

## 7 Renal Pathology Review

### Lesions Associated with Nephrotic Syndrome

- Some patients with nephrotic syndrome have (1) normal glomeruli by light microscopy → capillary loops are thin and delicate, mesangial areas are inconspicuous and not too cellular, capillary loops are widely patent, and there are no segmental lesions
- Others have (2) segmental sclerosing or collapsing lesions by light microscopy
- Still others have (3) diffuse nodular type of glomerulosclerosis

### Patient with Nephrotic Syndrome Who Has Normal Glomerulus DDX

- Minimal change disease, early membranous nephropathy
- **Minimal change disease**
  - MCD is very reversible lesion, steroid-responsive.
  - 7 yo child with nephrotic syndrome. 70% of kids with nephrotic syndrome have MCD. Treated empirically with a month of steroids, and if they don't respond, then biopsy
  - Normal light microscopy, negative immunofluorescence, and diffuse podocyte foot process effacement by EM. In normal EM, you see GBM and normal podocyte foot processes. In MCD nephropathy, you see GBM but the podocyte foot processes are completely effaced.
    - You also have **micro-villous transformation of podocyte** (swelling). This is a measure of podocyte injury
- **Early membranous nephropathy**
  - Looks normal on light microscopy, like MCD
  - In membranous nephropathy, you see diffusely thickened glomerular capillary walls. *It takes a while for this to occur though, so early on it can look normal.*
  - You see immune-complex deposits between the podocytes and GBM. Podocyte is injured and reacts to this by laying down new basement membrane.
  - By light microscopy, the deposits rest on the BM but there is no thickening of the BM. Over time, the BM thickens around the deposits and you get the **spikes**. Initially, the glomerulus looks normal by light microscopy.
  - However, if you do IF for IgG and C3, you can see the immune-complex deposits along the glomerular capillary wall → tells you it is membranous nephropathy and not minimal change disease
  - Subepithelial deposits: **Spike & dome pattern** on EM → membranous nephropathy
  - **Most membranous nephropathies are idiopathic**, but there can be secondary causes of membranous nephropathy (such as latent malignancies in older people, like adenocarcinomas). If a patient has a membranous nephropathy at age 60, they need to get a full workup, like chest X-ray and colonoscopy to find an occult malignancy. **Hepatitis B and C can be associated with membranous nephropathy.**

- **10 – 15 % of lupus nephritis is membranous.**
- How to differentiate lupus nephritis from idiopathic membranous nephropathy?
  - Membranous lupus nephritis (IgG, IgA, IgM, C1q, and C3 staining) and tubuloreticular inclusions, a response to interferon (in lupus and HIV) **vs.** idiopathic membranous nephropathy (mostly IgG and C3 staining)

*Patient with Nephrotic Syndrome with Segmental Glomerulosclerosis/Capillary Collapse*

- Prototype is **FSGS**, but not all lesions with segmental sclerosis are FSGS. You can see segmental scars in membranous glomerulopathy as well.
  - Collapsing variant, glomerular tip lesion variant, classic FSGS variant
- If you have several normal glomeruli and some with segmental sclerosis, you need to do IF to rule out forms of membranous nephropathy, which can have segmental scars if long-standing.
  - **You'll have IgM and C3 staining in these hyalinosis lesions in FSGS, but not in membranous nephropathy (which would have IgG staining).**
- *What type of FSGS is it when you have narrowed it down with IgM and C3 immunofluorescence?*
- **Collapsing FSGS** is very aggressive → leads rapidly to chronic renal failure.
  - Characterized by collapse of the glomerular tuft AND swelling & hyperplasia of the podocytes. **Collapsing glomerulopathy is a podocyte disease** (de-differentiation, swelling, and proliferation of podocytes). Normally, podocytes don't proliferate (they are terminal cells).
    - In collapsing FSGS, they re-enter the cell cycle, and can almost look like a crescent here. They are not contiguous with the Bowman's capsule like a crescent.
  - Some collapsing variant of FSGS is idiopathic and some is HIV-associated. By EM, they can be differentiated. **Tubuloreticular inclusions** → HIV-associated collapsing FSGS, not idiopathic FSGS.
- **Glomerular tip lesion** → tend to be highly responsive to steroids
- **Classic FSGS** is somewhere in between these 2

*Patient with Nephrotic Syndrome with Nodular Glomerulosclerosis*

- Could be (DDx): Diabetic nephropathy → most common, light chain deposition disease (LCDD), and amyloidosis
- Diabetes is common, LCDD is rare, and amyloidosis is uncommon
- **Diabetes should come to your mind first with nodular glomerulosclerosis.** To know that it is diabetes-associated, you have to look at the silver-stain.
  - Diabetic nodules are comprised of **basement membrane matrix** → positive on PAS stain and very strongly positive on **silver stain**
  - By contrast, amyloid deposits and deposits of light chains in LCDD do not stain in silver stain because they are not basement membrane matrix. So you see lots of silver-negative material.

- **Amyloidosis** – matrix has glassy, acellular look on H&E. Most importantly, the whole glomeruli stains very strongly on Congo-red stain. If you polarize the Congo-red stain, you get light green color. **Congo-red positivity is very specific for amyloidosis.** This is an amyloidosis causing nephrotic syndrome. Congo-red positivity is enough to give you diagnosis of amyloidosis. On EM, you'll see fine non-branching fibrils.
  - You need to determine where the amyloid is coming from.
    - If patient has rheumatoid arthritis, it is probably **AA amyloidosis** or **secondary amyloidosis**.
    - If older patient with history of back pain or lambda light chain in urine, it's probably **AL amyloidosis**.
  - **Do immunofluorescence staining for kappa or lambda, immunoperoxidase staining for AA protein. This determines if it is AA or AL, and if AL, then if it is kappa or lambda.**
  - Amyloidosis begins in mesangium and spreads peripherally
- **LCDD** can be resolved by IF as well, stain for kappa and lambda. Glomerular capillary walls and particularly the **tubular basement membrane** lights up for one light chain (primarily kappa) and not other. Congo red stain is negative.
  - Fine granular deposits (light chains) in subendothelial location and in tubular basement membranes on EM

#### Kidney Diseases Associated with Renal Insufficiency

- Divided into those that are glomerular and non-glomerular

#### Glomerular-Involved Renal Insufficiency

- Very chronic diseases
- If one *presents* with renal insufficiency and not necessarily nephrotic syndrome, then one has to think of **glomerulonephritis** and **thrombotic microangiopathies (DDx)**
- **Glomerulonephritis** is characterized by hematuria, usually renal insufficiency, proteinuria (usually not nephrotic), and often hypertension; oftentimes there is edema in GN due to poor function
  - In GN, you very often see **RBC casts (essential finding of patients with GN in urine, but not ALWAYS)**. When glomeruli become damaged and leaky to RBCs, RBCs aggregate in tubules as water is resorbed in the distal tubules and Tamm-Horsfall protein is added → RBCs stick together and the urine washes them down. You see the casts of the tubular lumen (RBC casts).
  - Morphologically, GN can be classified as **focal** (fewer than 50% of glomeruli, which are usually segmentally affected), **diffuse** (more than 50% glomeruli involvement), or **crescentic**.
  - Segmental hypercellularity is often seen in GN. This is what distinguishes GN. **GN is characterized by hypercellularity (focal or diffuse) within the glomerulus.**
  - **Hypercellularity in glomeruli** differentiates GN from those forms of glomerular disease that have nephrotic syndrome (which have normal cellularity usually).
    - **Focal GN** → DDx is **IgA nephropathy**, two forms of **lupus** which can be focal (mesangial deposits and proliferation – class II and focal proliferative – class III)
    - To differentiate: In IgA nephropathy, you see IgA deposits on IF in the mesangium. C3 is almost always present with the IgA. C1q is ALWAYS absent (IgA does not activate the classical complement pathway). **If you see C1q, think lupus.**

- **Lupus** can pretty much look like anything on light microscopy (LM). Depend on patient history first. Look for lupus serologies (ANA).
  - In lupus nephritis (class III and IV – proliferative forms), you often see **wire loops (subendothelial deposits in glomerular capillary walls)**. Seen in many cases but not all.
  - Some things you always see in lupus nephritis: full house antibody staining of IgG, IgA, IgM, C3, and **C1q**
  - C1q is even present in the less severe class II and V lesions
  - By EM, you will see **tubuloreticular inclusions** (not specific for lupus, because HIV-associated collapsing FSGS also has this)
  
- **Diffuse proliferative GN** – DDx: post-infectious glomerulopathy, diffuse proliferative lupus nephritis, IgA nephropathy, membranoproliferative, lupus type IV
  - Acute post-infectious GN is characterized by diffusely hypercellular glomeruli with many many neutrophils
  - Coarse granular IgG and C3 in the glomerular capillary loops; **characteristic subendothelial humps by EM**
  - Membranoproliferative GN – diffuse form of GN; **hypercellular glomeruli and hyperlobulated glomeruli; lobular-accentuated appearance**
  - PAS stain or silver stain → **double contours** or tram tracks of GBM seen with negative space between (the cytoplasm and subendothelial deposits between)
  - EM shows IgG and C3 in glomerular capillary walls, which excludes lupus.
  - Deposits in mesangium and subendothelial deposits and duplication of basement membrane over the deposits → characteristics of membranoproliferative GN (**double contour**)
  - **Serum C3 value is very important for MP GN.**
    - **Only 3 types of glomerular diseases give you low serum C3: acute post-infectious, membranoproliferative GN, and diffuse proliferative lupus nephritis**
    - **So if you have a low serum C3 in a diffuse proliferative GN, you know it's not IgA nephropathy and it's not idiopathic membranous nephropathy and it's not HUS.**
  
- **Crescentic GN**
  - **DDx:**
    - immune-complex mediated crescentic GN, including lupus, membranoproliferative GN, post-infectious GN, and IgA nephropathy
    - Pauci-immune forms of crescentic GN, including
      - P-ANCA (anti-myeloperoxidase) positive - **microscopic polyangiitis**
      - C-ANCA (anti-proteinase 3) positive - **Wegener's granulomatosis**

- anti-GBM antibody disease
- Crescentic GN is a severe form of GN, which if not treated early and aggressively, can progress rapidly to ESRD (regardless of etiology)
- Used to be called RPGN (**rapidly-progressive GN**)
- Treatment is very different depending on what the cause of the crescentic GN (is it immune-mediated like post-infectious? Is it lupus nephritis? Is it ANCA-associated? Is it anti-GBM antibody disease?)
- Serologies can be helpful here (lupus serologies, ANCA serologies, blood tests for antibodies to GBM – against Goodpasture antigen)
- But you have to look at the tissue to determine the etiology of the crescentic GN
- If you have active nephritic syndrome with renal failure, and pulmonary disease evidenced by something like hemoptysis or rapid white-out of lung, DDx is likely vasculitis or anti-GBM disease. → this is what's causing the crescentic GN.
- Anti-GBM disease (cause of crescentic GN)
- **antibodies to portion of type IV collagen** (part of glomerular basement membrane and pulmonary alveolar basement membranes). Diagnosis requires **LINEAR staining** of IgG in glomerular capillaries by IF. **Direct reaction of antibody with basement membrane protein that is diffuse distributed** → smooth staining, even, and linear, not lumpy like in an immune-complex disease.
- Antibody can cross-react with pulmonary alveolar BM, giving a pulmonary-renal syndrome referred to as **Goodpasture's disease**
- **20 – 30% of patients with Anti-GBM disease are ANCA positive. Just because you have positive ANCA doesn't mean you DON'T have anti-GBM disease, though this is fairly uncommon compared to ANCA GN**
- In ANCA GN, it is Pauci-immune, so you do not see a lot by IF. In anti-GBM antibody disease, you see the nice linear staining of GBM for IgG on IF. You see huge cellular crescent outside the glomerular tuft in Bowman's capsule, which does not stain with anti-GBM antibody.
- Anti-GBM antibody cross-reacts with pulmonary alveolar BM.

### Thrombotic Microangiopathies

- Another cause of renal insufficiency (along with glomerulonephritis – focal, diffuse, and crescentic)
- Two main classes of TMAs: those that involve primarily **glomeruli and arterioles** (present with hematuria and proteinuria because they involve glomeruli, nephritic picture) and those that involve **arterioles and arteries**
- **DDx for TMAs that involve glomeruli and arterioles: HUS, TTP (main 2), anti-phospholipid syndrome, drug-induced, pregnancy-related**
  - In these forms of thrombotic microangiopathy (HUS and TTP), you see thrombi in the arterioles and in the glomerular capillaries.

- You see RBC fragments. These patients have hemolytic anemia with **schistocytes** in the periphery because they clot off arterioles and glomerular capillaries → RBCs that try to get through become sheared and you get this fragmentation of RBCs. **Microangiopathic hemolytic anemia.**
- In terms of prognosis for **HUS**, the **epidemic form** (associated with diarrhea) has good prognosis → only glomerular and arteriolar involvement.
  - **Non-epidemic form** (D<sup>-</sup> form) has a guarded prognosis and involves arteries as well as arterioles and glomeruli.
  - **The smaller the vessels involved → the better the prognosis.** Best prognosis is glomeruli only. Worst prognosis is all 3.
- **DDx for TMAs that involve arteries and arterioles: scleroderma and malignant hypertension**
  - You can tell them apart clinically usually
  - **On kidney biopsy, you can't tell scleroderma and malignant hypertension apart – has to be resolved serologically and clinically**
  - Both have **mucoïd intimal hyperplasia** in arteries with massive thickening of intima with edematous appearance, with marked narrowing of lumen (think malignant hypertension or scleroderma)
  - Glomeruli on these biopsies have ischemia because not a lot of blood is getting to glomeruli → glomerular capillaries are collapsing because they are not being perfused (but no podocyte hyperplasia, so it's not collapsing glomerulopathy). This is just low perfusion (ischemic glomeruli with low GFR).

### Tubulointerstitial Diseases

- Cause renal insufficiency with no hematuria
- These are patients who present with renal failure with little or no proteinuria and little or no hematuria; but **there can be WBCs and WBC casts in the urine**
- **DDx for patient with acute renal failure and WBCs in the urine: interstitial nephritis or infection (pyelonephritis)**
  - You can tell it is pyelonephritis if you can grow something in culture and if it has a lot of neutrophils.
  - A patient who has a *Staph* cellulitis on leg and you treat them with antibiotic → develops ARF and you see no RBCs in urine, but you do see WBCs and eosinophils in urine → this is an acute interstitial nephritis due to antibiotic
- **Biopsy of interstitial nephritis** → interstitial inflammation (primarily neutrophils, but also lymphocytes, and lots of eosinophils). Two drugs that cause this are antibiotics and NSAIDs (90% of drug-induced interstitial nephritis together).
  - You see eosinophils more with antibiotics than NSAIDs.
  - The two classes of drugs that cause interstitial nephritis are antibiotics and NSAIDs.
- **Biopsy of pyelonephritis** → acute infection of kidney. Mostly ascending infection into bladder seeded in the context of vesicoureteral reflux or obstruction. You see **intra-tubular neutrophils** (HALLMARK OF ACUTE PYELONEPHRITIS). Interstitial inflammation with neutrophils and lymphocytes. **The intra-tubular neutrophils are the key here.**

- If you have acute renal failure, no WBCs in urine, no RBCs in urine, and no proteinuria → you could have acute tubular necrosis or light chain cast nephropathy. → now you consider **primary tubular disorders: acute tubular necrosis and light chain cast nephropathy (DDx)**
  - **Light chain cast nephropathy** and renal failure could be the first manifestation of multiple myeloma → especially in older people.
    - Occurs in dehydrated people, older people → acute renal failure and acute oliguria (don't make a lot of urine).
    - Biopsy here will show dense light chain casts within tubules
    - You see fractured casts with hard edges → typical of light chain cast nephropathy
    - There is **cellular reaction to casts** (cells of macrophage origin). These cells engulf and phagocytize the casts. These can form **multinucleated giant cells (which are virtually pathognomonic for light chain cast nephropathy)**
  - **Acute tubular necrosis** (two faces – ischemic, where you have acute hypotensive episodes (post-surgically or in dehydration) or toxic).
    - With **ischemic acute tubular necrosis** → Decreased perfusion of kidney. These patients get acute hypotensive episodes which can happen post-surgically or in dehydration.
      - These patients don't have a whole lot of necrosis (misnomer) → sparse interstitial tubular cells → **proximal tubular cells become flattened and simplified**. So instead of having tall columnar appearance, they are flattened and squamous-like → very difficult to discern from distal tubules. This is **distalization** of the proximal tubule.
      - Diffuse flattening of the proximal tubular cells is seen in ischemic acute tubular necrosis, which is a misnomer because there isn't that much necrosis
    - **Toxic acute tubular necrosis** occurs with drugs, especially with gentamicin, heavy metal poisoning, antifreeze
      - **Diffuse necrosis** (not a misnomer like ischemic ATN) of proximal tubular epithelial cells → suggests a toxin, not ischemic ATN
    - In both of these (ischemic and toxic), you see interstitial edema but not much interstitial inflammation

### Pathology Review

Look at Learning Objectives for each lecture.

Look at what's in each box.

For **Forensic Pathology**, only memorize the things she said know. Know the difference between cause of death, mechanism of death, and manner of death. Know difference between cut and laceration.

When you have automobile accident, how do you get all the bruises?

Gun-shot wounds

Difference between entrance wound and exit wound.

### Renal

#### ➤ Minimal change disease

- On LM, you see normal glomerulus
- On EM, you see effacement of podocyte foot processes
- Signs of MCD are selective proteinuria
- Common in children

#### ➤ Segmental Sclerosis and Hyalinosis

- Proteinuria and foot process effacement are common here
- Know histologic variants here
- **Collapsing glomerulopathy** – a form of focal sclerosing and hyalinosing disease; HIV-associated

#### ➤ Membranous GN (Membranous Glomerulopathy)

- Caused by immune complex deposition in the basement membrane
- Very distinctive pattern on IHC
- Seen most often in **lupus**

#### ➤ Diabetic Nodular Sclerosis (Kimmelstiel-Wilson Nodules) → DEFINITELY KNOW THIS

- Hyalinizing, sclerosing glomerulopathy
- Risk factors for getting kidney disease in diabetes. **Not all diabetics get kidney disease**

#### ➤ Crescentic Glomerulopathy

- End-stage of lots of glomerular processes
- Lots of things cause crescentic change

- What diseases cause this? KNOW WHICH ONES DO CAUSE THIS AND WHICH ONES DON'T.

➤ **IgA Nephropathy**

- Most common disease on renal biopsy
- Proliferation in mesangium
- IgA deposits in mesangium

➤ Match up an IF with a light microscopic pattern

➤ **Malignant Hypertension**

- Intimal thickening
- Onion-skinning around it (mucoïd)
- Benign hypertensive changes causes hyaline nodularity to vessels, not the onion-skinning

➤ **Post-Streptococcal GN**

- Hypercellularity of glomerulus
- Inflammatory cells in glomerulus → neutrophils
- Know clinical presentation
- Cause of nephritic syndrome
- Gross hematuria

➤ **Acute Tubular Necrosis**

- Not necrotic tubules, but you see flattening of cells
- Drugs can cause this
- Pre-renal low perfusion can cause this
- This is the main cause of acute renal failure

➤ **Interstitial Nephritis**

- In the interstitium, you see lots of inflammatory cells
- NSAIDs, penicillin causes this
- Eosinophils are present

➤ **Acute Pyelonephritis**

- Neutrophils in the tubule lumens
- Common with UTIs
- Risk factors for pyelonephritis (reflux nephropathy, obstruction, manipulation of urinary tract, etc)

➤ **Hemolytic Uremic Syndrome**

- Diffuse thrombi in glomerular capillaries
  - KNOW ALL ABOUT THIS DISEASE
  - If someone eats a lousy hamburger, and three weeks later they get hematuria, it can be HUS
  - Know the different associated for HUS
- 

**Pulmonary**

**Diffuse Alveolar Damage**

- Key is **hyaline membranes**
- Gives you **acute respiratory distress syndrome (ARDS)** → in babies or adults
- What factors cause acute alveolar damage?

**Asbestosis**

- Asbestos bodies seen on H & E
- Asbestosis causes three things:
  - **Pulmonary fibrosis**
  - **Lung cancer**
  - **Mesothelioma**

**Sarcoidosis**

- Granulomas in lung
- Many other things cause granulomas
- Sarcoidosis is only a disease by exclusion
- First you have to rule out TB, fungi, foreign bodies
- Know the fungi that occur in the lung

**Interstitial Fibrosis**

- Idiopathic pulmonary fibrosis can cause this
- Looks like really diffuse fibrous bands
- Alveoli are pushed together

### **Emphysema**

- If you see free-floating alveoli, that shouldn't be
- Hyperinflated lungs
- Caused by smoking, or alpha-1 antitrypsin deficiency

### **Adenocarcinoma of the Lung**

#### **Small Cell Carcinoma**

- Most aggressive of lung cancers
- Almost always presents with metastases before you know something is going on in lungs

#### **Clear Cell Carcinoma of Kidney**

- Most common type of renal cancer
- Most benign is **oncocytoma** → extremely benign

#### **Wilms Tumor**

- Most common type of childhood renal cell carcinoma
- Prognosis is good in many cases if you diagnose early

#### **Polycystic Kidney Disease**

- Associated with liver disease, pancreas disease
- Looks like a ball of marbles

**15 Pathophysiology Review***Glomerular Filtration Lecture*

- $CrCl = U_{Cr} / P_{Cr} \times V / 1440$  (creatinine clearance)
- Serum creatinine – around 1 is normal
- Dependent on muscle mass
- Not a linear relationship between what creatinine is and what GFR is; it is exponential
- You can have very small change in serum creatinine that indicates big change in GFR
- Formulas to estimate GFR:
  - MDRD Formula (considers serum creatinine, age, gender, race)
  - Cockcroft-Gault:  $(140 - \text{age}) / P_{Cr} \times \text{Weight} / 72 \times 0.85$  (if women)
    - If serum creatinine rises, GFR will fall.
    - Older people → GFR falls as well.
    - Creatinine is based on muscle mass. If you are a woman with same creatinine as a man, then you probably have poor GFR.
    - African-Americans have more muscle mass than whites, so you have higher serum creatinine.
- Know that  $P_{GC}$  is what changes and helps us if the GFR goes up or down. **Auto-regulation**: at a range of pressures, we can keep our GFR fairly constant. For most pressures, you can keep GFR relatively constant.
- If pressure is low, you sense that pressure is low in afferent arteriole → turn on **renin, angiotensin II, aldosterone**
  - Angiotensin II constricts efferent more than afferent → helps you maintain GFR
  - Prostaglandins can dilate the afferent more than the efferent → helps you maintain GFR when your GFR is low
- When GFR is very high (with high BP or hypertension), you want to keep GFR intact
  - **Myogenic response** – if you have high pressure, afferent arteriole stretches and then responds to close back down (reflexive)
  - **Tubuloglomerular feedback** – you have macula dense in the glomerulus. The bulk of things is absorbed in the proximal tubule and loop of Henle. If you have a big load of things going downstream of this area, then the downstream parts can't handle it (the distal tubule and collecting duct).
    - The **macula densa** detects too much chloride coming through → releases **adenosine** → it constricts afferent arteriole so that you can get a lower GFR (back to normal) so that you can get slower flow through the glomerulus and extract (reabsorb) more

- **Types of Proteinuria**
- If GBM is intact, albumin doesn't get out because the podocytes have negative charge and you can't get it out of the blood into the urine. If it does get out, you think there is glomerular damage (nephrotic syndrome could be the cause).
- **Urine protein electrophoresis**, normally you don't have a lot of alpha, beta, gamma, or albumin.
  - In MCD, you get a lot of albumin out in the urine and nothing else really leaks. Not too much tubular damage. You have **selective glomerular proteinuria**.
  - All the other glomerular diseases have **non-selective proteinuria**
  - Albumin leak and tubular proteinuria problem superimposed on each other
  - **Tubular proteinuria: Tubular proteins do leak out**, but proximal tubules suck back the small proteins that do go out → you get spilling of smaller fraction of proteins, and a little albumin as well
  - **Multiple myeloma**: overproduction of light chain in the gamma fraction (so you see an increase in the gamma fraction).

#### *Tubular Function Lecture*

Don't need to know specifics

#### *Nephrotic Syndrome Case*

- There are primary causes (kidney-specific) and secondary causes of nephrotic syndrome
- The syndrome is:
  - Urine protein > 3 gm/day
  - Normal < 100 mg/day
  - Hypoalbuminuria
  - Edema
  - Hypercholesterolemia
- If you have severe nephrotic syndrome, you have predisposition for blood clots (can cause pulmonary embolism → death or go into the renal system).

#### *Sodium Balance Lecture*

- Carotid body sensors → turns on sympathetic NS as well as ADH
  - Increases cardiac output, heart rate, and causes vasoconstriction
  - Turns on RAA system → detected by renal afferent arteriole system
- Renal afferent arteriole sensors
  - At glomerulus, the RAA system that is activated helps to maintain the GFR

- Potent vasoconstrictor
  - RAA system: At tubular level (nephron), you suck up  $\text{Na}^+$  in proximal tubule
  - Aldosterone causes you to suck up  $\text{Na}^+$  in the collecting duct as well
- Most common cause of edema is **congestive heart failure**.
  - Here you don't get much contractility → carotid body doesn't sense fullness → activates sympathetic and thus RAA system → renal afferent arteriole activates RAA further → you suck up more  $\text{Na}^+$  in nephrons → edema
- In **cirrhosis of liver**, the liver is damaged.
  - With scarring, you get ascites due to leakage of fluids
  - With splanchnic circulation, you get pooling of blood. Instead of straight line bloodflow, it is stuck there, so the carotid body and renal afferent arteriole turn on sympathetic and RAA to try to get volume back
- With **nephrotic syndrome**
  - Causes of edema for nephrotic syndrome
    - Very low albumin
    - Primary sodium retention (tubules could just be dysfunctional and work improperly and just take up  $\text{Na}^+$ )
- Diuretics can be used to help you pee out this  $\text{Na}^+$

### *Water Balance Lecture*

#### **Hyponatremia**

- When you drink water normally, you maintain balance by sucking up sodium chloride within water in the tubules.
- You also don't have ADH around, so water just goes out of the collecting duct → you pee out water
- This is what you do in response to water load
- Hyponatremia = hyperwateremia
- The problem isn't too little salt, but rather too much water
- Decreased osmolality = hyponatremia → this is most of the cases you'll see (like 120  $\text{Na}^+$  rather than 140)
- Firstly, look at volume status
  - Hypovolemia → trauma or diarrhea (isotonic loss)
    - You have very low  $\text{Na}^+$  and low  $\text{H}_2\text{O}$
    - Poor skin turgor

- Dry mucous membranes
- Flat JVP
- Orthostatic hypotension
- Sensors sense this and turn on RAA → sucking up more  $\text{Na}^+$
- If you have uncontrollable blood loss or cholera and your effective extracellular volume is 10% down. Normally ADH responds to increasing serum osmolality (because you're losing water). Carotid body can also turn on ADH, and it causes a huge increase in ADH when you are more than 10% down on effective extracellular volume. It sees that the RAA system is not effective.
- ADH is also a vasopressor, so it constricts. It causes you to take up water in the nephrons. Only 1/3 of that water is extracellular, and 2/3 is intracellular.
- Thus, you suck up water, and you become hyponatremic to try to maintain your volume. This occurs in true hyponatremia & true volume depletion.
- Treatment: volume is down here, so replace fluids. Ameliorate the stimulus.
- Hypervolemia
  - Edema
  - Ascites
  - Elevated JVP
  - Total body sodium is up
  - CHF, cirrhosis, nephrotic syndrome
  - Effective volume seems low because of low contractility in CHF or low detected pressure due to other two. You sacrifice volume fullness for perfect serum sodium.
  - Treatment: Restrict dietary  $\text{Na}^+$  and  $\text{Cl}^-$ . You could give diuretics. You have to fix their nephrotic syndrome (primary cause must be fixed)
- Euvolemic
  - No edema, no dry mucous membranes, middle category
  - Volume status is okay
  - You just have too much water due to cortisol deficiency, hypothyroidism, SIADH (paraneoplastic) → you just have excessive ADH around → this causes hyponatremia
  - Treatment: water restriction because you are holding on to too much water. You don't need  $\text{Na}^+$  restriction here.
- To treat hyponatremia, you should not fix it too quickly.
- Osmolality:  $2 \times [\text{Na}^+] + (\text{BUN} / 2.8) + (\text{glucose} / 18)$
- Normal serum Osm is about 280 – 285.

- If you have hyponatremia, osmolality may go to 245 → water goes into brain and can expand → you can get herniation through the foramen magnum. The brain responds by trying to get sodium and potassium out of the head. After 2 – 3 days, the Osm goes back up to like 250 and the brain can shrink back. This is chronic hyponatremia. If serum sodium is low, and you try to fix it as quick as possible. If you make it 285 on the outside and you are 245 on the inside → water comes out and brain shrinks and pulls away from dura → central pontine myelinolysis
- **Dilutional hyponatremia**
  - Hyperosmolar hyponatremia (if glucose is very high for example in diabetes)
  - You actually have right amount of sodium, but since you have such high glucose, you increase ECF volume to dilute the glucose, but this also dilutes the sodium → you get hyponatremia
  - Normally, glucose just goes into cells because you have insulin around, but this doesn't work in diabetics.

### *Hypernatremia*

- If you are deprived of water, for example
- You turn on ADH and have thirst response
- With ADH, you take water channels in pre-formed vesicles and put them into membranes in principal cells in the collecting duct → water gets sucked back into the blood
- Urine osmolality will become very high here. This is what you normally do to concentrate urine.
- Hypernatremia is only with hyperosmolar states.
- Look at volume status
  - Hypovolemic
    - Occurs with most other diarrheas (you lose more water than sodium usually).
    - Treatment: Give NaCl and water
  - Hypervolemic
    - Edema, blood pressure is high
    - Sodium bicarbonate could be given if the person is in cardiac arrest
    - You could have hyperaldosteronism (serum sodium is being sucked up too fast); to treat, take out adenoma
    - Treatment: usually corrects by itself
  - Euvolemic
    - Water levels are down here (opposite of SIADH)
    - Diabetes insipidus
      - Central – brain cannot make ADH
      - Nephrogenic – you have plenty of ADH but your kidney does not respond to it due to V2 receptor defect due to lithium or hypercalcemia

- Treatment: give ADH and see if they concentrate their urine. If you give the ADH and nothing happens, they have nephrogenic DI. If you give ADH and they do respond, then they have central DI.
- **Anti natriuretic peptide** – makes you pee out  $\text{Na}^+$ . If you have volume up, the atrium will be stretched and you pee out more  $\text{Na}^+$ . This is important in normal states.
  - In CHF, you interestingly have tons of ANP. You can't pee this out however because the RAA and sympathetic outweigh it and you can't pee out the  $\text{Na}^+$ .

### *Potassium Lecture*

- Internal balance – shifting potassium
- Muscle and liver cells are major repository for potassium
- The main factors for shifting  $\text{K}^+$  inside cells are insulin and beta 2 receptors → causes  $\text{K}^+$  shift into cells. You have to shift the  $\text{K}^+$  into cells first before your kidneys get rid of it.
- How do your kidneys get rid of  $\text{K}^+$ ?
  - Collecting duct principal cell
  - Factors that affect this:
    - If you bring  $\text{Na}^+$  and  $\text{H}_2\text{O}$  you suck up  $\text{Na}^+$  and you release  $\text{K}^+$ .
    - If you have aldosterone, you get more activity of Na/K pump, so you get more  $\text{Na}^+$  reabsorption and more  $\text{K}^+$  excretion.
    - Normal  $\text{K}^+$  is 3.5 – 5 mEq

### *Hyperkalemia*

- Three main categories of hyperkalemia:
  - **Spurious** (if you have a lot of WBCs, platelets, or hemolysis during blood draws) → pseudohyperkalemia
  - **Shift** → in diabetics. If you have no insulin, you can't shift the  $\text{K}^+$  inside cells, and you get hyperkalemia
  - **Decreased renal excretion** → if no sodium and water are delivered to collecting duct, and there is no sodium to exchange, you can't excrete  $\text{K}^+$  and reabsorb  $\text{Na}^+$ 
    - **ACE inhibitors and low aldosterone can also cause this → hyperkalemia**
- Treatment of hyperkalemia
  - If you have ventricular fibrillation, you give calcium. This just stabilizes the membrane for severe arrhythmias.
  - Then you try to put potassium into cells → give insulin and glucose. You want to SHIFT it into cells
  - Finally, to get rid of the  $\text{K}^+$ , you get hemodialysis if you can't pee (oliguria) or you can use kayexylate (exchanges  $\text{Na}^+$  for  $\text{K}^+$  in gut and you defecate it out).

### Hypokalemia

- **Shift into cells** → seen with myocardial infarction (too much norepinephrine release → beta2 receptor stimulated → puts  $K^+$  into cells). Happens with severe stress.
- If you have heart disease, the low  $K^+$  can kill you.
- Excessive loss of  $K^+$ 
  - Renal loss
    - If  $U_{K^+} > 25$  mEq/day, then you are peeing out too much  $K^+$  when you should be holding on to it (kidney problem)
    - Diuretic could cause this
    - IF you are volume-depleted with diuretic → you activate aldosterone → you suck up  $Na^+$  and release  $K^+$
    - **BOARD Question. Vomiting is a renal loss of  $K^+$ .**
      - Why does vomiting cause renal loss of  $K^+$ . Stomach cells normally make HCl. Every time you put out an acid, you make bicarbonate. Pancreas takes bicarbonate and neutralizes acid in rest of intestine. However, if you are barfing, bicarbonate stays in pancreas and you get metabolic alkalosis. So kidney tries to get rid of sodium bicarbonate → which is delivered to principal cell and you lose potassium.
      - Since you are vomiting and your volume is low, you turn on RAA → you suck up  $Na^+$  and lose  $K^+$ . Thus, vomiting is a renal loss of  $K^+$ .
  - Gut loss
    - If  $U_{K^+} < 25$  mEq/day, then you have diarrhea
  - Differentiate with 24 hour urine potassium.
- In hypokalemia,  $H^+/K^+$  turns on and  $H^+$  is spit out so you get metabolic alkalosis

### Acute Renal Failure Lecture

- **Prerenal ARF** – glomerulus is not getting enough flow (could have true volume depletion with CHF or **hepatorenal syndrome** – associated with cirrhosis)
  - Very severe renal vasoconstriction despite other vessels being dilated
- **Postrenal ARF** – stone, prostate tumor, gynecological tumor
  - Diagnosed on ultrasound where you can see dilated calyces in the kidney because downstream in the bladder or ureters there is a stone and you can't urinate
- **Renal ARF**
  - **Acute Tubular Necrosis**
    - Can be caused iatrogenically by **contrast dyes, aminoglycosides**
    - Can be caused by rhabdomyolysis (toxic to tubules)

- Can also be caused by prolonged ischemic → tubular death
  - In the loop of Henle, you see Tamm-Horsfall protein binding to parts of proximal tubule → so you see muddy brown granular casts in ATN.
- **Acute Interstitial Nephritis**
  - Caused by many drugs (penicillin, NSAIDs)
  - Normally not inflamed (no inflammatory cells). You'll usually see lots of edema between tubules
  - You see eosinophils → indicates allergic reaction in tubules
  - In urine, you see WBCs in urinary space and stick to Tamm-Horsfall protein. Instead of granular cast, you see WBC casts and WBCs.
- Glomerulonephritis
- Breakdown of barrier
- Different types of rapidly-progressive crescentic GN
- Crescent is being made
  - Caused by:
    - Immune-complex disease (deposits in mesangial cells) → lupus
    - Anti-GBM disease (antibody attacking the GBM) → linear immunofluorescence
    - Pauci-immune – you don't see much on IF; ANCA-positive (Wegener's, microscopic polyangiitis).
  - In urine, you see lots of protein because of barrier leak. You see RBCs as well (schistocytes) → RBCs stick onto Tamm-Horsfall protein and make RBC casts. This is classification scheme for acute renal failure.
- Clinically, look at urine sodium, urine osmolality, FeNa, BUN/Cr between pre-renal and post-renal (ATN) state
  - Urine sodium
    - Low in pre-renal (< 20 mEq/L)
    - High in ATN (>40 mEq/L)
  - Urine osmolality
    - High in pre-renal (> 500 mOsm/kg)
    - Low in ATN (300 – 350)
  - FeNa
    - <1% in pre-renal

- >2% in ATN
- BUN/Creatinine Ratio
  - More than 20:1 in prerenal states
  - Less than 20:1 in ATN (post-renal)
    - Why is this? Because urea nitrogen passively follows sodium and water in proximal tubule. In renal failure, you don't filter as much, so BUN and creatinine are both elevated in blood, so both go up. If you are pre-renal, tubules are sucking up BUN, urea nitrogen goes back into blood and the ratio goes up. This can't happen in ATN because the tubules are dead, so the ratio is less than in ATN (post-renal).

### *Metabolic Acidosis Lecture*

- Whatever bicarbonate gets filtered by proximate tubule, you have to be able to reclaim that. Tubules are responsible for that. Proximal tubules are responsible for this.
- To avoid acidosis, you HAVE to reclaim this bicarbonate that you've filtered.
- The intercalated cell in collecting duct takes  $H^+$  and pees it out three different ways
  - Free HCl (0.1 mEq contribution)
  - As titratable acid (like  $H_2PO_4$ ) (35 mEq contribution)
  - Ammonia → Ammonium chloride (35 mEq contribution)
- You can only make pH in urine so acidic (like pH 4).
- **In acidosis, you have to have some way to get rid of the  $H^+$ . You have to have a way to generate a lot of ammonia to get rid of the  $H^+$ .**
- **Ammonia is your defense against an acidosis.** So the 35 mEq contribution normally for ammonia goes up to like 300!.
- Approaching acid-base problems:
  - Look at pH. Normal 7.4. Lower than 7.4 → acidemia
  - Look at bicarbonate. Normal 24. If lower → then you have metabolic acidosis contributing to acidemia
  - As part of metabolic acidosis, you have to have **pulmonary compensation**.
    - $pCO_2$  is normally 40. If you have lower bicarbonate,  $pCO_2$  should be lower as well (because you're trying to get rid of acid).
    - **Expected  $pCO_2 = 1.5 (HCO_3^-) + 8 \pm 2$**
  - Calculate the serum anion gap:  $Na^+ - (Cl^- + HCO_3^-)$
  - Two categories of acid:  $H^+X^-$  (extra anion in blood, that's why you have the gap).
  - If you have serum anion gap greater than 11, then think SLUMPED (high anion gap metabolic acidosis)

- Salicylic acid, lactic acid, uremia, methanol, phosphates, ethylene glycol, diabetic ketoacidosis
  - First, think of methanol and ethylene glycol.
- If measured osmolality is greater than the calculated osmolality by more than 10, then you know there is an extra osmolal that is in the blood that is not  $\text{Na}^+$ , BUN, or glucose (from the normal osmolality equation).
  - If serum anion gap  $< 1$ , then think of hydrochloric acid (no extra anion). You could be losing bicarbonate in stool, you could be losing bicarbonate in urine (where you have proximal RTA), or if you are unable to excrete RTA (distal RTA – type IV).
  - *Diarrhea*
    - **Urine anion gap:** when serum anion gap is normal, is measured by urine sodium + urine potassium – **urine chloride. This is an indirect measurement of ammonium secretion.** We assume this chloride is from 3 things: NaCl, KCl,  $\text{NH}_4\text{Cl}$ .
    - If you're having a lot of diarrhea, you should be making a lot of ammonium.
    - Urine anion gap is negative (high) with diarrhea because you have a lot of  $\text{NH}_4^+$ . Look at equation!
  - *Urine Loss*
    - You can pee out bicarbonate if you have a proximal RTA
    - In distal RTA, you cannot pee out acid, your urine is paradoxically alkaline, and acid builds up in the blood → classic distal RTA
    - You can become hypokalemic because you have negative charge in the tubular lumen and you get  $\text{K}^+$  loss into the urine.
    - In type IV RTA (hypoaldosterone type), you get aldosterone turning on  $\text{H}^+$  secretion. If you don't have aldosterone, you can't get rid of acid because you don't have the extra push to get rid of  $\text{H}^+$ . Also, if you have lost aldosterone, you get hyperkalemic. This is why with type IV, you get hyperkalemia. Additionally, in the proximal tubule, you have a lot of  $\text{K}^+$  in the cell, and you pump  $\text{H}^+$  into the blood to become neutral
      - Serum potassium elevated
      - Urine anion gap is 0 to something positive because you cannot make  $\text{NH}_4\text{Cl}$ . It is elevated in both distal RTA and type IV RTA.

#### *Metabolic Alkalosis*

- Generation phase and maintenance (kidney is not excreting the bicarbonate) phase of alkalosis
- Usually, this occurs because you are losing acid (vomiting, diuretic) → this is what starts the alkalosis.
- Maintenance of alkalosis
  - Lower ECF volume
  - Aldosterone
  - Hypokalemia
  - Chloride depletion

- In collecting duct, you have principal cell and intercalated A cell and intercalated B cell.
- Intercalated A cell have  $H^+$  pump into lumen and  $H^+/K^+$  pump ( $H^+$  into lumen).
- Intercalated B cell...
- If you vomit, you lose HCl and get volume depleted → turn on RAA. Aldosterone causes you to suck up  $Na^+$  via the principal cells in the collecting duct → it's easier to get rid of  $K^+$  and  $H^+$  because . Directly affects  $H^+$  secretion.
- Aldosterone for metabolic alkalosis is bad. You don't want to be peeing out acid.
- Hypokalemia → you shift and put  $H^+$  inside cell. Stimulus for glutamine to make ammonia. More ways to get rid of  $H^+$ . This is bad for metabolic alkalosis. If you are hypokalemic, you pee out  $H^+$  → bad for metabolic alkalosis.
- Chloride depletion → chloride passively follows sodium. By the time you get to the distal collecting duct, chloride will be low. When you vomit and are chloride depleted (volume depleted too), you get a larger gradient of blood → tubular lumen chloride. So you get more  $Cl^-$  movement into the tubular lumen →  $H^+$  follows it.
- These 4 things maintain the alkalosis. **KNOW THESE FOUR THINGS**
- **Classification of metabolic alkalosis (by urine chloride concentration)**
  - Urine chloride low (< 25 mEq/L)
    - Vomiting (volume-depleted)
    - Stopped diuretic use (remote)
    - If you replaced NaCl, then you would cure this problem
  - Urine chloride high (> 25 mEq/L)
    - Primary hyperaldosteronism → total body chloride is up (you're sucking up NaCl), so you can't just treat with NaCl
    - Bartter's syndrome (like being on loop diuretic forever)
    - Giving NaCl for these two does not help
- Compensation for metabolic alkalosis. For every 1 mEq increase in the bicarbonate > 24, the  $pCO_2$  will increase by 0.7x that number (e.g.  $40 + 0.7x$ ).
- Don't need to know water deficits, bicarbonate deficits formulae.

#### *Genetic Renal Diseases*

- **Alport Syndrome**
  - Major type is X-linked where you have problem with type IV collagen
  - Proteinuria, hematuria, eventually on dialysis
  - Other things associated with this are deafness and lenticonus
- **Congenital Nephrotic Syndrome**

- Involves nephrin (molecule in slit diaphragm). Podocyte protein problem. This is a glomerular problem.

➤ **Bartter's Syndrome**

- $\text{Na}^+/\text{K}^+/\text{2Cl}^-$  is blown away, so it looks like you're on a loop diuretic
- Hypokalemia
- Metabolic alkalosis
- Hypercalciuria
- Not hypertensive usually because they can't suck up NaCl
- JUST LIKE FUROSEMIDE ALL THE TIME
- DON'T KNOW EACH TYPE

➤ **Liddle Syndrome**

- Sodium channel in principal cell
- This channel is always on, so you get constant  $\text{Na}^+$  reabsorption into blood → hypertension
- Hypokalemic because the more  $\text{Na}^+$  you take up, the more  $\text{K}^+$  you lose
- Metabolic alkalosis because along with losing  $\text{K}^+$ , you can lose  $\text{H}^+$

➤ **Polycystic kidney disease**

- Autosomal dominant (men and women involved)
- Aneurysms ("worst headache of my life")

*Nephrolithiasis*

➤ **Struvite stone (infection stone)**

- Urine urea →  $\text{NH}_4^+$ . You get alkaline urine.
- Struvite stone is magnesium, ammonium, phosphate.
- Alkaline pH predisposes you to phosphate stones

➤ **Uric acid stone**

- Precipitates in acidic urine (opposite of struvite)
- Can have gout, diarrhea
- Can have abnormally acidic urine
- Not seen on plain X-ray, which picks up calcium
- X-ray negative

➤ **Calcium oxalate stone**

- Enteric hyperoxaluria. In gut, you get bile acids and FFAs absorbed in the small bowel. If you have calcium and oxalate in the gut, they bind together and you defecate it out.
  - If you have small bowel disease, bile acids can bind up calcium in the gut. Oxalate has nothing to bind to → you reabsorb oxalate and pee it out. You have small bowel disease here (could be Crohn's disease or malabsorption).
  - Distal RTA
    - Classic Type I
    - Acidosis and inability to pee acid, so you have alkaline urine → precipitates phosphate stones
    - Acidosis decreases citrate in the urine
  - Formulas to know: creatinine clearance, compensation for metabolic acidosis, compensation for metabolic alkalosis
- 

#### *Hypertension Lecture*

- BP equals cardiac output x SVR (systemic vascular resistance)
  - **SVR is increased in essential (primary) hypertension → why your BP goes up**
    - Sympathetic nervous system could cause this. Angiotensin II also causes you to press your vessels.
    - Endothelin is also a pressor.
    - Because of constant vasoconstriction, you have chronically elevated SVR due to SNS, RAA, and endothelin going up → arteriolar remodeling
  - **Secondary causes of hypertension**
    - **Renal artery stenosis**
      - If you have cholesterol ball upstream of glomerulus, you get upregulation of angiotensin II → renal artery disease
    - **Pheochromocytoma** → tumor in adrenal glands where you get increased epinephrine and norepi all the time → causes hypertension
    - **Primary hyperaldosteronism** → sucking up Na<sup>+</sup> all the time
- 

#### *Chronic Kidney Disease Lecture*

- Higher stage = worse GFR
- Use MDRD formula to classify people in stages
- What happens when you have chronic kidney disease?
- You have decreased number of nephrons working, so the ones that remain are picking up the slack and doing an unfair share of work. Total excretion is still okay for now.
- If you only have like 10% of nephrons, your total excretion may not be good enough because you don't have enough nephrons to filter it out.

- If you can't get rid of  $\text{Na}^+$ , for example, you get hypertension and edema.
  - Increased preload → in chronic kidney disease
  - You also can't get rid of  $\text{K}^+$  and  $\text{H}^+$  (metabolic acidosis)
  - Can't get rid of water even though they drink a lot
  - Uremia → buildup of toxin where you get nauseous and you vomit. Lethargy, seizures.
  - With chronic kidney disease, you try to do dialysis or transplant.
  - Anemia in CKD.
    - You don't make enough erythropoietin → you become anemic.
    - Patients don't absorb iron as well, so you get iron deficiency as well.
    - Arteriovenous malformations → blood loss.
  - Bone disease
    - Kidney takes vitamin D and makes it the active form (1,25)
    - CKD patients have less 1,25 Vitamin D → calcium decreases → so you increase PTH and chew up bone to make  $\text{Ca}^{2+}$  higher → you can get fractures
    - Ability to get rid of phosphate is less → so you get increased serum phosphate. Phosphate complexes with calcium and can deposit in coronary vessels
- 
- Peritoneal dialysis – more freedom
  - Hemodialysis – you are there three times per week
  - Dialysis gets you by, but a renal transplant is the way to go unless there is a big contraindication.
- 
- Dr. Miller
  - Know slides in big font

**32 Pulmonary Pathophysiology Review**➤ **Know equation:**

- A-a gradient
  - $DAa = [(P_B - 47)F_iO_2 - P_aCO_2/0.8] - P_aO_2$
- Pulmonary Vascular Resistance
  - $PVR = P_{PA} - P_{LA} / Q$
- Compliances
  - $V_T / P_X = (\text{tidal volume} / \text{appropriate transmural pressure})$
  - $1/C_{RS} = 1/C_L + 1/C_{CW}$

**PFTs**

- Interpretation of PFTs
  - Disease classifications
  - **Know the determinants of lung volumes**
  - Disease / PFT correlations
- Interpretation of **arterial blood gases (ABGs)**
  - Hypoxia (causes and their differentiation)
    - Alveolar air equation
  - Hypercarbia
- **Spirometry**
  - FEV<sub>1</sub>/FVC
  - FVC (obstructive vs. restrictive)
- Lung volumes
  - Restrictive vs. hyperinflated with air trapping
- Diffusing capacity
  - Lung vs. extra-pulmonary disease
- **Arterial Blood Gases**
  - pH: acidosis or alkalosis

- $P_aCO_2$ : respiratory or metabolic
  - pH relative to  $P_aCO_2$ ...
- 

### Chest radiograms

- Know patterns with diseases
- 

### Interstitial Lung Disease

- Know what patient looks like
    - Symptoms, exam, Chest X-ray, PFTs
  - Etiologic categories and examples
    - Environmental (occupational and hypersensitivity), connective tissue, drugs, idiopathic, miscellaneous
    - IPF
    - Silicosis
    - Sarcoidosis
- 

### COPD

- **Epidemiology – KNOW THIS**
  - Risk factors
  - What does a patient look like? (pink puffer vs. blue bloater)
  - Treatment
- 

### Asthma

- Epidemiology
- Causative factors
  - Disease ( $T_H1$  vs.  $T_H2$  imbalance, tendency for allergies)
  - Triggers
- Exacerbation
  - Severity assessment, management
- Long-term therapy
  - Step care therapy, controller medications

- Know how patient with mild asthma vs. severe asthma looks. How are drugs layered onto these patients?
- 

### **Pulmonar Vascular Disease**

- Pressure-flow relations
    - Ideas of recruitment and distensibility
  - Causes of pulmonary hypertension
    - Anatomic approach
    - Prevalence (common vs. uncommon types)
  - Effects of Hypoxia on pulmonary vasculature
    - Adaptive and maladaptive HPV
  - **Primary idiopathic pulmonary arterial hypertension (PAH) → know about this!!**
    - Epidemiology and treatment
- 

### **ARDS**

- Patient presentation
  - Common causes
  - Factors favoring fluid flux
  - Treatment
    - Mechanical ventilation principles, PEEP
    - Outcomes
- 

### **Sleep-Disordered Breathing**

- Epidemiology
    - Obesity, sleep apnea
  - Obstructive sleep apnea
    - Critical closure
    - Patient presentation
    - Treatment: CPAP
  - Obesity hypoventilation syndrome
    - Versus OSA
-

### Ventilatory Failure

- Demand vs. capacity balance
  - Hyperinflation
    - COPD, Asthma
  - Effects of critical illness
    - Shock states, recovery
  - Respiratory muscle failure
    - Recognize
    - Treat
- 

### Infectious Lung Disease

- Lists
    - Bugs vs.
      - Age
      - Chest X-ray
      - Host
      - Setting
      - Etc.
- 

### Bronchopulmonary Dysplasia

- Why does prematurity cause BPD?
  - What does surfactant do?
  - Risk factors?
  - Prevention and treatment?
  - What happens to these kids when they get older?
- 

### Cystic Fibrosis

- Epidemiology
  - Prevalance, age, outcomes
- Pathophysiology
  - Chloride channel range of defects → **know the range of defects here**

- Sweat test, genotyping
  - Multiple organ manifestations
  - Treatment
    - Patient presentation
- 

### **Pediatric Upper Airways Disease**

- Know various causes of obstruction in kids
  - Choanal stenosis
  - Tonsils / adenoids
  - Laryngomalacia
  - ...
- 

### **Pediatric Lower Airways Disease**

- Congenital
    - Vascular rings, malacias (also inflammatory)
  - **Infectious bronchiolitis**
    - RSV, other viruses
  - Asthma
    - Epidemiology
- 

### **Pleural Pathophysiology**

- Forces governing fluid in the pleural space
    - Same as ARDS (Starling Equation)
  - Approach to diagnosis
    - Thoracentesis
  - Common causes of transudates / exudates
- 

- Emphysema and pulmonary fibrosis share all of the following pathophysiologic abnormalities except:
  - Elevated residual volume (RV in fibrosis is low)
- Treatment for this disorder includes all the following EXCEPT mucolytic therapy (chronic bronchitis has a lot of mucus production, but it is not helpful in emphysema)

- Viral infections, cold, and exercise are common triggers of asthma, but not bacterial infections.
- The main cause of pulmonary hypertension in COPD is alveolar hypoxia (pulmonary hypoxia → vasoconstriction)
- **Compliance is the change in volume divided by the change in transmural pressure**
- Hypoxia
  - 100% O<sub>2</sub> will not correct the hypoxia →
  - Normal alveolar-arterial O<sub>2</sub> gradient on room air →
  - Most likely to have →
-