ACID BASE BALANCE
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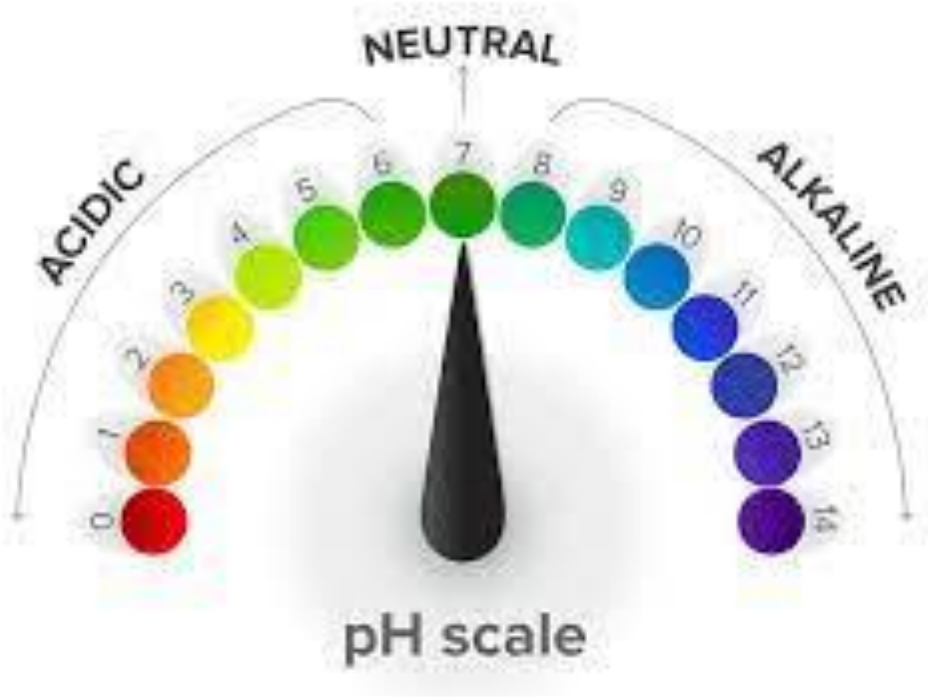


Acid-Base balance

- **Acid** is a substance whose dissociation in water releases hydrogen ions (H^+) Produces more acidic solution & **decrease** in pH $HCL \rightarrow H^+ + Cl^-$
- **A base** releases hydroxyl ions (OH^-) in aqueous solution.

This results in increase in pH of the solution

- $NaOH \rightarrow Na^+ + OH^-$

Amphoteric substances

Some substances, such as amino acids & proteins,

act acids as well as bases

Maintenance of blood pH

- The normal pH of the blood is maintained in the narrow range of <u>7.35- 7.45</u> (slightly alkaline).
- The body has developed three lines of defense to regulate the body's acid-base balance.
- 1- Blood <u>buffers</u>
- 2- <u>Respiratory</u> mechanism
- 3- <u>Renal</u> mechanism
- <u>Blood buffers</u>:
- A buffer may be defined as a solution of a weak acid & its salt with a strong base

Blood contains three buffer systems

- Bicarbonate buffer
- Phosphate buffer
- Protein buffer
- Bicarbonate buffer system:
- Sodium bicarbonate & carbonic acid ($NaHCO_3$- H_2CO_3) is the most predominant buffer system of ECF.
- Carbonic acid dissociates into hydrogen and bicarbonate ions.

$$H_2CO_3 \longleftrightarrow H^+ + HCO^-_3$$

- The blood pH 7.4, the ratio of bicarbonate to carbonic acid is 20: 1
- The bicarbonate concentration is much higher (20 times) than carbonic acid in the blood.
- This is referred to as alkali reserve.

Respiratory mechanism for pH regulation

- A rapid mechanism.
- 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. All of this CO_2 is eliminated from the body in the expired air via the lungs

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

The respiratory centre is highly sensitive to changes in the pH of blood.

Decrease in blood pH causes hyperventilation to blow off co_2 & reducing the H_2CO_3 concentration

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

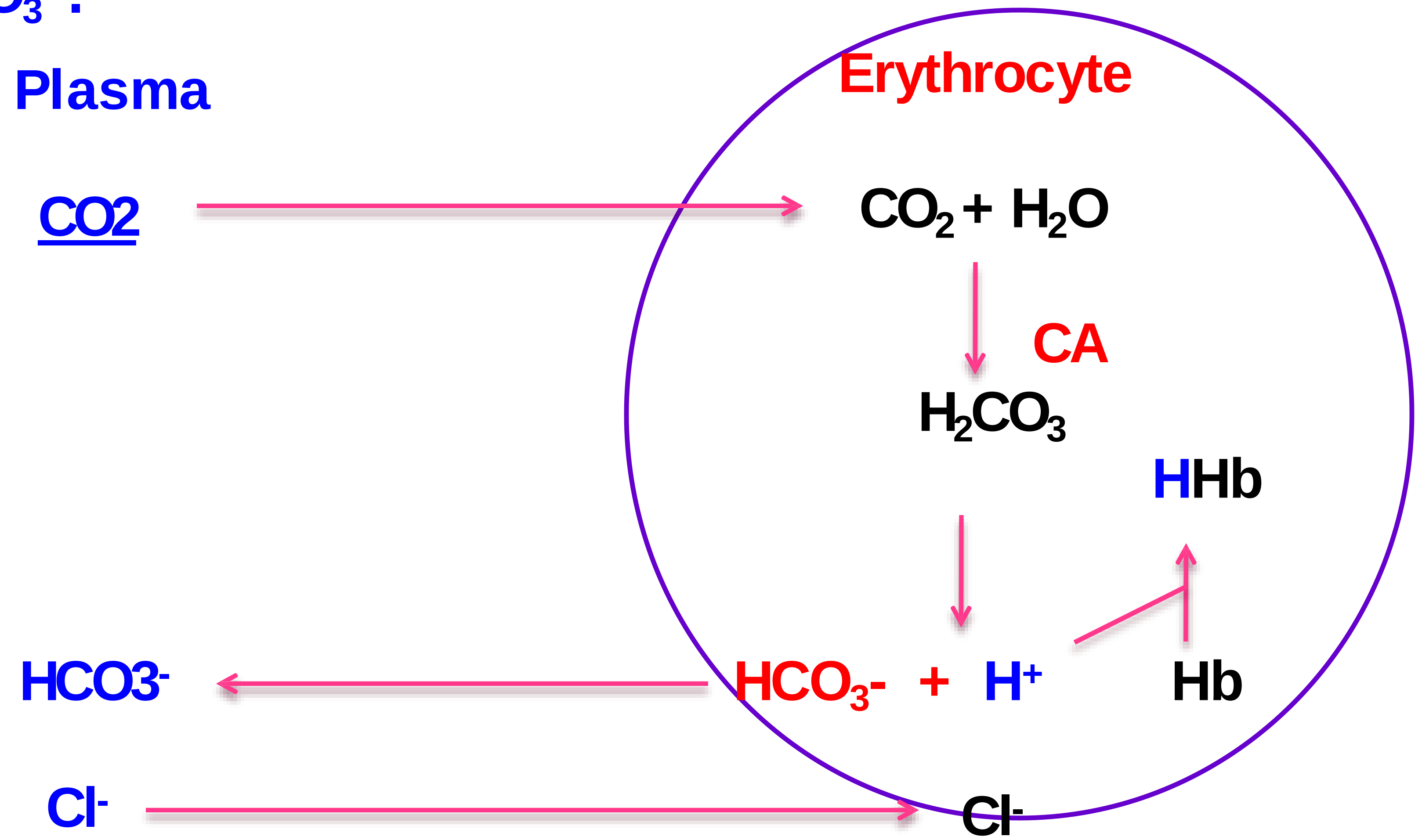
Hemoglobin as a buffer

- Hemoglobin binds to H^+ ions & helps to transport CO_2 as HCO_3^- with a minimum change in pH.
- In the lungs, hemoglobin combines with O_2, H^+ ions are removed which combine with HCO_3^- to form H_2CO_3 & is dissociates to release CO_2 to be exhaled.

Generation of HCO_3 by RBC

- Due to lack of aerobic metabolic pathways, RBC produce very little CO_2.
- The plasma CO_2 diffuses into RBC along the concentration gradient, it combines with water to form H_2CO_3 by Carbonic anhydrase.
- In RBC, H_2CO_3 dissociates to produce H^+ & HCO_3^-
- The H^+ ions are buffered by Hemoglobin.
- As the concentration of HCO_3^- increases in the RBC, it diffuses into plasma along with concentration gradient, in exchange for Cl^- ions, to maintain electrical neutrality.

This is **referred to as chloride shift**, helps to generate HCO_3^- .



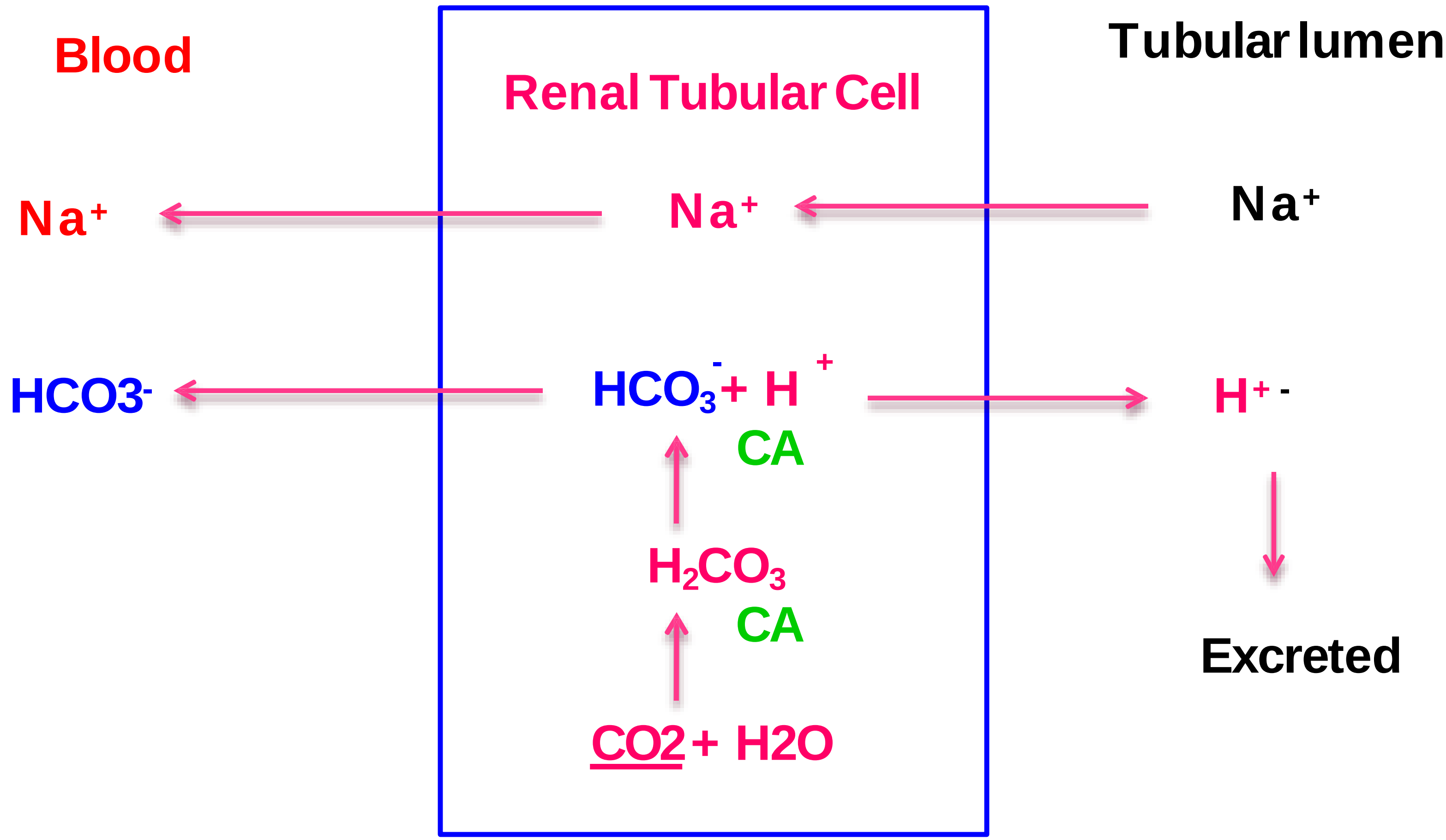
Renal mechanism for pH regulation

- The kidneys plays an important role in the regulation of pH through:
- 1-Excretion of H^+ ions
- 2-Reabsorption of Bicarbonate
- 3-Excretion of titratable acid
- 4-Excretion of ammonium ions

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 & is coupled with generation of HCO_3^-.
- Carbonic anhydrase catalyses the production of carbonic acid (H_2CO_3) from CO_2 & H_2O in renal tubular cells.
- H_2CO_3 then dissociates to H^+ & HCO_3^-
- H^+ ions are secreted into tubular lumen in exchange for Na^+
- Na^+ in association with HCO_3^- is reabsorbed into blood

Excretion of H^+ ions

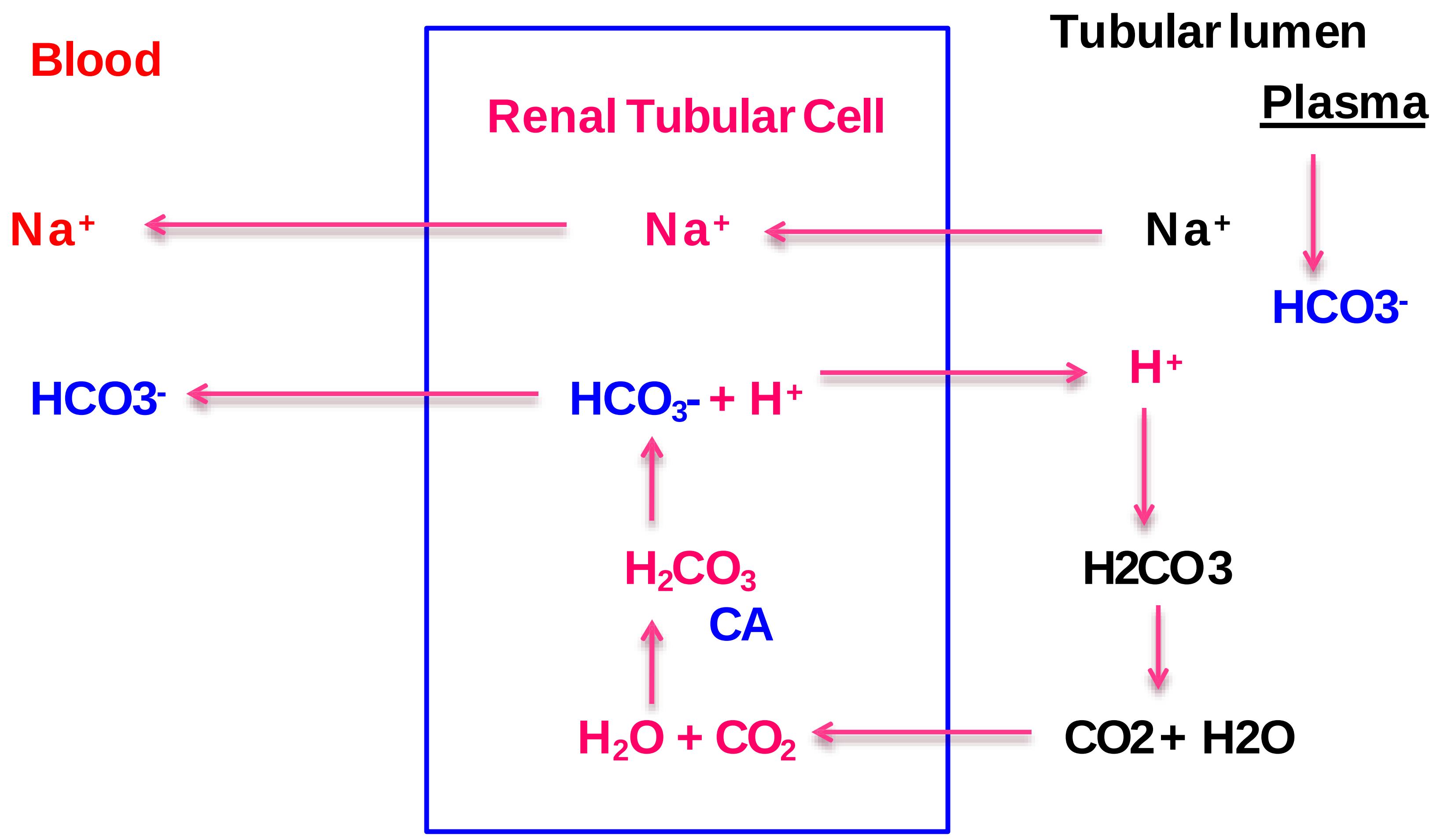


Reabsorption of Bicarbonate

- This mechanism is responsible to conserve blood HCO_3^-, with simultaneous excretion of H^+ ions.
- Bicarbonate freely diffuses from plasma into tubular lumen.
- HCO_3^- combines with H^+, secreted by tubular cells, to form H_2CO_3.
- H_2CO_3 is then cleaved to form CO_2 and H_2O.
- As the CO_2 concentration builds up in the lumen, it diffuses into the tubular cells along the concentration gradient.

- In the tubular cell, CO_2 again combines with H_2O to form H_2CO_3 which then dissociates into H^+ & HCO_3^-
- The H^+ is secreted into the lumen in exchange for Na^+.
- The HCO_3^- is reabsorbed into plasma in association with Na^+.
- Reabsorption of HCO_3^- is a cyclic process without net excretion of H^+ or generation of new HCO_3^-

Reabsorption of bicarbonate



Excretion of titratable acid

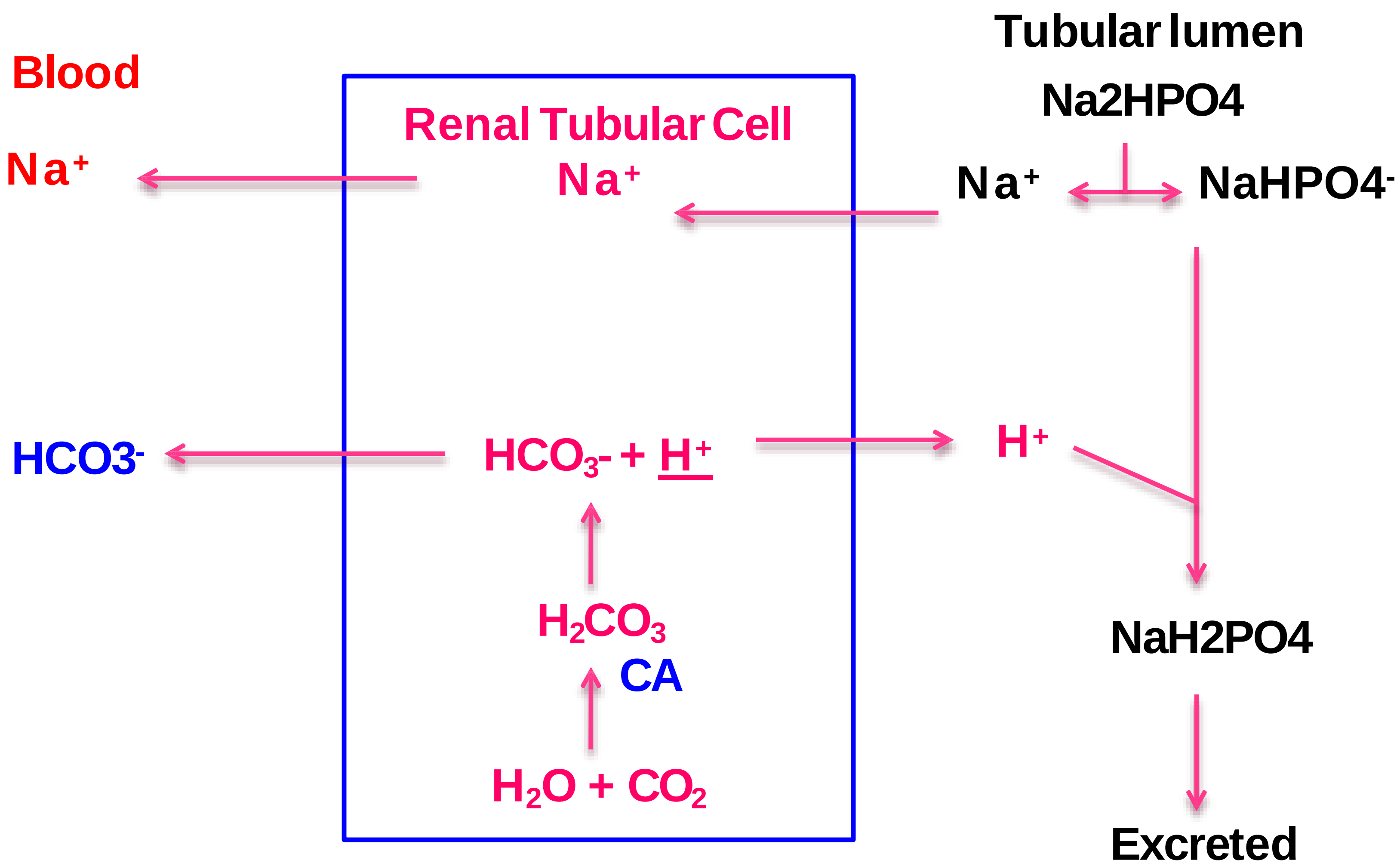
- Titratable acidity is a measure of acid excreted into urine by the kidney.
- Titratable acidity refers to the number of milliliters of N/10 NaOH required to titrate 1 liter of urine to pH 7.4.
- Titratable acidity reflects the H^+ ions excreted into urine.

- H^+ ions are secreted into the tubular lumen in exchange for Na^+ ion.
- This Na^+ is obtained from the base, disodium hydrogen phosphate (Na_2HPO_4).
- This combines with H^+ to produce the acid, sodium dihydrogen phosphate (NaH2PO4), in which form the major quantity of titratable acid in urine is present.
- Tubular fluid moves down the renal tubules,

  more and more H^+ ions are added, resulting in the acidification of

  urine. Causes a fall in the pH of urine as low as 4.5.

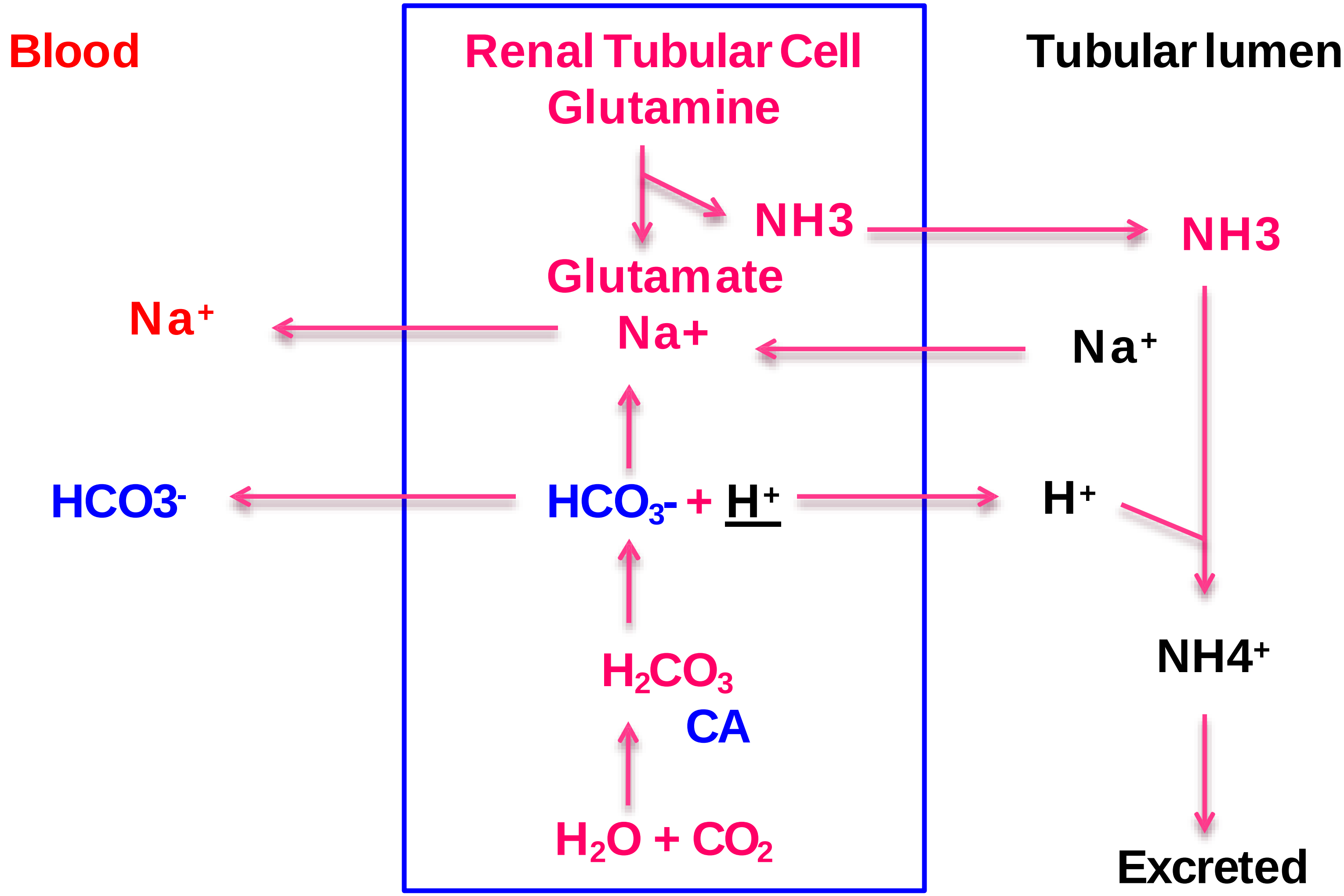
Excretion of titratable acid



Excretion of ammonium ions

- The H^+ ion combines with NH_3 to form ammonium ion (NH_4^+).
- The renal tubular cells deaminate glutamine to glutamate and NH_3 by the action of enzyme glutaminase.
- The liberated NH_3 diffuses into the tubular lumen where it combines with H^+ to form NH_4^+.
- Ammonium ions cannot diffuse back into tubular cells and excreted into urine.

Excretion of ammonium ions



Acidosis

Blood PH tend to ↓

Results from formation of **excessive acids**
More than the capacity of the body to eliminate them

Respiratory acidosis

Metabolic acidosis

Respiratory acidosis

↑ CO_2 (CO_2 RETENTION) due to

- Bronchial asthma
- Chronic bronchitis
- Emphysema
- Pneumonia
- Respiratory centre inhibition
- Asphexia

↑ CO_2 → ↑ blood H_2CO_3

Respiratory acidosis

↑CO_2 → ↑ blood H_2CO_3

→ HCO_3^- not changed

→ ↓ HCO_3^-/H_2CO_3 (N=20:1)

→ ↓blood PH

(Uncompensated respiratory acidosis [acidemia])

How to compensate?

Kidney reabsorbs more HCO_3^-

Till normal HCO_3^-/H_2CO_3 (20:1)

→ PH reach 7.4

Metabolic acidosis

↑ acids or ↓ bases (HCO_3^-) in blood

→ ↓ blood HCO_3^-

→ blood H_2CO_3 not changed

→ ↓ HCO_3^-/H_2CO_3 (N=20:1)

→ ↓blood PH

(Uncompensated metabolic acidosis [acidemia])

<u>How to compensate?</u>

↓ PH→ ++ chemoreceptors in respiratory centre→ hyperventilation→ loss of CO_2→↓H_2CO_3

Till normal HCO_3^-/H_2CO_3 (20:1)

→ PH reach 7.4 (Compensated metabolic acidosis)

Causes of Metabolic acidosis

1- ↑ blood acids

↑ production

- ↑ lactic acid in muscular exercise
- ↑ ketone bodies in Ketosis due to Diabetes mellitus
- ↑ acids from metabolism of different food stuffs (diet) as pyruvic , lactic, phosphoric and nucleic acids.

↓ excretion

- failure of excretion by the kidney in chronic renal failure

Causes of Metabolic acidosis

1- ↑ base loss

- **Diarrhea**: Intestinal juices are alkaline being rich in Na^+ & K^+ bicarbonate
- **Vomiting**: due to low intestinal obstruction
- **Hyperkalemia**:

  * ↑renal tubular reabsorption of Na^+ in exchange with K^+

  → stop of Na^+/ H^+ exchange

  * Na^+ reabsorption will be in the form of NaCl not $NaHCO_3$ > HCO_3^- will be excreted in the form of $KHCO_3$ in urine.

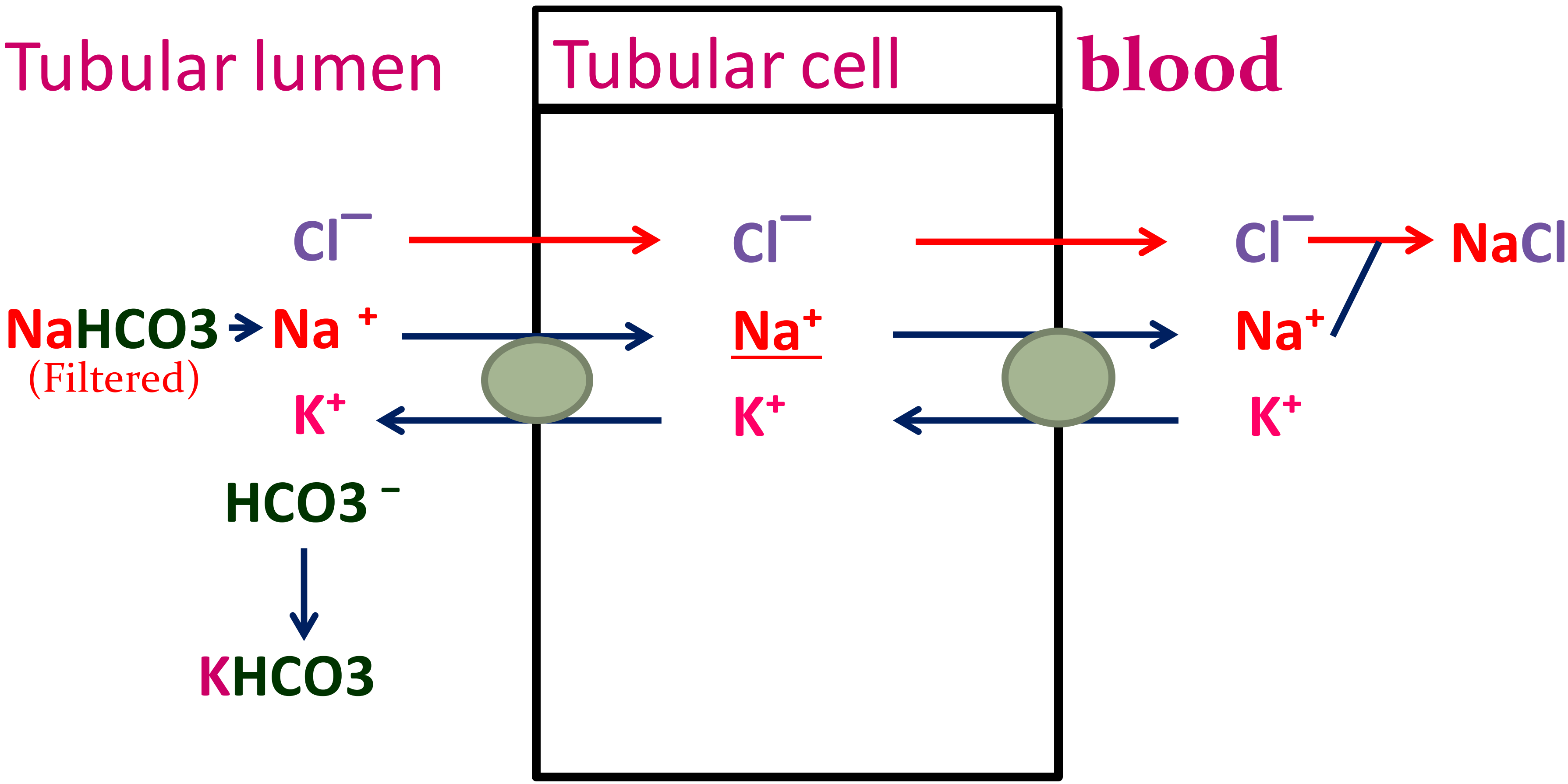
  HCO_3^- loss in urine → metabolic acidosis (Alkaline urine)

  ↑ Cl in blood→ hyperchloremic acidosis (Acidic blood)

The alkaline urine& acidic blood is called <u>paradoxical acidosis</u>

Causes of Metabolic acidosis

1- ↑blood acids



Alkalosis

Blood PH tend to ↑

Results from formation of excessive bases
More than the capacity of the body to neutralize & eliminate them

Respiratory alkalosis

Metabolic alkalosis

Respiratory alkalosis

↑ CO_2 loss due to

- fever
- encephalitis
- high altitude
- late stages of salicylate poisoning
- hystrical hyperventilation

↓ CO_2 → ↓ blood H_2CO_3

Respiratory alkalosis

↓ CO_2 → ↓ blood H_2CO_3
↘ HCO_3^- not changed

→ ↑ HCO_3^-/H_2CO_3 (N=20:1)

→ ↑ blood PH

(Uncompensated respiratory alkalosis [alkalemia])

<u>How to compensate?</u>

-- of renal tubular reabsorption of HCO_3^-

Kidney excretes more HCO_3^-

Till normal HCO_3^-/H_2CO_3 (20:1)

→ PH reach 7.4

(Compensated respiratory alkalosis)

Urine will be alkaline because of ↑ secretion of K^+ & HCO_3^- in urine

Metabolic alkalosis

↑ bases or ↓ acids in blood

→ ↑ blood HCO_3^-

↘ blood H_2CO_3 not changed

→ ↑ HCO_3^-/H_2CO_3 (N=20:1)

→ ↑blood PH

(Uncompensated metabolic alkalosis [acidemia])

How to compensate?

↑ PH→ - - - chemoreceptors in respiratory centre→ hypoventilation→ CO_2 retention →↑H_2CO_3

Till normal HCO_3^-/H_2CO_3 (20:1)

→PH reach 7.4 (Compensated metabolic alkalosis)

Causes of Metabolic alkalosis

1- ↑absorption of bases

- Intake of high vegetable and fruit diet: They contain Bicarbonate salts and citrate salts. Citrate salts will be transformed into bicarbonate salts by krebs cycle
- Intake of drugs containing bicarbonate & citrate salts (drugs used for treatment of hyperacidity & peptic ulcer)

Causes of Metabolic alkalosis

2- ↑loss of acids

- Prolonged <u>suction</u> of gastric juice
- <u>Vomiting</u> due to high intestinal obstruction
- <u>Hypokalemia:</u>

  *↓renal tubular reabsorption of Na^+ in exchange with K^+

  → instead there is Na^+/ H^+ exchange

  * Na^+ reabsorption will be in the form of NaHCO3 not NaCl →

  # Cl^- loss in urine in the form of NH4Cl→ hypochloremia and acidic urine

  ↑ NaHCO3 in blood→ alkalosis(alkaline blood)

The acidic urine& alkaline blood is called paradoxical alkalosis

- <u>Cushing syndrome</u>: →Na& water retention & K excretion→ hypokalemia