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# **BCH 450**

# **Biochemistry of**

# **Specialized Tissues**

## **VII. Renal Structure, Function & Regulation**



# Kidney Function

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1. Regulate Extracellular fluid (ECF) (plasma and interstitial fluid) through formation of urine.  
Primary function.
2. Regulate volume of blood plasma.  
Blood Pressure (BP).
3. Eliminates waste products from the blood.
4. Regulate concentration of electrolytes.  
 $\text{Na}^+$ ,  $\text{K}^+$ , and  $\text{HCO}_3^-$  and other ions.
5. Regulate pH.

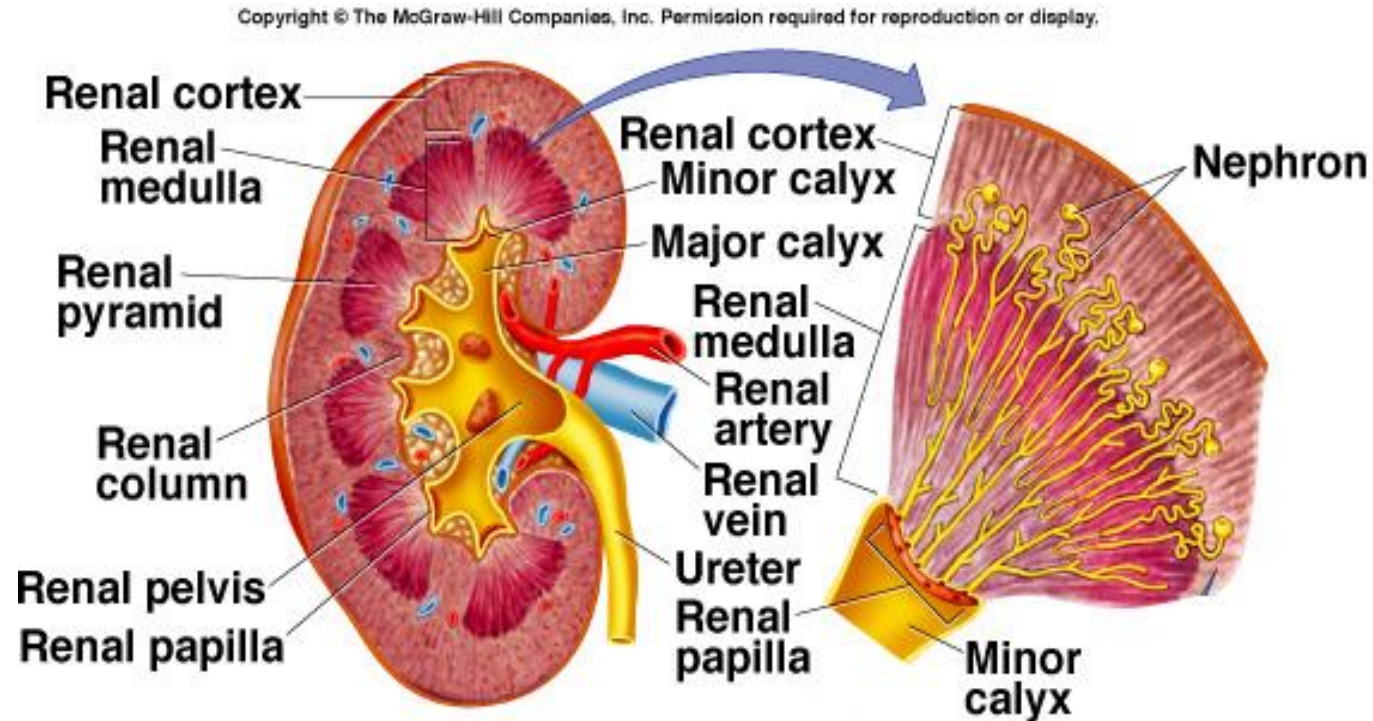
# Structure of the Kidney

## Outer cortex:

- Contains many capillaries.

## Medulla:

- Renal pyramids separated by renal columns.
- Pyramid contains minor calyces which unite to form a major calyx.

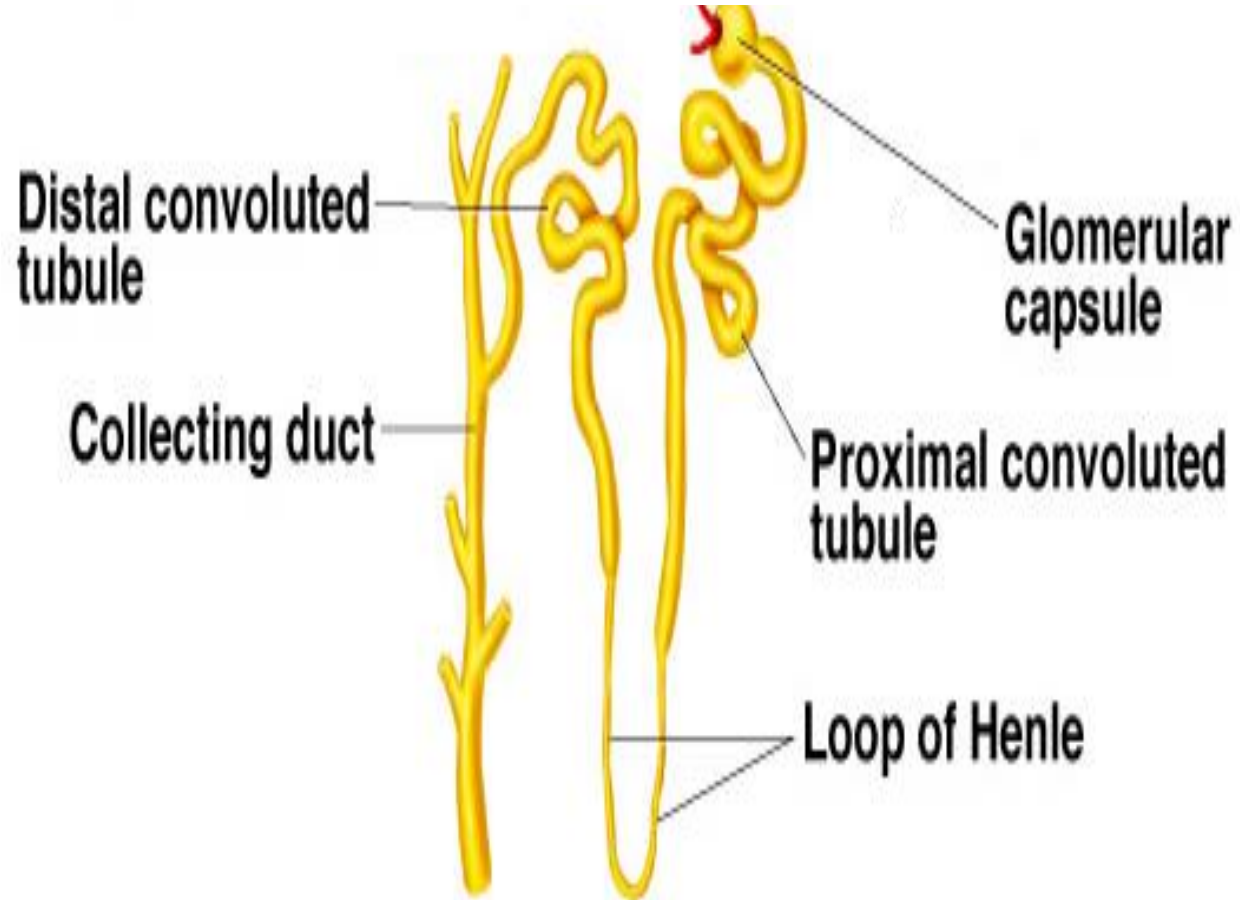


- Major calyces form renal pelvis.
- Renal pelvis collects urine.
- Transports urine to ureters.

# Nephron

- Functional unit of the kidney.
- Consists of:
  - Blood vessels:
    - Vasa recta.
    - Peritubular capillaries.
  - Urinary tubules:
    - PCT.
    - LH.
    - DCT.
    - CD.

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# Renal Blood Vessels

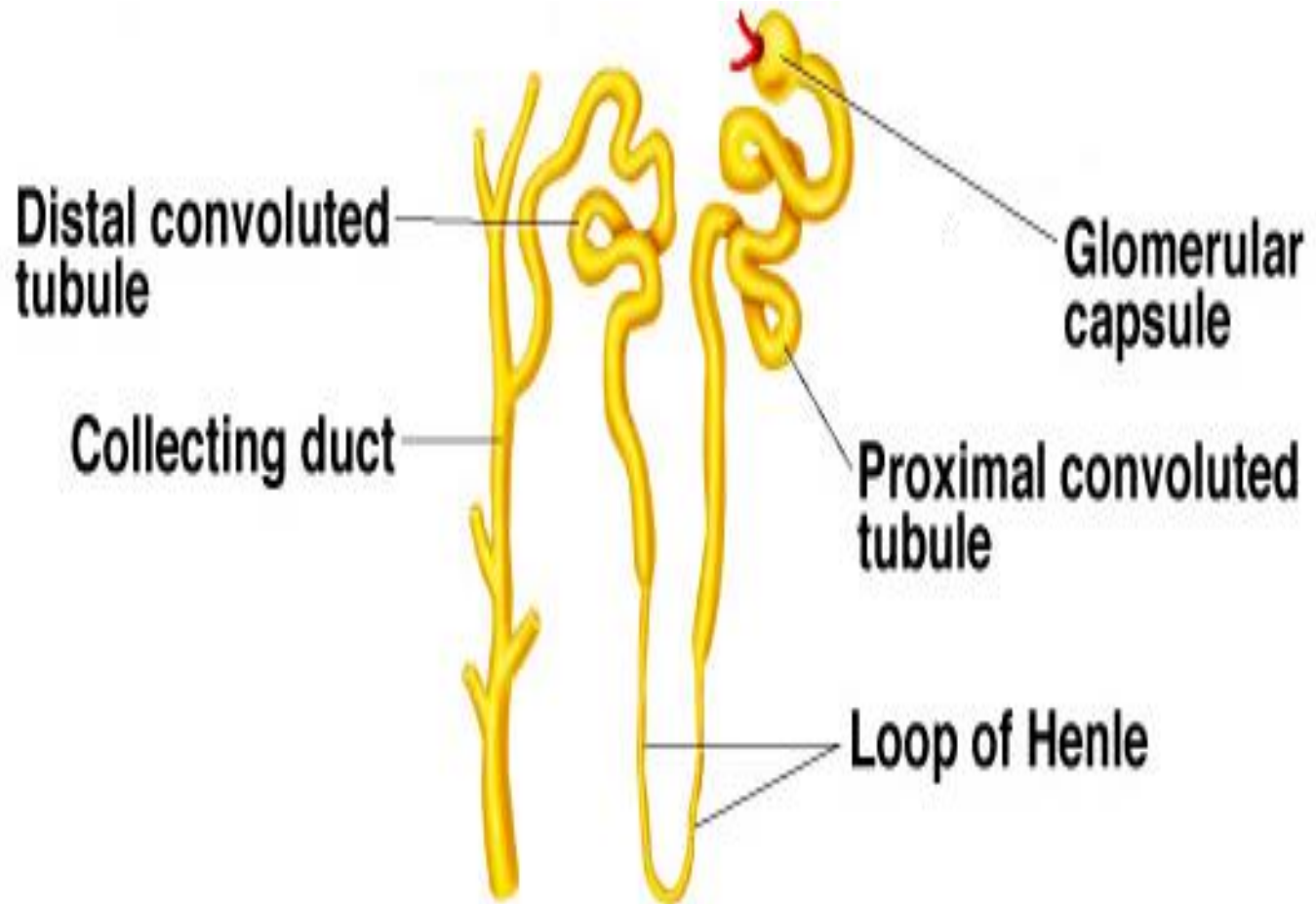
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- **Afferent arteriole:**
  - Delivers blood into the glomeruli.
- **Glomeruli:**
  - Capillary network that produces filtrate that enters the urinary tubules.
- **Efferent arteriole:**
  - Delivers blood from glomeruli to peritubular capillaries.
- **Peritubular capillaries:**
  - Deliver blood to vasa recta.

# Nephron Tubules

- Glomerular capsule.
- Proximal convoluted tubule (PCT).
- Descending and ascending limbs of Loop of Henle (LH).
- Distal convoluted tubule (DCT).
- Collecting duct (CD).

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# Glomerular Capsule

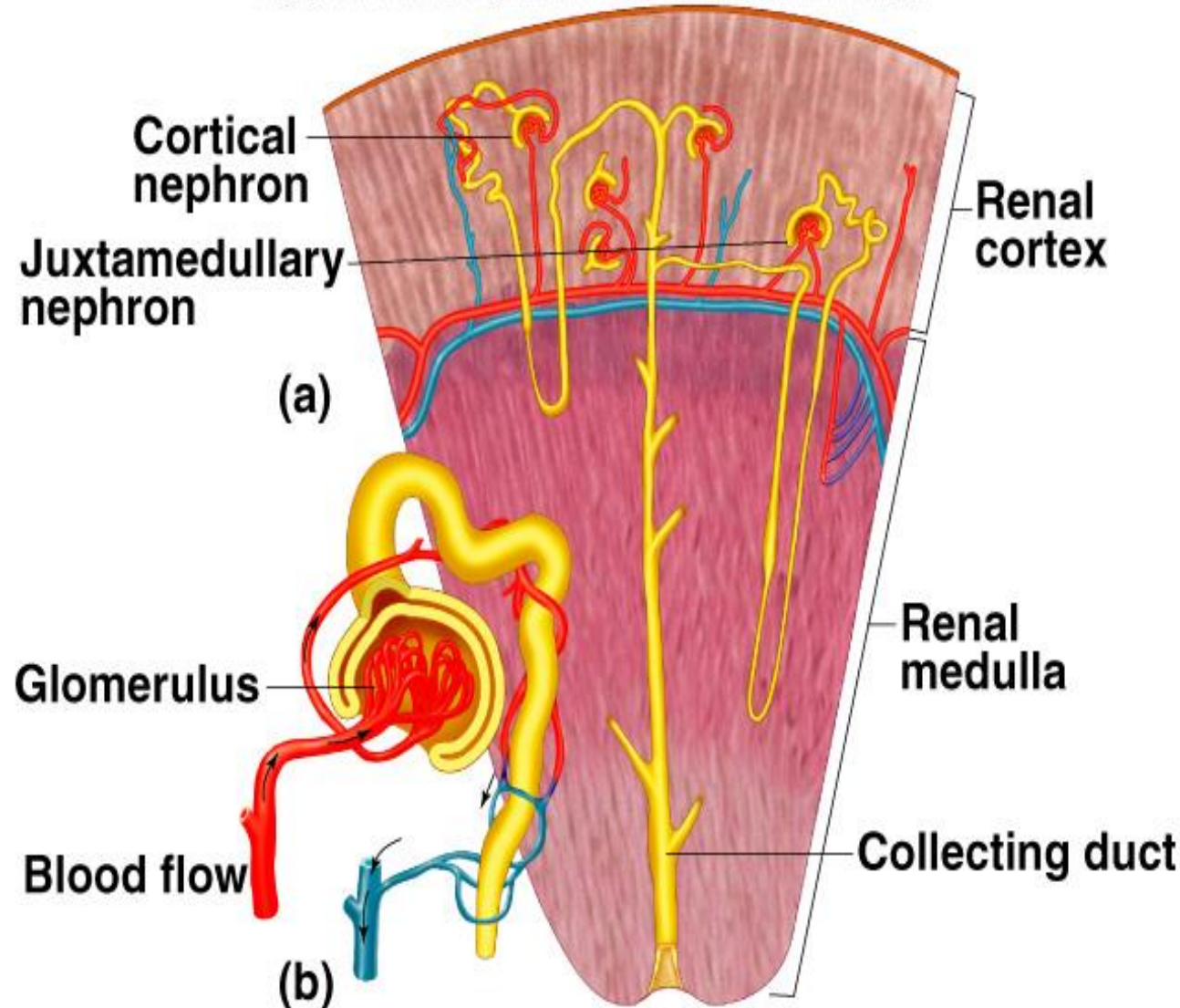
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## ■ Bowman's capsule:

- Surrounds the glomerulus.

- Location where glomerular filtration occurs.

- Filtrate passes into the urinary space into PCT.





# Proximal Convoluted Tubule

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- Single layer of cuboidal cells with millions of microvilli.
  - Increase surface area for reabsorption.





# Loop of Henle

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- Fluid passes from PCT to LH.
- Descending limb:
  - H<sub>2</sub>O reabsorption.
- Ascending limb:
  - Active transport of Na<sup>+</sup>.
  - Impermeable to H<sub>2</sub>O.



# Distal Convoluted Tubule

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- Contains few microvilli.
- Functions:
  - Secretion.
  - Reabsorption.
- Terminates in CD.

# Type of Nephrons

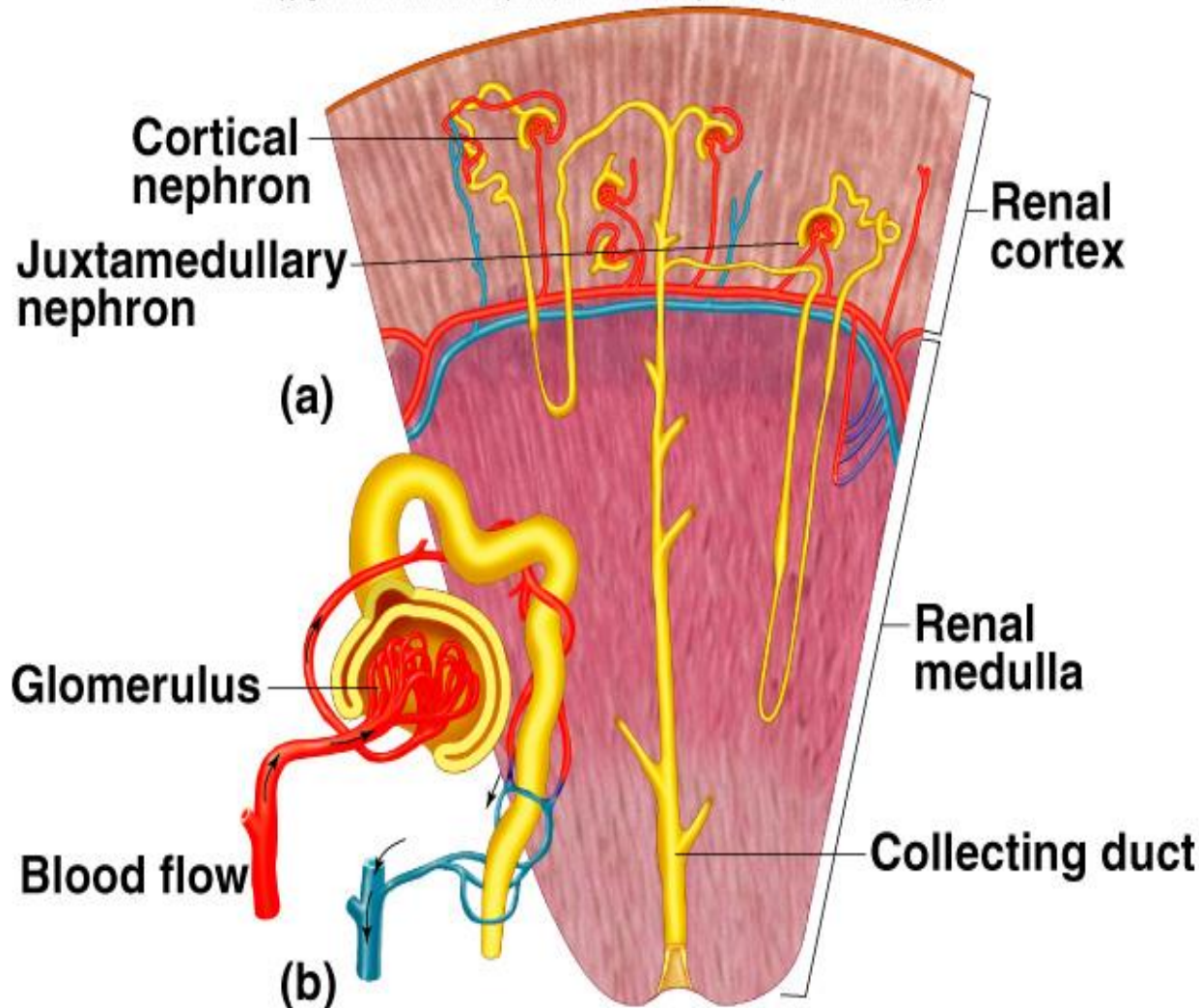
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## ■ Cortical nephron:

- Originates in outer 2/3 of cortex.
  - Osmolarity of 300 mOsm/l.
- Involved in solute reabsorption.

## ■ Juxtamedullary nephron:

- Originates in inner 1/3 cortex.
  - Important in the ability to produce a concentrated urine.
- Has longer LH.





# Collecting Duct

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- Receives fluid from the DCT of several nephrons.
- Passes through renal pyramid into minor calyx.
- Functions:
  - Reabsorption.
    - H<sub>2</sub>O reabsorption influenced by ADH.
  - Secretion.



# Glomerular Ultrafiltrate

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- Fluid that enters glomerular capsule is called ultrafiltrate.
  - Glomerular filtration:
    - Mechanism of producing ultrafiltrate under hydrostatic pressure of the blood.
      - Process similar to the formation of tissue fluid by other capillary beds.
- Glomerular filtration rate (GFR):
  - Volume of filtrate produced by both kidneys each minute.
    - Averages 115 ml/min. in women; 125 ml/min. in men.



# Regulation of GFR

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- Vasoconstriction or dilation of the afferent arterioles affects the rate of blood flow to the glomerulus.
  - Affects GFR.
- Mechanisms to regulate GFR:
  - Sympathetic nervous system.
  - Autoregulation.
- Changes in diameter result from extrinsic and intrinsic mechanisms.



# Reabsorption of Salt and H<sub>2</sub>O

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- Return of most H<sub>2</sub>O from the urine filtrate back into the peritubular capillaries.
  - About 180 L/day of ultrafiltrate produced; however, only 1–2 L of urine excreted/24 hours.
- Obligatory water loss:
  - Minimum of 400 ml/day urine necessary to excrete metabolic wastes (obligatory water loss).



# Significance of PCT Reabsorption

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- 65%  $\text{Na}^+$ ,  $\text{Cl}^-$ , and  $\text{H}_2\text{O}$  reabsorbed across the PCT into the vascular system.
- 90%  $\text{K}^+$  reabsorbed.
- Reabsorption occurs constantly regardless of hydration state and hormones.
- Energy expenditure is 6% of calories consumed at rest.





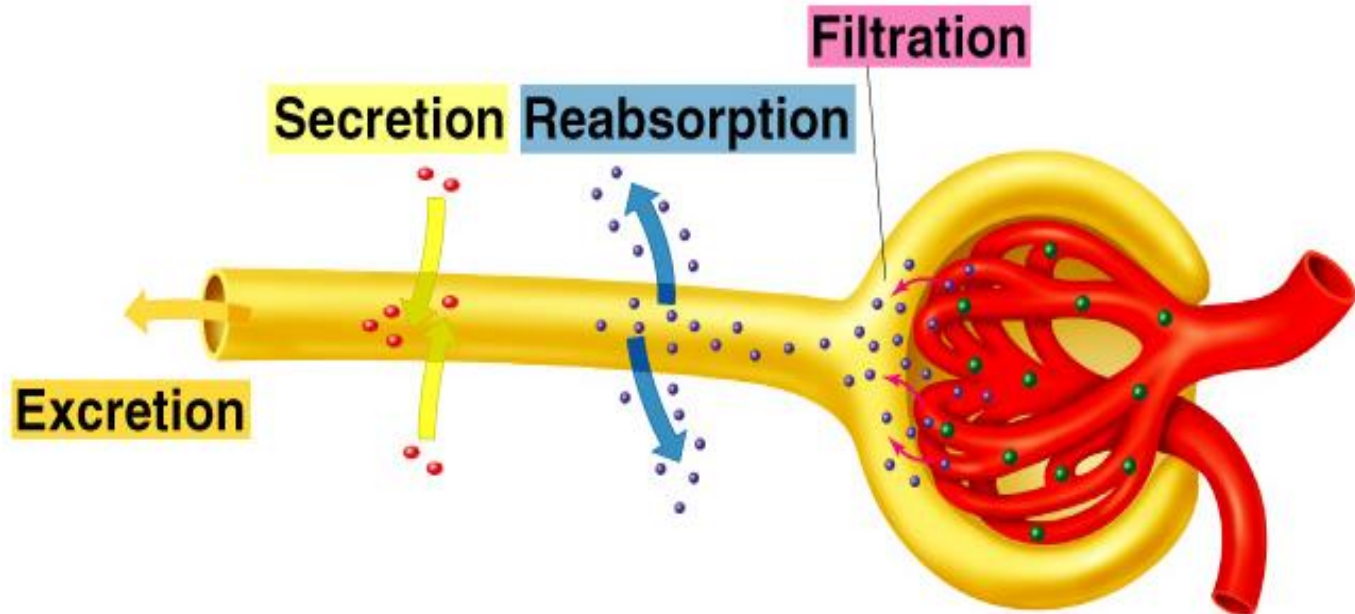
# Collecting Duct

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- Medullary area impermeable to high [NaCl] that surrounds it.
  - The walls of the CD are permeable to H<sub>2</sub>O.
- H<sub>2</sub>O is drawn out of the CD by osmosis.
  - Rate of osmotic movement is determined by the # of **aquaporins** in the cell membrane.
- Permeable to H<sub>2</sub>O depends upon the presence of **Anti Diuretic Hormone (ADH)**.

# Secretion

- Secretion of substances from the peritubular capillaries into interstitial fluid.
  - Then transported into lumen of tubule, and into the urine.
- Allows the kidneys to rapidly eliminate certain potential toxins.



# Transport Process Affecting Renal Clearance

- **Renal clearance:** The ability of the kidneys to remove molecules from plasma and excrete those molecules in the urine.
- If a substance is not reabsorbed or secreted, then the amount excreted = amount filtered
- **Quantity excreted (mg/min) = V x U**
  - V = rate of urine formation;
  - U = inulin concentration in urine
- GFR-Glomerular Filtration Rate
  - If a substance is not reabsorbed or secreted, then the amount excreted = amount filtered in the glomerulus



# Renal Plasma Clearance

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- Volume of plasma from which a substance is completely removed in 1 min. excreted in the urine.
- Substance is filtered, but not reabsorbed or secreted:
  - All filtered will be excreted.



# Renal Plasma Clearance

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$$\text{Renal plasma clearance} = \frac{V \times U}{P}$$

- $V$  = urine volume per min.
- $U$  = concentration of substance in urine
- $P$  = concentration of substance in plasma



# Clearance of Urea

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- Urea is secreted into blood and filtered into glomerular capsule.
- Urea clearance is 75 ml/min
  - 40-60% of filtered urea is always reabsorbed.
- Passive process due to presence of carriers for facilitative diffusion of urea.



# Measurement of Renal Blood Flow

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- Not all blood delivered to glomeruli is filtered in the glomerular capsules.
  - Most of glomerular blood passes to the efferent arterioles.
  - 20% renal plasma flow filtered.
- Substances in unfiltered blood must be secreted into tubules to be cleared by active transport.



# Glucose and Amino Acid Reabsorption

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- Filtered **glucose** and **amino** acids are normally reabsorbed by the nephrons.
  - In PCT occurs by secondary active transport with membrane carriers.
- **Renal transport threshold:**
  - Minimum concentration of substance in plasma that results in excretion of that substance in the urine.
    - Renal plasma threshold for glucose = 180-200 mg/dl.





# Electrolyte Balance

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- Kidneys regulate  $\text{Na}^+$ ,  $\text{K}^+$ ,  $\text{H}^+$ ,  $\text{Cl}^-$ ,  $\text{HCO}_3^-$ , and  $\text{PO}_4^{-3}$ .
  - Control of plasma  $\text{Na}^+$  is important in regulation of blood volume and pressure.
  - Control of plasma of  $\text{K}^+$  important in proper function of cardiac and skeletal muscles.
  - Match ingestion with urinary excretion.



# K<sup>+</sup> Secretion

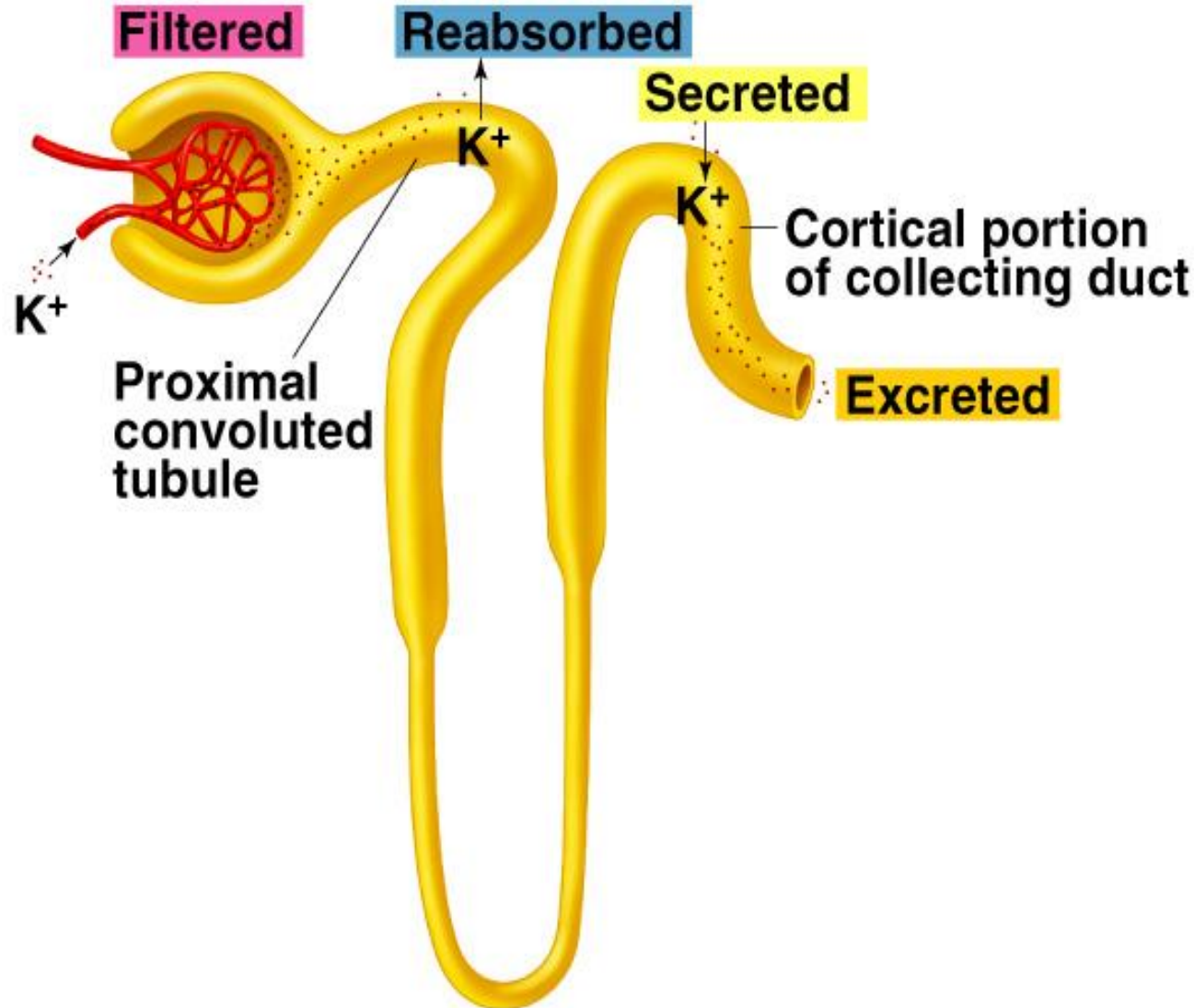
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- 90% filtered K<sup>+</sup> is reabsorbed in early part of the nephron.
- Secretion of K<sup>+</sup> occurs in Collecting Duct.
  - Amount of K<sup>+</sup> secreted depends upon:
    - Amount of Na<sup>+</sup> delivered to the region.
    - Amount of aldosterone secreted.
  - As Na<sup>+</sup> is reabsorbed, lumen of tubule becomes charged.
    - Potential difference drives secretion of K<sup>+</sup> into tubule.

# K<sup>+</sup> Secretion (continued)

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- Final [K<sup>+</sup>] controlled in CD by aldosterone.
  - When aldosterone is absent, no K<sup>+</sup> is excreted in the urine.
- High [K<sup>+</sup>] or low [Na<sup>+</sup>] stimulates the secretion of aldosterone.
- Only means by which K<sup>+</sup> is secreted.





# Renal Acid-Base Regulation

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- Kidneys help regulate blood pH by excreting  $H^+$  and reabsorbing  $HCO_3^-$ .
- Most of the  $H^+$  secretion occurs across the walls of the PCT in exchange for  $Na^+$ .
  - Antiport mechanism.
    - Moves  $Na^+$  and  $H^+$  in opposite directions.
- Normal urine normally is slightly acidic because the kidneys reabsorb almost all  $HCO_3^-$  and excrete  $H^+$ .
  - Returns blood pH back to normal range.

# Reabsorption of Bicarbonate- $\text{HCO}_3^-$



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- Powerful Buffer
- Water + Carbon Dioxide → Carbonic Acid →  
■  $\text{H}^+$  + Bicarbonate $^-$
- Apical membranes of tubule cells are impermeable to  $\text{HCO}_3^-$ .
  - Reabsorption is indirect through  $\text{CO}_2$  formation.



# Diuretics

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- Increase urine volume excreted.
  - Increase the proportion of glomerular filtrate that is excreted as urine.
- Loop diuretics:
  - Inhibit NaCl transport out of the ascending limb of the LH.
- Thiazide diuretics:
  - Inhibit NaCl reabsorption in the 1<sup>st</sup> segment of the DCT.
- Ca inhibitors:
  - Prevent H<sub>2</sub>O reabsorption in PCT when HCO<sub>3</sub><sup>-</sup> is reabsorbed.
- Osmotic diuretics:
  - Increase osmotic pressure of filtrate.



# Kidney Diseases

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- **Acute renal failure:**
  - Impaired ability of kidneys to excrete wastes and regulate homeostasis of blood volume, pH, and electrolytes.
    - Rise in blood [creatinine].
- **Glomerulonephritis:**
  - Inflammation of the glomeruli.
  - Autoimmune disease by which antibodies have been formed at the glomerulus basement.
    - Leakage of protein into the urine.



# Kidney Diseases (continued)

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- Renal insufficiency:
  - Nephrons are destroyed.
  - Clinical manifestations:
    - Salt and H<sub>2</sub>O retention.
    - Uremia.
    - Elevated plasma [H<sup>+</sup>] and [K<sup>+</sup>].
- Kidney Stones (as seen with Melamine)
- Dialysis:
  - Separates molecules on the basis of the ability to diffuse through selectively permeable membrane.