# 21 WATER, ELECTROLYTE, AND ACID-BASE BALANCE

The organism possesses tremendous capacity to survive against odds and maintain homeostasis. This is particularly true with regard to water, electrolyte and acid-base status of the body. These three are interrelated, hence they are considered together for the discussion.

## WATER AND LIFE

Water is the solvent of life. Undoubtedly, water is more important than any other single compound to life. It is involved in several body functions.

### Functions of water

1. Water provides the aqueous medium to the organism which is essential for the various biochemical reactions to occur.

2. Water directly participates as a reactant in several metabolic reactions.

3. It serves as a vehicle for transport of solutes.

4. Water is closely associated with the regulation of body temperature.

### Distribution of water

Water is the major body constituent. An adult human contains about 60% water (men 55-70%; women 45-60%).

A 70 kg normal man contains about 42 litres of water. This is distributed in intracellular (inside the cells 28l) and extracellular (outside the cells 14l) compartments, respectively known as ***intracellular fluid*** (*ICF*) and ***extracellular fluid*** (*ECF*). The ECF is further divided into interstitial fluid (10.5 l) and plasma (3.5 l). The distribution of water in an adult man is given in ***Table 21.1***.

## WATER TURNOVER AND BALANCE

The body possesses tremendous capacity to regulate its water content. In a healthy individual, this is achieved by balancing the daily water intake and water output (***Fig.21.1***).

### Water intake

Water is supplied to the body by ***exogenous*** and ***endogenous*** sources.

**Exogenous water :** Ingested water and beverages, water content of solid foods-constitute the exogenous source of water. Water intake is highly variable which may range from 0.5-5 litres. Ingestion of water is mainly controlled by a ***thirst centre*** located in the ***hypothalamus***.

**Endogenous water :** The ***metabolic water*** produced within the body is the endogenous water. This water (300-350 ml/day) is derived from the oxidation of foodstuffs. It is estimated that 1 g each of carbohydrate, protein and fat, respectively, yield 0.6 ml, 0.4 ml and 1.1 ml of water. On an average,

**TABLE 21.1 Distribution of water in an adult man, weighing 70 kg**

| *Compartment* | *% Body weight* | *Volume (l)* |
|---|---|---|
| Total | 60 | 42 |
| Intracellular fluid (ICF) | 40 | 28 |
| Extracellular fluid (ECF) | 20 | 14 |
| Interstitial fluid | 15 | 10.5 |
| Plasma | 5 | 3.5 |



ECF > ICF = Osmosis
ECF < ICF = Dehydration
Thirst

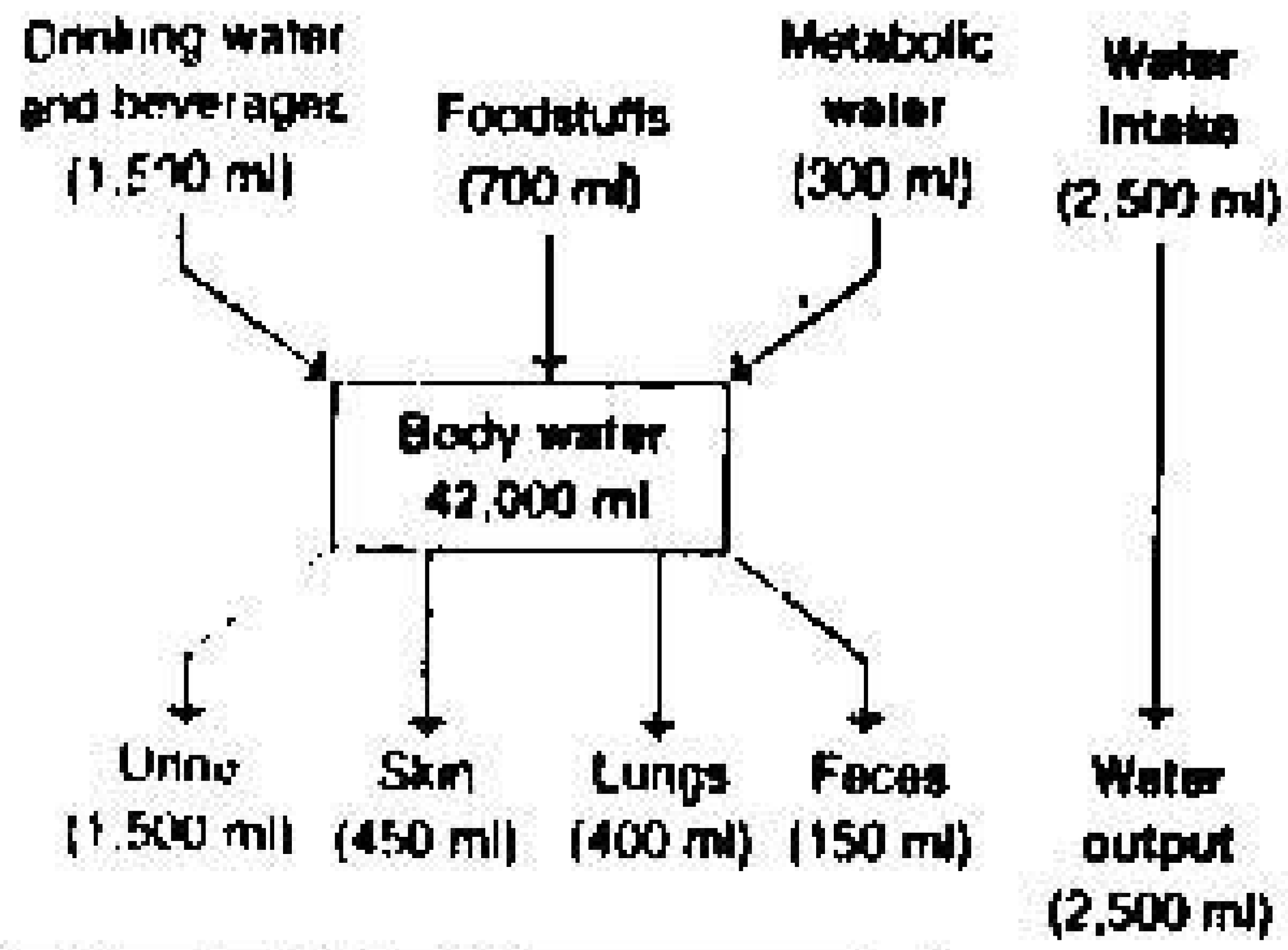


*Fig.21.1 : Water balance in the body, represented by daily intake and output (values are variable).*

about 125 ml of water is generated for 1,000 Cal consumed by the body.

### Water output

Water losses from the body are variable. There are four distinct routes for the elimination of water from the body—urine, skin, lungs and feces.

**Urine :** This is the major route for water loss from the body. In a healthy individual, the urine output is about 1-2 l/day.

**Hormonal regulation of urine production :** It is indeed surprising to know that about 180 litres of water is filtered by the glomeruli into the renal tubules everyday. However, most of this is reabsorbed and only 1-2 litres is excreted as urine. Water excretion by the kidney is tightly controlled by *vasopressin* also known as ***antidiuretic hormone (ADH)*** of the posterior pituitary gland. (ADH causes increased water reabsorption from renal tubules, and thus less urine output).

***Diabetes insipidus*** is a disorder characterized by the deficiency of ADH which results in an increased loss of water from the body.

**Skin :** Loss of water (450 ml/day) occurs through the body surface by perspiration. This is an unregulated process which mostly depends on the atmospheric temperature and humidity.

**Lungs :** During respiration, some amount of water (about 400 ml/day) is lost through the expired air.

The loss of water by perspiration (via skin) and respiration (via lungs) is collectively referred to as ***insensible water loss.***

**Feces :** Most of the water entering the gastrointestinal tract is reabsorbed by the intestine. About 150 ml/day is lost through feces in a healthy individual. Fecal loss of water is tremendously increased in diarrhea.

The abnormalities associated with water balance —dehydration and overhydration—will be described, following a discussion on electrolyte balance.

## ELECTROLYTE BALANCE

Electrolytes are the compounds which readily dissociate in solution and exist as ions i.e. positively and negatively charged particles. For instance, NaCl does not exist as such, but it exists as a cation ($Na^+$) and an anion ($Cl^-$). The concentration of electrolytes are expressed as milliequivalents (mEq/l) rather than milligrams.

### Electrolyte composition of body fluids

Electrolytes are well distributed in the body fluids in order to maintain the osmotic equilibrium and water balance. The total concentration of cations and anions in each body compartment (ECF or ICF) is equal to maintain electrical neutrality.

There is a marked difference in the concentration of electrolytes (cations and anions) between the extracellular and intracellular fluids. ***$Na^+$*** is the principal ***extracellular cation*** while ***$K^+$*** is the ***intracellular cation.*** This difference in the concentration is essential for the cell survival which is maintained by ***$Na^+$-$K^+$ pump*** (for details, ***Refer Chapter 33***)

### Osmolality of plasma

Osmolality is a measure of the solute particles present in the fluid medium. The osmolality of plasma is in the range of *285-295 milliosmoles/kg.* Sodium and its associated anions make the largest contribution (~90%) to plasma osmolality. Osmolality is generally measured by osmometer.

### Regulation of electrolyte balance

Electrolyte and water balance are regulated together, and the kidneys play a predominant role in this regard. The regulation is mostly achieved through the hormones aldosterone, ADH and renin-angiotensin.

**Aldosterone :** It is a mineralocorticoid produced by adrenal cortex. Aldosterone increases $Na^+$ reabsorption by the renal tubules at the expense of $K^+$ and $H^+$ ions. The net effect is the retention of $Na^+$ in the body.

**Antidiuretic hormone (ADH) :** An increase in the plasma osmolality (mostly due to $Na^+$) stimulates hypothalamus to release ADH. ADH effectively increases water reabsorption by renal tubules.

**Renin-angiotensin :** The secretion of aldosterone is controlled by renin-angiotensin system.

### Dehydration

Dehydration is a condition characterized by *water depletion in the body*. It may be due to insufficient intake or excessive water loss or both. Dehydration is generally classified into two types.

1. Due to loss of water alone.
2. Due to deprivation of water and electrolytes.

### Osmotic imbalance and dehydration in cholera

Cholera is transmitted through water and foods, contaminated by the bacterium *Vibrio cholerae*. This bacterium produces a toxin which stimulates the intestinal cells to secrete various ions ($Cl^-$, $Na^+$, $K^+$, $HCO_3^-$ etc.) into the intestinal lumen. These ions collectively raise the osmotic pressure and suck the water into lumen. This results in diarrhea with a heavy loss of water (5–10 liters/day). If not treated in time, the victims of cholera will die due to dehydration and loss of dissolved salts. Thus, cholera and other forms of severe diarrhea are the major killers of young children in many developing countries.

*Oral rehydration therapy (ORT)* is commonly used to treat cholera and other diarrheal diseases.

### Overhydration

Overhydration or water intoxication is caused by excessive *retention of water in the body*. This may occur due to excessive intake of large volumes of salt free fluids, renal failure, overproduction of ADH etc.

## ACID-BASE BALANCE

The *normal pH* of the blood is maintained in the narrow range of 7.35–7.45, i.e. slightly alkaline.

Maintenance of blood pH is an important homeostatic mechanism of the body. In normal circumstances, the regulation is so effective that the blood pH varies very little.

## MAINTENANCE OF BLOOD pH

The body has developed three lines of defense to regulate the body's acid-base balance and maintain the blood pH (around 7.4).

I. Blood buffers

II. Respiratory mechanism

III. Renal mechanism.

### I. Blood buffers

A buffer may be defined as a solution of a weak acid (HA) and its salt (BA) with a strong base. The buffer *resists the change in pH* by the addition of acid or alkali and the buffering capacity is dependent on the absolute concentration of salt and acid. It should be borne in mind that the buffer cannot remove $H^+$ ions from the body. It temporarily acts as a shock absorbant to reduce the free $H^+$ ions. The $H^+$ ions have to be ultimately eliminated by the renal mechanism (described later).

The blood contains 3 buffer systems.

1. Bicarbonate buffer
2. Phosphate buffer
3. Protein buffer.

**1. Bicarbonate buffer system :** Sodium bicarbonate and carbonic acid ($NaHCO_3-H_2CO_3$) is the most predominant buffer system of the extracellular fluid, particularly the plasma. Carbonic acid dissociates into hydrogen and bicarbonate ions.

$$H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$$

By the law of mass action, at equilibrium

$$K_a = \frac{[H^+][HCO_3^-]}{[H_2CO_3]}$$

($K_a$ = Dissociation constant of $H_2CO_3$).

The equation for bicarbonate buffer may be written as

$$pH = pK_a + \log \frac{[HCO_3^-]}{[H_2CO_3]}$$

The general equation referred to as *Henderson-Hasselbalch equation* for any buffer is written as

$$pH = pK_a + \log \frac{[Base]}{[Acid]}$$

**Blood pH and the ratio of $HCO_3^-$ to $H_2CO_3$ :** The plasma bicarbonate ($HCO_3^-$) concentration is around 24 mmol/l (range 22-26 mmol/l). Carbonic acid is a solution of $CO_2$ in water. Its concentration is around 1.2 mmol/l.

At a blood pH 7.4, the ratio of bicarbonate to carbonic acid is 20 : 1. Thus, the bicarbonate concentration is much higher (20 times) than carbonic acid in the blood. This is referred to as ***alkali reserve***, and is responsible for the effective buffering of $H^+$ ions, generated in the body. In normal circumstances, the concentration of bicarbonate and carbonic acid determines the pH of blood.

2. **Phosphate buffer system :** Sodium dihydrogen phosphate and disodium hydrogen phosphate ($NaH_2PO_4$ – $Na_2HPO_4$) constitute the phosphate buffer. It is mostly an intracellular buffer and is of less importance in plasma due to its low concentration.

3. **Protein buffer system :** The plasma proteins and hemoglobin together constitute the protein buffer system of the blood. The buffering capacity of proteins is dependent on the pK of ionizable groups of amino acids.

## II. Respiratory mechanism for pH regulation

Respiratory system provides a rapid mechanism for the maintenance of acid-base balance. This is achieved by regulating the concentration of carbonic acid ($H_2CO_3$) in the blood.

The large volumes of $CO_2$ produced by the cellular metabolic activity endanger the acid-base equilibrium of the body. But in normal circumstances, all of this $CO_2$ is eliminated from the body in the expired air via the lungs, as summarized below.

$$H_2CO_3 \xrightleftharpoons{\text{Carbonic anhydrase}} CO_2 + H_2O$$

Any decrease in blood pH causes hyperventilation to blow off $CO_2$, thereby reducing the $H_2CO_3$ concentration. Simultaneously, the $H^+$ ions are eliminated as $H_2O$.

Respiratory control of blood pH is rapid but only a short term regulatory process, since hyperventilation cannot proceed for long.

## III. Renal mechanism for pH regulation

The role of kidneys in the maintenance of acid-base balance of the body (blood pH) is highly significant. The renal mechanism tries to provide a permanent solution to the acid-base disturbances.

**Urine pH normally lower than blood pH :** The pH of urine is normally acidic (~6.0). This clearly indicates that the kidneys have contributed to the acidification of urine, when it is formed from the blood plasma (pH 7.4). In other words, the $H^+$ ions generated in the body in the normal circumstances, are eliminated by acidified urine.

**Carbonic anhydrase and renal regulation of pH :** The enzyme carbonic anhydrase is of central importance in the renal regulation of pH which occurs by the following mechanisms.

1. Excretion of $H^+$ ions
2. Reabsorption of bicarbonate
3. Excretion of titratable acid
4. Excretion of ammonium ions.

1. **Excretion of $H^+$ ions :** Kidney is the only route through which the $H^+$ can be eliminated from the body. $H^+$ excretion occurs in the proximal convoluted tubules (renal tubular cells) and is coupled with the regeneration of $HCO_3^-$. The process is depicted in *Fig.21.2*, and briefly described.

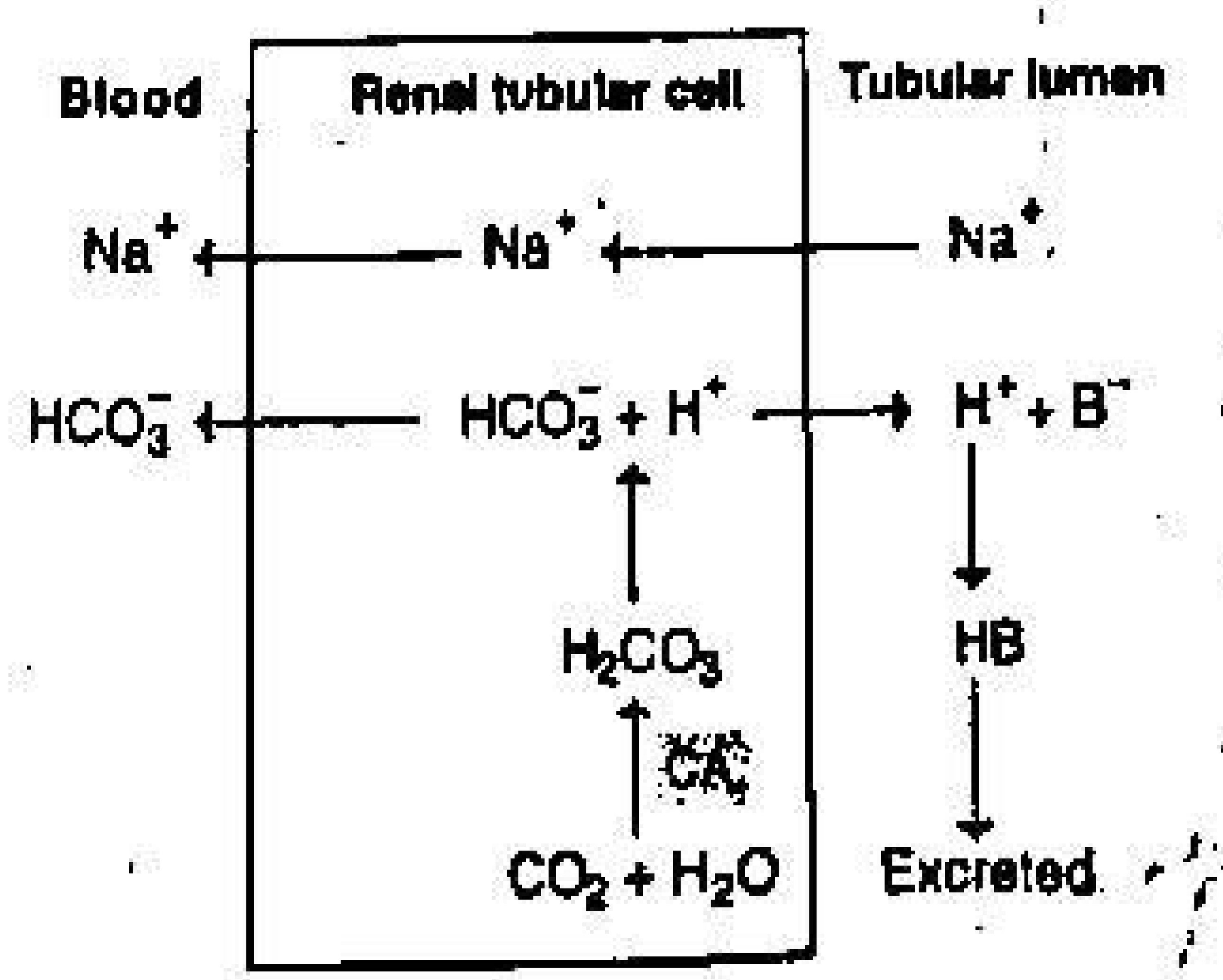


*Fig.21.2 : Renal regulation of blood pH–Excretion of H+ ions (CA–Carbonic anhydrase).*

Carbonic anhydrase catalyses the production of carbonic acid ($H_2CO_3$) from $CO_2$ and $H_2O$ in the renal tubular cell. $H_2CO_3$ then dissociates to $H^+$ and $HCO_3^-$. The $H^+$ ions are secreted into the tubular lumen in exchange for $Na^+$. The $Na^+$ in association with $HCO_3^-$ is reabsorbed into the blood. This is an effective mechanism to eliminate acids ($H^+$) from the body with a simultaneous generation of $HCO_3^-$. The latter adds up to the alkali reserve of the body. The $H^+$ combines with a non-carbonate base and is excreted in urine.

2. **Reabsorption of bicarbonate** : This mechanism is primarily responsible to conserve the blood $HCO_3^-$, with a simultaneous excretion of $H^+$ ions. The normal urine is almost free from $HCO_3^-$.

3. **Excretion of titratable acid** : Titratable acidity is a measure of acid excreted into urine by the kidney. This can be estimated by titrating urine back to the normal pH of blood (7.4). In quantitative terms, titratable acidity refers to the number of milliliters of N/10 NaOH required to titrate 1 liter of urine to pH 7.4. Titratable acidity reflects the $H^+$ ions excreted into urine which resulted in a fall of pH from 7.4 (that of blood).

4. **Excretion of ammonium ions** : This is another mechanism to buffer $H^+$ ions secreted into the tubular fluid. The $H^+$ ion combines with $NH_3$ to form ammonium ion ($NH_4^+$). Ammonium ions cannot diffuse back into tubular cells and, therefore, are excreted into urine.

$NH_4^+$ is a major urine acid. It is estimated that about half to two-thirds of body acid load is eliminated in the form of $NH_4^+$ ions.

### Carbon dioxide—the central molecule of pH regulation

As is observed from the foregoing discussion, $CO_2$ is of central importance in the acid-base balance of the body. It has the ability to combine with $H_2O$ to from $H_2CO_3$ which can dissociate to $HCO_3^-$ and $H^+$. A summary of the interaction between the lungs, erythrocytes and kidneys in handling $CO_2$ to maintain pH of the blood is depicted in *Fig.21.3*. The $CO_2$ generated by aerobic metabolism may be exhaled via lungs, or converted to $HCO_3^-$ by erythrocytes and kidneys to add up to the alkali reserve of the body.

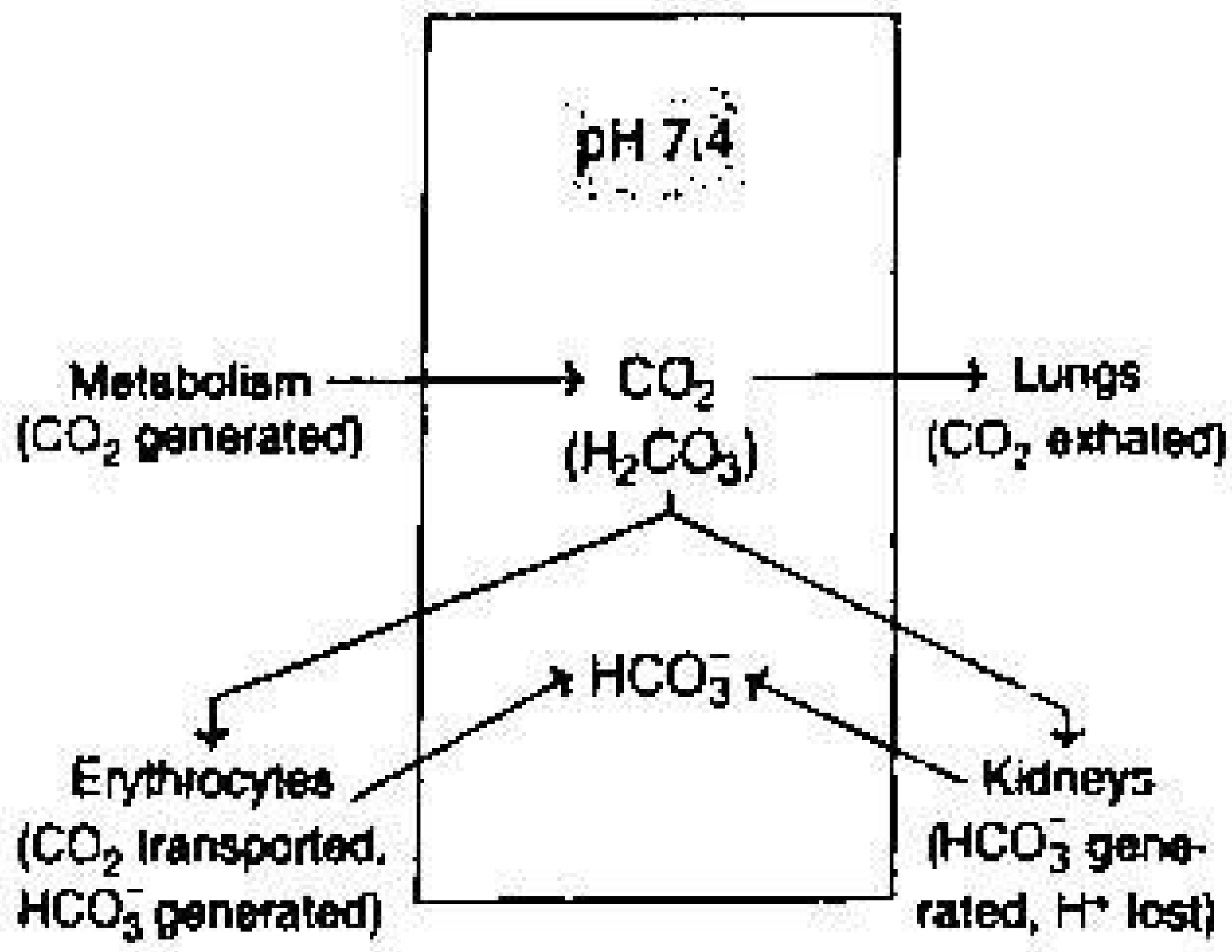


*Fig.21.3 : Carbon dioxide—the central molecule of blood pH regulation.*

## DISORDERS OF ACID-BASE BALANCE

The body has developed an efficient system for the maintenance of acid-base equilibrium with a result that the pH of blood is almost constant (7.4). The blood pH compatible to life is 6.8-7.8, beyond which life cannot exist.

For a better understanding of the disorders of acid-base balance, the Henderson-Hasselbalch equation must be frequently consulted.

$$pH = pK_a + \log \frac{[HCO_3^-]}{[H_2CO_3]}$$

It is evident from the above equation that the blood pH ($H^+$ ion concentration) is dependent on the relative concentration (ratio) of bicarbonate ($HCO_3^-$) and carbonic acid ($H_2CO_3$).

The acid-base disorders are mainly classified as

1. Acidosis—a decline in blood pH
   - (a) Metabolic acidosis—due to a decrease in bicarbonate.
   - (b) Respiratory acidosis—due to an increase in carbonic acid.
2. Alkalosis—a rise in blood pH
   - (a) Metabolic alkalosis—due to an increase in bicarbonate.
   - (b) Respiratory alkalosis—due to a decrease in carbonic acid.

The four acid-base disorders referred to above are primarily due to alterations in either bicarbonate or carbonic acid. It may be observed that the metabolic acid-balance disorders are caused by a direct alteration in bicarbonate concentration while the respiratory disturbances are due to a change in carbonic acid level (i.e. $CO_2$).

### Compensation of acid-base disorders

To counter the acid-base disturbances, the body gears up its homeostatic mechanism and makes every attempt to restore the pH to normal level (7.4). This is referred to as compensation which may be partial or full. Sometimes the acid-base disorders may remain uncompensated.

The principal acid-base disturbances, along with the blood concentration of $HCO_3^-$ and $H_2CO_3$, in acute and compensated states are given in the *Table. 21.2.*

For the acute metabolic disorders (due to changes in $HCO_3^-$), respiratory compensation sets in and regulates the $H_2CO_3$ (i.e. $CO_2$) by hyper- or hypoventilation. As regards acute respiratory disorders (due to changes in $H_2CO_3$), the renal compensation occurs to maintain the $HCO_3^-$ level, by increasing or decreasing its excretion.

### Anion gap

Anion gap is defined as the difference between the total concentration of measured cations ($Na^+$ and $K^+$) and that of measured anion ($Cl^-$ and $HCO_3^-$). The anion gap ($A^-$) in fact represents the ***unmeasured anions in the plasma*** and it is around 15 mEq/l (range 8–18 mEq/l) in healthy individuals.

### Metabolic acidosis

The primary defect in metabolic acidosis is a ***reduction in bicarbonate concentration*** which leads to a fall in blood pH.

The most important cause of metabolic acidosis is due to an excessive production of organic acids which combine with $NaHCO_3^-$ and deplete the alkali reserve.

$$NaHCO_3^- + \text{Organic acids} \longrightarrow \text{Na salts of organic acids} + CO_2$$

Metabolic acidosis is commonly seen in ***severe uncontrolled diabetes mellitus*** which is associated with excessive production of acetoacetic acid and β-hydroxybutyric acid (both are organic acids).

**Compensation of metabolic acidosis :** The acute metabolic acidosis is usually compensated by hyperventilation of lungs. This leads to an increased elimination of $CO_2$ from the body (hence $H_2CO_3^-$), but respiratory compensation is only

[illegible]

| *Disorder* | *Blood pH* | *[$HCO_3^-$]* | *[$H_2CO_3$]* |
|---|---|---|---|
| Metabolic acidosis | | | |
| Acute | ↓ | ↓ | → |
| Compensated (by ↑ ventilation) | ↘ or → | ↓ | ↓ |
| Respiratory acidosis | | | |
| Acute | ↓ | → | ↑ |
| Compensated ($HCO_3^-$ retained by kidney) | ↘ or → | ↑ | ↑ |
| Metabolic alkalosis | | | |
| Acute | ↑ | ↑ | → |
| Compensated (by ↓ ventilation) | ↗ or → | ↑ | ↑ |
| Respiratory alkalosis | | | |
| Acute | ↑ | → | ↓ |
| Compensated (↑ $HCO_3^-$ excretion by kidney) | ↗ or → | ↓ | ↓ |

↑ : Increased; ↓ : Decreased; → : Normal; ↘ : Marginally decreased; ↗ : Marginally increased.

short-lived. Renal compensation sets in within 3-4 days and the $H^+$ ions are excreted as $NH_4^+$ ions.

### Respiratory acidosis

The primary defect in respiratory acidosis is due to a ***retention of $CO_2$*** ($H_2CO_3$↑). There may be several causes for respiratory acidosis which include depression of the respiratory centre (overdose of drugs), pulmonary disorders (bronchopneumonia) and breathing air with high content of $CO_2$.

The renal mechanism comes for the rescue to compensate respiratory acidosis. More $HCO_3^-$ is generated and retained by the kidneys which adds up to the alkali reserve of the body. The excretion of titratable acidity and $NH_4^+$ is elevated in urine.

### Metabolic alkalosis

The primary abnormality in metabolic alkalosis is an *increase in $HCO_3^-$ concentration*. This may occur due to excessive vomiting (resulting in loss of $H^+$) or an excessive intake of sodium bicarbonate for therapeutic purposes (e.g. control of gastric acidity).

The respiratory mechanism initiates the compensation by hypoventilation to retain $CO_2$ (hence $H_2CO_3$↑). This is slowly taken over by renal mechanism which excretes more $HCO_3^-$ and retains $H^+$.

### Respiratory alkalosis

The primary abnormality in respiratory alkalosis is a ***decrease in $H_2CO_3$ concentration***. This may occur due to prolonged hyperventilation resulting in increased exhalation of $CO_2$ by the lungs. Hyperventilation is observed in conditions such as hysteria, hypoxia, raised intracranial pressure, excessive artificial ventilation and the action of certain drugs (salicylate) that stimulate respiratory centre.

The renal mechanism tries to compensate by increasing the urinary excretion of $HCO_3^-$.

## SUMMARY AND BIOMEDICAL / CLINICAL CONCEPTS

1. *Water is the solvent of life and constitutes about 60% of the total body weight, distributed in intracellular and extracellular fluids.*
2. *Electrolytes are distributed in the intracellular and extracellular fluids to maintain the osmotic equilibrium and water balance. $Na^+$ is the principal extracellular cation while $K^+$ is the intracellular cation.*
3. *The normal pH of blood is maintained in the narrow range of 7.35–7.45. The metabolism of the body is accompanied by an overall production of acids. The body has developed three lines of defense (blood buffers, respiratory and renal mechanisms) to regulate the acid-base balance and maintain the blood pH.*
4. *The acid-base disorders are classified as acidosis (metabolic or respiratory) and alkalosis (metabolic or respiratory), respectively, due to a rise or fall in blood pH. The metabolic disturbances are associated with alterations in $HCO_3^-$ concentration while the respiratory disorders are due to changes in $H_2CO_3$ (i.e. $CO_2$).*

- *Kidneys play a predominant role in the regulation of water, electrolyte and acid-base balance.*
- *Electrolyte and water balance regulation occurs through the involvement of hormones—aldosterone, ADH and renin-angiotensin.*
- *Vegetarian diet has an alkalizing effect on the body. This is attributed to the formation of organic acids such as sod[illegible] which can deplete $H^+$ ions by combining with them.*
- *Uncontrolled diabetes mellitus is associated with metabolic acidosis, commonly referred to as ketoacidosis (due to the overproduction of ketone bodies)*