pH & ACID BASE BALANCE

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What is pH?

- It is the negative log of the hydrogen ion concentration.
- pH = -log [H+]

What is pH?

- pH is a unit of measure which describes the degree of acidity or alkalinity (basic) of a solution.
- It is measured on a scale of 0 to 14.
- Low pH values correspond to high concentrations of H^+ and high pH values correspond to low concentrations of H^+.

Ph Value

- The pH value of a substance is directly related to the ratio of the hydrogen ion and hydroxyl ion concentrations.

- If the H+ concentration is higher than OH- the material is acidic.

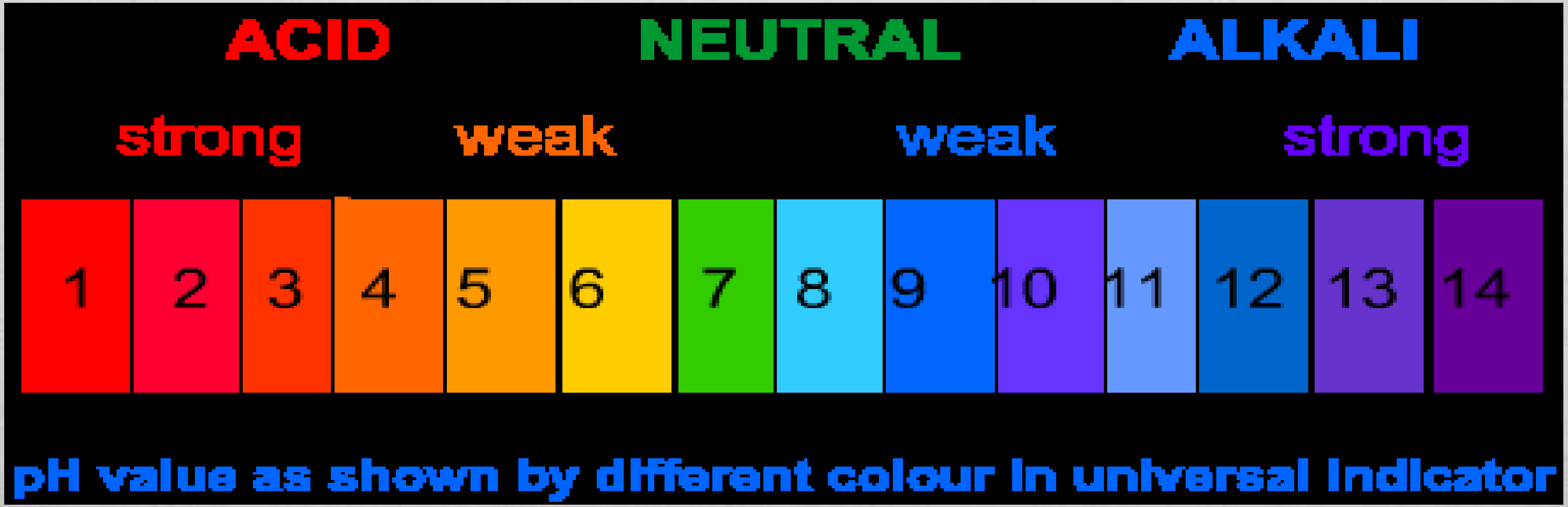
- If the OH- concentration is higher than H+ the material is basic.

- 7 is neutral, < is acidic, >7 is basic

The Ph Scale

- The pH scale corresponds to the concentration of hydrogen ions.

- For example pure water H+ ion concentration is 1 x 10^- 7 M, therefore the pH would then be 7.



Acid

- **Any compound which forms H^+ ions in solution (proton donors)**
- eg: Carbonic acid (H_2CO_3) releases H^+ ions

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

Base

- **Any compound which combines with H^+ ions in solution (proton acceptors) or gives OH^- ions.**
- eg:Bicarbonate($HCO3^-$) accepts H+ ions
- $HCO_3^- \; H^+ \longrightarrow H_2CO_3$
- $NaOH \longrightarrow Na^+ + OH^-$

6 Strong Acids		6 Strong Bases	
$HClO_4$	perchloric acid	$LiOH$	lithium hydroxide
HCl	hydrochloric acid	$NaOH$	sodium hydroxide
HBr	hydrobromic acid	KOH	potassium hydroxide
HI	hydroiodic acid	$Ca(OH)_2$	calcium hydroxide
HNO_3	nitric acid	$Sr(OH)_2$	strontium hydroxide
H_2SO_4	sulfuric acid	$Ba(OH)_2$	barium hydroxide

ACID BASE BALANCE

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

- The pH of intracellular fluid is rather variable. Thus, for erythrocytes the pH is 7.2, while for skeletal muscle, it may be as low as 6.0.

- Maintenance of blood pH is an important homeostatic mechanism of the body.

BUFFERS

- Buffers are weak acid or weak base which resist the pH changes when a small amount of **acid or base is added**.

- Typically a mixture of a weak acid and a salt of its conjugate base or weak base and a salt of its conjugate acid.

TYPES OF BUFFERS

Two types :

- ACIDIC BUFFERS –

Solution of a mixture of a weak acid and a salt of this weak acid with a strong base.

E.g. CH_3COOH + CH_3COONa

(weak acid) (Salt)

- BASIC BUFFERS –

Solution of a mixture of a weak base and a salt of this weak base with a strong acid.

e.g. NH_4OH + NH_4Cl

(Weak base) (Salt)

HOW BUFFERS WORK

- Equilibrium between acid and base.

- Example: ACETATE BUFFER
  - $CH_3COOH \leftrightarrow CH_3COO^- + H^+$

- If more H^+ is added to this solution, it simply shifts the equilibrium to the left, absorbing H^+, so the $[H^+]$ remains unchanged.

- If H^+ is removed (e.g. by adding OH-) then the equilibrium shifts to the right, releasing H^+ to keep the pH constant

•HANDERSON HASSELBALCH EQUATION

- Lawrence Joseph **Henderson** wrote an equation, in 1908, describing the use of carbonic acid as a buffer solution.

- Karl Albert **Hasselbalch** later re-expressed that formula in logarithmic terms, resulting in the **Henderson–Hasselbalch equation**.

The Henderson-Hasselbalch Equation derivation

$$HA \rightleftharpoons H^+ + A^- \qquad K_a = \frac{[H^+][A^-]}{[HA]}$$

take the -log on both sides

$$-\log K_a = -\log [H^+] - \log \frac{[A^-]}{[HA]}$$

apply p(x) = -log(x)

$$pK_a = pH \quad -\log \frac{[A^-]}{[HA]}$$

and finally solve for pH…

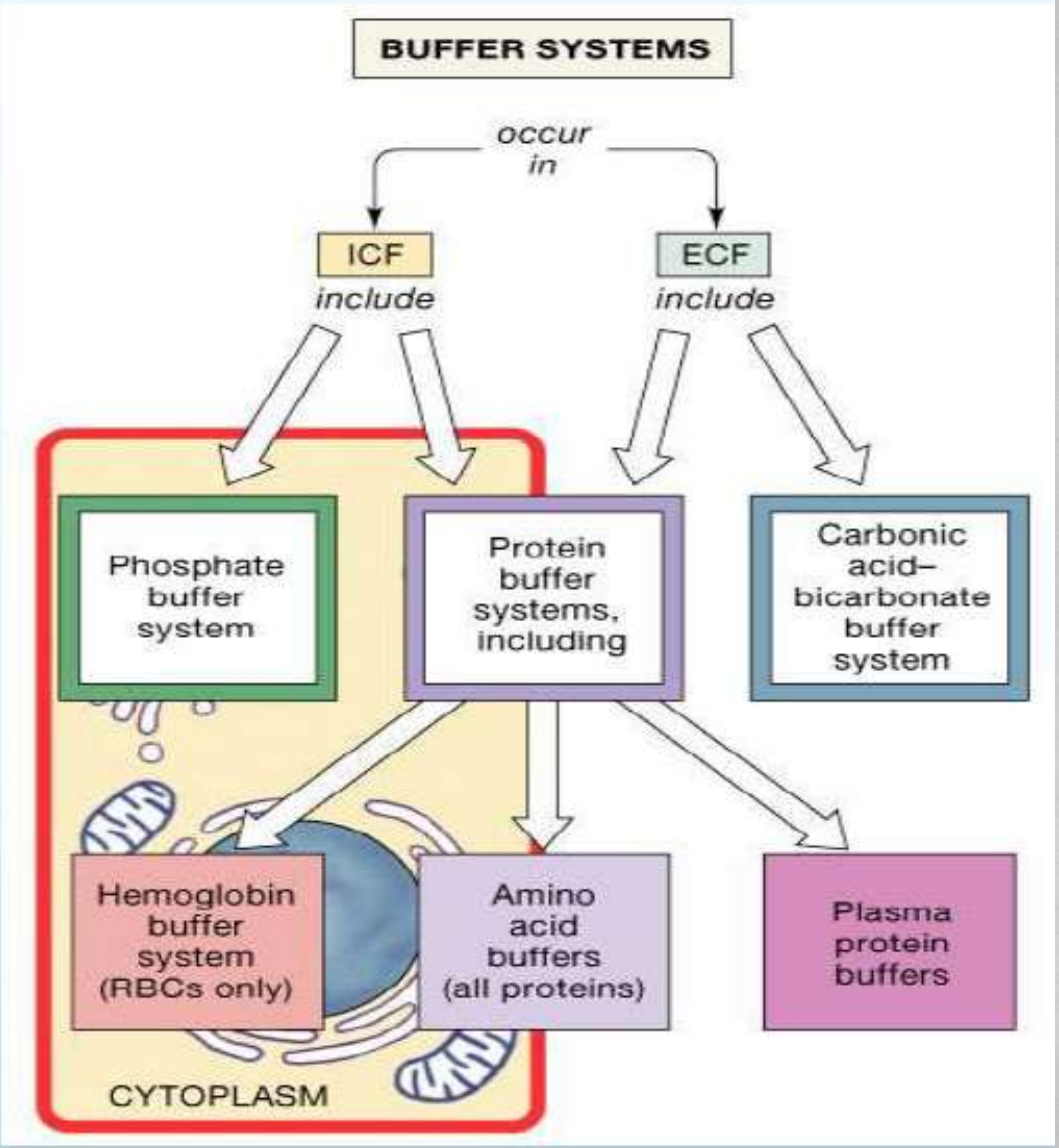
$$pH = pK_a + \log \frac{[A^-]}{[HA]} = pK_a + \log \frac{[\text{Proton acceptor}]}{[\text{Proton donor}]}$$

- \- The greater the buffer capacity the less the pH changes upon addition of H^+ or OH^-

- Choose a buffer whose pK_a is closest to the desired pH.

- pH should be within $pK_a \pm 1$

BUFFER SYSTEM IN BODY FLUIDS

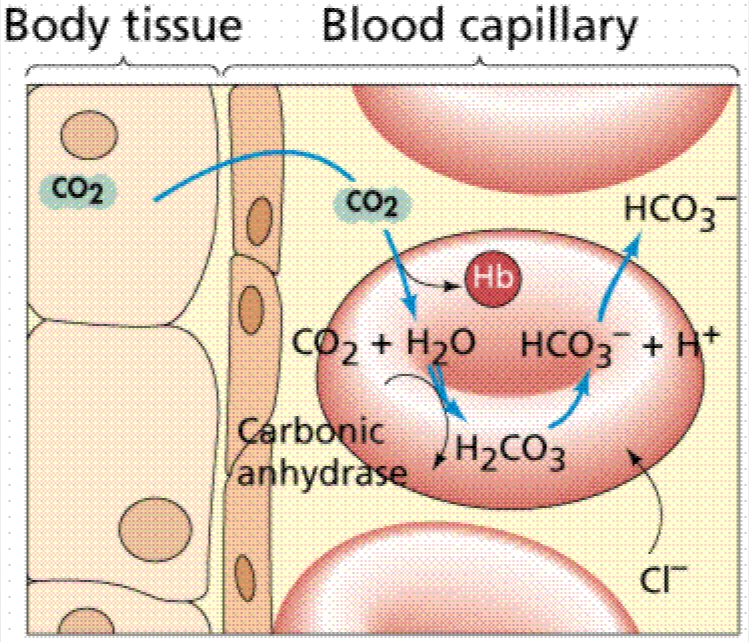


MAINTENANCE OF BLOOD pH

- 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



- It is a **first line of defense.**
- The blood contains 3 buffer systems.

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

1. Bicarbonate buffer system

- Sodium bicarbonate and carbonic acid (NaHCO3 – H2CO3) is the most **predominant buffer system of the** extracellular fluid, particularly the plasma.
- Carbonic acid dissociates into hydrogen and bicarbonate ions.
- The carbonic acid-hydrogen Bicarbonate ion buffer is the most important buffer system.
- Carbonic acid, H2CO3, acts as the weak acid Hydrogen carbonate, $HCO3^-$, acts as the conjugate base

- **Bicarbonate buffer system**
- H_2CO_3 ------> H+ + HCO_3^-
- When pH is rising:

  H_2CO_3 + H+ ---> HCO_3^-
- When pH is falling:

  H_2CO_3 H+ <----- HCO_3^-.

ADVANTAGES & DISADVANTAGE

ADVANTAGE

- •Bicarbonate buffer system is quite efficient as compared to other buffer system since it is present in very high concentration & it produce H_2CO_3 from which CO_2 is exhaled out.

DISADVANTAGE:

- Bicarbonate is very weak buffer & hence pKa is very far away from physiological pH.
- Cannot protect the ECF from pH changes due to increased or depressed CO_2 levels.

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.
- Consists of anion $H_2PO_4^-$ (a weak acid)(pKa-6.8)
- Works like the carbonic acid–bicarbonate buffer system.

- The phosphate buffer system ($HPO_4^{2-}/H_2PO_4^-$) plays a role in plasma and erythrocytes.
- $$H_2PO_4^- + H_2O \leftrightarrow H_3O^+ + HPO_4^{2-}$$
- Any acid reacts with monohydrogen phosphate to form dihydrogen phosphate

dihydrogen phosphate monohydrogen phosphate

$$H_2PO_4^- + H_2O \leftarrow HPO_4^{2-} + H_3O^+$$

- The base is neutralized by dihydrogen phosphate

dihydrogen phosphate monohydrogen phosphate

- $$H_2PO_4^- + OH^- \rightarrow HPO_4^{2-} + H_3O^+$$

- When pH is rising: $H_2PO_4 \dashrightarrow H^+ + HPO_4^{--}$;
- When pH is falling: $H_2PO_{4} \leftarrow\!\!\text{-----}\, H^+ + HPO_4$

Limitations of Phosphate Buffer Systems

- Provide only temporary solution to acid–base imbalance
- Do not eliminate H+ ions
- Supply of buffer molecules is limited
- The normal ratio in plasma is 4:1 and this is kept constant by the help of kidneys for which phosphate buffer system is directly related to the kidneys.

3. The Protein Buffer System

- The protein buffer system is part of body mechanism for controlling blood H+ ion concentration both ECF & ICF
- More concentrated than either bicarbonate or phosphate buffers.
- 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.

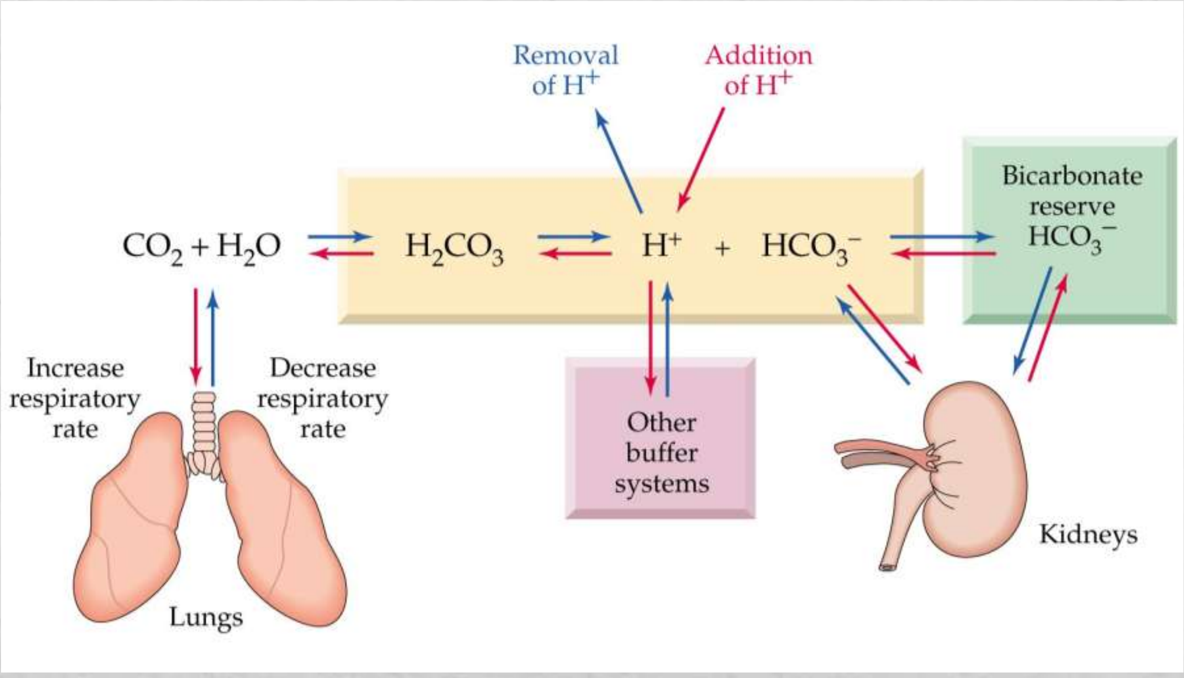
ROLL OF AMINO ACIDS IN BUFFER SYSTEM

- The carboxyl groups release H+ when pH rises and amino groups bind H+ when pH falls.
- In acidic media protein act as base , NH2 group takes up H+ and formed NH3. Here, protein become positively charged.
- In alkaline media , protein act as acid and acidic group (COOH) dissociate in to COO- & H+.
- In this case protein become negatively charged.

✓ If pH climbs, the carboxyl group of amino acid acts as a weak acid.

✓ If the pH drops, the amino group acts as a weak base.

2. RESPIRATORY BUFFER SYSTEM



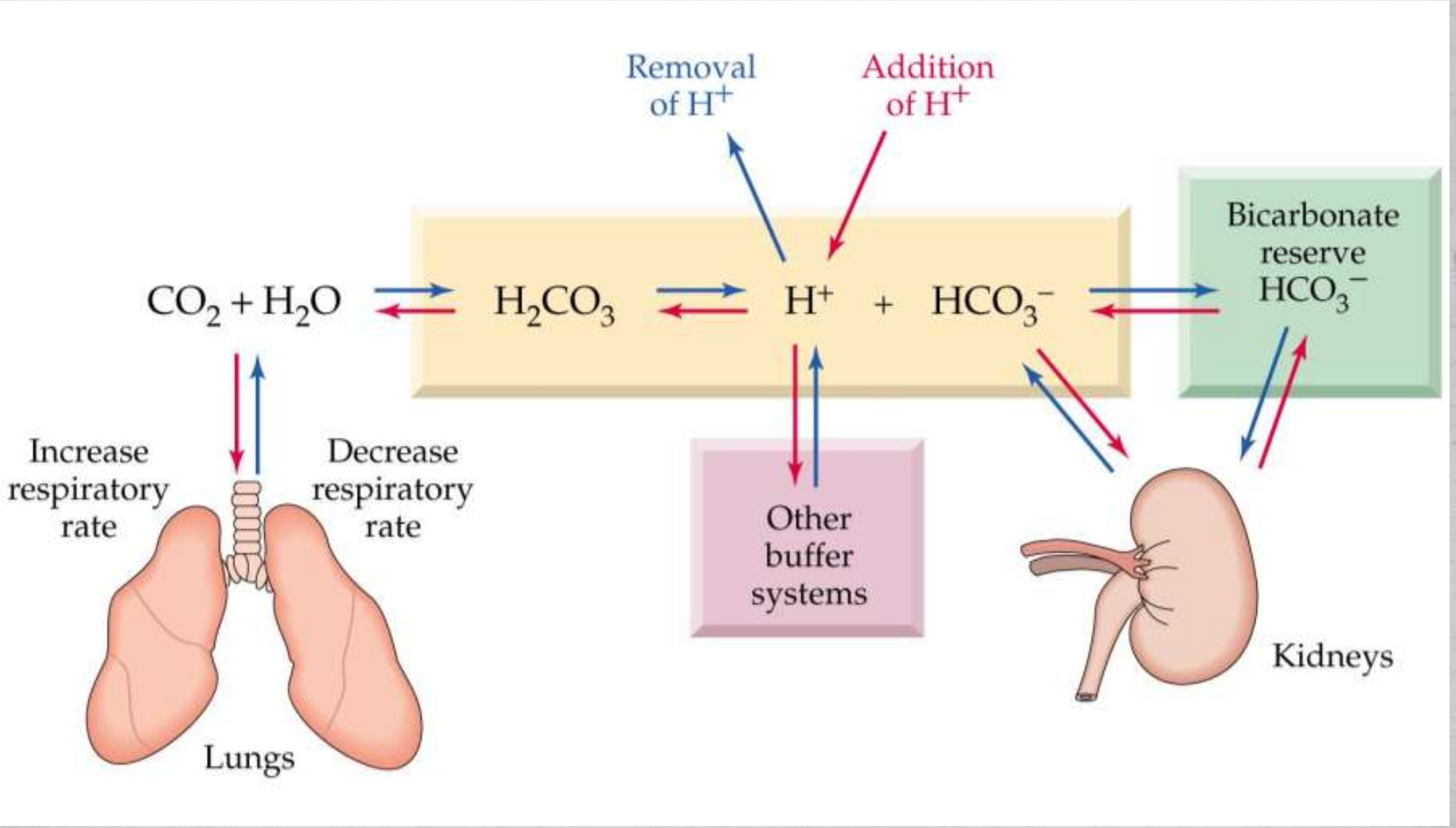
RESPIRATORY ACID-BASE CONTROL MECHANISMS

- When chemical buffers alone cannot prevent changes in blood pH, the respiratory system is the second line of defense against changes.
- Eliminate or Retain CO_2
- Change in pH are RAPID
- Occurring within minutes
- $PCO_2 \propto VCO_2/VA$

- The large volumes of CO2 produced by the cellular metabolic activity endanger the acid base equilibrium of the body. But in normal circumstances, all of this CO2 is eliminated from the body in the expired air via the lungs.

$$H_2CO_3 \xleftrightarrow{\text{Carbonic anhydrase}} CO_2 + H_2O\cdot$$

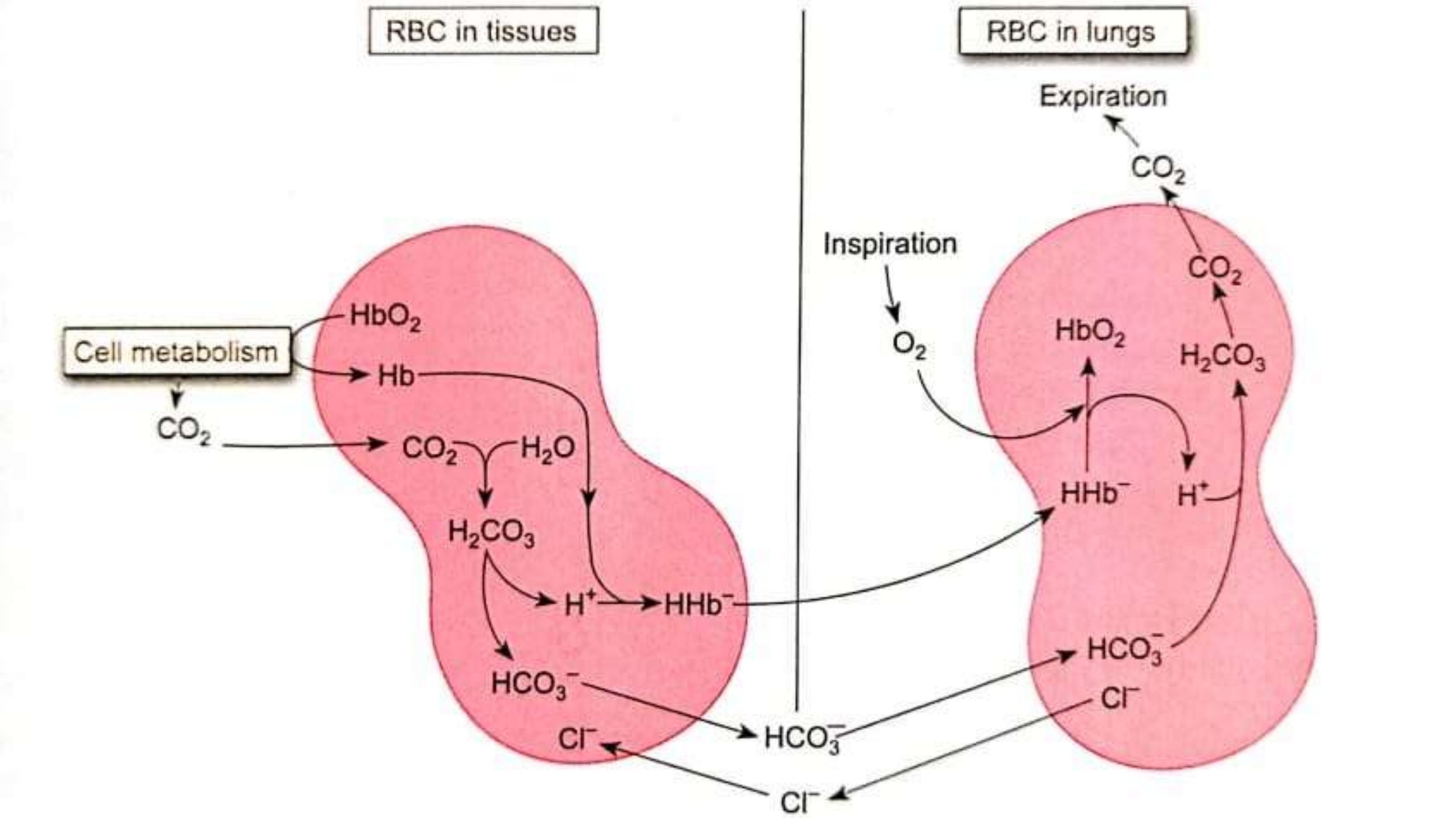
- The rate of respiration (or the rate of removal of CO2) is controlled by a respiratory centre, located in the medulla of the brain.
- This centre is highly sensitive to changes in the pH of blood.
- Any decrease in blood pH causes hyperventilation to blow off CO2, thereby reducing the H2CO3 concentration. Simultaneously, the H+ ions are eliminated as H2O.



Removal of H^+
Addition of H^+
$CO_2 + H_2O$
H_2CO_3
H^+ + HCO_3^-
Bicarbonate reserve HCO_3^-
Increase respiratory rate
Decrease respiratory rate
Other buffer systems
Lungs
Kidneys

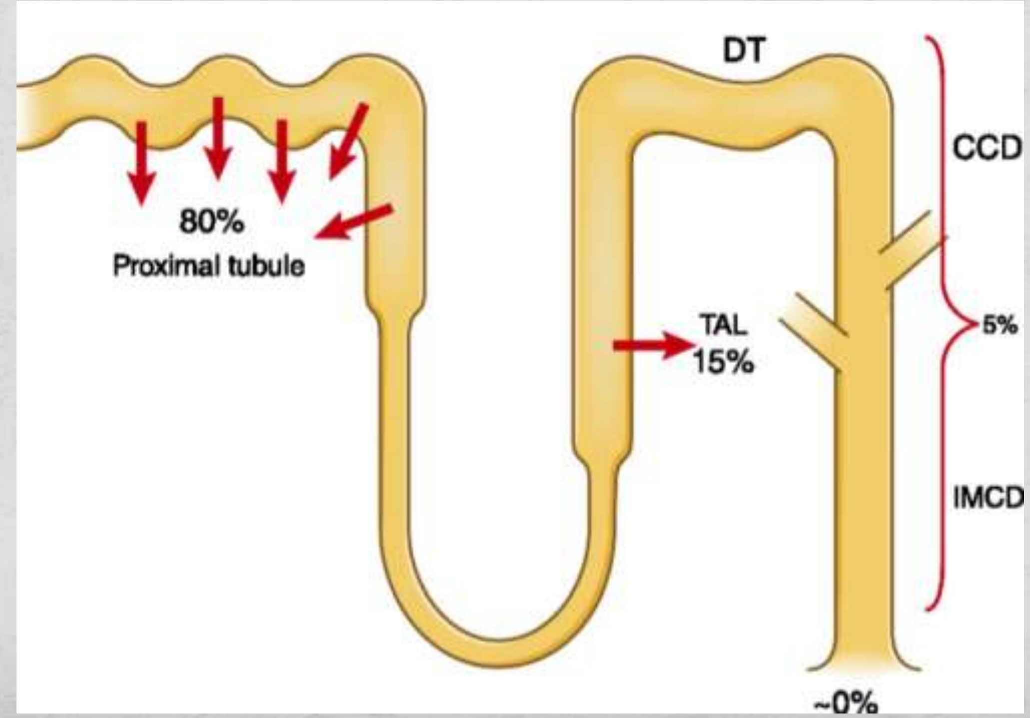
Hemoglobin as a buffer

- Hemoglobin of erythrocytes is also important in the respiratory regulation of pH.
- At the tissue level, hemoglobin binds to H^+ ions and helps to transport CO_2 as HCO_3^- with a minimum change in pH (referred to as **isohydric transport).**
- **In the lungs, as** hemoglobin combines with O_2, H^+ ions are removed which combine with HCO_3^- to form H_2CO_3.
- The latter dissociates to release CO_2 to be exhaled



: Role of RBC and Hb in acid base balance

III. Renal mechanism



Renal mechanism for pH regulation

- Renal mechanism for pH regulation is 3rd line of defense.
- The **renal mechanism tries to** provide a **permanent solution to the acid-base disturbances.**

- 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).

Renal mechanism for pH regulation

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.

i. 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 HCO3 – .

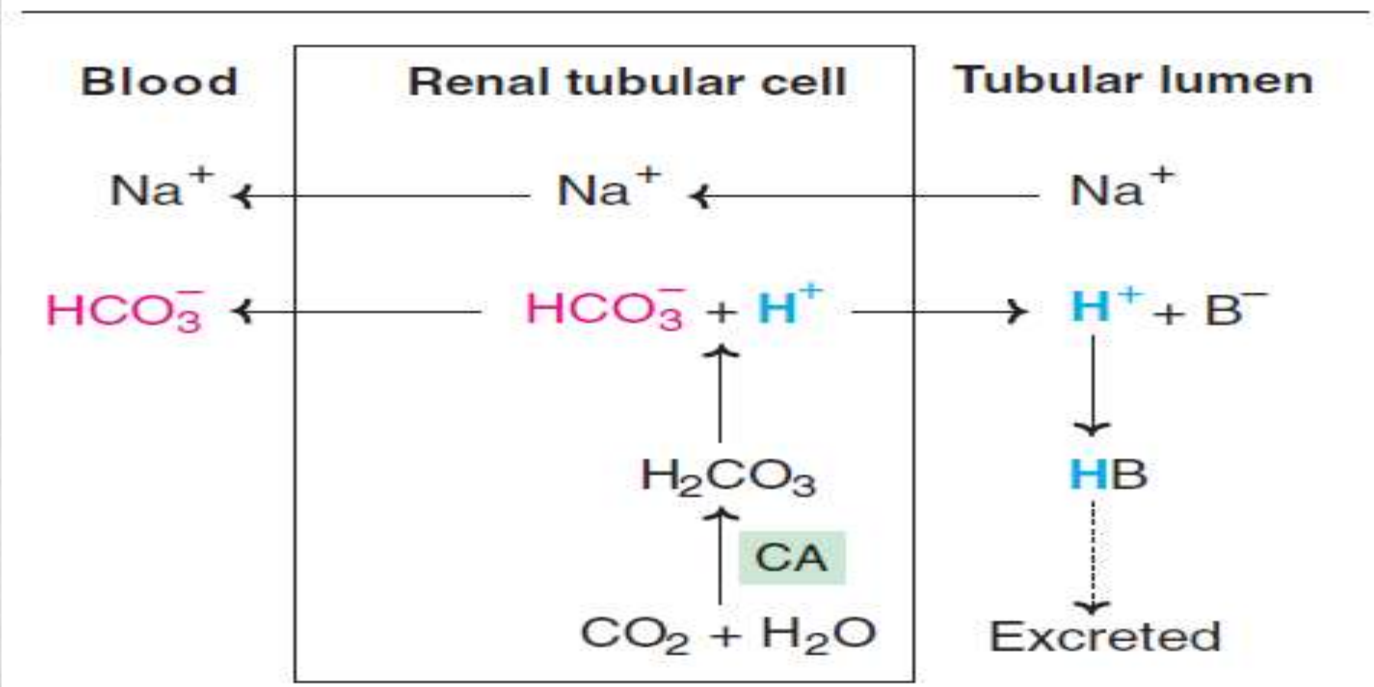


Fig. 21.5 : Renal regulation of blood pH–Excretion of H^+ ions (CA–Carbonic anhydrase).

ii. Reabsorption of bicarbonate :

- **This mechanism** is primarily responsible to conserve the blood HCO3 – , with a simultaneous excretion of H+ ions. The normal urine is almost free from HCO3 – .

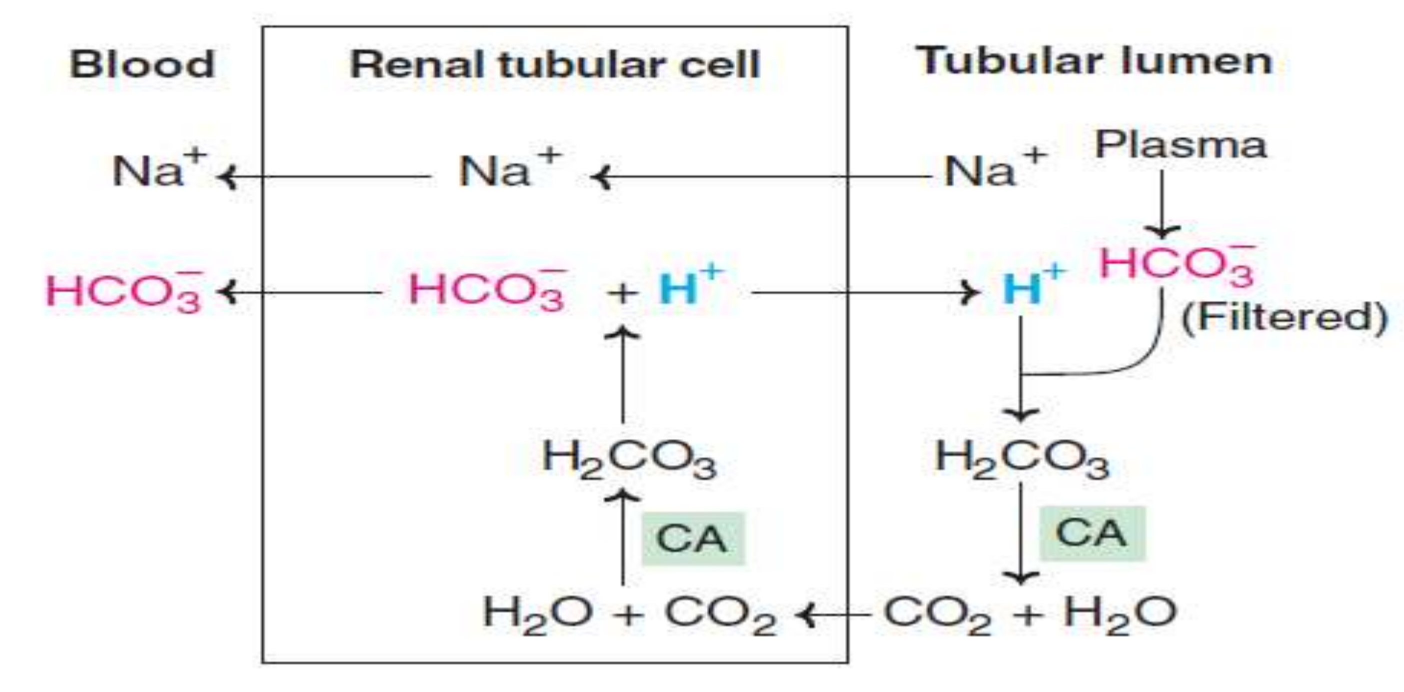


Fig. 21.6 : Renal regulation of blood pH–Reabsorption of bicarbonate (CA–Carbonic anhydrase).

iii. 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.
- H+ ion is secreted into the tubular lumen in exchange for Na+ ion. This Na+ is obtained from the base, disodium hydrogen phosphate (Na2HPO4).

iii. Excretion of titratable acid:

- The latter in turn combines with H+ to produce the acid, sodium dihydrogen phosphate (NaH2PO4), in which form the major quantity of titratable acid in urine is present.
- This causes a fall in the pH of urine to as low as 4.5. Any further fall in the pH will cause depletion of Na+ ions.

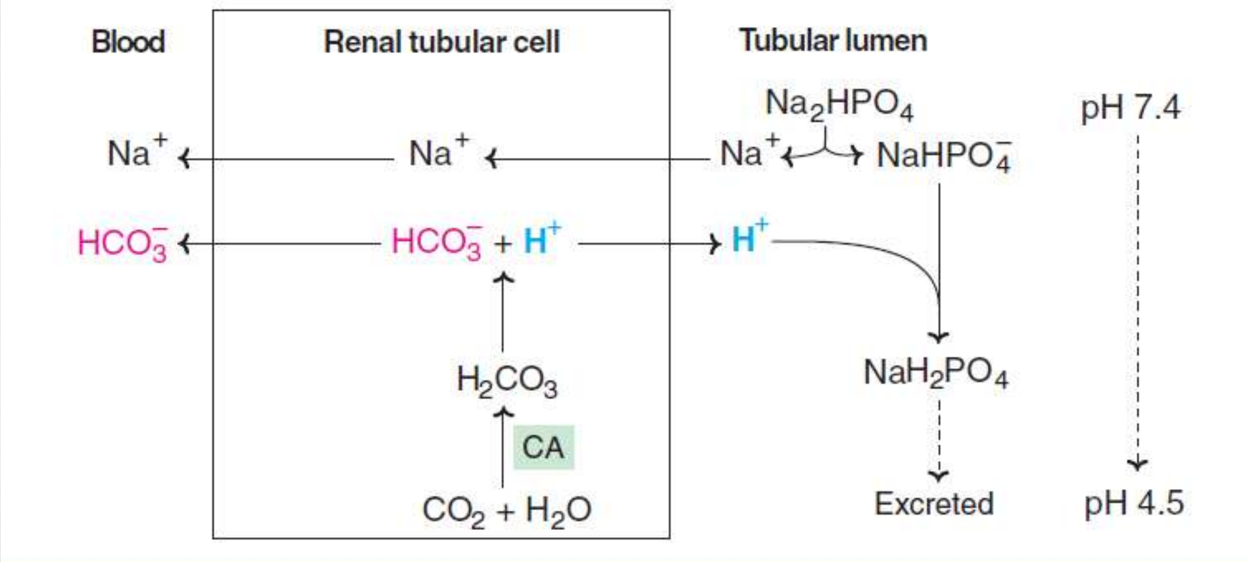


Fig. 21.7 : Renal regulation of blood pH–Excretion of titratable acid by phosphate buffer mechanism (CA–Carbonic anhydrase).

iv. Excretion of ammonium ions :

- This is another mechanism to buffer H+ ions secreted into the tubular fluid.
- The H+ ion combines with NH3 to form ammonium ion (NH4+).

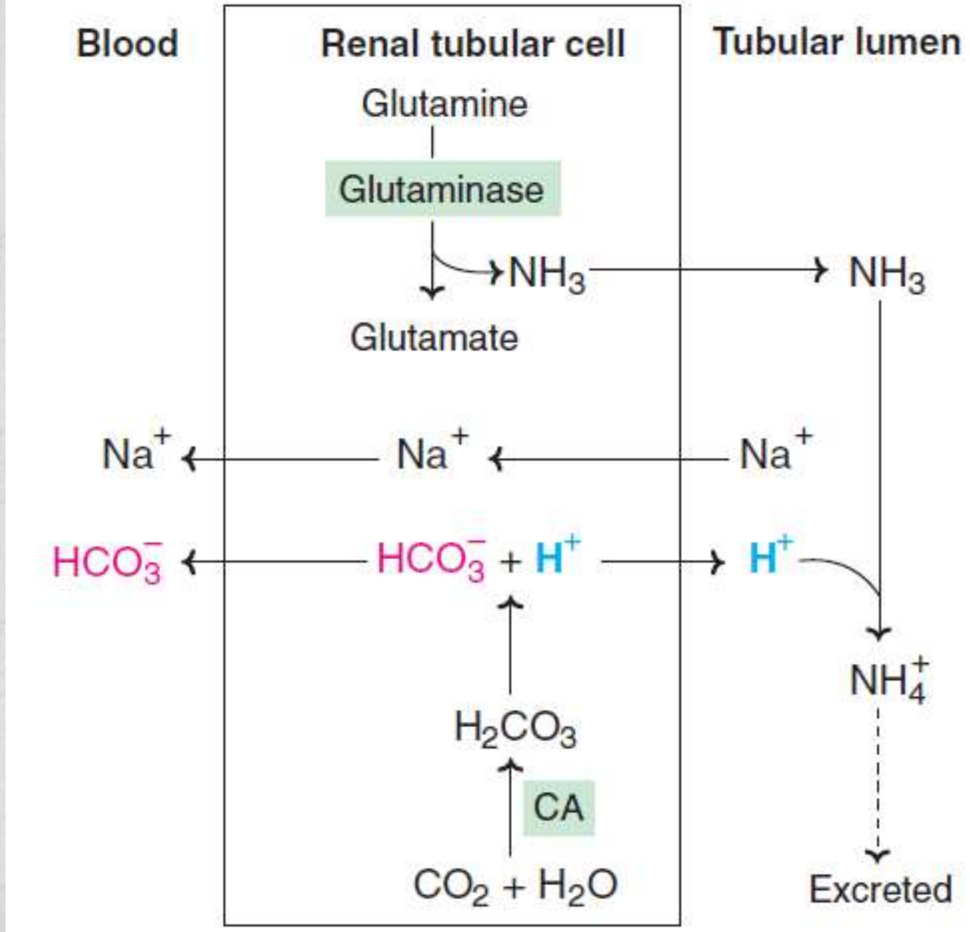


Fig. 21.8 : Renal regulation of blood pH–Excretion of ammonium ions (CA–Carbonic anhydrase).

Carbon dioxide—the central molecule of pH regulation

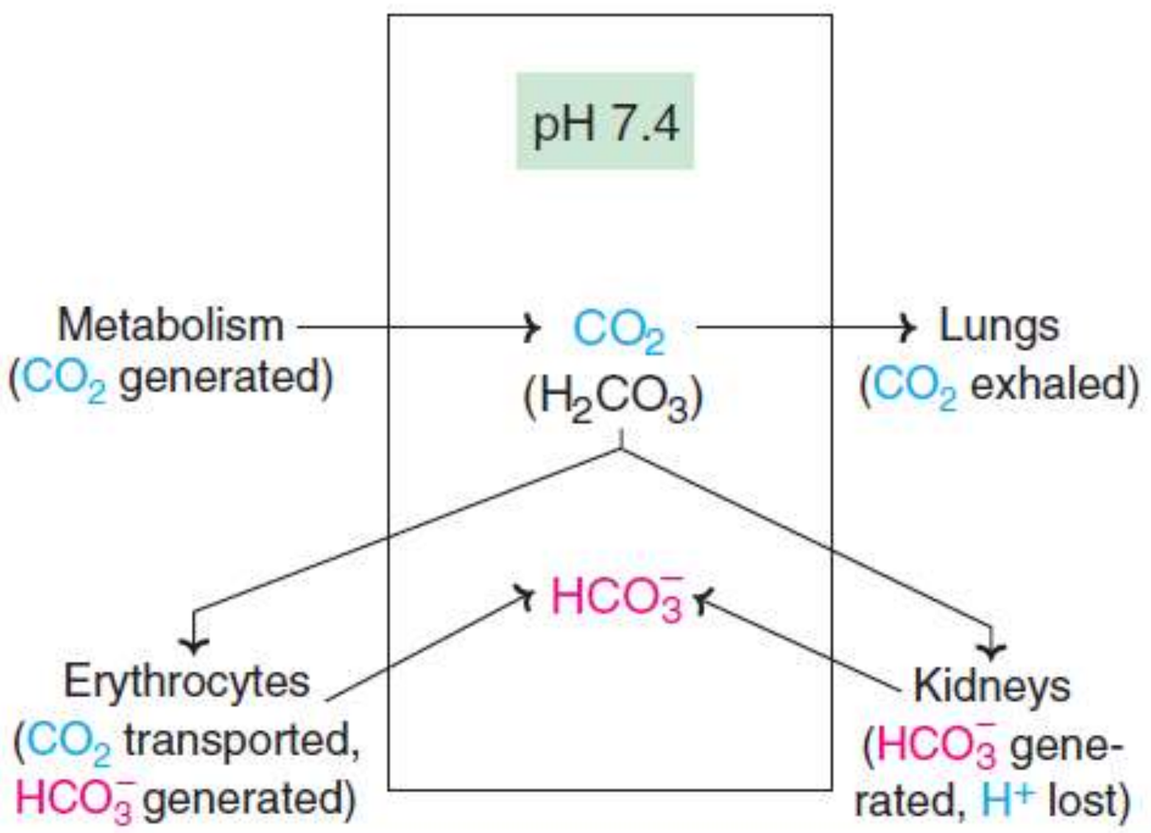


***Fig. 21.9 :** Carbon dioxide—the central molecule of blood pH regulation.*

DISORDERS OF ACID-BASE BALANCE

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 terms **acidemia and alkalemia,** respectively, refer to an increase or a decrease in [H+] ion concentration in blood. They are, however, not commonly used.

TABLE 21.4 Major clinical causes of acid-base disorders

Metabolic acidosis	*Respiratory acidosis*
Diabetes mellitus (ketoacidosis)	Severe asthma Pneumonia Cardiac arrest
Renal failure	Obstruction in airways
Lactic acidosis	Chest deformities
Severe diarrhea Renal tubular acidosis	Depression of respiratory center (by drugs e.g. opiates)
Metabolic alkalosis	*Respiratory alkalosis*
Severe vomiting	Hyperventilation
Hypokalemia	Anemia High altitude
Intravenous administration of bicarbonate	Salicylate poisoning

TABLE 21.6 Acid-base disorders with primary changes and compensatory mechanisms

Disorder	*Primary change*	*Compensatory mechanism*	*Timescale for compensation*
Metabolic acidosis	Decreased plasma bicarbonate	Hyperventilation (decrease in pCO_2)	Minutes to hours
Metabolic alkalosis	Increased plasma bicarbonate	Hypoventilation (increase in pCO_2)	Minutes to hours
Respiratory acidosis	Increased pCO_2	Elevation in plasma bicarbonate; increase in renal reabsorption of bicarbonate	Days
Respiratory alkalosis	Decreased pCO_2	Reduction in plasma bicarbonate; decrease in renal reabsorption of bicarbonate	Days

Table 21.5 Acid-base disorders along with the concentrations of bicarbonate (HCO_3^-) and carbonic acid (H_2CO_3) in plasma

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.*

thank you!