

## REGULATION OF ACID-BASE BALANCE

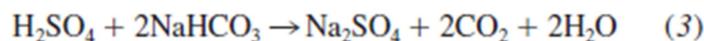
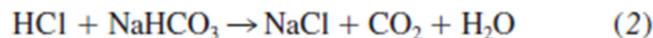
### Q. What is the possible working principle of the acid-balance system?

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  $CO_2$  produced (20 mol/day) is excreted, and there is no impact on the systemic acid-base balance. Because of the following reaction:



**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  $H_2SO_4$ ). These acids, often referred to as “non-volatile acids,” are rapidly buffered:



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.,  $NH_4Cl$  and  $(NH_4)_2SO_4$ ]. In the process of excreting  $NH_4$ ,  $HCO_3^-$  is generated and returned to the blood to replace the  $HCO_3^-$  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  $HCO_3^-$ , 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  $HCO_3^-$ .

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 $HCO_3^-$ reabsorption.

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  $H^+$  secretion 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