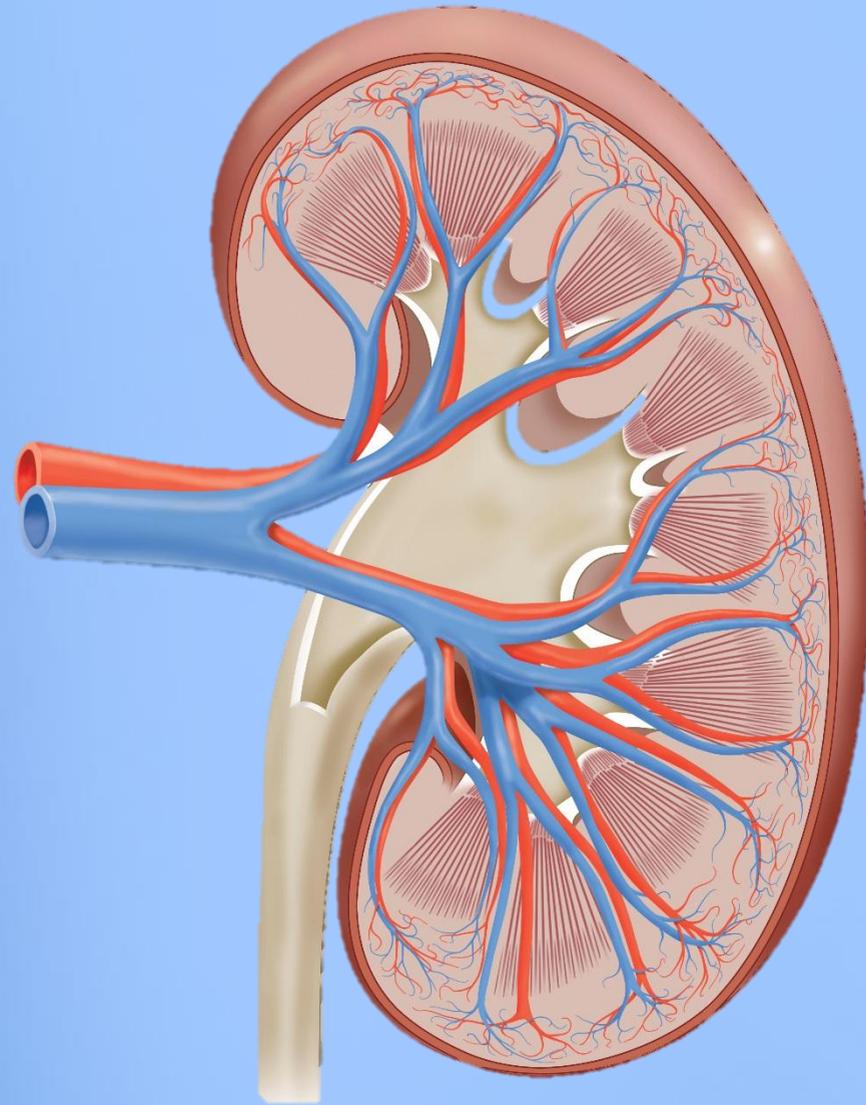


5 & 6

# REABSORPTION AND SECRETION



Renal Block

# Objectives

Define tubular reabsorption, tubular secretion, transcellular and paracellular transport.

Identify and describe mechanisms of tubular transport & Describe tubular reabsorption of sodium and water

Revise tubule-glomerular feedback and describe its physiological importance

Identify and describe mechanism involved in Glucose reabsorption

Study glucose titration curve in terms of renal threshold, tubular transport maximum, splay, excretion and filtration

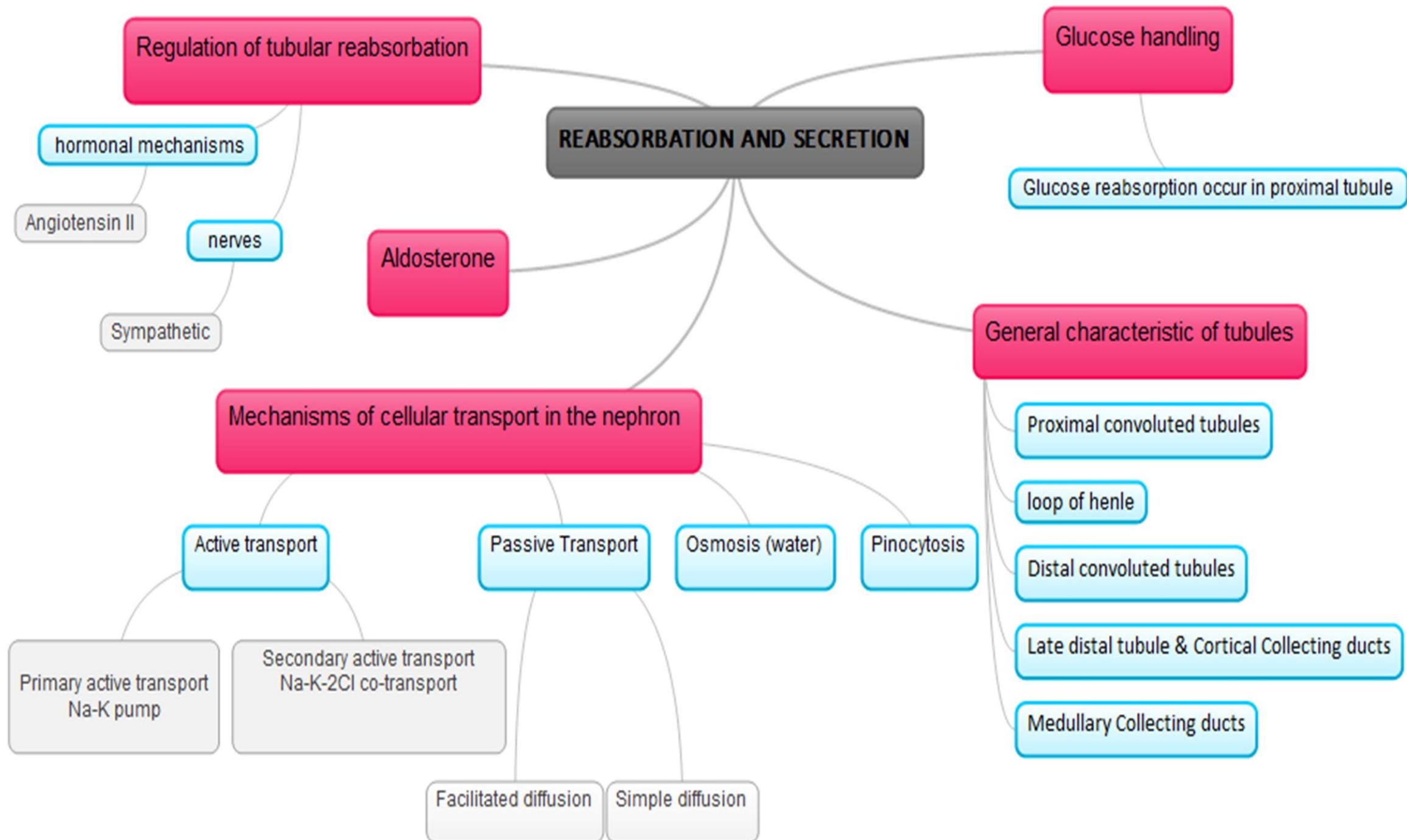
Identify the tubular site and describe how Amino Acids,  $\text{HCO}_3^-$ ,  $\text{PO}_4^-$  and Urea are reabsorbed

Describe tubular secretion with PAH transport and  $\text{K}^+$

Identify and describe the characteristic of loop of Henle, distal convoluted tubule and collecting ducts for reabsorption and secretion

Identify the site and describe the influence of aldosterone on reabsorption of  $\text{Na}^+$  in the late distal tubules.

# Mind Map



# Reabsorption and Secretion

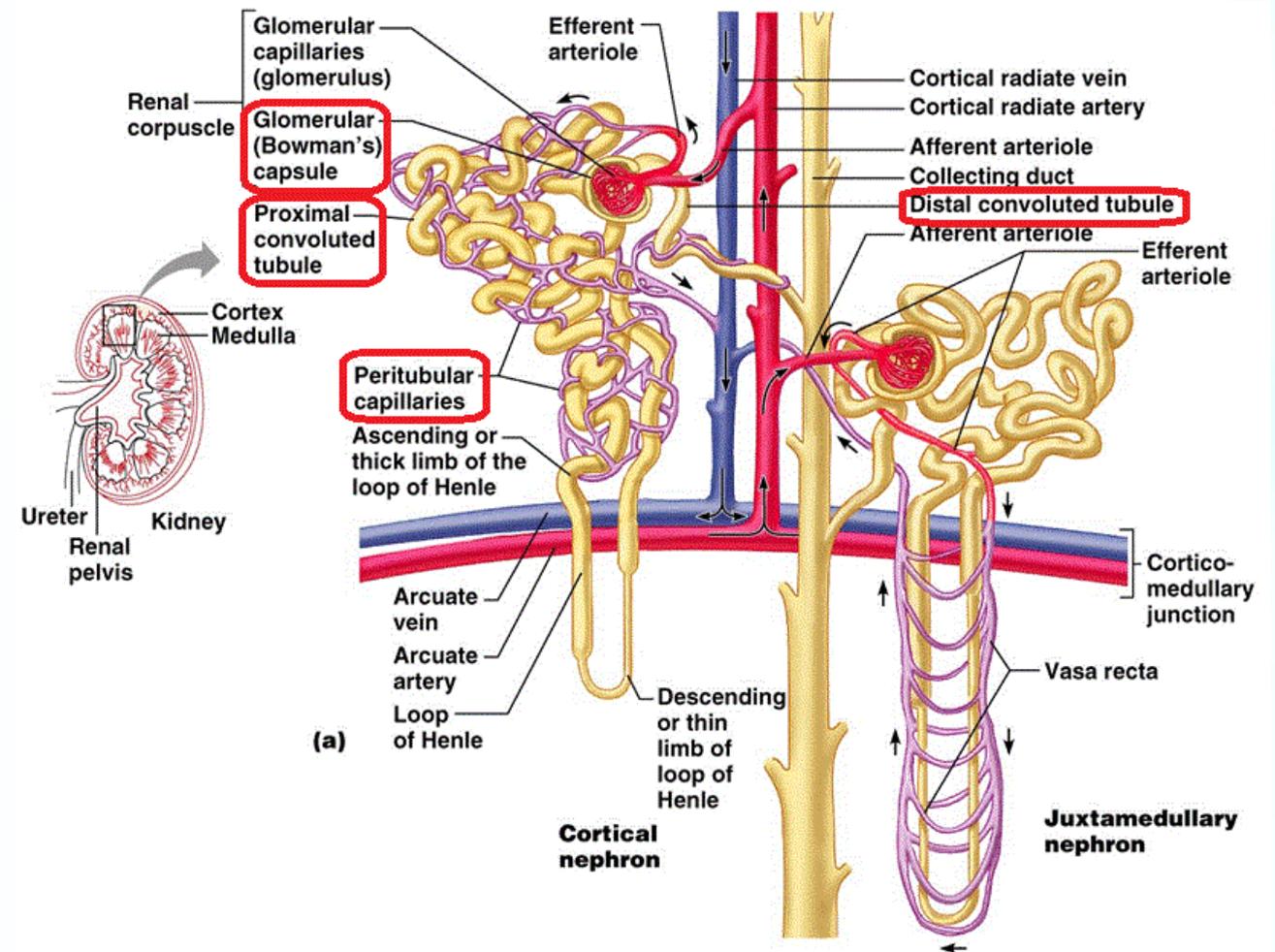
As the glomerular filtrate enters the renal tubules, it flows sequentially through the successive parts of the tubule:

The proximal tubule → the loop of Henle<sub>(1)</sub> → the distal tubule<sub>(2)</sub> → the collecting tubule → finally, the collecting duct, before it is excreted as urine.

Along this course, some substances are selectively reabsorbed from the tubules back into the blood, whereas others are secreted from the blood into the tubular lumen.

The urine represents the sum of three basic renal processes: glomerular filtration, tubular reabsorption, and tubular secretion:

**Urinary excretion** = Glomerular Filtration – Tubular reabsorption + Tubular secretion



# Mechanisms of cellular transport in the nephron are:

## Active transport

“Active transport can move a solute against an electrochemical gradient and requires energy derived from metabolism”

### Primary active transport

Transport that is coupled directly to an energy source such as **ATP**

#### Sodium-potassium pump

(found in **basolateral membrane** along renal tubules)

H<sup>+</sup>-pump

### Secondary active transport

Transport that is coupled indirectly to an energy source due to **concentration gradient of ion**

Na-K-2Cl co-transport

glucose-sodium co-transport (SGLT)

amino acid-sodium co-transport

H<sup>+</sup>/Na counter-transport

## Passive Transport

### Simple diffusion

(without carrier protein)

Cl, HCO<sub>3</sub><sup>-</sup>, urea, creatinine

### Facilitated diffusion

(require carrier protein)

Glucose and amino acids at the basolateral border (GLUT)

## Osmosis

**Water** is always reabsorbed by a passive (nonactive) physical mechanism called osmosis, which means water diffusion from a region of **low solute concentration (high water concentration)** to one of **high solute concentration (low water concentration)**.

## Pinocytosis \ exocytosis

### (Additional reading)

The proximal tubule, reabsorb **large molecules such as proteins** by pinocytosis. In this process, the protein attaches to the brush border of the luminal membrane, then invaginates to the interior of the cell until it is completely pinched off and a vesicle is formed containing the protein. Once inside the cell the protein is digested into its constituent amino acids, which are reabsorbed through the **basolateral membrane** into the interstitial fluid. Because pinocytosis requires energy, it is considered a form of **active transport**.

(1) Co-transport : movement of two molecules in the same direction but they opposite in concentration gradient

(2) Counter-transport: movement of two molecules in opposite direction based on their concentration gradient

# Tubular Reabsorption

## The ways of transport:

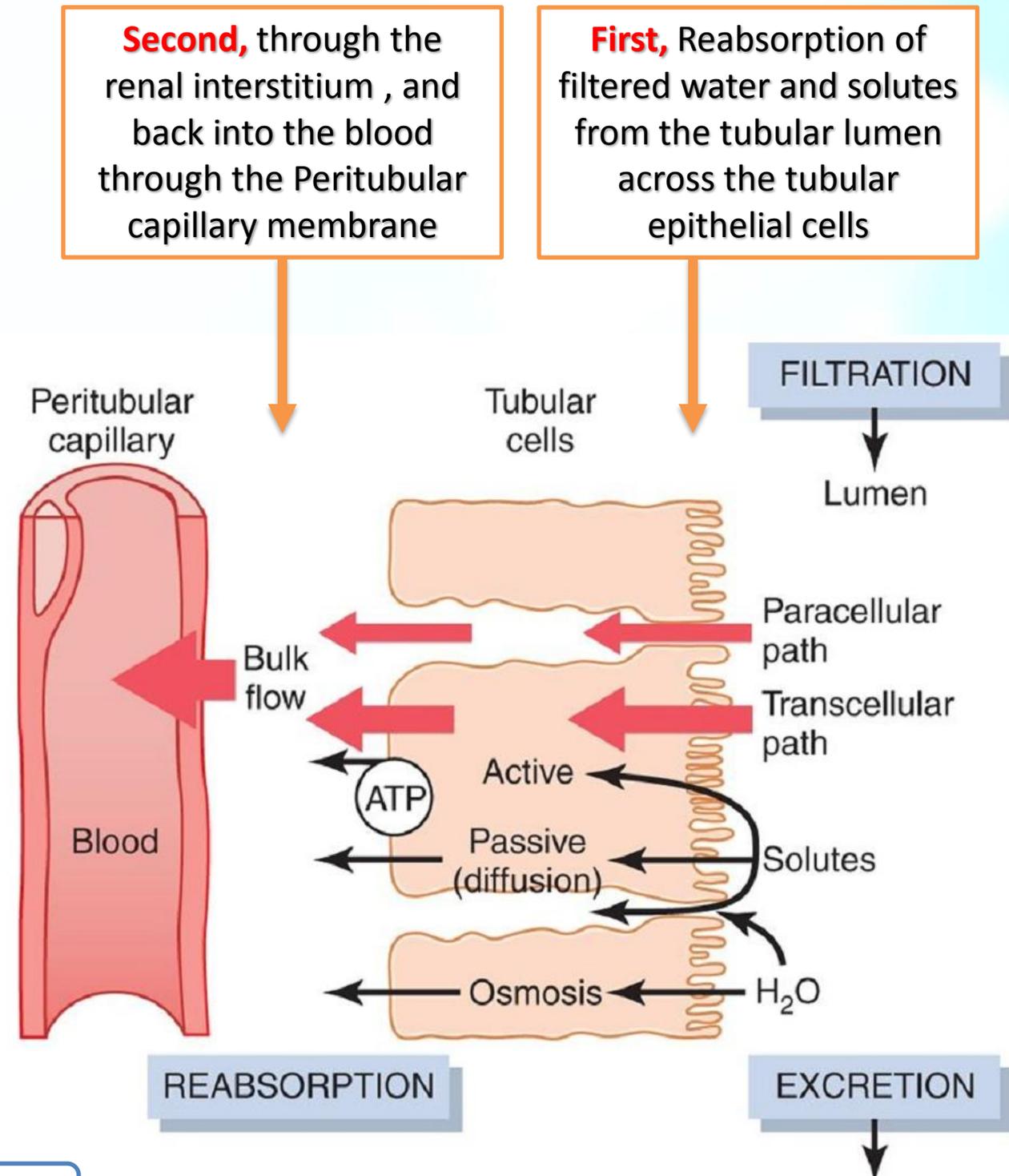
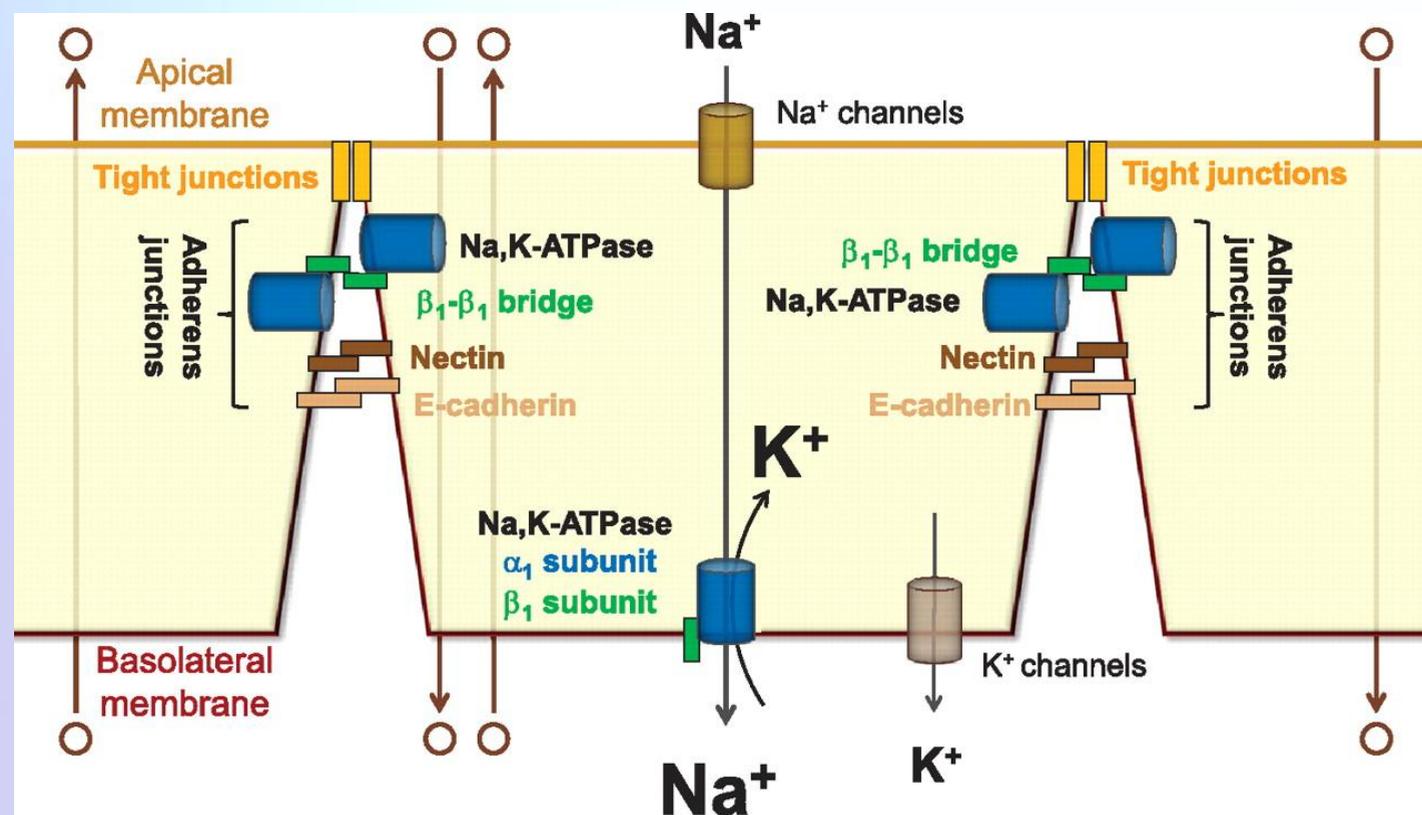
1- From lumen of tubules (Apical membrane"1") to epithelial cells then from epithelial cells to interstitium (Basolateral membrane):

A-Transcellular route: (through the cell membrane)

B-Paracellular route: (between spaces of tight cell junction)

2- From interstitium (basolateral space) to the Peritubular capillaries: By ultrafiltration (bulk flow) that is mediated by:

**hydrostatic and colloid osmotic forces**



(1) Apical membrane = brush border which is numerous to help in reabsorption

# How is transportation take place from tubules to interstitium?

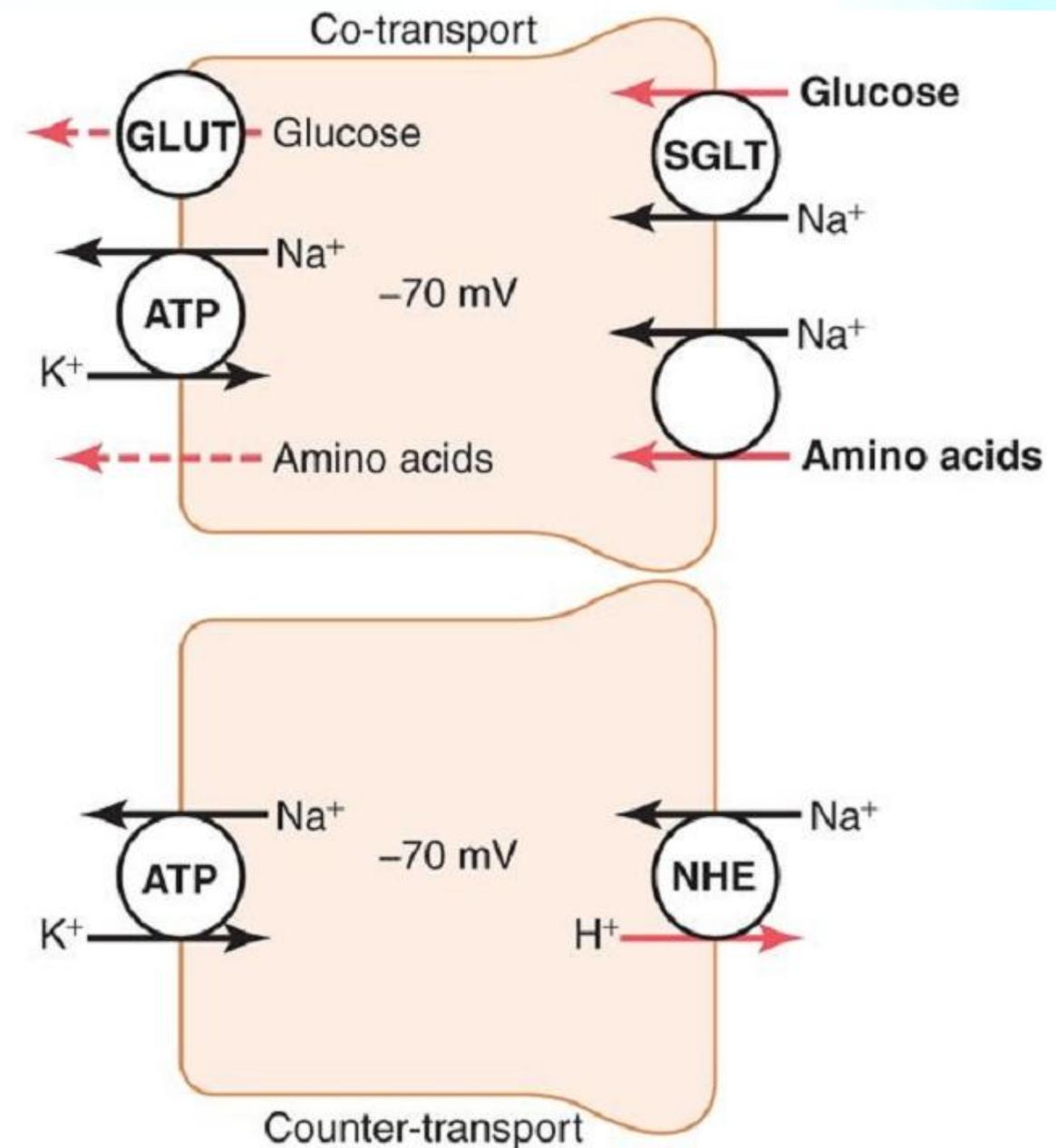
1. :

- A. Sodium diffuses across the **luminal membrane** (also called the apical membrane) into the cell **down an electrochemical gradient** (with other substances such as glucose, amino acids etc.) established by the sodium -potassium ATPase pump on the basolateral side of the membrane.
- B. Other molecules like water and Cl , Ca etc. by osmosis and diffusion

2. :

- A. Sodium is transported across the basolateral membrane against an electrochemical gradient by the sodium -potassium ATPase pump
- B. other substances will across the basolateral membrane by passive diffusion

3. Sodium , water , and other substances are reabsorbed from the interstitial fluid into the Peritubular capillaries by **ultrafiltration (bulk flow "1")**, a passive process driven by the hydrostatic and colloid osmotic pressure gradients



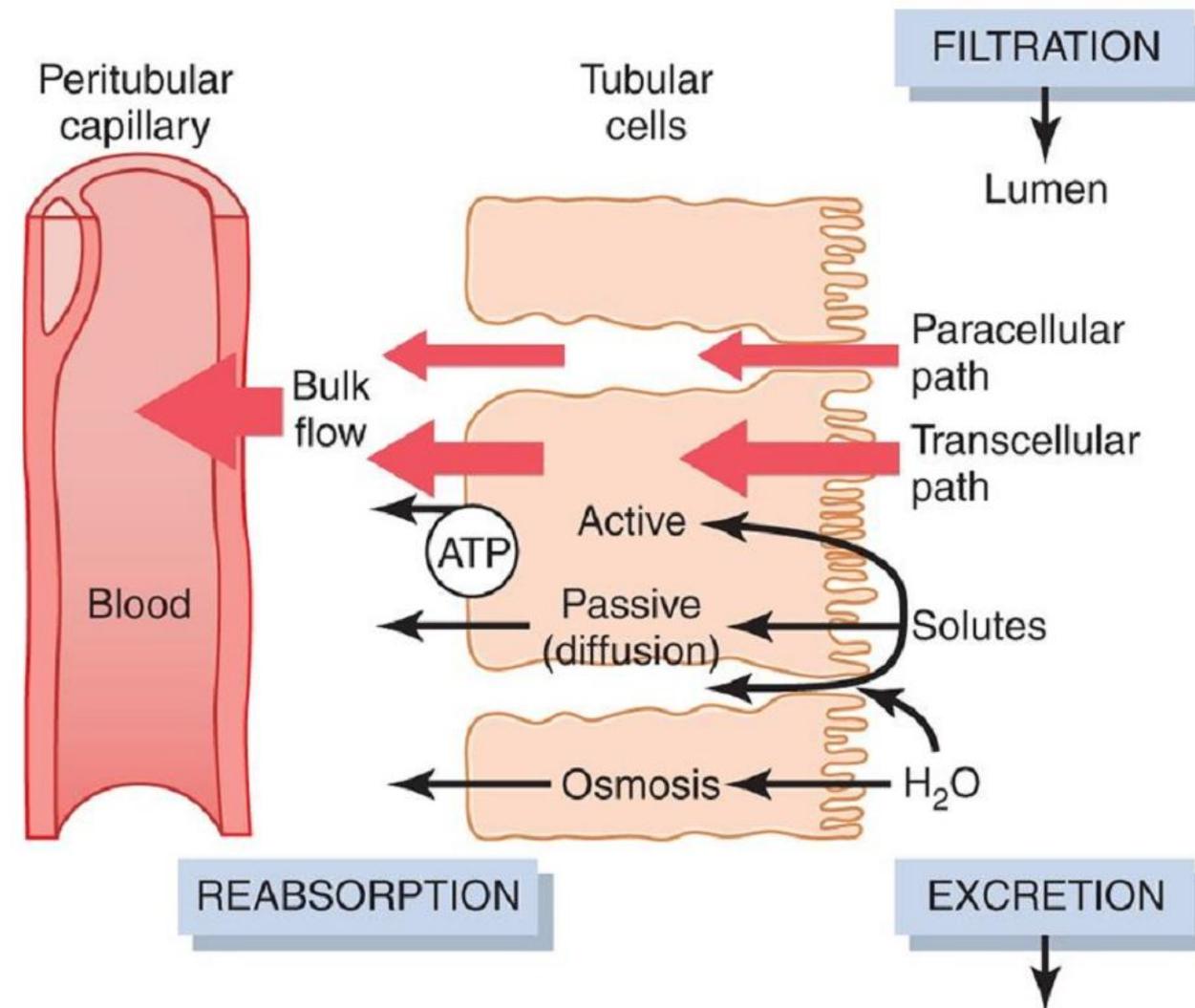
(1) Bulk flow = movement of water with other substances  
While diffusion = movement of substances without water.

# How ultrafiltration take place?

In Peritubular capillaries the high plasma **oncotic pressure** is due to fluid filtration in glomerulus

**increase GFR** → increase oncotic pressure & decrease hydrostatic pressure in efferent & Peritubular capillaries → increase bulk flow from lateral space to Peritubular capillaries → increase reabsorption

**decrease GFR** → decrease oncotic pressure & increase hydrostatic pressure → decrease bulk flow → fluid go back to lumen through tight junction → decrease reabsorption



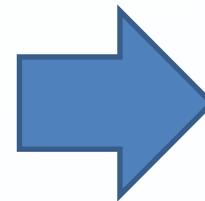
# General characteristic of tubules

## Proximal convoluted tubule

1- Proximal tubules is **coarse adjustment** (reabsorption a most of of water and solutes)

3-100% of glucose and amino acids reabsorbed

2- Solute reabsorption in the proximal tubule is isosmotic (equal amount of solute and water are reabsorbed)



- (1) **Concentrate urine** = remove water from fluid
- (2) **Dilute urine** = remove solutes from urine

\* The main function of tubules is **concentrate urine** and that has done in **loop of henle of Juxtamedullary nephron**

\* **Sodium-potassium pump** that found in **distal convoluted tubules** is under control of **aldosterone**

## Loop of henle

1- Responsible for producing a **concentrated urine** in the medulla.

2- When **ADH (antidiuretic hormone)** is present, **water is reabsorbed and urine is concentrated.**

### **Descending limb: (concentrate urine "1")**

- 1- **water** permeable and allow **absorption of 25% of filtered H<sub>2</sub>O.**
- 2- It is **impermeable to Na-CL.**
- 3- fluid become **hyper-osmolar**

### **Thin ascending limb: (dilute urine "2")**

- 1- **impermeable to H<sub>2</sub>O**
- 2- permeable to **NaCl (passive)**
- 3- By the end of ascending limb of loop, the tubular fluid becomes **hypo-osmolar**

### **Thick ascending limb: (dilute urine)**

- 1- **impermeable to H<sub>2</sub>O**
- 2- **Na-K-2Cl co-transport** occur in this part. **(active)**
- 3- the tubular fluid becomes **hypo-osmolar** to plasma in this part

## Distal convoluted tubules

- 1- Distal tubule is **fine adjustment** (reabsorption a fine amount of water and solutes by hormonal control based on body needs)
- 2- The first portion of DCT forms part of **Juxtaglomerular Apparatus**, that provides feedback control of GFR and RBF of the same nephron.
- 3- The next early portion has the same characteristics as **ascending limb of Henle** that is
  - 1- impermeable to water
  - 2- absorbs solutes.So it is called the **diluting segment** & the osmotic pressure of the fluid ~ 100 mOsm/L.

Continues in renal pelvis,  
ureters, urinary bladder  
and urethra

## Late distal convoluted tubules & cortical collecting ducts

- 1- Composed of two types of cells:
  - a. **Principal cells:** absorb  $\text{Na}^+$  &  $\text{H}_2\text{O}$  and secrete  $\text{K}^+$
  - b. **Intercalated cells:** absorb  $\text{K}^+$  & secrete  $\text{H}^+$
  - Secretion of  $\text{K}^+$  and reabsorption of  $\text{Na}^+$  controlled by aldosterone.
- 2- **water permeability under ADH control. (works under body needs)**
- 3- **Impermeable to Urea.**

## Medullary collecting ducts

- 1- Under ADH control. (works under body needs)
- 2- **Highly permeable to urea.**
- 3- Final site for processing urine.
- 4- Secretes  $\text{H}^+$  helps to:
  - a- maintain blood pH
  - b- reabsorb  $\text{HCO}_3^-$  and generate new  $\text{HCO}_3^-$

	Reabsorption	Secretion
Proximal convoluted tubules	<ul style="list-style-type: none"> <li>- Poorly reabsorbed of creatinine and urea</li> <li>- 60% - 75% of sodium and water</li> <li>- 90% of HCO<sub>3</sub>, K<sup>+</sup>, Ca and Cl<sup>-</sup></li> <li>- 100% Glucose and amino acids</li> </ul>	<ul style="list-style-type: none"> <li>- H<sup>+</sup></li> <li>- Urea</li> <li>- ammonia</li> </ul>
Descending loop of henle	-25% of water (H <sub>2</sub> O)	_____
Thin ascending loop of henle	- Sodium chloride (NaCl)	_____
Thick ascending loop of henle	<ul style="list-style-type: none"> <li>- Sodium</li> <li>- Potassium</li> <li>- Chloride</li> </ul>	_____
Distal convoluted tubules	<ul style="list-style-type: none"> <li>- Sodium in response to <b>aldosterone</b></li> <li>- Water in response of <b>ADH</b></li> <li>- Calcium in response of <b>parathyroid hormone</b></li> </ul>	- Potassium in response of <b>aldosterone</b>
Late distal tubule & Cortical Collecting ducts	<ul style="list-style-type: none"> <li>a. Principal cells: absorb Sodium Na<sup>+</sup> &amp; H<sub>2</sub>O</li> <li>b. Intercalated cells: absorb Potassium K<sup>+</sup> &amp; HCO<sub>3</sub></li> <li>- Water in response of <b>ADH</b></li> <li>- Sodium in response to <b>aldosterone</b></li> <li>- Calcium in response of <b>parathyroid hormone</b></li> </ul>	<ul style="list-style-type: none"> <li>a. <b>Principal cells:</b> secrete K<sup>+</sup></li> <li>b. <b>Intercalated cells:</b> secrete H<sup>+</sup></li> <li>Potassium in response of <b>aldosterone</b></li> </ul>
Medullary Collecting ducts	<ul style="list-style-type: none"> <li>- Water in response of <b>ADH</b></li> <li>- <b>Highly permeable to urea</b> ( to maintain osmolarity of medulla )</li> </ul>	- H <sup>+</sup>

	Site	Between	Functions
<b>Primary Active Transport</b>			
Sodium-potassium pump	All renal tubules	Basolateral membrane	Reabsorption of sodium and secrete potassium to maintain the intracellular and extracellular balance of Na and K
<b>Secondary Active Transport</b>			
H <sup>+</sup> /Na counter-transport	Proximal convoluted tubules, Distal convoluted tubules and collecting ducts	Apical membrane	Reabsorption of sodium and secrete hydrogen ion and It is coupled with bicarbonate transport
HCO <sub>3</sub> /Na co-transport	Proximal convoluted tubules, Late distal convoluted tubules and collecting ducts	Basolateral membrane	Reabsorption of sodium and bicarbonate
Na-K-2Cl co-transport	Thick ascending limb of henle's loop	Apical membrane	Reabsorption of sodium, potassium and two chloride to dilute water
glucose-sodium co-transport (SGLT)	Proximal convoluted tubules	Apical membrane	Reabsorption of sodium and glucose
Amino acid-sodium co-transport	Proximal convoluted tubules	Apical membrane	Reabsorption of sodium and amino acid
<b>Simple diffusion</b>			
Passive NaCl transport	Thin ascending limb of henle's loop	Apical membrane	Reabsorption of NaCl to dilute fluid in tubules
Passive channels of K <sup>+</sup> , Cl <sup>-</sup> , Ca etc.	All renal tubules	Apical membrane & Basolateral membrane	Reabsorption and secretion
<b>Facilitated diffusion</b>			
Glucose transporter (GLUT)	Proximal convoluted tubules	Basolateral membrane	Reabsorption of glucose to interstitial fluid
<b>Osmosis</b>			
Water	<b>All renal tubules except:</b> 1- thin and thick ascending limb and 2- early portion of distal convoluted tubules	Apical membrane & Basolateral membrane	Reabsorption of water

# Glucose handling

## GLUCOSE REABSORPTION

- Glucose enter the tubular cells by secondary active transport “co-transport”, It use **SGLT** “a specific transport protein “which needs Na” .
- Then it's cross the cell membrane into the interstitial spaces by facilitated transport “passive transport” which use **GLUT's** “do not need Na” .
- Glucose reabsorption occur in **proximal tubule** .

- Essentially all glucose is reabsorbed
- The renal **threshold** for glucose= **180 mg/dl**
- the **tubular transport maximum** for glucose  
Tmg = **375 mg/min** in **men** and **300 mg/min** in **women**.

**What is the difference between renal threshold and tubular transport maximum ?**

**Renal threshold** : it's the rate that glucose **begins** to appear in the urine .

**transport maximum for glucose** : **all** nephrons have reached their **maximal** capacity to reabsorb glucose “maximum saturation of transporters”

**What cause the excretion of glucose in urine before reach to its maximum transport?**

**not** all nephrons have the **same** transport maximum for glucose, and some of the nephrons therefore begin to excrete glucose **before** others have reached their transport maximum

# Reabsorption of bicarbonate

1

- First of all, bicarbonate ( $\text{HCO}_3^-$ ) attaches itself with hydrogen ( $\text{H}^+$ ) then it becomes  $\text{H}_2\text{CO}_3$  in the lumen

2

- Carbonic Anhydrase will break  $\text{H}_2\text{CO}_3$  down to water ( $\text{H}_2\text{O}$ ) + carbonic dioxide ( $\text{CO}_2$ ) which diffuses into the proximal tubule

3

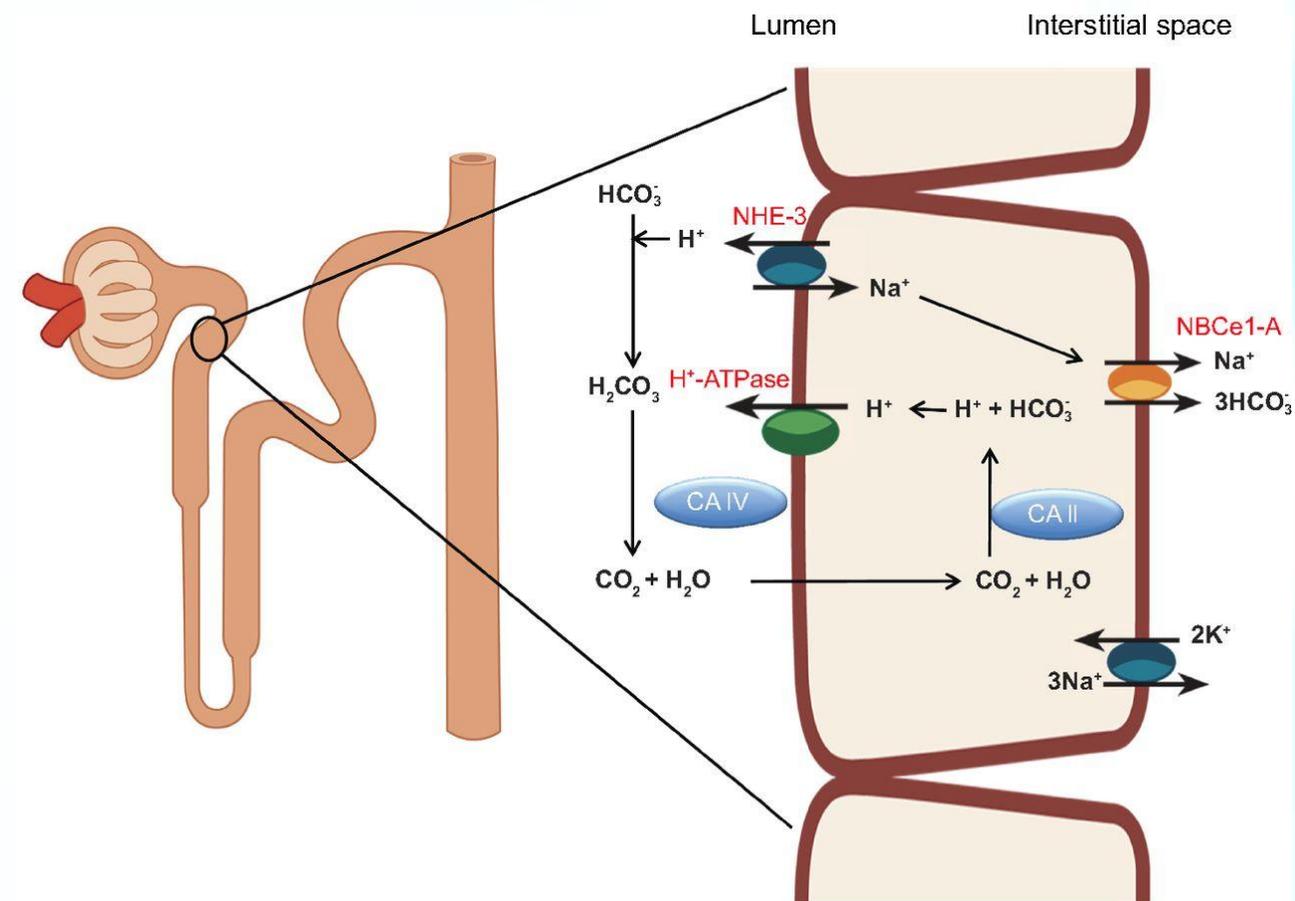
- Carbonic Anhydrase will convert the water ( $\text{H}_2\text{O}$ ) + the carbon dioxide ( $\text{CO}_2$ ) to  $\text{HCO}_3^- + \text{H}^+$

4

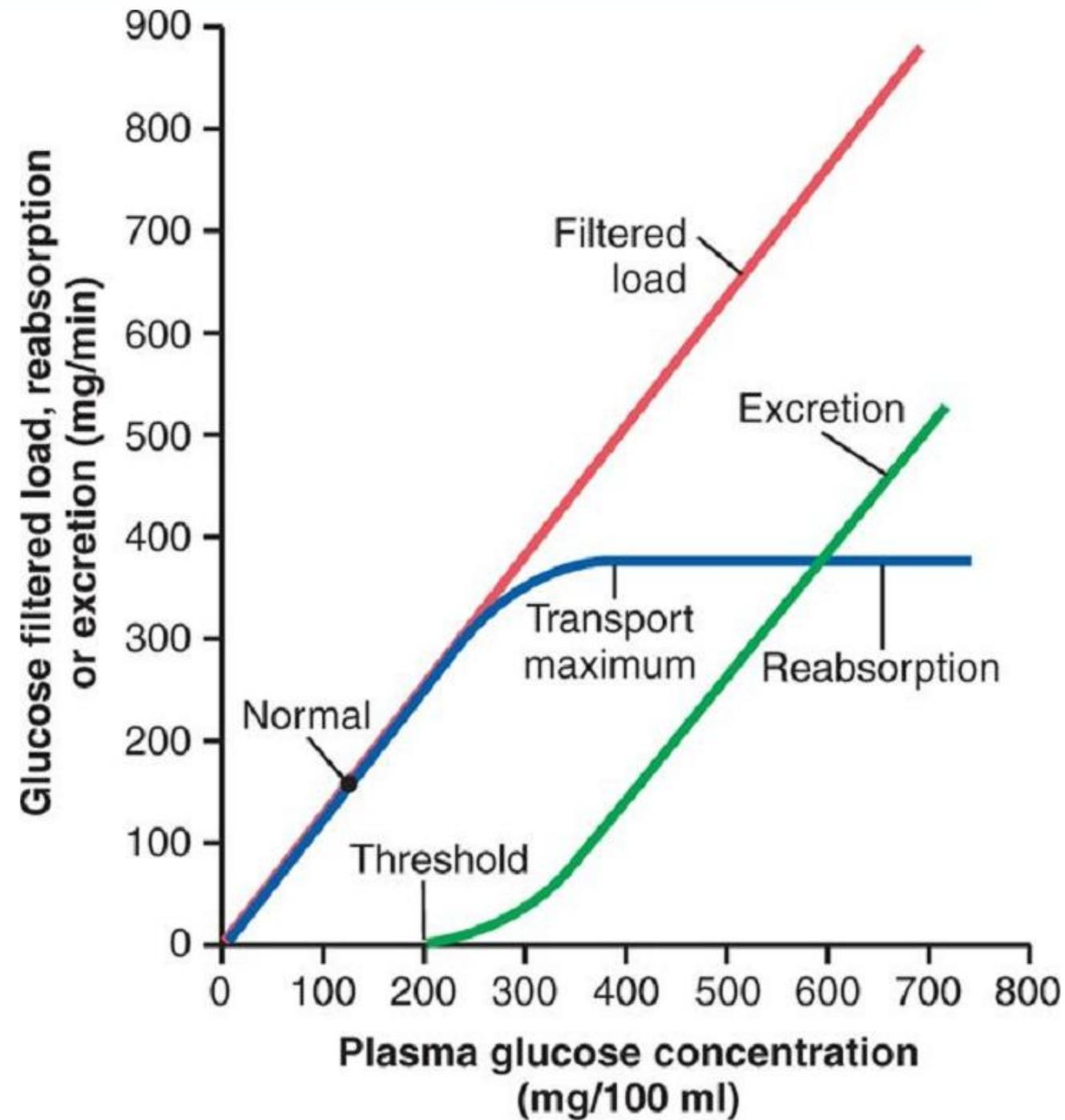
- Hydrogen will transport out and sodium (Na) will come in the proximal tubule

5

- Lastly, the  $\text{HCO}_3^-$  will go into the blood



## Glucose titration curve



Relations among the filtered load of glucose, the rate of glucose reabsorption by the renal tubules, and the rate of glucose excretion in the urine

# Regulation of tubular reabsorption

There must be a balance between tubular reabsorption and glomerular filtration. This is controlled by local, nervous & hormonal mechanisms.

1. **Glomerulotubular balance:** prevents overloading of distal parts when GFR increases.

2. **Peritubular capillary reabsorption** is regulated by **hydrostatic and colloidal pressures through the capillaries.**

3. **Arterial blood pressure:** if increased it reduces tubular reabsorption. **(increase in blood pressure will reduce GFR in response of myogenic mechanism and the decrease reabsorption)**

4. **Nervous Sympathetic:**  
-Increases Na<sup>+</sup> reabsorption.

5-**Tubuloglomerular feedback:** it will observe concentration of **sodium chloride** by **macula dense** in **distal tubules** and what will lead to:

- 1- constriction and dilatation of afferent arteriole which affect on GFR
- 2- release **renin** which increase **reabsorption of sodium** and play a role in **production of angiotensin II**

6-**Hormonal:**

- **Angiotensin II :** release aldosterone
- **ADH :** H<sub>2</sub>O reabsorption
- **ANP :** Sodium excretion and diuresis
- Parathyroid hormone:** Increases Ca reabsorption & decreases phosphate reabsorption

- (1) ADH: Antidiuretic hormone
- (2) ANP: atrial natriuretic peptide
- (3) Diuresis: increase urine output

# Aldosterone

## Function

- 1-increases Sodium reabsorption
- 2-stimulates Potassium secretion

## When does it secreted?

- (1) Increased extracellular potassium concentration.
- (2) Increased angiotensin II levels, which typically occur in conditions associated with **sodium and volume depletion or low blood pressure (so it will increase blood pressure)**

## Site of secretion

- Aldosterone, secreted by the **zona glomerulosa cells** of the **adrenal cortex**.

## Mechanism of action

- by stimulating the sodium-potassium ATPase pump on the **basolateral side of the cortical collecting tubule membrane**.
- Aldosterone also increases the sodium permeability of the luminal side of the membrane .

## Diseases associated with aldosterone

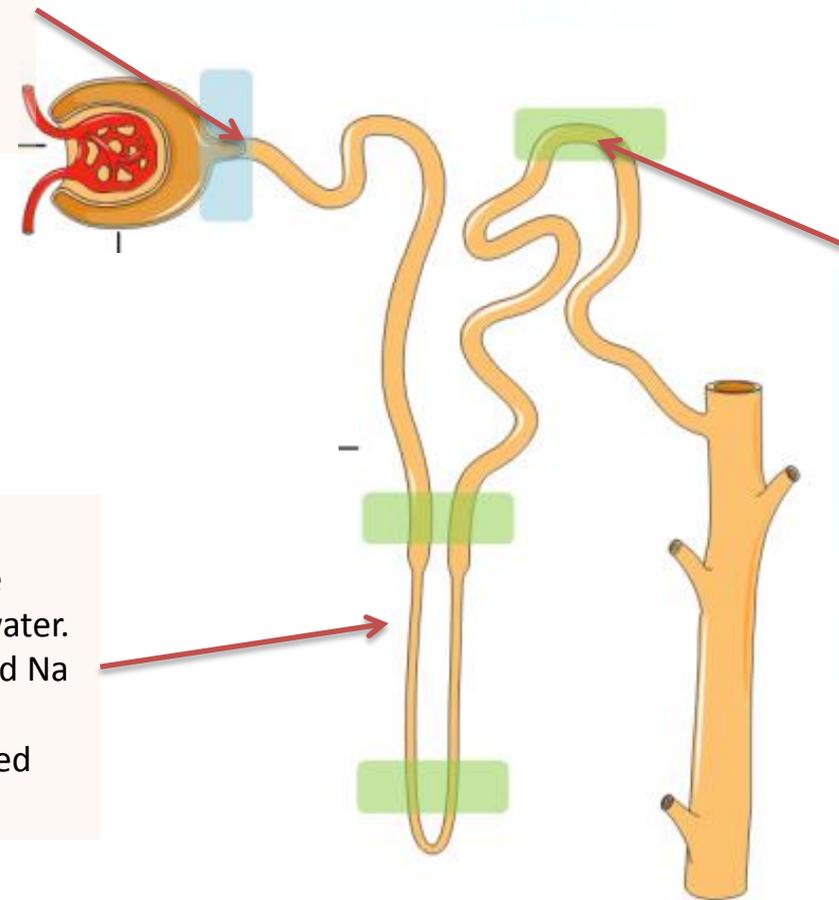
- Absence of aldosterone, as occurs with adrenal destruction or malfunction (**Addison's disease**)
- Excess aldosterone, as occurs in patients with adrenal tumors (**Conn's syndrome**) is associated with:
  - 1- sodium retention
  - 2- decreased plasma potassium concentration

# Summary

- Absorption **through apical membrane** is done **passively**.
- Movement of **Na through basal membrane** is done **Na/K ATPase**.
- $\uparrow$  GFR  $\rightarrow$   $\uparrow$  Absorption
- **Sympathetic**  $\rightarrow$   $\uparrow$  Na absorption
- **ADH**  $\rightarrow$   $\uparrow$  H<sub>2</sub>O absorption
- **Aldosterone**  $\rightarrow$   $\uparrow$  Na absorption + K excretion
- **ANP**  $\uparrow$  Na excretion

## Proximal tubules:

- 1- has the greatest effect in all tubules.
- 2- the fluid inside it is isosmotic.

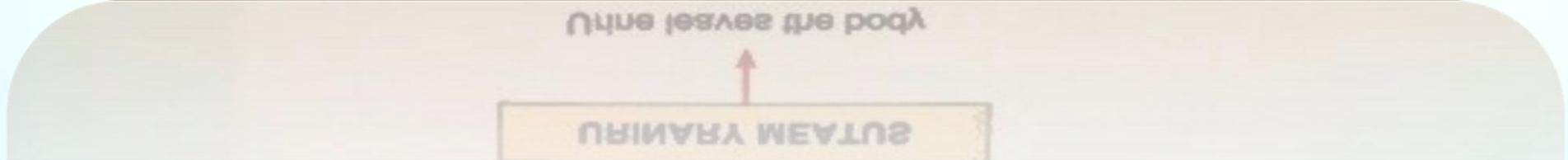
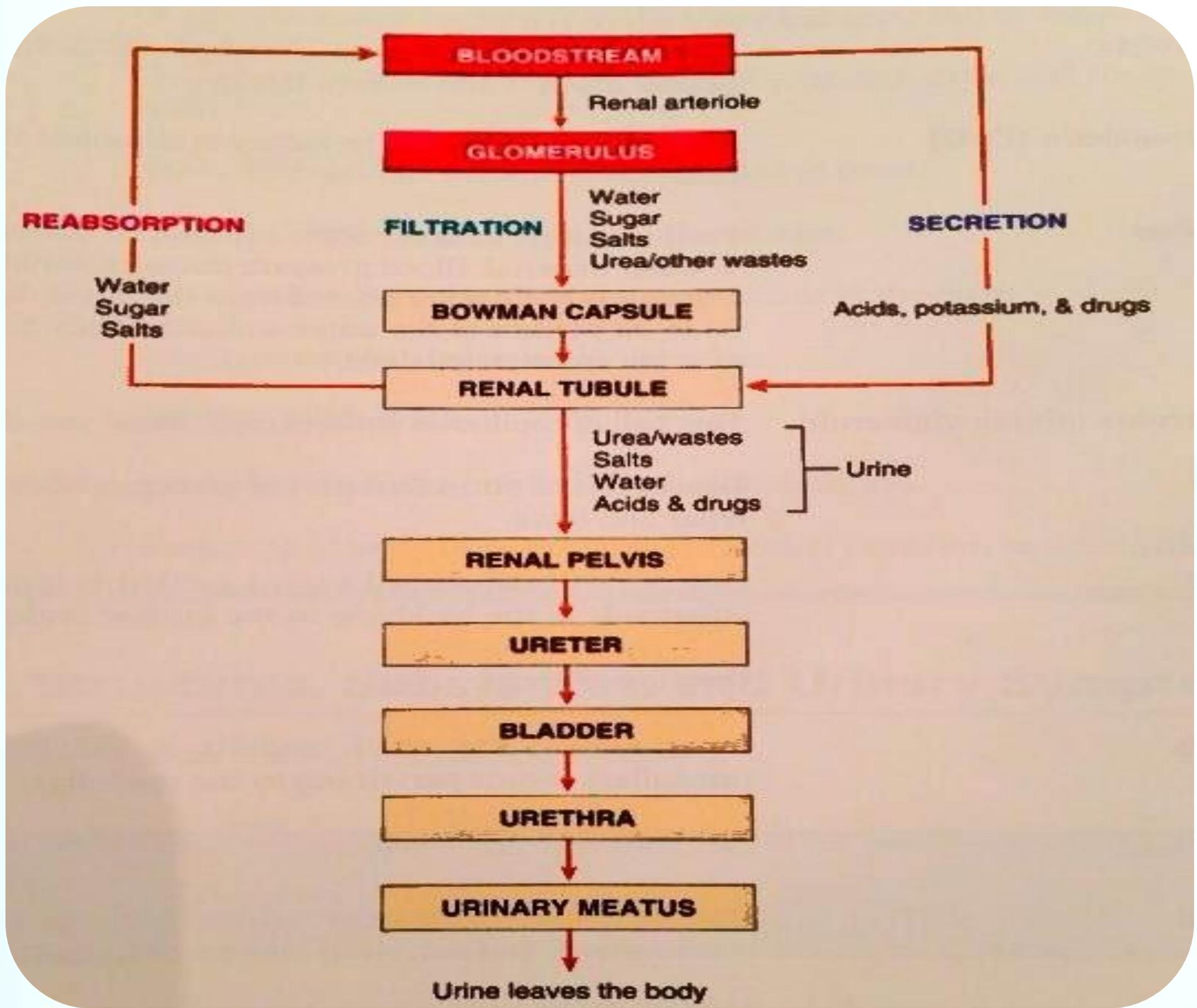


## Loop of Henle:

- \* Descending: concentrate urine by reabsorption of water.
- \* Thin ascending: Absorbed Na Cl
- \* Thick ascending: Absorbed Na 2Cl K

## Distal tubules:

- 1- Has **mucla densa** which is Na sensitive + excretes renin.
- 2- has principal cell: Na + H<sub>2</sub>O absorption & K secretion
- 3- has intercalated cell: absorbs K and secretes H<sup>+</sup> (controls pH)



# MCQS

**Q1: One of these examples is control passively:**

- A/Transport maximum
- B/Transcellular reabsorption
- C/Paracellular reabsorption
- D/co-transport

**Q2: where is Sodium-potassium specific pumps?**

- A/Basement membrane
- B/Basolateral membrane
- C/Interstitial wall
- D/Cytoplasmic membrane

**Q3: Where can you found sodium-potassium pump? In between..**

- A/Tubular lumen & tubular cell.
- B/interstitial fluid & tubular lumen.
- C/ interstitial fluid, tubular cell & tubular lumen.
- D/interstitial fluid & tubular cell

**Q4: When 3 Na / 2 K pumped in Basolateral membrane, the net result is:**

- A/High intracellular Na concentration
- B/Low Extracellular Na concentration
- C/↑ osmolarity in the basolateral space
- D/↓osmolarity in the basolateral space.

**Q5: Most of filtered water is reabsorbed in:**

- A/ Proximal convoluted tubule (PCT)
- B/Distal convoluted tubule (DCT)
- C/Ascending loop of henle
- D/Descending loop of henle

**Q6: Glucose reabsorption is the difference between:**

- A/the amount of glucose filtered and the amount Secreted
- B/the amount of glucose filtered and the amount excreted.
- C/the amount of glucose reabsorbed and the amount excreted.
- D/the amount of glucose reabsorbed and the amount secreted

**Q7: When plasma glucose reach which called “glucose renal threshold” , How much is glucose level in vein that will lead to appear in urine ?**

- A/250mg/dl
- B/375 mg/dl
- C/180mg/dl
- D/200mg/dl

**Q8: How much is maximum absorptive capacity for glucose in men?**

- A/375mg/min
- B/200mg/dl
- C/250mg/min
- D/300mg/min

Ans: 1-C, 2-B, 3-D, 4-C, 5-A, 6-B, 7-C. 8-A,

# MCQS

**Q9: Amino acid is reabsorbed in Basolateral membrane by :**

- A/ATP
- B/ Diffusion
- C/ Co-transport with Na
- D/Na<sup>+</sup>/K<sup>+</sup> ATPase

**Q10: What is the main important mechanism for Na exchange on Bicarbonate reabsorption ?**

- A/Reabsorption of HCO<sub>3</sub>
- B/Secreted H<sup>+</sup>
- C/Diffuses CO<sub>2</sub>
- D/Filtered HCO<sub>3</sub>

**Q11: At the end of descending loop of henle the osmolarity will be :**

- A/Decrease
- B/No change
- C/Minimal change
- D/Increase

**Q12: Which site has a high permeability of water:**

- A/Thick ascending loop of henle
- B/Thin ascending loop of henle
- C/Early portion of Distal convoluted tubule
- D/Thin descending loop of henle

**Q13: Which of the following is a site of NaCl diffuses passively ?**

- A/Proximal convoluted tubule (PCT).
- B/ thin ascending loop.
- C/ Distal convoluted tubule (DCT ).
- D/ thick ascending limb .

**Q14: the amount of water, solute reabsorption and secretion depends on :**

- A/Age
- B/Wight
- C/ body's needs
- D/secreted H<sup>+</sup>

**Q15: During Reabsorption/secretion of H<sub>2</sub>O in Late Distal Tubules and Collecting Tubules, the H<sub>2</sub>O is more dependent on :**

- A/Angiotensin II
- B/principal cells
- C/Aldosterone
- D/Anti-Diuretic hormone

Ans: 9-B, 10-B, 11-D, 12-D, 13-B, 14-C, 15-D.