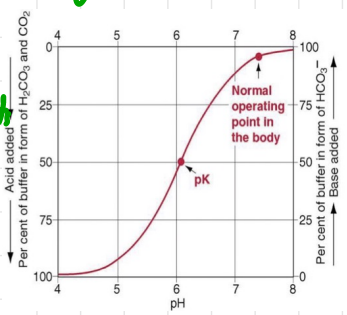
★Topic 1:- Acid-Base balance

- **Mechanisms of Hydrogen ion regulation:-** H^+ is precisly regulated at $3\text{-}5\times10^{-8}$ mole/L (pH: 7.2 / 7.4)
  - Body fluid chemical Buffers:- Rapid but tumporary.
  - Respiratory:- Rapid, eliminate CO_2 ($\uparrow H \rightarrow \uparrow$ventilation $\rightarrow \uparrow CO_2$ Loss).
  - Kidney:- slow & powerful, eliminates non-volatile acids (secrete H, Reabsorbs & new HCO_3^-).

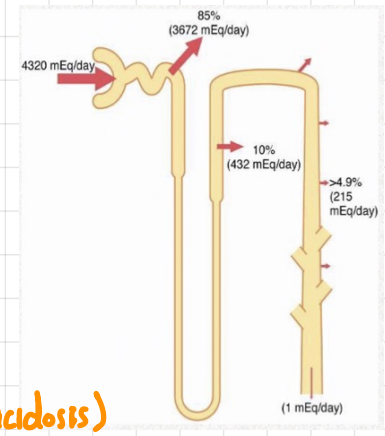
- **Buffer system**
  - Types
    - Bicarbonate:- most important, ECF, $H_2O + CO_2 \xleftrightarrow{CA} H_2CO_3 \longleftrightarrow H^+ + HCO_3^-$
    - phosphate:- Renal, $HPO_4^- + H^+ \longleftrightarrow H_2PO_4$
    - Ammonia:- Renal, $NH_3 + H^+ \longleftrightarrow NH_4^+$
    - proteins:- intracellular, $H^+ + Hb \longleftrightarrow HHb$,

    ·60-70% of Buffering is in the cells.
  - importance:- Normal H^+ (optimal) concentration = 0.00004 mmol/L, Amount of non-volatile acids produced ~ 60-80 mmol/day → 47,500 times > normal H^+ concentration, pH 6.8-8 → die
    - non-volatine acids cannot be eliminated by Respiratory system.
  - equation:- $pH = pK + \log(HCO_3^-/\alpha PCO_3)$, $\alpha = 0.03$, $pK = 6.1$ ($\uparrow HCO_3 \rightarrow \uparrow pH$, $\uparrow PCO_2 \rightarrow \downarrow pH$).
    - effectiveness of buffer system depends on → Concentrations of Reactants.
      → pK of system & pH of Body fluids.
  - Bicarbonate Buffer system:- it's the most important in ECF even though the concentration of the components are low & pK = 6.1, which is not very close to normal pH (7.4), Because the components of the system (CO_2 & HCO_3) are Highly regulated by Lungs & Kidney.

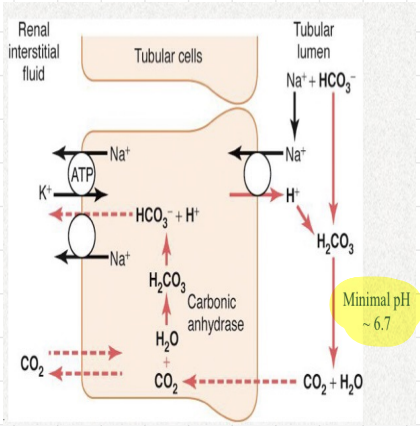


- **Respiratory Regulation of Acid-Base Balance:-** $\uparrow H \rightarrow \uparrow$ventilation $\rightarrow \downarrow PCO_2$
  - $\downarrow PCO_2$ ($\uparrow H + HCO_3 \rightarrow H_2CO_3 \longrightarrow H_2O + CO_2$)
  - Feedback gain:- 1.0 to 3.0.
  - corrects:- 50 - 75%.

- **Renal Regulation of Acid-Base balance:-** more potent.
  - Eliminate non-volatile acids (H_2SO_4, H_3PO_4) ~ 80 mmol/day.
  - filtration of HCO_3 ~ 4320 mmol/day
  - Secretion of H^+ ~ 4400 mmol/day
  - Reabsorption of HCO_3 ~ 4319 mmol/day → needs
  - production of new HCO_3 ~ 80 mmol/day
  - Excretion of HCO_3 ~ 1 mmol/day
    - 1 HCO_3^- Reabsorbed → 1 H^+ secreted (↑ in alkaloss, ↓ in acidosis)

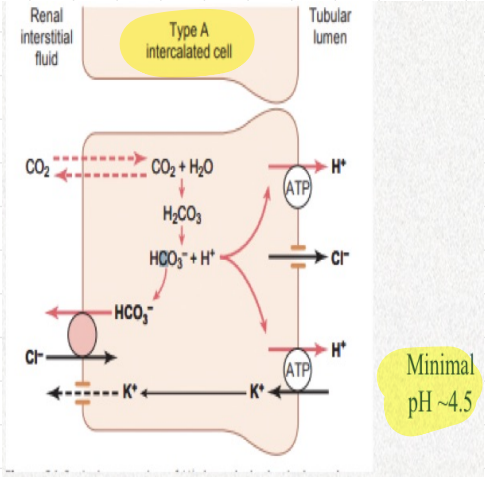


Proximal tubule & thick Henle



Secrete H^+
↓
$+ HCO_3$
↓
H_2CO_3
↓
$CO_2 + H_2O$
↓
$HCO_3 + H^+$
↓ Reabsorbed ↘ Secrete

Late distal & collecting tubules

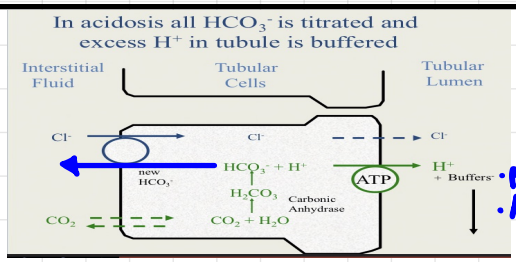


- H^+ATpase:- powerful against large gradiant (4.5)
- H^+/K^+:- stimulated by hypokalemia.

- **Regulation of H^+ secretion:-** $H_2O + CO_2 \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^-$ / $pH = pK + \log(HCO_3/\alpha\, PCO_2)$
  - respiratory acidosis:- ↑PCO_2 → ↑H^+ secretion
  - metabolic (↓Buffer, ↓HCO_3) or respiratory acidosis
    - ↑H extracellular → ↑H^+ secretion.
    - ↑Buffer → ↑H^+ secretion.

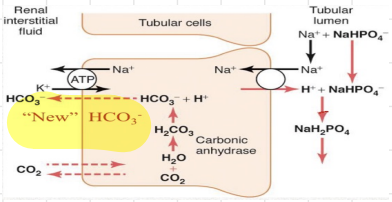
- **Renal compensation for Acid-Base disorders**
  - Acidosis:- ↑H^+ secretion, ↑HCO_3^- Reabsorption, production of new HCO_3^-.
  - Alkalosis:- ↓H^+ secretion, ↓HCO_3^- Reabsorption, Loss of HCO_3^- in urine (↓Reabsorption → ↑secretion).

Buffers → new HCO_3



- phosphate
- Ammonia

Buffered by phosphate → New HCO_3^-

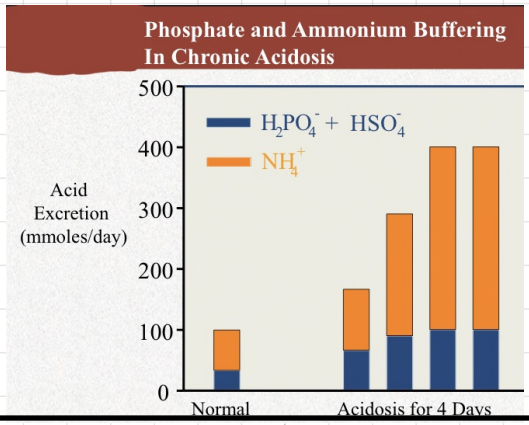


- This process Helps to secrete more H^+.

- **importance of Buffers**
  - min urine pH = 4.5 (3.5×10^{-5} mole/L).
  - max H^+ of urine = 0.03 mmol/L.
  - Kidney must excrete 60 mmol of non-volatile acids each day, to excrete this as free H^+ → $\frac{60}{0.03}$ → 2000 L/day.

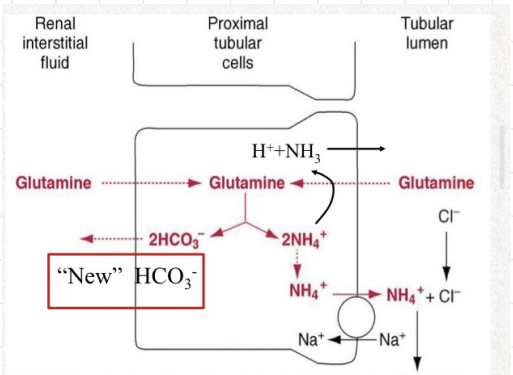
- **phosphate as a tubular fluid Buffer**
  - ↑concentration of phosphate, pK = 6.8 (close).
  - Buffers about 30 mmol/day H^+ (100 mmol/day phosphate is filtered but 70% Reabsorbed).
  - not major in chronic acidosis:- Buffering capacity does not change much with acid-Base disturbance

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

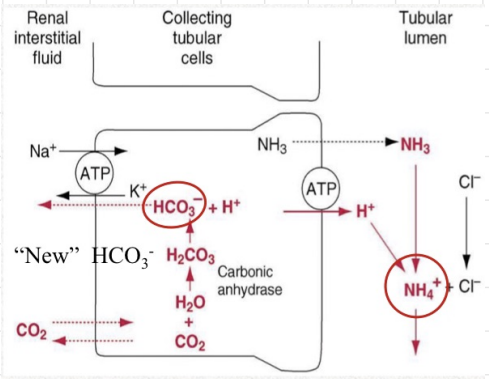


- **Acidosis**
  - ⬇
  - More ammonia (NH_3) by the Body glutamine.
  - ⬇
  - More useful in chronic.

- **production & secretion of NH_4 & HCO_3^- by PCT**
  - DCT, thick Loop of Henle



- **Buffering of H^+ secretion by NH_3 in collecting tubules.**



★Topic 2 :- Acid-base balance -2.

- **Total H^+ secretion** = H^+ secreted (HCO_3 reabsorption) + titratable acid ($NaHP_o$) + NH_4 excretion
  = 432o + 3o + 3o = 438o

  (titratable acid: non-volaite)

- **Net H^+ excretion = Net HCO_3 addition =**
  H^+ excreted by buffers not HCO_3 (new HCO_3) − New H^+ (HCO_3 excreted)
  ↳ titrable acids + NH_4 (3o + 3o) − HCO_3 excretion (1) = 59.

- **Renal consmpensation** → Acidosis:- ↑HCO_3 addition = ↑H^+ excretion (can increase to 500 mmol/d).
  ↳ Alkalosis:- ↑HCO_3 excretion = ↑H^+ addition.

- **classification**

Plasma				
Disturbance	pH	HCO_3^-	pCO_2	Compensation
metabolic acidosis	↓	↓	↓	↑ ventilation, ↑ renal HCO_3 production
respiratory acidosis	↓	↑	↑	↑ renal HCO_3 production
metabolic alkalosis	↑	↑	↑	↓ ventilation, ↑ renal HCO_3 excretion
respiratory alkalosis	↑	↓	↓	↑ renal HCO_3 excretion

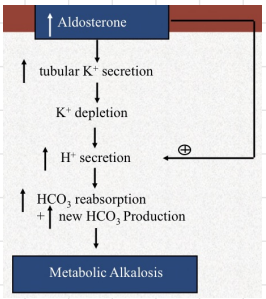
Metabolic Acidosis (↓PH<7.4, ↓HCO_3<24)

- Causes:- aspirin poisioning (↑H^+ intake), DM (↑H^+ production), diarrhea (HCO_3 loss), Renal tubular acidosis (↓H^+ secretion = ↓HCO_3 Reab), CA inhibitor (↓H^+ secretion).
- Renal Response:- ↓HCO_3 filt. → ↑HCO_3 Reab → ↑Buffers → ↑New HCO_3^-
- Respiratory compensation:- ↑ventilation → ↓PCO_2.

↑volume → ↓Aldosterone

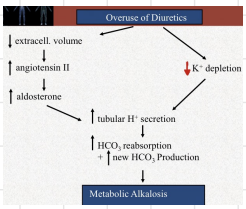
Respiratory Acidosis (↓PH<7.4, ↑PCO_2>40 mmHg)

- Causes:- Brain damge, pneumonia, emphysema, Lung disorders.
- Renal Response:- ↑H^+ secretion → ↑HCO_3 Reab → ↑Buffers → ↑New HCO_3^-.



metabolic Alkalosis (↑PH>7.4, ↑HCO_3^->24)

- Causes:- ↑Base intake ($NaHCO_3$), Vomiting, mineralocorticoid excess, diureticsoveruse
- Renal Response:- ↑HCO_3 filtration → ↓HCO_3 Reab → ↑HCO_3 excretion = ↓H^+ excretion.
- Respiratory Compensation:- ↓ventilation → ↑PCO_2.
- ↑Aldoslerone :- ↑K secretion → ↓K → ↑H secretion = ↑HCO_3 Reab → new HCO_3^-. → metabolic alkalosis
- Diuretics overdose → ↓volume → ↑RAAS → ↑H secretion = ↑HCO_3 Reab
  ↳ ↓K → ↑H^+ secretion = ↑HCO_3 Reab



Respiratory alkalosis (↑PH>7.4, ↓PCO_2 < 40mmHg).

- Causes:- ↑attiude, psychic (fear, pain).
- Renal Response:- ↓H^+ secre. → ↓HCO_3 Reab → ↑HCO_3 excretion = ↓H^+ excretion (↑Reab).

mixed Acidosis:- ↑PCO_2 + ↓HCO_3.

mixed Alkalosis:- ↓PCO_2 + ↑HCO_3.

- **Anion Gap (Dx)** = unmeasured anions = $Na^+ - cL^- - HCO_3^-$ (8-16 mEq/L)
  - in body fluids :- total cations = total anions (electrical balance)
  - Hyperchloremic metabolic acidosis
    - normal anion gap = Na^+ − ↑cL − ↓HCO_3
    - Causes:- Diarrhea (HCO_3 Lost), Renal tubular acidosis & CA inhibitors & Addisons (↓H^+ secretion).
  - normochloremic metabolic acidosis
    - ↑unmeasured anions = ↑anion gap = Na^+ − normal cL^- − ↓HCO_3^-
    - causes:- DM (Ketoacidosis), Lactic acidosis, aspirin (acetysalicylic acid) poisoning, methanol poisoning, starvation.

- Buffering of H^+ by something other than HCO_3^- → new HCO_3^-
- titrable acid is H_2PO_4 not NH_4 because PKA of NH_4 is 9.1 far away from urine pH so it wont dissostae from H^+.