Acid Base Balance

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PROGRAMME OUTCOMES

- PO1- Demonstrate comprehensive knowledge and application of the Trisutra concept to explore root causes, identify clinical manifestations of disease to treat ailments and maintain healthy status.
- PO2- Demonstrate knowledge and skills in Ayurveda, acquired through integration of multidisciplinary perspectives and keen observation of clinical and practical experiences.

COURSE OUTCOMES

- CO1- Explain all basic principles & concepts of Kriya Sharir along with essentials of contemporary human physiology and biochemistry related to all organ systems.

- **Teaching learning methods-** lecture with power point presentation
  Domain- Cognitive/comprehension
  Must to know / desirable to know / Nice to know- Must to know
  Millers pyramid- Knows how(applied knowledge)
  Bloom taxonomy- Understand

Introduction

1. An Acid is a substance that acts as a **proton (i.e. H+) donor**. The acids (such as hydrochloric and sulphuric acids) that are 100% ionized in solution are known as **strong acids**; while carbonic and lactic acids, which do not completely ionize in solution, are **weak acids**. The acidity of a solution refers to the free (unbound) H+ concentration in the solution.

2. A Base is a substance that **accepts protons (i.e. H+) in solution** e.g. bicarbonate ion (HCO^{3-}), phosphate ion (HPO_4^{2-}), acetate ion ($CH3COO^-$), proteinate$^-$, $HbO2^-$ and Hb^-. **Strong bases** are 100% ionized in solution while **weak bases** are only partially ionized.

3. The body produces large amounts of acid in two forms:

(i) Carbonic acid (H_2CO_3) is called volatile acid because CO_2 can be formed from H_2CO_3 and, in turn can be eliminiated by the lungs, and

(ii) **Non Carbonic acids** cannot be converted to CO_2 and, therefore, are called Non-volatile or fixed acids e.g H_2SO_4 (a product of protein catabolism), HCl, phosphoric acid (H_3PO_4 a product of phospholipid metabolism), ketoacids (aceto-acetic acid and beta hydroxy-butyric acid) and lactic acid.

However, body fluids are maintained in an alkaline state (pH = 7.4).

- **4. Sources of H+**
- **(i) As an end product of metabolism:** the greatest source of H^+ is CO_2 produced as end product of cellular metabolism, the amount of CO_2 produced during a day in a normal individual is capable of forming 20- 40 mEq of H^+
- **(ii) Diets** which are high in protein, generate between 50-100 mEq of H+ per day. High protein diets contain large amounts of phosphorus and sulphur ; oxidation of these complexes forms anions of phosphate (PO_4^{3-}) and sulphate (SO_4^{2-}) which lead to formation of non carbonic acid e.g. H_3PO_4 and H_2SO_4
- **(iii) Renal tubular generation of H^+.** Therefore, in renal failure, failure to excrete normal acid load leads to acidosis.
- **(iv) Waste products of metabolism** form acid phosphate ($H_2PO_4^-$).
- **(v) Strenuous exercise** leads to formation of lactic acid from skeletal muscles.

- **(vi) Under some pathological conditions** such as starvation or uncontrolled diabetes mellitus accumulation of organic acids such as acetoacetic acid and beta-hydroxybutyric acid occurs.
- **(vi) Ingestion of acidifying salts** e.g. NH_4Cl and $CaCl_2$ which in effect add HCl to the body.
- **5. Compensatory Mechanism**

Whenever there is a change in pH beyond the normal range, some compensatory changes occur in the body to bring the pH back to normal level. There are three processes available for acid removal i.e. for maintaining the concentration of H^+ within normal limits:

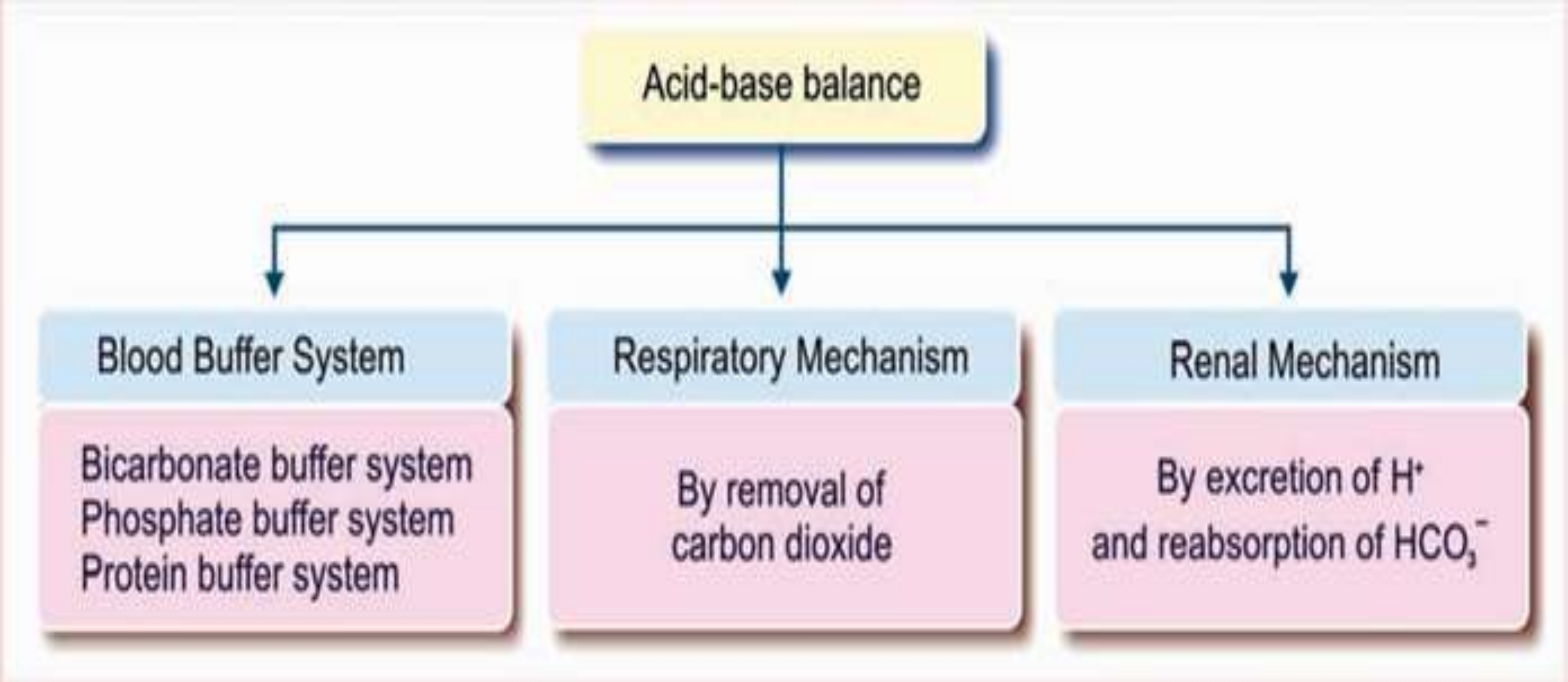
(i) Acid- Base buffer system, i.e combination of free H^+ with:

(a) a blood buffer e.g. HCO_3^-, haemoglobin; or

(b) an intracellular buffer e.g;. organic or inorganic phosphate

(ii) Reduction of Carbonic acid and elimination of CO2 via respiration.

(iii) Reduction of non-carbonic acid by renal elimination of H^+


Acid-base balance
Blood Buffer System
Bicarbonate buffer system
Phosphate buffer system
Protein buffer system
Respiratory Mechanism
By removal of carbon dioxide
Renal Mechanism
By excretion of H^+ and reabsorption of HCO_3^-

- Among the three mechanisms, the acid-base buffer system is the fastest one and it readjusts the pH within seconds.
- The respiratory mechanism does it in minutes. Whereas, the renal mechanism is slower and it takes few hours to few days to bring the pH back to normal.
- However, the renal mechanism is the most powerful mechanism than the other two in maintaining the acid base balance of the body fluids.

REGULATION OF ACID-BASE BALANCE BY ACID-BASE BUFFER SYSTEM

An acid-base buffer system is the combination of a weak acid (protonated substance) and a base – the salt (unprotonated substance). Buffer system is the one, which acts immediately to prevent the changes in pH. Buffer system maintains pH by binding with free H^+.

- **Types of Buffer Systems**
- Body fluids have three types of buffer systems, which act under different conditions:
  1. Bicarbonate buffer system
  2. Phosphate buffer system
  3. Protein buffer system.
- **1. Bicarbonate Buffer System**
- It is present in ECF (plasma). It consists of the protonated substance, carbonic acid ($H_2 CO_3$) which is a weak acid and the unprotonated substance, $HCO3^-$, which is a weak base. $HCO3^-$ is in the form of salt, i.e. sodium bicarbonate ($NaHCO_3$).

- **Mechanism of action of bicarbonate buffer system**
- Bicarbonate buffer system prevents the fall of pH in a fluid to which a strong acid like hydrochloric acid (HCl) is added. Normally, when HCl is mixed with a fluid, pH of that fluid decreases 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 HCl combines with $HCO_3^–$ of $NaHCO_3$ and forms a weak H_2CO_3 . This H_2CO_3 in turn dissociates into CO_2 and H_2O.

$$HCl + NaHCO_3 \rightarrow H_2CO_3 + NaCl$$

$$\downarrow$$

$$CO_2 + H_2O$$

- Bicarbonate buffer system also prevents the increase in pH in a fluid to which a strong base like sodium hydroxide (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 NaHCO3 . NaHCO3 is a weak base and it prevents the increase in pH by the strong NaOH.
- This buffer system plays an important role in maintaining the pH of body fluids than the other buffer systems.
- **2. Phosphate Buffer System**
- This system consists of a weak acid, the dihydrogen phosphate ($H_2PO_4^-$ protonated substance) in the form of sodium dihydrogen 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 intracellular fluid (ICF), in red blood cells or other cells, as the concentration of phosphate is more in ICF than in ECF.
- **Mechanism of phosphate buffer system**
- When a strong acid like hydrochloric acid is mixed with a fluid containing phosphate buffer, sodium dihydrogen phosphate (NaH_2PO_4 - weak acid) is formed. This permits only a mild change in the pH of the fluid.
- $HCl + Na_2HPO_4 \rightarrow NaH_2PO_4 + NaCl$

(strong acid) (weak acid)

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 pH.

$NaOH + NaH_2PO_4 \rightarrow Na_2HPO_4 + H_2O$

(strong base) (weak base)

- **3. Protein Buffer System**
- Protein buffer systems are present in the blood; both in the plasma and erythrocytes.

Protein buffer systems in plasma

- Elements of proteins, which form the weak acids in the plasma are:
- **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.
- Protein buffer systems in plasma are more powerful because of their high concentration in plasma

- **Protein buffer system in erythrocytes (Hemoglobin)**
- 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 a more powerful buffer than oxygenated hemoglobin.
- When a hemoglobin molecule becomes deoxygenated in the capillaries, it easily binds with H+, which are released when CO_2 enters the capillaries. Thus, hemoglobin prevents fall in pH when more and more CO_2 enters the capillaries.

- **PULMONARY REGULATION OF ACID BASE BALANCE**
- Lungs play a role in maintenance of acid base balance of the body by regulating the carbon dioxide content in blood.
- Carbon dioxide is produced during various metabolic reactions in the tissues of the body. When it enters the blood, carbon dioxide combines with water to form carbonic acid. Since carbonic acid is unstable, it splits into hydrogen and bicarbonate ions.
- $CO_2 + H_2O \rightarrow \mathbf{H_2CO_3 \rightarrow H^+ + HCO_3^-}$

  Entire reaction is reversed in lungs when carbon dioxide is removed from blood into the alveoli of lungs.

  $H^+ + HCO_3^- \rightarrow \mathbf{H_2CO_3 \rightarrow CO_2 + H_2O}$

  As carbon dioxide is a volatile gas, it is practically blown out by ventilation.
- When the respiratory system compensates for metabolic pH disturbances, the effect occurs in minutes to hours.

- **RENAL REGULATION OF ACID-BASE BALANCE**
- **1.** The kidneys are responsible for clearing the body of metabolically produced non-carbonic acids. Therefore, normal urine reaction is acidic in nature.
- **2.** The kidneys perform two major functions:
- **(i)** The kidneys stabilize the standard HCO_3^- pool by obligatory reabsorption (mainly by PCT) and by controlled reabsorption of filtered HCO_3^- (by the DCT and CT) .
- **(ii**) The kidneys excrete a daily load of 50-100 mEq of metabolically produced non-carbonic acid, which represents a H^+ excretion of 1 mEq/kg of body weight/day.

3 Role of Kidney in Preventing Metabolic Acidosis

Kidney plays an important role in preventing metabolic acidosis by excreting $\mathbf{H^+}$

Excretion of $\mathbf{H^+}$ occurs by three mechanisms:

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

- **BICARBONATE MECHANISM**
- All the filtered HCO_3^- in the renal tubules is reabsorbed. About 80% of it is reabsorbed in PCT, 15% in Henle loop and 5% in DCT and collecting duct.
- The reabsorption of HCO_3^- utilizes the H+ secreted into the renal tubules. **H+** secreted into the renal tubule, combines with filtered HCO_3^- forming carbonic acid (H_2CO_3).
- H_2CO_3 dissociates into CO_2 and H_2O in the presence of carbonic anhydrase. CO_2 and H_2O enter the tubular cell and combines to form H_2CO_3. It immediately dissociates into H+ and HCO_3^-.
- 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 sodium bicarbonate (NaHCO3). Now, the H+ is secreted into the tubular lumen from the cell in exchange for Na+.
- Thus, for every hydrogen ion secreted into 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.

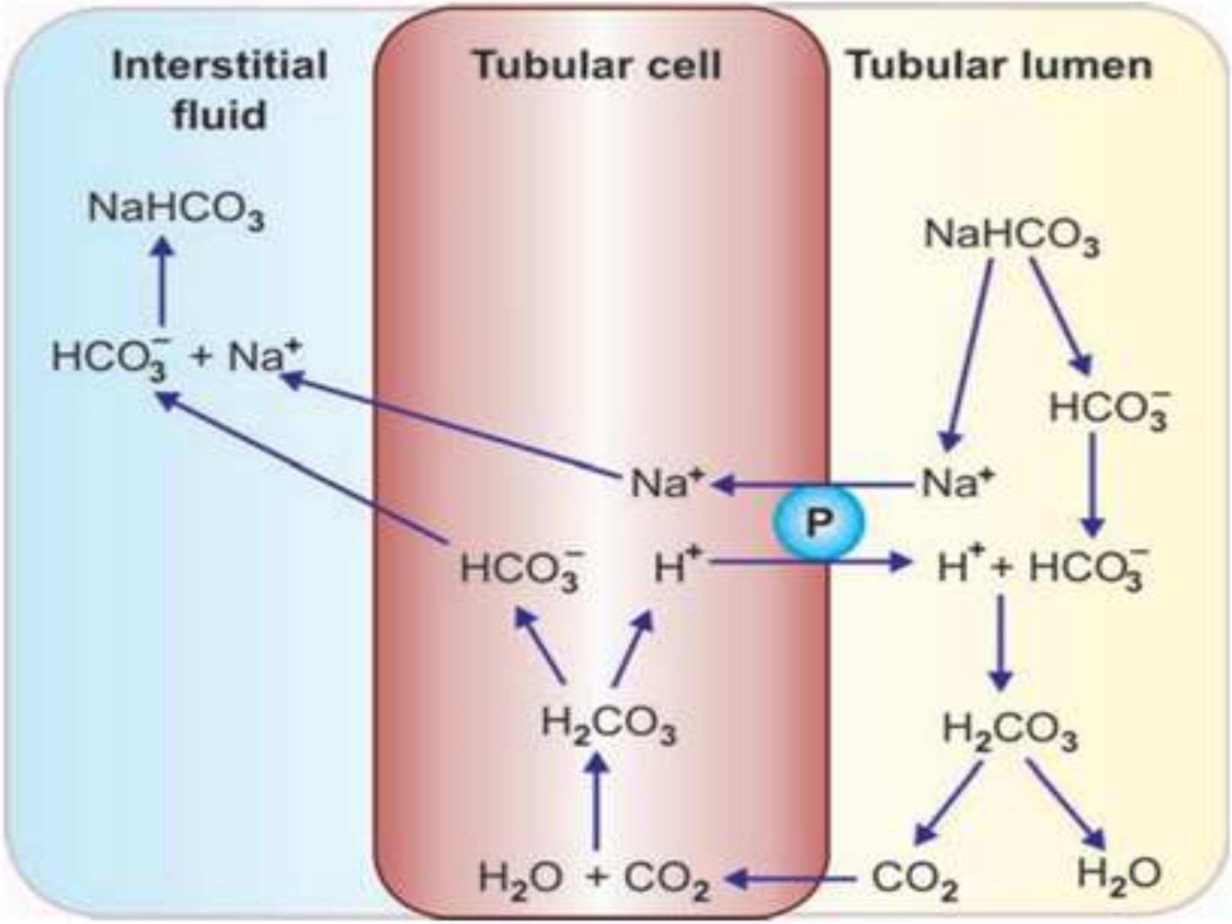


FIGURE 54.1: Reabsorption of bicarbonate ions by secretion of hydrogen ions in renal tubule. P = sodium-hydrogen antiport pump

- **PHOSPHATE MECHANISM**
- In the tubular cells, CO_2 combines with H_2O to form H_2CO_3. It immediately dissociates into H+ and **HCO_3^-**
- **HCO_3^-** from the tubular cell enters the interstitium. Simultaneously, Na+ is reabsorbed from renal tubule under the influence of aldosterone.
- Na+ enters the interstitium and combines with **HCO_3^-** H+ is secreted into the tubular lumen from the cell in exchange for Na+. H+, which is secreted into renal tubules, reacts with phosphate buffer system. It combines with sodium hydrogen phosphate to form sodium dihydrogen phosphate.
- Sodium dihydrogen phosphate is excreted in urine. The H+, which is added to urine in the form of sodium dihydrogen, makes the urine acidic. It happens mainly in distal tubule and collecting duct because of the presence of large quantity of sodium hydrogen phosphate in these segments.

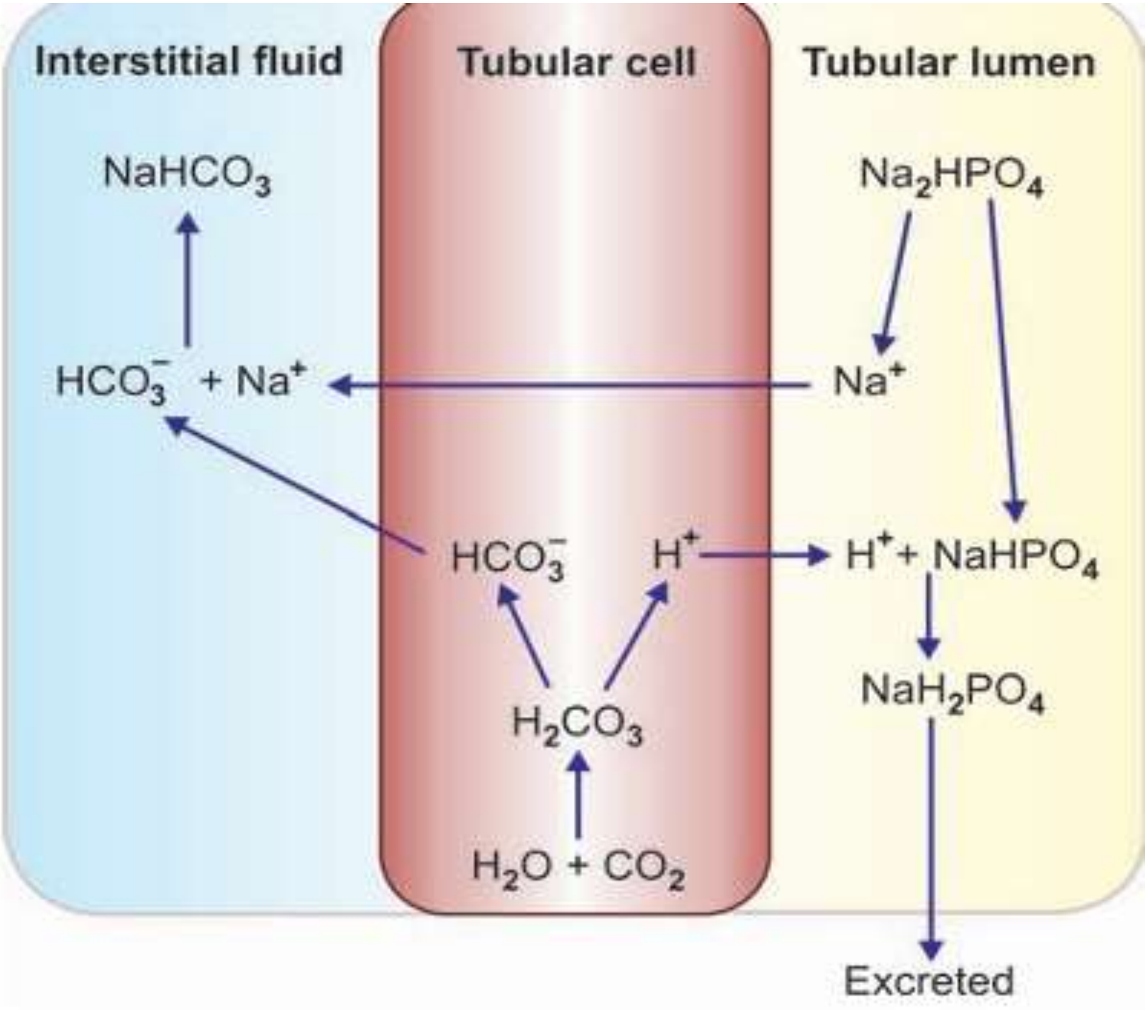


FIGURE 54.2: Excretion of hydrogen ions in combination with phosphate ions

- **AMMONIA MECHANISM**
- This is the most important mechanism by which kidneys excrete H+ and make the urine acidic.
- In the tubular epithelial cells, ammonia (NH3) is formed when the amino acid glutamine is converted into glutamic acid in the presence of the enzyme glutaminase. Ammonia is also formed by the deamination of some of the amino acids such as glycine and alanine .
- NH3 formed in tubular cells is secreted into tubular lumen in exchange for sodium ion. Here, it combines with H+ to form ammonium (NH4). The tubular cell membrane is not permeable to NH4. Therefore, it remains in the lumen and then excreted into urine.
- Thus, H+ is added to urine in the form of NH4 compounds resulting in acidification of urine. For each NH4 excreted one HCO3– is added to interstitial fluid. This process takes place mostly in the proximal convoluted tubule because glutamine is converted into ammonia in the cells of this segment.

THUS, BY EXCRETING H+ AND CONSERVING HCO3–, KIDNEYS PRODUCE ACIDIC URINE AND HELP TO MAINTAIN THE ACID-BASE BALANCE OF BODY FLUIDS.

Assessment

1. Write short notes on:

(i) Major buffer systems in kidney

(ii) Renal regulation of acid base balance

(iii) Volatile and non-volatile acid.

(iv) Buffer system in the kidney

2.Draw diagrams:

(i) Dibasic phosphate system

(ii) Ammonia buffer system

3. MCQ.

(i) False about volatile acid:

(a) Forms carbonic acid from CO2 (b) H2C03 is an example

(c) Forms CO2 from carbonic acid (d) Can be eliminated by the lungs

(ii) Greatest source of H+ in the body is:

(a) End product of cellular metabolism (b) High protein diet

(c) Synthesized by renal tubular cells (d) Waste product of metabolism

(iii) Major source of ammonia production in renal tubular cells is by:

(a) Deamination of glutamine (b) Deamination of glutamic acid

(c) Deamination of other amino acids: glycine, asparagine, alanine

(d) Comes directly from arterial blood

(iv) Not a true statement regarding fixed acids:

(a)Also called non-volatile acids or non-carbonic acids

(b) Cannot be converted to CO2 (c) Can be formed from H2CO3

(d) Ketoacids is an example

(v) The buffer system in the kidney to excrete H+ is all except:

(a) Bicarbonate (b) Ammonia

(c) Dibasic phosphate (d) Urate

THANKS