Lecture-8

Regulation of acid-base balance

Balance between acid and based is essential for metabolic processes. Reaction of any solution depends on free hydrogen ions concentration ($[H^+]$). The term used to indicate $[H^+]$ is pH . pH is negative logarithm of hydrogen ions concentration:

$$pH = - \log [H^+]$$

pH depends on balance between $[HCO_3]$ and CO_2. CO_2 concentration is regulated by lungs. Bicarbonate ion $[HCO_3]$ is a base, metabolized mainly in kidneys. CO_2 dissolves in plasma, forming carbonic ion (H_2CO_3), which is main acid component of blood, as it's difficult to determine H_2CO_3 concentration directly, acid component is expressed as carbon dioxide concentration in normal CO_2 to HCO_3 ratio is approximately 1/20. In different cases of acid base disturbances when acid content increases - acidosis will develop, if base content increase – alkalosis will develop.

Regulation of acid - Base Balance

The main buffer systems are following:

1. **Bicarbonate buffer:** The most important extracellular buffer produced by kidneys, has the largest buffering capacity.
2. **Haemoglobin buffer:** Main intracellular buffer of the blood.
3. **Protein buffer:** An extracellular buffer together with bicarbonate buffer, represented by plasma proteins.
4. **Phosphate buffer:** It takes part in hydrogen ions excretion in renal tubules, is not of great importance in blood.

Main blood buffer systems:

Buffer system	Buffering capacity (%)
Bicarbonate	53
Haemoglobin	35
Protein	7_
Phosphate	5

Cellular mechanisms of regulation of acid-base: Change in blood pH causes activation of cellular mechanisms of maintaining constancy of hydrogen ions concentration in extra-cellular fluid:

• If pH increases hydrogen ions move from cells to extracellular fluid in exchange of potassium ions that enter the cells and alkalosis is usually accompanied by hypokalaemia.

- If pH decreases hydrogen ions enter the cells in exchange of potassium ions that leaves the cells and acidosis may cause hyperkalaemia. In such a way electro-neutrality law is maintained by cellular regulation. According to it, the sum of the positive and negative charges (cations and anions) is equal. So, hydrogen to potassium exchange between ECF and ICF should be equal.

Organ mechanisms of regulation of acid-base:

- **Respiratory mechanisms:** Lungs are responsible for volatile acid (carbon dioxide) emanation. CO_2 content in plasma depends on alveolar ventilation. Changes in pH lead to stimulation of chemo-receptor's in the brain stem, causing a compensatory mechanism; therefore changing the respiratory rate. In acidosis alveolar ventilation increases, $PaCO_2$ decreases and pH tends to return to normal. These changes occur rapidly, but it takes 12 to 24 hours to stabilize acid-base status. Alkalosis causes hypoventilation and rise in $PaCO_2$, that leads to fall in pit.

- **Renal mechanisms:** Renal mechanisms are the most complex and effective. Renal compensation occurs by three main mechanisms:
  1. Bicarbonate ions reabsorption in proximal tubules
  2. Bicarbonate ions regeneration in distal tubules
  3. Hydrogen ions excretion.

CO_2 reacts with water to produce carbonic acid into the renal tubular cells. Carbonic acid dissociates to yield H^+ and HCO_3^- reaction is catalyzed by carbonic anhydrase. Bicarbonate ion enter the systemic circulation, is secreted into the lumen. The secretion is coupled to the reabsorption of Na* and electro neutrality preserved. The secreted reacts with filtered bicarbonate to produce carbonic acid that dissociate into carbon dioxide and water. Hydrogen ions excretion begins at the second stage when the whole bicarbonate is reabsorbed. HPO_4 ion can't be reabsorbed from renal tubules because of charge, but it can bind secreted hydrogen ions. Produced H_2PO_4 - is excreted in urine, HCO_3 is reabsorbed into the blood.

After depletion of the latter mechanisms, the kidneys switch to ammonia buffer (NH_3/NH_4^+). The main source of ammonia is glutamine deamination. As NH_3 has no charge, it moves freely across the tubular cell membrane and appears in the urine, where it binds scatted proton to produce ammonium ions (NH_4^+). NH_4^+ can't be reabsorbed because of its charm. This process is termed as ammoniogenesis.