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 Regulate 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 D₃) 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$_2$O within Renal Tubular cells:

  **Carbonic Anhydrase**

  \[
  \text{CO}_2 + \text{H}_2\text{O} \rightleftharpoons \text{H}_2\text{CO}_3 \rightleftharpoons \text{H}^+ + \text{HCO}_3^-
  \]

- 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 HCO₃⁻ ions used up in the buffering process and maintaining the plasma [HCO₃⁻] within normal limits;

• Secretion of H⁺ ions by Tubular cells serves initially to reabsorb HCO₃⁻ ions from GF to prevent lost from body,

• When all the HCO₃⁻ ions have been reabsorbed, any deficit due to buffering process is regenerated,

• Mechanism for Reabsorption of HCO₃⁻ ions is different from the Regeneration of HCO₃⁻ 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 \( \text{HCO}_3^- \) ions reabsorbed from Glomerular Filtrate (GF)?

- \( \text{HCO}_3^- \) are freely filtered via Glomerular membrane;
- \([\text{HCO}_3^-]\) in GF is equivalent to that in Plasma,
- If \( \text{HCO}_3^- \) are not reabsorbed by Renal Tubules then the buffering capacity of plasma would rapidly deplete,
- Reabsorption of \( \text{HCO}_3^- \) ions occurs mostly in Proximal Convoluted Tubules (Fig. 2)
  - In Tubular Lumen \( \text{HCO}_3^- \) filtered via Glomerulus combine with \( \text{H}^+ \) secreted from Tubular cell forming Carbonic Acid (\( \text{H}_2\text{CO}_3 \));
  - \( \text{H}_2\text{CO}_3 \) is converted to \( \text{CO}_2 \) and \( \text{H}_2\text{O} \) catalyzed by **Carbonic Anhydrase-II**, located in brush border of Tubular cells;
• CO₂ produced diffuses into Tubular cell membrane,
• The CO₂ interacts with H₂O again to form H₂CO₃ in a reaction catalyzed by Carbonic Anhydrase-II,
• The H₂CO₃ formed dissociates to form HCO₃⁻ and H⁺ ions;
  • HCO₃⁻ ions formed diffuse into blood plasma and H⁺ ions are transported into Tubular Lumen in exchange for Na⁺
• Thus almost all the HCO₃⁻ ions in the Glomerular Filtrate are Reabsorbed or Reclaimed (Fig. 2);
Fig. 2: Diagram to illustrate reabsorption of $\text{HCO}_3^-$ ions by Renal Tubules
How are the Bicarbonate ions Regenerated?

- After reabsorption of $\text{HCO}_3^-$ ions is completed, process of regeneration compensates for any deficit in $[\text{HCO}_3^-]$ reabsorbed,
- Mechanisms for reabsorption of $\text{HCO}_3^-$ ions and for the regeneration of $\text{HCO}_3^-$ ions are different,
- These two processes are very similar and are sometimes confused,
- Mechanism of Regeneration of $\text{HCO}_3^-$ is shown in Fig.3.
Fig. 3: Regeneration of Bicarbonate ions by Renal Tubules

- **Na⁺**
- **HCO₃⁻**
- **CO₂**
- **H₂CO₃**
- **Carbonic Anhydrase**
- **CO₂ + H₂O**

| Peri-tubular Capillary | Renal Tubular cell membrane | Renal Tubular Lumen |
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 (HPO₄²⁻) and Ammonium (NH₃) buffers are the predominant buffers in Renal tubules and Urine,
- **HPO₄²⁻ ion** is freely filtered in the Glomerulus, then passes down the Tubule where it combines with an H⁺ ion to form H₂PO₄⁻ (**Fig. 4**);
Fig. 4: Formation of Phosphate Buffer in Renal Tubules

Glomerulus (Glomerular Membrane)

Na$^+$

K$^+$

HCO$_3^-$

HCO$_3^-$ + H$^+$

H$_2$CO$_3$

Carbonic Anhydrase

H$_2$PO$_4^{1-}$

KH$_2$PO$_4$

Peri-tubular Capillary | Renal Tubular cell membrane | Renal Tubular Lumen
• 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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<th>Peri-tubular Capillary</th>
<th>Renal Tubular cell membrane</th>
<th>Renal Tubular Lumen</th>
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Glomerulus (Glomerular Membrane)

Na⁺ → Na⁺
K⁺ → K⁺
H⁺ → H⁺

Glutamine + ATP → Glutaminase → Glutamate + NH₃

NH₄⁺ → NH₃ → Cl⁻
REFERENCES

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