PHYSIOLOGY

Acid – Base Balance 1

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اعداد

لجنة التبيضات

Acid – Base Balance

Regulation of H+ concentration is very important because it affects the function of all enzyme systems of the body, as any change in H+ concentration may alter most of cellular functions.

Sources of H+:

1. Diet:
    - ❖ Protein diet produce more fixed acids than bases.
2. Intermediary Metabolism.
    A. Volatile acids (Carbonic acid)
    - ❖ Carbonic acid formed from Co2 that result from oxidation of glucose and triglycerides during anaerobic metabolism. About 300 L are produced daily in normal adult.

    B. Fixed acids
    - ❖ As lactic acid from oxidation of carbohydrates in hypoxic states
    - ❖ And Ketoacids that result from oxidation of fat in uncontrolled diabetes mellitus

Normal H+ conc = 0.00004 m eq / L

PH= - log H+

PH = 7.4

The PH is inversely proportional to with H+ concentration.

Defensive Mechanisms against changes in H+ concentration:

There are 3 mechanisms:

1. Buffer system - Rapid Mechanism (takes minutes)
    - ❖ by immediate combination of H+ with extracellular and intracellular buffer system.
2. Respiration regulation - Intermediate mechanism (takes hours)
    - ❖ in which reduction of carbonic acid is by elimination of Co2 by respiratory system.
3. Renal Regulation - Slow mechanism (takes days)
    - ❖ by increased rate of H+ excretion and bicarbonate Reabsorption by renal tubules.

<u>1- Rapid Mechanism (Buffer system)</u>

- Definition of Buffer:
  It is defined as any substance that can give or accept H+ if an alkali or an acid is added respectively to minimize the change in PH.
- It consists of a combination of a weak acid and the salt of a strong base.
- The most effective **extracellular** buffer system is <u>bicarbonate system</u>.
- The most important **intracellular** buffer systems are <u>phosphates and proteins</u>. (viiiiiiip)

A-Bicarbonate buffer system:

- It consists of combination of carbonic acid and bicarbonate
- This system accounts **for 65 % of buffering capacity i**n <u>plasma</u>
- And **40 % of buffering action in the whole body.**
- Bicarbonate is regulated by the **kidney** (Metabolic component)
- Carbonic acid is under **respiratory regulation** (Respiratory component).

Acids like HCl will be neutralized by the bicarbonate salts:

Addition of an acid as (HCl) it will be neutralized by NaHCo3-.

HCl + NaHCo3 → NaCl + H2Co3

So strong acid (HCL) is converted into weak acid (H2Co3) and neutral salt (NaCL)

Addition of an alkali (NaOH) it will be neutralized by carbonic acid

NaOH + H2Co3 → NaHCo3 + H2O

So strong alkali is neutralized to neutral salt and water.

N.B: We use the concentration of Co2 instead of H2Co3 because it is easy to assay and it is a mirror of H2Co3 because when H2Co3 concentration increases the concentration of Co2 increase. So we can use Co2 instead of H2Co3.

B-Phosphate buffer system:

- **intracellular buffer and tubular fluid buffer**
- **Its two elements are:**
  - Phosphoric acid (H2PO4)
  - Phosphate salt.
- It is an effective buffer system because its concentration is high intracellular and in tubular fluid

C-Protein buffer system:

- It is a powerful system because of its high concentration in intracellular fluid and in plasma.
- Amino acids can act as an acid (Proteinic acid) and or alkali (Na proteinate)
- **In RBCs Hb is a powerful buffer.**

Note: Phosphate buffer system and protein buffer system neutralize with H+ as it inside the cell, as if any H+ exit the cell it will be neutralized by bicarbonate system.

2-Respiratory regulation (Intermediate Mechanism):

The respiratory system has the ability to eliminate the excess H2Co3

- Because H2Co3 ↔ H2O + CO2 So
  - **In acidosis** → ↑ H2CO3 → ↑ CO2 in the blood → stimulate Respiratory center → ↑ rate of respiration and elimination of the excess CO2 leading to decreased acid in the blood and so correcting acidosis.
  - **In alkalosis** (the reverse occurs) i.e. decreased level of H2CO3 leads to decreased CO2 concentration and inhibit R.C leading to CO2 retention in the blood and increased H2CO3 so correcting alkalosis.

3-Renal Regulation (Slow Mechanism):

Renal compensation in acid base disturbances takes place through Excretion or absorption of H+ and HCO3 This occur in two ways:

1-Directly by retaining or excreting H

2-Indirect by changing Reabsorption or excretion of HCO3 buffer.

In the proximal tubule:

- ❖ Hydrogen ion secretion and bicarbonate Reabsorption.
- ❖ The proximal tubule is responsible for Reabsorption of most of the HCO3- that enters the nephron at the glomerulus.
- ❖ Mechanism:
  a- H+ is secreted from the cells into the lumen in exchange with filtered Na+ using Na+ - H+ antiport protein
  b- b-The secreted H+ combine with filtered HCO3 forming H2CO3 that dissociates in the lumen into CO2 + H2O.
  c- c- CO2 diffuse to the tubular cells and combine with H2O to form H2CO3 that dissociate into H+ and HCO3-
  d- d- The HCO3 in the tubular cell is transported out of the cell on basolateral side by HCO3- - Na + symport protein.
- ❖ Net result: Filtered Na+ and HCO3 are reabsorbed H+ is secreted.

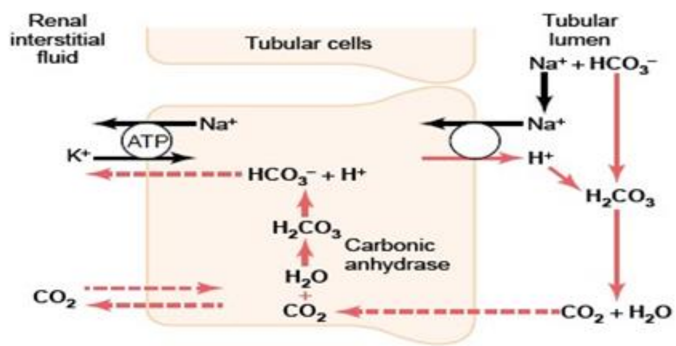


Figure: H+ secretion and HCO3- reabsorption in PCT.

In distal tubule:

- ❖ The distal nephron (<u>distal tubule and collecting duct</u>) plays a significant role in fine regulation of acid – base balance.
- ❖ It contains two types of intercalated cells.
  - ➢ **In acidosis**, type (A) intercalated cells secrete H+ and reabsorb bicarbonate.
  - ➢ **In alkalosis** type (B) intercalated cells secrete HCO3 and reabsorb H+
- ❖ Intercalated cells are characterized by high concentration of **carbonic anhydrase** in their cytoplasm, <u>this enzyme allows them to convert large amounts of CO2 into H+ and HCO3-</u>

❖ The H+ is pumped out of the intercalated cells by H+ - ATPase or ATPase that exchanges H+ for K+

❖ The HCO3 leaves the cell by means of HCO3 - CL- antiport exchanger

The next Figure shows how type A intercalated cell works in times of acidosis secreting H+ and reabsorbing HCO3 by a process similar to H^+ secretion in proximal convoluted tubules except for specific H^+ transporters in distal nephron **which are**

a- H+ - ATPase

b- H+ / K+ ATPase

While in proximal tubule it is Na+ - H+ antiport protein.

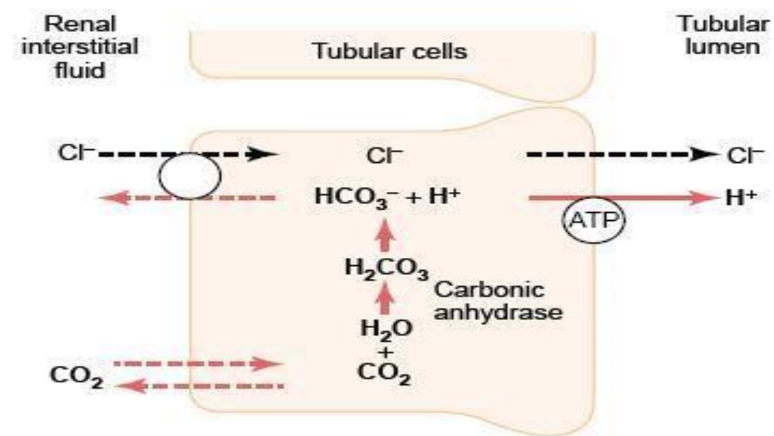


Figure (2): Primary active secretion of hydrogen ions through intercalated cells

Note: the proximal tubule cells have a constant method of dealing with H^+ (it always pumps H^+ out and Na^+ in by the antiport and passively move $HCO3^-$ from the cell to the extracellular fluid). Whereas the distal tubule intercalated cells act as response to either acidosis or alkalosis

الأنابيب الملتوية البعيدة هي التي تتخلص من حالات ارتفاع حموضة الدم او انخفاضها

In acidosis:

The kidney secretes H+ into the lumen of both proximal and distal tubules using direct (distal) and indirect (proximal) active transport If H^+ is secreted rapidly by this mechanism in the tubular fluid its concentration is increased and tubular pH drops rapidly to (4.5) leading to stoppage of H^+ secretion.

So, for H^+ secretion to continue more and more in acidosis it must be carried and transported by Ammonia and phosphate ions to become in non-ionized state i.e. ammonia and phosphate ions in urine act as urinary buffers trapping H+ and allowing more H+ to be secreted.

While H+ is being secreted, the kidney makes new HCO3 from CO2 and H2O and HCO3 is reabsorbed into the blood to act as buffer to increase the pH.

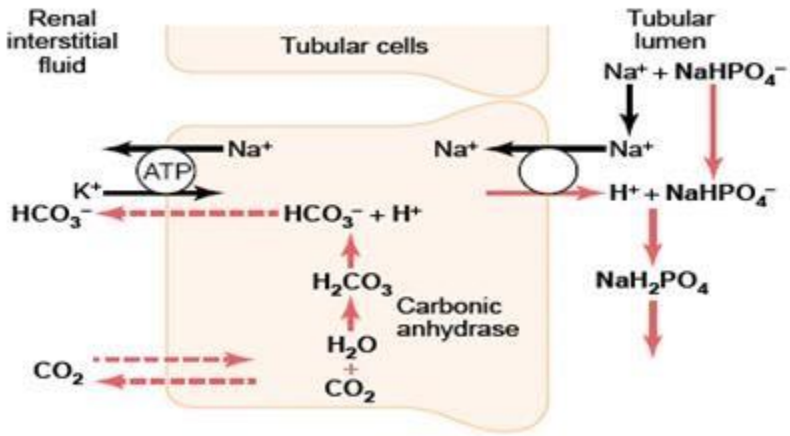
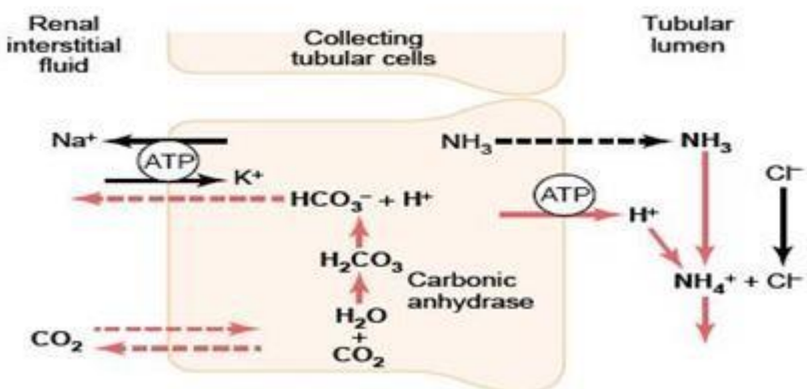


Figure (3): Buffering of secreted hydrogen ions by filtered phosphate (NaHPO4).



ملاحظة جانبية

NH_3 is Neurotoxic

NH_4 in urine = Bad odor

Figure (4): Buffering of hydrogen ion secretion by ammonia (NH3) in the collecting tubules.

In alkalosis:

In alkalosis the kidney reverses the process described above by secreting HCO3 into the lumen, and absorbing H+ in an effort to bring pH back into normal range. H^+ are reabsorbed into extracellular fluid on basolateral border by H^+ ATPase and H^+ - K^+ ATPase

The H^+ - K^+ ATPase of the distal nephron provides link between H^+ and K^+ creates an increase in K^+ excretion and hypokalemia, while in acidosis the kidney secretes H+ into urine and reabsorbs K+ leading to hyperkalemia.

Role of the liver in regulation of Acid – base balance:

1. Transform ammonia to urea (Neutral)

2. Transformation of Lactic acid (produced during exercise) to glycogen
3. In alkalosis it transforms glucose into lactic acid.
4. In alkalosis it increases the production of ketone bodies.

Disturbances of acid –base balance

- The 3 compensatory mechanisms Buffer, Ventilation and Renal excretion Keep the plasma PH at its normal value 7.4, but under some conditions the production or loss of H+ and HCO3 is so extreme that compensatory mechanisms fail to maintain PH homeostasis.

- The normal range of the PH is 7.38 – 7.42.
  Unlike other homeostasis parameters pH has a narrow normal range

- Drop of PH below 7.38 leads to acidosis
- Rise of PH above 7.42 leads to alkalosis.

- Also, the cause May be **Metabolic** (Acidosis or alkalosis) if the disturbance is in HCO3 i.e. arises from acids or bases of non-CO2 origin
- But it is **Respiratory** (acidosis or alkalosis) if the disturbance is in PCO2 which result from hypo or hyper ventilation.

Some other notes:

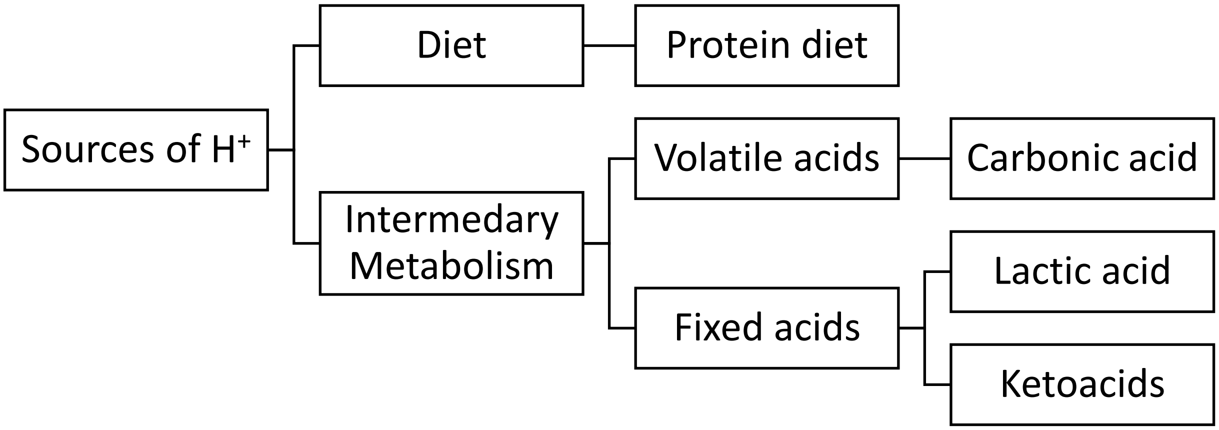
Note1: As well as increasing H^+ concentration lead to acidosis, decreasing HCO_3 will lead to acidosis

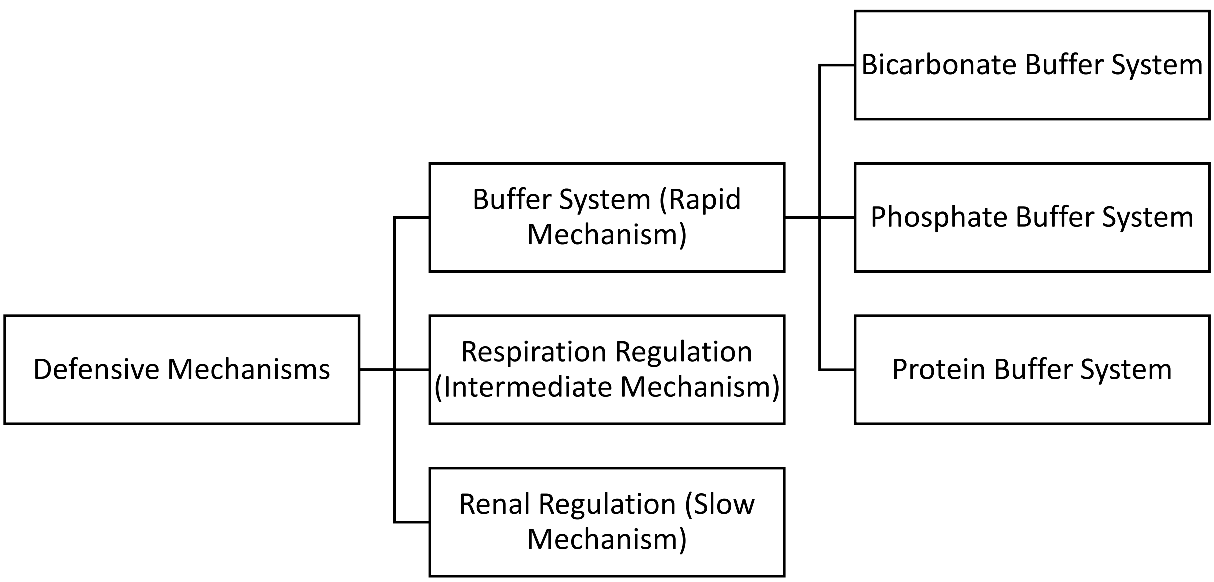
Note2: High protein and high fat diets will, when it metabolized, increase acids in blood thus the kidney throws H^+ down in urine ➔ form NH_4 ➔ Bad odor

معلومة عامة مش للحفظ

Acid –base balance

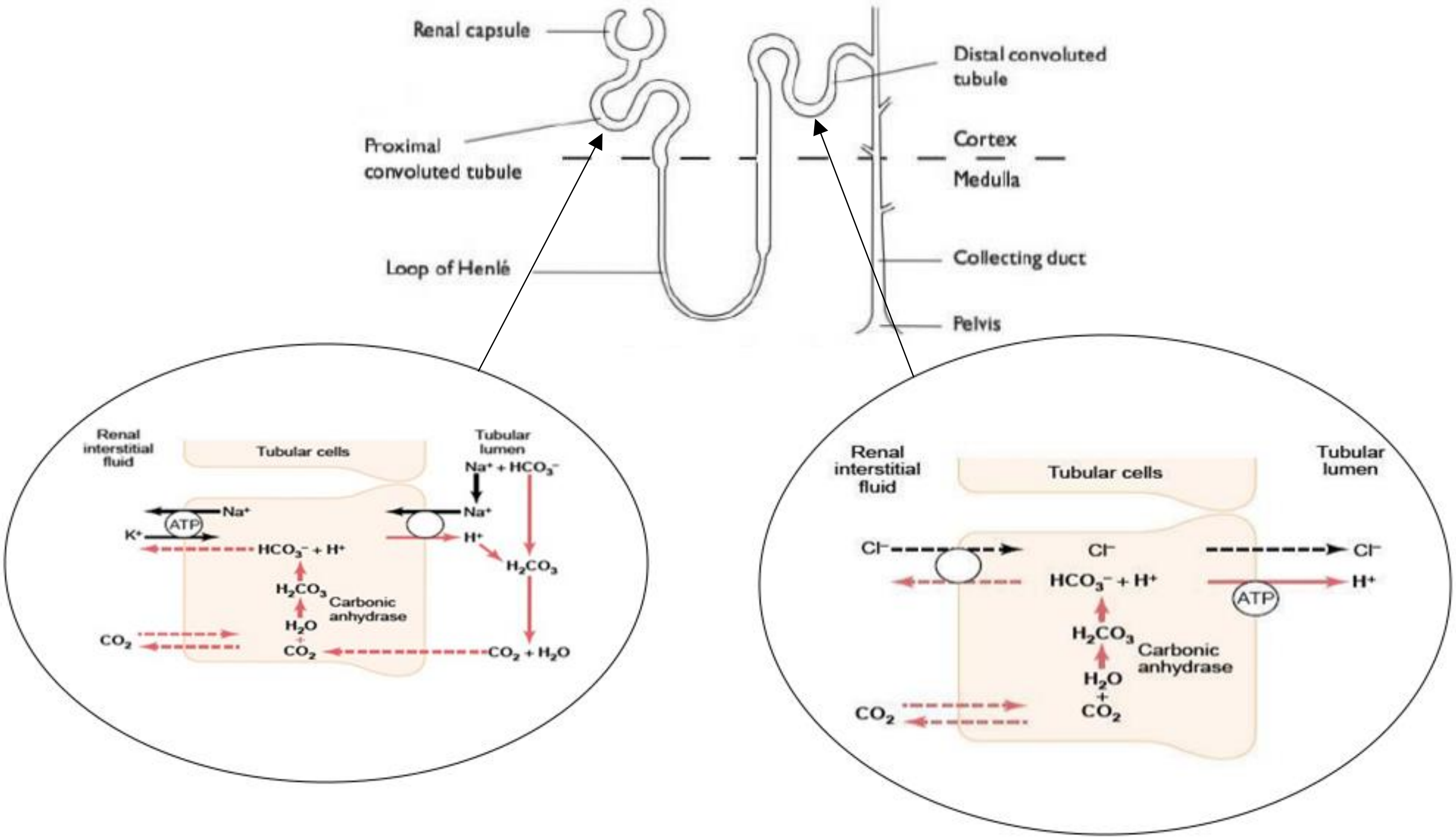
Mind Maps





Bicarbonate Buffer System

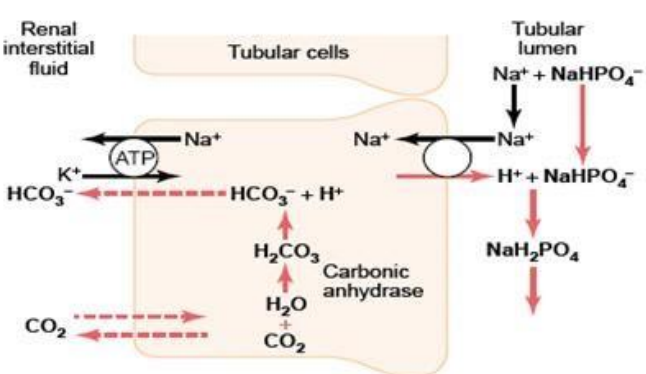
$$CO_2 + H_2O \xleftrightarrow{\text{Carbonic Anhydrase}} H_2CO_3 \longleftrightarrow HCO_3^- + H^+$$



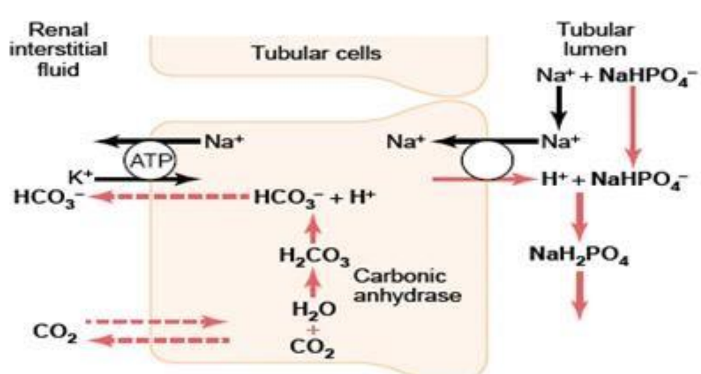
Basolateral side	Lumen side
HCO3- - Na + symport protein	Na+ - H+ antiport protein

Basolateral side	Lumen side
HCO3 - CL- antiport exchanger	1. H+ - ATPase 2. H+ / K+ ATPase

Buffering systems in the filtrate



Phosphate Buffering System



Ammonia Buffering System