ACID BASE BALANCE

Acid base balance is very important for the homeostasis of the body and almost all the physiological activities depends upon the acid base status of the body.

Hydrogen ion (H^+) and pH – An acid is the proton donor (the substances that liberate hydrogen ion). Hydrogen ion (H^+) contains only a single proton (positive charged particle) which is not orbited by an electron. Therefore, it is the smallest ionic particle. However, it is highly reactive. Because of this, the H^+ shows severe effects on the physiological activities of the body even at low concentration. The normal H^+ concentration in ECF is 38-42 nM/L.

pH- the pH is another term for H^+ concentration that is generally used now a day instead of hydrogen ion concentration. The negative logarithm of hydrogen ion concentration expressed in molarity is called pH.

$$pH = \text{Log } \frac{1}{H^+}$$

An increase in H^+ ion concentration decreased the pH (acidosis) and a reduction in H^+ concentration increased the P^H (alkalosis). An increase in pH by one fold requires a tenfold decrease in H^+ concentration. In healthy person, the pH of the ECF is 7.40 and it varies between 7.38-7.42.

H^+ (nM/L)	pH
10000	5.0
1000	6.0
100	7.0
10	8.0
1	9.0

Table- Relation between H^+ ion concentration and pH

Regulation of acid base balance-

Body is under constant threat of acidosis because of the production of large amount of acids. Generally two types of acids are produced in the body-

1. Volatile- it is almost totally removed through expired air by lungs.
2. Non volatile- nonvolatile acids are produced during the metabolism of nutritive substances such as proteins. For example- sulfuric acid is produced during the metabolism of sulfur containing amino acid such as cysteine, metheonine and hydrochloride acid is produced during the metabolism of lysine, arginine and histidine.

Whenever there is a change in pH beyond the normal range, some compensatory mechanism plays an important role to bring the pH to normal level. The body has three different mechanisms to regulate acid base status-

1. Acid Base buffer system
2. Respiratory mechanism
3. Renal mechanism

Regulation of acid base balance by acid base buffer systems

The buffer system maintains pH by binding with free H^+ ion. Acid base buffer system is the combination of a weak acid (protonated compound) and a base the salt (unprotonated compound). The buffer system is the one, which acts immediately to prevent the changes in pH. The body fluids have three types of buffer systems, which act under different conditions-

A. Bicarbonate buffer system- It consists of the protonated substance- carbonic acid (H_2CO_3) which is a weak acid and the unprotonated substance HCO_3^- which is a weak base. HCO_3^- is the form of salt, ie sodium bicarbonate ($NaHCO_3$).

Bicarbonate buffer system prevents the fall of pH in a fluid to which a strong acid like HCl is added. Normally, when HCl is mixed with a fluid, the pH of the fluid decrease quickly because the strong HCl dissociates into H^+ and Cl^-.

But, if bicarbonate buffer system ($NaHCO_3$) is added to the fluid with HCl, the pH is not altered much. This is because the H+ dissociated from the HCl combines with HCO_3^- of $NaHCO_3$ and forms a weak H_2CO_3. This H_2CO_3 is turn dissociates into CO_2 and H_2O.

$$HCl + NaHCO_3 \longrightarrow H_2CO_3 + NaCl$$
$$\downarrow$$
$$CO_2 + H_2O$$

The bicarbonate buffer system also prevents the increase in pH in a fluid to which a strong base like NaOH is added.

Normally, when a base (NaOH) is added to a fluid, Ph increases. It is prevented by adding H_2CO_3 which dissociates into H^+ and HCO_3^-. The hydroxyl group (OH) of NaOH combines with H^+ and forms H_2O. And Na^+ combines with HCO_3^- and forms $NaHCO_3$. $NaHCO_3$ is a weak base and it prevents the increase in pH by the strong NaOH.

Importance of bicarbonate buffer system

The bicarbonate buffer system is not powerful like the other buffer systems because of the large difference between the pH of the ECF (7.4) and the pK of the bicarbonate buffer system (6.1). But this buffer system plays an important role in maintaining the pH of the body fluid than the other buffer systems. It is because the concentration of two components (HCO_3^- and CO_2) of this buffer system is regulated separately by two different mechanisms. The concentration of HCO_3^- is regulated by kidney and the concentration of CO_2 is regulated by the respiratory system. These two regulatory systems operate constantly and simultaneously, making the system more effective.

B. Phosphate buffer system- This system consists of a weak acid, the hydrogen phosphate ($H_2PO_4^-$ protonated substance) in the form of sodium hydrogen phosphate (NaH_2PO_4) and the base, hydrogen phosphate (HPO_4^- unprotonated substance) in the form of disodium hydrogen phosphate (Na_2HPO_4).

Phosphate buffer system is useful in the ICF (in red blood cells or other cells) as the concentration of phosphate is more in ICF than in ECF. When a strong acid like HCl is mixed with a fluid concentrating phosphate buffer, sodium dihydrogen phosphate ($NaH_2PO_4^-$ weak acid) is formed. This permits only a mild change in the pH of the fluid.

$$HCl + Na_2HPO_4 \longrightarrow NaH_2PO_4 \text{ (weak acid)} + NaCl$$

If a strong base such as sodium hydroxide (NaOH) is added to the fluid containing phosphate buffer, a weak base called disodium hydrogen phosphate (Na_2HPO_4) is formed. This prevents the changes in P^H.

$$NaOH + NaH_2PO_4 \longrightarrow NaHPO_4 \text{ (weak base)} + H_2O$$

Importance of phosphate buffer system-

Phosphate buffer system is more powerful than bicarbonate buffer system as it has a Pk of 6.8 which close to the P^H of the body fluids, 7.4. In addition to ICF, phosphate buffer is useful in tubular fluids of kidneys also. It is because more phosphate ions are found in tubular fluids.

In the RBC, the potassium ion concentration is higher than the sodium ion concentration. So, the elements of phosphate buffer inside the RBC are in the form of potassium dihydrogen phosphate (KH_2PO_4) and dipotassium hydrogen phosphate (K_2HPO_4)

C. Protein buffer system- The protein buffer system are present in the blood; both in the plasma and erythrocytes.

a. Protein buffer in plasma- The elements of proteins, which form the weak acids in the plasma, such as- i. C-terminal carboxyl group, N-terminal amino group and side chain carboxyl group of glutamic acid.

ii. Side chain amino group of lysine

iii. Imidazole group of histidine

The protein buffer systems in plasma are more powerful because of their high concentration in plasma and their pK being very close to 7.4.

b. Protein buffer in erythrocyte- hemoglobin is the most effective protein buffer and the major buffer in blood. Due to its high concentration than the plasma proteins, hemoglobin has about six times more buffering capacity than the plasma proteins. The deoxygenated hemoglobin is more powerful buffer than oxygenated hemoglobin because of the higher pK. When a hemoglobin molecule becomes oxygenated in the capillaries, it easily bind with H^+ ions, which are released when CO_2 enters the capillaries. Thus, hemoglobin prevents fall in pH when more and more CO_2 enters the capillaries.

Regulation of acid base balance by respiratory mechanism

The lungs play an important role in the maintenance of acid-base balance by removing CO_2 which is produced during various metabolic activities in the body. This CO_2 combines with water to form carbonic acid. Since carbonic acid is unstable, it splits into H^+ ion and HCO_3^-.

$$CO_2 + H_2O \longrightarrow H_2CO_3 \longrightarrow H^+ + HCO_3^-$$

The entire reaction is reversed in lungs when CO_2 diffuses from blood into the alveoli of lungs.

$$H^+ + HCO_3^- \longrightarrow H_2CO_3 \longrightarrow CO_2 + H_2O$$

And CO_2 is blown off by ventilation. When metabolic activities increase, more amount of CO_2 is produced in the tissues and the concentration of H^+ ion increases. The increased H^+ ion concentration increases the pulmonary ventilation (hyperventilation) by acting through the chemoreceptors. Due to hyperventilation, the excess of CO_2 removed from the body.

Regulation of acid base balance by renal mechanism

Kidney maintains the acid base balance of the body by excreting hydrogen ions and retaining bicarbonate ions. The excretion of H^+ and retention of HCO_3^- occurs by three mechanisms:

1. Bicarbonate mechanism
2. Phosphate mechanism
3. Ammonia mechanism

Bicarbonate mechanism- In the tubular cells, CO_2 combines with water to form carbonic acid. It immediately dissociates into H^+ and HCO_3^- from the tubular cell enters the interstitium. Simultaneously Na^+ is reabsorbed from the renal tubule under the influence of aldosterone. HCO_3^- combines with Na^+ to form $NaHCO_3$. Now, the H+ is secreted into the tubular lumen from the cell in exchange for Na+.

Thus, for every H^+ ion secreted into the lumen of tubule, one bicarbonate ion is reabsorbed from the tubule. In this way, kidneys conserve the HCO_3^- .The reabsorption of filtered HCO_3^- is an important factor in maintaining pH of the body fluids.

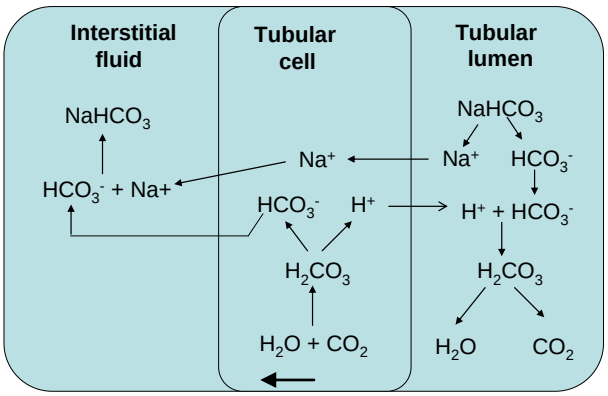

Fig- Reabsorption of bicarbonate ions by secretion of hydrogen ions in renal tubules

Phosphate mechanism: The H^+, which is secreted into the renal tubules, reacts with phosphate buffer system. It combines with sodium hydrogen phosphate. Sodium hydrogen phosphate is excreted in urine. The H^+, which is added to urine in the form of sodium hydrogen, makes the urine acidic. It happens mainly in the distal tubules and collecting duct because of the presence of large quantity of sodium hydrogen phosphate in these segments.

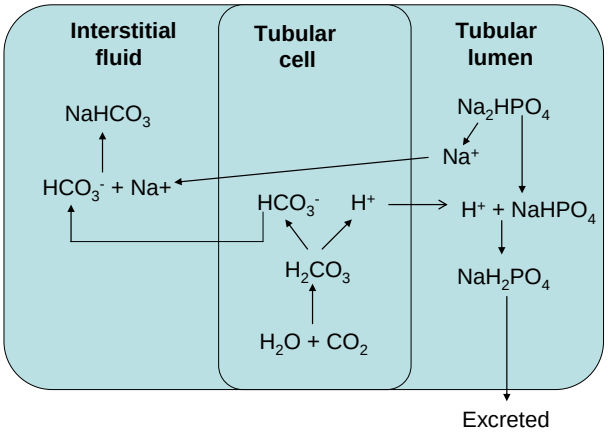

Fig- Excretion of hydrogen ions in combination with phosphate ions

Ammonia mechanism: The ammonia (NH_3) formed in tubular cells is secreted into the tubular lumen in exchange of sodium ion. Here, it combines with H^+ to form ammonium (NH_4). The tubular cell membrane is not permeable to ammonium. Therefore, it remains into the lumen and combine with sodium aetoacetate to form ammonium aetoacetate. Ammonium aetoacetate is excreted through urine. Thus, H^+ is added to urine in the form of ammonium compounds resulting in acidification of urine.

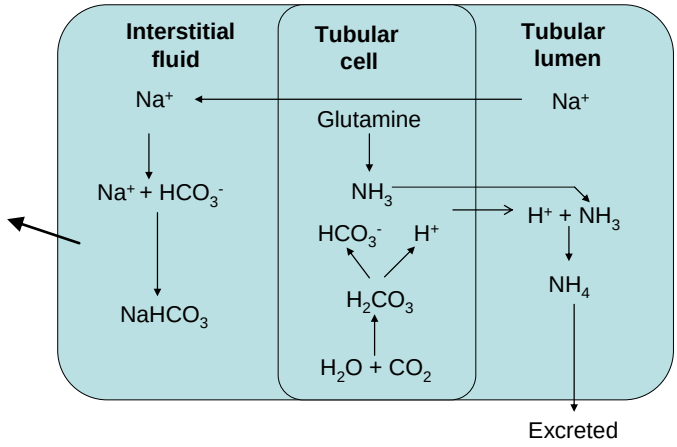

Fig- Excretion of hydrogen ions in combination with ammonia

Thus, by excreting H^+ and conserving HCO_3^-, Kidneys produce acidic urine and help to maintain acid- base balance of body fluids.

Disturbances of acid base status

Acidosis- Acidosis is the reduction in pH (increase in H^+ ion concentration) below normal range. The acidosis is produced by-

1. Increase in partial pressure of CO_2 in the body fluids particularly in arterial blood
2. Decrease in HCO_3^- concentration.

Acidosis usually two types-

A. **Respiratory acidosis-** Respiratory acidosis is the acidosis that is caused by alveolar hypoventilation. During hypoventilation the lungs fail to expel CO_2 which is produced in the tissues due to oxidation of carbohydrate, proteins and fats.

Causes of excess CO_2 in the body-

1. Airways obstruction due to bronchitis, emphysema etc.
2. Lung diseases like fibrosis, pneumonia etc.
3. Respiratory center depression by anesthesia, sedatives, cerebral trauma, tumors etc.
4. Neural diseases like polyomyelitis, paralysis of respiratory muscles.

CO_2 accumulates of in blood when it reacts with water to form carbonic acid which is called respiratory acid. Carbonic acid dissociates into H^+ and HCO_3^-. The increased H^+ concentration in blood leads to decrease in pH and acidosis occur. The normal partial pressure of CO_2 in arterial blood is about 40 mm Hg. When in increases above 60 mm Hg acidosis occurs.

B. Metabolic acidosis- Metabolic acidosis is the acid base imbalance characterized by excess accumulation of organic acid in the body which is caused by abnormal metabolic processes. Organic acids such as lactic acid, ketoacids and uric acids are formed by normal metabolism but their levels are increased due to abnormality in the metabolism.

Causes of metabolic acidosis-

1. Lactic acidosis as in circulatory shock
2. Ketoacidosis as in diabetes mellitus
3. Uric acidosis as in renal failure
4. Acid poisoning
5. Renal tubular acidosis due to decreased H^+ excretion.
6. Loss of excess HCO_3^- due to diarrhea

Alkalosis- Alkalosis is the increase in pH (decrease in H^+ ion concentration) above the normal range. The alkalosis is produced by:

1. Decrease in partial pressure of CO_2 in the arterial blood or
2. Increase in HCO_3^- concentration.

Alkalosis usually two types-

Respiratory alkalosis- Respiratory alkalosis is the alkalosis that is caused by alveolar hyperventilation. Hyperventilation causes excess loss of CO_2 in the body. Loss of CO_2 in the body lead to decrease formation of carbonic acid and decrease release of H^+, increase the pH leading to respiratory alkalosis. When the partial pressure of CO_2 in arterial decreases below 20 mm Hg, alkalosis occurs.

Causes of respiratory alkalosis-

1. Hypoxia in high altitude
2. Severe anemia and pulmonary disease like edema and embolism
3. Increase respiratory drive due to cerebral disturbances, voluntary hyperventilation and psychological and emotional trauma.

Metabolic alkalosis-Metabolic alkalosis is the acid-base imbalance caused by the loss of excess H^+ resulting in increased HCO_3^- concentration. Some of the endocrine disorders, renal tubular disorders, etc cause metabolic disorders leading to loss of H^+. It increases HCO_3^- and pH in the body leading to metabolic alkalosis.

Causes of metabolic alkalosis-

1. Vomiting and congenital diarrhea
2. Endocrine disorders such as Cushing's syndrome and Conn's syndrome
3. Diuretic therapy.