RENAL FUNCTION – An Overview

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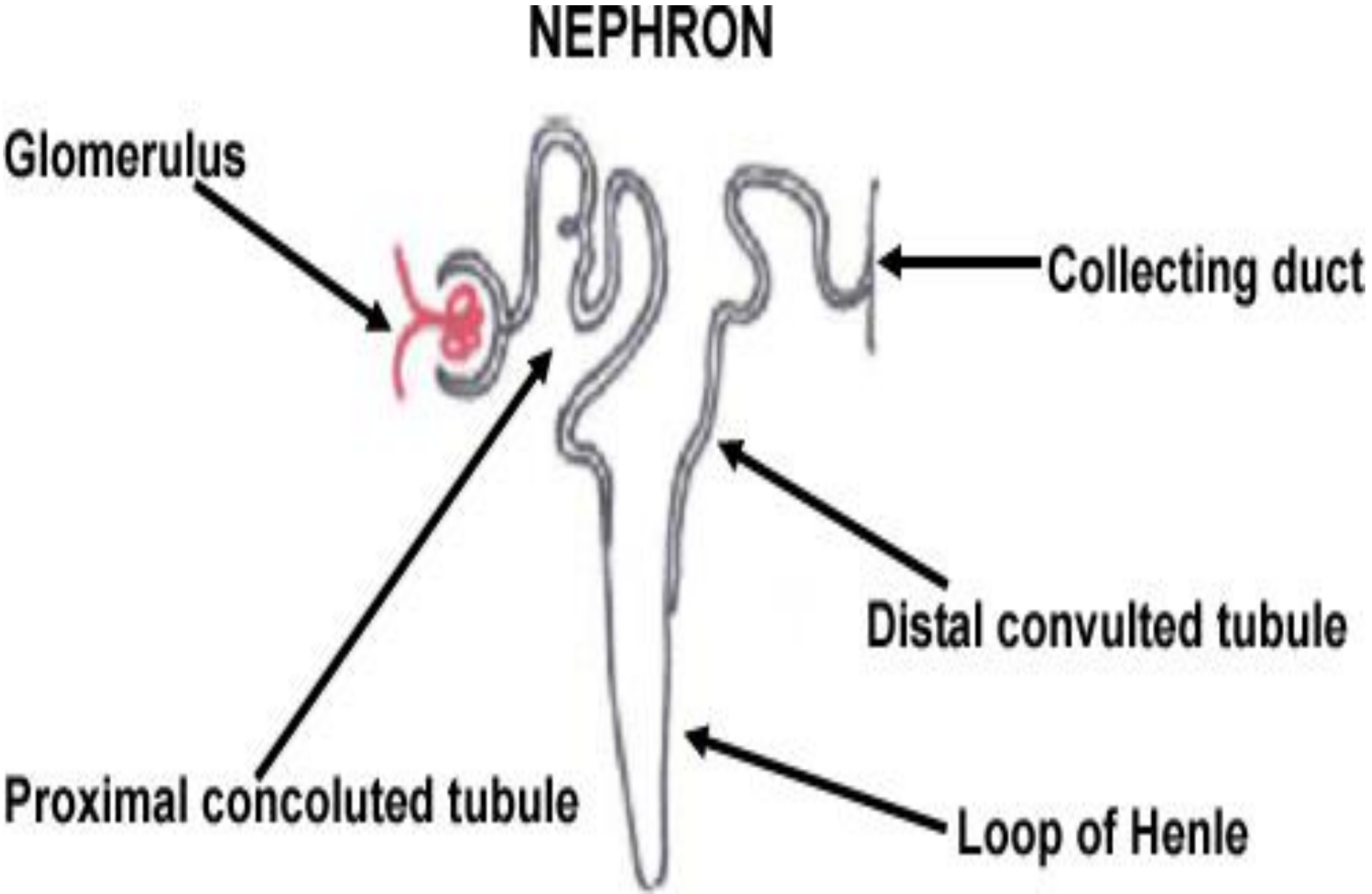
- Kidneys are the major excretory system in humans and other Ureotelic Organisms;
- Nephron is the Functional unit of the Kidneys **(Fig 1)**

Fig 1 http://www.dwp.gov.uk/publications/specialist-guides/medical-conditions



What are some basic functions of the kidneys?

- Kidneys form urine in which toxic waste products of metabolism are excreted;
- Three major processes used in formation of urine:
  - Glomerular Filtration,
  - Tubular Reabsorption,
  - Tubular Secretion;
- Glomerular Filtration Rate (GFR) is the maximum rate that plasma can be 'Cleared' of any substance by kidneys;
- Rate of GFR is about 140ml/min or about 180 litres/day;
- Filtration is accomplished by blood Hydrostatic pressure,
- Glomerular Filtrate (GF) is an Ultra filtrate of Plasma;

- Normal GFR depends on normal Renal Blood Flow and Pressure,
- Composition of GF is the same as plasma excluding the Plasma Proteins: Thus,
  - GF contains all the low mol wt compounds in plasma,
  - High mol wt compounds like, Proteins, RBC, WBC, various Enzymes etc are not filtered,
- Most of the fluid in GF are reabsorbed via Tubules and returned to the vascular system to maintain blood volume and pressure;

- Extent of Tubular reabsorption depends on the need to adjust blood composition and ability of the kidneys to reabsorb the various components in the GF;
- Kidneys play major role in excretion of Nitrogenous wastes, including products of Protein and Nucleic acid metabolism, such as: Urea, Creatinine, Creatine, Uric acid, Sulphate, Phosphate, Nitrate, Nitrite, etc.

What are some regulatory functions of the kidneys?

- Regulation of ECF Volume and Electrolyte to compensate for wide daily variations in Water and Electrolyte intake,
- Regulation of water,
- Regulation of Electrolyte,
- Participate in regulation of blood pressure,
- Participate in regulation of Calcium and Phosphate metabolism,
- Regulation of Acid-Base balance, which involves maintaining the pH (acidity/alkalinity) in body fluids,

What are some endocrine functions of the kidneys?

- Kidneys are under control of some hormones and productions of some hormones are under the control of the kidneys,
- **Arginine Vasopressin** (**AVP**): Acts on kidneys to Regulate fluid balance;
- **Aldosterone:** Acts on Kidney Tubules to Regulates Sodium & Potassium balance;
- **Parathyroid Hormone** (**PTH**): Acts via the Kidneys:
  - To promote Tubular Reabsorption of Calcium;
  - To promote Phosphate excretion;
  - For biosynthesis of 1,25-Dihydroxy-Cholecalciferol (Vitamin D_3) that regulates Calcium absorption by Gastrointestinal Tract;

- **Renin** produced by Juxtaglomerular cells in kidneys:
  - Renin catalyzes conversion of Angiotensinogen to Angiotensin-1,
  - Angiotensin Converting Enzyme (**ACE**) then converts Angiotensin-1 to Angiotensin II,
  - Angiotensin II stimulates biosynthesis of Aldosterone in the Adrenal Cortex,
- **Erythropoietin**: A peptide hormone that promotes biosynthesis of Hemoglobin,
  - Production of Erythropoietin is partly regulated by kidneys;

- **NB: Endocrine effects of kidneys remain intact until End Stage Renal Failure;**

How do the kidneys regulate Acid-Base balance?

- Kidney regulates Acid-Base Balance by controlling:
  - Re-absorption of Bicarbonate ions (HCO_3^-)
  - Secretion of Hydrogen ions (H^+)
- Both processes depend on formation of HCO_3^- ions H^+ ions from CO_2 and H_2O within Renal Tubular cells:

Carbonic Anhydrase

$$\mathbf{CO_2 + H_2O \leftarrow\!=\!=\!=\!=\!=\rightarrow H_2CO_3 \leftarrow\!=\!=\!=\!=\!=\rightarrow H^+ + HCO_3^-}$$

- H^+ ions formed are actively secreted into Tubular lumen in exchange for Na^+

IMPORTANT TO NOTE

- H^+ ions buffered in blood during metabolism are excreted via the kidneys, regenerating HCO_3^- ions used up in the buffering process and maintaining the plasma [HCO_3^-] within normal limits;
- Secretion of H^+ ions by Tubular cells serves initially to reabsorb HCO_3^- ions from GF to prevent lost from body,
- When all the HCO_3^- ions have been reabsorbed, any deficit due to buffering process is regenerated,
- Mechanism for Reabsorption of HCO_3^- ions is different from the Regeneration of HCO_3^- ions;

What renal mechanisms are used for elimination of Acids?

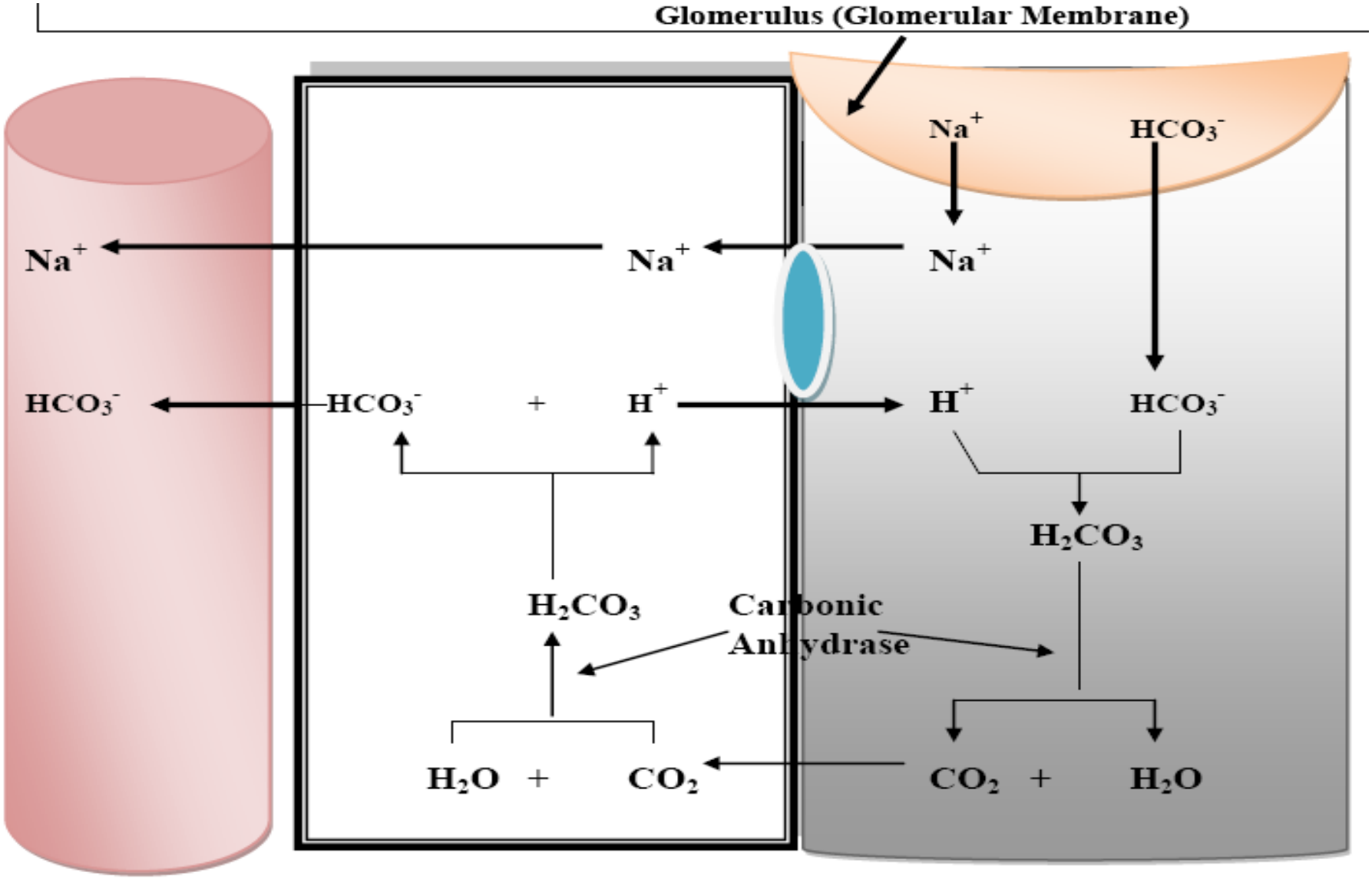
- Mechanisms for elimination of Acids:
  - **Re-absorption** of Bicarbonate (HCO_3 ions) by Proximal Renal Tubules, (**Fig. 2**)
  - **Regeneration** of HCO^-_3 by Distal Renal Tubules (**Fig. 3**)
  - **Phosphate buffer** formation in Distal Tubules (**Fig. 4**)
  - Production of **Ammonia (NH_3)** by Distal Renal Tubules for formation of Ammonium buffer (**Fig. 5**)

How are HCO_3^- ions reabsorbed from Glomerular Filtrate (GF)?

- **HCO_3^-** are freely filtered via Glomerular membrane;
- **[HCO_3^-]** in GF is equivalent to that in Plasma,
- If **HCO_3^-** are not reabsorbed by Renal Tubules then the buffering capacity of plasma would rapidly deplete,
- Reabsorption of **HCO_3^-** ions occurs mostly in Proximal Convoluted Tubules **(Fig. 2)**
  - In Tubular Lumen **HCO_3^-** filtered via Glomerulus combine with **H^+** secreted from Tubular cell forming Carbonic Acid (**H_2CO_3**);
  - **H_2CO_3** is converted to **CO_2** and **H_2O** catalyzed by **Carbonic Anhydrase-II**, located in brush border of Tubular cells;

- CO_2 produced diffuses into Tubular cell membrane,
- The **CO_2** interacts with **H_2O** again to form **H_2CO_3** in a reaction catalyzed by Carbonic Anhydrase-II,
- The **H_2CO_3** formed dissociates to form **HCO_3^-** and **H^+ ions**;
  - **HCO_3^-** ions formed diffuse into blood plasma and **H^+** ions are transported into Tubular Lumen in exchange for **Na^+**
- Thus almost all the **HCO_3^- ions** in the Glomerular Filtrate are Reabsorbed or Reclaimed (**Fig. 2**);

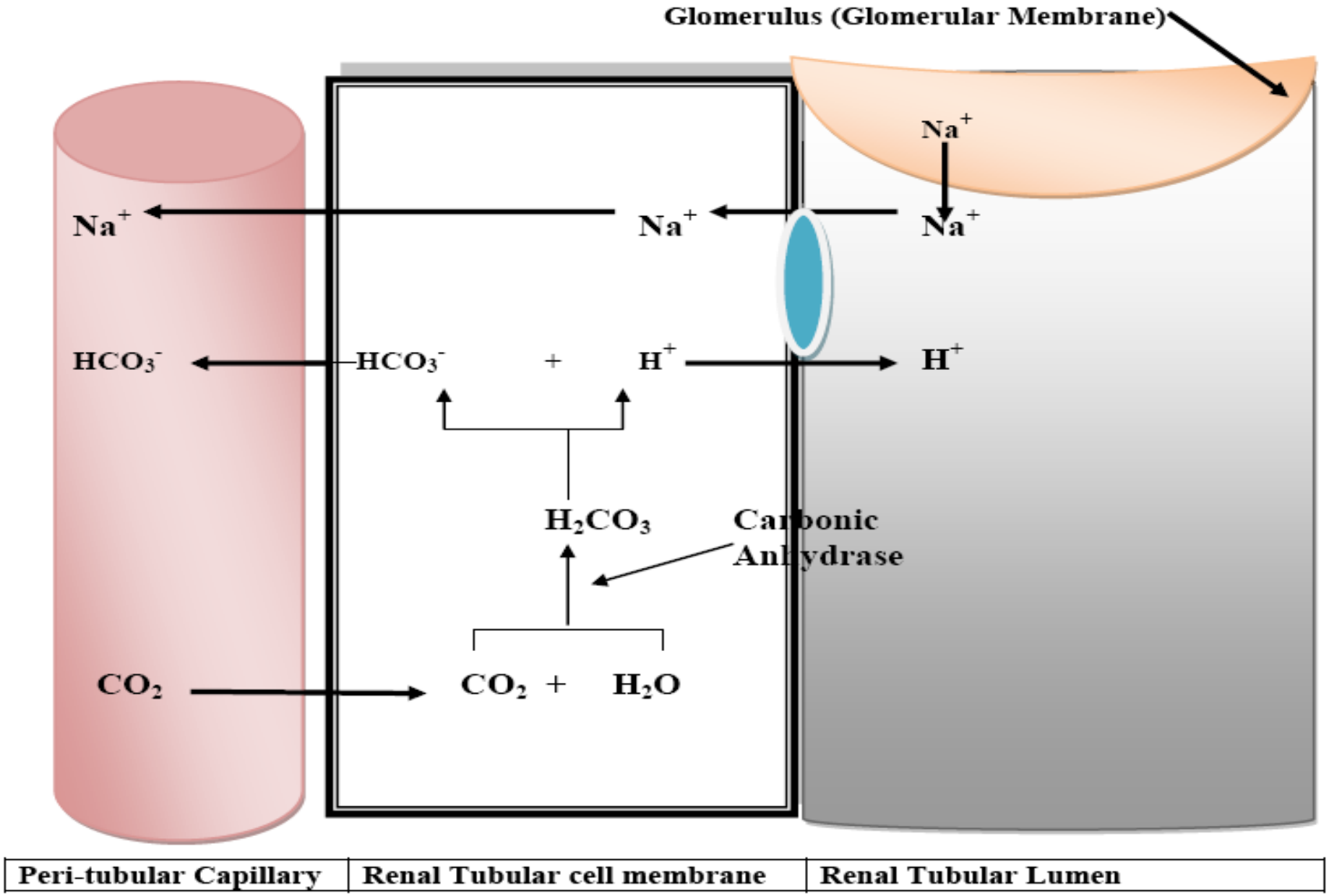
Fig. 2: Diagram to illustrate reabsorption of HCO_3^- ions by Renal Tubules



How are the Bicarbonate ions Regenerated?

- After reabsorption of **HCO_3^-** ions is completed, process of regeneration compensates for any deficit in **[HCO_3^-]** reabsorbed,
- Mechanisms for reabsorption of HCO_3^- ions and for the regeneration of HCO_3^- ions are different,
- These two processes are very similar and are sometimes confused,
- Mechanism of Regeneration of HCO_3^- is shown in **Fig.3**.

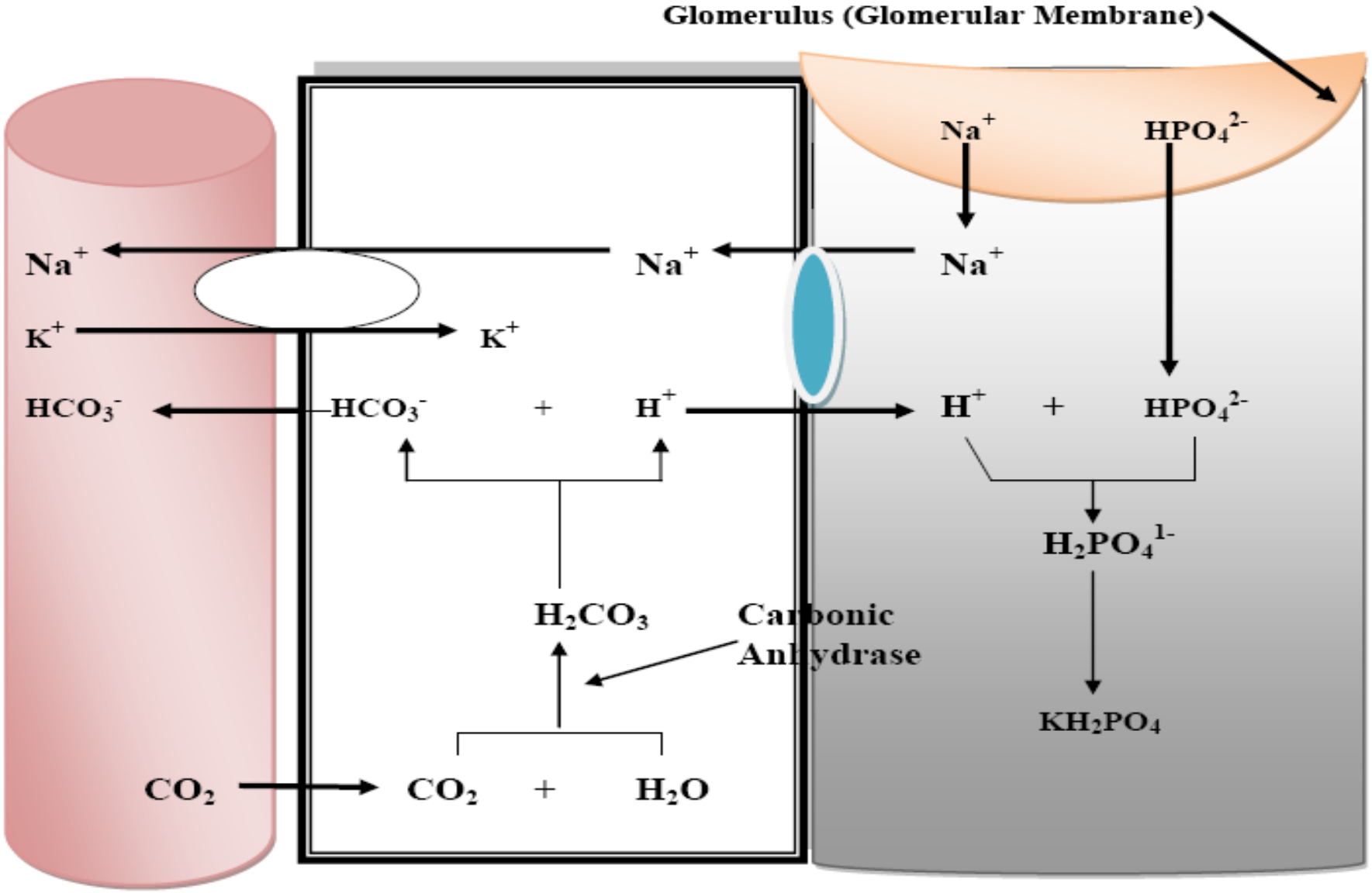
Fig. 3: Regeneration of Bicarbonate ions by Renal Tubules



How are H^+ ions excreted by the Renal Tubules?

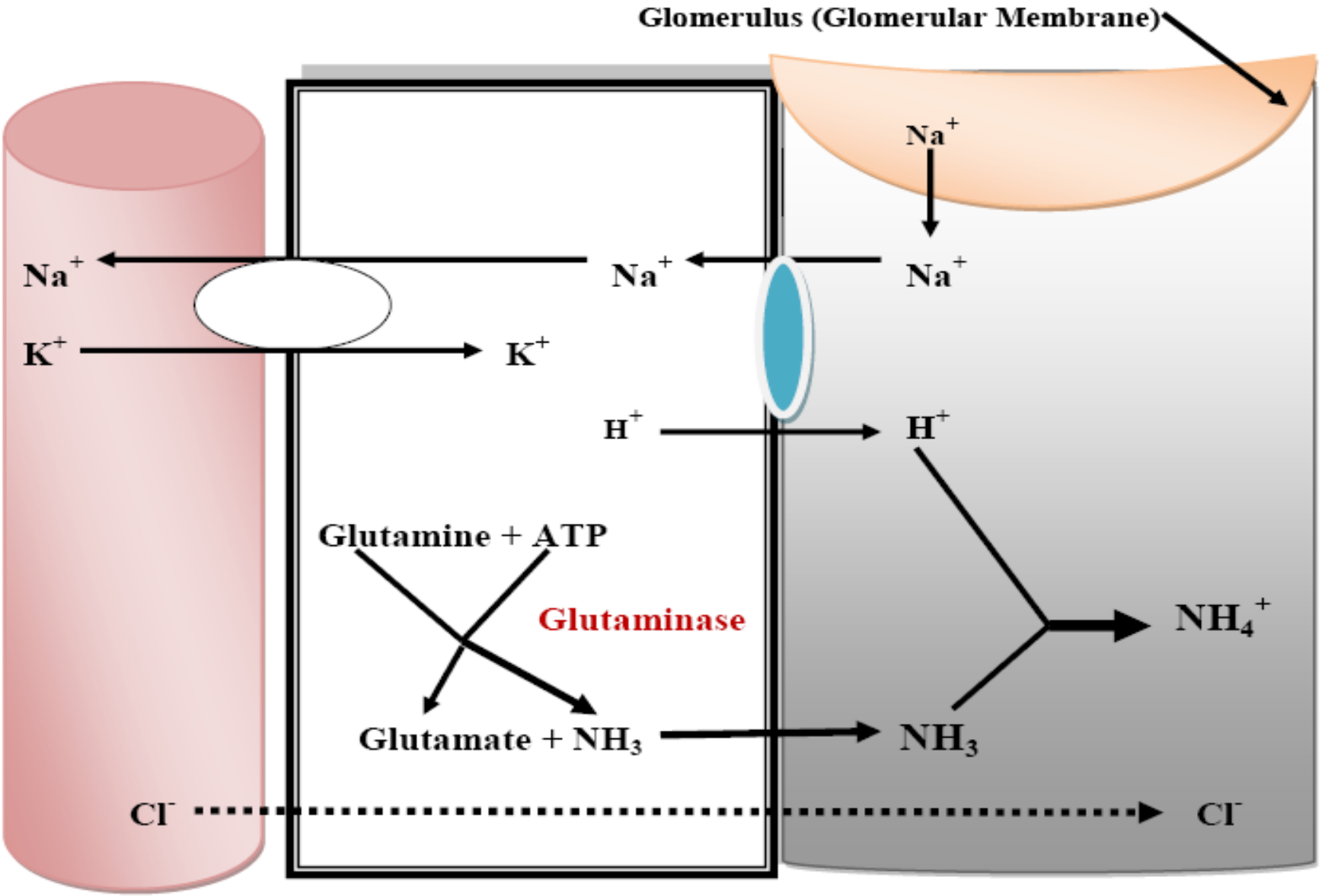
- **H^+ ions** are secreted in exchange for Na^+ ions,
  - Energy for this exchange is from **Na^+-K^+-ATPase** (Sodium-Potassium pump) that maintains the **[Na^+]** gradient,
- Secretion of H^+ ions is regulated by buffers
- Phosphate (HPO_4^{2-}) and Ammonium (NH_3) buffers are the predominant buffers in Renal tubules and Urine,
- **HPO_4^{2-} ion** is freely filtered in the Glomerulus, then passes down the Tubule where it combines with an H^+ ion to form $H_2PO_4^-$ (**Fig. 4**);

Fig. 4: Formation of Phosphate Buffer in Renal Tubules



- **Ammonia (NH_3)** is produced in Renal Tubular cells by the action of **Glutaminase** on the amino acid **Glutamine**,
- Glutaminase activity is optimally at lower (more acidic) than normal pH,
  - Thus, more Ammonia is produced during Acidosis, which enhances the buffering capacity of the Urine,
- Ammonia rapidly diffuses into Renal Tubular Lumen,
- In the Tubular Lumen, **NH_3** combines with **H^+ ions** to form **NH_4^+ ions** (Ammonium ions),
- NH_4^+ ions binds with Chloride ions and passed out in urine as **NH_4 Cl** (**Fig 5**).

Fig. 5: Formation of Ammonium Buffer in Renal Tubules



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