3/10/2007

Med Study Nephrology

Tests:

(1) Urine Dipstick Hematuria:

- may see ϕ RBC's on microscopic analysis
- if dip (+) + microscopic (−)

↓

think myoglobinuria / hemoglobinuria → can be seen w/ RBC lysis in very dilute urines

- if casts or dysmorphic RBC's → GN

(2) Urine Eosinophils:

- think drug-induced interstitial nephritis

(3) Proteinuria:

- best indicator of renal pathology
- normal 24-hr urine protein: <150 mg
  - >2.5g → glomerular dis.
  - <1 g/day → more likely interstitial renal dis.
- exceptions:
  - (1) Medullary Cystic kidney
  - (2) Obstructive uropathy

  can have normal urine sediment w/ minimal proteinuria
- Myeloma → light-chain deposition (Bence-Jones) ϕ picked up on dipstick (needs 24-hr. urine for immunoelectrophoresis)
- Transient → post-exercise, fevers, CHF, COPD
- Benign orthostatic Proteinuria
  - reverts when the pt. is supine

3/20/2007

④ Protein : Creat Ratio :

- can be a "spot" test
- ~ amount of protein in a 24-hr. urine

Ex.) spot protein : creat ratio of 3.5 ~ 3.5 g in a 24-hr. urine

⑤ μ-Albuminuria :

- earliest indicator of DM-Nephropathy
- too small to be picked up on dipstick
- Late DM-Nephropathy → nephrotic dipstick
- may also indicate early-stage glomerular dis other than DM (Ex.) HTN)
- False ⊕ Causes :
  - Ⓐ Alkaline urine (pH 78)
  - Ⓑ CHF
  - Ⓒ UTI
  - Ⓓ Concentrated urine

Serum Creat

- source → muscle tissue
- ↑'d muscle mass → ↑'d creat.
- rapid muscle breakdown → Rhabdo → acute ↑ in creat.
- cooking meats → converts creatine → creatinine (which can be absorbed thru GI tract)
- ↑'d age → ↓ muscle mass w/ ↓ GFR → creat should remain ~ the same
- Renal Toxins that can ↑ creat :
  - ① Cimetidine — also acetone + cefoxitin
  - ② Probenecid
  - ③ Bactrim (Trimeth/sulfa)

    (Ex.) AIDs pt. w/ ↑ creat being treated for PCP prophylaxis w/ Bactrim

  ↓ tubular secretion of creat.

3/22/2007

-Acetone / Cefoxitin may falsely ↑ creat

-BUN/creat ratio > 20:1 → prerenal azotemia or ↑'d protein breakdown

- BUN/creat ratio >20:1 indicates:

(1) Prerenal Azotemia (↓ flow + ↑ absorption)

OR

(2) ↑ Protein Breakdown

- ↑ protein intake
- GI Bleed
- TPN
- Catabolic States
- Steroids → ↑ protein turnover

GFR

-most accurate measure of renal function

-usually calculated as Creat Clearance (Cockcroft-Gault)

$CrCl = (140 - Age) \times IBW / creat \times 72$ (×0.85 women)

-Probenecid
- Cimetidine
- Trimethoprim

→ ↓ tubular secretion of creat.
↓ ↓ creat clearance (but normal GFR)

-Advanced Renal Dis. → ↑ secretion of creat tubular ↓ ↑ creat clearance (higher than actual GFR)

-creat clearance may be misleading as an estimate of GFR

FENA

-most useful in eval. ARF

-can use to differentiate prerenal azotemia vt. ATN

<2% → prerenal

>2% → ATN except w/ contrast-induced ATN → FENA can be <1%

$$FENA = \left(\frac{\text{urine } Na^{\oplus} / \text{serum } Na^{\oplus}}{\text{urine creat} / \text{serum creat}} \right) \times 100\%$$

Renal Bx

-used to diagnose causes of ARF, Nephrotic Syn. + GN

Acidemia / Alkalemia

-pH < 7.4 → acidemia + if > 7.4 → alkalemia

-Alkalemia:

-may cause diffuse paresthesias / numbness

-↑ pH → ↑ fraction of bound $Ca^{(2+)}$

↓ ionized $Ca^{(2+)}$

↓

hypocalcemia

Normal 70 kg man produces ~70 mEq/day of acid

3/28/2007

Acid-Base O/O's

Henderson-Hasselbach Equation:

$$HCO_3^{\ominus} + H^{\oplus} \rightleftharpoons H_2CO_3 \rightleftharpoons H_2O + CO_2$$

(H_2CO_3: carbonic acid)

$$pH = pk + \log\left(\frac{HCO_3^{\ominus}}{0.03 \times PaCO_2}\right)$$

OR

$$H^{\oplus} = 24\left(\frac{PaCO_2}{HCO_3^{\ominus}}\right)$$ → indicates that both kidneys + lungs partake in pH control

Resp. compensation can occur instantly in response to acidosis / alkalosis

vs.

Renal compensation will occur more slowly

Resp. D/o's: -If $PaCO_2$ ↓ 10 → pH will Δ 0.08 (acutely)

0.04 (chronic)

$HCO_3^{\ominus}$ will Δ −2 (acutely)

−5 (chronic)

- If P_aCO_2 ↑ 10 → pH will Δ −0.08 (acutely)
  −0.04 (chronic)
  $HCO_3^\ominus$ will Δ 1 (acutely)
  4 (chronic)

Metabolic D/O's: - If $HCO_3^\ominus$ ↓ 10 → $paCO_2$ will Δ −12
- If $HCO_3^\ominus$ ↑ 10 → P_aCO_2 will Δ 6

Anion Gap

$$HCO_3^\ominus + Acid^\ominus + H^\oplus \rightleftharpoons H_2O + CO_2 + Acid^\ominus$$

Blood Anions: $HCO_3^\ominus$, $Cl^\ominus$, Phosphate, Sulfate, Albumin, organic Acids

Blood Cations: $Na^\oplus$, $K^\oplus$, $Ca^{2\oplus}$, $Mg^{2\oplus}$

"True" Anion Gap = 0 b/c blood is neutral

$$(Na^\oplus + K^\oplus + Ca^{2\oplus} + Mg^{2\oplus}) - (HCO_3^\ominus + Cl^\ominus + \text{Phosphate} + \text{Sulfate} + \text{Alb} + \text{orgAcids}) = 0$$

Most of above are unmeasured

$$\text{Anion Gap} = Na^\oplus - (Cl^\ominus + HCO_3^\ominus)$$

OR

$$= (\text{Phosphate} + \text{Sulfate} + \text{Albumin} + \text{OrganicAcids}) - (K^\oplus + Ca^{2\oplus} + Mg^{2\oplus})$$

Normally = 24 − 12 = 12 mEq/L

↑'d AGap Metabolic Acidosis:

A) CRF → ↓ acid excretion (esp. NH_4)
B) Ketoacidosis → DM, alcoholic, starvation
C) Lactic Acidosis → Drugs, toxins, circulatory compromise
D) Poisons → Salicylate, Methanol, Ethylene Glycol

Normal AGap metabolic Acidosis:

A) RTA
B) Diarrhea
C) Carbonic Anhydrase Inhibs
D) Hyperal → TPN

urine AGap:
- useful when w/u normal AGap metabolic acidosis

$UAGap = UNa^{\oplus} + UK^{\oplus} - UCl^{\ominus}$

Normal: -10 to 10

4/2/2007

Metabolic Acidosis

Expected $pCO_2 = (1.5 \times HCO_3^{\ominus}) + 8 (\pm 2)$

Mechanisms:

① ↑ production - lactate or ketoacids
② $HCO_3^{\ominus}$ wasting → RTA vs. Diarrhea
③ ↓ acid excretion → RFailure
④ Poisonings → agents metabolized to acids

Normal AGap Acidosis

- aka - hyperchloremic → $\uparrow Cl^{\ominus}$ w/ $\downarrow HCO_3^{\ominus}$
- Causes:
  ① $HCO_3^{\ominus}$ loss → RTA vs. Diarrhea
  ② ↓ acid excretion by kidneys
  ③ organic acid ingestion (Ex.) NH_4

- $Cl^{\ominus}$ retained w/ $HCO_3^{\ominus}$ losses to maintain electric neutrality
= Use urine AGap to differentiate RTA from GI loses of $HCO_3^{\ominus}$ → urine AGap directly reflects renal excretion of $NH_4^{\oplus}$

- RTA → urine AGap > 10
- Extrarenal Normal AGap Acidosis (Ex.) GI losses) → urine AGap < -10 → urine $Cl^{\ominus}$ >>> (urine $Na^{\oplus}$ + urine $K^{\oplus}$)

4/3/2007

Delta AGap: allows calculation of an underlying non-anion gap metabolic acidosis w/ an anion gap acidosis

AGap - Normal AGap (Id)
↓
add this to the $[HCO_3]$

↑ AGap Acidosis

- ↓ $HCO_3^{\ominus}$ w/ out accompanying ↑ $Cl^{\ominus}$
  ↓
  to maintain electric neutrality, an unmeasured anion must be ↑'d
  1. ketoacidosis (Diabetic, alcoholic or starvation)
  2. Lactic Acidosis (including D-lactate)
  3. Uremia
  4. Toxins (salicylates, ethylene glycol (→ glycolic + oxalic acid), toluene + methanol (→ formic acid))

Alcoholic ketoacidosis:
- Tx → Dextrose
- classically volume depletion, normal $Cl^{\ominus}$ + ↑ AGap

Diabetic ketoacidosis:
- 50% → ϕ volume depleted → ↑ $Cl^{\ominus}$ + normal AGap

D-Lactic Acidosis:
- short bowel
- usually present w/ obtundation
- Tx → Dextrose

Methanol:
- metabolized to formaldehyde → formic acid
- ↑ AGap

Ethylene Glycol:
- metabolized to Glycolic Acid + Oxalic Acid
- ↑ AGap
- Calcium oxalate urine crystals/stones

Isopropyl Alcohol
- can have ketosis w/out acidosis
- Metabolized to acetone
- Stuporous
- "Fruity" smell
- Normal chems w/ ↑ ketones

Immediate w/u of unexplained ↑AGap Acidosis:

1. Urine/serum ketones
2. Lactate
3. Osmolar Gap

↓

Difference b/w measured + calculated osmolality

Calculated Osmolality = $(2 \times Na^{\oplus}) + (BUN/2.8) + (Glucose/18)$

Normal <10

↑ Osmolar Gap (>20) + ↑AGap Acidosis + Intoxication

↓

Must consider alcohol (or similar) ingestion

- Ethanol
- Methanol
- Ethylene Glycol
- Isopropyl Alcohol

Metabolic Alkalosis

-usually due to volume contraction → diuresis or vomiting

↓

urine $Cl^{\ominus}$ <10 mEq/L b/c ↑ NaCl absorption to maintain volume

If urine $Cl^{\ominus}$ >10 → think of other causes

- Cushing's Syndrome
- Primary Hyperaldosteronism
- Severe Hypokalemia
- ↑ $HCO_3^{\ominus}$ Intake

- may cause ↓ $K^{\oplus}$ due to ↑ $K^{\oplus}$ losses + ↑'d cellular uptake by cells in exchange for $H^{\oplus}$

-Tx: (A) Severe (pH >7.55): KCl, NaCl or HCl

-avoid KCl w/ RF

-avoid NaCl w/ HF

- use HCl inpt's w/ both RF + HF (0.1N solution
  NOT 0.3N → causes blood vessel breakdown
  - can only give HCl via central line
- NH_4Cl → oral
- Diamox (Acetazolamide): preferable oral drug
  - carbonic anhydrase inhib.
  ↓ $HCO_3^\ominus$ excretion

Acid-Base Problems

- Sequence of Steps:
  1. ABG → to eval. $PaCO_2$ + pH
  2. AGap
  3. Osmolar Gap
  4. Serum $HCO_3^\ominus$
  5. $Cl^\ominus$
  6. urine AGap (if AGap is normal)

4/4/2007

A) pH: Acidemic or Alkalemic

B) Resp vs. Metabolic → $PaCO_2$ and $HCO_3^\ominus$

C) Simple or Mixed
   - if simple then renal/pulm compensation is predicted by equations

Resp. Alkalosis: - For each Δ $PaCO_2$ of -10 → pH will ↑ by 0.08
- If pH Δ's less than that → compensatory metabolic acidosis

Acute Resp. Acidosis: - For each Δ $PaCO_2$ of 10 → pH will ↓ by 0.08
- If pH Δ's less than that → compensatory metabolic alkalosis
↓
check the PaO_2

- serum HCO_3^- or CO_2 → measured
- HCO_3^- from ABG's → derived

- Normal serum HCO_3^- : 23-28 mmol/L
- Acute Δ in ventilation → Δ in $PaCO_2$ → induces a compensatory response in HCO_3^-

↓

unable to recognize acutely
but w/ time → kidneys will either retain or excrete HCO_3^- in efforts to Δ pH back to normal

larger HCO_3^- Δ's in chronic vs. acute conditions

$PaCO_2$ + HCO_3^- should always move in the same direction

↓

If they do not move in the same direction (HCO_3^- should move in same direction as $PaCO_2$)

↓

3rd acid/base disturbance

- Normal Cl^- = 2/3 Na^+
- Cl^-: may be lower in endogenous metabolic alkalosis
  : may be higher in most metabolic acidoses except ↑AGap acidosis

Ex.) 100M patient w/ vomiting (similar for salicylates too)

135	75
3.2	24

ABG: 7.40/40/96

AGap: 36

Dx: ① ↑AGap Metabolic Acidosis → DKA
② ↓Cl^- → Metabolic Alkalosis → vomiting

pH is normal so both must be offsetting each other

Ex.) ① 7.56 / 20 / 90 → Acute Resp. Alkalosis
② 7.56 / 20 / 50 → Acute Resp. Alkalosis w/ Hypoxia
③ 7.44 / 25 / 90 → Chronic Resp. Alkalosis w/ Metabolic Acidosis / Compensation
④ 7.43 / 30 / 60 → Chronic Resp. Alkalosis w/ Metabolic Acidosis (Compensation) + Hypoxia
⑤ 7.40 / 40 / 50 → Hypoxia → Impending Failure
⑥ 7.24 / 60 / 80 → Acute Resp. Acidosis
⑦ 7.16 / 70 / 50 → Acute Resp Acidosis w/ Hypoxia
⑧ 7.37 / 60 / 60 → Chronic Resp. Acidosis w/ Metabolic Alkalosis / compensation + Hypoxia
⑨ 7.44 / 60 / 90 → Metabolic Alkalosis w/ Resp. Compensation
⑩ 7.36 / 28 / 90 → metabolic Acidosis w/ Resp. compensation

4/6/2007

Fluids + Electrolytes

-Normal osmolality: 282 ± 2 mOsm/kg H_2O

calculated Osmolality = $(2 \times Na^{\oplus}) + (\text{Glucose}/18) + (\text{BUN}/2.8)$

ADH Regulation:

-osmoreceptors → hypothalamus (primary stimulus)
-volume (stretch) receptors → LA (? pulm. veins)
-strongest stimulus for ADH release → volume loss ↓ hypotension
-ADH → acts on collecting duct
↑'d H_2O permeability
↓
↑'d urine concentration

Volume Status Assessment:

① Edematous → volume overload
② Clinical signs of volume loss → volume deficit
-If neither → Isovolemic

Clinical Signs of Volume Loss:

1. Tachycardia
2. Narrowed Pulse Pressure
3. Orthostasis
4. Resting Tachycardia w/ Hypotension

Hyponatremia

- the most common electrolyte abnorm.
- 1st steps of pt's w/ Hyponatremia:
  1. serum osmol.
  2. serum gluc.
  3. volume status

A) Isotonic: (By osmol.)
- proteins / lipids displace $Na^{\oplus}$ → pseudo hypo-$Na^{\oplus}$
- Ex.) Multiple Myeloma / Dyslipidemia
- ↑'d osmol gap
  - measured serum osmol → normal
  - calculated osmol → low (b/c $Na^{\oplus}$ is low)

B) Hypertonic: (By osmol.)
- Glucose / Mannitol → osmotic shift of H_2O out of cells → dilutes serum $Na^{\oplus}$ (increased)
- For each ↑ glucose by 100 mg/dL → $Na^{\oplus}$ ↓'s by 1.6

C) Hypotonic: (By osmol.)
- causes intracellular swelling → ↑'d neuromuscular excitability → seizures and eventually coma (acutely $Na^{\oplus}$ <120)
- if slowly ↓'d $Na^{\oplus}$ → cells re-equilibrate and do not swell
- serum $Na^{\oplus}$ reflects ratio of $Na^{\oplus}$ to total body water

↓

Decision Tree is based on Volume status

Hypovolemic Hypo-$Na^{\oplus}$

- involves both $Na^{\oplus}$ + free-H_2O losses but $Na^{\oplus}$ losses > free-H_2O

- Causes:
  - (A) Diuresis
  - (B) GI Losses (Vomiting / Diarrhea)
  - (C) Adrenal Insufficiency
    - ↓ aldosterone → ↓'d active $Na^{\oplus}$ resorption
      ↓
      ↑'d $K^{\oplus}$ ← $Na^{\oplus}$/H_2O wasting
      mild metabolic acidosis

Hypervolemic Hypo-$Na^{\oplus}$

- involves retention of $Na^{\oplus}$ + free-H_2O but free-H_2O > $Na^{\oplus}$
  ↓
  most pt's actually have normal-high total body $Na^{\oplus}$ stores

- Signs:
  - (1) JVD
  - (2) Edema (Dependent, usually)
- Causes:
  - (A) Low-output CHF
  - (B) Hypoalbuminemia
  - (C) Cirrhosis
  - (D) Nephrosis
  - (E) Renal Failure
- Tx:
  - (1) Restrict $Na^{\oplus}$ / H_2O
  - (2) Loop Diuretics or ACEI's/ARB's
  - (3) AVOID: -$Li^{\oplus}$ / Demeclocycline → ↓ GFR → ↑ salt retention
    - chronic thiazides
      ↓
      impair urinary diluting ability
      (use only loop diuretics)

- use caution w/ aggressive diuresis in cirrhotics w/ ↓ Creat Cl → ↓'d muscle mass (normal creat w/ ↓ GFR)
  ↓
  may lead to ARI

Eurolemic Hypo-$Na^{\oplus}$

- Causes: (A) SIADH (most commonly)
  (B) Psychogenic Polydipsia
  (C) Diuresis (w/ free-H_2O replacement)
  - $K^{\oplus}$ usually low
  - urate / BUN low → dilutional

- SIADH:
  - Causes: (1) CNS D/O's (Ex.) Meningitis)
    (2) Lung D/O's
    (3) Cancers (esp. small cell)
    - pancreas, duodenum, thymus too
    (4) Drugs: - chlorpropamide
    - phenothiazines
    - cyclophosphamide
    - clofibrate
    - vincristine
    (5) Emetic Response → ↑'s ADH
    (6) Old Age → ↑'d ADH
  - ✓ urine osmol to differentiate SIADH vs. Polydipsia (concentrated vs. dilute)
  - once SIADH Dx'd + w/u ⊖ (total body CT) → repeat w/u Q 1-2 yrs. for malignancy

Treatments:

- If hypovolemic → NS IVF's
- If severe symptoms (coma / seizures) → 3% NS plus loop diuretics
  1 L 3% saline → 512 mEq $Na^{\oplus}$
  - calculate $Na^{\oplus}$ deficit:

$$\text{Deficit} = [\text{weight (kg)} \times 0.6] \times 10$$

(60% × weight = Total Body Water; 10 = Goal Δ in $Na^{\oplus}$)

- Give deficit replacement over 8-12 hrs..

- If using 3% saline → correction rate should never be more than 1-2 mmol/hr
- If Euvolemic / Hypervolemic → fluid restrictions
- SIADH:
  - fluid restrictions
  - 900 mg/day Demeclocycline (sometimes useful in refractory cases)
    - inhibits ADH ~~secretion~~ stimulation of adenylate cyclase in renal tubules
    - side effx: A) Photosensitive skin Rash
      B) Normally Albumin-bound but free portion → Nephrotoxic
      - hypoalbuminemic pt's (Cirrhosis/Nephrosis)
      - ↓ dose + monitor renal funx.

Central Pontine Myelinolysis / Osmotic Demyelination Syndrome:
- important not to correct $Na^{\oplus}$ too quickly
- if $Na^{\oplus}$ corrected too quickly → cells ~~swell~~
- risk ↑'d w/ chronic hypo-$Na^{\oplus}$ corrected too quickly

- cellular Δ's can occur w/ too rapid a correction of any hyperosmolar state:
  - (A) Hypernatremia
  - (B) NKHC (Non-ketotic Hyperglycemic Coma)
  - (C) Uremia

  → - Cerebral edema
  - seizures
  - coma

Hypernatremia

- free-H_2O deficit → always hyperosmolar
- 1st step → determine volume status
  - Hypovolemia → High H_2O losses
- Tx: severe Hyper$Na^{\oplus}$ → NS 1st to correct hypotension then hypotonic IVF's

4/9/2007

~~***~~ Even NS is hypotonic vs. hyperosmolar serum

-Calculate Free-H_2O Deficit:

$$\text{Deficit} = (\text{Total Body water}) \times \left(\frac{\text{serum } Na^{\oplus} - 145}{145}\right)$$

$$= [0.6\ (\text{Body weight})] \times \left(\frac{\text{serum } Na^{\oplus} - 145}{145}\right)$$

- give the deficit over 24-48 hrs.
  - ↓ should ↓ $[Na^{\oplus}]$ by 0.5 mEq/L/hr

- Hypervolemia:
  - -unusual scenario and usually not serious
  - -Most likely mineralocorticoid excess (Primary Hyperaldo)
  - -serious situation: Ex.) ↑ amnts Na-$HCO_3^{\ominus}$ w/ ACLS
  - -Tx:
    - -Loop Diuretics
    - -Free-H_2O

-Euvolemia:
- -think DI
- -↓-free-H_2O intake
- -Central DI:
  - -recent NSurg, head trauma, brainca./mets
  - -Hyper $Na^{\oplus}$ w/ ↑ urine volume

H_2O-Restriction

-helpful in Dx of DI

-Normal healthy pt: serum osmol gets to 295
↓
↑ ADH
↑ urine osmol (>700)

(A) Central DI:
- ↓ ADH + ↓ urine osmol
- Give ADH → Desmopressin (DDAVP) → urine osmol ↑'s

(B) Partial Central DI:
- Chlorpropamide

(C) Nephrogenic:
- ↑ ADH but ↓ urine osmol
- Tx w/ DDAVP does not ↑ urine osmol
- Tx: Thiazide Diuretics

↑ADH / Normal Volume → Hypo-$Na^{\oplus}$ (SIADH)
↓ADH / Normal Volume → Hyper-$Na^{\oplus}$ (DI)

Urine Osmol
- Normal Range: 40-1400 mOsm/L
- Total Osmolar output / Day = Osmolality × output
  - Normally ~500 mOsm
- If 24-hr. solute output: >900 → osmotic cause of hyper-$Na^{\oplus}$ (Ex.) Hyperglycemia)
  : Normal → dilute urine (DI)

Renal Physiology
(1) Proximal Convoluted Tubule (PCT):
- reabsorbs ~90% of $HCO_3^{\ominus}$ → driven by $H^{\oplus}$ secretion
- Acidosis → ↑ $H^{\oplus}$ secretion + ↑ $HCO_3^{\ominus}$ reabsorption

$H^{\oplus} + HCO_3^{\ominus} \rightleftharpoons H_2CO_3$ (carbonic acid)

↓↑ carbonic anhydrase (proximal tubule brush border)

$H_2O + CO_2$

CO_2 reabsorbed by cells + converted back to $HCO_3^{\ominus}$

- Acetazolamide: (carbonic anhydrase inhib.)
  - diuresis w/ $HCO_3^{\ominus}$ wasting → metab. acidosis similar to Type II (proximal) RTA
- also Ca^{2+} reabsorbed
  - Tx for HyperCa^{2+} → IVF's (NS) + loop diuretics
    - (A) NS IVF's → volume expansion → ↑ proximal tubular flow → ↓ Ca^{2+} reabsorption
    - (B) ↓ Ca^{2+} reabsorption → ↑ downstream load
- also $K^{\oplus}$ reabsorbed → 100% of filtered $K^{\oplus}$ is reabsorbed here

to the distal tubules → ↓ Ca^{++} reabsorption → loop diuretics → even further ↓'d Ca^{++} reabsorption

↑ calciuresis

4/11/2007

(2) Loop of Henle:

A) Descending Limb:

- renal medulla is very hypertonic → free H_2O follows the osmotic gradient → ↑ free H_2O absorption

B) Ascending Limb:

- 25% of filtered NaCl is actively reabsorbed
- H_2O unable to follow the NaCl → tubular fluid becomes diluted

- Loop diuretics block the active reabsorption of Na^+ in the ascending limb

(Ex.) Furosemide - Lasix
Bumetanide - Bumex
Torsemide - Demadex)
Ethacrynic Acid - Edecrin)

- effective even w/ ↓ GFR's
- also ↑ Ca^{++} excretion
- Both Lasix + Bumex contain sulfa
- w/ Sulfa allergy → Edecrin

(3) Distal Tubule:

- Na^+ is actively reabsorbed
- H^+ (as salts → NH_4^+ or phosphate salts) + K^+ excreted

↓ formerly the Na^+/K^+ pump

but actually → Na^+ pump - K^+/H^+ electrical excretion gradient

- if Na^+ reabsorbed then must excrete a $^+$ charge to maintain electrical neutrality

- metabolic acidosis → more H^+ excretion vs. K^+
  ↳ also causes ↑ K^+ shifts out of cells
  ↓
  hyperkalemia

-hyperkalemia can also cause an acidosis
↑ K^+ excretion renally in deference to H^+ excretion → acidosis

-Aldosterone → facilitates active reabsorption of Na^+
- virtually all the K^+ in urine is due to distal tubular secretion

④ Collecting Duct:
-ADH acts here → ↑'s ductal H_2O permeability
-normal urine is dilute upon reaching the duct
↑'d free-H_2O reabsorption

Diuretics

① Spironolactone:
- aldosterone antag. → works in distal tubule → K^+-sparing → may cause acidosis

② Diuretics Acting on Early Distal Tubule:
- ↑ Na^+ load to late distal tubule → ↑ Na^+ uptake there w/ resultant ↑'d K^+ excretion
-Ex.) Thiazides + Loop diuretics

③ Triamterene / Amiloride:
-K^+-sparing → inhibit Na^+ reabsorption in distal tubular cells → ↓'d K^+/H^+ excretion

④ Thiazides:
-↓ Na^+/Cl^- reabsorption in early distal tubule + thick ascending limb
- much of the Na^+/Cl^- has been reabsorbed already in the PCT
-not effective w/ ↓GFR's (Creat Cl <20)
- longer ½-life vs. loop diuretics
-↓ Ca^{2+} excretion
- may act synergistically w/ loop diuretics
-Ex.) If Lasix maxed out → try low dose thiazide too

RTA:

- normal anion gap metabolic acidosis (hyperchloremic)
- Proximal RTA → Type 2
- Distal RTA's → Types 1 + 4
- Type 3 → very rare AR lack of carbonic anhydrase II
- K^+:
  - low (normal) in Types 1 + 2
  - high in Type 4

Type 1 RTA:

- distal defect w/ H^+ secretion → urine pH usually > 5.5 (despite the metabolic acidosis)
  - ↓ serum $[H^+]$ → acidosis
  - serum HCO_3 < 10
  - K^+ excretion is ↑'d due to ↓ H^+ excretion
    - ↓ hypokalemia
- commonly assoc. w/ hypercalciuria
- Causes:
  - (A) Autoimmune D/O's
    - Sjogren's
    - SLE
    - RA
  - (B) Hereditary Hypercalciuria
  - (C) Hyperparathyroidism
  - (D) Vit. D Intoxication
  - (E) Drugs
    - Amphotericin B
    - Li^+
  - (F) Hypergammaglobulinemia
    - Chronic Hepatitis
- commonly causes stones → ↓'d citrate excretion + hypercalciuria
- Tx:
  - Alkali therapy
  - Treat the underlying cause

Type 2 RTA:

proximal defect → the only proximal RTA

-similar effect w/ Acetazolamide → $HCO_3^\ominus$ wasting in the proximal tubule (usually serum $HCO_3^\ominus$ 12-20)

-once serum $[HCO_3^\ominus]$ ↓'s significantly and serum acidity triggers ↑'d $H^\oplus$ excretion in the PCT

↓

acid-base re-equilibration

-Early Type 2:

-urine pH very high

-Later Type 2:

-urine pH minorly acidic (<5.5) w/ ⊕ urinary AGap → urine $Ce^\ominus$ < urine $Na^\oplus$ + urine $K^\oplus$

-Causes:

Ⓐ Multiple Myeloma

Ⓑ Carbonic Anhydrase Inhibitors (Acetazolamide)

Ⓒ Amphotericin B

Ⓓ 6-Mercaptoparine

Ⓔ Heavy Metals

- Lead
- Copper
- Mercury
- Cadmium

Ⓕ Amyloidosis

Ⓖ Protein/carbohydrate/AAcid Metabolism d/o's

-Fanconi syndrome:

-generalized PCT dysfunction

-can be caused by same causes of Type 2 RTA above

-pt's also have phosphate/urate/glucose + AAcids losses →

- hypophosphatemia
- hypouricosuria
- renal glycosuria (glycosuria w/ normal serum glucose)

-Idiopathic Type 2 RTA → tx w/ $Na^\oplus$ restriction

Type 4 RTA:

- impaired $Na^{\oplus}$ pump - $K^{\oplus}/H^{\oplus}$ electrical excretion gradient mechanism
- due to aldosterone defic. or distal tubular resistance to aldosterone → ↓ urinary $NH_4^{\oplus}$
- $Na^{\oplus}$ does not exchange normally w/ $K^{\oplus}/H^{\oplus}$ → acidemia + hyperkalemia
- Causes: (A) Diabetic Nephropathy (Main cause) → Hyporeninemic Hypoaldosteronism
  - (B) Spironolactone
  - (C) Interstitial Nephritis
  - (D) obstructive Uropathy
  - (E) Renal Transplant
- Common Tx is Fludrocortisone (Florinef) → Synthetic adrenocortical steroid w/ very potent mineralocorticoid effect
  - but usually leads to too much fluid retention
- Tx: (1) Dietary restriction of $Na^{\oplus}$
  - (2) Lasix
- NSAID's may further ↓ renin output → may exacerbate the hyperkalemia
- distal RTA

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Potassium

- mild hyper - $K^{\oplus}$ → stimulates aldosterone release → ↑'d distal tubular reabsorption of $Na^{\oplus}$ in exchange for $K^{\oplus}/H^{\oplus}$

- Alkalosis
- Insulin
- β- Agonists
- Aldosterone

→ stimulate ↑'d cellular uptake of $K^{\oplus}$ → ↓'ing serum $K^{\oplus}$

- Acidosis
- α - Agonists

→ inhibit cellular uptake of $K^{\oplus}$ → ↑'ing serum $K^{\oplus}$

-virtually all urine K^+ is secreted by the distal tubule
(all filtered K^+ is reabsorbed in the PCT)

-↓'d urine Na^+ / ↓'d urine due to RF → ↑'d K^+ retention
↓
ϕNa^+ available to exchange for K^+ or H^+

① Hyper-K^+:

-Causes: Ⓐ ↓ Excretion → Drugs, RF, Hypoaldosteronism
↓
Addison's Dis.

Ⓑ ↑ Production
↓
Trauma + Tumor Lysis Syndrome

Ⓒ Volume Contraction

Ⓓ Hypertonic states (Ex.) Hyperglycemia → K^+ follows free-H_2O out of cells)

-Common Drug Causes:

Ⓐ ACEI / ARB's

Ⓑ β-blockers

-Hyporeninemic hypoaldosteronism (renal) → avoid NSAID's, ACEI/ARB's, β-blockers + Heparin

-Comatose Diabetics → avoid empiric D50 w/out 1st checking a fingerstick
↓
if DKA then pt. may be hyperkalemic already (hyperglycemic + acidotic)
↓
T'ing the hyperglycemia will ↑ K^+ movement out of cells following the free-H_2O
↓
↑'d serum K^+

-can cause / exacerbate existing metabolic acidosis
↓
K^+/H^+ now competing for excretion in distal tubules

-Tx: Ⓐ Immediate Tx → IV calcium (CaCl - 1 amp or Ca Glue - 3 amps)
- counters CV effex of ↑ K^+ w/in 5 mins.

Ⓑ Insulin / Glucose → drives K^+ into cells
- onset 15-30 mins and lasts 12-24 hrs.

(C) $NaHCO_3$ → also drives K^+ into cells
- onset 15-45 mins and lasts 12-24 hrs.

(D) K^+-Binding Resins (Ex.) Kayexalate)
- onset ~30 mins and lasts permanently
- the only permanent fix (other than HD) ↓ actually removes K^+ from GI tract so ↓ GI absorption
- the other tx's only act temporarily

- cardiac effects of ↑ K^+:
  - d/t to the large difference b/w intra + extracellular K^+ levels
  - EKG Δ's Include (In order of Appearance):
    1. Peaked T-waves
    2. PR Prolongation
    3. Loss of P-waves
    4. QRS widening
    5. severe Brady arrhythmias
  - Begin tx for hyperkalemia w/:
    1. K^+ ≥ 7.0 or
    2. EKG Δ's

(2) Hypo-K^+:
- serum K^+ levels do not ↓ below normal until ~200-300 mEq deficit
- Findings: (A) U waves on EKG
  (B) ↓'d DTR's
  (C) Rhabdomyolysis
- Causes: (A) Diuretics (Most common cause)
  (B) Hyperaldosteronism
  (C) ↑'d Insulin Levels / Alkalosis
  (D) GI Losses
  (E) Type I RTA
  (F) Drugs (Ex.) Gentamycin → Renal K^+ wasting)
  (G) Genetic D/O's (Ex.) Bartter Syndrome, Gitelman Syndrome + Liddle syndrome)

- Diuretics:
  - ↑'d urine K^+ + Cl^-
- Hyperaldosteronism:
  - HTN w/ hypokalemia → ~40% will have Hyperaldo
  - Primary: - Hyporeninemia
    - HTN
    - Hypokalemia
  - 2nd-ary: - Due to renovascular HTN
    - ↓ Hyperreninemic Hyperaldo
    - ↓ Renal Blood Flow (Ex.) RAS → ↑ Renin → ↑ Angiotensin II → ↑ Aldo
  - ? How to differentiate Primary vs. 2nd-ary:
    - give NS 2L over 3-4 hrs. and check aldo level
    - If aldosterone level suppressed → then 2nd-ary (w/u for RAS)
    - If not suppressed → then primary
- Insulin / Alkalosis:
  - insulin drives K^+ into cells
  - alkalosis → K^+/H^+ excretion in the distal tubule favors K^+ excretion to hold H^+ in setting of alkalosis
- Type I RTA:
  - distal tubular defect of H^+ secretion → K^+ excreted instead in exchange for Na^+ reabsorption
  - hyperchloremic (non-Anion Gap) acidosis
- GI Losses:
  - Laxatives, diarrhea, vomiting + fistulas
    - ↓ causes alkalosis too → further K^+ loss ↑
    - can also cause hyperreninemic hyperaldosteronism
- Gentamycin:
  - causes K^+ + Mag^{2+} renal wasting

- Bartter Syndrome:
  - AR d/o
  - abnormal NaCl transport in thick ax. limb of loop of Henle
    ↓
    $Na^{\oplus}$ / $Cl^{\ominus}$ / $K^{\oplus}$ wasting
- Gitelman Syndrome:
  - more mild form of Bartter's but w/ ↓ urine Ca^{++}
    ↓
    distinguishes from Bartter's
- Liddle Syndrome:
  - rare cause of HTN w/ Hypo-$K^{\oplus}$
  - primary $Na^{\oplus}$ retention
    ↓
    ↓ Renin + ↓ Aldosterone levels
    ↓
    differentiates this from HTN w/ Hypo-$K^{\oplus}$ due to Hyperaldosteronism
- Tx: - treat the underlying cause
  - oral supplements

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Calcium

- circulates as bound (w/ albumin) + inactive or unbound + active (~50:50 ratio)
- hypoalbuminemia → only bound form is ↓'d → ionized Ca^{++} does not ↓
  - for each ↓'d albumin by 1 → total calcium ↓ by 0.8
    but ionized Ca^{++} remains the same
- Pregnancy → ↑'d Ca^{++} absorption + excretion
  - $1,25\text{-}(OH)_2\text{-}D3$ (active Vit. D) > 2 x normal

① Hypercalcemia:

- usually incidental finding on asymptomatic patient
  ↓
  usually primary (1°) hyperparathyroidism
  (esp. if h/o neck radiation)
  or cancer
- Tx: - Lasix → ↑'s Ca^{++} excretion
  - If severe → NS IVF's @ 300 cc/hr x 1-2 L w/ Lasix
    ↓
    rapidly ↓'s Ca^{++}

① Hypocalcemia:

-Causes: (A) Hypoparathyroidism
(B) Pseudohypoparathyroidism
(C) Hypomagnesemia
(D) Rhabdomyolysis
(E) Renal Failure → ↓'d conversion of 1-OH-D3 → 1,25-(OH)$_2$-D$_3$ (active) → ↑ pTH
(F) Severe Pancreatitis

-Tx: (A) Hypocalcemia w/ Hypercalciuria:
-thiazide diuretics → ↓ Ca^{2+} excretion
-otherwise treat w/ Calcium/ Vit. D

Magnesium

① Hyper Magnesemia:

-rare

-Causes: (A) Magnesium-containing laxatives/antacids in pts. w/ renal failure
(B) Mag-Sulfate over infusion → eclampsia

-symptoms w/ levels > 4-6 mEq/L
- initially nausea
-sedation
-muscle weakness
-loss of DTR's
-paralysis (including cardiac + resp. muscles)

-Tx: -volume expansion
-induce diuresis
-Calcium to treat symptoms
-HD if needed

② HypoMagnesemia:

-Causes: (A) Drugs: -Ampho B -Pentamidine
- Loop Diuretics - Cyclosporine
- Gentamycin -Cisplatin

(B) Insulin

(C) EtOH withdrawal

(D) Hungry-Bone Syndrome

-Renal-wasting vs. redistribution

-Renal-wasting:

- w/ loop diuretics
- Gentamycin / Cisplatin → wasting persists even after drugs are stopped

-Redistribution:

- w/ EtOH w/drawal
- Insulin
- Hungry-Bone Syndrome
  - post-parathyroidectomy → bones will suck up Ca^{2+} / Mag^{2+}

-↓ Mag → ↓'d Ca^{2+} + ↓'d K^{+}

- in pt's w/ hypocalcemia or hypokalemia ↓ serum Mag^{2+}
  - b/c hypocalcemia/hypokalemia not correctable until body Mag^{2+} stores are repleniished

-refractory cardiac arrhythmias → assoc. w/ low body Mag^{2+} stores (not just serum hypomag → total body stores may be low w/ a normal serum Mag^{2+} level)

-Tx:

(A) Parenteral: 12 mL of 50% Mag-Sulfate (49 mEq) in 1 L D5W (over) x 3 hrs. then 80 mEq in 2L D5W (over) x 21 hrs.

(B) oral: Mag Oxide (less severe cases)

Phosphate

① Hypophosphatemia:

-acute or chronic

-Acute Causes: (A) ATN (esp. w/ rhabdomyolysis)

(B) IVF's w/ phosphates
(C) Tumor Lysis Syndrome

-Chronic Causes: (A) Hypoparathyroidism
(B) Chronic kidney dis.

-If phos > 5.5 mg/dL → tx w/ Ca^{++}-containing antacids (bind phos in GI tract, if Ca^{++} is low) or Renagel (Sevelamer)
if Ca^{++} × Phos product is >55

(2) Hypophosphatemia:
-think EtoH w/ EtoH ketoacidosis
-Symptoms/consequences: if phos < 1 mg/dL (A) Rhabdomyolysis
(B) Cardiomyopathy
(C) Resp. Failure (esp. diaphragmatic muscles)
(D) CNS D/o's → irritability, hyperventilation, profound muscle weakness, seizures, coma + death

-chronic malnutrition (Ex.) EtoH)
↑'d catabolic release of phosphate → excreted in urine
-may have normal phos level on admission
-but when resume diet → glycogen levels ↑ → cells take up phos (anabolic process) → ↓'s serum phos

-Also EtoH pt's w/ hepatic encephalopathy / resp. alkalosis usually given dextrose ℞ solutions → alkalosis/ glucose cause cellular uptake of phos → may ↓ phos serum levels → predisposes to ATN / Rhabdo

-Other Causes: (A) Phosphate-binding antacids
(B) DKA
(C) Re-Feeding Syndrome
- involves feeding malnourished pt's

↑'d carbohydrate loads
(Ex.) TPN in the ICU)

- Tx: -supplemental Phos (esp. w/ pt's in DKA, EtOH w/drawal + include phos in TPN orders)
- If renal failure then give less supplemental Phos

Volume contraction

① Vomiting:
- causes a metabolic alkalosis → gastric HCl losses
- ↓ serum $Cl^{\ominus}$
- Hypokalemia → Renal $K^{\oplus}$ wasting
  kidneys reabsorb $Na^{\oplus}$ to maintain volume and w/ alkalotic state, preferentially excrete $K^{\oplus}$ rather than $H^{\oplus}$'s w/ $Na^{\oplus}$ reabsorption

② Diarrhea:
- causes a metabolic acidosis → HCl ↑'s as $HCO_3^{\ominus}$ is lost in stools
- ↑ serum $Cl^{\ominus}$
- ↓ serum $HCO_3^{\ominus}$

③ Thiazide Diuresis:
- causes a metabolic alkalosis
- ↓ serum $Cl^{\ominus}$ w/ ↑ urine $Cl^{\ominus}$ (unlike vomiting)
  ↓
  effective HCl losses in urine
- thiazides → ↑ NaCl load distally
  ↑ $Na^{\oplus}$ for reabsorption → ↑ $H^{\oplus}$/$K^{\oplus}$ excretion
  ↓
  actually ↑ NaCl, HCl + KCl in urine

④ Osmotic Diuresis:
- Ex.) Mannitol or Hyperglycemia
- causes ↑'d uop w/ normal urine osmol
  ↑'d solute losses per day

⑤ Diabetes Insipidus (Nephrogenic or Neurogenic):
- can cause hyper-$Na^{\oplus}$ + volume contraction

- but if pt's can maintain fluid intake → will be euvolemic
- usually caused by $Li^{\oplus}$ intoxication → impairs kidney concentrating ability → Nephrogenic DI

Edema

- 2/3 of filtered $Na^{\oplus}$ / H_2O is passively reabsorbed in PCT
- Primary Hyperaldosteronism:
  - Hyporeninemic
  - ↑ $Na^{\oplus}$ and total body water → ↓ $Na^{\oplus}$ / H_2O reabsorbed in PCT to somewhat counterbalance the ↑'d aldosterone effect → little to ϕ edema
- 2nd-ary Hyperaldosteronism:
  - CHF, cirrhosis, nephrotic syndrome, hypoalbuminemia
  - kidneys see an effectively ↓'d intravascular volume ↓ ↑'s renin-angiotensin-aldosterone system and ↑'s PCT reabsorption of $Na^{\oplus}$/H_2O ↓ peripheral edema

Hypertension

- from JNC VII
- Stage I: SBP 140-159 or DBP 90-99 → must be avg'd from ≥ 2 reads taken from each visit after the initial ↑ read
- Stage II: SBP ≥ 160 or DBP ≥ 100
- 95% of cases → primary (essential/idiopathic)
- ↑ morbidity/mortality for men vs. women, blacks vs. whites
- HTN → nephrosclerosis → hyperuricemia

- Syndrome X (Metabolic Syndrome):
  - obese pts w/ ↓ glucose tolerance + HTN
  - insulin resistance → causes hyperinsulinemia → volume retention, vascular hypertrophy, sympathetic overactivity → HTN

-Follow-ups: (A) DBP <85 → re✓ in 2-3 yrs.
(B) DBP 85-90 → re✓ in 1 yr.
(C) DBP 90-104 → re✓ in 2 months
(D) 105-114 → w/u w/in 2 wks.
(E) ?115 → w/u immediately

-w/u: look for identifiable/reversible causes:
(A) Truncal obesity w/ striae → Cushing Syndrome
(B) Labile BP's → Pheochromocytoma
(C) Abd. Bruits (esp. w/ diastolic component) → RAS
(D) ↓BP in LE's w/ absent/delayed femoral pulses → Aortic Coarctation
(E) Abd./Flank Masses → PCKD
(F) ↑Creat /Abnormal UA → Renal Parenchymal Dis.
(G) Hypercalcemia → Hyperparathyroidism
(H) Hypok⊕ → Primary Hyperaldosteronism

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-Initial Lab w/u: (A) CBC
(B) CMP (esp. k⊕, Na⊕, creat, serum gluc)
(C) FLP
(D) 12-lead EKG

-Indications for further eval for 2nd-ary HTN: (only ~5% of cases)
(A) Abrupt onset
(B) Age < 30 yrs.
(C) Malignant HTN
(D) Refractory HTN
(E) Hypercalcemia
(F) Hypokalemia w/ kaliuresis
(G) Systolic/Diastolic epigastric bruits or lateralizing over the kidneys

★ systolic bruit alone → ∉ an indication ★

Most common 2nd-ary cause → renovascular HTN (Ex.) RAS
↓
causes 2nd-ary Hyperaldosteronism

Anti-HTN Meds

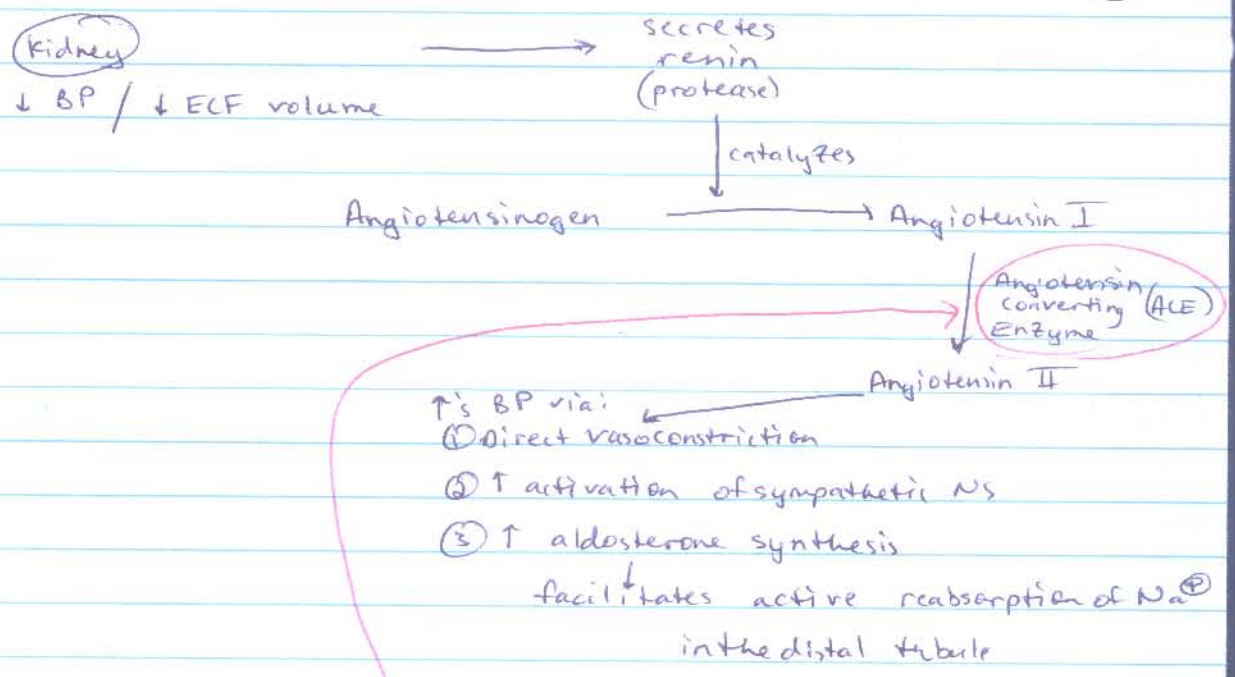
① Diuretics:

- thiazides → ϕ effective w/ creat cl < 20
- loop diuretics are effective ↗ but w/ shorter duration ↓ dose BID
- pt's must have moderate (not ↓ or ↑) salt intake to avoid hypo-$K^{\oplus}$
  - ↑ salt intake → ↑↑↑ $Na^{\oplus}$ load on distal tubule ↑ $K^{\oplus}$/$H^{\oplus}$ excretion/exchange
  - ↓ salt intake → ↑ $Na^{\oplus}$ load on distal tubule via actions of thiazides ↑ $K^{\oplus}$/$H^{\oplus}$ excretion/exchange
- avoid in pt's w/:
  - gout
  - orthostasis
  - dyslipids
- supplement $K^{\oplus}$ w/ diuretics + hypokalemia < 3.5
  - or w/ digoxin, glucose intolerance + CAD
- effective only w/ moderate dietary salt ↓'s

② β-Blockers:

- ↓ CO + sympathetic tone
  - ↳ ↓ renin production
- lipid-solubility → ↑'d solubility means ↓'d ½-life → (↑'d first pass effect) + ↑'d passage thru blood-brain barrier → ↑'d CNS side effex
  - highly lipid-soluble → Lopressor + Propranolol
  - least lipid-soluble → Atenolol + Nadolol ↓ ↑'d ½-lives + ↓'d CNS side effex
- Atenolol + Lopressor are β-1 selective (Nadolol, Pindolol, Propranolol + Timolol are not selective)
- Pindolol → some β-1 agonist activity
  - may be lost @ higher doses
- avoid β-blockers in pt's w/:
  - (A) Reactive airway dis.
  - (B) Dyslipids
  - (C) PVD

Renin-Angiotensin-Aldosterone System



③ ACE Inhibitors:

- inhibit Angiotensin I → II
  - ↓ causes ↓ Angiotensin II → ↓ aldosterone synthesis
    - ↓ Na⊕ reabsorption
- ↓ efferent tone (glomerulus)
  - ↓ glomerular capillary pressure + ↓ GFR
    - ↓'s progression of both DM + HTN nephropathies

④ Angiotensin II Receptor Blockers (ARB's):

- similar effex as ACEI's
- recommended for pt's unable to tolerate ACEI's
- act @ the Angiotensin II receptor levels

- give either ACEI/ARB for mild-to-moderate HTN w/ DM nephropathy
  - most effective w/ ↑/normal renin
  - minimal side effex
- avoid in ① pregnancy → teratogenic

④ Hyperkalemia (usually due to ↓ $K^{\oplus}$ excretion → ↓GFR w/ ALEI's/ARB's worsens this

⑤ Use w/ caution w/ ⓑ RAS or severe CHF ~~prevent~~ ↓GFR w/ ALEI's/ARB's → worsens azotemia

⑥ ↓ Renin dis.

⑤ CCB's:

- most effective in ↓ renin states

Tx of Essential HTN

- ↓'s complications (CVA, LVH, CHF, RF) except CAD
- lifestyle Δ's
- Pharmacologic Therapy:
  - begin w/ low-dose thiazide for Stage 1
  - Stage 2 → diuretic + 2nd agent
  - re✓ BP's in 1-2 months and ↑ doses as needed
  - may use other agent if co-morbidities indicate:
    - Ⓐ HF → ALEI's
    - Ⓑ CAD → β-blockers / ALEI's
    - Ⓒ DM → ALEI's
    - Ⓓ CKD → β-blockers / ACEI's (diuretics ϕhelpful if anuric)
- in the Elderly:
  - lifestyle Δ's
  - low-dose thiazide
  - isolated systolic HTN → diuretics 1st then add long-acting CCB as needed
- Special conditions:
  - Ⓐ Angina:
    - β-blockers and long-acting CCB's (ϕshort-acting)
  - Ⓑ Post-MI:
    - β-blockers to ↓ recurrent MI risk
    - ALEI's to ↓ HF risk

(C) LVH:

- major risk factor for CV events
- ALEI's / ARB's, CCB's, β-blockers → may cause regression of LVH (uncertain significance of regression)
  - ↓ effect w/ diuretics
  - ↓ effect w/ hydralazine
  - Minoxidil actually ↑'s LVH
- may have diastolic dysfunction → ⊖ inotropes are DOC's
  - ↓ avoid preload reducers + use caution w/ diuretics

(D) HF:

- ALEI's / ARB's
- β-blockers
- Aldosterone antags.
- ⊕/⊖ Digoxin / Diuretics

(E) Proteinuria:

- > 1 g / 24 hrs. → ALEI's / ARB's to goal BP's < 130/85

(F) DM:

- ALEI's / ARB's
- α-blockers, CCB's, diuretics too
- DM Nephropathy → ALEI's / ARB's

(G) Asthma:

- avoid β-blockers + α/β-blockers
- ALEI's / ARB's safe

(H) Gout:

- avoid diuretics

(I) LVA:

- do not treat aggressively if h/o HTN
  - ↓ cranial vessels require ↑ BP's to maintain perfusion
- CCB's (best option)
- avoid → central-acting agents (clonidine), nitroprusside ("steals" blood flow from brain)

HTN Crisis

- rapid ↓ BP required to limit end-organ damage

(A) Unstable Angina w/ ↑BP
(B) Acute MI w/ ↑BP
(E) Encephalopathy w/ ↑BP
(D) Acute Retinopathy w/ ↑BP → due to retinal artery spasm
(E) Nephropathy w/ ↑BP
(F) LV Failure w/ ↑BP
(G) Dissecting Aneurysm w/ ↑BP

- intense hyperreninemia may cause resulting hypokalemia
- Tx:
  - ↓ BP by 25% w/in minutes - 2hrs.
  - Goal BP 160/100 w/in 2-6 hrs.
  - oral Agents: Rapid onset
    - loop diuretics
    - β-blockers
    - α2 -blockers
    - CCB's
  - avoid SL Nifedipine → too many side effex
  - IV Agents:
    - Nitroprusside
    - Labetalol
    - CCB's

2nd-ary HTN

① Renovascular HTN:
  (A) RAS: - usually (B)
    - affex men >50
    - usually DM
  (B) Fibromuscular Dysplasia: - often (B) too
    - affex women <40
  (C) Vasculitis (esp. Takayasu)
  (D) Scleroderma (~50% have renovascular HTN)

-Dx:

-continuous (not just systolic) abd. bruit
-↓ serum $K^{\oplus}$ (hyperreninemic hyperaldosteronism)
↓ strongly suggestive
-screen via captopril renogram or Doppler u/s
-Arteriography: Gold standard
- Fibromuscular Dysplasia: string of beads
- RAS: usually single, proximal stenosis w/ distal dilation
-if (F) arteriography → confirm w/ renal vein renin test
-involved / uninvolved renin ratio >1.5
↓ functionally significant

-Tx:

-Angioplasty
-ACEI/ARB's → ↓BP + ↓GFR in the involved kidney
-if RAS is (B) → may worsen prerenal azotemia
↑RF
-DOC's for scleroderma

(F) Primary Hyperaldosteronism:

-aldosterone → promotes ↑ $Na^{\oplus}$ reabsorption (actively) in distal tubule
↓
H_2O (water) follows to maitain osmol
↓
↑ $Na^{\oplus}/H_2O$
↓
↑ intravascular volume
↓
↑ BP

-suspect in pt's w/ hypokalemia of unknow etiology (ϕ on diuretics)
-may / may not have HTN
-Causes: (A) Adrenal Adenoma (~70%)
-Conn syndrome
(B) Idiopathic (B) Adrenal Hyperplasia (~25%)

Ⓒ Adrenal carcinoma (<5%)

- rare

- if ϕ hypokalemic → do not consider this Dx

- Dx:

- ✓ stimulated plasma renin activity (PRA)

- if ↓/undetectable (to confirm) ↙ salt↑ + IV fluid load w/ 2L NS over 3-4 hrs. + ✓ aldosterone level

- if aldosterone level not suppressed then Dx made

- CT Abd to eval adrenals once above Ⓐ

- if pt. on ACEI's/ARB's:

- ✓ renin/aldosterone levels to see if aldosterone is suppressed

- if ϕ suppressed → Dx likely

- Tx: Ⓐ $Na^{\oplus}/H_2O$ restrictions

Ⓑ $K^{\oplus}$-sparing diuretics

- Aldactone

- Triamterene

- Amiloride

Ⓒ Adrenal Adenoma:

- surgical excision if unilateral

- Ⓑ → diuresis alone

- only ~1/3 of pt's w/ Ⓑ adenomas + HTN w/ be cured w/ surgery

③ Cushing Syndrome

④ Pheochromocytoma:

- rare

- chromaffin tissue origins

- 90% in adrenal medulla (other 10% abd or thorax)

- 10% Ⓑ, 10% malignant, 10% familial

- most pt's have sustained HTN/tachycardia

-assoc. w/ MEN II A + II B

-Dx:

-✓ 24-hr urine metanephrines, VMA ↑ catecholamines (metanephrines least sensitive)

- combo of above very sensitive/specific if collected when symptomatic, resting off meds

- CT of adrenals to find it

-if ϕ seen by CT:

Ⓐ Arteriography

Ⓑ Meta iodo benzylguanidine scintigraphy

-NorEpi analog

↓

concentrates in adrenals/pheo's

-Tx: surgical excision

-pre-op w/: - phenoxybenzamine (α-blocker) or Labetalol for BP control

- Propranolol for tachycardia

HTN w/ Pregnancy

① Latent Essential HTN

② Pregnancy-Induced HTN

-if before 3rd trimester → latent essential HTN

-Pregnancy-Induced HTN:

-PIH or preeclampsia

Risk Factors:
- creat ↑ 1.2 / lab / 100
- BP

-usually occurs in 3rd trimester of primigravidas

-stops w/ delivery

- HTN, proteinuria → post 20th week → Dx made

- assoc. w/ [redacted] hyperuricemia

-severe PIH w/ ↑ LFT's, ↓ plat's + μ- angiopathic hemolytic anemia → HELLP syndrome

-Tx: ① Bedrest

② Tx HTN

③ sometimes hospitalization

- Drugs: ① Methyldopa (DOC)
② Hydralazine
③ Labetalol / β-blockers / Clonidine / CCB's → limited experience

-avoid ACEI's / ARB's → teratogenic
-avoid Nitroprusside → cyanide poisoning
-avoid β-blockers if early pregnancy → growth retardation

Other Causes - 2nd-ary HTN

① OCP's
② Aortic Coarctation
③ Obesity
④ EtoH
⑤ Ca^{++} / K^{+} Deficiency

Renal Failure

① Pre-Renal
② Post-Renal
③ Intra-Renal

Pre-Renal Renal Failure

-due to a real or effective ↓ in renal blood flow
-Causes: ① ↓ intravascular volume (Ex.) Cirrhosis / Hypo-Albuminemia
② RAS
③ CHF / low-output states
④ Drugs - diuretics (most common)
- NSAID's
- ACEI's / ARB's
- IL-2 / cyclosporine / Tacrolimus → in transplant pt's.
⑤ Renal Emboli / Thrombi → may be prerenal or intrarenal

-NSAIDs:
-esp. likely to cause prerenal azotemia w/ renal function impairment → pt's are prostaglandin-dependent for normal function
-If ACEIs/ARB's cause prerenal azotemia → consider underlying RAS
-Lab w/u:
(A) BUN/creat high (usually >20 ratio)
(B) ↑ urine osmol (usually > 700)
(C) ↓ urine $Na^{\oplus}$ (usually < 20) → if tubular function is intact
(D) Normal urine sediment
(E) FENa → low ★ Best 1st test of ARI ★
-also low w/ acute GN
-to differentiate acute GN vs. prerenal azotemia → urine sediment + protein → normal → prerenal azotemia
-exam should include orthostasis measurements

$$FENa = \left(\frac{\text{urine } Na^{\oplus}}{\text{serum } Na^{\oplus}} \Big/ \frac{\text{urine creat}}{\text{serum creat}} \right) \times 100\%$$

Post-Renal Renal Failure

-Causes: (1) Bladder Outlet Obstruction
- prostatic hypertrophy
- prostatic stenosis/cancer
- bladder ca.
(2) (B) ureteral obstruction → rare
-Lab w/u:
(A) BUN/creat high → urea diffuses back into the system
(B) ↑ $K^{\oplus}$ → possibly assoc. Type IV RTA (distal)
-assoc. w/: -papillary necrosis/pyogenic kidneys
-sterile pyuria w/ WBC casts
-Symptoms: -renal colic / hematuria

Intra-Renal Renal Failure

-Causes: ① ATN
② Intratubular Obstruction
③ Glomerular Damage (Ex.) Acute GN)
④ Acute Interstitial Nephritis
⑤ vasculitis / Emboli / Thrombi / stenoses / HTN / scleroderma / Eclampsia
-most common vascular causes

-acute atheroembolic renal dis.:
-may have hypocomplementemia
-↑ESR
-eosinophilia
-Rash
-but ∅ RBC casts → differentiates from vasculitis

① ATN:
-most common intrarenal cause (~75%)
- 90% of those who improved did w/in 3 wks. + 99% w/in 6 wks.
- ½ to ⅓ of pt's w/ ATN will die

4/23/2007

-Causes: Ⓐ Transient Ischemia of kidneys
Ⓑ Toxic Insult to kidneys
Ⓒ ↓ Renal Perfusion → shock, surgery, burns, sepsis, trauma (most common cause)
Ⓓ Rhabdomyolysis → myoglobinuria
Ⓔ Hemoglobinuria
Ⓕ Heavy Metals
Ⓖ Contrast Dye
Ⓗ Drugs - Aminoglycosides
- Ampho B
- Cisplatin
- Foscarnet

more likely to resolve ↑

-Aminoglycosides: - induce PCT damage → non-oliguric ATN
- also cause hypomagnesemia

-Amphotericin B: - esp. induce ATN w/ doses > 3 grams

-direct nephrotoxin → can cause Types 1+2 RTA

-Cisplatin: - can also cause hypomagnesemia via hypermagnesiuria

-Lab w/u:

molality (urine) <400 but never <300 → isoosmolar

-urine Na^{+} >20 + FE_{Na} >1%

- urine sediment → large muddy-brown granular casts (sensitive but not specific)

Course:

-oliguric ATN → resolves w/in 1-4 wks.

- 1/4 ATN's is non-oliguric (usually aminoglycosides)

↑ risk of hyperkalemia

-Tx:

-treat the underlying cause

-treat hyper-K^{+} if present

-encourage PO intake → ↓ catabolic state

- Equalize I/o's

Rhabdomyolysis

-myoglobin causes rhabdo if:

① urine is acidic

② pt. is volume-depleted

-Causes: (A) Muscle/Tissue Trauma → comatose states, OD w/ sustained tissue compression or direct trauma

(B) Strenuous Exercise

(C) Seizures

(D) Heat Stroke

(E) Severe volume contraction

(F) Cocaine

(G) Hypophosphatemia

(H) Severe HypoK^{+}

-lab w/u: ① ↑↑↑ CK (confirmatory)

② If ϕ CK available → ↑K^{+}, ↑Phos, ↑↑Urate,

↓ Ca^{++} + disproportionately ↑ creat vs. BUN

③ Urine: - muddy brown casts
- heme⊕ w/out RBC's
- brown-pink urine supernatant

- occurs via:
  - Ⓐ ↓ 1,25-$(OH)_2$ D production due to renal injury
  - Ⓑ ↑ Phos due to renal injury + tissue breakdown

- PTH levels are ↑'d due to hypo-Ca^{++}
- hypocalemia (if the 1° (primary) cause) may not be evident initially
  hypoK^{+} causes ATN/Rhabdo → may induce a hyperK^{+}-ic state plus tissue injury may also cause a hyper-K^{+}-ic state → thus serum K^{+} may be normal or high w/ the initial cause being hypo-K^{+}-ic rhabdo

- Tx (ASAP):
  - NS volume replacement
  - Forced diuresis w/ urine alkalinization
- risk of hyper-Ca^{++} following tx
  ↓ avoid treating hypo-Ca^{++} unless symptomatic

Hemoglobinuria

- similar effect as rhabdo and same tx but mechanism is different
- ATN is due to mechanical obstruction vs. toxicity (rhabdo)

Intratubular Obstruction

- Causes:
  1. urate nephropathy
  2. Oxalate Deposition
  3. Hyper-Ca^{++} / Intrarenal Deposits
  4. Multiple Myeloma
  5. Drugs: Ⓐ Methotrexate Ⓒ Acyclovir Ⓑ Indinavir Ⓓ Sulfa's
  6. Cholesterol Atheroembolic Renal Dis.

- can be 2nd-ary to aortic manipulation or anticoagulants
  ↓
  "showers" of emboli
  ↓
  stepwise progression to renal failure

-Dx: - tissue biopsy confirming cholesterol emboli

Malignancy-Assoc. Renal Failure

-Causes: ① Lymphoma (more common than #2)
② Leukemia

-Lymphoma: -may infiltrate the kidney itself
-IL-2 → causes prerenal azotemia
-mTx/urate → related to tumor lysis, precipitate + cause obstruction (intratubular RF)
-Cisplatin → directly nephrotoxic (hypomag)
-Mitomycin C → causes HUS

-Leukemia: -rarely affect renal function
-↑↑↑ WBCs → treat prophylactically w/ Allopurinol to avoid urate Nephropathy
-avoid Probenecid → uricosuric agent
↓
worsens urate nephropathy
-maintain intravascular volume
-alkalinize the urine
-if Allopurinol allergy → Lasix, IVF's + alkalinize the urine

Wisdom Pearls

① EtOH → Think rhabdo
② Prosthetic valve → Think SBE w/ post-infex GN
③ CLL/Lymphoma Tx → Think urate Nephropathy
④ Drugs → Think Interstitial Nephritis

ARF Tx Pearls

-Lasix will ϕ help preserve renal function w/ ARF (esp. if ϕ

↑ in uop after 1st dose)

- Low-dose Dopamine should only be used w/ ↓BP's +ARF unresponsive to IVF boluses / volume resuscitation

Glomerular Disease

- Histology Review of Glomeruli:
  - specialized capillary plexus
  - surrounded by Bowman's capsule
  - capillary walls filter blood → ultrafiltrate passes into Bowman's capsule → conducted into tubules for processing
  - Filtration Process:
    1. Endothelium (capillaries)
    2. GBM
    3. Pores b/w epithelial foot processes (podocytes)

- Classes of Glomerular Dis:
  - (A) Nephritic:
    - acute/subacute inflammatory process → acute GN
    - presents w/: (1) Hematuria, (2) mild Proteinuria, (3) RBC casts (usually)
    - may progress to ↓
  - (B) Nephrotic:
    - presents w/: (1) Heavy Proteinuria, (2) Edema, (3) oval fat bodies in urine

4/24/2007

- Causes of Glomerular Dis:
  - (A) Idiopathic
  - (B) Immune Complex (Ag-Ab) → most commonly
    - Mesangial or
    - GBM
  - (C) Ab-Mediated → directed against the GBM

- Membranous + post infex GN → subepithelial deposits
- IgA Nephropathy → mesangial deposits
- FENa < 1% → Nephritis (+)/(−) prerenal azotemia
- Definitive Dx → Renal biopsy

A) Subepithelial Deposits:
   1. Membranous
   2. Post-Infections

B) Subendothelial Deposits:
   1. Diffuse
   2. Proliferative
   3. Lupus Nephritis
   4. Membranoproliferative GN

C) Mesangial Deposits:
   1. IgA Nephropathy

4/26/2007

Nephritic Urine
- variable proteinuria
- "active" urinary sediment → dysmorphic RBC's/WBC's w/ casts (mostly RBC casts but WBC's/granular also possible)
  - casts → always originate from renal tubules
    - granular casts → non-specific
    - muddy-brown casts → ATN more likely than GN
      - ↓ urine osmol
      - ↑ in GN
      - ↓ in ATN

- Causes:
  1. Post-Infex GN
  2. IgA Nephropathy (most common cause)
  3. Lupus Nephritis

Nephrotic Urine
- reflex defex in glomerular filtration barrier selectivity

- little inflammation, more like sclerosis
- heavy proteinuria (2.5-3.5 g/day or 40-50 mg/kg/day)
- urine fat (oval fat bodies, fatty/waxy casts + renal tubular cells w/ lipid droplets
- usually normal sediment except for fat
- Signs:
  - (A) Hypoalbuminemia (w/ 2nd-ary edema)
  - (B) Hypogammaglobulinemia → tendency for ↑'d infx. (protects against encapsulated organisms) esp. H. influenzae + Strep pneumo
  - (C) ↓ Thyroid-Binding Globulin → ↓ total thyroxine
  - (D) ↓ Iron-Binding Globulin → ↓ total iron levels
  - (E) ↓ Levels of Anti-Thrombin III → Hypercoagulable ↑ risks for PE / renal vein thromboses
  - (F) Dyslipidemia
  - (G) Pleural Effusions → Related to Hypoalbuminemia
  - (H) Ascites
  - (I) Pulm Edema/Congestion
    - (Interestingly) → unless h/o CHF
      - ↓ pulm. interstitium loses albumin @ same rates as blood → ∅ a large osmotic differential

Steps In Evaluating Glomerulopathies

1. Evaluate urine sediment → Nephritic vs. Nephrotic
2. Systemic D/O or Localized Renal D/O
3. If Nephritic → Complement Levels (Low vs. Normal)

4/27/2007

Nephritis

- Complement:
  - Low Complement → Lupus Nephritis
    - Post-Infx GN
    - Membranoproliferative GN
    - cryoglobulinemia
    - SBE
  - Normal Complement → vasculitis

Rapidly Progressive GN (RPGN)

- any nephritis may devolve to this
- renal failure w/in days to weeks → if untrtd → 100% injury (usually 3-4 mos)
- may be normal or low complement or present as systemic or kidney disease
- ANCA (+) RPGN always presents as a RPGN
  - always consider if RF is rapidly progressive + recent

- Causes:
  - (A) Idiopathic
  - (B) SLE
  - (C) Vasculitis → PAN + wegener's
  - (D) Goodpasture's → anti-GBM / linear deposits (kidneys + lungs)
    - RPGN + pulm. hemorrhage
  - (E) Wegener's
  - (F) PAN

- Classes:
  - (1) Immune-complex Dis. (45%): (IC) Lumpy-Bumpy / Granular (Type II)
    - Post-Infec GN
    - Lupus Nephritis — Tx: -steroids
    - IgA Nephropathy — -Cytoxan / cellcept
    - Membranoproliferative
    - Idiopathic
  - (2) Pauci-Immune Dis. (~50%): (Type III)
    - Microscopic Polyangiitis
    - wegener's Granulomatosis — Tx: -Immunosuppressives (Cytoxan) -steroids
    - Churg-Strauss
    - 80-90% are ANCA (+)
  - (3) Anti-GBM Dis. (~5%): Linear (Type I)
    - Goodpasture's (lung involvement too)
    - Localized Anti-GBM Dis.

- Urine:
  - (+) protein
  - RBC casts

- Bx:
  - crescents (75%) of glomeruli

- inflammatory crescents → dis. may respond to tx
- fibrous crescents → irreversible dis.
- w/u:
  ① ✓ ANCA + anti-GBM's
    - Anti-GBM w/ pulm. hemorrhage → Goodpasture's
    - Anti-GBM w/out pulm. hemorrhage → Anti-GBM GN
    - ⊕ ANCA + ϕ anti-GBM:
      Ⓐ Wegener's → Necrotizing pulm. granulomas (79% c-ANCA⊕)
      Ⓑ PAN → Systemic necrotizing arteritis
      Ⓒ Idiopathic ANCA⊕ crescentic GN → ϕ systemic findings

      (can have either p-ANCA or c-ANCA ⊕)

    - ANCA + Anti-GBM ⊖:
      - consider Ic Dis:
        Ⓐ Lupus Nephritis → anti-DS-DNA Ab's
        Ⓑ Post-Infex → ✓ complements (↓)
        Ⓒ Cryoglobulinemia → ✓ complements (↓) + cryoglobulin levels

- Tx:
  ① Corticosteroids
  ② Cyclophosphamide or Azathioprine

  - For SLE or ANCA⊕ vasculitis → cyclophosphamide ↓ ↓'s relapses ×3-fold
  - Cryoglob or Goodpasture's → plasmapheresis then alkylating agent (cytoxan) +/- steroids +DD

- C3:
  - used up in both intrinsic + extrinsic complement reactions
  - Ic Dis → ↓C3 levels
- CH50:
  - marker for the intrinsic pathway
  - normal w/ extrinsic activation

Nephritis w/ Low Complement Levels

- 1st step → Kidney or Systemic Presentation

Kidney Presentation:
1. Post-Infex GN
2. Membranoproliferative GN

Systemic Presentation:
1. SLE
2. SBE
3. Cryoglobulinemia

1. Post-Infex GN:

- aka diffuse endocapillary proliferative GN
- commonly assoc. w/ strep (Group A) but actually majority of cases → non-strep infex.
- Bx:
  - Diffuse glomerular cellular proliferation (affex all glomeruli)
  - Hump-shaped subepithelial deposits
- presents w/ hematuria + HTN
- Causes:
  1. Sepsis
  2. Viruses
- caused by Ab-Ag reactions
  - Ag is infecting agent
    - causes granular IgG/C3 deposits
      - hypocomplementemic ($\downarrow C_3$ / CH_{50})
        - x6-8 wks.

- Post-Strep GN:
  - Group A β-hemolytic strep
  - causes throat or skin (impetigo) infex 1st
    - then 1-6 wks. later → GN
      - ~10 days post throat infex.
      - ~14 days post skin-infex.
    - latent period differentiates from IgA Nephropathy (more immediate)
  - only will progress to RF if infection persists
    - tx w/ Abx
  - most recover w/in 6-8 wks (~1/3 will have histologic damage decades later)

- progression: rare but ↑common in adults vs. kids

② Membranoproliferative GN:

3 Types: ① Type I – endothelial deposits
② Type II – dense deposits
③ Type III – deposits throughout

- Causes: Ⓐ Hep C
  - mixed essential cryoglobulinemia
  - ↓ C_3/C_4/CH_{50} levels in 83% of pt's → C_3 level stays ↓ indefinitely (can help differentiate MPGN vs. Post-Infx GN)
  - ↑ RF factor
  - Ⓐ cryoglobulins
- Ⓑ Idiopathic
  - frequently progresses to RF (~50% after 10 yrs) + cell proliferation
  - has both BM Δ's → nephrotic component; → nephritic component
  - tends to recur w/ transplanted kidney in small %
- BM Δ's:
  - dense immune deposits → double-layered BM
- Presentation: (may look like combined nephritis/nephrosis)
  - hematuria
  - nephrotic-range proteinuria
  - RPGN
- Tx:
  ① Children → Prednisone
  ② Adults → Aspirin + Dipyridamole (anti-platelet)
  ③ If assoc. w/ Hep C → IFN

Nephritis w/ Normal Complement Levels

- 1st step → kidney or systemic Presentation

Kidney Presentation:
① ANCA⊕ RPGN
② IgA Nephropathy
③ Alport Syndrome

Systemic Presentation:
① Good pasture's syndrome
② Vasculitis
③ TTP/HUS

① ANCA⊕ RPGN:
- ϕ systemic presentation → ϕ wegener's or PAN
  ↓
  Idiopathic ANCA⊕ crescentic GN

5/9/2007

② IgA Nephropathy:

- aka Berger Disease
- most common GN world wide (>25%)
- mesangial proliferation / hypercellularity / small crescents
  - Ab/Ag reactions → IC deposition of IgA / C3 in mesangial matrix + skin
- usually normal serum complement levels
- more progressive in pt's w/ proteinuria

6/6/2007

- Presentation:
  - ① Gross Hematuria s/p URTI
  - (many) Microscopic Hematuria w/ proteinuria / progressive dis.
  - hematuria usually occurs during a viral illness or post-exercise
  - more common in males + Asians
- Prognosis: Z 1.4 → worse prognosis
  - tied to creatinine, BP + degree of proteinuria
    - if normal → good prognosis
  - ~50% w/ proteinuria have progressive dis.
- Treatment:
  - ϕ definitive consensus (steroids in short-term, ? Cytoxan / Imuran)
  - ACEIs / ARB's + fish oils → "appear" to help

③ IgM Nephropathy:

- similar as IgA Nephropathy above
- usually males and/or Asian w/ gross hematuria after exercising or s/p viral illness

④ Alport Syndrome:

- hereditary (usually X-Linked)
- chronic glomerulonephritis
- Nerve deafness
- Congenital Eye Abnormalities

mesangial cells in line without matrix b/w them

Nephritic w/ Normal Complement Levels – Systemic Presentation

① Goodpasture's Syndrome:
- char. by linear anti-GBM deposits in the kidneys/lungs
  ↓
  RPGN + pulm. hemorrhage

② Vasculitides:
- Wegener's Granulomatosis
- Polyarteritis Nodosa (PAN)
- Henoch-Schonlein Purpura (HSP) → children
  - may also affect skin, GI tract, joints, hematuria
    ↓
    erythema/urticaria/purpura

③ TTP/HUS → Thrombotic Thrombocytopenic Purpura/Hemolytic Uremic Syndrome

Nephrotic w/ Renal Presentation

① Minimal Change Dis:
- most common cause of nephrosis in kids <10 yrs. (~90%)
- causes nephrosis in ~15-20% of adults → 15-20% of nephroses in adults are due to minimal Δ dis.

6/7/2007

- Presentation:
  - usually gross proteinuria w/out hematuria or sudden edema
    ↑
    frothy/foamy urine
- Causes:
  - (A) Idiopathic (most common)
  - (B) NSAIDs
- Associations:
  - Hodgkin's Dis.
- Complications:
  - ① SBP
  - ② Pneumonia
  - } common causes of death if untreated
- Microscopic Analysis:
  - ϕ Δ on light microscopy → minimal Δ dis.
  - immunofluorescence → normal
  - EM → loss of epithelial foot processes (podocytes)
- sediment may show Maltese crosses (w/ polarized light)

-Tx:

Ⓐ steroids (DOC) → good response (90% resolve in days-weeks)

Ⓑ Cyclophosphamide (cytoxan) - 98% response rate

Ⓒ Cyclosporine

-carries the best prognosis of the nephrotic syndromes (~50% will resolve on their own)

-Bx if poor response to steroids

② Focal segmental Glomerulosclerosis (FSGS):

-usually idiopathic

-also causes diffuse foot process loss → similar to minimal Δ dis.

may be a more severe form of minimal Δ dis.

- IgM deposits

- renal sclerosis is only present in segments of the glomeruli (esp. juxtamedullary glomeruli) → eosinophilic as it moves toward the capsule

- most common cause of idiopathic nephrosis in AAmers.

-consider in young pts (15-30 y.o) w/ HTN, HIV⊕, obesity, sickle cell, heme malignancies or chronic vesicoureteral reflux or IVDU

-renal failure is slowly progressive

↓

may require HD in 5-10 yrs.

-Tx:

-long-term steroids to induce remission (up to 1 year)

-ACEI/ARB → ↓ proteinuria + ↑ prognosis w/ <2g proteinuria

-Prognosis:

-40% → partial or complete remission w/ steroids

-60% → ESRD w/in 10-yrs.

③ Membranous Nephropathy (or sometimes Epimembranous)

-usually idiopathic

-most common cause of nephrosis in non-diabetic adults

-Causes:

Ⓐ Infections (Ex.) Malaria, HBV, HCV + Syphilis

Ⓑ Drugs → Gold, penicillamine + NSAID's

Symptoms: ① ↑ LE Edema
② Nephrosis
③ Foamy urine → protein
④ Usually normotensive

Natural History (w/out tx):
- 1/3 progressive (10 yrs) → 75 g/24hr proteinuria, creat ↑↑ (>50 yrs) → risks: males, Zn↓
- 1/3 resolves
- 1/3 progressive but very gradual (decades)

⑤ Small underlying solid tumors (present in ~50% of cases) (esp. Lung/colon ca.)
age-appropriate cancer screening

⑥ SLE

- Bx Results: Classic IC dis.
  - involves all glomeruli → sclerotic D's
  - may have subepithelial IgG/C3 deposits or spikes (lumpy-bumpy) (silver methamine stain)
  - assoc. w/ hypocomplementemia only if due to SLE flare
- Prognosis:
  - women do better vs. men
  - ~30% (overall) progress to ESRD
- Tx:
  - Mild cases → spontaneous remission likely
  - Mod/Severe cases → corticosteroids plus cytotoxins (Ex.) cyclophosphamide or chlorambucil)
  - Pontiselli → alternate months of steroids vs. chlorambucil/cytoxan

Nephrotic w/ Systemic Presentation

6/8/2007

① Diabetic Nephropathy:
- most common cause of nephrosis in adults
- develops in ~30% of Type I DM's
- ↑ vascular retinopathy follows a decline in renal function
- Testing:
  - urine ↑-albumin → too small to detect by dipstick (30-300 mg/day)
  - spot urine protein/creatinine ratio → >30 mg/day → ⊕ test
  - should be done annually in all DM's
  - if ⊕ ↑-albumin → start ACEI/ARB even if normotensive

*serum creat is poor judge of GFR b/c ↓ muscle mass

- Histology:
  - diffuse nodular glomerular D's
- HD or transplant will be required w/ in 5-7 yrs. of onset of proteinuria
  - if Dx <5 yrs. ago or >35 yrs. ago then progression to ESRD unlikely

- if renal function declines rapidly → over months
  then look for another cause

- Tx:
  - (A) Excellent HTN control
  - (B) Excellent glucose control (DCCT)
  - (C) ACEI / ARB

  → all will slow the progression to RF

- as renal function worsens
  ↓ insulin requirements ↓ → 2nd'ary to ↓'d metabolism by kidneys
  - also causes ↓ renin levels
    ↓ hypo-reninemic hypoaldosteronism + Type IV RTA

② Amyloidosis:

- causes light-chain nephropathy → induces light-microscopy Dx's similar to DM

- Histology:
  - large hyaline-appearing nodular masses of glomeruli
    ↓ signifies amyloidosis or DM-Nephropathy
    ↓ differentiate via Congo Red stain
    ↓ amyloid will have an "apple green birefringence" on polarizing microscopy

- Types:
  - (A) AL: primary-type
    - assoc. w/ multiple myeloma
    - caused by a plasma cell clone line that produces a partially-degraded Kappa/lambda fragments
  - (B) AA:
    - due to chronic inflammation (Ex.) RA + FMF)
  - (C) Rarely may result from chronic skin infex via "skin popping" in drug addicts

Tx: FMF-associated type → colchicine

Pharmacotherapy

Causes of Nephrosis:

1. NSAID's (may also cause papillary necrosis)
2. Gold
3. Penicillamine
4. Trimethadione
5. Captopril (Rarely)

General Tx Guidelines of Nephrosis

- ↑ intraglomerular pressure → ↑ disease progression
  - ↳ ACEI/ARB's → good for ↓ing intraglomerular pressures
  - Low-protein diet ↗
- use caution w/ diuretics → nephrotics have difficulties maintaining intravascular volume
  - ↓
  - diuresis/ $Na^{\oplus}$-restriction → may induce prerenal azotemia
- Nephrosis → should never have assoc. hypocomplementemia
  - should never be assoc. w/ a nephritic-type sediment

Pearls

1. Prerenal Azotemia: Granular/Hyaline casts
2. Postrenal Failure: Blood/WBC casts; if due to papillary necrosis
3. Intrarenal Failure: ATN → muddy-brown granular casts

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Acute Interstitial Nephritis

- drug-induced hypersensitivity
- often presents w/ eosinophiluria
- sediment contains (typically):
  1. Eosinophils
  2. RBC's
  3. WBC's / WBC casts
  4. β-2 Microalbumin

- differs from GN in that it lacks
  - albumin
  - RBC casts
  - Fat Bodies

- Causes:
  1. Antibiotics → unrelated to dosage/duration
     - A. β-Lactams (esp. Methicillin)
     - B. Trimethoprim/Sulfamethoxazole (Bactrim)
     - C. Cephalosporins
     - D. Rifampin
     - E. Fluoroquinolones

     Classic triad includes:
     1. Fever
     2. Rash
     3. Eosinophilia
  2. NSAID's
     - typically ingested for months before symptoms occur
     - may not present w/ fever/rash/eosinophilia
     - usually presents w/ nephrosis too (very unusual for an AIN)
     - Microscopy may reveal minimal Δ glomerular Δ's
  3. Cimetidine
  4. Thiazides
  5. Phenytoin
  6. Allopurinol
  7. Sarcoidosis
  8. SLE
  9. Pyelonephritis
  10. Transplant Rejection

  → non-medication causes

Chronic Interstitial Nephritis

- Causes:
  1. Renal Outlet Obstruction
  2. Drugs:
     - A. Analgesics → papillary necrosis usually w/ analgesics & NSAIDs (large doses required (> 6 lbs. of drugs))
     - B. Cisplatin
     - C. Cyclosporine
  3. Metals:
     - A. Lead
     - B. Cadmium
  4. Sjogren's
  5. Sickle cell
  6. Multiple Myeloma

- consider CIN in pt. w/ a pain d/o who presents w/ proteinuria and ↑ creat.
  - ✓ for lead toxicity w/ EDTA
- also consider if pt. has glucosuria but a normal serum glucose → tubulointerstitial dis. (or pregnancy or Type II RTA)
  or
  Fanconi's Syndrome

NSAID's

- may cause both acute/chronic IN
  - key point → nephrotic range proteinuria → acute
    - if light proteinuria ‖ chronic ← or
    - if light w/ active sediment → Nephritis
- effectively ↓ GFR → ↓ renal blood flow via blocking prostaglandins → ϕ vasodilation → may induce a prerenal azotemic state
  - avoid in pt's w/ already ↓ GFR or low flow volume states (CHF)
- also ↓ renin release → ↑ hyperkalemia (esp. in pt's w/ hyporeninemic hypoaldosteronism)
- also avoid in prerenal stress states (Ex.) CHF or volume contraction) → in these pt's renin-angiotensin system is already activated for compensation → NSAID-induced ↓ renin release will lead to decompensation quickly

Chronic IV Drug Use

- Ricks:
  1. Acute Bacterial Endocarditis
     - causes focal or progressive GN via IC deposition
  2. septic Embolization
     - causes infarcts → hematuria
  3. Chronic/Progressive Focal Sclerosis
  4. Skin-Popping → chronic SQ infx → Amyloidosis

Chronic Kidney Disease (CKD)

- **Definition:**
  1. Kidney damage > 3 months (w/ or w/out a ↓ GFR) w/ pathological abnorms. or markers of kidney damage

     OR

  2. A GFR < 60 mL/min × > 3 months (w/ or w/out kidney damage)

- **Diagnostics:**
  - A) need to determine the original cause/insult
  - B) after ~75% of baseline nephrons are lost → remaining 25% are unable to maintain work
    - ↓
    - 2nd-ary hyperperfusion
    - Hypertrophy
    - ↓
    - Renal function accelerates quickly and progresses to failure quickly
    - (Hence the importance of A)

- **Causes/Hints @ Causes:**
  1. Diabetes (#1 cause)
  2. CHF
  3. Obstructive uropathy
  4. NSAID's
  5. Aminoglycosides → ATN
  6. β-Lactam Antibiotics
  7. Hypercalciuria
  8. Hyperphosphatemia
  9. HTN
  10. UTI's
  11. Lead Nephropathy → μ-cytic anemia, CKD + gout

  → Most are treatable/reversible so quick diagnosis paramount to preserving renal function

- **Systemic Effects:**
  - A) HTN
  - B) Normocytic/Normochromic anemia → ↓ epo levels

(C) Salt-Retention → volume overload

(D) Above 3 may lead to CHF

(E) Restless leg Syndrome / Peripheral Sensory Neuropathy

(F) Bone Disorders:

(1) ↑-Turnover D/O → osteitis Fibrosa Cystica
- ↑ pTH w/ ↑ osteoclast + blast activity

(2) ↓-Turnover D/O → osteomalacia / adynamic osteodystrophy
- prior causes included aluminum toxicity when aluminum used to be used as a phosphate binder
↓ now control hyperphos w/ $Ca^{(2+)}$-containing binders (Ex.) $CaCO_3$ or Ca-Acetate) or Renagel (Sevelamer)
↓ goal: Calcium/Phosphate Product < 55

↓ conversion of 1-$(OH)D_3$ → 1,25-$(OH)_2D_3$ by defective kidneys
plus ↑ serum phos
→ hyperparathyroid bone disease

- also may cause: ↓ glucose tolerance
- ↓ gonadal hormone production
↓ impotence / amenorrhea / infertility
- ↓ T_3 w/ normal TSH

- uremia may cause:
(1) uremic pleural Effusions
(2) uremic pericardial Effusions
(3) Hemorrhagic Pericarditis
(4) Anorexia
(5) ↑ AGap Metabolic Acidosis

- Gout (in CKD):
- exacerbations can still be treated w/ colchicine/NSAID's (colchicine preferred)
↓ must monitor creat while on treatment
- Allopurinol → ↓'s urate production → usually Ok in CKD (not contraindicated)

- Probenecid → ↑'s renal excretion of uric acid makes ↓ ϕ sense in CKD due to the fact that CKD implies a limited renal excretion to begin w/
  - should not be used to treat Gout in pt's w/ CKD

- (CKD) Treatment:
  - (A) slow progression w/ ACEI's/ARB's + ↓-protein diets (diet issue is less proven)
    - ACEI/ARB's → ↓ intraglomerular pressure
      - also suppresses angiotensin II which normally activates TNF-β to stimulate fibrosis
  - (B) Treat underlying Anemia (if normocytic/normochromic)
    - responds well to recombinant epo (Darbepoetin)
    - prior to starting tx → ✓ Fe stores and replete to normal levels

- Hemodialysis:
  - start w/ uremic symptoms and/or CrCl < 15 mL/min
  - start plans for HD earlier
  - forearm AV fistula lasts longest
  - Common Problems:
    - (A) Most common cause of death → CV disease
    - (B) #2 most common cause of death → infection
    - (C) Most common cause of admission → thrombosis or infection of the HD site
    - (D) Anemia
    - (E) ↑ Triglycerides / ↓ HDL
    - (F) ↑ AGap Metabolic Acidosis w/ a resp. alkalosis just after HD
    - (G) Metabolic Bone Dis.
      - either 2nd-ary hyperparathyroidism or vit. D-resistant osteomalacia (low-turnover renal osteodystrophy)

- HD does not cause vit. D or calcium loss

(4) Nutritional wasting
- may require supplementation (esp. folate / Fe)

- Continuous Ambulatory Peritoneal Dialysis (CAPD):
  - does not require a fistula
  - less CV strain (esp. heart)
  - the pt. infuses 2-3 L of hypertonic dextrose into their peritoneal cavity → gravity then subsequently drains it
  - 4-6 x QDay
  - Complications: (1) Peritonitis (usually skin flora → Gram (+)'s → staph epi or aureus OR then most common after Gram(+) skin flora are Gram(-)'s)
    - usually tx w/ outpt. antibiotics intraperitoneally
    (2) ↑ Protein Losses (~12 g / day)
    (3) ↑ water-soluble vit. Losses (esp. folate)

- ↓ GFR leads to re-dosing / frequency of certain drugs
  (Ex.) Vancomycin → w/ GFR <10% vanco doses can be streteled to Q7days sometimes

- Renal Transplant:
  - if transplant pt. presents w/ acute deterioration of function (w/in week of transplant):
    (A) ✓ cyclosporine / tacrolimus levels
    (B) ✓ renal u/s to r/o obstruction
    if both ok then go to C
    (C) Renal biopsy
  - Cyclosporine:
    - works via ↓ T-cell proliferation (but not function)
    - ∅ BM effects
    - side Effx: (1) Tremors
      (2) Nephrotoxicity

③ Hepatotoxicity
④ CNS-toxicity
⑤ HTN
⑥ oral Gum Hypertrophy

- metabolized by P-450 system
- Blood levels ↑'d by:
  - (A) Erythromycin
  - (B) Ketoconazole
  - (C) Diltiazem
- Levels ↓'d by:
  - (A) Phenytoin
  - (B) Carbamazepine
  - (C) Rifampin
  - (D) Phenobarbital

- Tacrolimus:
  - same MOA/profile as cyclosporine
  - induces diabetes
- Azathioprine: (Imuran)
  - has BM toxic effects (esp. leukopenia)
  - Allopurinol will ↑ levels
  - rarely used in modern medicine
- Mycophenolate Mofetil (MMF/ Cellcept):
  - newer agent
  - similar to Azathioprine but w/:
    - (A) Less BM toxicity
    - (B) ↑'d GI side effex
- any long-term immunosuppressive therapy → ↑'d risk of neoplasia
- Common complications:
  - (A) UTI's
  - (B) Pneumonia
  - (C) sepsis

  → most common post-transplant infex.
  - (D) CV Effex → most common cause of death

(E) CMV
(F) HSV → Acyclovir prophylaxis used
(G) PCP → Bactrim prophylaxis used
(H) Cataracts
(I) Aseptic Femoral Head Necrosis
(J) ↑-risk of post-transfusion hepatitis

-Common Recurring Diseases Post-Transplant:
1. RPGN
2. Mesangial Proliferative Dis. (IgA / Berger's Disease)
3. Membranoproliferative GN (only ~1/3 pt's will lose kidney through)
4. Idiopathic Focal Segmental Sclerosis

-Post-Infex GN + interstitial nephritis → will not recur

-both HD / CAPD / Renal transplant will reverse:
(A) Platelet Dysfunction
(B) Renal Osteodystrophy
(C) Sensory Neuropathy

-only Renal transplant will reverse:
(A) small-vessel calcifications
(B) Motor Neuropathy

Hereditary Diseases

1. Alport Syndrome
-aka Hereditary Nephritis
- either X-Linked or autosomal dominant w/ variable expression
- result of a connective tissue D/O (Type IV collagen) affex basement membranes (same target as Goodpasture anti-GBM Ag's)
-also affex cochlea (asso. w/ deafness) + lens
- Female X-Linked carriers → μ-scopic hematuria only
- Males affected → renal failure before 50 y.o.

- consider the Dx in pt's w/ persistent µ-scopic hematuria (onset @ birth) that worsens after an infection
  - include in diff. Dx w/ post-infectious GN and IgA nephropathy
- also consider Dx in female w/ µ-scopic hematuria whose FH is (+) for males dying young w/ renal issues
- Dx: via renal biopsy

(5) Polycystic Kidney Disease:
- autosomal dominant form → most common genetic dis. of the kidney
- assoc. w/ short arm of chrom. 16 mutation → suggests a tendency for the disease (↘ polycysteine ½)
- assoc. w/ renal/hepatic/pancreatic cysts and recurrent hematuria
- onset typically around age 20
- Symptoms/Course:
  1. Progressive Renal Failure
  2. HTN
  3. Flank Pain
- Assoc.:
  1. Hepatic cysts → rarely cause dysfunction
  2. Cerebral Aneurysms (rare ~1-5%) → Berry Aneurysm
     - no screening needed unless (+) FH of aneurysms or symptoms
  3. Diverticulitis
- Dx:
  - via imaging
- if pt w/ UTI/pyelonephritis → use lipid-soluble antibiotics → better penetration
  - Quinolones
  - Trimethoprim
  - Erythromycin
  - Chloramphenicol
  - Tetracycline
  - Clindamycin

③ Medullary Disease:

-2 main types:

Ⓐ Medullary Sponge Disease:

-dx'd via IVP → calcifications in renal pyramids

-rarely clinically significant → usually incidental

-assoc. w/: - ↑ PTH (Hyperparathyroidism)

- Hypercalciuria

- Renal calculi

Ⓑ Medullary Cystic Disease:

-can progress to renal failure

- presents w/ a normal UA w/out proteinuria in pt's usually <20 y.o.

Renal Cysts

- very common → ~50% >50 y.o. have cysts

- Benign if:

Ⓐ Asymptomatic

Ⓑ simple by U/S → well-defined margins, ϕ echo-densities or compressed surrounding tissues

-if not benign → consider PKD or surgical exploration to eval. for neoplasia / malignancy

Pregnancy w/ Renal Disease

① Pregnancy-Induced HTN (Pre-eclampsia):

-suspect w/:

-new-onset HTN

-new-onset proteinuria

-rapid wt. gain

-edema in 3rd trimester

-pt's have diffuse vasospasm, low-grade DIC w/ ↓plat's and ↓ anti-thrombin III

good dx test

-may develop HELLP syndrome (→ Hemolytic Anemia, Elevated Liver Functions + Low Platelets)

-Tx: Delivery ASAP

② SLE / Lupus Nephritis:
- if dis. in remission → ~90% chance of successful pregnancy
- if SLE flare during pregnancy → 1/4 fetuses abort (usually via thrombotic events → lupus anti-coag Ab)
- screen all pregnant lupus pt's for:
  - (A) Lupus Anti-Coagulant → ↑ risk of spontaneous abortion
  - (B) SSB Antibodies → ↑ risk for neonatal H Block

③ CKD:
- creat <2, ϕ HTN → ϕ ↑'d risk of abortion
  → ϕ ↑'d rate of renal dis. progression
  → ↑'d risk of pre-eclampsia

④ Post-Transplant:
- usually good outcomes if pt. is stable

Renal Stones

- ~2/3 of stones are calcium stones (Ca-Phos or Ca-Oxalate)
- other 1/3 are struvite or urate
  - struvite stones → phosphate w/ mixture of cations (Ca^{2+} / NH_4^+ / Mg^{2+})

-Initial w/u:
1. Stone Analysis
2. serum Ca^{2+} → to eval. for hyperparathyroidism
3. serum electrolytes / urine electrolytes → to eval. for RTA (Type I - Distal)

④ UA - C+S

⑤ Renal Imaging → CT (Toc) or IVP

-if stones are recurrent:

- ✓ urine volume
- ✓ urine urea
- ✓ urine cystine
- ✓ urine uric acid
- ✓ urine Ca^{2+}
- ✓ urine citrate
- ✓ urine Na^{+}
- ✓ urine creat.

-if signs of acute ureteral obstruction w/ a concurrent infec. → hospitalize pt. (↑'d risk of sepsis/papillary necrosis)

-Stone Inhibitors:

① Citrate
② Magnesium
③ Pyrophosphate

-Stone Inducers:

① Concentrated urine
② ↑ Excretion of stone-forming products
③ Hypercalciuria
④ Uric Acid
⑤ Hypocitraturia
⑥ Hyperoxaluria
⑦ Medullary Sponge Disease

-citrate chelates Ca^{2+} → prevents Ca^{2+} stones

-acidosis → induces hypocitraturia (<250 mg/day) + leaches calcium from bones → hypercalciuria →

6/15/2007

-Hypercalciuria: Ca^{2+}-stone-inducer

-Causes: (A) Hypervitaminosis D
(A) Distal RTA (Type I)
(C) Sarcoidosis
(D) Hyperparathyroidism

- ~50% of cases are idiopathic → usually due to ↑'d gut absorption of Ca^{2+} due to ↑'d renal production of $1,25(OH)_2-D_3$ or due to Ca^{2+} leak @ the renal level

Calcium Metabolism

Total Body Ca^{2+}: ~1.5 kg
Dietary Daily Ca^{2+}: ~1 g @ Day
80% actively reabsorbed → upper small bowel
20% lower small bowel
50%/50% → bound : ionized ratio

① Ca^{2+} - Phosphate Stones

- more common w/ RTA Type I - Distal RTA due to the hypercalciuria + primary hyperparathyroidism and acetazolamide
- Distal RTA (Type I) → alkaline urine (due to a distal defect in H^+ secretion) → ↑'d precipitation of $CaPO_4$
  - metabolic acidosis → predisposes to stone formation due to buffering of Ca^{2+} out of bones

② Ca^{2+} - oxalate stones → bipyramidal stones / envelope crystals

- assoc. w/ ↑ urinary oxalate, males 3:1
- vit. C + ethylene glycol → oxalate precursors → can lead to stones if taken in large amounts (large amt of ethylene glycol needed though so pt's will die from ingestion prior to stone formation)
- steatorrhea → also causes oxaluria
  - free FAcids in bowel chelate Ca^{2+} → oxalate gets absorbed and secreted in urine
- uricosuria also predisposes to oxalate stones → urate crystal acts as a nidus for stone formation
- Tx: (for both Ca^{2+}-oxalate + Ca^{2+}-Phosphate stones)
  - fluids
  - thiazide diuretics → ↓'s urinary Ca^{2+}
  - ↓ dietary protein + Na^+
  - give K^+-citrate
  - treat ↑'d uric acid
  - DO NOT ↓ calcium intake → ↑'s oxaluria

③ Struvite Stones: (Ca^{2+} / NH_4^+ / Mg^{2+} / Phos) →  → coffin-lid

- can cause staghorn calculi → think infection
  - NH_4^+ required for these stones is produced when urease breaks down urea
    - urease produced by Proteus, Pseudomonas, Yeast + staph (PPYS)

- Tx: (A) Stone removals → if all stones unable to be removed ↓ indefinite Abx
(B) Acidification of the urine
(C) Abx

(4) Cystine Stones:
- hexagonal crystals in urine → ⬡
- cystine → very insoluble
  - under-saturated in normal urine
- Homozygotes for cystinuria (AR-inheritance) → familial secrete large amnts of cystine in urine (~40 mg/day)
- Tx: (A) Fluids → rest of life
(B) Alkalinize the urine → keeps urine [cystine] normal ↑ prevents crystallization
(C) Penicillamine → forms soluble complexes w/ cystine
  - not greatly tolerated

(5) Urate Stones:
- usually seen w/ chronic acidic urine / ↑ urate in serum, pinkish-colored sediment, plates
- other causes:
  - (A) Myeloproliferative syndromes
  - (B) Chemotherapy
  - (C) Lesch-Nyhan Syndrome
  - → all can cause hyperuricosuria even w/ a normal urine pH
- Tx:
  - (A) Allopurinol (B)/(C) urinary alkalinization
  - avoid alkalinization of urine if hypercalciuria present too

(6) Phosphate Stones:
- brownish-color
- assoc. w/ alkaline urine

Acute Ureteral Obstruction

(1) must allow passage if possible
(2) cystoscopy to remove
(3) Percutaneous c/s Lithotripsy or Extracorporeal Shock-Wave Lithotripsy (ESWL)

Anemias of Kidney Disease

(1) CKD:

-↓'d erythropoietin → normocytic / normochromic
-target Hgb on epo tx is 11-12

② Good pasture's Syndrome:
- microcytic / hypochromic anemia
↓
chronic blood loss in lungs

③ Malignant HTN:
-may cause a microangiopathic hemolytic anemia + thrombocytopenia

④ Sickle Cell Disease:
-assoc. w/ small vessel occlusions
-↑'d frequency of hematuria
-also assoc. w/ papillary necrosis

Poisonings

① Aspirin Poisoning:
-assoc. w/ mixed resp. alkalosis + metabolic acidosis

② $Li^{\oplus}$ Poisoning:
- ↓ AGap 2nd-ary to ↑'d unmeasured cations

③ Bromide Poisoning:
-assoc. w/ marked hyperchloremia + ↓'d AGap 2nd-ary to pseudo hyperchloremia

Other Diagnoses

① Pregnancy:
-also assoc. w/ a resp. alkalosis

② Cushing's Syndrome:
-assoc. w/ $Cl^{\ominus}$-resistant metabolic alkalosis (urine $Cl^{\ominus}$ > 30 mEq/L)

6/23/2007

Small-vessel vasculitides

① Wegener's
② Microscopic Polyangiitis (not granulomatous, may affect lungs/kidneys)
③ Churg-Strauss
-similar to asthma → eosinophilic
-RFailure less likely than ①'s ①+② above

- Dx: ① ✓ ANCA's
② ✓ anti-proteinase III
③ ✓ myeloperoxidase

~~Goodpasture's~~ Granulomatosis

Tx: Ⓐ steroids (prednisone)
-pulse-dose
Ⓑ Cyclophosphamide (Cytoxan)
-pulse-dose x 3 months (until remission)
then Δ to Azathioprine (Imuran)
↓
to prevent relapse
-fertility issues, hemorrhagic cystitis + BM suppression common side effex
Ⓒ Plasmapheresis

Wegener's Granulomatosis

- pauci-immune crescentic necrotizing GN
↓
proliferative
RPGN → rapidly ↑'ing creat w/ ↓'ing GFR
- usually presents in older adolescents / young adults
- Symptoms: ① Renal Insufficiency
② Affects lungs → alveolar hemorrhages + pulm. nodules @ varying degrees of maturation
③ Sinus congestion
④ Skin/Eyes → Uveitis / Episcleritis
⑤ Neuritis (Poly or mono)
- if untx'd → death w/in 1 year
- Sediment:
- RBC casts
- Telescope urine sediment → proliferative RBC casts
↓
↑ likelihood of renal vasculitis

Renal Vein Thrombosis

- assoc. w/ RCC and PE's ← hypercoagulability
- large proteinuria (massive nephrosis)
↳ esp. AT III

Henoch-Schonlein Purpura (HSP)

- typically younger pt's
- palpable purpura (gravity-driven)
- discolored urine (brownish)
- arthritis-type complaints
- assoc. w/ GI bleeds
- IgA deposits

Myeloma Kidney

- elderly pt's
- bone pains
- anemia
- Renal Involvement:
  1. RTA (Type II) Proximal
  2. Fanconi's Syndrome
  3. Amyloidosis
  4. ARF
- Sediment → Cast nephropathy → eosinophilic casts

7/3/2001

Hemolytic Uremic Syndrome (HUS)

- usually seen in peds pt's
- char by:
  1. Anemia
  2. uremia
  3. Hemolysis
- Peripheral Smear:
  - A. Helmet cells
  - B. Schistocytes
- Assoc. w/:
  1. E. Coli 0157:H7 verotoxin
  2. chemo drugs
  3. preeclampsia / Eclampsia

Urinalysis

- If ⊕ dipstick for proteinuria → ✓ urine pH → if alkaline then likely not as significant as dipstick indicates (Ex. 3⊕ → 1⊕)

- RBC's:
  - normal 0-3/hpf → 100,000 - 200,000 @ Day
  - fractured RBC's → Glomerular Dis.

- Casts:
  1. Dirty Brown Granular Casts:
     - ATN → Tamhorsphil protein
  2. RBC Casts:
     - GN
  3. Fatty Casts:
     - brownish-colored @ low power
     - Assoc. w/ nephrotic states
  4. Broad Casts:
     - Twice size of normal casts
     - Assoc. w/ hydronephrosis or CKD
  5. Telescoping Sediment:
     - Nephritic (RBC casts) + Nephrotic (Fatty) = chronicity
     - Crescentic GN frequency vasculitic