Lec 10 & 11 ♡ Acid / Base

Background

- Renal, Respiratory & buffer system work together to maintain balance of acid / base
- normal pH is 7.2 - 7.4 which mirrors H^+ levels in
  - ↳ narrow range for normal enzymatic function the body
- Volatile acids are removed from body by CO_2 expiration
- non-volatile are organic acids, produced in greater quantity, & eliminated by titration
- narrow pH is maintained by:

Body fluid chemical buffers - 1st line, rapid, temporary
↳ Bicarbinate, ammonium / amonia, proteins, phosphate

Lungs - 2nd line, rapid, volitile only by CO_2 expiration

Kidney - 3rd line, most powerful, slower, non-volatile

Buffer System

- Buffers resist ↑ or ↓ in pH in ICF, ECF, & urine compartments by either accepting H^+ or OH^- or releasing H^+
- Buffer effectiveness depends on concentration of reactant (buffer) & PK & PH of body fluids
  - ↳ most effective when pK of buffer is close to pH of fluid .... ill explain

Bicarbonate

$$H_2O + CO_2 \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^-$$

- most important ECF buffer, & is a weak acid that dissociates into H^+ & HCO_3^- ... reaction can go either way depending on what the body needs

- using henderson hasselbalch equation, we can calculate pH...

why? b/c effectiveness is best when pH = pK

$$pH = pK + \log \frac{HCO3^-}{\alpha\, pCO2}$$

* bicarb pK = 6.1 * α constant = .03

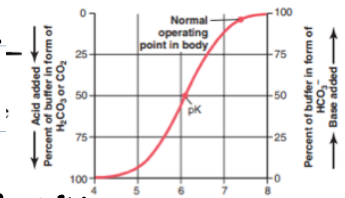
* we need HCO_3^- conc. & CO_2 conc. but... CO_2 conc. is difficult to obtain, so instead we use CO_2 partial pressure

$$pH = 6.1 + \log [HCO_3^-] / (.03 \times pCO_2)$$

* if HCO_3^- conc. = CO_2 conc. then pK will = pH

but heres the problem.... we said bicarb is most effective when pH = pK ... but body pH = 7.4 & bicarb pK is 6.1, so bicarb effectiveness is not at its best, but b/c bicarb conc. is very high, it is considered the best buffer

* when we have 50% acid & 50% base



pH will = 6, & bicarb will be most effective

Phosphate

$$HPO_4^{--} + H^+ \leftrightarrow H_2PO_4^-$$

- major intracellular & renal tubule electrolyte, so it is an important renal tubular buffer w/ a pK of 6.8 (which is close to urine pH)

Ammonia

$$NH_3 + H^+ \leftrightarrow NH_4^+$$

- renal tubular buffer

Proteins

$$H^+ + Hb \rightarrow HHb$$

- important intracellular buffer, but very slow (hours-days) b/c its hard for acids to enter cell to get titrated

notes

- normal H^+ conc = $4 \cdot 10^{-5}$ mmol / L & non-volitile acids produced = 1.9 mmol / L which is 47500 x greater than H^+ conc. so we need high buffering capacity to titrate these & maintain normal pH
- min & max pH a person can live w/ for only a few hours is 6.8 - 8

Respiratory Regulation

$H_2O + CO_2 \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^-$

- eliminates volatile acids by expiration of CO_2 thus ↑ H^+ loss
- in Acidosis, respiratory centers ↑ ventilation to rapidly eliminate volatile acids in the form of CO_2, & opposite happens in Alkalosis, to maintain H^+
- respiratory gain = 1-3, so it corrects 50-75% which is why we need kidneys

Renal Regulation w/ HCO_3^-

- eliminates non volatile acids by H^+ secretion & HCO_3^- reabsorption in intercalated cells ... it can also generate <u>new HCO_3^-</u> → this happens if we have too much H^+ & not enough HCO_3 to titrate it ... you will see

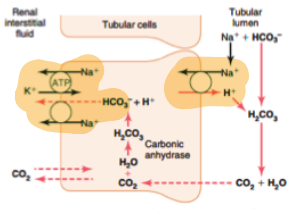
* 1:1 ratio, every HCO_3 reabsorbed must have 1 H^+ secreted

- 4320 mmol / day of HCO_3^- is filtered, 70-80% of this is reabsorbed in PCT, 10% reabsorbed in Thick ascending, & late distal & collecting reabsorb depending on body's needs (fine tuning) → acidosis = more reabsorption and vise versa

- so about 1 mEq/day of HCO_3^- excreted

lets talk about the mechanism in each segment

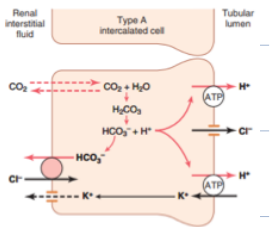
PCT & Thick ascending



- basal surface has Na^+/K^+ ATPase & HCO_3^-/Na^+ cotransporter that depend on this gradient; proximal surface has Na^+/H^+ exchangers ... Story time ... so.. carbonic acid (H_2CO_3) dissociate into H^+ & HCO_3^-. The HCO_3^- will be reabsorbed via cotransporter, & H^+ will be secreted into tubular lumen via Na^+/H^+ exchange. here, the H^+ will bind w/ filtered HCO_3^- in the lumen = H_2CO_3 → this will dissociate into H_2O & CO_2. The CO_2 diffuses back into the cell & binds w/ H_2O = H_2CO_3 which then dissociates again into H^+ & HCO_3^- ... its a cycle (1:1 ratio)

* this gives urine a pH of ~6.7

Late distal & Collecting (type A)



- basal surface has HCO_3^-/Cl^- exchanger, & proximal has H^+ ATPase & H^+/K^+ antiporter ... Story ..

H_2CO_3 dissociates into HCO_3^- & H^+ in the cell, the H^+ will be secreted by both channels & HCO_3^- reabsorbed by its channel ... 1:1 ratio again, & gives urine a pH of 4.5

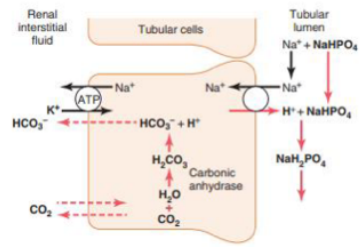
notes

so what happens in acidosis, when I have too much H^+... we undergo same processes, but eventually, all bicarb will be reabsorbed, but not all the excess H^+ will be secreted

(so some H^+ is not titrated)... this means we need another buffer, other than HCO_3^- to titrate ... & every time that that other buffer titrates H^+, a new HCO_3 will be generated

Phosphate

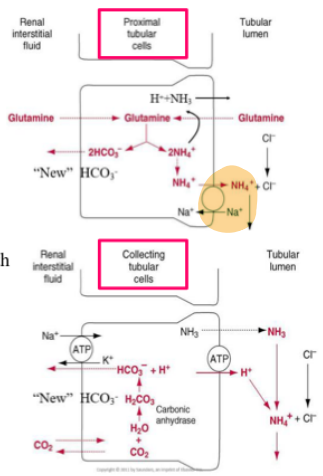
$$NaHPO_4^- + H^+ \rightarrow NaH_2PO_4$$



- filtered phosphate in tubular lumen binds w/ excess H^+ to make NaH_2PO_4 ... for every H^+ titrated, a new HCO_3^- is made in the cell
- about 100 mmol of phosphate is filtered / day, & titrates 30 mmol of H^+ / day, so about 70% of phosphate is reabsorbed

* phosphate is not the major buffer, because its buffering capacity does not change in chronic acidosis ... so we have....

Ammonia (NH_3) & Ammonium (NH_4)



- Glutamate is broken down into HCO_3^- & NH_4 in the tubular cells of PCT, Thick Ascending, & DCT. NH_4 is secreted in exchang for Na^+, & a new HCO_3^- will be generated
- in collecting duct cells, NH_4 breaks into NH_3 & H^+ to be secreted into tubular lumen ... in the lumen, they bind = NH_4 to be excreted, & a bicarb is made
- the source of NH_3 in tubular lumen can be either from the blood → tubular cell → tubular lumen ... or present in lumen in high concentration

* in chronic acidosis, NH_4 level ↑ b/c it is physiologically

regulated, meaning it is better than phosphate in chronic acidosis

Importance of Renal Tubular buffers

- minimum urine pH = 4.5 or $10^{-4.5}$, & must excrete at least 60 mmol/L of non-volatile acids / day
- H^+ conc. in urine is .03 mmol / L ... 60/.03 = 2000L
- this means tubular fluid volume must be 2000L/day in order to release 60 mmol on non volatile acid → this is illogical, so we titrate the H^+ w/ different buffers

Quantification of normal Renal acid / Base regulation

- nonvolatile acids eliminated = 80 mmol/day
- HCO_3^- filtration = 4320 mmol/day
- HCO_3^- reabsorption = 4319 mmol/day
- new HCO_3^- production = 80 mmol/day
- HCO_3^- excretion = 1 mmol/day
- titratable acid NaH_2PO_4 = 80 mmol/day
- NH_4^+ excretion = 30 mmol/day
- H^+ secretion = 4400 mmol/day

Total H^+ Secretion

- H^+ secreted in exchange for bicarb + H^+ of non volatile acid

$4320 + 30 + 30 = 4380$

Net H^+ Excretion

- H^+ excreted by buffers other than bicarb - H^+ added to blood

* H^+ added to blood = bicarb excretion, so ...

30 + 30 - 1 = 59 mmol/day

- the net HCO_3^- added to body is = to net H^+ loss
- the new HCO_3^- added to body = net H^+ excretion by buffers other than bicarb ... about 200 mmol/day but can ↑ to 500 by ↑ ammonium buffer in chronic acidosis
- in Alkalosis, net HCO_3^- loss can = 80 mmol/day

Acid Base Disorders

- Acidosis = pH less than 7.4 b/c of ↓ HCO_3^- or ↑ PCO_2
  - Kidney ↑ H^+ secretion & HCO_3^- reabsorption, or makes new HCO_3^-
- Alkalosis = pH more than 7.4 b/c of ↑ HCO_3^- or ↓ PCO_2
  - Kidney ↓ H^+ secretion & HCO_3 reabsorption so HCO_3 is lost in urine

Renal Compinsation

$$H_2O + CO_2 \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^-$$

Respiratory acidosis

- ↑ in pCO_2 will shift the equation to the right, so carbonic acid ↑ & more H^+ is made ... the kidney undergoes dual compensation effect by secreting extra H^+ & making new bicarb

Metabolic Acidosis

- ↓ bicarb in blood = ↓ pH ... dual compensation again by ↓ bicarb filtration, full bicarb reabsorption & titration of H^+ w/ other buffers

Respiratory Alkalosis

- ↓ pCO_2 = ↓ H^+ & ↓ H^+ secretion & bicarb reabsorption

... so excess bicarb in tubular fluid to be excreted