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-Intermedary Metabolism.

The body produce acids in 2 forms:

a-Volatile acids (carbonic acid)

b-Non volatile acids (Fixed acids)

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-Rapid Mechanism (takes minutes)

by immediate combination of H+ with extracellular and intracellular buffer system.

2-Intermediate mechanism (takes hours)

in which reduction of carbonic acid is by elimination of Co2 by respiratory system.

3-Slow mechanism (takes days)
by increased rate of H+ excretion and bicarbonate Reabsorption by renal tubules.

1- Rapid Mechanism (Buffer system)

Def 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 bicarbonate system.

The most important intracellular buffer systems are phosphates and proteins.(viiiiiiip)

A-Bicarbonate buffer system:
It consists of combination of carbonic acid and bicarbonate

This system accounts **for 65 % of buffering capacity i**n plasma and **40 % of buffering action in the whole body.** Bicarbonate is regulated by the kidney (Metabolic component) while the 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-.

$HCL + NaHCo3 \rightarrow NaCl + H2Co3$

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

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

$NaOH + H2Co3 \rightarrow NaHCo3 + H2O$

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 mainly an intracellular buffer.

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.

2-Respiratory regulation (Intermediate Mechanism):

The respiratory system has the ability to eliminate the excess H2Co3

Because $H_2Co_3 \leftrightarrow H_2O + CO_2$

So

In acidosis $\rightarrow \uparrow H_2CO_3 \rightarrow \uparrow CO_2$

In the blood $\rightarrow$ stimulate Respiratory center $\rightarrow \uparrow$ 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.

The proximal tubule.

Hydrogen ion secretion and bicarbonate Reabsorption.

1-The proximal tubule is responsible for Reabsorption of most of the HCO3- that enters the nephron at the glomerulus.

2-In the proximal tubule:

a- H+ is secreted from the cells into the lumen in exchange with filtered Na+ using Na+ - H+ antiport protein

b-The secreted H+ combine with filtered HCO3 forming H2CO3 that dissociates in the lumen into CO2 + H2O.

c- CO2 diffuse to the tubular cells and combine with H2O to form H2CO3 that dissociate into H+ and HCO3-

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.

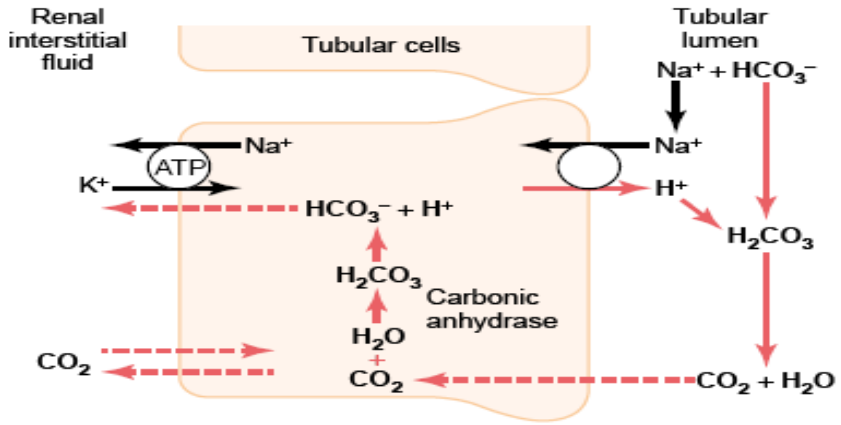


Figure (23): H+ secretion and HCO3- reabsorbtion in PCT.

3-In distal tubule:

The distal nephron (distal tubule and collecting duct) plays a significant role in fine regulation of acid – base balance.

It contain 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 ,this enzyme allows them to convert large amounts of CO2 into H+ and HCO3-

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

H+ - ATPase

H+ / K+ ATPase

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

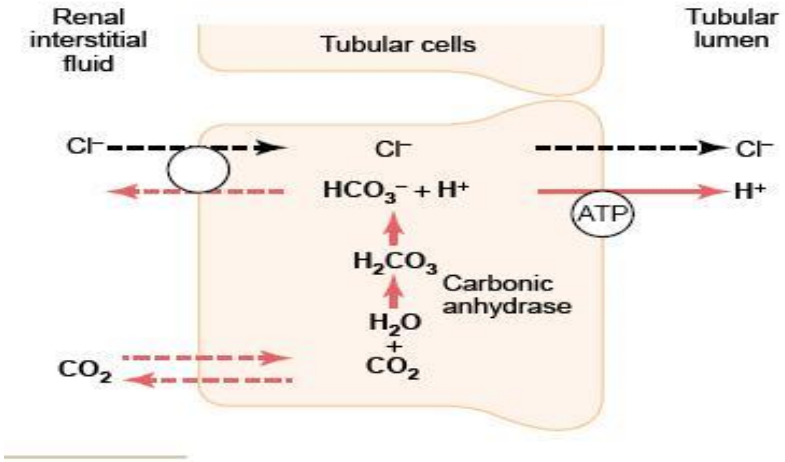


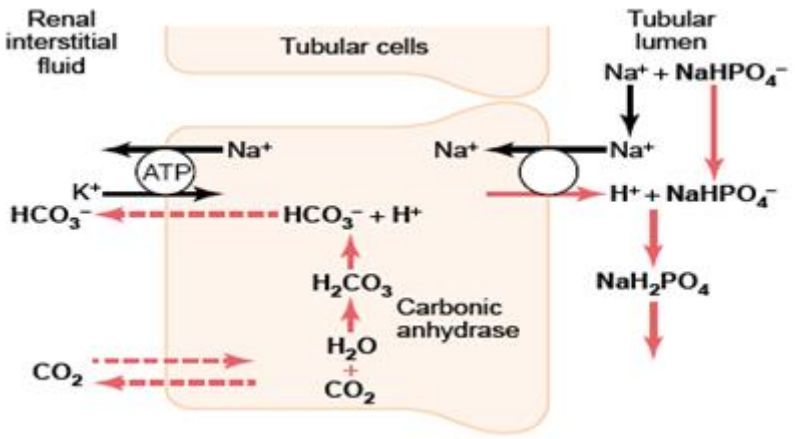
Figure (24): Primary active secretion of hydrogen ions through intercalated cells

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 make new HCO3 from CO2 and H2O and HCO3 is reabsorbed into the blood to act as buffer to increase the PH.



Figure(25): Buffering of secreted hydrogen ions by filtered phosphate (NaHPO4).

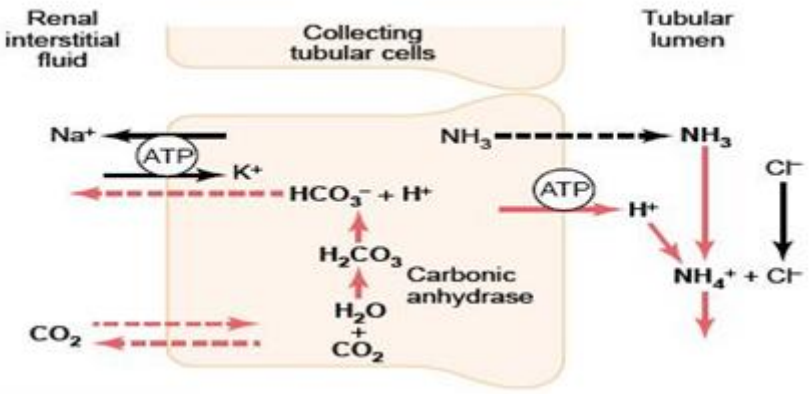


Figure (26): Buffering of hydrogen ion secretion by ammonia (NH3) in the collecting tubules.

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 transform 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 HCO_3 is so extreme that compensatory mechanisms fail to maintain PH homeostasis.

The normal range of the PH is 7.38 – 7.42.

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 HCO_3 i.e arises from acids or bases of non CO_2 origin but it is respiratory (acidosis or alkalosis) if the disturbance is in PCO_2 which result from hypo or hyper ventilation.