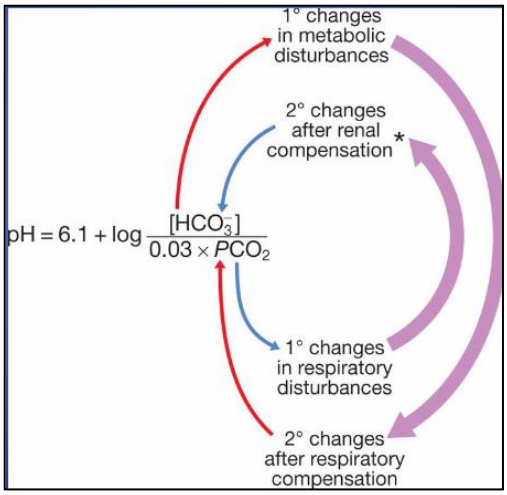
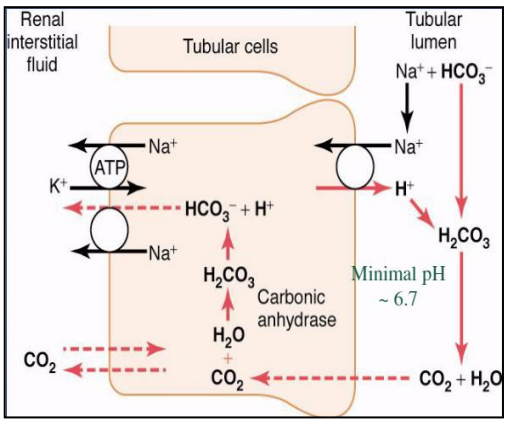
Unit I – Problem 3 – Physiology: Regulation of Acid-Base Balance

- Plasma concentration of $[H^+]$ is very small when compared to other ions (40 nmoles/L).
- **Normal range of pH:**
  - **Normal pH of the body**: 7.35-7.45 (a pH outside this range is life-threatening).
- **What are the buffer systems in the body?**
  - **Bicarbonate: it is the most important extracellular fluid buffer**
    - ✓ $H_2O + CO_2 \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3$
  - **Phosphate: it is an important renal tubular buffer**
    - ✓ $HPO_4^- + H^+ \leftrightarrow H_2PO_4^-$
  - **Ammonia: it is an important renal tubular buffer**
    - ✓ $NH_3 + H^+ \leftrightarrow NH_4^+$
  - **Proteins: they are considered as important intracellular buffers**
    - ✓ $H^+ + Hb \leftrightarrow HHb$
- **Importance of buffer systems:**
  - **Normal $[H^+]$ concentration** = 0.00004 mmol/L
  - **Amount of non-volatile (غير متبخّر) acid produced** = 80 mmol/L → 80 mmol/42L = 1.9 mmol/L which is 47,500 times more than normal $[H^+]$ concentration!
- **Bicarbonate buffer system:**
  - $H_2O + CO_2 \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3$
  - **pH = pKa (6.1) + log** $\frac{HCO_3}{0.03 \times pCO_2}$
  - It is the most important buffer in extracellular fluid even though the concentration of the components are low and the pKa of the system is 6.1, which is not very close to normal extracellular fluid pH (7.4).
  - The components of this system (CO_2 and HCO_3) are closely regulated by the lungs and the kidneys.
  - Notice that increased hydrogen ion concentration (↓pH) will stimulated alveolar ventilation and this will lower the pCO_2, decrease hydrogen ion concentration and increase pH (alveolar ventilation: it is the volume of gas per unit time that reaches the alveoli).



- **Renal regulation of acid-base balance:**
  - Kidneys eliminate non-volatile acids (H_2SO_4 and H_3PO_4).
  - Filtration of bicarbonate.
  - Secretion of $[H^+]$.
  - Reabsorption of bicarbonate.
  - Production of new bicarbonate.
  - Excretion of bicarbonate.

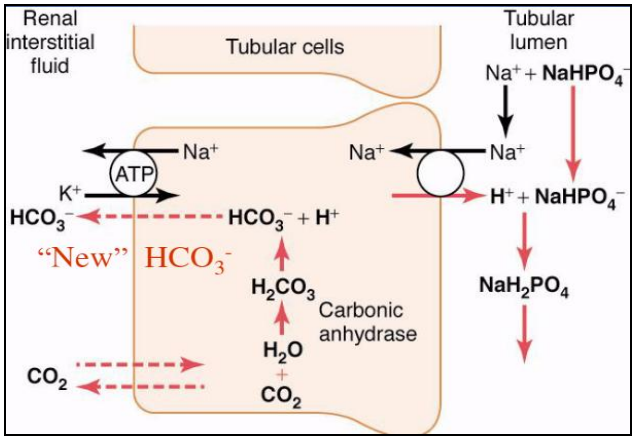
    Notice that kidneys conserve bicarbonate and excrete acidic or basic urine depending on body needs.



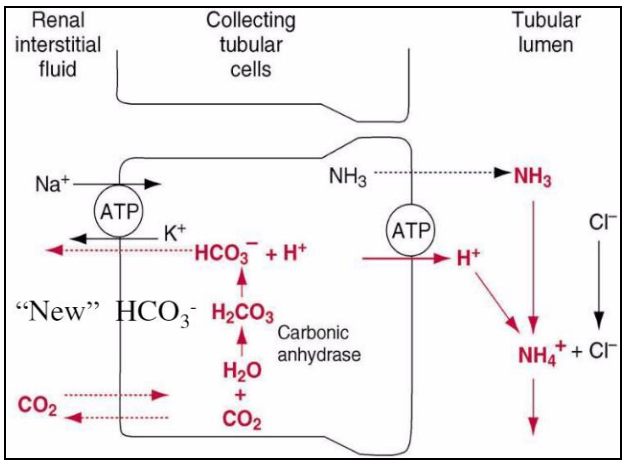
- **Reabsorption of bicarbonate in different segments of renal tubule:**
  - 85% of bicarbonate is reabsorbed in Proximal Convoluted Tubule (PCT)
  - 10% of bicarbonate is reabsorbed in thick ascending limb of loop of Henle.
  - > 4.9% of bicarbonate is reabsorbed in collecting duct.

Notice that for each bicarbonate reabsorbed, there must be a $[H^+]$ secreted (see the image in previous page).

- **Renal compensation for acid-base disorders:**
  - **Acidosis:**
    - ✓ Increased $[H^+]$ secretion to increase the pH.
    - ✓ Increased HCO_3^- reabsorption.
    - ✓ Production of new HCO_3^-
  - **Alkalosis:**
    - ✓ Decreased $[H^+]$ secretion.
    - ✓ Decreased HCO_3 reabsorption.
    - ✓ Loss of HCO_3^- in urine.
- **Why are renal tubular buffers important:**
  - Minimum urine pH = 4.5
  - The maximal $[H^+]$ of urine is 0.03 mmol/L
  - Yet, the kidneys must excrete, under normal conditions, at least 60 mmol of non-volatile acids each day. To excrete this as free $[H^+]$, this process would require 2000 L or urine per day!!!
- **The image below shows buffering of secreted $[H^+]$ by filtered phosphate ($NaHPO_4^-$) and generation of new HCO_3^-**



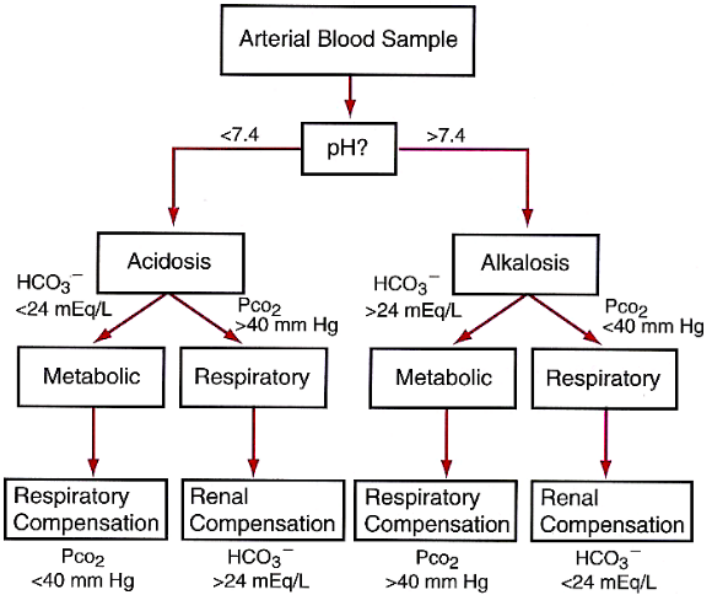
  - There is a high concentration of phosphate in tubular fluid (100 mmol/day of phosphate is filtered but 70% of it is reabsorbed).
  - Phosphate normally buffers about 30 mmol/day of $[H^+]$.
  - Notice that phosphate buffering capacity does not change much with acid-base disturbances (phosphate is not the major tubular buffer in chronic acidosis).
- **The image below shows buffering of hydrogen ion secretion by ammonia (NH_3) in collecting tubules:**



- **Classification of acid-base disorders:**

Acidosis: pH < 7.35	
Metabolic	↓ HCO_3^-
Respiratory	↑ pCO_2
Alkalosis: pH > 7.45	
Metabolic	↑ HCO_3^-
Respiratory	↓ pCO_2

	pH	pCO_2	HCO_3^-	Compensatory response
Metabolic acidosis	↓	↓	↓	Hyperventilation (immediate)
Metabolic alkalosis	↑	↑	↑	Hypoventilation (immediate)
Respiratory acidosis	↓	↑	↑	↑ renal HCO_3^- reabsorption (delayed)
Respiratory alkalosis	↑	↓	↓	↓ renal HCO_3^- reabsorption (delayed)



- **Anion gap:**
  - **Anion gap = Na^+ - (Cl^- + HCO_3^-)**
  - In metabolic acidosis, anion gap can be increased or normal (depending on the cause):
    - ✓ Increased anion gap (MUDPILES):
      - ❖ M: Methanol.
      - ❖ U: Uremia.
      - ❖ D: Diabetic ketoacidosis.
      - ❖ P: Propylene glycol.
      - ❖ I: Iron tablets.
      - ❖ L: Lactic acidosis.
      - ❖ E: Ethylene glycol.
      - ❖ S: Salicylates.
    - ✓ Normal anion gap (8-12 meq/L): HARD-ASS
      - ❖ H: Hyperalimentation.
      - ❖ A: Addison's disease.
      - ❖ R: Renal tubular acidosis.
      - ❖ D: Diarrhea.
      - ❖ A: Acetazolamide.
      - ❖ S: Spironolactone.
      - ❖ S: Saline infusion.
- When there is increased aldosterone production (which occurs with excessive use of diuretics) → there is increased [H^+] secretion → resulting in increased HCO_3^- reabsorption and production of new HCO_3^- → leading to metabolic alkalosis.