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) As lactic acid And Ketoacids

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.

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.

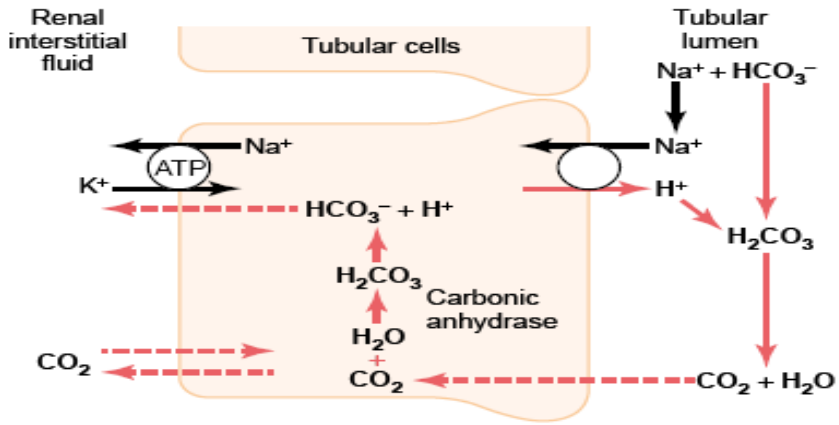


Figure (23): H+ secretion and HCO3- reabsorbtion in PCT.

3-In distal tubule:
The distal nephron (distal tubule and collecting duct) plays a significant role in fine regulation of acid – base balance.
It 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, 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 counter transprt
While in proximal tubule it is Na+ - H+ antiport protein.

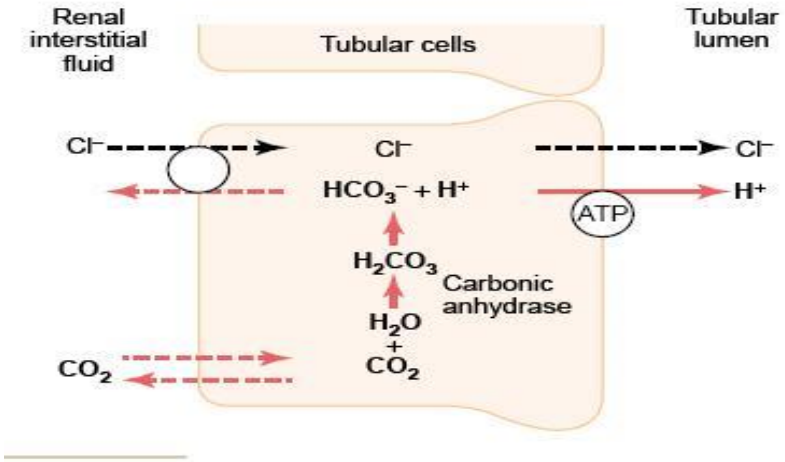
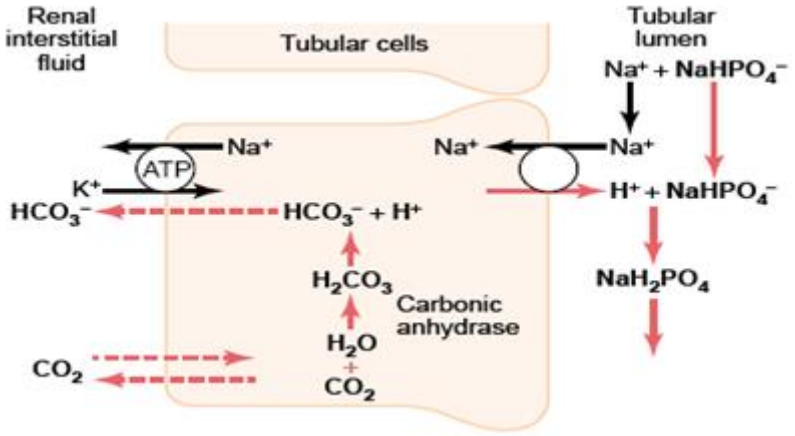


Figure (24): Primary active secretion of hydrogen ions through intercalated cells

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).

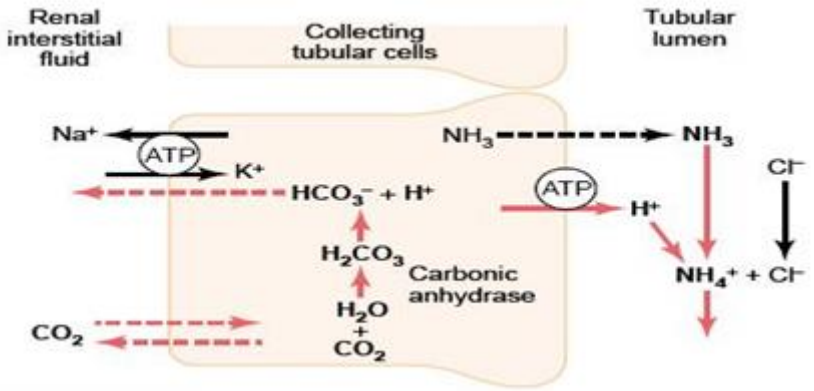


Figure (26): Buffering of hydrogen ion secretion by ammonia (NH3) in the collecting tubules.

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.

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.

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.

Acidosis

Two types:

1-Respiratory acidosis.

2-Metabolic acidosis.

1-Respiratory acidosis:

Characterized by an increase in PCO2 of artertial blood more than 45 mmHg ,which is normally 40 mmHG , this leads to an increase in H2CO3 in the blood ,while HCO3 remains constant.

Causes.

1-Inadequate ventilation to remove the produced CO2 leading to its retention as in bronchial asthma and emphysema that leads to inadequate alveolar ventilation.

2-Disorders in diffusion of CO2 from the blood to alveolar air across the pulmonary membrane e.g pulmonary fibrosis, pulmonary edema and pneumonia.

3-Disorders that lead to decreasing the movement of thoracic cage e.g chest trauma ,deformities ,weakness or paralysis of respiratory muscles e.g due to poliomyelitis

4-Conditions of decreased rate or depth of respiration caused usually by depression of respiratory center due to use of some narcotic drugs (e.g morphine) or sedatives e.g barbiturates

Compensation.

Because the proplem is of respiratory origin ,the body can not carry respiratory compensation , any compensation must be through renal mechanisms that secrete H+ and absorb HCO3

Secreted H+ allows urine to be more acidic

Reabsorption of HCO3 provides additional buffer that combines with H+ lowering the amount of free H+ and also raising the PH.

Metabolic Acidosis:

It occur when dietary and metabolic input of acids exceeds acid excretion

Metabolic causes include.

1-Lactic acidosis which result from anaerobic metabolism.

2-Keto- acidosis when there is excessive breakdown of fats or certain amino acids.

3-Ingested toxins that cause metabolic acidosis as methanol, asprin ,and ethylene glycol.

4-Diarrhea ,due to loss of HCO3 from intestine.

There is elevated H+ concentration

Decreased HCO3 concentration.

Compensation.

Elevated H+ and CO2 stimulate ventilation leading to decreased PCO2 to normal or even below normal due to hyperventilation.

Renal compensation also takes place by increased secretion of H+ ,with Reabsorption of HCO3

Renal compensation takes several days to reach full effectivness so usually no seen in acute disturbances since it start within 24 – 48 hours.

Alkalosis

2 types:
1-Respiratory alkalosis
2-Metabolic alkalosis.

1-Respiratory alkalosis.
Causes.
1-Hyperventilation due to wash of CO2.
Drop of CO2 decreases both H+ and HCO3 ,so low HCO3 in alkalosis indicate respiratory disorder ,the most common physiological cause of respiratory alkalosis is hysterical hyperventilation due to anexiety .The proplem can be corrected by allowing the patient to rebreath the exhaled CO2 by allowing the patient to breath into a paper bag ,the rise of arterial PCO2 corrects the proplem.
2-Metabolic alkalosis.
Caused by.
1-Excessive vomiting of acidic gastric contents.
2-Excess ingestion of bicarbonate containing antacids.
In both cases the resulting alkalosis reduces H+ concentration.

Metabolic alkalosis is characterized by
Decreased H+ concentration and PCO2
Increased HCO3 concentration.

Compensation.
Respiratory compensation is very rapid
Increased PH and drop of PCO2 depress ventilation leading to increased CO2 and creating more H+ and HCO3 so ventillatory compensation help to correct PH but elevates HCO3.
Renal compensation.
By HCO3 excretion and H+ Reabsorption.