The Physician Pharmacist: Renal

Renal Embryology:
-**Pronephros** = week 3 of development (then degenerates)
-**Mesonephros** = week 4 of development; functions as interim kidney for 1st trimester (persists in Male genital system as Wolffian Duct, forming ductus deferens + epididymis)
-**Metanephros** = Permanent; first appears in week 5, nephrogenesis completes ~week 36

- **Ureteric Bud** (Metanephric Diverticulum) = Ureter, Pelvises, Calyces, Collecting Ducts (complete by week 10)
- **Metanephric Mesenchyme** (Metanephric Blastema) = Ureteric bud interacts w/ this tissue ; interaction induces differentiation + formation of glomerulus through to DCT
- Aberrant Interaction btw these two tissues leads to malformations of kidney (Renal Agenesis, Multicystic Dysplastic Kidney)

-**Ureteropelvic Junction** = last to calize → Congenital obstruction (Most common cause of Prenatal Hydronephrosis) - Detected by Prenatal US

Potter Sequence:
-**Oligohydramnios** → compression of fetus → limb deformities, facial anomalies (low-set ears + retrognathia, flattened nose), Compression of chest - poor lung amniotic fluid aspiration triggering pulmonary hypoplasia (Primary Cause of Death))
-Causes = Chronic placental insufficiency, Reduced Renal Output of Fetus, ARPKD, Obstructive Uropathy, Bilateral Renal Agenesis
-"Babies who can't Pee in Utero develop Potter Sequence"
-POTTER:

- **Pulmonary Hypoplasia**
- **Oligohydramnios (trigger)**
- **Twisted Face**
- **Twisted Skin**
- **Extremity Defects**
- **Renal Failure (in utero)**

Horseshoe Kidney:
-Inferior poles of both kidneys fuse
-ascending from pelvis during fetal development, get trapped under Inferior Mesenteric a. (kidneys remain low in Abd)
-Functionally normal or Hydronephrosis, Renal stones, risk of renal cancer
-Commonly w/ Aneuploidy (Turner, Trisomies 13,18,21)

Congenital Solitary Functioning Kidney:
-being born with only one functioning kidney
-most asymptomatic if compensatory hypertrophy of contralateral kidney
Unilateral Renal Agenesis:
-Ureteric bud fails to develop and induce differentiation of Metanephric Mesenchyme → complete absence of Kidney + Ureter
Multicystic Dysplastic Kidney:
-Ureteric bud develops, BUT fails to induce differentiation of metanephric mesenchyme → nonfunctional kidney w/ Cysts + connective tissue
-usually Unilateral, bilateral = Potter Sequence

Duplex Collecting System:
-Bifurcation of Ureteric bud before it enters the metanephric blastema (creating **Y-shaped bifid Ureter**)
-Associated w/ Vesicoureteral Reflux, Ureteral Obstruction, risk of UTIs
-Presents w/ Hydronephrosis

Posterior Urethral Valves:
-membrane remnant in posterior (prostatic) urethra in males
-leads to Urethral Obstruction
-ddx prenatally = Bilateral Hydronephrosis + dilated/thick-walled bladder on US
-**Most common cause of bladder outlet obstruction in male infants**

Vesicoureteral Reflux:
-retrograde flow of urine from bladder to upper urinary tract
-causes = abnormal/insufficient insertion of ureter within vesicular wall (Ureterovesical Junction - UVJ) or secondarily via abnormally high bladder pressure
- risk of recurrent UTIs

Renal Anatomy:
-Left Renal Vein receives 2 additional veins (Left Suprarenal + Left Gonadal veins)
-Renal Cortex receives far more blood flow than Renal Cortex (Glomerulus - very sensitive to hypoxia/ischemic damage)
-Renal Transplant - Donor often gives Left Kidney b/c of longer renal veins
Ureters Course:

1. Arises from renal pelvis
2. Travels under gonadal arteries
3. Over common iliac a.
4. Under uterine artery/vas deferens (retroperitoneal)

-"Ureters flow Over the Iliacs, and Under the uterine artery/vas deferens"
-At risk for damage w/ gynecologic procedures (ligation of uterine artery)
-Ureter Blood Supply:

- Proximal = Renal a.
- Middle = Gonadal a, Aorta, Common/internal Iliac a.
- Distal = internal iliac + Superior Vesical a.

-Most Common points of Urethral Obstruction;

1. Ureteropelvic Junction (UPJ)
2. Pelvic Inlet
3. Ureterovesical Junction (UVJ)

Physiology:
-K+ intracellularly
-60-40-20 Rule = 60% total body water, 40% ICF, mainly composed of K+, Mg2+, organic Phosphates (ATP), 20% ECF mainly composed of Na+, Cl-, Bicarb, Albumin
-Plasma Vol = measured w/ Radiolabeled Albumin
-ECF = measured w/ Inulin or Mannitol
-Serum Osmol = 275-295

Glomerular Filtration Barrier:
-fenestrated capillary endothelium
-basement membrane w/ **Type IV Collagen** chains + Hapran Sulfate
-Visceral epithelial layer w/ Podocyte Foot Processes (FPs)
-Charge Barrier = (-) Glycoproteins prevent other (-) from getting through Albumin
-Size Barrier = fenestrated capillary endothelium; podocyte foot processes interpose w/ glomerular basement membrane(GBM); slit diaphragm (prevents entry of molecules > 4-5 nm)

Renal Clearance (Cl):
-Cl = ([Xurine] x Urine Flow Rate) / [Xplasma]
-Cl < GFR = net tubular reabsorption or not freely filtered substance
-Cl > GFR = there is a net tubular secretion of "X"
-Cl = GFR = no net secretion or reabsorption

Glomerular Filtration Rate (GFR):
-**Inulin** clearance = used to calculate GFR (b/c it's freely filtered and neither reabsorbed or secreted)
-Cl (inulin) = GFR = ([Inulin]urine x Urine flow rate) / Plasma inulin
-Normal GFR ~ 100 mL/min
-CrCl = approximate measure of GFR (slightly **overestimates GFR** b/c Cr is moderately secreted by renal tubules (meaning NOT every bit was actually filtered out of blood via GFR glomeruli)

Effective Renal Plasma Flow:
-eRPF = estimated w/ Para-Aminohippuric Acid (PAH) clearance
-there is 100% excretion of all PAH that enters the kidney
-Renal Blood flow (RBF) = RPF / (1- Hct)
-eRPF **underestimates** true renal plasma flow (RPF) slightly

Filtration:
-**Filtration Fraction (FF)** = GFR/ RPF
-Normal FF = 20%
-Filtered Load = GFR x Plasma Conc

Summary:
-GFR estimated w/ CrCl
-RPF = best estimated w/ PAH clearance
-NSAIDs constrict Afferent Arteriole (RPF, GFR, No change in FF)
-ACEI dilate Efferent Arteriole (RPF, GFR, FF)

Changes in Glomerular Dynamics: FF = GFR/RPF
1. Afferent Arteriole Constriction = GFR, RFP
2. Efferent Arteriole Constriction = GFR, RFP, FF
3. Plasma Protein Conc = GFR, -- RFP, FF
4. Plasma Protein Conc = GFR, --RFP, FF
5. Constriction of Ureter = GFR, --RFP, FF
6. Dehydration = GFR, RFP, **FF**

Calculation of Reabsorption and Secretion Rate:
-Filtered Load = GFR x Plasma Conc
-Excretion Rate = Flow Rate x Conc Urine
-Reabsorption Rate (RR) = Filtered - Excreted
-Secretion Rate = excreted - filtered
-**FeNa** = Fractional Excretion of Sodium

$$Fe_{Na} = (P_{Cr} \times U_{Na}) / (U_{Cr} \times P_{Na})$$

Glucose Clearance:
-at normal blood Glc levels, Glc is 100% reabsorbed in PCT by Na+/Glc Cotransporter (SGLT2)
-Glc > 200 mg/dL, saturates reabsorption transporters and Glc begins to remain in urine
-Pregnancy = GRF → higher filtration rates w/ Lower Glc transporter capacity = Glucosuria @ normal plasma Glc levels
-Splay Phenomenon = Glc transporter saturation is reached gradually, rather than sharply due to heterogeneity of nephrons

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Nephron Transport Physiology:

1. Early PCT:
-contains brush border
-reabsorbs ALL Glc, AAs, and Most Bicarb, Na+, Cl-, Phos, K+, Water, Uric Acid
-Isotonic Absorption
-Generates + secretes NH3 (allowing kidney to secrete more H+)
-**PTH = inhibits Na/Phos Cotransport → Phos Excretion**
-AngII = stimulates Na/H Exchange → Na+, Water, and Bicarb Reabsorption
-65-80% of Na+ and Water Reabsorbed
-SGLT2 Inhibitors Act here = Na+ (cardio benefits), Glc reabsorption (antidiabetic)
-Acetazolamide site of action (Carbonic Anhydrase inhibitor)

2. Thin Descending Loop of Henle:
-passively reabsorbs Water via medullary Hypertonicity
-Impermeable to Na+
-"Concentrating Segment" → making Urine Hypertonic
-Mannitol Site of Action (also PCT)

3. Thick Ascending Loop of Henle (TAL):
-reabsorbs Na+, K+ and Cl-
-indirectly induces paracellular (btw cells) reabsorption of **Mg2+, Ca2+** from (+) lumen potential generated by K+ backleak
-**Impermeable to water**
-makes urine less concentrated as it ascends
-10-20% Na+ reabsorbed
-**Loop Diuretic**

4. DCT:
-reabsorbs Na+, Cl-
-**Impermeable to Water**
-makes urine FULLY DILUTE (Hypotonic)
-PTH = Ca/N Exchange → Ca2+ reabsorption
-5-10% Na+ reabsorbed
-Thiazide Diuretics

5. Collecting Duct:
-reabsorbs Na+ in exchange for secreting K+ and H+ (regulated by **Aldosterone**)
-Aldosterone = acts on MC receptor → mRNA --. Protein synthesis
- Principal Cells =
  - apical K+ conductance
  - Na/K ATPase Pump
  - ENaC channel activity
  - Leads to K+ secretion
- a-Intercalated Cells =
  - Lumen negativity → H+ ATPase activity → H+ secretion → Bicarb/Cl exchanger activity
- **Spironolactone, Eplerenone** = decrease aldosterone receptor production (Na+, K+)
- **Amiloride, Triamterien** = inhibit apical side ENaCs

-**ADH = V2 Receptor → insertion of aquaporins H2O channels on apical side**
-3-5% of Na+ reabsorbed

Renal Tubular Defects:

-"Fanconi's BaGeLS" vs. "Fanconi Bartering, Gits Little Success"

1. Fanconi Syndrome:

-reabsorption defect in **PCT** → excretion of AAs, Glc, Bicarb, Phos (basically everything in PCT)

-Sxs:

- **Metabolic Acidosis (Proximal RTA) (H+)**
- **Hypophosphatemia (Phos)**
  - Growth Retardation + Rickets/Osteopenia
- **Hypokalemia (K+)**

-Causes:

- Hereditary (Wilson Dx, Tyrosinemia, Glycogen Storage Dx)
- Ischemia
- Multiple Myeloma (MM)
- Nephrotoxins/Drugs (Ifosfamide, Cisplatin)
- Lead Poisoning

-Common Volume depletion

2. Bartter Syndrome:

-Thick ascending Loop (**TAL**) defect (Na/K/Cl Cotransporter defect)

-sxs = Metabolic **Alkalosis**, **Hypokalemia, Hypercalciuria (Ca2+ urine)**

-Autosomal recessive

-Looks like Chronic Loop Diuretic Use

3. Gitelman Syndrome:

-**DCT** defect for NaCl reabsorption

-Metabolic **Alkalosis**, **Hypomagnesemia** (Mg), Hypokalemia (K), **HypOcalciuria**

-Autosomal Recessive

-Looks like Chronic Thiazide use (less severe than Bartter)

4. Liddle Syndrome:

-Gain of function mutation → Na+ channel degradation → Na+ reabsorption in Collecting Tubules **(CT)**

-Metabolic Alkalosis, Hypokalemia, **HTN, Aldo**

-Autosomal dominant

-Looks like Hyperaldosteronism but Aldo is absent

-Tx = Amiloride (ENaC inhibitor)

5. Syndrome of Apparent MC Excess (SAME):

-Hereditary **11b-HSD deficiency in Kidney**:

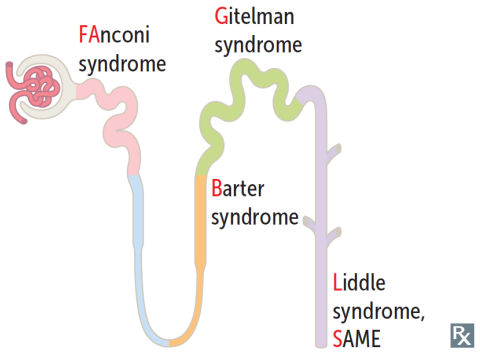
- Normally inactivates cortisol (much higher plasma conc) to Cortisone to avoid overstimulation of MC receptor (Na+, K+, H+)
- Deficient 11b-HSD = Cortisol → MC activity

-Sxs:

- **Metabolic Alkalosis**
- **Hypokalemia**
- **HTN**
- **serum Aldo level**

-Autosomal recessive (can be acquired via excessive Licorice intake - glycyrrhetinic acid inhibiting 11b-HSD)

-Tx = K+-sparring diuretics (MC effects) or Steroids (exogenous GC leads to endogenous cortisol production → MC receptor activation)



Relative Conc of Reabsorption/excretion along the PCT:

-From Highest excretion to lowest (most reabsorbed over time)

- PAH
- Creatinine ~ Inulin (clearance = GFR)
- Urea
- Chloride
- K+, Na+ = when solute and water reabsorbed at same rate (TF/P) = 1
- Bicarb
- AAs
- Glc

-Tubular inulin in conc (but not Amount) along the PCT as a result of water reabsorption

-Chloride reabsorption occurs slower than Na+ in early PCT, then matches rate of Na+ reabsorption more distally (both plateau at end)

RAAS:

1. Renin:

-secreted by JC cells

-released when renal perfusion pressure (PP) detected by Renal Baroreceptors in Afferent Arteriole, SNS discharge (B1 effect), NaCl delivery to macula densa

2. ACE:

-converts AngI to AngII in the Lung

-produced by vascular endothelial cells

3. AngII:

-maintains blood vol + pressure

-Affects baroreceptor function, limiting reflex bradycardia

1. AngII receptor Vasoconstriction → BP
2. Efferent Arteriole Constriction → FF → preserves GFR when RBF
3. Na/H+ Activity in PCT Cells → Na+, Bicarb, and Water reabsorption (permits contraction alkalosis)
4. Triggers Aldosterone secretion (Zona Glomerulosa of Adrenal Cortex) →
   a. A-intercalated cell = H+ secretion (H+ ATPase)
   b. Principal Cell activity (see 5.)
5. Principal Cell Activation:
   a. Na+ reabsorption, K+ secretion (K+ conductance, Na/K ATPase, ENaC)
   b. H20 Reabsorption from Aquaporins (ADH from Posterior Pituitary stimulated)

4. ANP, BNP:

-Atria (ANP), and Ventricles (BNP) in response to Vol → inhibits RAAS, relaxes VSM via cGMP→ GFR, Renin

-Dilates Afferent Arteriole, promoting Natriuresis

5. ADH (Vasopressin):

-regulates Serum Osmolality + Low BP

- H2O reabsorption + Urea reabsorption

6. Aldosterone (Aldo):

-regulates ECF vol, Na+ content → release in Hypovolemic states + Hyperkalemia (tries to)

Juxtaglomerular Apparatus (JGA):
-consists of mesangial cells, JC cells (modified smooth muscle of afferent arteriole), and Macula Densa (NaCl sensor located at the DCT)
-**JG Cells** = Secrete Renin in response to;
- renal blood pressure
- SNS tone (B1)

-**Macula Densa** = sense NaCl delivery to DCT → renin release → efferent arteriole vasoconstriction → GFR
-JGA maintains GFR via RAAS
-BB can BP by inhibiting B1-receptors of JGA → renin release

Kidney Hormone Functions:

1. Erythropoietin (EPO):
-from Interstitial Cells in Peritubular Capillary bed in response to Hypoxia
-Stimulates RBC proliferation in Bone marrow
-Given for Anemia for CKD

2. Calciferol (Vitamin D):
-PCT cells convert 25-OH vit D3 to 1,25-OH Vit D3 (Calcitriol - active form)
-Increases **Calcium absorption from small bowel**
-**1a-Hydroxylase** = stimulated by **PTH**

3. Prostaglandins:
-paracrine secretion vasodilates afferent arterioles to RBF
-NSAIDs block renal-protective PG Synthesis → constriction of Afferent Arteriole + GFR (AKI in low renal blood flow states)

4. Dopamine:
-secreted by PCT cells → promoting Natriuresis
-Low doses = dilates Interlobular arteries, afferent arterioles, efferent arterioles → RBF (little to no change in GFR)
-Higher Doses = Vasoconstrictor
-Fenoldopam = peripheral D1 Receptor agonist → vasodilation of systemic renal arterioles (GFR)

Potassium (K+) Shifts;
-Intracellular Shifts (Inducing Hypokalemia):
1. Hypo-osmolarity
2. Alkalosis
3. B-adrenergic Agonist (Na/K/ ATPase)
4. Insulin (Na/K ATPase)

-Extracellular Shifts (Causing HyperKalemia):
1. Digoxin (blocks Na/K ATPase)
2. HyperOsmolarity
3. Lysis of Cells (Crush Injury, Rhabdomyolysis, Tumor Lysis Syndrome)
4. Acidosis (H+)
5. B-Blockers
6. Low Insulin (high blood sugar)
7. Succinylcholine (Risk in Burns/Muscle Trauma)

Electrolyte Disturbances:
1. Sodium (Na+):
-Low = Nausea, Malaise, stupor, coma, seizures
-High = Irritability, stupor, coma

2. Potassium (K+):
-low = U waves + flattened T waves on ECG, Arrhythmias, Muscle Cramps, Spasms, Weakness
-High = Wide QRS + peaked T waves, arrhythmias, muscle weakness

3. Calcium (Ca2+):
-Low = tetany, seizures, QT prolongation, twitching (Chvostek), spasm (Trousseau sign)
-High = **Stones** (nephrolithiasis), **Bones** (pain), **Groans** (Abd pain), **Thrones** (Urinary frequency), **Psychiatric Overtones** (anxiety, AMS)

4. Magnesium:
-Low = Tetany, Torsades de Pointes, Hypokalemia, HypoCalcemia
-High = DTRs, lethargy, bradycardia, hypotensions, Cardiac arrest, hypocalcemia

5. Phos:
-low = bone loss, osteomalacia (adults), Rickets (Children)
-high = Renal stones, metastatic calcifications, hypocalcemia

Acid Base Physiology:
1. Metabolic Acidosis:
   a. pH, PCO2, Bicarb
   b. Hyperventilation (immediate)
2. Metabolic Alkalosis:
   a. pH, PCO2, Bicarb
   b. Hypoventilation (immediate)
3. Respiratory Acidosis:
   a. pH, PCO2, Bicarb
   b. Renal bicarb reabsorption (delayed)
4. Respiratory Alkalosis:
   a. pH, PCO2, Bicarb
   b. renal bicarb reabsorption (delayed)

-pH = 6.1 + log ([Bicarb] / 0.03 x Pco2)

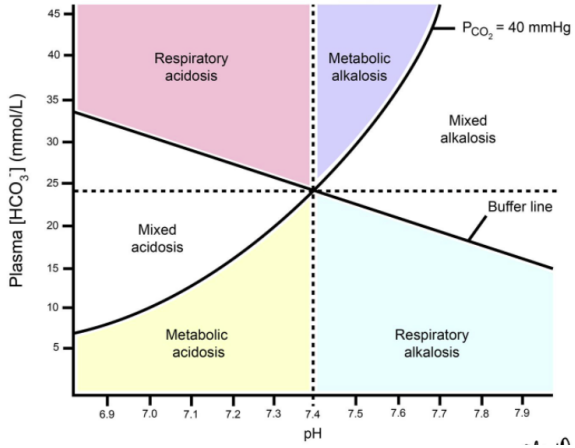
Winters Formula:
-predicted respiratory compensation for simple metabolic acidosis
-Measured PCO2 > predicted PCO2 --. Concomitant respiratory acidosis
-Measure PCO2 < Predicted PCO2 = concomitant respiratory alkalosis

PCo2 = 1.5 [Bicarb] + 8 +/- 2

Anion Gap = Na+ - (Cl- + Bicarb)
> 12 mEq/L

Anion Gap: **GOLDMARK**
1. Glycols (Ethylene Glycol)
2. Oxoproline (APAP metabolite)
3. Lactate (lactic acidosis)
4. D-lactate (exogenous lactic acid)
5. Methanol
6. ASA (late effect)
7. Renal Failure
8. Ketones (Diabetic, Alcoholic, Starvation)
9.

Normal Anion Gap: **HARDASS**
1. Hyperchloremia
2. Addison Dx
3. Renal tubular acidosis
4. Diarrhea
5. Acetazolamide
6. Spironolactone
7. Saline Infusion



Respiratory Acidosis Causes: "Hypoventilation"
-Airway Obstruction
-Acute Lung Dx
-Chronic Lung Dx
-Opioids, Sedatives
-Weakening of Respiratory Muscles

Respiratory Alkalosis Causes: "Hyperventilation"
-Anxiety attack/panic attack
-hypoxemia (hgih altitude)
-Salicylates (Early)
-Tumor
-Pulmonary Embolism
-Pregnancy

Metabolic Alkalosis Causes: "H+ loss/Bicarb Excess"
-Loop diuretics
-Vomiting
-Antacid Use
-Hyperaldosteronism

Nomenclature for Glomerular Disorders:

- **Focal** = < 50% of Glomeruli involved
- **Diffuse** = >50% of Glomeruli involved
- **Proliferative** = Hypercellular Glomeruli
- **Membranous** = Thickening of GBM
- **Primary Glomerular Dx** = Primary dx of kidney specifically impacting the glomeruli (Minimal Change Dx)
- **Secondary Glomerular Dx** = Systemic dx or dx of another organ system that also impacts the glomeruli (SLE, Diabetic Nephropathy)

Renal Tubular Acidosis:

CO2 + H2O → H2CO3 → H+ + Bicarb

Distal RTA Type 1:
-inability of **a-Intercalated** cells to secrete H+ (H+ ATPase) into the Urine (apical side) → no new bicarb is generated → metabolic acidosis
- Can't release H+ → H+ accumulates in cell turning off synthesis pathway (subsequently Bicarb too)
- Bicarb is normally released on the Basal side into the bloodstream

-Urine pH > 5.5
-Serum K+
-Causes:
- Amphotericin B Toxicity
- Analgesic Nephropathy
- Congenital Anomalies (obstruction)
- Autoimmunity (SLE)

- risk of **Calcium Phosphate** Kidney Stones (due to Urine pH and Bone Turnover needed for pH buffering of serum)

Proximal RTA Type 2:
-defect in PCT Bicarb Reabsorption → excretion of Bicarb in Urine → metabolic acidosis
-Urine can be acidified by a-Intercalated Cells in Collecting Duct, BUT not enough to overcome Bicarb excretion
-Urine pH =
- **< 5.5** when plasma Bicarb is below the reduced reabsorption threshold
- **> 5.5** when filtered bicarb exceeds resorptive threshold

-Serum K+
-Causes:
- Fanconi Syndrome
- Multiple Myeloma (MM)
- Carbonic Anhydrase Inhibitors (Acetazolamide)

- Risk for Hypophosphatemic Rickets (in Fanconi Syndrome)

Hyperkalemic Tubular Acidosis (RTA Type 4):
-HypOaldosteronism or aldosterone resistance → Hyperkalemia → NH3 synthesis in PCT → NH4 excretion
-Urine pH < 5.5 (or variable)
-Serum K+
-Causes:
- aldosterone production (Diabetic Hyporeninism, ACEI, ARBs, NSAIDs, Heparin, Cyclosporine, Adrenal Insufficiency)
- Aldosterone Resistance (K+ sparing diuretics, nephropathy duet obstruction, TMP-SMX)

Casts:
-Presence of casts indicates that the Hematuria/Pyuria is of Glomerular or Renal Tubular Oigin
-Hematuria w/ No Casts = Bladder Cancer, Kidney Stones
-Pyuria w/ No Casts = Acute Cystitis

1. RBC Casts:
- Glomerulonephritis
- HTNsive Emergency

2. WBC Casts:
- Tubulointerstitial Inflammation
- Acute Pyelonephritis
- Transplant Rejection

3.Granular Casts:
- Acute Tubular Necrosis (ATN) - "Muddy Brown" appearance

4. Fatty Casts: **"Oval Fat Bodies"**
- Nephrotic Syndrome (Maltese Cross)

5. Waxy Casts:
- End-Stage Renal Dx/CKD

6. Hyaline Casts:
- Nonspecific
- Normal finding = Dehydration, Exercise, Diuretic Therapy

-Forms via solidification of **Tamm-Horsfall Mucoprotein** (Uromodulin), secreted by renal tubular cells to prevent UTIs

Glomerular Diseases:

Nephritic Syndrome:

-Glomerular inflammation → GBM Damage → loss of RBCs into Urine → dysmorphic RBCs + Hematuria

Sxs:

-Hematuria

-RBC casts in urine

- GFR → Oliguria, Azotemia → Renin release + HTN

-Proteinuria (subnephrotic range of < 3.5 g/day)

Examples:

1. Acute Poststreptococcal Glomerulonephritis (PSGN)
2. Goodpasture Syndrome
3. IgA Nephropathy (Berger Disease)
4. Alport Syndrome
5. Membranoproliferative Glomerulonephritis (MPGN)

1. Acute Poststreptococcal Glomerulonephritis (PSGN):

-Children

-2-4 weeks after group A streptococcal infxn of Pharynx or skin

-Most resolve spontaneously in children (adults more likely to progress)

-Type III HSR - IC depositing in GBM

-Findings:

- Sxs = Peripheral Edema, Periorbital Edema, Tea/Cola-Colored Urine, HTN, (+) Strep titers/serology, Complement (C3) due to consumption
- **LM** = Glomeruli enlarged + Hypercellular
- **IF** = "**Starry Sky**" granular appearance ("Lumpy-Bumpy") due to IgG, IgM, C3 deposition along GBM and Mesangium
- **EM** = Subepithelial IC humps

2. Rapidly Progressive Glomerulonephritis (RPGN) (Crescentic):

-Poor prognosis

-rapidly deteriorating renal function (days - weeks)

-LM = Crescent Moon Shape (consist of Fibrin + plasma proteins (C3b) w/ Glomerular parietal cells, monocytes, macrophages)

-Several Presentations:

- **Goodpasture's Syndrome**:
  - Linear IF due to Antibodies against GBM + alveolar basement membrane
  - Hematuria/Hemoptysis
  - **Type II HSR**
  - Tx = Plasmapheresis
- **Granulomatosis w/ Polyangiitis (Wegeners)**
  - Negative IF/Pauci-Immune (No Ig/C3 Deposition)
  - PR3-ANCA
  - c-ANCA
- **Eosinophilic Granulomatosis w/ Polyangiitis (Churg-Strauss) or Microscopic Polyangiitis:**
  - Negative IF/Pauci-Immune (No Ig/C3 Deposition)
  - MPO-ANCA
  - p-ANCA
- Granular IF = Post-Strep GN, DPGN

3. Diffuse Proliferative GN (DPGN):

-Due to SLE ("Wire Lupus")

-Commonly both a Nephritic + Nephrotic Syndrome

-Findings:

- **LM = "Wire Looping"**
- **IF = Granular**
- **EM =** Subendothelial (sometimes Subepithelial or Intramembranous) IgG-based ICs w/ C3 Deposition

4. IgA Nephropathy (Berger Dx):

-Episodic Hematuria usually occurring concurrently w/ Respiratory/GI infections (IgA secreted by Mucosal Linings)

-IgA Vasculitis (HSP)

-Findings:

- **LM = Mesangial Proliferation**
- **IF = IgA-based IC deposits in mesangium**
- **EM = Mesangial IC deposition**

5. Alport Syndrome:

-Mutation in Type IV Collagen → irregular thinning + thickening + Splitting of GBM

-X-linked Dominant

-Triad: "Can't See, Pee, or hear a Bee"

1. **Eye problems** (Retinopathy, Anterior Lenticonus)
2. **Glomerulonephritis**
3. **Sensorineural Deafness**

-EM = Basket Weave (irregular thickening of GBM

6. Membrano-Proliferative Glomerulonephritis (MPGN):

-Nephritic Syndrome w/ Nephrotic features

-**Type I** = Hepatitis B/C Infxns

- Subendothelial IC Deposits w/ Granular IF

-**Type II** = C3 Nephritic Factor (IgG Autoantibody that stabilizes C3 Convertase → persistent Complement activation → C3 levels)

- Intramembranous Deposits (Dense Deposit Disease)

-Both Types = Mesangial Ingrowth → GBM Splitting → "Tram-track" on H&E and PAS stains

Nephrotic Syndrome:

-Podocyte Damage → impaired charge barrier → proteinuria

Sxs:

-massive proteinuria (>3.5 g/day) w/ Hypoabluminemia

-Edema

-Frothy Urine w/ Fatty Casts

-Hypercoagulable State (due to AT III loss in urine)

- Infection (due to loss of IgGs in urine + soft tissue compromise from edema)

Ex: "May be Primary (direct Podocyte Damage) or Secondary (podocyte damage from systemic process)

- Focal Segmental Glomerulosclerosis (FSGS)
- Minimal Change Disease
- Membranous Nephropathy
- Amyloidosis (secondary)
- Diabetic Glomerulonephropathy (secondary)

1. Minimal Change Disease (MCD):

-"Lipoid Nephrosis"

-Most Common cause of nephrotic syndrome in children

-Causes (**4 I's**) = Idiopathic, Infection, Immunizations, Immune Stimulus

-Tx = Excellent response to **Steroids**

-LM = Normal Glomeruli

-IF = Negative

-EM = **Effacement of Podocyte Foot Processes**

2. Focal Segmental Glomerulosclerosis (FSGS):

-high prevalence in black people

-Primary (Idiopathic) or Secondary (HIV, Sickle Cell, Heroin use, Obesity, Interferon Tx, Congenital)

-Tx = **POOR response to Steroids** (may progress to CKD)

-LM = segmental sclerosis + Hyalinosis

-IF = often negative (some focal deposits of IgM, C3, C1)

-EM = effacement of foot processes similar to minimal change dx

3. Membranous Nephropathy:

-"Membranous Glomerulonephritis" (MGN)

-Primary (antibodies to PLA2 Receptor), Secondary to drugs (NSAIDs, Penicillamine, Gold,) infxns (HBV, HCV, Syphilis)

-Tx = **POOR response to steroids**, may progress to CKD

-LM = diffuse capillary + GBM thickening

-IF = granular due to IC deposition

-EM = **"Spike and Dome"** appearance of Subepithelial Deposits

4. Amyloidosis:

-Kidney = most commonly involved organ

-associated w/ chronic conditions that predispose to Amyloid Deposition (AL Amyloid, AA amyloid, Prolonged Dialysis)

-LM = **Congo Red Stain = Apple-Green Birefringence** under polarized light due to Amyloid deposition in mesangium

5. Diabetic Glomerulonephropathy (DGN):

-Most common cause of ESRD in USA

-Mech:

1. Hyperglycemia → Non-enzymatic glycation of tissue proteins
2. Mesangial expansion = GBM thickening + permeability
3. Hyperfiltration (glomerular HTN and GFR)
4. Glomerular hypertrophy + glomerular scarring (glomerulosclerosis) → Progression to Nephropathy

-LM = **Mesangial Expansion, GBM thickening, Eosinophilic Nodular Glomerulosclerosis (Kimmelstiel-Wilson Lesions)**

Nephritic-Nephrotic Syndrome:

-Severe GBM damage → loss of RBCs into urine + impaired charge barrier → hematuria + Proteinuria

-Features of Both (>3.5 g/day proteinuria + nephritic)

-Can occur w/ any form of Nephritic Syndrome dependending on extent of inflammation

- Diffuse Proliferative Glomerulonephritis (DPGN)
- Membranoproliferative Glomerulonephritis (MPGN)

Kidney Stones:

-stones can lead to obstruction = hydronephrosis, pyelonephritis, AKI

-sxs = unilateral flank tenderness, colicky pain radiating to groin, hematuria

-calcium most common (80%) > Oxalate > Phos

1. Calcium Oxalate: "Hypocitraturia"

-radiopaque (X-ray, CT)

-shaped like envelope or dumbbell

-Cause = Ethylene Glycol (Antifreeze), Vitamin C Overdose, Hypocitraturia (urine pH), Malabsorption (Crohns)

-Tx = Thiazures, Citrate, Low-Sodium Diet

2. Calcium Phos: (pH)

-Radiopaque (X-ray, CT)

-Wedge-shaped Prism

-Tx = Low-Sodium Diet, Thiazides

3. Ammonium, Magnesium, Phos(Struvite):

- pH

-radiopaque (X-ray, CT)

-"Coffin Lid" / Staghorn Calculi

-15% of all stones

-Cause = Urease (+) Bugs (Proteus Mirabilis, Staphylococcus, Saprophyticus, Kleb) that hydrolyze urea to Ammonia → urine Alkalinization

-Tx = eradication of infxn, surgical removal of stone

4. Uric Acid: (pH)

-Radiolucent (X-ray), Visible on CT

-Rhomboid or Rosettes (Rhombus)

-RF = Urine vol, arid climates, acidic pH

-Strong association w/ Hyperuricemia (Gout)

-Common in Dx w/ cell turnover (Leukemia)

-Tx = Alkalinize urine, Allopurinol

5. Cystine: (pH)

-Faintly radiopaque (X-ray), Moderately (CT)

-Hexagonal Pattern ("Systine for Six Sides")

-Hereditary condition = **Cystine-reabsorbing PCT transporter is loss/defective** (cystinuria)

- reabsorption of **O**rnithine, **L**ysine, **A**rginine (**COLA**)

-(+) Sodium Cyanide Nitroprusside Test

-Staghorn Calculi can form

-Tx = Low Sodium diet, Alkalinization of Urine, Chelating Agents (Tiopronin, Penicillamine)

Hydronephrosis:
-distention/dilation of renal pelvis/calyces
-caused by obstruction (renal stones, severe BPH, congenital blockage, cervical cancer, damage to ureter)
-Dilation occuring proximal to site of pathology
- SCr if bilateral obstruction
-Compression, atrophy of renal cortex/medulla

Urinary Incontinence:

1. Stress Incontinence:
-mech = outlet obstruction (Urethral hypermobility or sphincter def.) → Leaking
-Often occurring w/ intra-abdominal pressure (Sneezing, Lifting, Valsalva Maneuver)
-(+) Bladder stress test
-Associated w/ Obesity, Pregnancy, Vaginal Delivery, Prostate Surgery
-Tx = Pelvic Flood Muscle Strengthening (Kegels), Weight loss, Pessaries

2. Urgency Incontinence:
-mech = Detrusor Overactivity → leak w/ urge to void immediately
-Associated w/ UTIs
-Tx = Kegels, Bladder training (timed voiding, distraction, relaxation), Antimuscarinics (Oxybutynin) or B3 Agonists (Mirabegron)

3. Overflow Incontinence:
-Mech = Incomplete Emptying (Detrusor UNDERactivity or outlet obstruction) → leak w/ overfilling, Postvoid residual on catheterization/US
-Associated w/ Polyuria (DM), Bladder outlet obstruction (BPH), Spinal Cord Injury (MS)
-Tx = catheterization, relieve obstruction (a-Blockers for BPH - Tamsulosin)

Acute Cystitis:
-inflammation of urinary bladder
-sxs = suprapubic pain, dysuria, urinary frequency, urgency **(Absent Systemic Signs - fever, chills)**
-RF = Females (Short Urethra), Sexual Intercourse, Indwelling Catheter, DM, Impaired Bladder Emptying
-Causes:
- E.coli (Most Common)
- Staph saprophyticus (sexually active women)
- Klebsiella
- Proteus Mirabilis (Ammonium Scent)

-Labs:
- (+) leukocyte esterase
- (+) nitrites (indicates Enterobacteriaceae)
- Sterile Pyuria suggests Urethritis via Neisseria Gonorrhoeae or Chlamydia Trachomatis

-Tx = Antibiotics (TMP-SMX, Nitrofurantoin)

Acute Pyelonephritis:
-neutrophils infiltrate renal interstitium
-Renal Cortex damaged (Sparing of Glomeruli/vessels)
-sxs = Fevers, Flank pain (**CVA tenderness**), N/V, Chills
-Causes = ascending UTI (E.coli most common), Hematogenous Spread to kidney
-(+) WBC in Urine w/ +/- WBC Casts
-CT = striated parenchymal enhancement
-RF = Indwelling catheter, Urinary obstruction, vesicoureteral reflux, DM, Pregnancy
-Complications = Chronic Pyelonephritis, Renal Papillary Necrosis, Perinephric Abscess, Urosepsis
-Tx = Antibiotics

Chronic Pyelonephritis:
-result from recurrent/inadequately treated episodes of acute pyelo (often secondary to other issue - chronic VUR, or kidney stones)
-Coarse, asymmetric corticomedullary scarring, blunted calyces
-Tubules have eosinophilic casts (resemble Thyroid tissue = **Thyroidization of Kidney**)
-**Xanthogranulomatous Pyelonephritis** (rare) = grossly orange nodules that mimic tumor; widespread kidney damage due to granulomatous tissue containing foamy macrophages (Often Proteus Infxn)

Acute Kidney Injury (AKI):

1. Prerenal Azotemia:
-Hypovolemia, CO, Effective Circulating Volume (HF, Liver Failure)
-pathogenesis = RBF → GFR → Reabsorption of Na+/H2O/Urea
- **Urine Osmol = > 500**
- **Urine Na+ = < 20**
- **FeNa = < 1%**
- **Serum BUN/Cr = > 20**

2. Intrinsic Renal Failure:
-Tubules + Interstitium:
- Acute Tubular Necrosis (ATN) = Ischemia, Nephrotoxins)
- Acute Interstitial Nephritis (AIN)

-Glomerulus:
- Acute Glomerulonephritis

-Vascular:
- Vasculitis
- Malignant HTN
- TTP-HUS

-pathogenesis (in ATN) = patchy necrosis → debris obstructing tubules and fluid backflow → GFR
- **Urine Osmol = < 350**
- **Urine Na+ = > 40**
- **FeNa = > 2%**
- **Serum BUN/Cr = < 15**

3. Postrenal Azotemia:
-Outflow Obstruction (Bilateral) = stones, BPH, Neoplasm, Congenital Anomalies
- **Urine Osmol = < 350**
- **Urine Na+ = Varies**
- **FeNa = Varies**
- **Serum BUN/Cr = Varies**

Acute Interstitial Nephritis (AIN):
-"Tubulointerstitial Nephritis" = acute interstitial renal inflammation
-Pyuria (classically Eos) + Azotemia occurring after admin of drugs that act as Haptens, inducing HSR
-**Diuretics, NSAIDs, PCNs/Cephs, PPIs, Rifampin, Quinolones, Sulfas**)
-Sxs = Fever, rash, pyuria, hematuria, CVA Tenderness (can be asymptomatic)

Acute Tubular Necrosis (ATN):
-MOST Common cause of AKI
-spontaneously resolves (can be fatal)
- FeNa
-Granular Casts (Muddy Brown)
-3 Stages:
1. Inciting Event
2. Maintenance Phase = **Oliguric** (1-3 weeks); Risk for Hyperkalemia (K), Metabolic Acidosis (H), Uremia
3. Recovery Phase = **Polyuric**; BUN + SCr , risk of HypOkalemia (Renal wasting of electrolytes)

-Causes:
- Ischemic = secondary to RBF (hypotension, shock, sepsis, hemorrhage, HF) causing death of tubular lumen → death of PCT and TAL
- Nephrotoxic = injury resulting from Toxic substances (AMinoglycosides, Contrast, Lead, Cisplatin, Ethylene Glycol), Crush Injury (Myoglobinuria), Hemoglobinuria = PCT susceptible

Diffuse Cortical Necrosis:
-acute generalized cortical infarction of both kidneys
-cause = Vasospasm + DIC
-seen in Obstetric Catastrophes (Abruptio Placentae), Septic Shock (Distributive shock)

Renal Papillary Necrosis:
-Sloughing of necrotic renal papillae → Gross Hematuria
-"Renal Papi = SAAD papi"
- Sickle Cell Dx/Trait
- Acute Pyelo
- Analgesics (NSAIDs)
- DM

Renal Osteodystrophy: "Pathologic Fractures"
-Hypocalcemia (Ca), Hyperphos (Phos), failure of Vit D hydroxylation = **All these due to kidney dx**
- Causing secondary Hyperparathyroidism (PTH) → Tertiary Hyperparathyroidism (chronically active for so lung w/ secondary that they remain hypertrophied and overactive permanently)

-high Phos → Binds w/ Ca2+ → tissue deposits → Serum Ca2+
- Calcitriol → intestinal Ca2+ absorption (causing Subperiosteal thinning of bones)

Consequences of Renal Failure:
-decline in renal filtration leads to retained nitrogenous waste + electrolyte disturbances
-**MAD HUNGER:**
1. **Metabolic Acidosis**
2. **Dyslipidemia (Trigs)**
3. **Hyperkalemia**
4. **Uremia**
5. **Na/H2O retention (HF, Pulm Edema, HTN)**
6. **Growth retardation/developmental delay**
7. **Erythropoietin def** (EPO → Anemia)
8. **Renal Osteodystrophy**

-2 Forms of Renal Failure; Acute (ATN), Chronic (HTN, DM, Congenital)
-Incremental reductions in GFR = used to define CKD
-Normal Phos levels maintained in early CKD due to levels of Fibroblast growth factor 23 (**FGF23**) = promoting renal excretion of Phos
-**Uremia** = syndrome from high urea in blood (Nausea, Anorexia, Encephalopathy w/ Asterixis, Pericarditis, Platelet dysf.); Tx = Dialysis

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Renal Cyst Disorders:

1. Autosomal Dominant Polycystic Kidney Dx (ADPKD):
-numerous cysts in cortex/medulla → causing bilateral enlarged kidneys destroying kidney parenchyma
-Flank pain, hematuria, HTN, Urinary Infxn, Progressive renal failure
-**Mutation of PKD1 (Chr 16), or PKD2 (Chr4 - less common)**
-Complications = CKD, HTN (Renin), Berry Aneurysms, Mitral Valve Prolapse (MVP), Hepatic Cysts, Diverticulosis
-Tx = ACEI/ARB (if HTN/Proteinuria)

2. Autosomal Recessive PKD (ARPKD):
-cystic dilation of Collecting Ducts
-Infant presentation
-associated w/ congenital hepatic fibrosis
-Significant Oliguric renal failure in utero → Potter Sequence (Pulm Hypoplasia)
-Born = HTN, Progressive renal failure, Portal HTN

3. Autosomal Dominant Tubulointerstitial Kidney Disease (ADTIKD):
-"Medullary Cystic Kidney Dx"
-Tubulointerstitial fibrosis + Progressive Renal Insufficiency w/ inability to concentrate urine
-Medullary cysts not visualized w/ US- poor prognosis

4. Simple Cysts:
-filled w/ ultrafiltrate (Anechoic on US)
-very common (account for most renal masses)
-found incidentally + often asymptomatic

5. Complex Cysts:
-septated, enhanced, solid components on imaging require follow-up or removal
-concern for Renal Cell Carcinoma

Renovascular Disease:
-unilateral or bilateral renal artery stenosis (RAS) → Renal Perfusion → Renin → AngII → HTN
-Most common cause of secondary HTN in adults
-Causes:
1. Atherosclerotic Plaques = Proximal 1/3rd of Renal artery, older males, smokers
2. Fibromuscular Dysplasia = distal 2/3rd of renal artery or segmental branches, young-middle aged females

-Unilateral RAS = affected kidney atrophies → asymmetric kidney size (Renin in Affected Kidney, but Renin in Unaffected)
-Bilateral RAS = sudden rise in Cr after starting ACEI, ARB, Renin Inhibitor due to interference of RAAS mediated renal perfusion
-sxs = severe refractory HTN, Flash pulmonary edema, epigastric/flank bruit
-commonly have stenosis in other major vessels

Renal/Bladder Cancer/Malignancy:

Renal Cell Carcinoma (RCC):
-**Polygonal Clear Cells** w/ accumulated lipids + Carbs (deletion of **Chr 3** gene - associated w/ **Von Hippel-Lindau Syndrome**)
-histo has lots of clear/white lipid droplets/accumulation
-Golden-Yellow (due to high lipid content)
-Originates in **PCT** → invades renal vein (Testicular **Varicocele** common if Left sided) → IVC → hematogenous spread → mets to Bones/Lungs
-sxs = Hematuria, Palpable Masses, Polycythemia, Flank pain, fever, weight loss)
-Triad:
1. Flank Pain
2. Palpable Masses
3. Hematuria

-MOST common primary renal malignancy
-Males 50-70 yo (higher rates if Tobacco/Obese)
-**Paraneoplastic Syndrome (PTHrP, Ectopic EPO, ACTH, Renin)**
-
-Tx = surgery/ablation, Immunotherapy (Ipilimumab), Often resistant to Chemo/Rads

Renal Oncocytoma:
-Benign epithelial cell tumor from **Collecting Ducts**
-well-circumscribed mass w/ central scar
-**Large eosinophilic cells w/ abundant mitochondria** w/o perinuclear clearing (opposite of RCC Clear cells)
-Sxs = Painless Hematuria, Flank pain, Abdominal Mass
-Tx = resection (also confirm it's not RCC)

Nephroblastoma: "Wilms Tumor"
-MOST common renal malignancy of early childhood (ages 2-4 yo)
-Embryonic Glomerular structures
-Sxs = large palpable, unilateral flank mass and/or hematuria w/ possible HTN
-Loss of Function of Tumor Suppressor genes **WT1 + WT2 on Chr 11**
-Part of Several Syndromes:
1. **WAGR Complex (WT1)**= Wilms Tumor, Aniridia (Absence of Iris), Genitourinary Malformations, Range of Developmental Delays
2. **Denys-Drash Syndrome (WT1)** = Wilms Tumor, Diffuse mesangial sclerosis (early onset Nephrotic syndrome), Dysgenesis of Gonads (male pseudohermaphroditism)
3. **Beckwith-Wiedemann Syndrome (WT2)** = Wilms Tumor, Macroglossia, Organomegaly, Hemihyperplasia, Omphalocele

Urothelial Carcinoma of the Bladder:
-"Transitional Cell Carcinoma" (TCC)
-MOST common tumor of urinary tract
-can be found in Renal Calyces, Renal pelvis, Ureters, Bladder
-Painless hematuria (no casts)
-Associated w/ Phenacetin, Smoking, Aromatic Amines (dyes), Cyclophosphamide (hemorrhagic cystitis)
-Histo = fibrovascular core + dysplastic urothelium

Squamous Cell Carcinoma (SCC) of Bladder:
-Chronic irritation of urinary bladder → squamous metaplasia → dysplasia + squamous cell carcinoma
-RFs:
1. Schistosoma Haematobium (middle east)
2. Chronic Cystitis
3. Smoking
4. Chronic Nephrolithiasis

-Painless Hematuria + No Casts

Mannitol:
-osmotic diuretic
- tubular fluid osmolarity → urine flow, intracranial/intraocular pressure
-Use = drug OD, elevated intracranial/intraocular pressure
-Site = PCT and Descending Limb
-sxs = Dehydration, Hypo/hypernatremia, Pulmonary Edema
-Contrianidcated in Anuria, HF

Acetazolamide:
-carbonic anhydrase inhibitor
-causes self-limited NaBicarb diuresis, and total body bicarb stores (Alkalinizes Urine)
-Use = Glaucoma, Metabolic Alkalosis, Altitude Sickness (Offsetting Respiratory Alkalosis), Idiopathic Intracranial HTN
-Sxs = **Proximal RTA (Type 2 - defect in Bicarb reabsorption in PCT→ metabolic acidosis, and urinary alkalosis)**, Paresthesias, NH3 toxicity, Sulfa allergy, Hypokalemia (K), Promotes CaPhos Stone formation (Insoluble at high pH)
-Acts in PCT

Loop Diuretics:

Furosemide, Bumetanide, Torsemide
-"Sulfonamide" Loop Diuretics → inhibit cotransport system (**Na/K/2Cl Channel**) in **TAL**
-Abolishes Hypertonicity of Medulla → preventing concentration of urine
- PGE (vasodilatory effect on Afferent Arteriole); Inhibited by NSAIDs
- Ca excretion(Ca blood)="Loops Lose Ca"
-Use = Edematous states (HF, Cirrhosis, Nephrotic Syndrome Pulm Edema), HTN, Hypercalcemia
-Sxs = **Ototoxicity, HypoKalemia (K), Hypomag (Mg), Dehydration, Allergy (Sulfa), Metabolic Alkalosis, Nephritis (Interstitial), Gout (Uric Acid)**

Ethacrynic Acid:
-Non-sulfonamide Inhibitor of **Na/K/2Cl** of TAL
-Diuresis in pts allergic to sulfa drugs
-Similar to Furosemide, but more Ototoxic( )

Thiazides: **HCTZ, Chlorthalidone, Metolazone**
-mech = Inhibit NaCl reabsorption in early **DCT** → Diluting Capacity of Nephron (Ca2+ Excretion)
-use = HTN, HF, Idiopathic Hypercalciuria, Nephrogenic Diabetes Insipidus, Osteoporosis
-Sxs = Hypokalemic Metabolic Alkalosis, Hyponatremia, Hyperglycemia, Hyperlipidemia, Hyperuricemia, Hypercalcemia (Sulfa Allergy)

Potassium-Sparing Diuretics: "Collecting Tubule"
-Spironolactone, Eplerenone = competitive Aldosterone Receptor antagonists in Cortical Collecting Tubule
-Amiloride, Triamterene = block Na+ channels at the same part of the tubule
-use = Hyperaldosteronism, K+ Depletion, HF, Hepatic Ascites (Spironolactone), Nephrogenic DI (Amiloride), Antiandrogen (Spironolactone)
-Sxs = Hyperkalemia (K) - can lead to arrhythmias, Endocrine effects w/ Spironolactone (Gynecomastia, Antiandrogen effects)

Electrolyte Changes:
-Urine NaCl = w/ all diuretics (Conc varies based on potency of diuretic effect) - serum NaCl may
-Urine K+ = Loops + Thiazides
- **pH (Acidemia):**
  - **CAI → bicarb reabsorption**
  - **K+ sparing → aldo blockage prevents K+ secretion and H+ secretion**
  - **Hyperkalemia → k+ entering all cells (via H+/K+ Exchanger) in exchange for H+ exiting cells**
- **pH (Alkalemia):**
  - Loops and Thiazides cause Alkalemia via;
    - Volume contraction → Ang II → Na/H Exchanger in PCT → Bicarb reabsorption (Contraction Alkalosis)
    - K+ loss leads to K+ exiting all cells (H+/K Exchanger) in exchange for H+ entering cells
    - In low K+ state, H+ (rather than K+) is exchanged for Na+ in cortical collecting tubule → alkalosis + "Paradoxical Aciduria"

-Urine Ca2+: w/ Loops (Loops Lose Ca), w/ Thiazides (Enhanced Ca2+ reabsorption)

ACEI: Captopril, Enalapril, Lisinopril, Ramipril
-Inhibit ACE (Lungs) → AngII → GFR by preventing constriction of efferent arterioles
- Renin due to loss of negative feedback
-inhibition of ACE, also prevents inactivation of Bradykinin (Potent vasodilator)
-use = HTN, HF (mortality), Proteinuria, Diabetic Nephropathy, prevent unfavorable heart remodeling as a result of chronic HTN
-Chronic Kidney Dx (Diaetic Nephropathy), ACEI intraglomerular pressure, slowing GBM thickening
-Sxs:
- Cough
- Angioedema (contraindicated in C1 esterase def)
- Teratogen (Fetal Renal Malformations)
- Cr (GFR)
- Hyperkalemia (K), Hypotension

-Use w/ Caution in Bilateral Renal Artery Stenosis (further GFR → Renal Failure)

ARB: Losartan, Candesartan, Valsartan
-selectively blocks AngII at AT1 receptor (no in bradykinin)
-sxs = Hyperkalemia, GFR, Hypotension, Teratogen

Aliskiren: Direct Renin Inhibitor (blocking ANgiotensinogen to Ang I)
-Hyperkalemia, GFR, Hypotension, Angioedema, No use preg or with ACEI/ARB

	BP	Renin	Aldo	Mg2+	Urine Ca2+
SIADH (ADH)				-	-
Primary Hyperaldosteronism (Aldo)			▮	-	-
Renin-Secreting Tumor		▮		-	-
Bartter Syndrome (TAL - Na/K/Cl)	-			-	▮
Gitelman Syndrome (DCT - Mg2+ due to charges) - Mg reabsorption in TAL	-				▮

Liddle Syndrome (GOF - ENaC) / SAME (11b-HSD def)				-	-

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