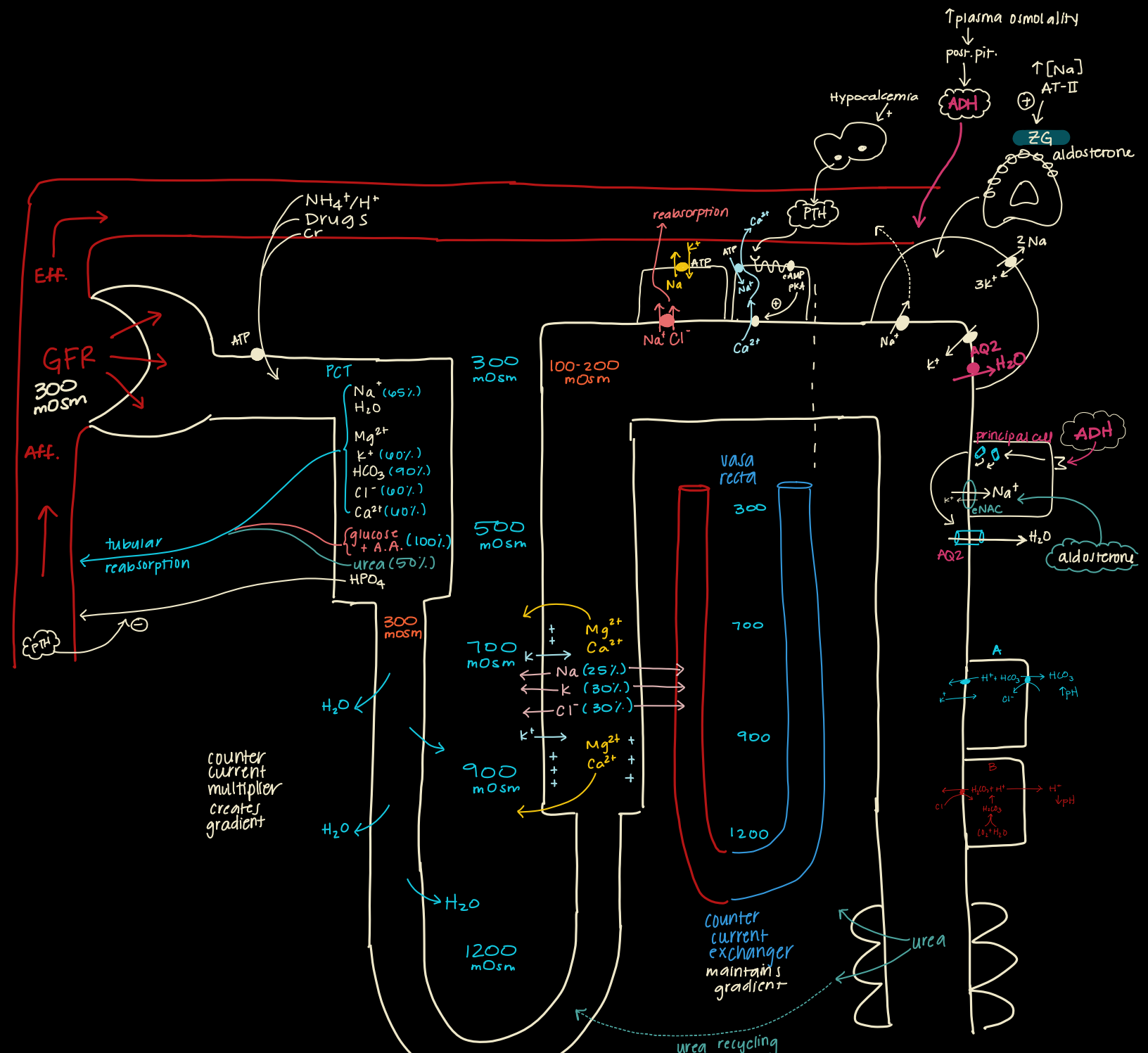
LO1 HY

Table 1

Urine Component	False Positive	False Negative
Leukocytes	Contamination, trichomonas, drugs/foods coloring urine red, low urine specific gravity (increases cell lysis)	Recent antibiotic therapy, glycosuria, proteinuria, elevated urine specific gravity (impedes cell lysis), low bacteria urine count, high vitamin C, oxidizing drugs (cephalexin, nitrofurantoin, gentamicin, tetracycline)
Nitrites	Contamination, dipstick exposure to air, phenazopyridine	Drugs/foods coloring urine red, elevated urine specific gravity, high urobilinogen, pH < 6, high vitamin C, specific bacteria (S. saprophyticus, Pseudomonas, Acinetobacter, and enterococci (at least most))
Protein	Alkaline/concentrated urine, phenazopyridine	Acidic/dilute urine, protein that is not albumin (Bence Jones in multiple myeloma)
Blood	Dehydration, exercise, menstrual blood, myoglobinuria	Captopril, acidic urine, high vitamin C, elevated urine specific gravity
Glucose	Ketones, levodopa, bleach, hydrogen peroxide	Elevated urine specific gravity, uric acid, high vitamin C
Ketones	Acidic urine, elevated urine specific gravity, several drug metabolites, heavily pigmented urine	Delayed urine analysis, predominance of beta-hydroxybutyric acid



A 63-year-old male has GFR 15% of normal. What is the most likely effect of his renal function on calcium homeostasis?

A. Hypercalcemia, high PTH and negative Ca++ balance
B. Hypercalcemia, low PTH and positive Ca+ balance
✓ C. Hypocalcemia, high PTH and negative Ca++ balance
D. Hypocalcemia, low PTH and positive Ca+ balance

pH = 7.15 ↓ Acidosis
PCO_2 = 30 mmHg ↓
$[HCO_3^-]$ = 10 ↓ Metabolic
$[Cl^-]$ = 100
$[Na^+]$ = 145

145 − [110] = 35 ↑
High Anion Gap
∴ excess metabolic acid
↓
could be xs production (Ketoacidosis) OR renal failure to excrete

if it were NAGMA, it would be due to bicarb LOSS, & replacement w/ chloride
= Hyperchloremic NAGMA

↓
★Urine Anion Gap★ (limited by type of acid)
to measure amount of acid excreted
$UAG = [Na^+] + [K^+] - [Cl^-]$

if there is net excretion of acid, UAG is negative.

are the kidneys properly compensating?
75 + 50 − 150
125 − 150 = ⊖ ✓

75 + 50 − 100
125 − 100 = ⊕ NO

pH 7.15 ↓
HCO_3 ↓ Metab acidosis
PCO_2 ↑↑ Resp. acidosis
PO_2 ↓

7.32 ↓ Acidosis
HCO_3 ↓ 22-26 Metabolic
CO_2 ↓ 35-45
PAG: 140 − 115 → High AG = excess acid in system
25 ↑

Normal pH 7.36 (↓?)
HCO_3^- ↑
PCO_2 ↑↑ Respiratory acidosis

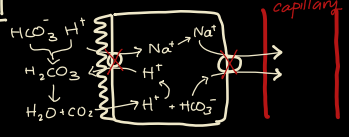
pH 7.32 ↓
HCO_3 ↓ Metab. acidosis
PCO_2 ↓
low GFR or RTA ← NAGMA
140 − (130) = 10

LO8 HY:

RTA = ↑acidity in blood bc kidneys can't get rid of protons or reabsorb bicarb = NAGMA (Hyperchloremia)

Renal Tubular Acidosis causes frickin ACIDOSIS

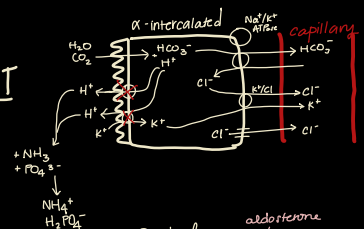
PCT



Type II: cant reabsorb bicarb
distal intercalated cells intact & acidify urine
- Fanconi syndrome
  - phosphaturia
  - glucoturia
  - proteinurea
  caused by Tetracyclines
- Hypokalemia

Type III: PCT & PCT carbonic anhydrase deficiency

DCT

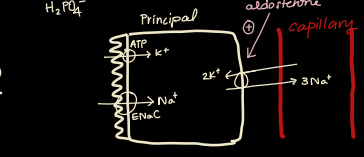


Type I: cant acidify urine
cant secrete H^+
- Lithium / Ampho B
- defect in H^+ ATPase
  H^+/K^+ ATPase
  HCO_3^-/Cl^- EX
- alkaline urine
  = calculia

Hx of RA or kidney stones

If you suspect RTA: UAG should be checked
urine Na^+ K^+ - Cl^- should be ⊖ due to metab. acidosis
BUT WILL BE ⊕ IN RTA!

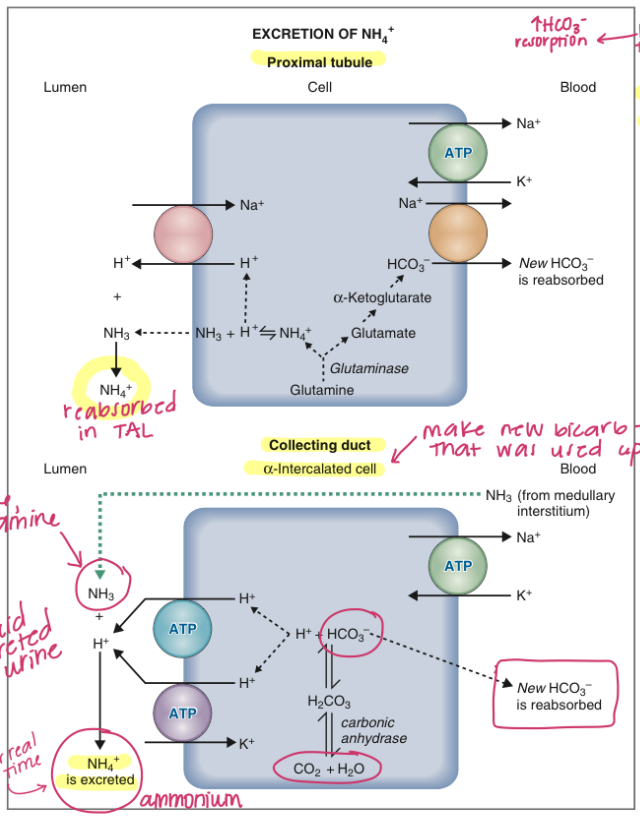
CD



Type IV: aldosterone deficiency
- principle & Intercalated
Ex: Addison's dz
or ENaC mutation
↓ Na^+/K^+ ATPase
↓ H^+ ATPase @ intercalated
= Hyperkalemia
acidemia
↓ ammonium in urine

Ex: Hypovolemia
↓ Na^+ in cell = ↓ reabsorption
- SLE
- Lithium

Non-Volatile Acids
↓
↓HCO_3^- in plasma
↓ prox tubule ↑HCO_3^- resorption
↓ collecting duct ↑H^+ excretion ↑HCO_3^- generation
Buffering titratable acids NH_4^+
setting of acidosis



make new bicarb to replenish any that was used up buffering fixed acid.

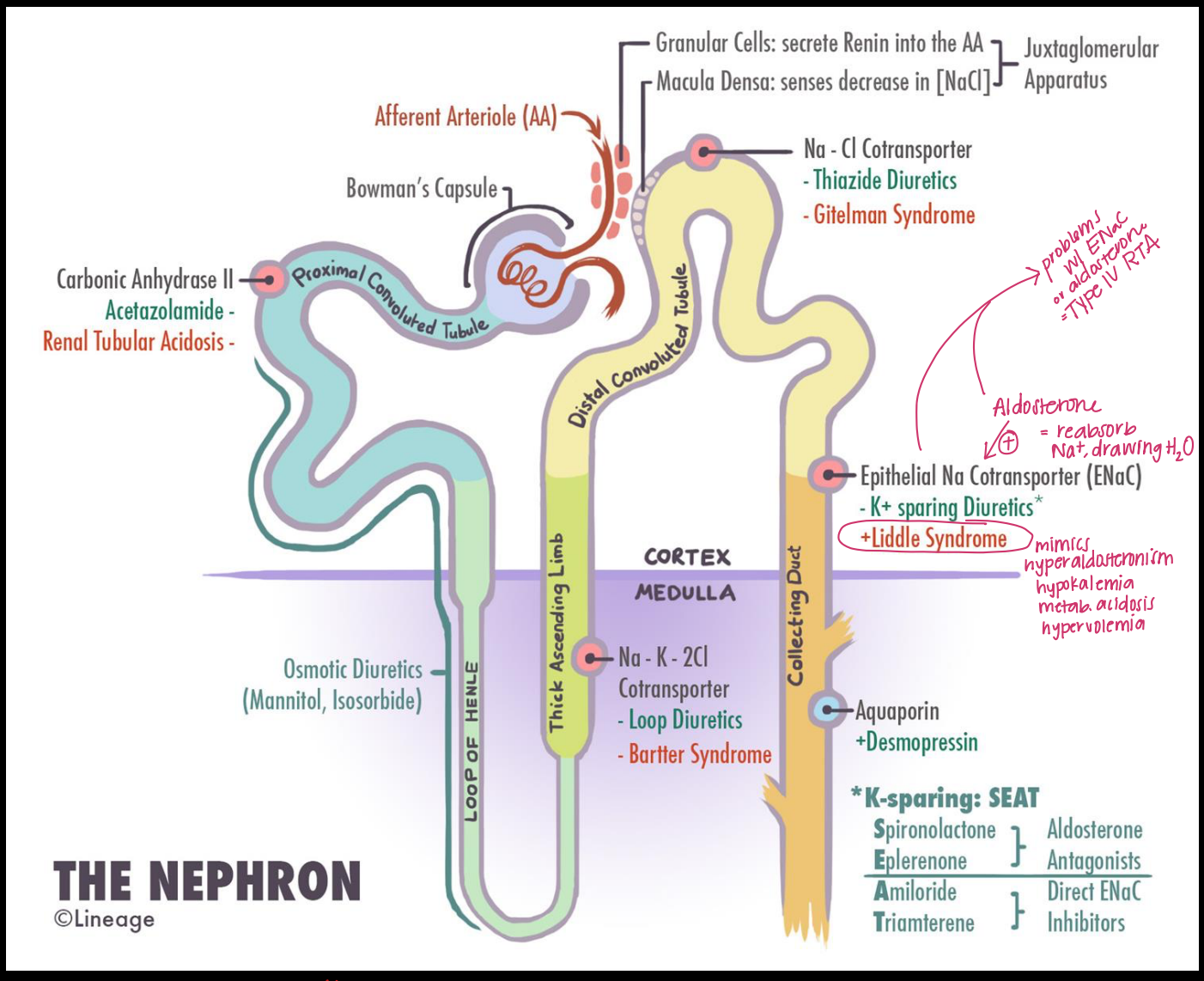
NH_3 Ammonia = adaptable made from glutamine

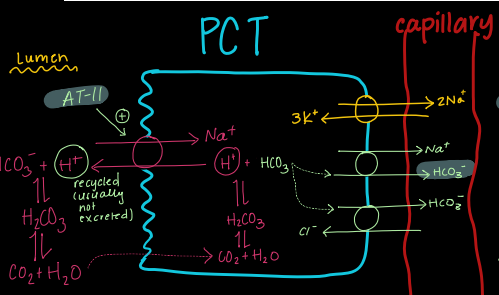
acid excreted in urine

could damage nephron... ∴ we use titratable acids & ammonia

for real this time

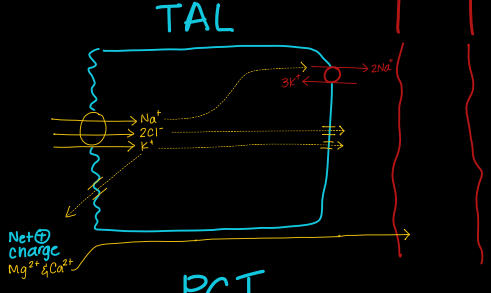
Figure 7–8 **Mechanism of excretion of H^+ as NH_4^+.** In the proximal tubule, NH_3 is produced from glutamine in the renal cells. H^+ is secreted by Na^+-H^+ exchanger and NH_3 diffuses into the lumen. NH_4^+ is reabsorbed by Na^+-K^+-$2Cl^-$ cotransporter in the TALH and deposited in the medullary interstitial fluid (not shown). In the collecting ducts, NH_3 diffuses from the medullary interstitium into the lumen, combines with secreted H^+ in the lumen, and is excreted as NH_4^+. ATP, Adenosine triphosphate. TALH, thick ascending limb of loop of Henle.

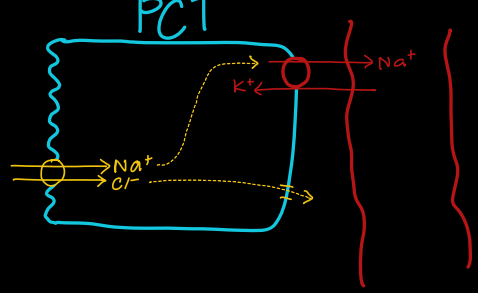




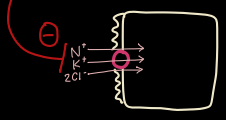
Na+/H+ exchanger (NHE3)
★ under influence of AT-II
↑ Na+/HCO3- reabsorbed
∴ ECF volume contraction stimulates alkalosis
→ contraction alkalosis also caused by thiazide & loop diuretics

★ upregulated during acidemia
★ aldosterone antagonist = causes acidosis by blocking H+-ATPase & NaH Exchanger



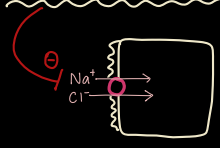


Bartter syndrome: defective NKCC channel @ TAL



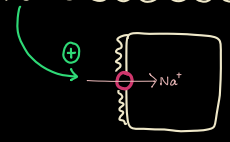
∴ loss of Cl^-, Na^+, & K^+ in urine
→ Naturesis → Hypovolemia → ↑aldosterone → HYPOKALEMIA & METABOLIC ALKALOSIS + hypocalcemia?

Gitelman Syndrome: impaired function of Na^+/Cl^- cotransporter @ DCT
(mimics thiazide diuretic)



∴ mild naturesis & RAAS activation ∴ Normal BP
↓K^+ ↓Mg^{2+} ↑Ca^{2+} → METABOLIC ALKALOSIS

Liddle syndrome: gain of function mutation of ENaC



∴ increased reuptake of Na^+ / H_2O = pseudoaldosteronism [↓aldosterone ↓Renin] ⊖ feedback
→ HTN + Hypokalemia + metab. ALK

For Respiratory Acidosis:

↑HCO_3 1/10↑CO_2

if pCO_2 = 62

40 → 62 ↑ of 20

∴ expect ↑ of 2 of HCO_3^-

26 + 2 = 28

For Chronic Resp. Acidosis:

like COPD/CHF

Expected $\Delta HCO_3^- = \frac{3.5(\Delta pCO_2)}{10}$

Before Exam: Re-read the last 5 slides of tutoring powerpoints

free water loss
- burns, hyperglycemia, ventilated pts

SG: **Osmolality**: "amount of Na^+ in water" serum osmolality = $2 \times [Na^+]$ the body maintains osmolality via **ADH** (+) acting on kidney → AQ2 during ★ hypovolemia (stronger stimulus than osm)

tonicity: in reference to fluid

Hypotonic	fluid shifts into cells (ECF → ICF)
Isotonic	fluid stays @ ECF
Hypertonic	fluid shifts out of cells (ICF → ECF)

urea & glucose usually diffuse / are transported BUT @ high concentrations contribute to tonicity → Hyperglycemia = osmotic diuresis

ANION GAP

Serum AG = $Na^+ - Cl^- - HCO_3^-$
represents acid in system that is being added (rather than loss in HCO_3^-)

★ **HAGMA** ∴ AG >12 means acid is being added
MUDPILES

- **Lactic Acidosis**: L-form, look for signs of **SEPSIS**, shock, or metformin use (?) → order lactate level

- **DKA**: ↑Acetoacetic Acid & β-hydroxybutyrate (not measured on dipstick)
young pt w/ Type I DM → Hyperosmolar state → brain swelling & osmotic diuresis = volume DEPLETION
↳ fruity breath, polydipsia
WBOT
★ As you tx w/ fluids, can transform to NAGMA so → tx w/ LR
★ Hyperglycemia does NOT cause DKA! Insulin deficiency DOES.
↳ lipolysis, ↑FFA, ↑ketogenesis, ↓alkali reserve

- **Toxic alcohol ingestion**: HAGMA + osmolar gap ↑ SOG
WBOT
metnanol: MOONSHINE + BLINDNESS
ethylene glycol: antifreeze + Ca OXALATE CRYSTALS ⊠
propylene glycol: IV medications (propofol)
ethanol: (toxic amounts) but can also be used to TREAT metnanol & ethylene glycol toxicity
★ Fomepizole (⊖) inhibits alcohol dehydrogenase

- **Alcoholic ketoacidosis**: poor nutrition + alcohol abuse = volume depletion from N/V
characterized by ethanol induced hypoglycemia & lactic acidosis ↑NADH
↳ general malnutrition deficiency: ↓K^+, ↓Mg^{2+}, ↓PO_4^{2-}

★ **NAGMA**: loss of bicarb was compensated for by RISE IN CHLORIDE
HARDPASS
★ check serum Cl^- → fills gap
★ check urine anion gap: UAG = (urine Na^+ + urine K^+) − urine Cl^-

URINE ANION GAP

UAG = NH_4^+ excretion by kidneys measurement → used in NAGMA
★ WBOT
(+) kidneys not secreting NH_4^+ = RTA I & IV
(⊖) kidneys are secreting NH_4^+ = GI or RTA II

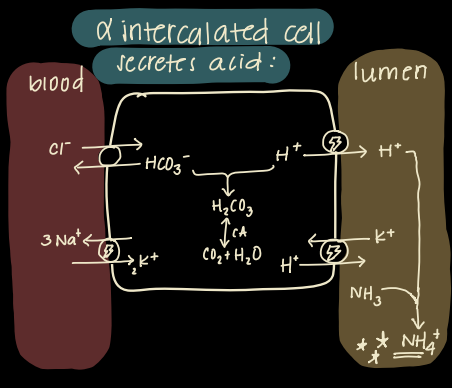
RTA	I	II	IV
Where	DCT	PCT	DCT/CD
serum K^+	↓	↓	↑
urine pH	↑	↓	↓

RTA

★ **Type I** = can't acidify urine: α-intercalated cell @ DCT not working
↑pH of urine
Hypo kalemia bc defective H^+/K^+ ATPase & H^+-ATPase
(+) UAG bc kidney NOT secreting NH_4^+
★ sickle cell & autoimmune dz amphotericin B ★

★ **Type II** = impaired bicarb reabsorption @ PCT
↓pH of urine bc α intercalated cells intact
Hypokalemia bc
(⊖) UAG bc kidney can secrete NH_4^+ (problem w/ bicarb)
★ Fanconi & topiramate ★

★ **Type IV** = aldosterone problem
acidic urine
hyperkalemia
(+) UAG
@ CD
★ Diabetic Nephropathy ACE-I/ARB/NSAIDs Aldosterone inhibitors TMP|SMX ★



ACID/BASE compensations vs secondary pathophysiology:

★ Metabolic Acidosis:

1. AG
2. Winters formula: checks if respiratory compensation was appropriate $pCO_2 = 1.5[HCO_3^-] + 8 \pm 2$
   - if CO_2 is lower than expected = 2° Resp Alkalosis
   - if CO_2 is higher than expected = 2° Resp Acidosis
3. if HAGMA → ΔΔ ratio determines secondary metabolic disorder

DELTA DELTA

$$\Delta\Delta \text{ ratio} = \frac{AG - 12}{24 - 12}$$

- <1 = NAGMA + HAGMA
- 1-2 = HAGMA only
- >2 = HAGMA + metab. alk

4. if NAGMA → UAG
   - ⊕ = kidney problem (RTA I or II)
   - ⊖ = diarrhea or RTA II

★ Metabolic Alkalosis

post-hypercapnea

check for compensation by $CO_2 = [0.7 \times \Delta HCO_3^-] + 40 \pm 2$

★ [if lower than expected → Resp. Alkalosis; if higher than expected → Resp. Acidosis]

metab. alkalosis w/ high urinary kt = gitteman or barrter syndrome + liddle

★ WBOT ★ caused by diuretics → volume depletion → ↑aldosterone → ★★ Potassium & chloride depletion

GENERATION & MAINTENANCE

loss of acid — loss of volume

★ Respiratory Acidosis

check for compensation by comparing $\Delta HCO_3 : \Delta pCO_2$

Kind of important...

- <1:10 : 2° metab acidosis
- 1:10 : acute resp. acidosis
- 1:2 : chronic resp. acidosis
- <1:2 : 2° metab alkalosis

caused by hypoventilation, opioids!! CNS depression, MG, etc.

★ Respiratory Alkalosis

caused by hyperventilation, hypoxia from PE, anxiety, vent settings too high

---

★ sCr: depends on diet, muscle mass, pregnancy, etc. but measures GFR

★ BUN/Cr: basis of diagnosis of ACUTE kidney injury

★ WBOT

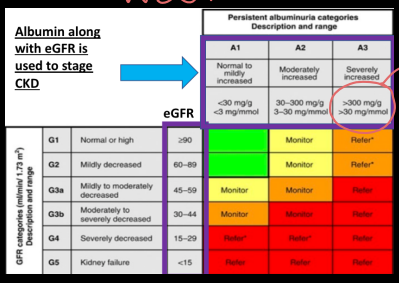
- ≥20: pre-renal → HYPOTENSION → ↓GFR = ↑BUN, Na^+, H_2O reabsorption
- <10: Renal → tubule necrosis or ischemia → ↓GFR due to clog ∴ BUN resorption impaired
- 10-15: Post-Renal → kidney stones

↑BUN
- → Azotemia = ↑nitrogen in blood ∴ kidney damage ★Hypotension!!
- → Uremia = urea in blood ∴ more severe kidney damage

BUN/Cr ↑0.3 Cr from baseline = acute kidney injury

★ WBOT ★

★ eGFR = staging chronic kidney dz
- < 60 = monitor
- < 30 = refer
- use w/ Proteinuria
  - > 30 = monitor
  - > 300 = refer



→ Nephrotic ★★ Syndrome
= podocyte disruption
(referring to protein)

★ WBC = pyelonephritis
+ CVA tenderness → sepsis

★ Hematuria > 3 RBC = abnormal
= Acanthocytes (dysmorphic RBC) → Nephritic syndrome = GLOMERULONEPHRITIS
(autoimmune, SLE, or post strep)

URINALYSIS scenarios:

2+ Blood, No RBC = Rhabdomyolysis
Nitrite +, 3+ WBC = UTI/pyelo
3+ Blood w/ isomorphic RBC ± crystals & flank pain = stone = lower kidney dysfunction
Oxalate crystals ☒ = ethylene glycol

EABV: amount of fluid that's perfusing
★ strongest stimulator of RAAS = Hypovolemia / ↓EBV → triggers ADH no matter what
∴ in CHF & cirrhosis ↑TBW → fluid overload (maybe hyponat.)
↑Renin = ↑AT-II = ↑Aldosterone
- efferent arteriole constriction ↑GFR
- ↑Na+ reabsorption = HTN = Hypokalemia = metabolic alkalosis?

★ Aldosterone ↑ENaC, ↑ROMK, ↑Na^+/K^+ ATPase ↑H^+ ATPase

Hypoaldosteronism vs Hyperaldosteronism
- Hypoaldosteronism = Hypotension, Hyperkalemia, Hyponatremia, salt cravings = Hypotonic contraction = metabolic acidosis!
- Hyperaldosteronism = HTN, hypervolemia, hypokalemia = Hypertonic expansion, Metab alkalosis

HOW DO YOU EVALUATE FOR HYPER/HYPOALDOSTERONISM on clinical basis

↓VOLUME STATUS: impacts ↑ADH & turns on RAAS system

★ SIADH:

★ Diabetes Insipidus:
- central: No ADH secretion = Pituitary tumor tx: desmopressin
- nephrogenic: No kidney response to ADH = lithium (bipolar tx) tx: thiazides

WBOT

RAAS System

↓NaCl delivery to JG cells
Hypotension / ↓C.O. = ↑SNS β1 stimulation
CHF
→ Renin → AT-II → Aldosterone → ↑Na^+/H_2O Retention
- → constrict efferent arteriole ↑GFR
- → constrict vasculature ↑TPR

★ Electrolyte Abnormalities

Hyponatremia: <135
- ★ volume status → SXS of
  - ★ Hypervolumia: JVD, edema, swollen
  - ★ Hypovolemia: tachycardia, ↓BP, prolong. cap refill

Hypovolemia: dehydration, vomiting, diarrhea, diuretics
Euvolemia: SIADH; NORMAL PE
Hypervolemia: Heart Failure → volume overload
SXS:
- ★ Rapid correction = osmotic demyelination syndrome

Hypernatremia: >145 irritable/coma
Hypovolemia: RENAL causes = loop diuretics; extrarenal = BURNS, SWEATING
Euvolemia: diabetes insipidus
Hypervolemia: Hyperaldosteronism, Cushings
- ★ Rapid Correction = cerebral edema

★ WBOT: cannot correct hypokalemia w/o first correcting hypomagnesemia

Hypokalemia: U-WAVE
caused by: Alkalosis, β agonists, Insulin ← Albuterol, WBOT

Hyperkalemia: PEAKED T-WAVES
caused by: lysis of cells (chemo), Acidosis, β-blockers, Succinylcholine

pseudohyperkalemia: fist clenching

★★ WBOT TREATMENT:
1. IV calcium gluconate TO STABILIZE MYOCARDIUM
2. IV insulin or Albuterol
3. IV loop diuretics

★ Hypocalcemia: U-wave, ↑QT MUSCLE SPASMS (Trousseau, Chvostek)
WBOT CKD = phosphate retention = ↑FGF23 = ↓Vit.D = ↓Ca^{2+} & ↑PTH = phosphate excretion
→ Bone disease & vascular calcification ↑Ca^{2+}

★ Hypercalcemia: wide QRS; stones, bones, groans, & psych. overtones
caused by anything that ↑PTH

pH

<7.35 Acidotic

Guillan Barre, COPD, hypoventilation syndromes, drug overdose (opiates)

↑CO_2 Respiratory

Acute
$\Delta HCO_3 = \frac{\Delta pCO_2}{10}$

Chronic
$\Delta HCO_3 = \frac{3.5\Delta pCO_2}{10}$
#: 40

check for compensation:
- = 1-2 : 10 acute resp. acidosis
- = 3-4 : 10 chronic resp. acidosis
- < 1-2 : 10 2° metab acidosis
- > 3-4 : 10 2° metab. alkalosis

↓HCO_3^- Metabolic

<22

winter's formula:
$pCO_2 = 1.5 \times HCO_3 + 8 \pm 2$

if CO_2 is lower than expected
= Respiratory Alkalosis

if CO_2 is higher than expected
= Respiratory Acidosis

$AG = Na^+ - Cl^- - HCO_3$

NAGMA
- H
- Addisons
- RTA
- Diarrhea
- Pathypocapneic
- Acetazolamide
- Saline
- S (succinylcholine?)

HAGMA
- Methanol → Blindness
- Uremia
- DKA + Metformin toxicity
- Paraldehyde
- Iron tox. & Isoniazid
- Lactic Acidosis
- Ethylene glycol → Ca^{2+} oxalate crystals in urine ☒
- Salicylates = aspirin

$UAG = Na + K - Cl$

(−) GI (Kidney wasting HCO_3) → RTA II, Diarrhea

(+) Kidney (Not secreting NH_4^+) → RTA I ($\downarrow K^+$, $\uparrow$pH urine); RTA IV ($\uparrow K^+$, $\downarrow$pH urine <5.5)

$\Delta\Delta = \frac{AG - 12}{24 - HCO_3}$ = expected HCO_3

- < 1 : HAGMA + NAGMA
- 1-2 : HAGMA only
- > 2 : HAGMA + metab. alkalosis

>7.45 Alkalotic

Thiazide & loop diuretics

↓CO_2 Respiratory

check for compensation:
$\frac{\Delta HCO_3}{\Delta CO_2} \rightarrow$
- = 1-2 : 10 → acute resp. alk
- = 3-4 : 10 → chronic resp. alk
- < 1-2 : 10 → 2° metab. alk
- > 3-4 : 10 → 2° metab. acidosis

↑HCO_3^- Metabolic

$CO_2 = 0.7(\Delta HCO_3) + 40$

① $PCO_2 = 0.7(HCO_3^- - 24) + 40$

② Hypercalcemia?
(9-11) normal
- NO → urine chloride
  - normal → GI → NGT
  - >20 → urinary K^+
    - <30 → laxative abuse
    - >30 → BP
      - ↑ -Hyperald -Hypercortisol
      - ↓ - gitelman - barter - diuretics - liddle's - licorice

pH 7.31 ↓ acid
PCO_2 80 ↑ acid
HCO_3 38 ↑ alk
Resp. acidosis + metabolic alk

= 1-2 : 10
= 3-4 : 10 chronic resp. acidosis
< 1-2 : 10
> 3-4 : 10

$\Delta HCO_3 = 14$ (3.5/10)
$\Delta CO_2 = 40$

	I	II	IV
Where	DCT	PCT	DCT/CD
serum K^+	↓	↓	↑
urine pH	↑	↓	↓
UAG	⊕	⊖	⊕

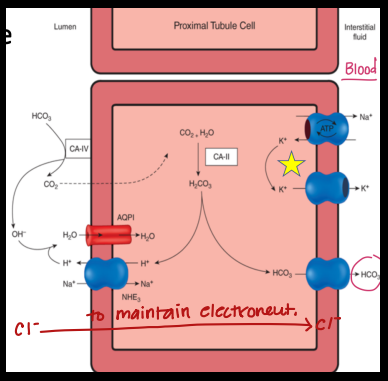
7.33 ↓
CO_2 40 -
HCO_3 18 ↓
Metab acidosis w/ hyperkalemia

louis

L03 ACID/BASE :

How the kidneys reabsorb HCO_3^- : @PCT via NHE_3 (stimulated by AT-II) ⊖ impaired by RTA II

How the kidneys regenerate HCO_3^-



Gitelman vs Barter
= Magnesium levels!