REGULATION OF ACID-BASE BALANCE

Q. What is the possible working principle of the acid-balance system?

i)In a typical diet, the majority of calories are ingested in the form of carbohydrates and fats. The complete metabolism of carbohydrates and fats requires O_2 and insulin and yields CO_2 and H_2O. With normal lung function, the CO2 produced (20 mol/day) is excreted, and there is no impact on the systemic acid-base balance. Because of the following reaction:

$$CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow HCO3^- + H^+$$

Alterations in ventilation: by changing the PCO_2 of the blood, will alter blood pH (e.g., an increase in PCO_2 produces **acidosis**, whereas a decrease in PCO_2 produces **alkalosis**).

ii)The metabolism of the amino acids in protein may produce either acids or alkali depending on the specific amino acid. However, the metabolism of dietary protein produces net acids (e.g., HCl of H_2SO4). These acids, often referred to as "non-volatile acids," are rapidly buffered:

$$HCl + NaHCO_3 \rightarrow NaCl + CO_2 + H_2O \qquad (2)$$

$$H_2SO_4 + 2NaHCO_3 \rightarrow Na_2SO_4 + 2CO_2 + 2H_2O \qquad (3)$$

iii)The CO_2 generated in this buffering process is excreted by the lungs, whereas the Na salts of the acids are excreted by the kidneys, principally with NH_4 [e.g., NH4Cl and (NH4)2SO4]. In the process of excreting NH_4, $HCO3^-$ is generated and returned to the blood to replace the $HCO3^-$ lost in titrating the nonvolatile acid.

iv)Other dietary constituents result in the generation of alkali. For example, when organic anions are metabolized to CO_2 and H_2O, H is consumed (i.e., HCO_3^- is produced). From a dietary perspective, fruits and vegetables result in the **generation of alkali**, whereas meat, grains, and dairy products generate acid.

v)In addition, the diet may contain various acids and alkalis that, when absorbed via the gastrointestinal tract, contribute to the net acid/alkali load to the body.

vi)Finally, each day, HCO_3^- is lost in the feces and thus imparts an acid load to the body. In a healthy individual consuming a "typical Western diet," there is a net addition of acid to the body. This acid, referred to as **net endogenous acid production** (NEAP), results in an equivalent loss of $HCO3^{-1}$, which must then be replaced.

vii)Importantly, the *kidneys excrete acid and*, in the process, generate HCO_3^-.

Thus, the systemic acid-base balance is maintained when **renal net acid excretion (RNAE)** equals NEAP. RNAE excretion can be quantitated by measuring the excretion of NH_4, titratable acid (TA), and $HCO3^-$.

It is important for students to recognize that RNAE excretion is accomplished by the transport of H^+ and HCO_3^- by the cells of the **nephron**.

viii)Through the action of various H^+ and HCO_3^- transporters, the kidneys reabsorb the filtered load of HCO_3^-, titrate urinary buffers, excrete NH_4, and acidify the urine. In the following sections each of these processes is reviewed.

Q.State the role of renal tubule in HCO_3^- reabsorpotion.

i)The cells of the nephron secrete H^+ into the tubular fluid and, in so doing, reabsorb the filtered load HCO_3^-. The contribution of each segment of the nephron to this process is shown in Figure 2.

At a plasma HCO_3^- concentration of 24 meq/l and *a glomerular filtration rate of 180 l/day*, the filtered load of HCO_3^- is > 4,300 meq/day. Approximately 80% of this filtered load is reabsorbed by the proximal tubule. An additional 16% is reabsorbed by the thick ascending limb and distal convoluted tubule, and the remainder (4%) is reabsorbed by the collecting duct.

ii)The cellular mechanisms by which H^+ and HCO_3^- are transported across the apical and basolateral membranes of **the proximal tubule** are shown in Figure 3.

iii)H^+secretion across the apical membrane occurs **by two mechanisms**. The primary mechanism is a Na^+/H^+ antiporter [Na^+/H^+ exchanger 3 (NHE3)]. It is estimated that two-thirds of proximal HCO_3^- reabsorption occurs via H^+ secretion by NHE3.

iv)Vacuolar H^+-ATPase provides another mechanism for apical H^+ secretion and is responsible for approximately one-third of HCO_3^- reabsorption.

v)As shown in Figure 3, **carbonic anhydrase (CA)** plays an important role in H^+ section and HCO_3- reabsorption.

vi)Within the cell, CA-II facilitates the generation of $H^+$and HCO_3^-. The H^+ is then secreted into the tubular fluid