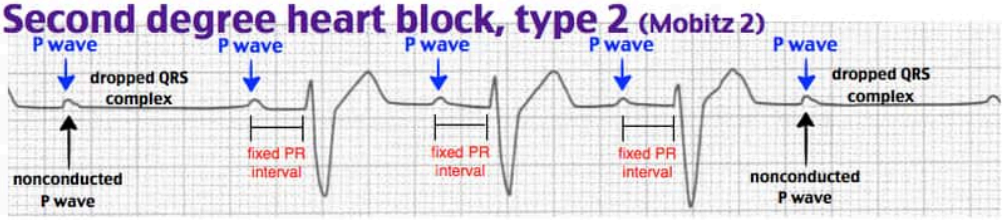
- **First Degree Heart Block**



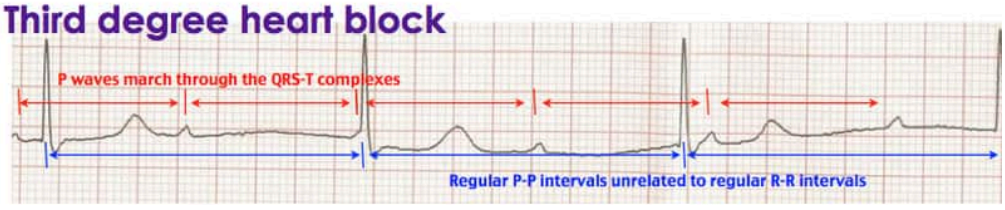
- **Second degree heart block, type I (Wenckebach/Mobitz I)**



- **Second degree heart block, type 2 (Mobitz 2)**

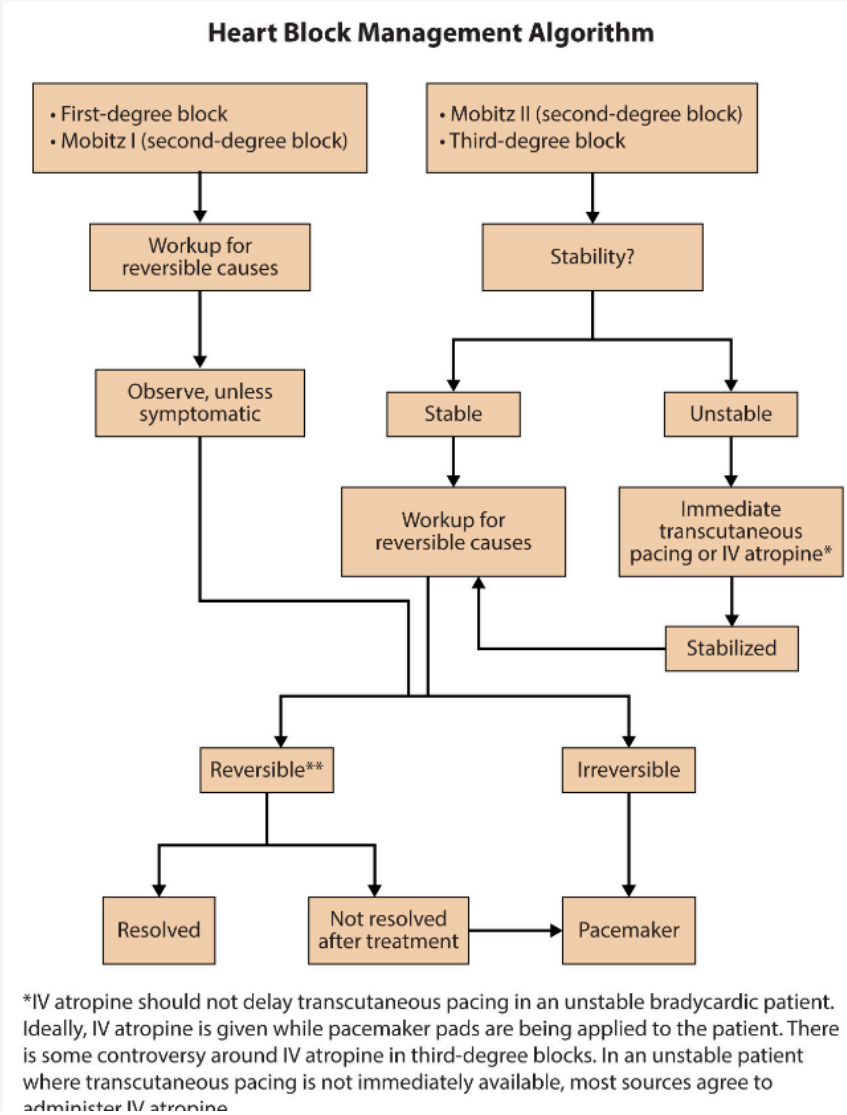


- **Third degree heart block**



-

Atrioventricular block			
	Clinical presentation	**ECG features**	**Management**
First degree	Asymptomatic	PR interval prolongation	Observation
Mobitz type I second degree	Usually asymptomatic	Progressive PR interval lengthening followed by dropped QRS complex	Observation (rarely PPM placement)
Mobitz type II second degree	Fatigue, lightheadedness, syncope	Constant PR interval with randomly dropped QRS complexes	PPM placement
Third degree (complete)	Fatigue, lightheadedness, syncope	Complete dissociation of P waves & QRS complexes	PPM placement



- **Labs**

        - Troponin T- elevated several hours after
    - **Arteries**
        - Most common = Left anterior descending (LAD)
        - Posterior descending artery arises from the right circumflex a.
        - coronary arteries fill during **<u>diastole</u>**
            - propranolol + cocaine= vasospasm
        - systemic arteries fill during systole
        - MI → arrhythmias < 48 hours= V tachycardia, V fibrillation

Mechanical Complications of AMI		
Complication	**Time Course**	**Clinical Findings**
Papillary muscle rupture	Acute or within 3-5 days	New holosystolic murmur at apex (mitral regurgitation) Severe Pulmonary edema
Interventricular septum rupture	Acute or within 3-5 days	New holosystolic murmur at lower left sternal border (ventricular septal defect (VSD)
Ventricular free wall rupture	Within 5 days to 2 weeks	Pericardial effusion with tamponade
Left ventricular aneurysm	2 weeks to several months	Dyskinetic myocardial wall

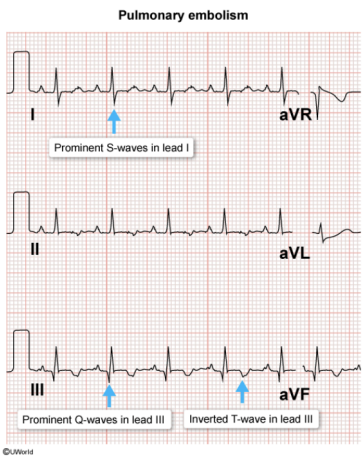
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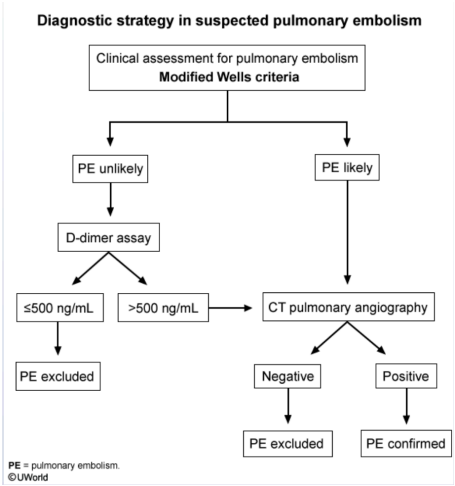
Mechanical complications of acute myocardial infarction				
Complication	**Time course**	**Involved coronary artery**	**Clinical findings**	**Echocardiogram findings**
Right ventricular failure	Acute	RCA	• Hypotension • Clear lungs • Kussmaul sign	• Hypokinetic RV
Papillary muscle rupture	Acute or within 3-5 days	RCA	• Severe pulmonary edema • New holosystolic murmur	• Severe mitral regurgitation with flail leaflet
Interventricular septum rupture	Acute or within 3-5 days	LAD (apical septal) or RCA (basal septal)	• Chest pain • New holosystolic murmur • Biventricular failure • Shock	• Left-to-right ventricular shunt • ↑ O_2 level from RA to RV
Free wall rupture	Within 5 days* to 2 weeks	LAD	• Chest pain • Shock • Distant heart sounds	• Pericardial effusion with tamponade
Left ventricular aneurysm	Up to several months	LAD	• Subacute heart failure • Stable angina	• Thin & dyskinetic myocardial wall

*50% occur within 5 days.
LAD = left anterior descending; **RA** = right atrium; **RCA** = right coronary artery; **RV** = right ventricle.

- **Arrhythmias**
    - **Congenital long QT syndrome**
        - Voltage gated potassium channels
        - Delayed repolarization
        - Sensorineural hearing loss
        - Torsades de pointes, PVT
        - Syncope
        - Tx: beta blockers
- **Cardiomyopathy**
    - **hypertrophic cardiomyopathy**: asymptomatic. can cause sudden death in young patients.
        - murmur intensifies with valsalva maneuver

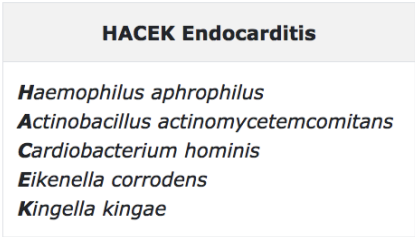
        - Seen in infants of diabetic mothers
        - tx: **beta blockers** is symptomatic (slows HR, decrease myocardial contractility)
    - **Restrictive** → diastolic heart failure , -OSIS
        - **Hemochromatosis**: iron overload, DM, bronzing, elevated LFTs, arthropathy
            - High ferritin, low TIBC, high serum iron
        - **Amyloidosis**
            - Protein deposits in kidney, joints, heart
            - Proteinuria
        - **Sarcoidosis**
            - B/L hilar LN, uveitis, erythema nodosum, cough
            - Heart and lung noncaseating granulomas
- **Pulmonary embolism**
    - sudden SOB, tachycardia, **DVT** or blood clot, hypercoagulable (females taking OCP), smoking
    - Shock, marbled skin
    - Injury of long bones (humerus, femur), hx of immobilization, cancer, travel
    - Dx:
        - CT pulmonary angiography: transition from infarct to melting sign
        - LE doppler US for DVT (homans sign= pain with dorsiflexion)
        - Westermark sign, hampton hump, fleischner sign
    - EKG: negative T waves in precordial leads, RBBB, Right axis deviation, sinus tachycardia (up= right, down= left)
    - Dx: Well's criteria
    - S1Q3T3
        - S waves in lead 1, Q waves in lead 3, T waves in lead 3





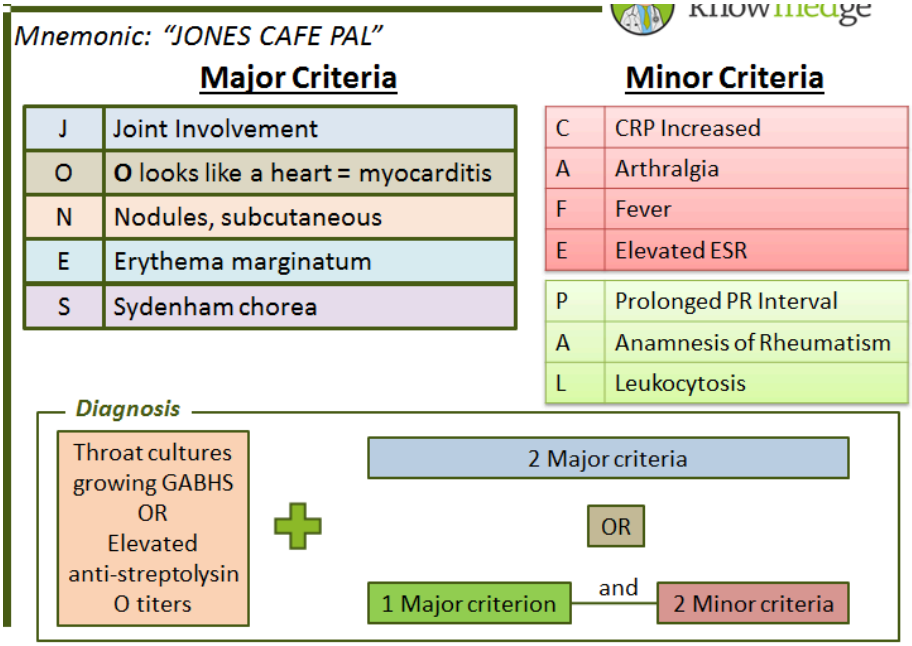
Type of Obstructive Shock	Pathophysiology	CVP	PCWP	CO	Etiologies
Pre-pulmonary	• Right ventricular failure due to obstruction prior to left-sided filling OR • Decreased preload OR • Inadequate right ventricle filling	↑	↓	↓	• PE • Tension pneumothorax • Pericardial tamponade • Severe pulmonary hypertension
Post-pulmonary	• Obstruction occurs after pulmonary circulation involving outflow of the left heart	↑	↑	↓	• Aortic stenosis • Mitral stenosis • Aortic dissection

    -

- **DVT**
  - Anticoagulation:
    - Warfarin (cant be started alone bc protein C and S are cleared before Vit K dependent clotting factors.
    - Bridging therapy= heparin + warfarin for 5 days
    - Warfarin for 3 months, **INR 2.0-3.0**
  - IVC filter
    - Give if already on anticoagulation
    - Stops thrombus from going to lungs
- **Arterial thrombosis**
- **Cardioembolic disease**
  - Uneven pulses
- **Acute endocarditis**
  - Most common= Staph aureus (tricuspid) right sided heart murmurs, worse with expiration
  - complication= emboli, destruction to valve
  - Mitral valve endocarditis - strep viridans
  - Prophylaxis: mechanical valve, hx of endocarditis, VSD/ ASD
  - Strep bovis endocarditis: colonoscopy bc associated with malignancy and bacteremia
  - Culture negative: HACEK
    - 

- **Infective endocarditis**
  - IV Drug abuse, tricuspid valve
  - next steps: **blood culture from 3 sites —> empiric Abx → TTE → TEE**
  - ECHO of tricuspid valve (no heart murmur), REGURGITATION, holosystolic
    - Aortic valve endocarditis= perivalvular abscess (fever, conduction abnormalities), bicuspid valve
  - findings: janeway lesions, roth spots
  - Septic emboli → splenic abscesses, infarctions anywhere, lung abscess
  - Perivalvular abscess can occur in those with persistent bacteremia or heart block
  - Prevention: Abx for 6 months only for High-risk procedures AFTER surgical repair
  - Tx: **pencillin** → **clarithromycin** (penicillin allergy, syphilis endocarditis); ampicillin and ceftriaxone (strep viridans, bovis); nafcillin and gentamicin (MSSA); vanco and gentamycin (MRSA)
    - STAPH endocarditis= **Vancomycin**
    - **STREP endocarditis= ceftriaxone**
    - If penicillin allergy → macrolides, clindamycin, keflex cephalosporin
  - Valve replacement
    - Prosthetic valve endocarditis with valve dysfunction or bacteremia
    - Uncontrolled infection with abscess, fistula, conduction defects despite IV abz for 1 week
    - Systemic embolizations despite IV abx for 1 week

- Severe annular disease → CHF



-

Physical Exam Finding	Description	Pathogenesis	Incidence
Janeway lesions	Nontender erythematous macules on palmar and plantar surface of hands and feet	Vascular (embolic)	2.20%
Osler nodes	Tender violacious nodules classically on pads of fingers and toes	Immunologic	6.70%
Roth spots	Exudative hemorrhagic lesions with pale centers on retinal exam	Immunologic	3%
Splinter hemorrhage	Nontender linear red marks vertically under nail plate	Vascular (embolic)	39%

Indications for Surgery in Infective Endocarditis			
Heart Failure	**Uncontrolled Infection**	**Prevention of Embolization**	**Prosthetic Valve**

• Refractory pulmonary edema or cardiogenic shock (emergent surgery)
• Persistent heart failure despite medical therapy (urgent surgery)
	• Abscess
	• Fistula
	• Pseudoaneurysm
	• Enlarging vegetation
	• Persistent fever
	• Positive blood cultures despite 7–10 days of appropriate antibiotic therapy
	• Heart block
	• Resistant organisms:
	  ◦ Fungi
	  ◦ Staphylococci
		• Vegetation > 10 mm with embolization (urgent surgery)
		• Vegetation > 15 mm
		• Recurrent embolization events or persistent vegetation despite therapy
			• Patients with prosthetic valve endocarditis and any high-risk features:
			  ◦ Heart failure
			  ◦ Abscess
			  ◦ Persistent fever

- **Nonbacterial thrombotic endocarditis**
  - Seen with SLE, antiphospholipid Ab (clots)
  - Valvular insufficiency is uncommon
  - Tx: anticoagulation, manage disease
- **Prosthetic valve thrombosis**
  - Presents ~ heart failure
  - Need to be adequately anticoagulated= INR 2.5-3.5
- **Myocarditis**
  - Enterovirus coxsackie B → diarrhea/ vomit → chest pain and tachycardia
  - Viral myocarditis → eccentric hypertrophy and decompensated heart failure
    - PVB19, HHV6, Cox, adenovirus, Influenza, HIV
- **Pericarditis**
  - Most common cause is coxsackie, URI, neoplasia, tuberculosis, autoimmune
  - Diffuse PR depression and ST elevation
  - **Friction rub**
  - Next best step: **Echocardiogram** → trend troponins, POC ultrasound, chest radiography to evaluate heart size) → no additional testing needed if uncomplicated pericarditis
  - EKG: diffuse ST elevation with concave upward, improved with leaning forward
  - Tx: oral NSAID + oral PPI (protect from NSAID) + oral colchicine +/- pericardiocentesis and d/c home
    - Reproducible with palpation: costochondritis
    - Vague pain with hx of infection: myocarditis
  - Admission if:
    - Fever, elevated troponins, trauma, anticoagulation treatment, immunosuppression, large effusion, tamponade, subacute course
- **Constrictive pericarditis**

-

Features of constrictive pericarditis	
Etiology	• Idiopathic or viral pericarditis • Cardiac surgery or radiation therapy • Tuberculous pericarditis (in endemic areas)
Clinical presentation	• Fatigue & dyspnea on exertion • Peripheral edema & ascites • ↑ Jugular venous pressure • Pericardial knock may be heard • Pulsus paradoxus • Kussmaul's sign
Diagnostic findings	• ECG may be nonspecific or show atrial fibrillation or low-voltage QRS complex • Imaging shows pericardial thickening & calcification • Jugular venous pulse tracing shows prominent x & y descents

- **Aneurysm (pulsatile mass)**
  - abdominal bruit, femoral artery aneurysm
  - saphenous varices (bruit, not pulsatile)
  - risks= smoking
- **Aortic dissection******
  - acute onset, tearing paint that radiates to the back
  - Chest pain with widened mediastinum on chest x-ray, can present with flank pain **+/- hypovolemic shock**
  - Risk factor is hypertension, Marfan, congenital anomalies, pregnancy
  - Surgical repair for type a descending Arabic dissection. Type B descending aortic dissections are managed medically.
  - Complications are rupture, occlusion, retrograde dissection, cardiac Tamponade
  - Aneurysms greater than 5.5 cm need elective surgical repair
  - Aneurysms less than 5 cm are monitored with serial ultrasound or other imaging
  - Work up: **CTA** (type A or B) shows double lumen
  - **tx**: blood pressure control —> beta blockers (esmolol, **labetalol**), CCBs to reduce cardiac output
    - Prevents advancement of dissection flap, occlusion of branch vessels
    - Lower CO, reduce fluctuations of pulse pressure with alpha blocker or arterial vasodilator to lower MAP
    - Labetalol is nonspecific alpha 1 and beta 1 blocker
  - 2nd line: vasodilator (nitro) to reduce preload, nicardipine, clevidipine
  - Emergency surgical repair
- **Coarctation of aorta**
  - Weakened pulses in UE +/- LE depending on arctation
- **Subclavian steal syndrome**
  - Proximal stenosis of subclavian artery
  - Asymmetric pulses in UE
- **Arrhythmia**
  - A fib= pulmonary v.
  - AVNRT= AV node
  - A flutter= tricuspid isthmus
  - AVRT/ WPW= bundle of kent

- **Valvulopathy**
  - **Murmurs → get an ECHO**
    - healthy adult asymptomatic= transthoracic echo
    - opening snap= mitral stenosis
    - crescendo-decrescendo= aortic stenosis
    - Blowing holosystolic= mitral regurgitation
  - Grade of murmurs *work up if < grade III
    - I: S1S2 > murmur
    - II: S1S2 = murmur
    - III: S1S2 < murmur
    - IV: palpable thrill
    - V: stethoscope ½ off chest
    - VI: without stethoscope

Cardiac Murmurs and Associated Conditions				
Condition	**Location[1]**	**Timing**	**Quality**	**Radiation**
Pulmonary stenosis	Pulmonary	Midsystolic	Harsh	Left shoulder
Aortic stenosis	**Aortic**	**Midsystolic**	**Harsh**	**Carotid arteries**
Ventricular septal defect	Tricuspid	Holosystolic	Harsh	Precordium
Mitral insufficiency	Mitral	Holosystolic	Blowing	Left axilla
Tricuspid insufficiency	Tricuspid	Holosystolic	Blowing	Apex
Aortic insufficiency	Mid-left sternal edge	Early diastolic	Blowing	Sternum
Pulmonary insufficiency	Pulmonary	Early diastolic	Blowing	Sternum
Mitral stenosis	Apex	Late diastolic	Rumbling	None
Tricuspid stenosis	Tricuspid	Late diastolic	Rumbling	None

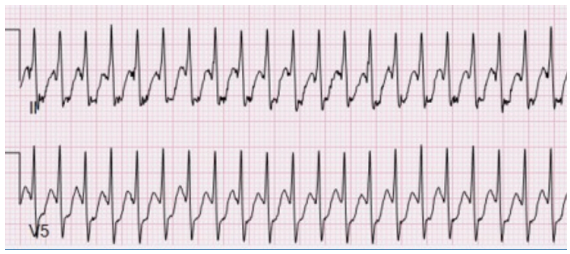
Heart Murmurs	
Systolic	
Mitral Valve Regurgitation	• Holosystolic, high-pitched • Loudest at the apex, radiates to the axilla • Enhanced with squatting and a hand grip
Tricuspid Valve Regurgitation	• Holosystolic, high-pitched • Loudest at the left lower sternal border • Enhanced with inspiration
Aortic Stenosis	• Crescendo-decrescendo systolic ejection • Loudest at the heart base, radiates to the carotids • Decreased with Valsalva
Ventricular Septal Defect	• Holosystolic, harsh-sounding murmur • Loudest at the left lower sternal border • Enhanced with a hand grip
Mitral Valve Prolapse	• Late systolic crescendo with a mid-systolic click • Best heard over the apex • Click occurs earlier with Valsalva or standing
Diastolic	
Aortic Regurgitation	• High-pitched early diastolic blowing decrescendo murmur • Enhanced with a hand grip
Mitral Stenosis	• Opening snap with delayed rumble, late diastolic • Enhanced with expiration
Continuous	
Patent Ductus Arteriosus	• Continuous machine-like murmur • Best heard at the left infraclavicular area

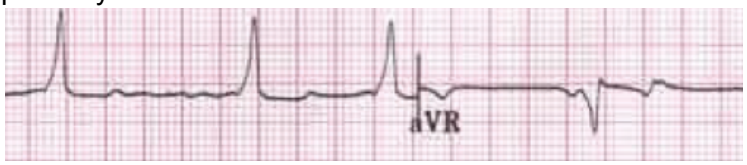
Maneuver	Physiologic Effect(s)	Diagnostic Relevance
Inspiration	• ↑ venous return to right atrium	• ↑ intensity of right heart sounds and murmurs (eg, tricuspid, pulmonic)
Hand grip	• ↑ afterload	• ↑ intensity of mitral regurgitation (MR), aortic regurgitation (AR), and ventricular septal defect (VSD) • ↓ intensity of hypertrophic obstructive cardiomyopathy (HOCM) and aortic stenosis (AS) • Later onset of click and murmur for mitral valve prolapse (MVP)
Rapid squatting	• ↑ venous return • ↑ preload • ↑ afterload	• ↓ intensity of HOCM • ↑ intensity of MR, AR, and VSD • Later onset of click and murmur for MVP
Standing up	• ↓ preload	• ↓ intensity of benign (physiologic) murmurs • ↓ intensity of AS • ↑ intensity of HOCM • Earlier onset of click/murmur for MVP
Valsalva		

- **Aortic stenosis**
  - asymptomatic AS= good

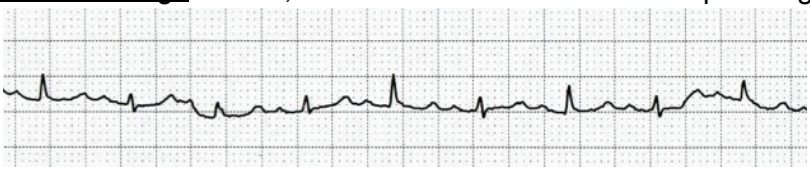
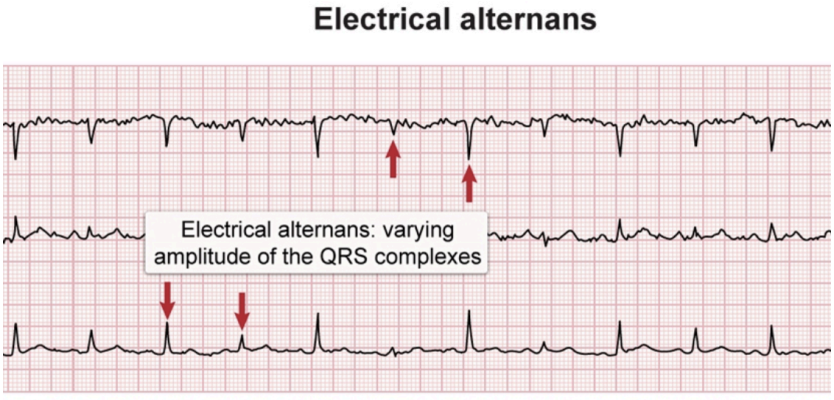
        - serial Echos q 6-12 months
    - symptomatic aortic stenosis= poor 3 year prognosis
        - symptoms: syncope, dyspnea, angina with exertion
        - LVH → long standing → dilation
        - Bicuspid valve; Old men with chest pain, syncope, CHF, due to atherosclerosis and calcium deposition
        - Low volume, slow rising carotid pulse (pulsus parvus et tardus)
        - Single and soft second heart sound; mid-late peak systolic murmur
        - diagnostic: systolic **crescendo-decrescendo** murmur → ECHO
            - valve area < 1, gradient > 40
            - Parvus et tardus
        - tx: valve replacement (if surgical candidates) diuretics, beta blockers
            - balloon valvuloplasty if not good surg candidate
            - percutaneous balloon valvuloplasty
            - palliative care
- **Aortic regurgitation**
    - Weak and floppy aortic valve, more blood stays in heart → dilated CM
    - Due to infection, infarction, aortic dissection
    - Acute: cardiogenic shock, flash pulmonary edema, chest pain
    - Chronic: CHF symptoms, chest pain
    - Widened pulse pressure and eponym parade
    - Dx: diastolic murmur at 2nd ICS on right, rumbling murmur
    - Tx: replacement, refer to cardiothoracic surgery for aortic valve replacement
- **Mitral stenosis**
    - Rheumatic heart disease
    - Younger patients 20-30s with CHF or A fib
    - Dx: rumbling diastolic murmur at apex, **opening snap**
    - Tx: balloon valvuloplasty
    - Complications: LVH, cardiomyopathy, syncope, angina
- **Mitral regurgitation**
    - Fluid builds up in atria → atrial stretch → atrial fibrillation
    - Dx: apex, **holosystolic** murmur, high pitched and blowing
    - Tx: replacement
- **Mitral valve prolapse**
    - Murmur gets better with more blood in heart
    - Loud with valsalva and handgrip, soft with squatting
    - Congenital, seen in young women
    - Mitral regurgitation but better with more blood (leg lift, squatting)
    - Tx: hydration, beta blocker
- **Hypertrophic cardiomyopathy**
    - Due to sarcomere mutation → hypertrophic and obstructive ventricular septum that occludes the outflow
    - Worsened with valsalva
    - Patient is young athlete with SOB, syncope, exertion
    - Dx: systolic murmur, squats make it better, **ECG**
    - Tx: stay hydrated, beta blocker (increase filling time)
- **Dilated cardiomyopathy**
    - S3 heart sound
    - Due to chronic valvulopathy or heart failure
    - Causes: ALCOHOL
- **VSD**

    - Holosystolic murmur with late diastolic rumble in kiddos
    - small= resolves
    - large= surgery (RDS, pulmonary HTN)
- **Tetralogy of fallot**
    - Pulmonary stenosis, overriding aorta, VSD, RVH → right to left shunt with cyanosis
    - Murmur heard relates to VSD = holosystolic murmur at Left lower sternal border
    - Cyanosis in newborn period (blue lips) with eating
- **Transposition of the great vessels**
    - Supplemental oxygen does not correct
    - Cyanosis in 24 hours, single S2
    - Egg on a string
- **Hypoplastic left heart syndrome**
    - Cyanosis, no murmur, single S2
    - Delayed presentation with PDA closes
- **PDA**
    - Continuous machine like murmur
- **ASD**
    - Wide fixed and split S2
    - Ostium secundum defect; ostium primum defect associated with trisomy 21
    - Left to right shunt → relative volume overload → delayed closure of the pulmonic valve
    - Uncorrected → Eisenmenger syndrome due to pulmonary remodeling, PAH and shunt reversal → cyanosis
- **Syncope**
    - Decreased perfusion to the brain
    - POTS (postural orthostatic tachycardia syndrome)
        - hypotension, racing heart, dizzy/ light headed, fainting
        - dx: tilt table test, ECG, Echo
    - Orthostatic hypotension
        - order EKG and BP when sitting and standing
        - Due to decreased baroreceptor sensitivity , arterial stiffness, decreased NE, low sensitivity of myocardium to SNS
- **Palpitations**
    - if occurs during sleep or at work = cardiovascular causes
    - anxiety, panic attacks, drugs
- **Arrhythmias**
    - **Atrial fibrillation**
        - Absent A wave
        - Apixaban does not require frequent lab draws, unlike eliquis/ warfarin
        - Rate control > rhythm control
        - Due to atrial remodeling with electrical activity that arises from pulmonary vein ostia
        - Most common causes of hypertension and coronary atherosclerosis. I SMART CHAP
            - Inflammatory, surgery, medication's, atherosclerosis, rheumatic heart disease/mitral stenosis, they were toxicosis, congenital heart disease, hypertensive disease, alcohol, pulmonary embolism, **AGE**
        - Tx: rate control (beta blockers: propranolol of hyperthyroid), digoxin, CCB (verapamil, diltiazem), electrical or chemical cardioversion with ibutilide

resorts sinus rhythms
    - Unstable: direct cardioversion
    - Stable: beta blocker, diltiazem come over uphill or to Jackson
    - Anticoagulation with warfarin to reduce risk of stroke
    - 
- **Atrial flutter**
    - Regular rate atria 250-300, ventricular rate 125-150
    - F waves
    - 

- **Torsades de pointes**
    - Electrolyte imbalance → Ventricular fibrillation
    - Low K, low Mg, TCA overdose, antipsychotics
    - Tx: IV magnesium sulfate
- **Wolf-parkinson white syndrome**
    - Short PR interval with QRS > 120 with slurred deflection representing early ventricular activation via bundle of kent
    - Ventricular preexcitation syndrome with symptomatic tachycardia, delta wave, short PR interval and prolonged QRS
    - Causes atrial fibrillation
    - Delta waves
    - Tx: cardioversion or antiarrhythmics: procainamide
    - Avoid CCBs, digoxin, beta blockers, adenosine with accessory conduction pathways
    - 

- **Tricuspid regurgitation**
    - Prominent V waves, absent x descent
    - IV drug use and carcinoid syndrome
- **Pericardial effusion**
    - Flattened y descent
- **Atrioventricular block**
    - Cannon A waves= jugular venous pulsation
- **Supraventricular tachycardia**
    - Reentry currant due to 2 conduction pathways thru AV node
        - Fast pathway with long refractory period + slow pathway with short refractory period
    - Narrow QRS, QRST

        - Sudden onset, sudden offset
        - Regular with atrial rate 150-220
        - #1 vagal maneuver, carotid sinus massage, ice water → adenosine
            - Stable: adenosine
            - Unstable: cardioversion
        - 
    - **Ventricular tachycardia**
        - Wide QRS, 3 or more consecutive beats w/ QRS < 120 @ rate > 120
        - Find underlying cause! ELECTROYLTES
        - Tx: stable → amiodarone, lidocaine
        - Tx: Unstable: cardioversion
        - 
    - **Torsades de pointes**
        - Tx: IV Mg (stabilizes the membrane)
    - **Ventricular fibrillation**
        - Defibrillation
    - **Pulseless electrical activity**
        - CPR
    - **Cardiac tamponade**
        - “Enlarged cardiac silhouette with pleural effusion” secondary viral pericarditis , muffled heart sounds → pericardiocentesis
        - Pulsus paradoxus: inspire, decrease preload → systolic pressure drops by 10
        - Electrical alternans, dampened voltage and undulating
        - Kussmaul sign: inhale, JVD increases due to less compliant right heart
        - 
        - 

- Vasculitides
- **temporal arteritis**
    - tx:high dose glucocorticoids
    - dx: temporal biopsy
- **Medications**
    - Amiodarone: monitor TSH, free T4
    - hypo/ hyperthyroid
- EKGs
    - hypokalemia: inverted T waves, u waves
    - Hyperkalemia: peaked T waves
        - CKD missed dialysis, crush injury
    - hypomagnesemia: torsades de pointes

Respiratory

- **Emma Holliday**
    - Suspect PE → heparin!
    - Check O2 sats → give O2 if < 90%
    - If signs of pneumonia → give CXR
    - Pulmonary edema → give nitrates, lasix, morphine
    - Recurrent pneumonia → swallow study
    - Typical pneumonia → amoxicillin
    - Atypical pneumonia → azithromycin
    - Dyspnea → COPD, asthma, interstitial lung disease, pneumonia, anxiety
    - Non-smoker Young person with obstructive lung disease= alpha-1 antitrypsin deficiency
    - Kid with inspiratory stridor when supine, better in prone → **laryngomalacia**
    - Chronic cough + mucopurulent sputum= bronchiectasis → PSEUDOMONAS
    - Smoker with chronic cough, permanent damage to conducting airways = bronchiectasis
    - Decreased diffusion capacity of lung → interstitial thickening, restrictive
    - Decreased FEV1/FVC= restrictive
    - normal/ Increased FEV1/FVC= obstructive
    - Increased PCWP → left heart failure
    - Postoperative lung morbidity → DLCO and FEV1
    - Chronic Lung disease → multifocal atrial tachycardia (hypoxia accentuates P waves)
    - Pulmonary Langerhans:

Pulmonary Langerhans cell histiocytosis is a rare condition that presents with non-specific symptoms in young adults. The most common of these is dyspnea and a nonproductive cough, but the possibilities also include chest pain (often pleuritic), fatigue, weight loss, or fever. Many of these patients will present after incidental findings on a chest radiograph or after a spontaneous pneumothorax. The classical findings on a chest radiograph (which can be diagnostic) are:

1. Ill-defined or stellate nodules (2-10 mm, typically middle and/or upper lobe)
2. Reticular and nodular opacities (typically middle and/or upper lobe)
3. Upper zone cysts (or honeycombing in advanced disease)
4. Normal lung volume
5. Normal costophrenic angle

Infective Pediatric Airway Disorders				
Epiglottitis	**Tracheitis**	**Laryngotracheitis**	**Laryngotracheobronchitis**	**Laryngotracheobronchopneumonitis**

• Drooling
• Airway compromise
• High fever
• Thumbprint sign on x-ray
	• Can present like croup, but with fulminant disease
	• Can have steeple sign on x-ray
	• Usually similar to epiglottitis
	  ◦ Drooling
	  ◦ High fever
		• Barking cough
		• Stridor
		• Viral symptoms (croup)
			• Croup + lower airway inflammation without consolidation
			• Often caused by viruses other than parainfluenza
				• Croup + pneumonia
				• Often a postviral bacterial infection

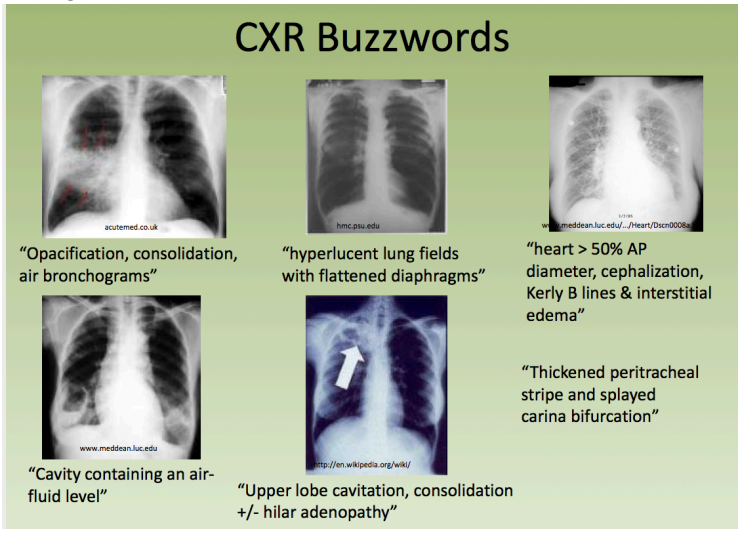
- **Next best step…**
  - Swallow study→ Dysphagia, recurrent pneumonia
  - Bronchoscopy → airway obstruction
  - CT scan of chest → resolution of pneumonia
  - Xray→ primary pulmonary pathology
  - Bronchodilator → Bronchospasm
  - BAL → ID infectious organism in severe/ persistent pneumonia
  - Open lung bx → interstitial lung disease, pulmonary nodule. Mass
  - Sputum AFB → mycobacterial
  - Laryngoscopy and endotracheal intubation → epiglottitis with H flu
  - PET → cancer
  - Diffuse alveolar hemorrhage → Bronchoscopy/ Bronchoalveolar lavage → High dose corticosteroids
  - Pulmonary nodule → < 4 reassure, > 4 work up
    - Compare to CXR, no change in 2 years= done
    - Increased size, no CXR – CT
  - Bloody nose
    - Damage to kiesselbach plexus
    - Compression of nares → anterior nasal packing → silver nitrate cauterization → topical cocaine
  - Pneumonia
    - When to admit. Unstable vitals, elevated urea and confusion

CURB-65	Clinical Feature	Points
C	Confusion	1
U	Urea > 7 mmol/L	1
R	RR ≥ 30	1
B	SBP ≤ 90 mm Hg OR DBP ≤ 60 mm Hg	1
65	Age > 65	1

CURB-65 Score	Risk group	30-day mortality	Management
0 -1	1	1.5%	Low risk, consider home treatment
2	2	9.2%	Probably admission vs close outpatient management
3-5	3	22%	Admission, manage as severe

    -

Bacterial Pneumonia	
Community-acquired	• *Streptococcus pneumoniae* (most common bacterial cause) • *Haemophilus influenza* • *Moraxella catarrhalis* • *Staphylococcus aureus* • Group A streptococci • Aerobic gram-negative bacteria (eg, *Enterobacteriaceae* such as *Klebsiella* spp or *Escherichia coli*) • Microaerophilic bacteria and anaerobes (associated with aspiration) • ***Pseudomonas aeruginosa* (immunocompromised, underlying structural lung disease)**
Hospital-acquired	• Methicillin-susceptible *Staphylococcus aureus* • Methicillin-resistant *Staphylococcus aureus* • *Pseudomonas aeruginosa*
Ventilator acquired	• Methicillin-susceptible *Staphylococcus aureus* • Methicillin-resistant *Staphylococcus aureus* • *Pseudomonas aeruginosa* • *Stenotrophomonas maltophilia* • *Acinetobacter* spp
Atypical	• *Legionella* spp • *Mycoplasma pneumoniae* • *Chlamydia pneumoniae* • *Chlamydia psittaci* • *Coxiella burnetii*

- **Chest x ray**
  - Opacification, consolidation, bronchogram= pneumonia
  - Hyperlucent lung fields, flat diaphragm= COPD
  - Heart > 50% AP diameter, Kerley B lines, interstitial edema= CHF
  - Cavity with air fluid level= abscess (anaerobics)
  - Upper lobe cavitation, consolidation, hilar LN= TB
    - Acute (days)= staph aureus
    - Mechanical heart valve= staph epid
  - Thickened peritracheal stripe and splayed carina bifurcation= Left atrial enlargement, cancer in mediastinal
  - 

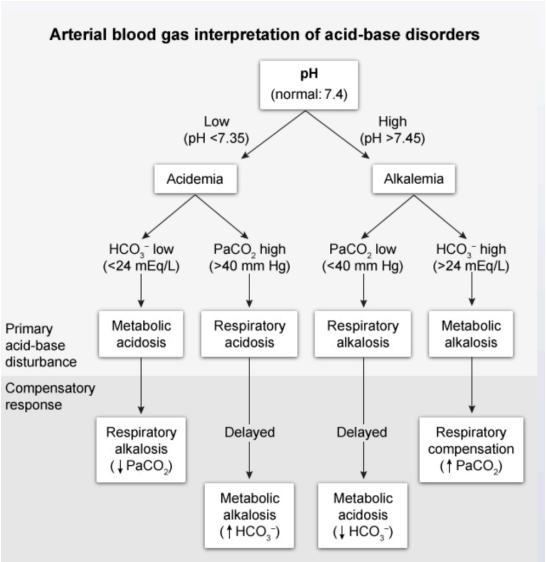
- **Pulmonary nodules**
  - #1 compare to old CXR (new or increasing?)

- Popcorn calcification = hamartoma (most common)
- Concentric calcification= old granuloma
- Good signs:
  - Pt < 40 yo, < 3 cm, well circumscribed
  - Tx: CXR or CT scans every 2 months
- Spicules= bad cancer
  - Risk factors like smoking, > 3cm, eccentric calcification
  - Open lung biopsy to remove nodule
  - Most common in non-smokers: adenocarcinoma
    - Peripheral cancer
    - Mets to liver, bone, brain, adrenal glands
    - Exudative pleural effusion with high hyaluronidase
  - SCC
    - Central tumor, **low PTH, high Ca**
    - **High PTHrp**
    - Paraneoplstic = hypercalcemia due to PTHrp
    - Low PO4 and high Ca
  - Small cell carcinoma
    - Central tumor
    - Superior sulcus syndrome
    - Pancoast tumor ~ horner syndrome
    - Tx: sensitive to chemotherapy, radiation
    - Lambert Eaton Syndrome: ptosis better with 1 minute of muscle contraction
      - Ab to pre-synaptic calcium channels
    - SIADH: old smoker with low Na, euvolemic, high urine Osm
      - Tx: fluid restriction +/- 3% saline in < 112
  - Large cell carcinoma
    - Peripheral cavitation and metastatic
    - Easier to resect

- **ABGs**
  - **ROME: respiratory opposite, metabolic equal**
  - pH: 7.35-7.45
  - PaCO2: 35-45 mmHg
  - HCO3: 21-27 mEq/L
  - PaO2: > 80 mmHg
  - SaO2 > 95%
  - PaO2
    - LOW: COPD, smoker status
    - high: oxygen support

Respiratory acidosis	Low pH High CO2	**Alveolar hypoventilation** - Sedative OD, obesity, brainstem dz, COPD, asthma Causes H+ to shift off albumin, ionized electrolytes bind onto it (causes hypocalcemia) Tx: O2, treat underlying cause Intubation with mechanical ventilation, bronchodilators

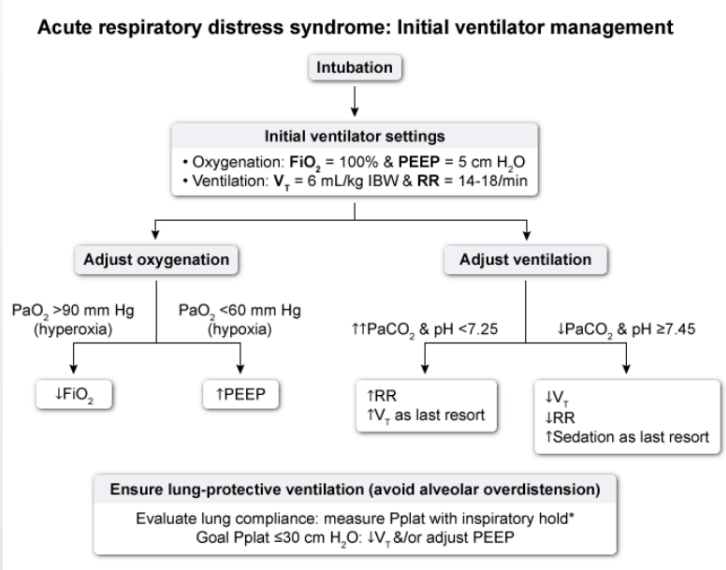
Respiratory alkalosis	high pH Low CO2	Alveolar hyperventilation - Anxiety, PE, pneumonia w/ sepsis, aspirin OD
Metabolic acidosis *calculate anion gap Na + K - Cl Normal = 3-10	Low pH Low HCO3	DKA, lactic acidosis, type 1 RTA, diarrhea Anion gap: lactic acidosis, ketoacidosis, methanol, ethylene glycol, salicylate, uremia MUDPULES= anion gap nonAG= CAGE= (chloride, acetazolamide/ addison disease, GI lises, extra diarrhea, diuretic, RTAs
Metabolic alkalosis	High pH High HCO3 Urine Cl: High- renal problem Low- GI problem	Mineralocorticoid excess, loop or thiazides, milk-alkali syndrome, bicarb ingestion, vomiting Overdiuresis tx: IV K and Cl, fix underlying cause



Etiology of Respiratory Acidosis		
Category	**Etiologies**	**Comments**
Central	Medications	Anesthetics, opioids, sedatives
	Stroke	Brainstem circulation affecting respiratory centers
	Infection	Encephalitis, meningitis
Airway	Obstruction	Impaired ventilation due to decreased airway flow (mucus plug, asthma, mass/tumor)
	Bronchoconstriction	
Parenchymal	Emphysema	Impaired gas exchange at the alveolar-capillary membranes
	Interstitial lung disease	
	Adult respiratory distress syndrome (ARDS)	
	Barotrauma	
Neuromuscular	Myasthenic syndromes	Weakness leading to inability to maintain ventilatory efforts
	Muscular dystrophies	
	Myelopathies	
Structural	Kyphoscoliosis	Anatomical restriction impairing ventilation
Miscellaneous	Obesity	Restriction due to abdominal size, higher incidence of sleep apnea syndromes and obesity hypoventilation syndrome

- **Positioning**
  - Left lateral decubitus- venous embolism (bubble gets stuck in RV)
  - Right lateral decubitus
  - Prone→ prevent atelectasis, improve oxygenation in RDS
  - Supine → arterial embolism to stop clot from going to brain
  - Semirecumbent → Ventilator associated pneumonia
  - Pneumonia
    - Lay side of pneumonia UP, decreases perfusion of poorly ventilated areas and decreases V/Q mismatch
    - Hypoxic pulmonary vasoconstriction = lungs reduce perfusion to affected area, preserve V/Q
  - Dead space ventilation
    - Pulmonary embolism
  -
- **Ventilator settings**
  - Increase PEEP if PaO2 < 60 (recruit more alveoli, improves lung compliance, increases MAP). Best for ARDS
    - Increased PEEP= increased plateau pressure
    - Plateau pressure= elastic pressure + PEEP
      - Increased PP with PTX, pulmonary edema, pneumonia, atelectasis, right mainstem intubation
  - FiO2 is started ASAP and weaned to avoid O2 toxicity
  - Increase TV if PaCO2 is high and acidosis

- Extubation readiness: spontaneous breathing trial
  - pH > 7.25
  - PaO2 > 60
  - Intact inspiratory effort and mental alertness
  - Normal ABG with minimal ventilator settings



- **Pulmonary function tests**
  - https://step2.medbullets.com/pulmonary/120664/pulmonary-function-tests
  - Obstructive: reduced FEV1/ FVC, normal FVC, increased RV, DLCO reduced
    - reversibility= increase in **FEV1 > 12% or 200mL with bronchodilators**
  - Restrictive: normal FEV1/ FVC, reduced FVC, reduced RV

	Obstructive	Restrictive	Mixed
FEV1:FVC	**Reduced** ⩽70%	**Normal** >70%	**Reduced** ⩽70%
FEV1	**Reduced** <80%	Variable	**Reduced** <80%
FVC	**Normal** >80%	**Reduced** <80%	**Reduced** <80%
TLC	**Normal / Increased**	**Reduced** <80%	Variable
RV	**Normal / Increased**	**Reduced**	Variable
DLCO	**Reduced:** emphysema **Normal:** asthma, chronic bronchitis	**Reduced:** parenchymal **Normal:** chest wall / neuromuscular	

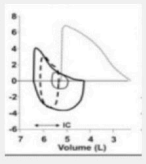
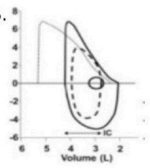
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	Obstructive	Restrictive
Examples	Asthma COPD Emphysema	Interstitial lung dz (sarcoid, silicosis, asbestosis. Structural- super obese, MG/ALS, phrenic nerve paralysis, scoliosis
FVC	↓ <80% predicted	↓ <80% predicted
FEV1	↓ <80% predicted	↓ <80% predicted
FEV1/FVC	↓ <80% predicted	Normal
TLC	↑ >120% predicted	↓ <80% predicted
RV	↑ >120% predicted	↓ <80% predicted
Improves >12% with bronchodilator	Asthma does COPD and Emphysema don't.	Nope
DLCO reduced	Reduced in Emphysema 2/2 alveolar destruction.	Reduced in ILD due to fibrosis thickening distance

-

Differential diagnosis based on DLCO			
	Obstructive pattern (FEV1/FVC <70% predicted)	**Restrictive pattern (FEV1/FVC >70% predicted, FVC <80% predicted)**	**Normal spirometry**
Low DLCO	• Emphysema	• Interstitial lung diseases • Sarcoidosis • Asbestosis • Heart failure	• Anemia • Pulmonary embolism • Pulmonary hypertension
Normal DLCO	• Chronic bronchitis • Asthma	• Musculoskeletal deformity • Neuromuscular disease	
Increased DLCO	• Asthma	• Morbid obesity	• Pulmonary hemorrhage • Polycythemia

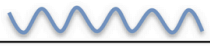
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Pattern	Spirometry Parameters	Flow-Volume Loops	Examples
Obstructive	↓ ↓ FEV_1 ↑ TLC ↓ FVC ↓ FEV_1/FVC ratio ↓ DLCO	A. 	• Chronic bronchitis • Emphysema • Asthma • Bronchiectasis
Restrictive	↓ FEV_1 ↓ TLC ↓ FVC ↔ or ↑ FEV_1/FVC ratio ↓ DLCO	B. 	• Idiopathic pulmonary fibrosis • Sarcoidosis • Hypersensitivity pneumonitis • Interstitial lung disease from collagen vascular diseases

-

- **Oxygen treatment & Critical Care**
  - Room air: 21%
  - nasal cannula: temporary stabilization
  - Venturi mask
  - non rebreather mask: high concentration of O2
  - noninvasive positive pressure ventilation: improves survival and quality of life
  - **PEEP**: improves Oxygenation by recruiting flooded alveoli
    - Reduce shunting. Increase pressure gradient
  - **Mechanical ventilation**
    - Measure airway pressures
      - Peak airway pressure= resistive pressure + plateau pressure
        - Increased PP suggests increased airway resistance
      - Plateau pressure: pressure during inspiratory hold maneuver when pulmonary airfow/ resistance are both 0
      - plateau pressure= elastic pressure + PEEP
    - PCO2 high (hypoventilating) → increase TV and RR
    - PCO2 low (hyperventilation) → increase PEEP and FiO2
- **Respiration patterns**

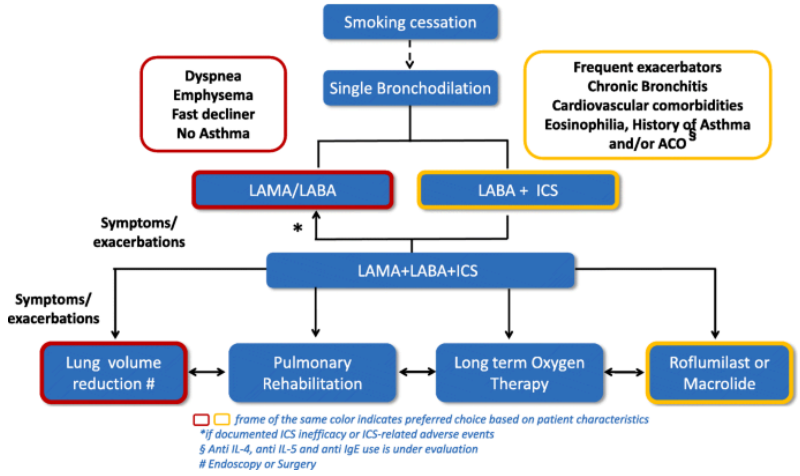
Breathing Patterns

Condition	Description	Causes	Diagram
Eupnea	Normal Respiratory Rate	Normal	
Tachypnea	Increased respiratory rate	Fever Anxiety Shock	
Cheyne-Stokes	Increasing and then decreasing respiratory rate and volume followed by period of apnea	Congestive Heart Failure Brain Stem Injury Central Sleep Apnea	
Biot's	Rapid deep respirations with short pauses	Head Injury Multiple CNS Conditions	
Kussmaul's	Deep Increased respirations	Metabolic (DKA, Renal Failure, etc)	

  - Seesaw respirations : paradoxical respiratory movements by chest wall or respiratory pathology
- **COPD/ emphysema**
  - Obstructive lung disease due to chronic remodeling changes and alveolar destruction and fibrosis —> dyspnea, sputum (white—> yellow-green), cough and wheeze → progressive obstructive expiratory changes
  - history of smoking ** Counsel on smoking cessation
  - Dx: productive cough > 3 mo for > 2 years , FEV1/ FVC ratio DECREASED < 0.7
    - Prognosis: FEV1 is best indicator
    - Reversibility > 12% or 200mL increase in FEV1
    - Once dyspnea sets in, FEV1 reduced by half

Table 2–1 • CLASSIFICATION OF COPD SEVERITY			
Stage	**Classification**	**Findings**	**Treatment**
0	At risk	Cough, sputum production Normal spirometry	Vaccines and address risk factors (exposure to tobacco smoke, occupational dust/chemicals, or smoke from home cooking/ heating fuel)
I	Mild COPD	$FEV_1/FVC < 0.7$ $FEV_1 \geq 80\%$ predicted With or without symptoms	Short-acting bronchodilators
II	Moderate COPD	$FEV_1/FVC < 0.7$ FEV_1 50%-80% predicted With or without symptoms	Long-acting bronchodilators
III	Severe COPD	$FEV_1/FVC < 0.7$ FEV_1 30%-50% predicted With or without symptoms	Inhaled steroids
IV	Very severe COPD	$FEV_1/FVC < 0.7$ FEV_1 <30% predicted FEV_1 <50% predicted with chronic hypoxemia	Long-term oxygen therapy and consider surgical interventions

- **Polycythemia** = low Hct; **Respiratory acidosis**
- Improved mortality: O2 > 18 hours + smoking cessation
  - Smoking cessation leads to least postop pulmonary complications
- WHEN TO START OXYGEN: PAO2 < 88%
- **Tx: STOP SMOKING → SABA → LAMA → LABA → ICS → PDE4 i + Steroids**
  - **Oxygen decreases morbidity and mortality**
  - **Stage 1: Inhaled Albuterol prn, ipratropium, tiotropium (antimuscarinic for bronchodilation);**
  - **Stage 2: + beta agonist (LABA= Salmeterol), theophylline (narrow TD, PDE inhibitor)**
  - **Stage 3 & 4: + Inhaled steroids (fluticasone) + oxygen therapy**
- **Z-pack/ azithromycin:** has antiinflammatory component
- Mucolytic: acetylcysteine for thick secretions
- Methylxanthines (aminophylline, theophylline)= PDE inhibitors → bronchodilation. Used for uncontrolled asthma or severe COPD
- Indication for O2= PaO2 < 55, < 88%, cor pulmonale
- Goal 94-95% bc COPD is chronic CO2 retainers, need hypoxia to drive respirations
- Preventative: Pneumococcus w/ 5 year booster
- Rare cause: alpha-1 antitrypsin deficiency
- Hypertrophic osteoarthropathy= finger clubbing = CANCER → get CXR
  - 
- Increased AP diameter “barrel chest,” flattened diaphragms, increased lucency.
  - acute exacerbation: Abx, bronchodilators, systemic corticosteroids
  - interventions: stop smoking, long-acting BD, ICS, influenza and pneumococcal polysaccharide vaccination
- Mild COPD (I): FEV1 > 80% predicted —> ALBUTEROL Short BD
- Moderate COPD (II): FEV 50-80% —> SALMETEROL long BD (tiotropium)
- Severe COPD (III): FEV1 30-50% —> INHALED ICS

- Very severe COPD (IV): FEV1 < 30% —> long-term oxygen
  - O2% < 88%, PaO2 < 55
- **COPD exacerbation**
  - Wheezing, dyspnea, cough → mechanical ventilation
  - Sputum color changing, increased dyspnea, change from baseline
  - Due to air pollutants > viral or bacterial infection
    - Tx: short acting bronchodilator + systemic steroids (prednisolone)
      - **Abx** (macrolides/ z-pack) and **steroids/ glucocorticoids**, O2 with sats 88-92%
      - NIPPV to keep airway open, increase PEEP, avoid excess O2 → intubation with mechanical ventilation is last step
    - Next steps:
      - Sputum culture: pneumococcus, H. flu, moraxella, klebsiella, pseudomonas
- **Chronic bronchitis**:
  - cough, sputum production most days for at least 3 months, for 2 consecutive years.
- **Emphysema**:
  - SOB due to enlarged respiratory bronchioles and alveoli from destruction of tissue
- 

Acute exacerbation of chronic obstructive pulmonary disease	
Cardinal symptoms	• Increased dyspnea • Increased cough (more frequent or severe) • Sputum production (change in color or volume)
Diagnostic testing	• Chest x-ray: Hyperinflation • ABG: Hypoxia, CO_2 retention (chronic &/or acute)
Management	• Oxygen (target SpO_2 of 88%-92%) • Inhaled bronchodilators • Systemic glucocorticoids • Antibiotics if ≥2 cardinal symptoms • Oseltamivir if evidence of influenza • NPPV if ventilatory failure • Tracheal intubation if NPPV failed or contraindicated

Asthma vs COPD			
	Asthma	**COPD**	**Late-stage COPD**
FVC	Normal/↓	Normal/↓	↓/↓↓
FEV_1	↓	↓	↓↓
FEV_1/FVC	↓	↓	↓↓
Bronchodilator response	Reversible	Partially reversible/ nonreversible	Usually nonreversible
Chest x-ray	Normal	Normal	Hyperinflation, loss of lung markings
DLCO	Normal/↑	Normal/↓	↓

- **Asthma****
  - presents earlier in life, episodic exacerbations that return to baseline
  - viral illness or environmental
  - **Next steps**: methacholine challenge even if PFT is normal
  - Asthma exacerbations → mucus hypersecretion, mucus plug → alveolar collapse, trachea pulled toward side of atelectasis
  - Reversibility of airflow obstruction with bronchodilator (complete reversal FEV1/ FVC > 70%)
  - Serum eosinophils are nonspecific
  - Aspirin related asthma → NSAID avoidance and montelukast
  - Complications: allergic bronchopulmonary aspergillosis

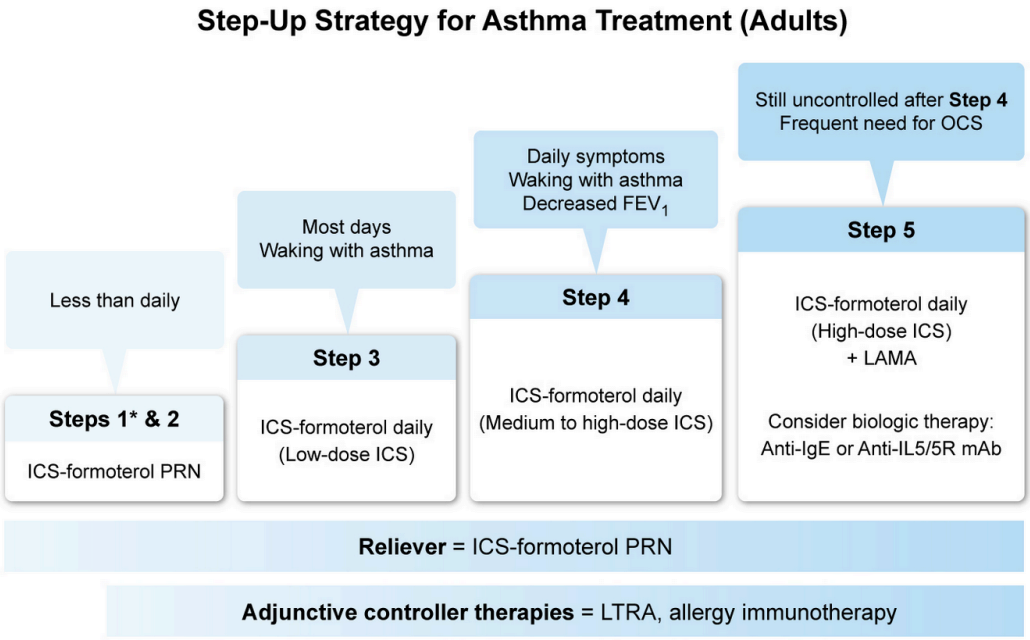
Mild intermittent asthma	2x/ week Normal PFT	Albuterol (rescue inhaler)
mild persistent asthma	4x/ week Normal PFT	Albuterol + inhaled CS
Moderate persistent asthma	Daily symptoms, night cough,	LABA (salmeterol) + ICS

	FEV1 decrease 60-80%	
Severe persistent asthma	Daily symptoms, night cough 4x/ week, FEV1 < 60%	Albuterol +ICS + salmeterol + montelukast and oral steroids , theophylline
Exacerbation	Normalizing PCO2= impending respiratory failure	Inhaled albuterol, PO/ IV steroids Intubation

Asthma Severity Classified by History				
Determinants of Severity	**Intermittent**	**Persistent-Mild**	**Persistent-Moderate**	**Persistent-Severe**
Symptoms	• ≤ 2 days per week	• > 2 days per week but not more than 1 time daily	• Daily	• Throughout the day
Nighttime awakenings	• ≤ 2 times per month	• 3–4 times per month	• > 1 time weekly but not nightly	• Often nightly
Rescue inhaler use	• ≤ 2 days per week	• > 2 days per week but not more than 1 time daily	• Daily	• Several times daily
Limitations on activity	• None	• Minor	• Moderate	• Severe
Lung function	• Normal FEV_1 between exacerbations; FEV_1 > 80% predicted, FEV_1/FVC normal	• FEV_1 > 80% predicted, FEV_1/FVC normal	• FEV_1 > 60% < 80% predicted, FEV_1/FVC reduced 5%	• FEV_1 < 60% predicted, FEV_1/FVC reduced > 5%
Initiation step (for treatment of patients not on current asthma therapy)	• Step 1	• Step 2	• Step 3	• Step 4/5/6

- tx: O2, bronchodilators —> inhaler, steroids —> long acting beta agonist, leukotriene receptor antagonist (montilukast), mast cell stabilizer (inhaled cromolyn
- Give **oral prednisone/ systemic glucocorticoids** for 5-7 days to prevent relapse and decrease need for hospitalization
- ask about baseline O2, prior exacerbations, increased use of oxygen, ever been

intubated



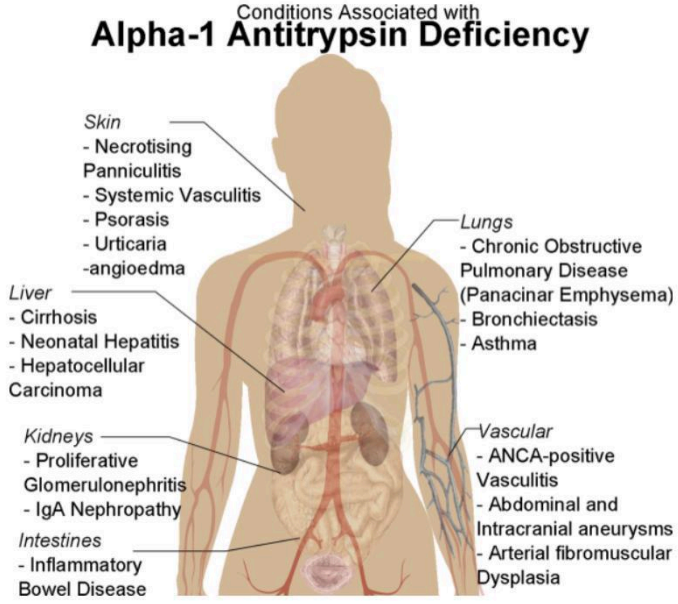
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Classification of Asthma Severity				
Severity	**Intermittent**	**Peristent**		
		Mild	**Moderate**	**Severe**
Symptoms	≤2 days/week	>2 days/week but not daily	Daily	Throughout the day
Nighttime awakenings	≤2 days/month	3 to 4 times/ month	>1 time/week but not nightly	Often 7 times/week
SABA use for symptoms	≤2 days/week	>2 days/week but not daily	Daily	Several times per day
Interference with normal daily activity	None	Minor limitations	Some limitations	Extremely limited

- **Exercise induced bronchoconstriction**
  - Hyperventilation → cooler air triggers mast cell degranulation
  - Decreased exercise tolerance, asthma symptoms
  - > 15% FEV1 decline with exercise
  - ICS and beta agonist (budeside-formoterol)
- **Restrictive lung disease****
  - **Pulmonary fibrosis**
    - Diffuse infiltration
    - Decreased FEV1 and FEV1: FVC ratio > 0.7
  - **Sarcoidosis / Lofgren syndrome**
    - Young AA female, Hilar LN, increased ACE and hypercalcemia
    - Erythema nodosum

        - Macrophages makes Vit D, increased alpha-1 hydroxylase
        - Uveitis conjunctivitis → refer to ophtho
        - Reduced diffusion capacity for carbon monoxide
        - Tx: biopsy, non-caseating granulomas
        - Tx: steroids / glucocorticoids (advanced stage with lung involvement), Hilar LN alone, just expectant management
    - **Silicosis**
        - 1cm nodule in Upper lobes w/ **eggshell calcifications**
        - Increased risk if TB → annual TB test
        - Construction, mining, silica dust, glass production
    - **Asbestosis**
        - "Works as plumber"
        - Most common cancer is bronchogenic carcinoma, mesothelioma
        - Reticulonodular process in lower lobes with pleural plaques
        - Restrictive pattern: decreased FVC, TLC; elevated FEV: FVC ratio
        - Bx: bronchogenic carcinoma >> mesothelioma
    - **Hypersensitivity pneumonitis**
        - Farmer's lung, patchy lower lobe infiltrates, thermophilic actinomyces, hot tubs
        - B/L ground glass and reticular infiltrates with centrilobular nodules
        - Mixed type III and IV
    - **Allergic bronchopulmonary aspergillosis**
        - Aspergillus fumigatus
        - Uncontrolled asthma despite ICS
        - Fixed infiltrate on CXR
        - + antigen skin test, IgE
    - **Invasive aspergillosis**
        - Immunocompromised
        - Neutropenic fever
        - Hemoptysis
        - Halo sign on CXR
        - Tx: voriconazole and echinocandin (caspofungin)
- **Anaphylaxis**
    - Rash, wheezing , hypotension
    - Tx: IM epinephrine → IV epinephrine
    - Endotracheal intubation: upper airway edema
    - IV glucocorticoids also given, takes hours to kick in
- **Tracheomalacia**
    - Shoft tracheal cartilage due to intubation
    - SOB, cough, **expiratory stridor (wheezing) worsene with crying, feeding, coughing**
- **Paradoxical vocal cord motion**
    - Cords close on breathing → obstruction
        - Exercise, cough, acid reflux
- **Cystic fibrosis**
    - Chronic, recurrent respiratory infection
    - Obstructive lung disease
    - Malabsorption of vitamin ADEK, elevated PTT, meconium ileus
    - Due to Cl channel
- **Pneumothorax**
    - Air in pleural space → decreased breath sounds on affected side

    - Tachycardia, tachypnea
    - Associated with barotrauma from mechanical ventilation
    - **Spontaneous PTX**
        - Collapsed lung without tension
        - Occurs out of the blue
        - Dyspnea, pleuritic chest pain
        - Tracheal deviation to ipsilateral side, elevated hemidiaphragm, hyperlucency
        - Elevated JVD
        - Tx: watch and wait if small enough, otherwise perform needle aspiration → thoracostomy with chest tube placement→ pleurodesis
    - **Tension PTX**
        - Hypotension, decreased breath sounds, depressed hemidiaphragm
        - Tx: needle decompression → chest tube
- **Rib fracture**
    - Decreased TV and normal lung compliance
- **Hemothorax**
    - +/-Decreased lung sounds, dullness to percussion
    - Due to trauma, rupture intercostal arteries
    - No JVD
    - Tx: chest tube and drainage
- **Alpha-1 antitrypsin deficiency**
    - PANacinar emphysema
    - young adults with wheezing, pursed lips, intercostal retractions
    - Early emphysema, reduced FEV1
    - Unopposed proteolytic activity due to insufficient inhibition of neutrophil elastase



- **TRALI**
    - transfusion related lung injury
    - SOB, crackles in lungs
- **TACO**
    - Transfusion associated circulatory overload
    - SOB, crackles, decreased EF%, high BNP

- **Acute hypersensitivity pneumonitis**
  - Detailed occupational and exposure history
  - Recurrent URI due to exaggerated immune response
  - Cxr: diffuse reticular interstitial opacities
  - PFT: restrictive pattern
  - Tx: self-resolving
- **Acute respiratory distress syndrome**
  - Hypoxemia associated with diffuse pulmonary infiltrates, can be due to sepsis
  - Increased alveolar capillary permeability → impaired gas exchange, reduced lung compliance
    - Direct: pneumonia (bacterial, viral), contusion, inhalation injury
    - indirect: sepsis, non-thoracic trauma, hemorrhagic shock, burn injury
  - Xray findings
  - Takes hours- days to develop
  -

Acute respiratory distress syndrome: pathogenesis & diagnosis	
Risk factors & pathogenesis	• Direct (eg, pneumonia, inhalation) or indirect (eg, sepsis, pancreatitis, trauma) lung injury • Inflammatory cell activation & ↑ permeability ↔ fluid & cytokine leakage into alveoli
Pathophysiology	• ↓ Lung compliance (alveolar flooding) → ↑ work of breathing • Severe V/Q mismatch (intrapulmonary shunt) → severe hypoxemia • ↑ Hypoxic pulmonary vasoconstriction → ↑ RV afterload & acute PHTN
Diagnosis	• New bilateral alveolar opacities within 1 week of inciting insult • Edema not explained by cardiac failure or volume overload • Hypoxemia with PaO_2/FiO_2 ≤300

- **Pulmonary embolism**
  - Acute hypoxemia
    - Give Heparin!
    - Check O2 sats
  - Hypercoagulable state
  - Pleuritic chest pain, tachypnea, wedge shaped infarct, hemoptysis
  - Pulmonary angiography is gold standard
  - Tx: heparin right away → heparin
  - Surgical thrombectomy if life threatening
  - IVC filter if not on chronic coagulation
  - Workup → V/Q scan, spiral CT

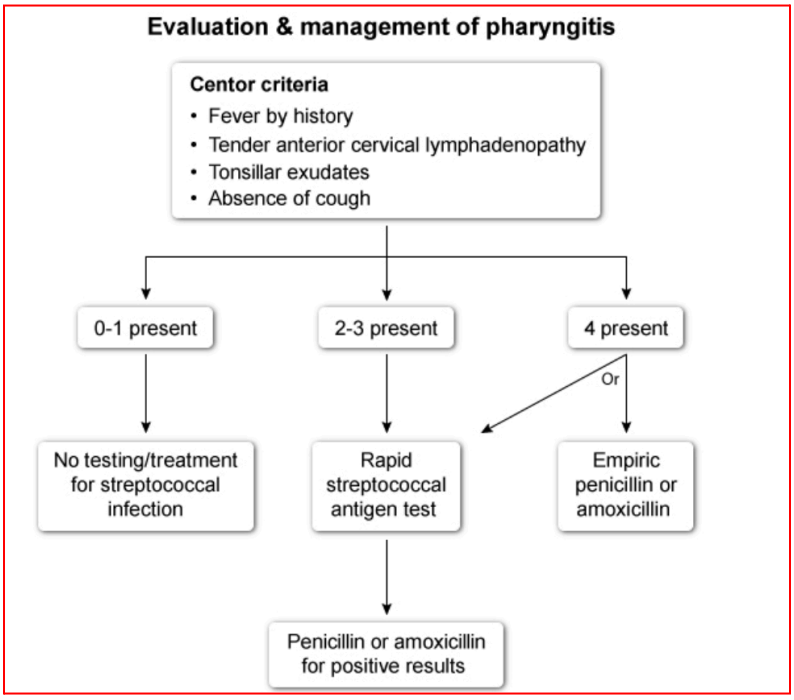
Hemodynamic Changes in Obstructive Shock		
Variable	Cardiac tamponade	Pulmonary embolism or pneumothorax
Left ventricular end diastolic pressure (preload)	↓	↓
Central venous pressure	↑	↑
CO	↓	↓
SVR	↑	↑
Heart rate	↑	↑
PCWP	↑	Normal or ↓

- **Pulmonary hypertension**
  - Due to idiopathic HTN (tx: bosentan, PDE5i; left heart disease (tx: loops and ACE/ ARB); Chronic lung disease/ hypoxemia (tx: underlying lung disease); pulmonary artery obstruction
  - **Hypoxemia** is common mechanism due to COPD→ vascular remodeling, elevated PVR, pulmonary HTN
  - MAP > 25
  - Right ventricular heave
  - secondary to left heart failure
  - treat with loop diuretics (furosemide) and ACEi/ ARB
  - Biopsy: arterial intimal hyperplasia

Clinical features of pulmonary hypertension	
Classification	• Pulmonary *arterial* hypertension (WHO group 1) • Left heart disease (group 2) • Lung disease (eg, COPD, ILD) (group 3) • Pulmonary artery obstruction (eg, CTEPH) (group 4) • Other causes (eg, sarcoidosis) (group 5)
Symptoms	• Dyspnea, fatigue • Exertional chest pain & syncope • Abdominal distension, weight gain
Signs	• Loud P2 • Left parasternal lift, right ventricular heave • Holosystolic murmur of tricuspid regurgitation • JVD, ascites, peripheral edema

- **Idiopathic primary PAH**
  - not due to heart failure
  - tx: bosentan, prostanoids, PDE5 inhibitors
  - normal PCWP
    - Right heart catheterization can tell CHF from pulmonary HTN
- **Pseudoallergic drug reaction**

    - 1st dose drug reaction with shortness of breath, not as severe as true allergic reaction
- **Urticaria**
    - large pruritic red wheals
- **Angioedema**
    - painless deep subQ swelling in facial region
- **Anaphylaxis**
    - hypotension, shock, widespread vasodilation, respiratory distress, bronchospasms, laryngeal edema, GI/ uterine contraction, urticaria and angioedema
    - tx: epinephrine 1:1000 in dose of 0.2 mg SQ or IM
    - ABCs, intubate if unable to breathe
- **Conjunctivitis**
    - self-limited infection of palpebral or bulbar conjunctiva
    - most common eye disease in FM due to bacterial or viral, allergy or chemical irritants
    - Staph, Strep, Haemophilus, moraxella, pseudomonas
    - no vision change or photosensitivity
    - tx: sulfonamide 3x/ day
- **Keratoconjunctivitis (pink eye)**
    - highly contagious, adenovirus
    - associated with URI, preauricular LN
    - red conjunctiva with watery discharge
    - tx: compress, steroids
- **Tonsillitis**
    - Edema of soft palate → airway compromise, spread of infection into deep neck tissue or posterior mediastinum, post strep sequelae
    - **Peritonsillar abscess** → incision and drainage + Abx
        - Muffled voice, drolling
        - Dx: none needed
    - Group A strep most common cause
- **Croup (laryngotracheitis)**
    - 6 month-3 yo kid with barking cough, inspiratory stridor
    - Parainfluenza viral infection
    - Tx: humidified air and corticosteroids
        - Severe: corticosteroids + nebulized racemic epinephrine
- **Allergic rhinitis**
    - asthmatic with chronic nasal congestion
    - swollen nasal turbinates (boggy), pale, blue-gray, watery snot, post-nasal drip
    - findings:
        - “allergic shiners” dark circles under eyes
        - nasal crease (horizontal/ transverse crease along bridge from repeated rubbing)
        - nasal polyps
        - dennie-morgan lines- creases below inferior eyelid
        - cobblestoning of posterior pharynx, tonsillar hypertrophy
        - septal abnormalities
    - IgE mediated inflammation to airborne pathogens, allergen sensitization on mast cells —> histamine, tryptase, kinase, chymase —> LKs and PGD2 → treatment: Nasal budesonide (intranasal corticosteroids)
        - perennial (year round)

        - seasonal
        - occupational
    - tx: antihistamines, decongestants, intranasal steroids
        - 1st line: inhaled corticosteroids (mild-mod; best for long-term management), + antihistamines and decongestants (severe)
            - xs use of topical decongestants cause rebound congestions
            - rebound hyperemia with chronic us or with discontinuation
                - Rhinitis Medicamentosa due to prolonged nasal decongestant use → injured vascular endothelium → rebound congestion, beefy red nasal mucosa → tx: cessation of nasal spray
        - antihistamines: diphenhydramine, hydroxyzine
            - anticholinergic side effects
        - 2nd gen antihistamines: loratidine, cetirizine
            - less sedating
    - Leukotriene inhibitors (zafirlukast, montelukast, zileuton): allergic rhinitis and maintenance of asthma
    - oral corticosteroids
        - peptic ulcer, poor wound healing, reduced bone density
    - desensitization therapy: gradually increased antigen concentration.
- **Pharyngitis**
    - Centor criteria: fever, anterior cervical LN, tonsillar exudates, absence of cough
        - If a lot of symptoms (bacterial)→ do rapid antigen detection test
        - Tx: penicillin
    - 

- **Sarcoidosis**
    - Decreased diffusion capacity for CO, hypercalcemia ACE elevation
    - Increased ALP
    - B/L lymphadenopathy
- **Smoking**
    - #1 cause of preventable death (cancer, cardiac, cerebrovascular, COPD)

- USOSTF recommends screening adults and pregnant patients for tobacco use
- smoking cessation counseling:
  - ask, advise, assess willingness to quit, assist to quit, arrange f/u and support
    - ask about smoking cessation with each encounter. smokers require multiple attempts before quitting
  - nicotine withdrawal: mood changes (anxiety, irritable), difficulty concentrating, increased
- Tx:
  - Bupropion: 7-12 weeks —> 6 months maintenance (dont use if seizure activity)
    - causes insomnia and dry mouth; contraindicated in eating disorders
    - safe in pregnancy , can be used in combination with other nicotine supplement
  - varenicline: partial nicotinic agonist (increase smoking cessation); , nicotine inhaler, patches
    - causes nausea, abnormal vivid dreams
-

- **Upper respiratory illness**

Distinguishing features of common upper respiratory illnesses			
	Viral upper respiratory syndrome	**Influenza**	**Streptococcal pharyngitis**
Onset of symptoms	Slow, stepwise, migratory, or evolving	Abrupt & often dramatic	Variable
Upper respiratory symptoms	Rhinorrhea, coryza, sneezing, mild pharyngitis	Usually mild	Predominantly pharyngeal symptoms
Systemic symptoms	Usually mild	Prominent with possible high fever, myalgias, headache	Variable with possible fever & myalgias
Examination findings	Nasal edema with normal or slightly erythematous pharynx	Variable but often unremarkable	Pharyngeal erythema, tonsillar hypertrophy & exudates, tender cervical lymph nodes

-

- **Pneumonia**
  - sick contacts, immunosuppression (RA or cancer), COPD/ Asthma, alcohol use, loss of consciousness
  - **Chemical pneumonitis**
    - Self-limited inflammatory response, direct pulmonary injury
    - Pregnancy is risk factor
    - Upper lung segments
  - **bacterial pneumonia**: lobar
    - #1 strep pneumonia (macrolide, beta lactam)
    - H. flu: COPD and sickle cell (TMP-SMX, beta-lactam)
    - CAP or HAP

- Anaerobic
  - Poor dentition, foul smelling, lung abscess with air-fluid level
  -

Lung abscess	
Pathophysiology	• Aspiration of oropharyngeal/gingival anaerobes • Risk factors: dysphagia, substance abuse, seizures • Pneumonitis → pneumonia → abscess/empyema
Manifestations	• Subacute fever, night sweats, weight loss • Cough with putrid sputum
Diagnosis	• Cavitary infiltrates with air-fluid levels • Cultures rarely useful
Treatment	• Ampicillin-sulbactam, imipenem, meropenem • Alternate: clindamycin

- **alcoholic: aspiration pneumonia** (gram negative and gram positive); tx: ampicillin, aminoglycosides
  - currant red jelly: klebsiella
- mortality: RR > 30/ min, hypotension, confusion, disorientation, BUN > 20, > 65 yo
- Dullness to percussion and diminished breath sounds
- repeat CXR if superinfection or parapneumonic process

- **Atypical pneumonia**: patchy B/L infiltrates
  - **Legionella**: aerosolized water (macrolides, fluoroquinolones)
    - Urine antigen: serotype 1
    - Culture of transtracheal aspirate is most sensitive
  - **mycoplasma** (macrolides, erythromycin)
    - Teens with Walking pneumonia → Cough, fever, dyspnea, pleuritic chest pain
    - Cold agglutinins (IgM) → hemolytic anemia
    - Mild anemia with normal MCV
    - Erythromycin is 50s ribosomal subunit inhibitor
    -

***Mycoplasma* pneumonia**	
Epidemiology	• Respiratory droplets • Close quarters/young (eg, school, military) • Fall or winter
Clinical	• Indolent headache, malaise, fever, persistent dry cough • Pharyngitis (nonexudative) • Macular/vesicular rash
Diagnostic	• Normal leukocyte count • Subclinical hemolytic anemia (cold agglutinins) • Interstitial infiltrate (chest x-ray)
Treatment	• Usually empiric • Macrolide or respiratory fluoroquinolone

- **Pleural Effusions**
  - **Empyema**: purulent fluid, foul smelling
    - Lower lobe= aspiration = anaerobic
    - Most common CAP= pneumococcal
  - **malignant pleural effusion**
    - Serosanguinous on thoracentesis

        - **Chylothorax**
        - **Light's criteria**

	Light's Criteria	
	Transudate	Exudate
Pleural:Serum Protein	< 0.5	≥ 0.5
Pleural:Serum LDH	< 0.6	≥ 0.6
Pleural fluid LDH	< 2/3 upper limit of normal	> 2/3 upper limit of normal
Main Causes	• Heart failure • Cirrhosis • Nephrotic syndrome • Pulmonary embolism	• Malignancy • Bacterial/Viral pneumonia • Tuberculosis • Pulmonary embolism • Pancreatitis • Esophageal rupture • Collagen vascular disease • Chylothorax/Hemothorax

        -
    - **Bronchiectasis**
        - Pseudomonas, TB, H flu, Staph aureus, MAC
        - Due to repeated inflammation/ infection
        - Dx: atelectasis and scarring, peripheral opacities, mucous plugs
        - Tx: IV abx, antiviral varicella
    - **Viral pneumonia**
        - Rhinovirus > coronavirus, adenovirus
    -

Purulent discharge in addition to mucosal edema and erythema	Bacterial sinusitis
Mucosa is either normal or mildly edematous, and shiny or glassy-appearing, clear nasal discharge	Viral URI
Mild mucosal edema that is boggy and pale or bluish in color as well as clear nasal discharge	Allergic rhinitis

    - **Recurrent pneumonia**
        - Bronchial obstruction, aspiration, immunodeficiency, BOOP
    -

Common causes of recurrent pneumonia	
Same lung lobe*	**Bronchial obstruction** • Extrinsic: neoplasm, adenopathy • Intrinsic: bronchiectasis, foreign body **Recurrent aspiration** • Altered consciousness: seizure, sedatives, antipsychotics, alcohol, illicit drugs • Dysphagia: neurologic disorder, esophageal motility issue • Poor dental hygiene • Gastroesophageal reflux
Different lung lobes	• Immunodeficiency: HIV, leukemia, CVID • Sinopulmonary disease: cystic fibrosis, immotile cilia • Noninfectious: vasculitis, BOOP

- **Pleural effusion**
    - > 1 cm
    - **Transudative** if **LDH < 200, LDH/ serum < 0.6, protein/ serum < 0.5**

        - CHF, nephrotic, cirrhotic
        - Low glucose= RA
        - High lymphocytes= TB
        - bloody= malignancy, PE
    - **Exudative**
        - Parapneumonic, cancer
    - **Transudative**
        - CHF, cirrhosis
    - Complicated if ph < 7.2, gluc < 60, gram + → insert chest tube for drainage
    - **Light's criteria**
        - Exudate
            - High protein, high LDH
        - Transudate
            - Low protein, low LDH
        -

Light's criteria for pleural effusions		
	Transudate	**Exudate**
Protein (pleural/serum)	≤0.5	>0.5
LDH (pleural/serum)	≤0.6	>0.6
	Pleural LDH ≤ two-thirds upper limit of normal serum LDH	Pleural LDH > two-thirds upper limit of normal serum LDH
Common causes	• Hypoalbuminemia (cirrhosis, nephrotic syndrome) • Congestive heart failure • Constrictive pericarditis	• Autoimmune disease • Esophageal rupture • Infection (parapneumonic, TB, fungal, empyema) • Malignancy • Pancreatitis • Post-CABG • PE

- **Tuberculosis**
    - close contact
    - screening: skin tuberculin test or interferon test → CXR
        - 5- 10 mm induration 48-72 hours= positive
        - > 5mm positive in immunocompromised, primary TB, close contact with TB
        - > 10 mm positive in recent immigrants from high risk areas, health care workers, children < 4, homeless, prisoners, alcoholics, DM, IVDA
        - Latent TB= positive screening and negative CXR
            - Start isoniazid
            - Tuberculin test false positive with BCG vaccine
    - Disseminated tuberculosis = caseating granulomas on biopsy
    - Tx: isoniazid daily for 9 months
        - RIPE → idiosyncratic toxicities
        - rifampin= hepatotoxicity, orange/ red fluids, induces CYP
        - isoniazid= hepatotoxicity, inhibits CYP
        - Pyrazinamide= hepatotoxicity
        - Ethambutol= optic neuropathy

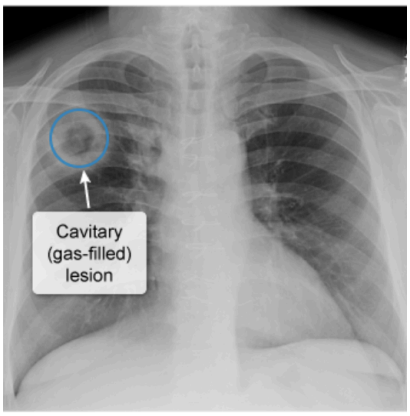
Anti-Mycobacterial Medications			
Drug	**Mechanism of Action**	**Adverse Effects**	**Notes**
Rifamycins (rifampin and rifabutin)	• Inhibits DNA-dependent RNA polymerase	• Hepatotoxicity • Red or orange body fluids • CYP450 inducer • Cutaneous flushing	• Rifabutin has less CYP450 effect, thus favored for HIV patients • Mutations occur due to decreased binding to RNA polymerase • Resistance occurs rapidly if used as monotherapy

Isoniazid	• Inhibits synthesis of mycolic acids	• Hepatotoxicity
		• Inhibits CYP450
		• Drug-induced systemic lupus erythematosus
		• Vitamin B6 deficiency
		  ○ peripheral neuropathy
		  ○ sideroblastic anemia
		  ○ co-administer with pyridoxine (B6) to reduce side effects
			• May be used as monotherapy for prophylaxis and latent TB
			• Mutations occur due to underexpression of enzyme required to convert drug into active metabolite

Pyrazinamide	• Unknown but may work through host phagolysosomes	• Hepatotoxicity • Hyperuricemia • Arthralgias	-
Ethambutol	• Inhibits arabinosyltransferase and disrupts cell wall carbohydrate polymerization	• Optic neuropathy ○ red-green color blindness	• Drug resistance due to increased production of arabinosyltransferase

■

●



○

- **Nocardia**
  - Partially acid fast branching bacteria
  - Tx: TMP-SMX
- **Bacterial sinusitis**
  - Strep pneumonia, H influenza
  - Tx: amoxicillin-clavulanate, doxycycline (if allergic to penicillins)
  - Symptom management: Antihistamine/ analgesic, ipratropium nasal spray, NSAIDS
  - Chronic > 12 weeks, polymicrobial
- **Acute bacterial rhinosinusitis**
  - Infection of paranasal sinuses after > 10 days of URI (cough, congestion, sore throat) → intracranial extension
  - HA, lethargy, vomiting in morning, AMS
  - Next step: CT scan
  - Tx: viral (supportive), bacterial = persistent fever (Abx)
- **Chronic Rhinosinusitis**
  - 2-4 cardinal symptoms: nasal drainage, nasal obstruction, facial pain/ pressure, hyposmia/ anosmia
- **Viral bronchiolitis**

    - < 2 yo with cough and SOB, due to RSV
    - Afebrile, mild wheezes
    - Cxr: increased interstitial markings and peribronchial cuffing, absence of consolidation
    - Tx: supportive
- **ARDS**
    - pneumocytes repair > regeneration —> interstitial lung disease/ fibrosis
    - Inflammation → impaired gas exchange, hypoxia despite increased oxygenation/ PEEP
    - Due to sepsis, gastric aspiration, trauma, ow perfusion, pancreatitis
    - Dx:
        - 1.) PaO2/FiO2 < 200 (<300 means acute lung injury)
        - 2.) Bilateral alveolar infiltrates on CXR
        - 3.) PCWP is <18 (means pulmonary edema is non cardiogenic)
    - Tx: mechanical ventilation, PEEP
        - Oxygenate w/o causing injury to lungs, low tidal volume ventilation
        - Prevent overdistension of collapsed alveoli
        - Low TV can cause mild hypercapnic respiratory acidosis (that is ok)
        - Use NMS blocking agents
        - Increase alveolar recruitment
        - Prone positioning
- **Bronchiolitis obliterans**
    - Chronic inflammation in bronchioles → connective tissue and obstructive lung disease
    - Seen with cardiomegaly
- **Pneumothorax**
    - **Next best step → Chest xray**
    - tension PTX: needle thoracostomy, stab wound
        - need to reduce pressure in thoracic cavity before ABCs
    - hemothorax
    - spontaneous pneumothorax
    - Non Tension Pneumothorax
        - Decompression sickness “the bends” “the chokes”
            - Painful joints after scuba diving, dissolved nitrogen in tissues from rapid ascent
            - Tx: IV fluids, oxygen, hyperbaric oxygen therapy
- **Hemoptysis**
    - infection (TB), lung cancer
    - order CXR —> CT —> Bronchoscopy
- **Pulmonary hypertension**
    - order Echocardiography
-

Health promotion / Disease prevention

- **Health INsurance**

Plan	Available Providers	Payment Details	Specialist/Referrals Choice
Exclusive Provider Organization	Limited, unless emergency care	—	No referral needed
Health Maintenance Organization	Limited, unless emergency care	Denies care that is not evidence-based	Need referral from primary care physician
Point of Service	Can be out of network	Higher co-pays and deductibles if out of network	Need referral from primary care physician
Preferred Provider Organization	Can be out of network	Higher co-pays and deductibles for all services	No referral needed
Accountable Care Organization	Voluntarily enrolled providers	Medicare	Voluntarily enrolled specialist

- **Medicare**
  - Part A: stays in hospital, nursing facility, hospice
  - Part B: doctor feed, medical supplies, outpt care, diagnostic testing
  - Part C: Bundle of A, B, D delivered to private insurance companies approved by medicare
  - Part D: prescription drugs
- **Adult health maintenance visit**
  - purpose of these visits are to identify the patient's health concerns, manage medical conditions, identify risks for future health problems, screening, healthy life-style promotion
    - **Primary prevention**: prevents disease before it occurs
      - Immunizations
    - **secondary prevention:** promotes early detection of disease or condition (mammogram, eye exam, colonoscopy)
    - **tertiary**: therapy and rehab measures once disease is diagnosed
      - screening tests (USPSTF)
        - high prevalence in population, sensitive and specific, cost-effective, acceptable to patients
        - Grade A and B recommendations are offered bc there is high benefit
        - immunoglobulins
    - **Cardiovascular**: Leading cause of death in men
      - Hypertension
      - lipids (men > 35, women < 45 yo, > 20 yo with risk factors)
        - men 45-79: daily aspirin
      - US for abdominal aortic aneurysm AAA (men 65-75 smokers)
        - Men, smokers, HTN
        - < 6cm for men good. > 6 cm bad
          - Expanding 1cm/year is at risk of rupture
          - Surgical evaluation and endovascular repair if > 5.5 cm
    - **Cancer**
      - colorectal cancer (> 50 yo M:F)
        - guaiac test, colonoscopy
      - prostate cancer (PSA or digital exam not recommended)
      - Lung cancer: annual low-dose CT of chest in smokers
      - breast: mammogram, BRCA
        - BRCA screening not indicated for fmhx of endometrial

cancer or breast cancer at advanced stage

- **Psych**
  - depression
  - tobacco use
  - alcohol abuse
- **Immunizations**:
  - **Tdap** booster: every 10 years and in those who did not receive one as an adult
  - pertussis: healthcare workers, childcare providers (grandparents
  - **influenza**: recommended annual
  - **pneumococcal**
    - PPSV-23 and PCV-13 recommended > 65 yo
  - meningococcal:
  - hep A and hep B with risk factors of exposure and chronic liver disease
  - varicella: recommendations for those with no reliable immunization history

Infectious disease

- **High yield**

Causes of Pneumonia by Patient Age	
Age Group	**Common Pathogens***
Birth–20 days	• Group B *Streptococcus* • *Escherichia coli* • *Listeria* species
3 weeks–3 months	• Respiratory syncytial virus • Parainfluenza • Influenza A or B • Adenovirus • *Streptococcus pneumoniae* • **Chlamydia trachomatis** • *Hemophilus influenza*
3 months–5 years	• Respiratory syncytial virus • Parainfluenza • Influenza A and B • Adenovirus • *Streptococcus pneumoniae* • *Hemophilus influenza* • *Streptococcus pyogenes* • *Staphylococcus aureus*
5 years–young adulthood	• Viral pathogens • *Mycoplasma pneumoniae* • *Streptococcus pneumoniae* • *Chlamydia pneumoniae* • *Staphylococcus aureus* (post-influenza pneumonia) • *Streptococcus pyogenes*
*Pathogens are listed in general order of predominance.	

- Community acquired pneumonia → ceftriaxone
- Lyme disease, bulls eye rash, new england= Doxycycline
- Kids with sinus infection= H flu, Moraxella, strep pneumo = amoxicillin clavulanate
- Group A strep → rheumatic fever, sydenham chorea (jerking, hypotonia, behavioral changes), erythema marginatum (pink plaques with serpiginous borders and central clearing)--> penicillin
- Tampon with diffuse rash → Toxic Shock syndrome= staph EXOtoxin, negative blood culture
- Lone star tick → ehrlichiosis → leukopenia, thrombocytopenia, elevated liver labs → doxycycline
- Notify health department for HIV, syphilis, gonorrhea, HSV (reportable diseases)
- Unpasteurized milk= listeria
- EBV= infectious mono= Aspirin
- Parvovirus= severe anemia, slapped checks
- Lice = topical spinosade/ topical pyrethrin → malathion
- Dandruff= selenium sulfide
- Diphtheria= corynebacterium = non-motile, nonencapsulated gram positive

bacillus
- Haemophilus influenza= pleomorphic gram negative coccobacilli
- Group A strep= gram positive diplococci
- Parenteral nutrition infection
  - Infectious risks with parenteral nutrition (PN) include *Staphylococcus aureus*, coagulase-negative staphylococci, aerobic gram-negatives, *Candida* species, and *Malassezia* species. *Candida*
- Typical pneumonia= strep pneumo, h flu, moraxella
  - outpt= amoxicillin
  - atypical= azithromycin
  - inpt= fluroquinolone
  - aspiration= clindamycin (anaerobes)
- HAP= E coli, pseudomonas, staph aureus (VAP in right lower lobe)
  - zosyn/ cefepime= pseudomonas
- HIV
  - Pneumocystis= TMP-SMX
  -

Prophylaxis for HIV Opportunistic Infections			
Infection	**CD4 Count (cells/mcL)**	**Primary Prophylaxis**	**Alternative Prophylaxis**
***Pneumocystis jirovecii* pneumonia**	< 200	TMP-SMX, 1 DS tablet daily	• Atovaquone • Dapsone • Aerosolized pentamidine
Toxoplasmosis	< 100	TMP-SMX, 1 DS tablet daily	• Dapsone + pyrimethamine + leucovorin • Atovaquone suspension ± pyrimethamine (+ leucovorin if pyrimethamine is used)
Mycobacterium avium* complex infection	< 50	Azithromycin, 1200 mg weekly	• Clarithromycin • Rifabutin

- PPD
  - 15 mm < +
  - 10 mm< + (incarcerated, health care worker, immigrant)
  - 5 mm < + HIV, close contact with TB → treat for TB
- PPD+ next step → CXR
  - Cavitations + symptoms: RIPE + B6 2 months → RI for 4 months
  - Negative CXR: isoniazid 6 months
  - BCG vaccine? Still do the work up
- **TB meds**

        - pyrazinamide= uric acid, gout
        - ethambutol= eye problems
        - rifampin= orange fluid
        - isonizid= neuropathy
    - **Meningitis**
        - Strep, H flu, neisseria → tx vancomycin + ceftriaxone
            - Rash = neisseria
        - Kids and elderly= GBS, listeria → ampicillin
            - Long term effect: hearing loss >> seizures
        - HA, fever, nuchal rigidity, kernig and brudzinski sign
    - Malaria
        - Antimalarial Drug Considerations

Drug	Considerations
Primaquine	Never to be used in G6PD deficient patients or in pregnancy
Mefloquine	Causes neuropsychiatric side effects and should not be used in patients with depression or psychosis
Chloroquine	*P. falciparum* is highly resistant
Atovaquone-proguanil	Never to be used in pregnancy or in renal failure
Quinine	Never used in G6PD deficient patients, and may cause thrombotic thrombocytopenic purura or hemolytic-uremic syndrome
Doxycycline	Never to be used in pregnancy and patients should not have prolonged sun exposure

    - **Parasites**
        - Praziquantel → essentially everything
        - Diethylcarbamazine → filariasis (elephantitis)
    - **Viral meningitis**
        - Hsv, echovirus, enterovirus
        - TB= basilar enhancement
        - HSV= temporal lobes
    - **UTI**
        - Tx: TMP-SMX, nitrofurantoin, fluoroquinolones
    - **STI**
        - Chlamydia= doxycycline, azithromycin (eyes)
        - gonorrhea= ceftriaxone
        - Trichomoniasis= metronidazole
        - High risk for co-infection= doxy and ceftriaxone
        - Syphilis
            - Primary
            - Secondary = condyloma accuminata (wart)

Stages of Syphilis			
Stage	**Timing**	**Findings**	**Treatment**
Primary	• 3–90 days post inoculation	• Chancre • Inguinal adenopathy	• 1 dose of penicillin G IM (preferred) • Ceftriaxone • Doxycycline
Secondary	• 2–3 months after chancre	• **Condyloma lata** • Hepatitis • Maculopapular rash (palms and soles) • Malaise, fever, general adenopathy • Meningitis (not tabes dorsalis) • Uveitis	• Same as primary • IV penicillin if meningitis or pregnant (desensitize if allergic)
Latent	• Early (< 12 months) • Late (≥ 12 months)	• No symptoms	• Early: same as primary • Late: 3 doses of penicillin G
Tertiary	• 1–30 years post-infection	• Argyll-Robertson pupils • Ascending aortic aneurysm • Dementia • Focal nervous system deficits or general paresis • Gummas • Tabes dorsalis	• Same as for late latent • IV penicillin if neurosyphilis or pregnant (desensitize if allergy)
IM = intramuscular; IV = intravenous.			

- **Bioterrorism**
  - **Anthrax**
    - Bacillus anthracis, Gram positive rod
    - Spores → cutaneous anthrax (necrotic ulcers), pulmonary anthrax (flu, hemorrhage)
    - Tx: Ciprofloxacin, Doxy, penicillin, clindamycin + anthrax immunoglobins
  - **Botulism**
    - Clostridium botulinum
    - Tx: antitoxin, respiratory support
  - **Brucellosis**
    - Doxy + rifampin
  - **Plague**
    - Yersinia pestis
    - Ulceroglandular disease: sepsis, meningitis, pneumonia
    - Tx: isolation, ciprofloxacin or other fluoroquinolone or streptomycin
  - **Coxiella (Q fever)**
    - Supportive → doxy + hydroxy if chronic query fever
  - Ricin toxin
    - Supportive, charcoal or gastric lavage if ingested
  - **Vaccinia**
    - Small pox
    - Prodrome → vesicular rash outpurse → large pustules

        - Tx: respiratory isolation, antiviral (cidofovir), smallpox vaccine
    - Tularemia
        - Tx: streptomycin, gentamicin (kids), doxy or cipro

Centers for Disease Control and Prevention Bioterrorism Designations			
Parameter	**Category A**	**Category B**	**Category C**
Description	• Easily disseminated or transmissible • High mortality rate • Potential to cause significant public panic and disruption • Requires specialized public-health preparedness	• Moderate ability to disseminate • Moderate morbidity and low mortality rates • Requires enhancement to diagnostic and surveillance capabilities of the Centers for Disease Control and Prevention	• Emerging pathogens that could be disseminated easily based on availability • Ease of production • Potentially high mortality and morbidity rates
Examples	• Anthrax • Botulism • Ebola • Plague • Tularemia • Smallpox	• Brucellosis • Ricin toxin • Query fever • Salmonella • Shigella • Typhus • *Vibrio cholerae*	• Hantavirus • Nipah virus

- **Aspergillosis**

Commonly Used Systemic Antifungal Classes				
Parameter	**Amphotericin B**	**Azoles**	**Echinocandins**	**5-fluorocytosine**
Examples	• Amphotericin B deoxycholate • Liposomal amphotericin B • Amphotericin B lipid complex	• Fluconazole • Voriconazole • Posaconazole • Itraconazole • Isavuconazole	• Caspofungin • Anidulafungin • Micafungin	• 5-fluorocytosine or flucytosine
Side effects	• Nephrotoxicity	• Hepatic toxicity • QT prolongation • Cytochrome P450 changes affect the metabolism of numerous drugs	• Mild hepatic toxicity • Infusion reactions	• Bone marrow suppression • Hepatic toxicity
Pearls	• First-line treatment for mucormycosis • Second-line treatment for most other diseases	• Fluconazole treats most *Candida* species	• Good broad-spectrum antifungals for patients with unknown fungal illnesses	• Not used for monotherapy • Resistance develops rapidly

- **Next step**
    - Needle stick HIV+ → HIV serology, > 3 antivirals
- **Vaccines**
    - Live vaccines contraindicated in immunocompromised
    - Mild illness, low grade fever, Abx therapy, prematurity not contraindications
    - HIV patient → dont give MMR, polio, varicella
        - Pneumococcal and meningeal okay

        - Hepatitis A and B
            - If exposed to HepA + person → HepA vaccine or Ig
        - PCP prophylaxis at CD4 < 200
        - Toxo prophylaxis at CD4 < 100
            - TMP-SMX or Dapsone (sulf allergy)
        - PPD > 5mm, latent TB tx recommended
    - **DTap**- every 10 years with prior Tdap vaccine
    - **23-valent pneumococcal vaccine**= > 65 yo with CHF, renal disease, liver, disease, smokers, diabetes
    - **Influenza**- always recommended
    - **HPV** vaccine- young < 26 yo
    - **Hepatitis vaccines**- liver disease
    -

Killed/Inactivated Vaccines OK for use in immunosuppressed	**Live Vaccines** Generally avoid in immunosuppressed
Influenza	Varicella
Pneumococcal (13 and 23)	Influenza inhaled (intranasal)
Tetanus	Measles
Pertussus	Mumps
Diphtheria	Polio (oral)
Hepatitis A	Rotavirus (oral, injectable)
Hepatitis B	Rubella
Typhoid (injection)	Herpes zoster (zostavax)
Meningitis (ACWY)	Smallpox
Rabies	Typhoid (oral)
Japanese encephalitis	Yellow fever
Tick-borne encephalitis	

- **Meningitis**
    - Lethargic baby with bulging fontanelle
    - Long term complication: hearing loss
    - Most common= strep pneumo, H flu, N meningitidis
        - Tx: high dose steroids → ceftriaxone
    - Close contacts to N meningitidis → rifampin
    - Old and young= listeria
        - Tx: ampicillin
    - Brain surgery= Staphylococcus → tx: vanco
    - TB= RIPE + steroids
    - Lyme= ceftriaxone
    - Streptococcus tx: empiric with steroids; examine for elevtated ICP/ CT, the LP

    - Dx: Lumbar puncture gram stain, WBC > 1000, low glucose
- **Pneumonia**
    - First dx step: CXR
    - Most common: **Strep pneuo**
        - Tx: macrolide, FQ, 3rd gen ceph
    - Most common bug, healthy: **mycoplasma**
        - cold agglutinins IgM;
        - tx: macrolide, QG, doxycycline
    - Hospitalized w/in 3 mo or in hospital > 5-7 days= **H flu**.
        - Tx: 2-3rd ceph
        - Encapsulated, gram negative rod
        - Pseudomonas, klebsiella, E coli MRSA
    - Alcoholics with currant jelly sputum= **Klebsiella.**
        - Tx: w/ 3rd ceph
    - Old men with HA, confusion, diarrhea and ab pain: **legionella**
        - Dx: urine antigen
        - Tx: macrolide, FQ, doxy
    - Flu then pneumonia → **MRSA** → tx: vancomycin
    - Cattle farmer with V/ D → **Q fever. Coxiella burnetii** → tx: doxy
    - Rabbit: **francisella**. Tx: streptomycin, gentamicin
    - Atypical pneumonia, no intracellular organisms on gram stain → **chlamydophila pneumonia**
    - Parrot breeder → **chlamydia psittaci**
    - Kids with bronchiolitis or pneumonia → **RSV**→ **d/c and follow closely**
    - Mild cold, lymphocytosis and coughing up blood= **Pertussis**
    - Asthma or CF with hemoptysis= **allergic bronchopulmonary aspergillosis**
    - Alcoholic, drug abuse, seizure with pneumonia= **aspiration pneumonia** (klebsiella)
- **Antibiotics (**online medEd)
    - Azithromycin= atypical pneumonia
    - Amoxicillin and azithromycin= community acquired pneumonia
    - Streptomycin = tularemia, francisella
    - Penicillin = gram positive Staph aureus
    - Ampicillin + gentamicin= GBS sepsis and E coli
    - Amoxicillin/ clavulanate= polymicrobial, animal bites of skin, aspiration pneumonia
    - Aminopenicillins= amoxicillin-clav, ampicillin-sulb) + beta lactamase inhibitor= gram negatives, Strep
    - Ciprofloxacin = UTI, acute sinusitis, skin infection, abdominal infections
    - Antipseudomonal penicillin= + beta lactamase inhibitor (piperacillin- tazo, tic-sulb)
    - Carbapenems (meropenem)= pseudomonas
    - Monobactams (aztreonam)
    - Nafcillin= soft tissue staph infection
    - Vancomycin= MRSA, C. difficile → Fisaxomicin for refractory cases
    - Clindamycin = MSSA, chlamydia
    - Daptomycin, linezolid
    - Cephalexin, cefazolin (GP)= uncomplicated skin infections, respiratory tract infections, otitis media, bone infections
    - Ceftriaxone (GN)= H influenza (epiglottitis)
    - Cefepime = pseudomonas?

- Metronidazole= gut and vagina
- clindamycin= used everywhere else
- Rules:
  - If sick, go broad. Less Abx resistance
  - Escalate quickly? Add a bunch
  - De-escalate slowly
  - Target cultures + sensitivities
  - Empiric treatment and go down ladder

- **Bacterial**
  - Mayo, cream= Staph aureus
  - B cereus= reheated rice
  - Mahi mahi= scombroid poisoning, serotonin
  - MSSA= nafcillin, dicloxacillin
  - MRSA= vancomycin, doxycycline, linezolid
  - CAP= ceftriaxone, azithromycin (moxifloxacin if beta lactam)
  - HCAP = vancomycin + PipTazo
  - meningitis= vanco, ceftriaxone, steroids, ampicillin if immunocompromised
  - Dog bite= Pasteurella multocida: GN coccobacillus
  - Pharyngitis= strep pyogenes
    - GP cocci
  - tetanus= C. tetani, spore forming rods
  - Immigrated with IFN gamma assay -> CXR to confirm if active or latent infection
  - daycares= shigella
  - watery diarrhea,oysters = vibrio
  - Lyme= borrelia burgdorferi, motile, spiral-shaped spirochetes; ixodes tick
  - legionella
    - legionnaires disease: flue, fever, respiratory symptoms and diarrhea
    - dx: urine sample ag, sputum culture on buffered charcoal-yeast extract
  - gastric ulcer= H pylori
  - UTI=nitrofurantoin (Macrobid) > amoxicillin > levofloxacin if allergic . No ciprofloxacin
    - Complicated cystitis (underlying disease, pregnancy, hospitalization)
      - Urine culture + blood culture needed

Treatment of acute cystitis & pyelonephritis in nonpregnant women	
Uncomplicated cystitis	• **Nitrofurantoin** for 5 days (avoid in suspected pyelonephritis or creatinine clearance <60 mL/min) • **Trimethoprim-sulfamethoxazole** for 3 days (avoid if local resistance rate >20%) • **Fosfomycin** single dose • Fluoroquinolones only if above options cannot be used • Urine culture needed only if initial treatment fails
Complicated cystitis*	• **Fluoroquinolones**** (5-14 days), extended-spectrum antibiotic (eg, ampicillin/gentamicin) for more severe cases • Obtain sample for urine culture prior to initiating therapy & adjust antibiotic as needed
Pyelonephritis	• **Outpatient:** Fluoroquinolones (eg, ciprofloxacin, levofloxacin) • **Inpatient:** Intravenous antibiotics (eg, fluoroquinolone, aminoglycoside ± ampicillin) • Obtain sample for urine culture prior to initiating therapy & adjust antibiotic as needed

        - **Pyelonephritis**= ceftriaxone IV, ciprofloxacin oral
        - **Cellulitis**
            - Staph= clindamycin, vancomycin
            - Strep= amoxicillin, ceftriaxone
- **Buzzwords**
    - Rash @ wrists, ankles, fever and HA, high liver enzymes, low platelets= **Rickettsia (rocky mountain spotted fever)**
        - Tx: doxycycline / tetracycline
    - Target rash, fever, VII palsy, meningitis, AV block= lyme disease
        - Tx: amox < 8, heart or CNS diseases= IV ceftriaxone
    - Tick bite, no rash, fever, HA, dec PLTs and WBC, increase ALT
        - Ehrlichiosis
        - Morulae intracellular inclusion
    - Immune suppressed, cavitary lung, weight loss
        - Gram + branching partially AF= nocardia
        - Tx: TMP-SMX
    - Neck or face infection with draining yellow material
        - Sulfur granules
        - Gram + anaerobic branching= actinomyces
        - Tx: high dose PCN for 6-12 weeks
    - Ringing in ears
        - Viral labyrinthitis → steroids
        - Tx: meclizine
    - Oily, foul stool after swimming
        - Giardia
        - Tx: #1 tinidazole, nitazoxanide → metronidazole, paromomycin

- **Salmonella vs Shigella**
    - H2S, black precipitates= salmonella
        - peanut butter, undercooked chicken, produce

        - fever, bloody diarrhea, cramps 8-72 hours after infection
    - **Shigella dysenteriae**
        - Aerobic, glucose fermenting, GNR
        - Highly contagious
        - Severe infection, high fever, abdominal pain, tonic-clonic seizures
        - Bloody and mucous diarrhea
    - **Typhoid fever**= much more severe
        - Chills, diaphoresis, anorexia, dry cough, dull frontal HA, myalgias
    -

Salmonella Characteristics		
Characteristic	**Non-Typhoidal Salmonella**	**Typhoidal Salmonella**
Organisms (most common)	*Salmonella enterica* typhimurium *Salmonella enterica* enteritidis	*Salmonella enterica* Typhi *Salmonella* Paratyphi
Epidemiology	Contaminated food including eggs, fresh produce, meats, nuts, and spices Contact with reptiles, amphibians, or poultry	Contaminated food or water, typically in unvaccinated individuals that travel to endemic regions.
Onset	8-72 hours following exposure	5-21 days after exposure
Clinical manifestations	Gastroenteritis: diarrhea, nausea, vomiting, fever, abdominal cramping	Enteric fever (also called Typhoid fever): fevers, chills, salmon-colored rash ("rose spots"), bradycardia, constipation or diarrhea, hepatosplenomegaly
Complications	Usually self-limited	Sepsis, intestinal bleeding, chronic carriage, death

- **Botulism**
    - Clostridium botulinum inhibits <u>presynaptic Ach release at NMJ</u>
    - B/L cranial neuropathy, facial weakness, symmetric descending muscle weakness, diaphragm weakness
    - SNARE protein cleaved → prevents fusion of vesicles that contain Ach with presynaptic membrane and inhibits Ach release.
    - Symmetric, descending muscle weakness, diaphragm weakness with respiratory failure.
    - dx : toxin analysis
    - Tx: equine serum heptavalent botulinum antitoxin
- **Parasites**
    - **Entamoeba histolytica**
        - Bleeding > 2 weeks, amebic abscess, fever, RUQ pain
        - Complications: pleural effusion, rupture
        - Dx: stool PCR
            - Drainage recommended for pyogenic bacterial liver abscess
        - Tx: metronidazole + intraluminal abx
    - **Liver flukes**
        - Clonorchis sinensis, Diphyllobothrium latum
        - Causes biliary disease
    - **Fish tapeworms**
        - Megaloblastic anemia, B12 deficiency
    - **Taenia solium**
        - Pork, tapeworm eggs → cysticercosis
    - **Echinococcus granulosus (dog tapeworm)**
        - Farmer with complex liver cysts w/ septations
        - Tx: albendazole, percutaneous therapy > 5 septation, surgery
- **Meningitis**

Bacterial meningitis		
Risk group	**Common organisms**	**Empiric antibiotics**
Age 2-50	*Streptococcus pneumoniae, Neisseria meningitidis*	Vancomycin + 3rd-generation cephalosporin
Age >50	*S pneumoniae, N meningitidis*, *Listeria*	Vancomycin + ampicillin + 3rd-generation cephalosporin
Immunocompromised	*S pneumoniae, N meningitidis*, *Listeria,* gram-negative rods	Vancomycin + ampicillin + cefepime
Neurosurgery/penetrating skull trauma	Gram-negative rods, MRSA, coagulase-negative *staphylococci*	Vancomycin + cefepime
• 3rd-generation cephalosporins: ceftriaxone or cefotaxime • Alternatives to cefepime: ceftazidime or meropenem • Alternative to ampicillin: trimethoprim-sulfamethoxazole for *Listeria*		

- Tx: Ampicillin, cefepime, vancomycin, dexamethasone
  - 3rd gen cephalosporin penetrates BBB
  - vancomycin: strep pneumoniae coverage
  - Dexamethasone
- **Neisseria Meningitidis**
  - meningitis + petechial rash in college student +/- splenectomy
  - Long term neurological deficit: hearing loss
  - Rifampin (DNA dependent RNA polymerase) prophylaxis —> causes red-orange body fluids
  - ceftriaxone: beta-lactam inhibits cell wall production
  - ciprofloxacin (fluoroquinoline, inhibits DNA gyrase)
  - Dx: fibrinogen → DIC
- **STDS**
  - **Gonorrhea**
    - Pustular rash, polyarthralgia, tenosynovitis
    - Dx: NAAT of urogenital site
  - **Syphilis**
    - Treponema pallidum
    - Dx: DFA
    - Ulcerative chancre → Fever and rash → symmetric, maculopapular on trunks, extremities, palms and soles → secondary and tertiary with systemic involvement
    - Neurosyphilis, argyll-robertson pupil
    - Tx: Penicillin G

Syphilis treatment		
Stage	**First line**	**Alternate**
Primary (chancre)	Penicillin G IM × 1	Doxycycline × 14 days
Secondary (diffuse rash)		
Early latent (asymptomatic)*		
Late latent (asymptomatic)*	Penicillin G IM × 3	Doxycycline × 28 days
Tertiary (eg, CV, gummata)		
Neurosyphilis (eg, meningitis, ocular)	Penicillin G IV × 10-14 days	Ceftriaxone IV × 14 days**
Stages of Syphilis			
Stage	**Timing**	**Findings**	**Treatment**
Primary	• 3–90 days post inoculation	• Chancre • Inguinal adenopathy	• 1 dose of penicillin G IM (preferred) • Ceftriaxone • Doxycycline
Secondary	• 2–3 months after chancre	• **Condyloma lata** • Hepatitis • Maculopapular rash (palms and soles) • Malaise, fever, general adenopathy • Meningitis (not tabes dorsalis) • Uveitis	• Same as primary • IV penicillin if meningitis or pregnant (desensitize if allergic)
Latent	• Early (< 12 months) • Late (≥ 12 months)	• No symptoms	• Early: same as primary • Late: 3 doses of penicillin G
Tertiary	• 1–30 years post-infection	• Argyll-Robertson pupils • Ascending aortic aneurysm • Dementia • Focal nervous system deficits or general paresis • Gummas • Tabes dorsalis	• Same as for late latent • IV penicillin if neurosyphilis or pregnant (desensitize if allergy)
- **Chlamydia**
  - Recurrent dysuria, chronic prostatitis
  - Negative urine culture
  - Tx: azithromycin, doxy
- **Haemophilus ducreyi**
  - Painful genital ulcerations
- **HSV**
  - Small vesicular and ulcerative lesions

- **Viral**
  - Filovirus
    - Dengue and marburg virus

        - Transmitted by mosquito
    - Ebola
        - Transmitted by direct contact with bodily fluids
    - Hepatitis
        -

	HBsAg	HBeAg	IgM anti-HBc	IgG anti-HBc	Anti-HBs	Anti-HBe	HBV DNA
Acute HBV							
Early phase	+	+	+				+++
Window phase			+				+
Recovery phase				+	+	+	Likely +
Chronic HBV carrier	+			+			
Acute flare of chronic HBV	+	Likely +	+	+			+
Vaccinated for HBV					+		
Immune due to natural HBV infection				+	+		

anti-HBc = hepatitis B core antibody; **anti-HBe** = hepatitis B e antibody; **anti-HBs** = hepatitis B surface antibody; **HBeAg** = hepatitis B e antigen; **HBsAg** = hepatitis B surface antigen; **HBV** = hepatitis B virus.

    - **Herpes zoster**
        -

Classification of herpes zoster pain		
Pain	**Timeframe**	**Treatment**
Acute herpetic neuralgia	Persists ≤30 days from rash onset	NSAIDs, analgesics
Subacute herpetic neuralgia	Persists >30 days but resolves within 4 months of rash onset	NSAIDs, analgesics
Postherpetic neuralgia	Persists >4 months from rash onset	Tricyclic antidepressants, gabapentin, pregabalin

        - **Acute shingles** → valacyclovir
        - **Postherpetic neuralgia > 4 months** → gabapentin, TCA, pregabalin
            - Not associated with viral replication
    - **HIV/ AIDS******
        - Patient who travels a lot for work, sex with many strangers
        - Acute retroviral syndrome: 2-3 weeks s/p exposure but 3 weeks before seroconversion (LN, fever, fatigue, HA, pharyngitis)
        - Young patient with new b/L bells palsy
        - Unexplained thrombocytopenia and fatigue, weight loss > 10%
        - Thrush, multidermatomal zoster, Kaposi sarcoma

CD4 count	Opportunistic infection
<500	Tuberculosis, Bacterial pneumonia, Heroes zoster, Oropharyngeal, Candidiasis, Non Typhoid Salmonelosis, Kaposy sarcoma, Non Hodgkin lymphoma
<200	Pneumocystic Jirovecy Pneumonia, Cronic Herpes Simplex Ulcer, Oesophageal Candidiasis, Isospora Belli Diarrhea, HIV wasting syndrome, HIV Associated dementia
<100	Cerebral Toxoplamosis, Cryptococal meningitis, Cryptospordiasis, Microspordiasis, Cytomegalovirus infection and disseminated *Mycobacterium avium* complex Progressive multifocal leucoencephalopathy
<50	Cytomegalovirus infection, *Mycobacterium avium* complex (mac), Toxoplasmodium gondi

- Tx: HAART
  - CD4 < 350
  - VIRAL > 55,000, preggo > 1000
  - GI, leukopenia, macrocytic anemia= Zidovudine
  - Pancreatitis, peripheral neuropathy= didanosine
  - Sensitivity rash= Abacavir
  - nephrolithiasis= indinavir
  - Sleepy confusion= efavirenz
  - Post-exposure prophylaxis
    - AZR, lamivudine and nelfinavir for 4 weeks
- **Vaccine and prophylaxis for HIV**
  - Vaccines if CD4 > 400
  - Abx prophylaxis: TMP-SMX
  - CD4 > 500 -350= no prophylaxis
  - CD4 < 250= PCP ⇒ TMP-SMX or Dapsone or atovaquone
  - CD4 < 100= TOXO⇒ Pyrimethamine + leucovorin
    - + toxo serology= tmp-smx
  - CD4 < 50= MAC prophylaxis⇒ **Azithromycin** (not recommended)
  -
- **PCP**
  - B/L diffuse symmetric interstitial infiltrate, elevated LDH
  - CXR → bronchoscopy w/ BAL
  - Dx: methenamine silver, Beta-d-glucan, increased serum LDH
  - Tx: TMP/SMX → Dapsone, primaquine- clinda, pentamidine
    - also used to treat staph aureus
  - Steroids when PaO2 < 70, A-a gradient > 35
  - Prophylaxis CD4 < 200= TMP-SMX →Dapsone, Atovaquone, pentamidine (if G6PD deficient(
- **Colitis**
  - **Cryptosporidium**
    - severe watery diarrhea + fever < 50
  - **Microsporidia**
    - Watery diarrhea, no fever

        - Oocysts acid fact
    - **MAC**= watery diarrhea, high fever < 50
        - Azithromycine weekly
    - **CMV**= hematochezia, low fever → < 50
        - Dx: colonoscopy/ biopsy
    - **Kaposi** = hematochezia, no fever
    -

Common causes of diarrhea in patients with AIDS		
Organism	**CD4 count**	**Symptoms**
Cryptosporidium	<180/mm^3	• **Severe watery diarrhea** • Low-grade fever • Weight loss
Microsporidium/*Isosporidium*	<100/mm^3	• Watery diarrhea • Crampy abdominal pain • Weight loss • **Fever is rare**
Mycobacterium avium complex	<50/mm^3	• Watery diarrhea • **High fever (>39 C [102.2 F])** • Weight loss
Cytomegalovirus	<50/mm^3	• **Frequent, small-volume diarrhea** • **Hematochezia** • **Abdominal pain** • Low-grade fever • Weight loss

- **Esophagitis**
    - **Candida**: oral fluconazole (give systemic) for 3-5 days
        - Common cause of dysphagia + LN
    - **CMV**
        - EGD confirm dx
        - Tx: IV ganciclovir
            - Multisystem infection → foscarnet
- **Neurologic signs**
    - Multiple ring enhancement: TOXO
        - Pyrimethamine sulfadiazine + folic acid 6 weeks → biopsy CNS lymphoma
    - One ring enhancing lesion
        - CNS lymphoma
        - EBV infection of B cells
        - Tx: HAART
    - **HIV-associated dementia**
        - Long standing untreated HIV
        - Apathy, attention impairment, subcortical motor symptoms
    - **HSV encephalitis**
        - Deja Vu aura with 500 RBCs in CSF, elevated proteins and lymphocytes
        - HSV encephalitis in temporal lobe
        - Tx: acyclovir
    - **Meningitis**
        - **Cryptococcus** + india ink
        - AIDS associated cryptococcal meningoencephalitis
        - Work-up: CT
        - Dx: lumbar puncture

        - Tx: **amphotericin B** IV 2 weeks → **fluconazole** maintenance
    - **PML (progressive multifocal leukoencephalopathy)**
        - Hemisensory loss, visual impairment, babinski
        - , JC virus demyelination grey-white jxn
        - Brain biopsy is gold standard
    - **Memory problems and gait disturbance**
        - AIDS-dementia complex
        - Serum, CSF, MRI to r/o treatable causes
    - **Cryptococcus**
        - Amphotericin B
- **Neutropenic fever****
    - Never do rectal exam bc can cause bacteremia
    - Cancer patient, immunosuppressed with fever and pancytopenia
    - Temp > 101/3
    - Abs PMN > 500
    - Mucositis, chemo causes bacteremia
    - 1st get blood culture → start 3-4th gen cephalosporin (ceftazidime, **cefepime**)- need to cover pseudomonas
        - Piperacillin- tazobactam, meropenem, imipenem-cilastatin- need **pseudomonas coverage**
        - Add vanco if line infection or if septic shock develops, MRSA
        - Add ampho B is no improvement (possible fungal infection)
        - If mouth lesions, add fluconazole for candida
        - Add acyclovir for HSV coverage
- **Severe systemic fungal infections**
    - IV amphotericin B
- **Bacillary angiomatosis**
    - Homeless, lice, cats
    - HIV CD4 < 100
    - Vascular cutaneous lesions, fever, organ involvement, liver lesions
    - Fever, weight loss, exophytic masses
    - Tx: HAART, doxycycline, erythromycin
- **Histoplasmosis**
    - Disseminated → tx: amphotericin B

Vaccines for adults with HIV	
Vaccine	**Indications**
HAV	• Chronic liver disease (including HBV & HCV) • Men who have sex with men • IV drug users
HBV	• All patients without documented immunity to HBV
HPV	• All patients age 11-26
Influenza	• Annually for all patients (inactivated formulation)
Meningococcus (serogroups A, C, W, Y)	• All patients age 11-18 • Large groups living in close proximity (eg, college students, military recruits, incarcerated individuals) • Asplenia or complement deficiency
Pneumococcus	• PCV13 once • PPSV23 8 weeks later, 5 years later & at age 65
Tetanus, diphtheria & pertussis	• Tdap once (repeat with each pregnancy in women) • Td every 10 years
Live vaccines (eg, MMR, varicella-zoster) are contraindicated if $CD4^+$ cell count <200/mm^3	

Opportunistic infections in HIV		
Infection	**CD4 cell count**	**Prophylaxis**
Pneumocystis jirovecii	• <200/mm^3 **OR** • Oropharyngeal candidiasis **OR** • History of PCP infection	Trimethoprim-sulfamethoxazole **Alternate therapies:** • Dapsone • Atovaquone • Pentamidine
Toxoplasma gondii	<100/mm^3 & positive IgG antibody	Trimethoprim-sulfamethoxazole **Alternate therapies:** • Dapsone **plus** pyrimethamine **plus** leucovorin • Atovaquone ± pyrimethamine **plus** leucovorin
Histoplasma capsulatum	<150/mm^3 & endemic area	Itraconazole
VZV	Close contact with person with chickenpox or shingles & no history of prior disease or negative antibody to VZV	VariZIG or IVIG administered within 4 days of exposure

- **Tetanus**
  - Patients who have not received updated tetanus every 10 years should be vaccination with Tdap
  - Tetanus IG best for Uncertain vaccine status with severe wound
Tetanus prophylaxis		
	Clean or minor wound	**Dirty or severe wound**
≥3 tetanus toxoid doses	• Tetanus toxoid-containing vaccine* only if last dose ≥10 years ago • **No** TIG	• Tetanus toxoid-containing vaccine* only if last dose ≥5 years ago • **No** TIG
Unimmunized, uncertain, or <3 tetanus toxoid doses	• Tetanus toxoid-containing vaccine* only • **No** TIG	• Tetanus toxoid-containing vaccine* **PLUS** • TIG
*Booster given as tetanus/diphtheria (Td) toxoids adsorbed or tetanus toxoid/reduced diphtheria toxoid/acellular pertussis (Tdap)		
- **Tuberculosis**
  - Symptomatic TB→ CXR
  - Screening:
    - > 15mm, > 10mm in prison, healthcare, nursing home, DM, etOH,

chronically ill, > 5mm AIDS, immunosuppressed
        - If PPD+ → CXR
        - If CXR+ → do AFB on sputum
        - If AFB + → RIPE for 6 months (12 months for meningitis, 9 months if pregnant)
        - Chemoprophylaxis (INH for 6 month) for kiddos < 4 exposed to TB
    - **RIPE therapy**
        - **Rifampin**: DNA dependent RNA polymerase, induced CYP450→ red orange secretions
        - **Isoniazid**: KatG ⇒ rash, B6 depletion, peripheral neuropathy and sideroblastic anemia
        - **Pyrazinamide**: proton transmembrane → hepatotoxicity, hyperuricemia
        - **Ethambutol**: inhibits arabinosyl transferase → optic neuritis (red and green color vision)

Tuberculosis Drug Treatment

Drug	Mechanism	Resistance	Toxicity
Rifampin	Inhibits DNA-dependent RNA polymerase	Efflux pump activation	• CYP induction • Red-orange secretions • Hepatotoxicity (esp. when combined with other hepatotoxic drugs)
Isoniazid	Activated by KatG to prevent the synthesis of mycolic acids, which are required for cell walls	• Mutations in *katG* gene • Efflux pump activation	• Peripheral neuritis (prevented with concomitant vitamin B6) • Lupus-like rash (esp. in slow acetylators) • Hepatotoxicity
Pyrazinamide	Pyrazinoic acid formation collapses the transmembrane proton motive force and inhibits enzyme function	Efflux pump activation	• Hepatotoxicity • Hyperuricemia • Should not be used in pregnancy
Ethambutol	Inhibits arabinosyl transferase to stop cell wall production	• Efflux pump activation • Possibly mutations in *embB* genes	Optic neuritis

- **Yeast/ fungus**
    - **Sporothrix***
        - Decaying plant matter, landscaper / gardener
        - Inoculation → papule → ulceration, nonpurulent odorless drainage → proximal lesions along lymphatic chain
        - Dx: cultures/ biopsy or aspirate → cigar shaped yeast with narrow based budding
        - Tx: itraconazole
    - **Mucormycosis**
        - Diabetics, ketoacidosis, malignancy, stem cell transplants
        - Acute, aggressive nasal congestion with necrotic, purulent discharge
        - Rhino-orbital-cerebral mucormycosis
        - Tx: surgical debridement, amphoB
    - **Histoplasmosis**
        - Asymptomatic pulmonary infection
        - Immunocompromised may develop skin lesions
        - Ohio-river valley
    - **Blastomyces**
        - Wart-like lesions, violaceous nodules, skin ulcers
        - Osteomyelitis, prostatitis, orchitis
        - Mild pulmonary disease

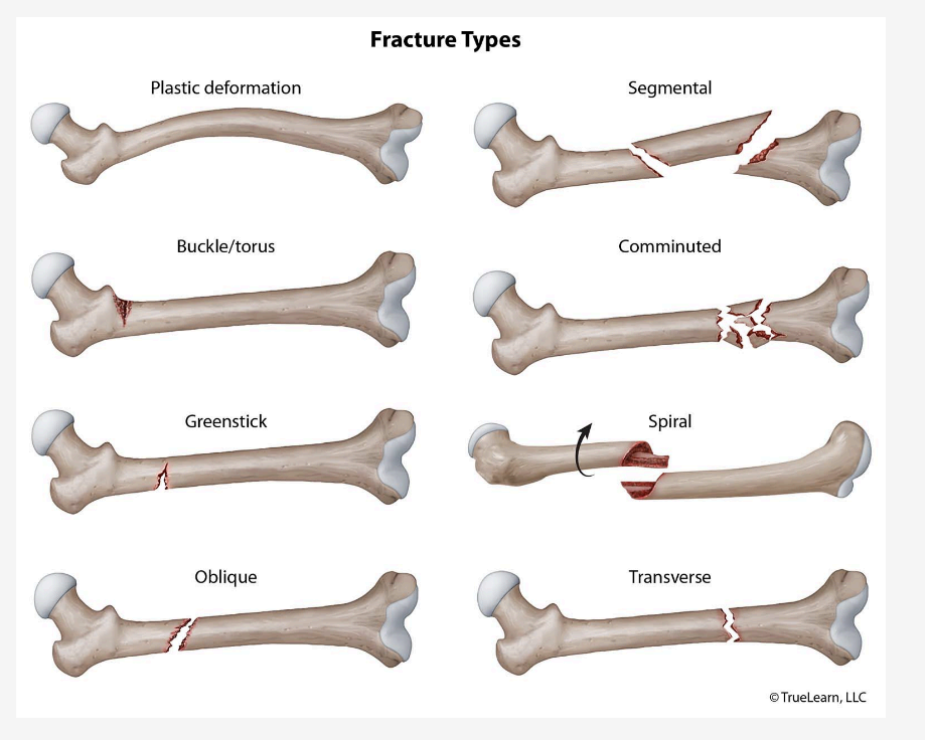
        - Wisconsin
    - **Coccidioides**
    - **Thermophilic actinomyces**
        - Farmer's lung
- Tick-Borne illnesses

Tick-Borne Illness				
Disease	**Tick**	**Pathogen**	**Area**	**Treatment**
Anaplasmosis	• *Ixodes pacificus* • *Ixodes scapularis*	Anaplasma phagocytophilum (intracellular bacteria)	Pacific coast, midwest, northeast	Doxycycline
Babesiosis	*Ixodes scapularis*	Babesia microti (parasite)	Midwest, northeast	Atovaquone + azithromycin
Colorado tick fever	*Dermacentor andersoni*	Colorado tick fever virus (ds-RNA virus, coltivirus family)	Rocky mountains	Supportive care
Ehrlichiosis	*Ambylomma americanum*	Ehrlichia chaffeensis (intracellular bacteria)	South central US	Doxycycline
Lyme disease	• *Ixodes scapularis* • *Ixodes pacificus*	Borrelia burgdorferi (bacteria, spirochete)	Midwest, northeast Pacific coast	Doxycycline or Cefuroxime or Amoxicillin
Rocky Mountain spotted fever	• *Dermacentor variabilis* • *Dermacentor andersoni* • *Rhipicephalus sanguineus*	Rickettsia rickettsii (intracellular bacteria)	Rocky mountains, southern midwest	Doxycycline
Tularemia	• *Dermacentor variabilis* • *Dermacentor andersoni* • *Ambylomma americanum*	Francisella tularensis (facultative intracellular bacteria)	Throughout US	Doxycycline or Ciprofloxacin

Radiology

- **Imaging modalities**
    - MRI
        - w/ contrast
        - w/o contrast
    - CT
    - Xray
        - cervical : 3-4 views
        - Radiation less than 50 rads is recommended in pregnancy
    - Guided Biopsy
        - Need surgery consult to ensure biopsy tract is resected, worry about sampling location and have it approved
    - Esophageal
        - Gastrografin (less toxic to tissues, esp for booerhave syndrome)
    - Gastric-GI
        - Barium study
- **ABCDE**
    - Airway
    - Bone, breathing
    - Circulation
    - Diaphragm
- **Patterns**
    - Interstitial “wirey”
    - Alveolar “fluffy”

    - sunburst= cancer (osteosarcoma)
    - Banana sign= neural tube defect
    - Bird beak= achalasia
- **RUQ pain= US**
    - **Cholecystitis**
        - fluid= hypoechoic, sludge= more dense, stones= hyperechoic
        - Wall Thickening
        - collapsed= ruptured gall bladder
        - Doppler: blood vessels, hyperemia (inflammatory response)
        - Positive sonographic murphy's sign
    - Ddx: choledocholithiasis, pancreatitis, hepatitis, liver abscess, subhepatic appendicitis (appendix not always in RLQ)
    - Complications: gangrenous cholecystitis (most common), becomes ischemic when there's a blockage; emphysematous cholecystitis (common in DM; fistula (bosser nelli syndrome- stone gets into small bowel)
- **RLQ pain= CT**
    - Appendicitis, ovarian torsion, colon cancer
- **Chest pain**
    - Xray
        - Tension PTX: tracheal deviation
        - Right diaphragm usually higher, so compare diaphragms
        - Compression of heart, decreased return to heart; mass effect of great vessels
- **Atraumatic knee pain**
    - Xray → malignancy order chest CT & MRI → biopsy
    - Osteomyelitis, osteosarcoma, ewing sarcoma
        - Osteosarcoma: pagets, irradiation, fibrous dysplasia
            - Bimodal (very young- very old) male
    - Giant cell tumor
    - Unicameral bone cyst
    - Osteosclerosis, periosteal inflammation, pathologic fracture
    - Soft tissue components, fractures, extension into joint space
- **Traumatic knee pain**
    - Xray → MRI
        - ACL and PCL
- **Brain depth study**
    - Normal: uptake to brainstem and cerebellum, cerebrum
    - Nuclear medicine injects radiotracer
    - No uptake= brain death
- **Stroke**
    - CT, CTA, MRI, DWI

- 

Surgery

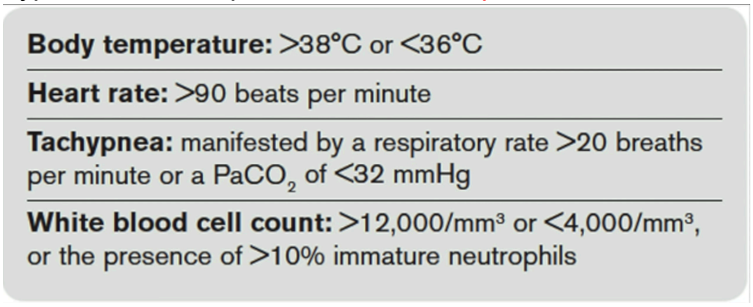
- [Mer's Cheat sheet]

Emergency Medicine

- [Mere's cheat sheet]
- **Resources:** Emergency Medicine PreTest® Self-Assessment and Review, 5e, Case files on access medicine
- **Fluids**
  - When calculating maintenance fluid rates for pediatric patients, use either the **Holliday-Segar formula** (per the table above) or the 4-2-1 rule:
  - 4 mL/kg/hour for the first 10 kg
  - 2 mL/kg/hour for the next 10 kg
  - 1 mL/kg/hour for every kg after 20 kg.
  -
- **Trauma care**
  - **Airway**
  - **Breathing**
  - **Circulation**
    - 1-2 IV, 1-2 crystalloid (less is best)
  - **Chest and Pelvis Xray**
  - **D**
  - **E**
  - **FAST exam-** look at all 4 quadrants on US
- **Acute blood loss**
  - Where's the blood: Chest, abdominal cavity, pelvis, leg, brain
    - Hemothorax → chest tube
    - Pelvic fracture (look at SI joint and pubic symphysis for widening)

- **Severe respiratory distress/ failure**
  - Retractions and accessory muscle use, fragmented speech, cannot laie supine, diaphoresis, agitation. Avoid intubating asthmatics, if possible
  - **Foreign body**
    - < 3 yo coughing
    - Cxr inspiratory and expiratory → esophagus vs. trachea/ bronchi (right mainstem bronchi)
    - Life saving techniques
      - If at corina → push object down R mainstem bronchus, lay patient on right side, intubate and ventilate left lung and wait until pulmonology arrives
  - **Angioedema**
    - Allergic, ACE-inhibitor induced, NSAID-induced, C1q esterase deficiency
    - Swelling of upper airway, tongue → epinephrine, nasal airway
  - **Infections**
    - **Epiglottitis**
      - Hib conjugate vaccine
      - Gram negative coccobacillus
      - Stridor, drooling, tripod, refuse to swallow, Thumb sign
      - Intubate
      - Dx: Lateral neck radiographs
    - **Ludwig angina**
      - Submandibular space infection, edema in sub mylohyoid and sublingual space. Elevated floor of mouth
      - "Muffled voice"
      - Due to **strep viridans,** polymicrobial from dental infection → tooth roots infected
      - Next step: CT, Abx (ampicillin-sulbactam, clindamycin), remove tooth
        - FYI Osteonecrosis from bisphosphonates!
    - **Peritonsillar abscess**
      - Hot potato voice, trismus (can't open mouth), uvular deviation
      - Next steps: none
      - Dx: CT scan neck if PTA has spread to deep spaces
      - Tx: needle aspiration or I&D + Abx for group A strep and respiratory anaerobes
    - **Retropharyngeal abscess**
      - Prevertebral soft tissue space widened
      -
  - **Airway trauma**
    - Burns or smoke inhalation requires early intubation
    - Larynx fracture after blunt trauma if severe neck pain and dysphonia
    - blunt/ penetrating trauma can cause hemorrhage, anatomic distortion, swelling
- **Needle sticks**
  - #1 clean the wound
  - Post-exposure prophylaxis if HbsAg positive
  - If immunized, give IgG
  - IFN-alpha for acute hepatitis C
- Lacerations
  - Lidocaine with dilute epinephrine (**1:100,000** to 1:400,000) is the preferred

local anesthetic mixture to use prior to skin suturing in vessel-rich areas of skin.

- **Code status**
  - Full code: do everything
  - DNR: no CPR or chest compressions
  - DNI: no intubation
- **Stability**
  - if vitals are fine, asymptomatic
    - A fib: asymptomatic CCB, beta blocker outpatient
    - CHF + A fib: amiodarone, digoxin and symptomatic
  - unstable (SOB, abnormal BP, hypoxemia)
- **SIRS criteria**
  - 2/4 = SIRS
    - > 20 breaths
    - HR > 90
    - WBC > 12K or < 4K
  - + source of infection = SEPSIS
  - + end organ damage or hypotension = SEVERE sepsis
  - Hypotension unresponsive to fluids= septic SHOCK
  - 

- **Gun shot**
  - Xray → CT w/o contrast
  - Find entrance and exit tract (not always linear, can have multiple), look at structures hit. Always look at diaphragms! Look at bowel perforation, vessels
  - Bright white= active blood
  - Assault rifle bullets (shockwave injuries to surrounding structures)
- **Poisonings/ OD**

	Intoxication	Withdrawal
Alcohol	CNS depression Impaired coordination, nystagmus	Agitation, seizures, hyperexcitability tx : clonidine for HTN in alcohol withdrawal
Amphetamines	CNS excitation	CNS depression
Benzodiazepine	CNS depression (fatal with opioid and alcohol) Tx: Flumazenil	Agitation, seizures, hyperexcitability
Cocaine- stimulant	CNS excitation, euphoria Don't give beta blockers!	CNS depression, dysphoria, Crash, vivid dream, hyperphagia, drug craving, por

	Tx: IV phentolamine	concentration
Cannabis	Mild euphoria, Munchies	none
Synthetic cathinones **Bath salts/ amphetamine analogs**	Severe agitation, combative,psychosis, delirium, myoclonus, seizures	
Caffeine	CNS stimulation, focus	headaches
Opioids (heroin, xanax) Can be smoked, snorted, injected	Sedation, euphoria, constipation, Miosis **Naltrexone, Naloxone (IV)**	Agitation, abdominal pain, diarrhea, mydriasis, YAWNING, PILOERECTION **Methadone, buprenorphine, naltrexone**
PCP	Aggression, belligerent, psychosis, homicidal Vertical and horizontal nystagmus, superhuman strength Tx: lorazepam	
MDMA	Bruxism, euphoria, sensory distortions, emotional closeness, severe hyperthermia	
Methamphetamine	Delusions, textile hallucinations, aggressive behavior, poor dentition, excoriations, skin picking Like a manic episode	
LSD	Synthesia / sensory blending	
Inhalants	Short lived high Patchy brain changes	
Tramadol		Can induce seizures

Common Heavy Metal Poisoning			
Variable	**Lead**	**Arsenic**	**Mercury**
Acute symptoms	• Abdominal pain • Constipation • Fatigue • Headache • Anemia • Central nervous system issues, if there are significantly elevated levels	• Severe nausea • Vomiting • Diarrhea • Abdominal pain • Garlic odor of breath and stool in severe poisoning • QTc prolongation, which may lead to: ◦ Shock ◦ Acute respiratory distress syndrome ◦ Arrhythmia	• Cough • Stomatitis • Inflammation of the gums • Nausea • Vomiting • Diarrhea • Conjunctivitis • Dermatitis
Chronic symptoms	• Distal motor and sensory neuropathy • Anemia	• Hyperpigmented and hypopigmented skin lesions • Hyperkeratosis of the skin • Symmetrical sensorimotor polyneuropathy	• Neuropsychiatric features: ◦ Anxiety ◦ Irritability ◦ Insomnia ◦ Depression ◦ Tremor
Sources	• Occupational exposures: ◦ Batteries ◦ Ammunition ◦ Paint ◦ Mining ◦ Plumbing • Contaminated water: ◦ Via lead pipes ◦ Via old buildings using lead paint	• Contaminated drinking water via pesticides • Contact with pressure-treated wood • Occupational sources: ◦ Semiconductors ◦ Fuel combustion ◦ Metallurgy ◦ Smelting	• Organic mercury may be ingested via heavy intake of fish with high levels: ◦ Swordfish ◦ Shark ◦ Mackerel • Elemental mercury may be absorbed via: ◦ Smelting operations ◦ Tooth fillings in dental offices
Antidote	• Chelating agents: ◦ Succimer ◦ **Dimercaprol**	• Chelating agents: ◦ Succimer ◦ Dimercaprol	• Chelating agents: ◦ Succimer ◦ Dimercaprol

- **Organophosphate poisoning**
  - DUMBBELLS: diarrhea, urination, miosis, bronchospasm, emesis, lacrimation, salivation
  - Measure AchE esterase activity
    - Tx: **atropine**, pralidoxime

Organophosphate poisoning	
Common exposures	• Pesticide: farmer/field worker, pediatric ingestion, suicide attempt • Nerve agent: multiple patients presenting with similar symptoms
Manifestations	• Muscarinic: ◦ **D**iarrhea/diaphoresis ◦ **U**rination ◦ **M**iosis ◦ **B**ronchospasms, bronchorrhea, bradycardia ◦ **E**mesis ◦ **L**acrimation ◦ **S**alivation • Nicotinic: muscle weakness, paralysis, fasciculations
Management	• Remove patient's clothes, irrigate skin • Atropine reverses muscarinic symptoms • Pralidoxime reverses nicotinic and muscarinic symptoms (administer after atropine)

- **Anticholinergic/TCA toxicity**
  - Antidote: physostigmine
  - Sodium bicarb → reduce effects of cardiac sodium channels
- **ethylene glycol**
  - Anion and osmolar gaps
  - Flank pain and hematuria (renal stones)
- **Potassium hydroxide**
  - People that drink drain cleaner
  - Ulcerative lesions in esophagus
- **Acetaminophen/ salicylate toxicity**
  - metabolized by liver via glucuronidation and sulfation, takes hours for levels to rise > 24 hours
  - kills the liver over days.
  - High lactic acid, anion gap metabolic acidosis
  - Dx: arterial blood gas
  - tx: sodium bicarbonate

Salicylate Toxicity Symptoms		
Severity	**Salicylate Levels (mg/dL)**	**Symptoms**
Mild	40 – 80	Tinnitus, nausea, vomiting, headache, tachypnea, and generalized pain are common.
Moderate	80 – 100	Tachypnea and tachycardia are more pronounced with more severe neurological symptoms (confusion, slurred speech, hallucinations).
Severe	>100	Cerebral and pulmonary edema lead to encephalopathy and seizures. Hypoventilation replaces hyperventilation and there is need for intubation.

- **Carbon monoxide poisoning**
  - hypoxemia (CO displaces O2 from Hgb —> prevents O2 delivery)
  - vehicle admission or wood burning stove, fire
  - Labs: increased carboxyhemoglobin, tissue hypoxia, EPO, secondary polycythemia
  - tx: 100% O2 or hyperbaric O2
- **Cyanide poisoning**
  - vinyl burning
  - binds cytochrome oxidase in mitochondria
  - bitter almond or metallic taste
  - tx: hydroxocobalamin —> forms cyanocobalamin
  - nitrates induce methemoglobin —> binds cyanide
- **Methemoglobinemia**
  - Cyanosis and dyspnea, normal PaO2
  - OD nitroglycerine, dapsone, antimalarials, **benzocaine**
  - Tx: methylene blue/ synthetic blue dye
- **Beta blockers OD**
  - tx: glucagon (activates cAMP)
  - activated charcoal
  - bradycardia, bradypnea
  - Propranolol —> sodium bicarbonate OD
- **Radiation**
  - Acute radiation syndrome
    - Tachycardia, N/V/D → anemia and encephalopathy
    - Dx: Geiger-Muller counter

- **Hemorrhage**
  - Blood can hide in the pelvis, abdomen, chest
  - pelvic fracture:
    - urethral injury posterior —> do retrograde urethrography —> suprapubic catheterization
      - Never insert foley
- **Pulmonary Emergencies**
  - **Flail chest**
    - > 2 rib fractures → paradoxical movement of chest wall
  - **Pulmonary contusion**
    - blunt/ penetrating trauma → fluid in alveolar spaces
    - Hypoxia if large enough
    - Control pain, pulmonary toilet, lung expansion, ventilation/ oxygenation
  - **Pulmonary embolism**
    - Tachycardia, tachypnea, pleuritic chest pain
    - Prolonged immobility, hospitalization, pregnancy, injury, infection, smoking
    - Start on heparin bridge therapy → go to warfarin
    - CT chest + LE doppler US
    - Graded: low risk, sub-massive, Massive PE
    - TPA thrombolysis
  - **Rib fractures**
    - Stabilize
    - Multimodal analgesia and epidural for pain control
- **Appendicitis**
  - RLQ pain
  - Due to fecalith lodged in appendix lumen

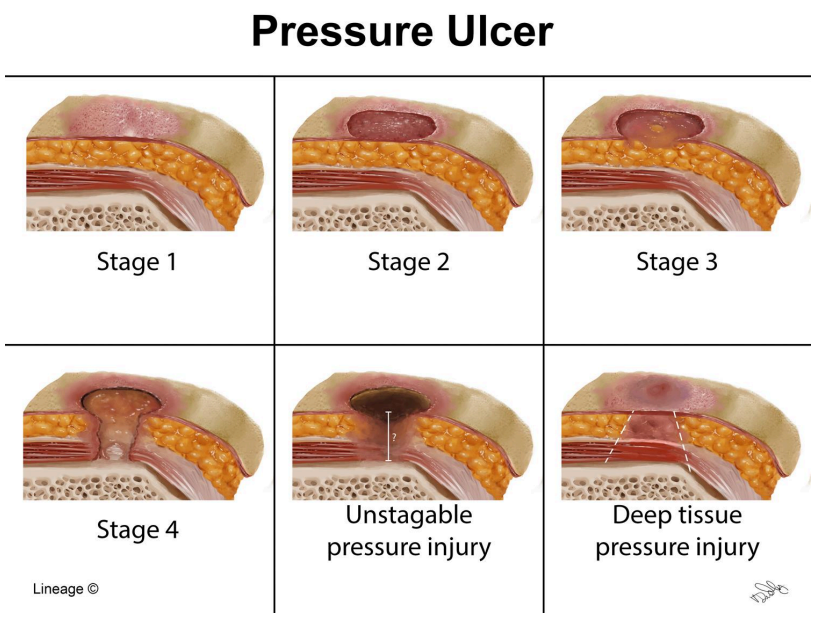
- Stump appendicitis: appendicitis in pt with appendectomy
- Interventions: good peripheral IV access, IV opioid pain meds, IV fluids, start IV cefoxitin

- **Anaphylaxis**
  - triggers: drugs, venoms, out of the blue
  - itchy, rash, hypotension, angioedema
  - more rapid onset, more severe; can present in hours- days
  - Tx: Epinephrine, antihistamine, fluid resuscitation,
  -

Diagnostic criteria for anaphylaxis	
Anaphylaxis is likely if there is rapid symptom onset & any 1 of the following criteria:	
1	Skin/mucosa involvement (eg, hives, lip/tongue swelling) & either hypotension or respiratory distress
2	Involvement of ≥2 organ systems after exposure to a likely allergen • Skin/mucosa (eg, hives, lip/tongue swelling) • Respiratory (eg, wheezing, stridor, dyspnea) • Cardiovascular (eg, hypotension, tachycardia, syncope) • Gastrointestinal (eg, abdominal pain, vomiting, diarrhea)
3	Hypotension after exposure to a known allergen

- **Non-allergic angioedema**
  - bradykinin mediated (ACEinhibitors, C1 inhibitor deficiency)
  - slower onset, no urticaria, pruritis or hypotension
    - C1 inhibitor concentrate
    - kallikrein inhibitor
    - antihistamine
- **Hypertensive emergency**
  - any elevated BP that causes organ damage
    - CNS: stroke, pulmonary edema, kidneys AKI, Acute MI, aortic dissection
    - tx: rapidly lower BP, IV short acting agents
      - Labetalol > sodium nitroprusside
      - BP < 25% in first hour
- **Hypotensive emergency**
  - Peaked T waves= hyperkalemia= succinylcholine (depolarization)
  - Hypotension, tachycardia
- **Hyperthermic emergency**
  - elevated temp > 104F —> end organ damage
  - AMS, seizure, AKI, muscle rigidity, rhabdo, ARDS, DIC
  - Heat Stroke
    - elderly pts on anticholinergics, volume depleted, athlete
    - tx: evaporated cooling, ice packs, target level 101F
    - immersion in cold water
  - Malignant hyperthermia > 113
    - halothane, isoflurane, AD Mutation in ryanodine or DHP receptor
    - tx: cooling and dantrolene
  - NMS
    - fever, AMS, lead pipe rigidity, hyperthermia
  - Serotonin syndrome
    - less severe hyperthermic reaction by 2+ serotonergic meds (MAOi + SSRI)
    - hyperreflexia and myoclonus
    - Linezolid has serotonergic effects

- **Hypothermic emergency**
  - **Frostbite**
    - Pallor, anesthesia, blistering
    - Tx: rapid rewarming in water path
    - Debridement and thrombolysis if severe
- **Encephalopathy**
  - Delirium- acute change in cognitive function for days
    - give haldol for agitation in elderly
    - early mobilization is preventative, post ICU, open curtains during day
    - frequent orientation
  - Coma= absent cortical function
    - CNS imaging, LP helpful, treatment is supportive
    - Acute hypoglycemia= 50% dextrose
  - Anoxic brain injury= damage to CNS from prolonged tissue hypoxia
    - edema and loss of gray-white matter demarcation
- **Burn victims**
  - Fluid replacement: Body surface x weight x 4L/kg / 8 hours
  - Hyperkalemia common
- **Critically ill patients**
  - **Nutrition**
    - Enteral nutrition via feeding tube
      - Initiating early, reduces infections and mortality. Maintains gut integrity
      - Can be tailored. Start low and increased as tolerated
    - Total parenteral nutrition
      - Only used in patients who cannot tolerate feeding tube
      - Increased risk of infection (central line)
  - **Ulcers***
    - Management: air bed (reduces pressure), **wet to dry dressings**, silver sulfadiazine cream and sterile dressing (promote regrowth and cleanliness); skin grafts
    - Grade 1
    - Grade 2
    - Grade 3-4
      - Debridement of ulcer with necrotic tissue
      - Full thickness tissue loss with subQ fat, eschar, erythema



- Skin grafts
  - Can undergo malignant degeneration
  - Red, painful granulation tissue that does not heal at site of prior skin graft
  - Delayed graft failure= skin does not adhere to the wound bed
- CABG
  - Must take DAPT to prevent intracoronary stent

Epidemiology

	95% confidence interval	99% confidence interval
Null value outside confidence intervals	$p < 0.05$	$p < 0.01$
Null value inside confidence interval	$p \geq 0.05$	$p \geq 0.01$

		Disease		Predictive Value	
		⊕	⊖		
Test	⊕	**A** True Positive (TP)	**B** False Positive (FP)	Positive Predictive Value (PPV) $\frac{TP}{TP+FP} = \frac{A}{A+B}$	Total Positive Results (A + B)
	⊖	**C** False Negative (FN)	**D** True Negative (TN)	Negative Predictive Value (NPV) $\frac{TN}{FN+TN} = \frac{D}{C+D}$	Total Negative Results (C + D)
Sensitivity & Specificity		Sensitivity $\frac{TP}{TP+FN} = \frac{A}{A+C}$	Specificity $\frac{TN}{FP+TN} = \frac{B}{B+D}$		
		All diseased patients (A + C)	All non-diseased patients (B + D)		

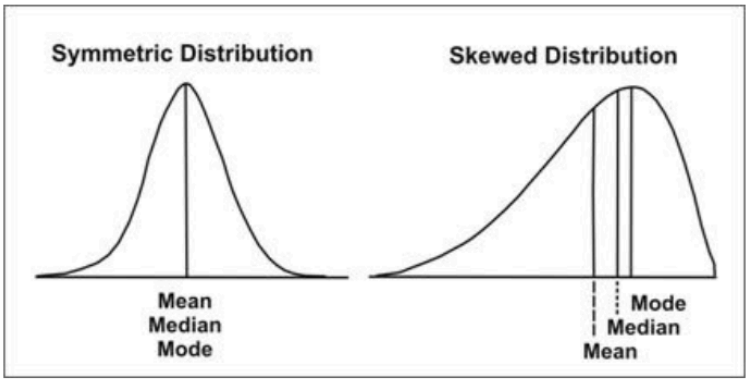
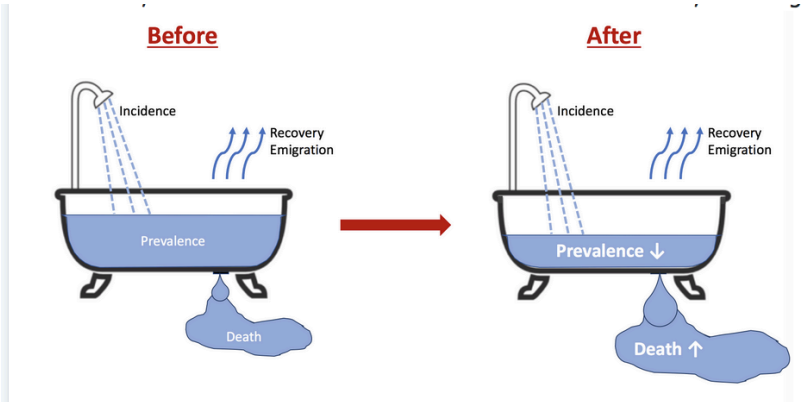
	Case report	Case series report	Ecological study	Cross-sectional (prevalence) study
Description	Report of disease presentation, treatment, and outcome in **single subject or event**	Report of disease course or response to treatment that is compiled by aggregating **several similar patient cases**	A study that assesses **links between exposure and outcome** – typically used if the outcome is rare	A study that **determines the prevalence of exposure and disease** at a specific point of time
Study method	• An unusual outcome in a single subject is described in detail • Generally, unique findings are reported • Can help in formulation of a hypothesis	• Assess aggregated data of similar patient cases • They all receive same intervention • No control group	• Assess aggregated data; at least one variable is at group level • Observation is entire country or large population of people	• Prevalence of disease and other variables measured simultaneously at a particular point in time (snapshot of population) • Can reveal association between risk factors and disease • Can help examine population and eventually support diagnostic tests
Disadvantages	• Lack of generalizability • Cannot assess causality	• Selection bias (researcher self-selects cases studied) • Cannot assess causality	• Ecological fallacy (make inferences about individual in a group based on group characteristics) • Cannot assess causality	• Cannot directly measure incidence or risk • Cannot assess causality
Example	Examining a single case of cervical cancer in a 25-year-old female	Collecting and examining several cases of pericarditis at a local hospital system	Determining incidence of cholera deaths based on specific locations to identify exposure	Investigating number of patients with both coronary artery disease and hypertension in 1998

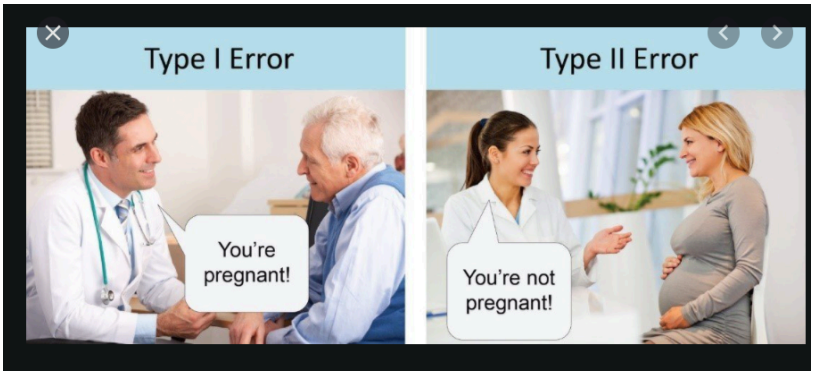
- **Prevalence vs incidence**
  - Drug causes longer life= increased prevalence
  - Increased prevalence= increased PPV, decreased NPV
- **Negative predictive value**
  - Truly negative with negative test
  - “Truly cancer free”
- **Positive predictive value**

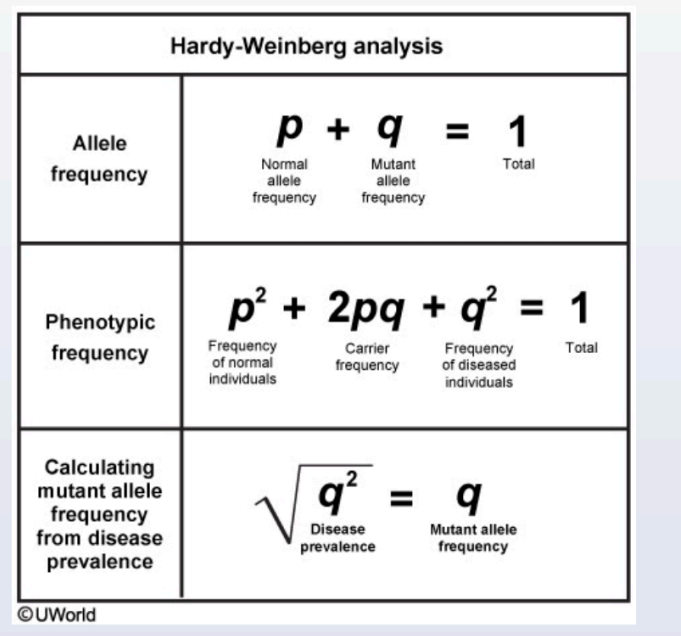
    - Truly positive with positive test
- **Sensitivity**
    - % of people who have a positive test result
- **Specificity**
    - % of people who have a negative test result

ANOVA	Analysis of variance compares **mean** **of quantitative** variable in **>** **3** independent groups (concentration in various age groups)
Chi-square test	Association between **2 categorical variables** (male, female and presence/ absence) Proportions “high” vs “normal” in 2 groups, observed vs expected
t-test	Compares the **mean** of QUANTITATIVE and categorical variables between 2 groups
Correlation analysis	Linear relationship between 2 quantitative variables
Logistic Regression analysis	Association between 1 or more independent variables (risk factors) and 1 quantitative dependent outcome (lab value) while adjusting for other variables → adjusted values reduce confounding factor → calculate line of best fit.
Case-control study - ODDS ratio - A/B / C/D	**Patients with disease and without disease, then determine exposures associated with disease, RISK FACTORS** cases= + disease controls= - disease Look at how groups are different, find exposure. Retrospective and observational. Identify risk factors for disease. Control group= people with out the disease regardless of exposure
Cross-sectional study - **Prevalence**	Prevalence study, snap shot that uses surveys to look at exposure and outcome in a disease of interest. One point in time **Odds ratio**: 2 groups are identified as cases or controls according to an outcome, frequency of exposure to the risk factors is compared
Cohort study **Relative risk** A/ A+B / C/ C+D	**Relative ris**k= risk of disease in **exposed/ unexposed**, observational, retrospective or prospective. People with a **risk factor**, see what happens to them Association between exposure to a risk and an outcome in an exposed group. < 1= exposure decreases risk (1- RR= % reduction) = 1 no effect > 1= exposure increases risk of disease If the confidence interval includes the null, not statistically significant.
Attributable risk percent	% of cancer attributed to smoking

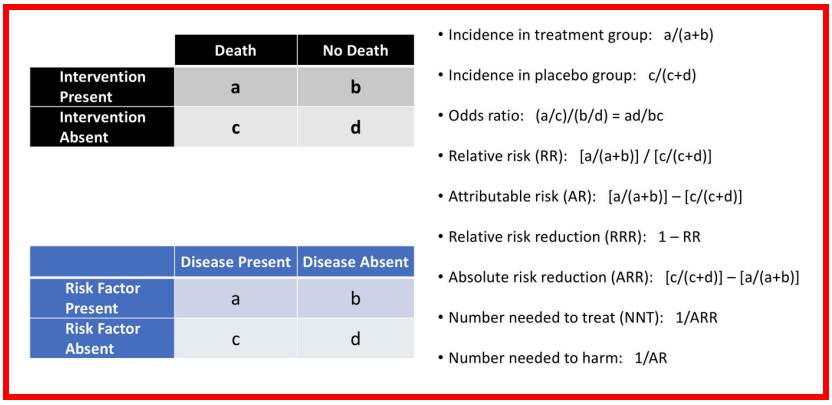
	ARP= 100 x risk in exposed - risk in unexposed/ exposed) 100 x (RR-1)/ RR A/ A+B - C/ C+D nnt= 1/ arr
NNT	ARR → NNT= 1/ ARR
Hypothesis	• 2 correct decisions: ◦ Fail to reject a true H_0 (ie, determine there is no correlation when one truly doesn't exists) ◦ **Reject a false H_0** (ie, determine there is a correlation when one truly exists) • 2 incorrect decisions: ◦ Type I error: reject a true H_0 (ie, determine there is a correlation when one truly doesn't exist) ◦ **Type II error: fail to reject a false H_0** (ie, determine there is no correlation when one truly exists)
Confounding bias	Confounding variables can arise with **matching** **RANDOMIZATION minimizes confounding variable bias** Association that does not consider an important variable. Stratification makes data nonsignificant in Both groups
Effect modification	Natural phenomenon that affects one group, so there are different measures of association. The effect of the main exposure on the outcome is modified by the presence of another variable
Selection bias	Loss to follow up leading to differences in groups.
Recall bias	Retrospective, forgotten or faded details of events/ exposure
meta-analysis	Large data, need very small P-value to decrease false positives
Intention to treat	Include all subject regardless of what happens. Need to know effects, including those who stopped. Avoids attrition, dropout. Leads to conservative estimate
Per-protocol principle	Study that only includes adherent patients, excludes nonadherent
Positive skew	“Ameanba” tail to right, **Mean** > median> mode
Negative skew	Taili to left, **Mode** > median > mean

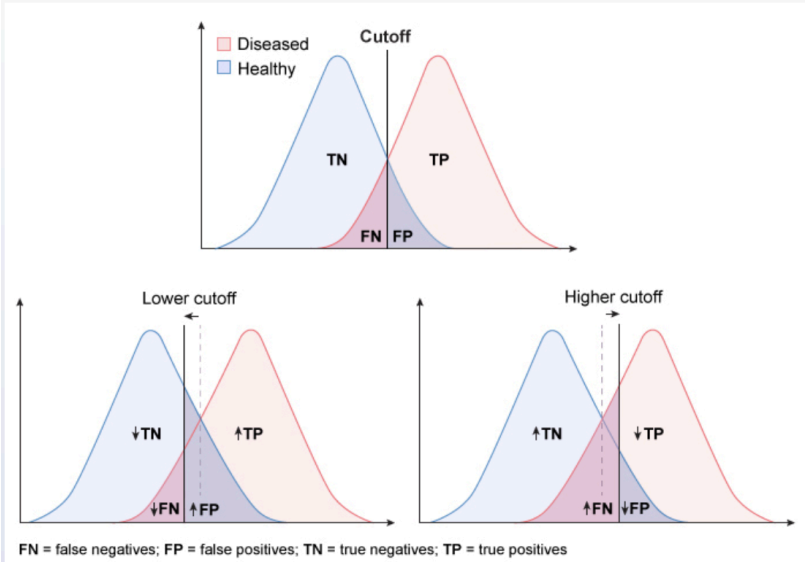
	
Hypothesis	H0= no association (null)- cross-sectional study - Risks are the same (cohort study) H1= association (p value < very small 0.05)
P value	small= very small probability results were due to chance Reject the null if p value < 0.05, accept alternative hypothesis Probability that a type 1 error has occurred and the null hypothesis is erroneously rejected. % chance of finding an average difference of that percentage or greater
power	Probability the test will reject the null hypothesis Increased power with more participants
Standard deviation	Variation of values with in a sample population
Standard error of the mean	Variation of sample means from the true population
incidence	Number of **new cases** of a disease in population at risk over time **Cumulative incidence** - New cases/ population at risk - those already with disease
Prevalence	Total number of cases in the population over a given time - **Increased duration increases prevalence** 

<table>
<tr><td>Randomization</td><td>Goal to prevent selection bias and produce comparable groups that are similar in underlying characteristics
Increases likelihood that any difference between groups is due to treatment only</td></tr>
<tr><td>Maintenance dose
Loading dose
Half-life</td><td>
<table>
<tr><th>Pharmacokinetic parameter</th><th>Formula</th><th>Note</th></tr>
<tr><td>Half life</td><td>$V_d \times 0.7 / CL$</td><td>Steady-state concentration is achieved in 4-5 half-lives.</td></tr>
<tr><td>Maintenance dose</td><td>$C_{ss} \times CL \times$ dosing interval</td><td>Maintenance dose is decreased in patients with renal or hepatic impairment.</td></tr>
<tr><td>Loading dose</td><td>$V_d \times C_{ss}$</td><td>Loading dose is affected by body weight and composition.</td></tr>
</table>
Renal disease: loading dose is same, maintenance dose is lowered
MD= Cp x CL/ bioavailability
</td></tr>
<tr><td>Validity</td><td>External validity: determines if an experiment can be generalized and conclusions applied to groups</td></tr>
<tr><td>Type 1 vs type 2 error</td><td>
</td></tr>
</table>

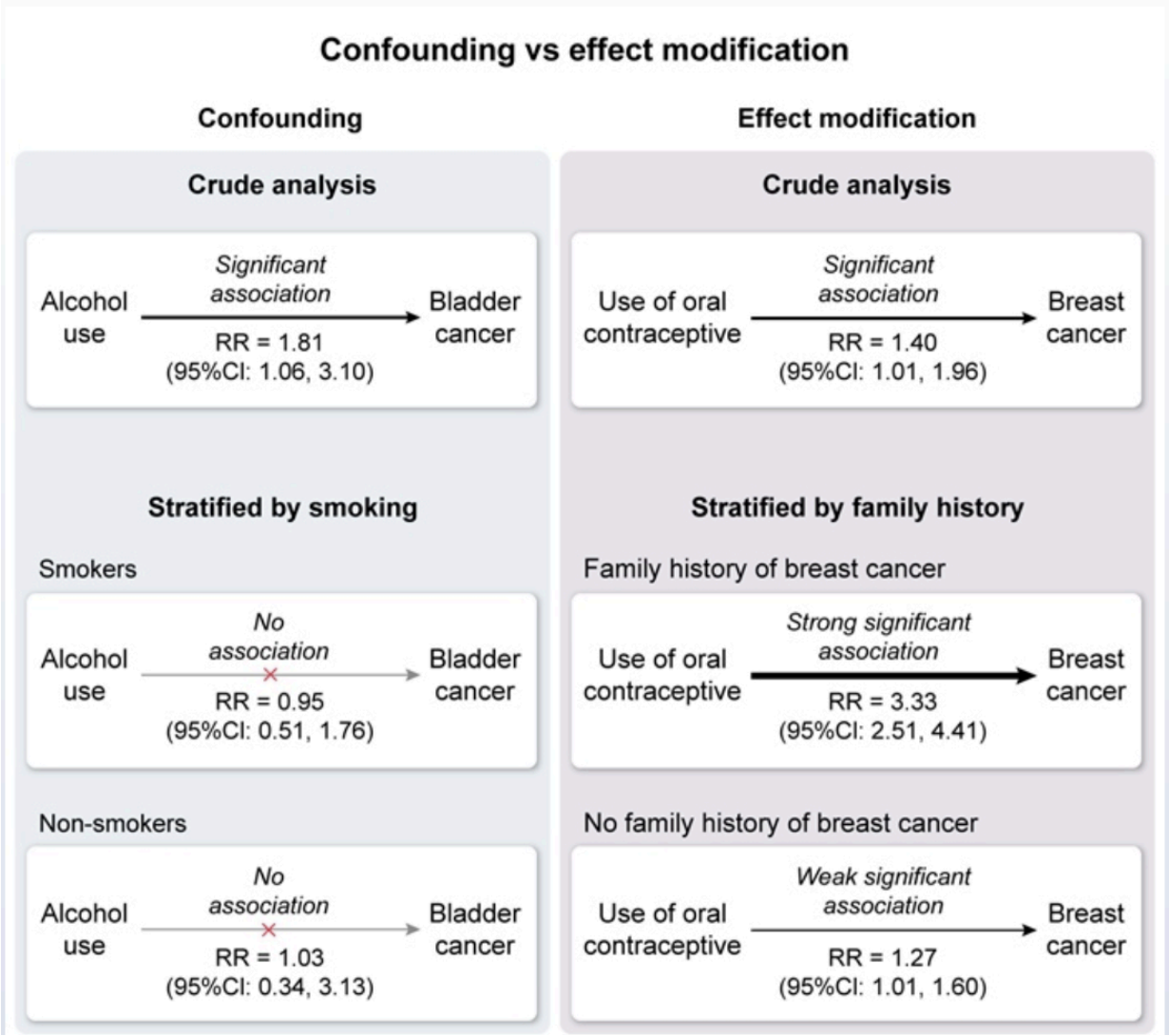
<table>
<tr><td>Hardy weinberg</td><td>

Autosomal recessive= ¼
Carrier frequency in population = ALLELES → q^2= 1/x → 2q= carrier status / frequency</td></tr>
<tr><td>68-95-99.7 rule</td><td>Standard variation of the mean/ interval
- 68: mean +/- SD
- 95: mean +/- 1.96 x SD/ sqr(n)
- 99.7: mean +/- 2.58 x SD</td></tr>
<tr><td>Ethics laws</td><td>cruzan= remove life sustaining treatments
schloendorff= informed consent
tarasoff= warn person and authorities, contain patient</td></tr>
<tr><td>Clinical trials</td><td><table>
<tr><th>Phase</th><th>Characteristics</th><th>Purpose</th></tr>
<tr><td>Preclinical</td><td>Evaluation on at least two nonhuman animal species before trials or use on humans.</td><td>Evaluation for harms before use on humans (assess carcinogenic, teratogenic, fertility effects, etc.). Dosing.</td></tr>
<tr><td>Phase 1</td><td>Preapproval phase. Initial testing in small groups (20-100). Healthy volunteers or individuals with the condition.</td><td>Examine safety, side effects, and effective dosages.</td></tr>
<tr><td>Phase 2</td><td>Preapproval phase. Controlled or uncontrolled trials of 20 to 200-300 subjects who have the disease.</td><td>Additional data on safety and efficacy. Develop and refine research questions, methods, and protocols.</td></tr>
<tr><td>Phase 3</td><td>Preapproval phase. Usually at least two independent randomized controlled trials. Study group may be compared to conventional treatment. Usually 300-3000 subjects.</td><td>Designed to address whether the drug or device provides benefit to the target population. More effectively addresses safety and side-effects than previous phases.</td></tr>
<tr><td>Phase 4</td><td>Postapproval phase. Usually involves thousands of users after FDA approval. Involves patients' physicians in a normal medical setting.</td><td>Safety and efficacy. Important information of use of drug or device in more normal, non-experimental settings for patients.</td></tr>
</table></td></tr>
<tr><td>Reportable disease</td><td>Four STDs are nationally notifiable, chlamydia, gonorrhea, syphilis, and chancroid,</td></tr>
</table>

	
NPV and PPV	More prevalence= greater PPV Less prevalence= greater NPV
Bias	**Response bias**: surveys where people give desirable responses to questions perceived to be sensitive (health behaviors) → inaccurate and incorrect conclusions (underreporting) **Admission rate bias**: different admission rates for certain cases. **Lead-time bias:** screening test diagnoses a disease earlier than it would have appeared by natural history alone. **Nonresponse bia**s: respondents differ from nonrespondents that threaten the generalized study **Regression of the mean**: first assessment of a variable reveals an extreme, but repeat assessments are more average

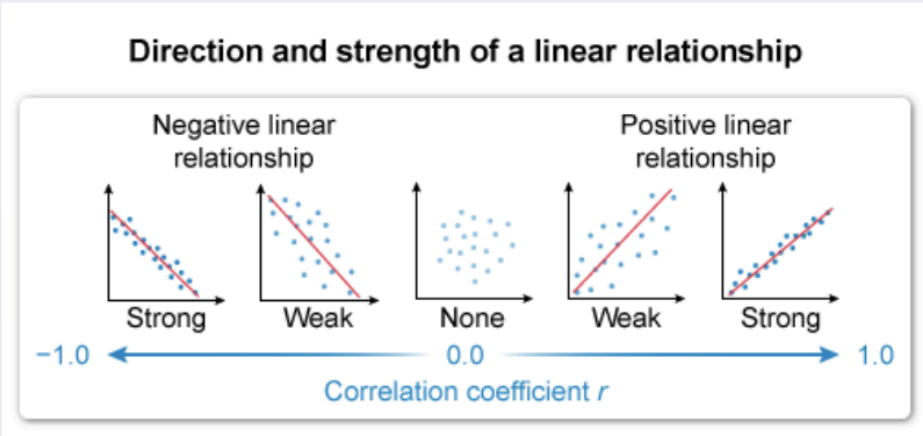


Prevalence & PPV/NPV	
Prevalence ↑	• PPV ↑ • NPV ↓
Prevalence ↓	• PPV ↓ • NPV ↑



$$\text{prevALence} = \frac{\text{ALL cases}}{\text{Population @ risk}}$$

$$\text{iNcidence} = \frac{\text{New cases}}{\text{Population @ risk}}$$



Research studies

- case-control study= Odds ratio
    - Exposure of people with disease and non-disease (control)
- Cohort study = relative risk

Medical Error Analysis Tools	
Barrier Analysis	• Identifies **barrier solutions** to error ◦ Physical, eg, locked cabinets for medications ◦ Administrative, eg, surgical time-out ◦ Team based, eg, standard forms used during transition of care
Common Cause Analysis	• Identifies a common system error that contributed to separate events across an entire system
Failure Modes and Effects Analysis	• **Occurs before** the implementation of a program or initiative • Used to identify **potential sources** of system failure
Morbidity and Mortality and Improvement Conferences	• **Forum** for detailed discussion of adverse events/medical errors and systemic issues • Allows for discussion among physicians and/or other health care team members • Goal is to improve system-wide processes
Root Cause Analysis = Event Analysis	• Identifies **system** factors that contributed to the error

History & physical

- **Interpreters**
    - on boards, always use an interpreter service (in reality, family members act as interpreters)
        - address patient directly
        - go sentence by sentence, don't overcomplicate issues
- **Discharge instructions**

    - early primary care follow-up
    - improve provider-to-provider communication
        - discharge summary, hand off, list of pending test results
    - improve patient education at discharge
        - med reconciliation by nurse and pharmacist
        - assess social and economic needs
- **Health care**
    - fee for service: reimbursement for service, traditional payment method
        - volume-base
    - capitation: payment per patient per month of care, augmented by meeting or exceeding quality and cost measures
    - Pay for performance: financial reward based on quality, safety, and cost measures
- **Medical Errors**
    - ***Table 1: Types of Medical Errors Based on Level of Intent***

Type	***Description***	***Example***
Slip	• *Incorrect execution of a correct action* • *Action that did not occur as planned*	• *Nasogastric tube is inserted, but it curls up in the patient's mouth.*
Lapse	• *Missed or forgotten action* • *Memory error*	• *Nurse forgets to put up the side rail on a patient's bed*
Mistake	• *Correct execution of an incorrect action* • *Action was thought to be correct but was not* • *Action occurs as intended, but it was the incorrect action*	• *Phlebotomist draws blood into tubes labeled with the wrong patient's name*
Violation	• *Deliberate action that violates rules, procedures, or standards*	• *Surgeon does not mark the site of the surgery because the surgeon is behind schedule*

Table 2: Categories of Medical Errors Based on Position in the Patient Care Process	
Category	**Definition/Examples**
Medication	• Ordering: prescribed medication causes an adverse reaction because of a known interaction with a medication the patient is already taking • Transcribing: order is written for 5.0 mg, but 50 mg is transcribed • Dispensing: hydroxyzine is dispensed instead of hydralazine • Administering: concentrated insulin (U-500) is given instead of the ordered U-100 insulin
Surgical	• Wrong patient • Wrong site • Wrong surgery • Retained object • Failure to take appropriate precautions (eg, preoperative antibiotics)
Diagnostic	• Failure of timely and accurate diagnosis • Failure to communicate with the patient • Overdiagnosing, overtesting, or overtreating
Transition of Care	• Any error occurring during a transition of care, including medication errors • Transition of care: ◦ Regular provider to on-call or covering provider ◦ ICU to the floor ◦ Discharge to home ◦ Transfer to a skilled nursing or acute rehabilitation facility
Teamwork and Communication	• Teamwork: an intern notices that a patient has not been receiving DVT prophylaxis but does not mention this to anyone during rounds • Communication: a physician orders a potassium for a patient with mild renal failure taking an ACE-inhibitor but forgets to ask a staff member to call the patient to schedule the test

- **Root cause analysis**
  - Identification Of fundamental, system-level factors that cause error
  - Interprofessional rounds, improve teamwork, communication, oversight and reduce wrong-patient error
- Medicaid: < 65, disabled, blind, dependent children
- Medicare: > 65, or with certain disabilities, ESRD

Management

- **Smoking cessation**: varenicline, Bupropion, Nicotine patch/ replacement

	Advantages	**Disadvantages and Precautions**	**Adverse Events**
Varenicline	Oral; works by blocking reward from smoking and relieving nicotine withdrawal	Avoid use in patients with history of suicidal ideation; use with caution in renal insufficiency; monitor for neuropsychiatric symptoms	Nausea, insomnia, abnormal dreams, headache
Bupropion	Oral; blunts postcessation weight gain	Contraindicated in patients with seizure disorders; monitor for neuropsychiatric symptoms	Insomnia, headache, dry mouth, agitation
Nicotine Replacement (lozenge, gum, nasal spray, patch, inhaler)	Can combine methods to provide sustained and as-needed nicotine replacement; patch, gum, and lozenge are over the counter	Gums and lozenges can have unpleasant taste; patch cannot be altered to provide craving relief	Patch: skin irritation Lozenge/gum: mouth irritation, heartburn

- **Alcohol counseling**
  - CAGE questions: Cut back? Angry? Guilty? Eye opener?
- **Bias**

Common Types of Cognitive Biases leading to Medical Error	
Type	**Description**
Aggregate	• The mistaken belief that population (eg, **aggregate**) **data does not apply** to the individual patient scenario, leading a physician to ignore guidelines
Anchoring	• Clinical decisions based on **initial judgment/impression** and failing to change from initial impression/diagnosis despite additional information
Availability	• **Use of recent examples/experiences** in forming a clinical impression instead of a careful assessment of the data
Commission	• The tendency towards **action** rather than inaction
Confirmation	• Gathering and interpretation of medical data which **confirms** the diagnosis, to the exclusion of conflicting information
Framing	• Decision/judgment made based on how a **problem/situation is presented**
Hindsight	• When knowledge of the outcome **influences perception of past events**, hindering understanding or critical appraisal of events (e.g. physician simply concludes they "knew it all along" and does not critically evaluate the situation)
Omission	• The tendency towards **inaction** rather than action based on fear of being held responsible for the outcome
Recency	• Using **recent** instead of older information, even if the older information is more relevant
Regret	• Overestimating the possibility of a diagnosis with devastating consequences in order to eliminate potential **regret** if the diagnosis is missed
Search-Satisfying Error	• **Discontinuing the search** for the answer once any finding has been discovered
Sunk-Cost effect	• Physicians continue to commit to a diagnosis because there has been a **large amount of time, energy, and resources devoted** to a diagnosis

-

Bioethics

- **Torts liability**
  - Duty= requirement for care
  - Breach of duty= failure to meet standard of care
  - injury= harm
  - causation= acts/ omissions in breach of duty that cause harm
- **Vicarious liability**
  - Liable for negligent acts or omissions by employees

The Four Elements of Torts Liability	
Element	**Definition**
Duty	Requirement (once physician-patient relationship is established) that care provided meets standard of care
Breach of duty	**Failure to meet the standard of care for a given circumstance**
Injury	Any harm (not necessarily physical) that occurs to a patient
Causation	The physician's acts or omissions in the breach of duty are the cause of the injury

Labs

- **Serum albumin to ascites gradient (SAAG)**
  - Transudative > 1.1

        - Protein > 2.5= HF, veno-occlusive disease, pericardial disease
        - Protein < 2.5= cirrhosis
    - Exudative < 1.1
        - Infection, malignancy, nephrotic syndrome, pancreatic ascites

Etiology of Transudative Versus Exudative Ascites	
Transudative with SAAG >1.1 g/dL	**Exudative with SAAG <1.1 g/dL**
• Cirrhosis • Alcoholic hepatitis • Heart failure • Budd-Chiari syndrome • Portal vein thrombosis • Tamponade	• Pancreatitis • Serositis • Nephrotic syndrome • Peritoneal tuberculosis • Peritoneal carcinomatosis

- **Tumor Markers**
    - Useful for monitoring treatment response

Tumor Markers	
Marker	**Associated Cancer**
Prostate-specific antigen (PSA)	Prostate
CEA	Colon
Cancer antigen 19-9 (CA19-9)	Pancreatic
Cancer antigen 125 (CA125)	Ovarian
Alpha-fetoprotein (AFP)	Hepatocellular or germ cell
Calcitonin	Medullary thyroid

- **Hepatitis**
    - Hep A
    - Hep B
    - Hep C: IVDA
    - Hep D
    - Hep E: fetal demise, intrapartum hemorrhage

Serologic Patterns of Hepatitis B Infection

	Surface antigen	E-antigen	Core antibody	Surface antibody
Acute infection	Positive	Positive	Positive IgM	Negative
Chronic infection	Positive	Positive or negative	Positive IgG	Negative
Resolved, old, past infection	Negative	Negative	Positive IgG	Positive
Vaccination	Negative	Negative	Negative	Positive
Window period	Negative	Negative	Positive IgM, then IgG	Negative

Hepatitis Virus Features				
Virus	**Genome**	**Transmission**	**Risks**	**Chronic Potential?**
Hepatitis A virus	ssRNA	Enteric	Contaminated food/water, day care, travel	No
Hepatitis B virus	dsDNA	Parenteral	Sex, injection drug use, mother-to-child transmission	Yes (10%)
Hepatitis C virus	ssRNA	Parenteral	Injection drug use, blood transfusions, sex	Yes (>50%)
Hepatitis D virus	ssRNA	Parenteral	Coinfection with hepatitis B virus	Yes (<5% coinfection, 80% superinfection)

Ethics
139 Ethics Qs and As.pdf

Key Health Care Organizations in the United States	
Organization	**Notable Duties**
Centers for Medicare and Medicaid Services	• Administration of Medicare, Medicaid (in association with state organizations), HIPAA, SCHIP, CLIA, and other health-related programs • Mandates quality measures for hospitals and providers participating in the CMS
Food and Drug Administration	• Federal agency that sets standards of safety, efficacy, and security of human and veterinary drugs, medical devices, and other health concerns
Joint Commission	• Provides optional accreditation programs to hospitals and other health care groups
National Committee for Quality Assurance	• Provides recommendations for health care quality based on evidence review
National Institutes of Health	• The primary federal agency for medical research
National Health Council	• Works with patient advocacy organizations
National Practitioner Data Bank	• Maintains confidential records on health care providers • Operated by the Department of Health and Human Services
Occupational Safety and Health Administration	• Federal agency under the Department of Labor • Establishes and enforces workplace safety standards

Surrogate Decision Makers		
Durable Medical Power of Attorney	**Legally Appointed**	**Next of Kin**
Also known as a healthcare proxy, this is an individual designated as a decision maker if the patient is incapacitated.	An example of this is a court-appointed guardian for an individual who is designated by the courts as incompetent or a minor.	The next of kin is the decision maker if a patient lacks decision-making capacity and has no advance directives or a designated surrogate decision maker. Priority is spouse, adult children, parents, siblings, then other relatives.

- Impaired physician
  - Dr shows up impaired to work (alcohol or drugs) what do you do?
    - Alert hospital chief or staff → report to medical board/police

Professional Responsibilities and Resources for Physicians
Professional responsibilities: • A commitment to professional competence through lifelong learning • Integrity in dealing with patients • Respect for patient confidentiality • Preservation of the physician-patient relationship • Continuous improvement of health care delivery • Just distribution of medical resources
Resources for impaired physicians: • Federation of State Physician Health Programs

1. failure modes and effects analysis
2. 5 Whys technique
3. root cause analysis
4. cause and effect diagram
5. gap analysis
6. Ishikawa (or fishbone) diagram
7. fault tree analysis

CDM cases

Cystic Fibrosis

- Lab work needed: CBC, CMP, Blood culture, Chest x-ray, Puls Ox, Liver function panel, saline, Sputum culture, gram stain of sputum
- Specific lab test: chloride sweat test
- Antibiotics: look at culture sensitivities → piperacillin and tazobactam
- Lumbar puncture is necessary to r/o meningitis in kiddos 3-36 months old
- Treatment of weight and oily stools → digestive enzymes/ pancreas
- Additional treatment: chest physiotherapy, vitamins, influenza vaccine, pneumococcal vaccine, pulmonary medicine referral, nutritionist referral, albuterol

Pelvic Inflammatory Disease

- Physical exam: genital exam
- Tests: CBC, BMP, LFTs, bHCG, HIV, Gram stain, VDRL test, Hep B and Hep C screen, saline if vomiting/diarrhea
- Bacteria: Neisseia gonorrhea
- Imaging: pelvic ultrasound
- Tx:
    - Outpatient: oral ceftriaxone and doxycycline +/- metronidazole
    - Inpatient: IV cefoxitin and IV doxyxyline
- Other interventions: sexual education, treat partner, give tylenol, ondansetron and admit for treatment if ill

Upper GI bleed

- Labs: BMP, CBC, Type and screen
- Discontinue NSAID and prescribe oral PPI
- Blood transfusion (instability), IV omeprazole, consult gastroenterology for EGD, 2 large bore peripheral IVs, IV octreotide, IV ceftriaxone, blood transfusion, IV fluid resuscitation with crystalloids, ICU admission, endoscopy

Upper GI Bleeding			
Etiology	**Laboratory Testing**	**Other Workup**	**Treatment**
Varices Gastropathy Aorto-enteric fistula Angiodysplasia Peptic ulcer disease Malignancy Marginal ulcers Esophagitis	CBC BMP Type and Screen Liver function testing Troponin	EKG Chest or abdominal imaging (if concerned for perforation) CT angiography if embolization if needed	IV proton pump inhibitors IV octreotide (if concerned for varices) Antibiotics (if cirrhosis) Blood transfusions as indicated Fluid resuscitation Endoscopy (if no perforation)

Dizziness

- TITRATE= timing, triggers, targeted exam
    - Recent illnesses, headaches, tinnitus, focal neurologic symptoms
    - Vertigo
        - Test of skew (head impulse and nystagmus)
        - Head, ears, eyes, nose and throat exam
        - Visualize eardrum and ocular testing
        - Dix-hallpike
    - Work up
        - MRI brain
        - CT head without contrast
        - Hospital admission

Etiologies of Vertigo						
Condition	**Peripheral Vertigo**				**Central Vertigo**	
	Ménière Disease	**Benign Paroxysmal Positional Vertigo**	**Vestibular Neuritis**	**Labyrinthitis**	**Cerebellar Hemorrhage**	**Brainstem Infarction (Wallenberg Syndrome)**
Demographics	• Typically younger patients (20–40 years)	• Older patients (> 50 years)	• Typically younger patients (20–40 years)		• Cardiovascular risk factors • Typically older patients (> 50 years)	
Symptoms	• Acute onset • Multiple, intermittent • Hearing loss • Tinnitus	• Acute onset • Multiple, intermittent • Triggered by head movement (rolling over in bed)	• Acute onset • Continuous • Nausea/vomiting • Usually improvement after about 1–3 days		• Acute onset • Nausea/vomiting • Symptoms may still be present > 3 days • Appear more ill	
Physical examination findings	• Sensorineural hearing loss	• Positive Dix-Hallpike test • Intact hearing	• Suppressible horizontal nystagmus • Ability to ambulate • Intact hearing	• Unilateral hearing loss	• Nystagmus not suppressible • Inability to ambulate • Dysarthria, limb dysmetria (+/–)	• Abnormal eye movements with ipsilateral Horner syndrome • Sensory loss with ipsilateral loss of corneal reflex • Hoarseness, dysphagia • Ipsilateral limb ataxia
Diagnosis	Clinical – Based on history and physical examination				MRI (CT if unavailable)	
Treatment	• Triamterene and hydrochlorothiazide	• Epley maneuver	• Meclizine • Prednisone		• Reduce CV risk • Physical therapy	
CV = cardiovascular.						