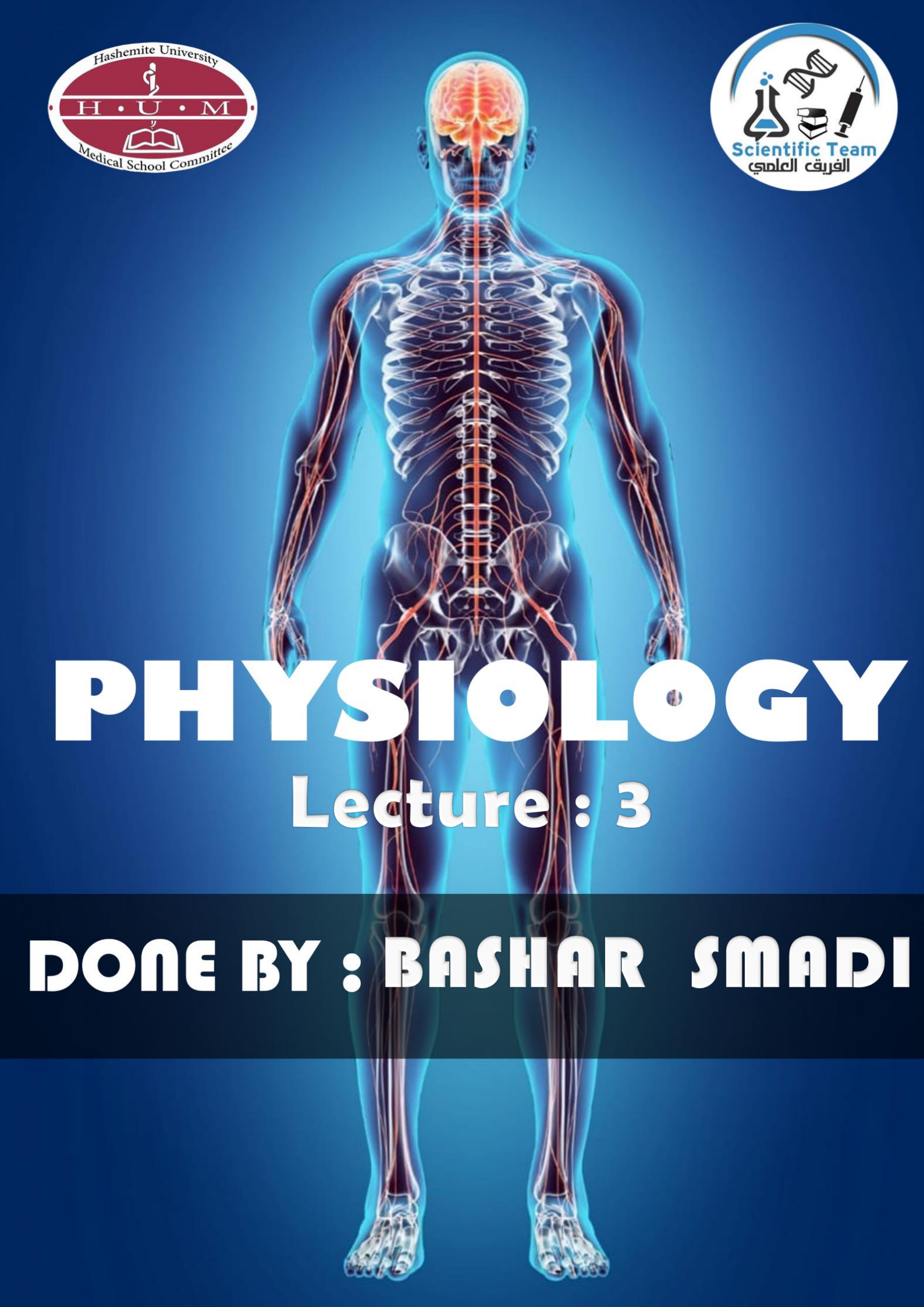


PHYSIOLOGY

Lecture : 3

DONE BY : BASHAR SMADI

Renal Tubular Reabsorption and Secretion-I

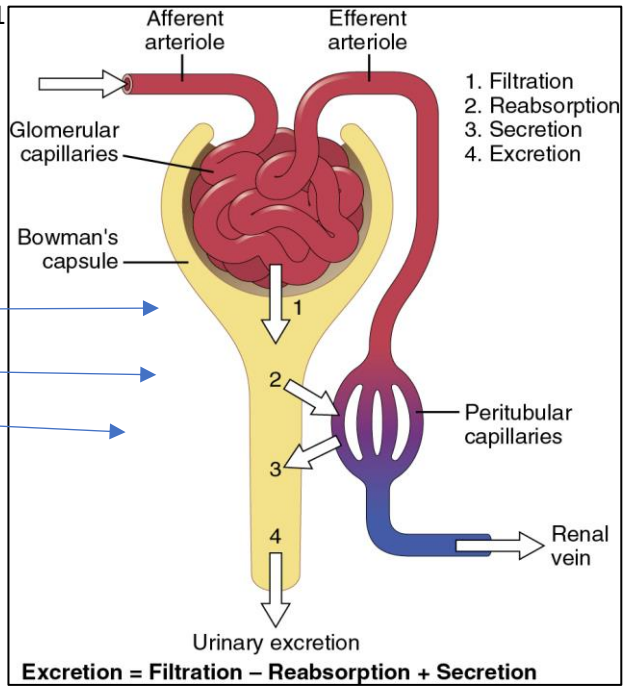
Basic Mechanisms of Urine Formation

the urine that is formed and all the substances in the urine represent the sum of three basic renal processes:

1. Glomerular filtration
2. Tubular reabsorption
3. Tubular secretion

so

Urinary excretion = filtration – Reabsorption + secretion



Glomerular filtration

• Filtration = GFR × Plasma concentration

(This calculation assumes that the substance is freely filtered and not bound to plasma proteins.)

لان ال filtration رح يكون قليل او معدوم اذا كانت bound to plasma proteins زي ما قلنا في المحاضرة السابقة

large quantities small quantities

Table 28-1 Filtration, Reabsorption, and Excretion Rates of Different Substances by the Kidneys

	Amount Filtered	Amount Reabsorbed	Amount Excreted	% of Filtered Load Reabsorbed
Glucose (g/day)	180	180	0	100
Bicarbonate (mEq/day)	4320	4318	2	>99.9
Sodium (mEq/day)	25,560	25,410	150	99.4
Chloride (mEq/day)	19,440	19,260	180	99.1
Potassium (mEq/day)	756	664	92	87.8
Urea (g/day)	46.8	23.4	23.4	50
Creatinine (g/day)	1.8	0	1.8	0

Changes in tubular reabsorption and glomerular filtration are closely coordinated to avoid large fluctuations in excretion

•الارقام ليست للحفظ بهذا الجدول

ال glucose كله filtered و Reabsorbed ما في اي شي بيظهر بال urine
ال urea نصها Reabsorbed ونصها Excreted
ال Creatinine كله filtered ما في عندنا Reabsorption
وباقي المواد يلي بالجدول هم electrolytes فاذا Mostly reabsorbed

● the processes of glomerular filtration and tubular reabsorption are quantitatively large relative to urinary excretion for many substances

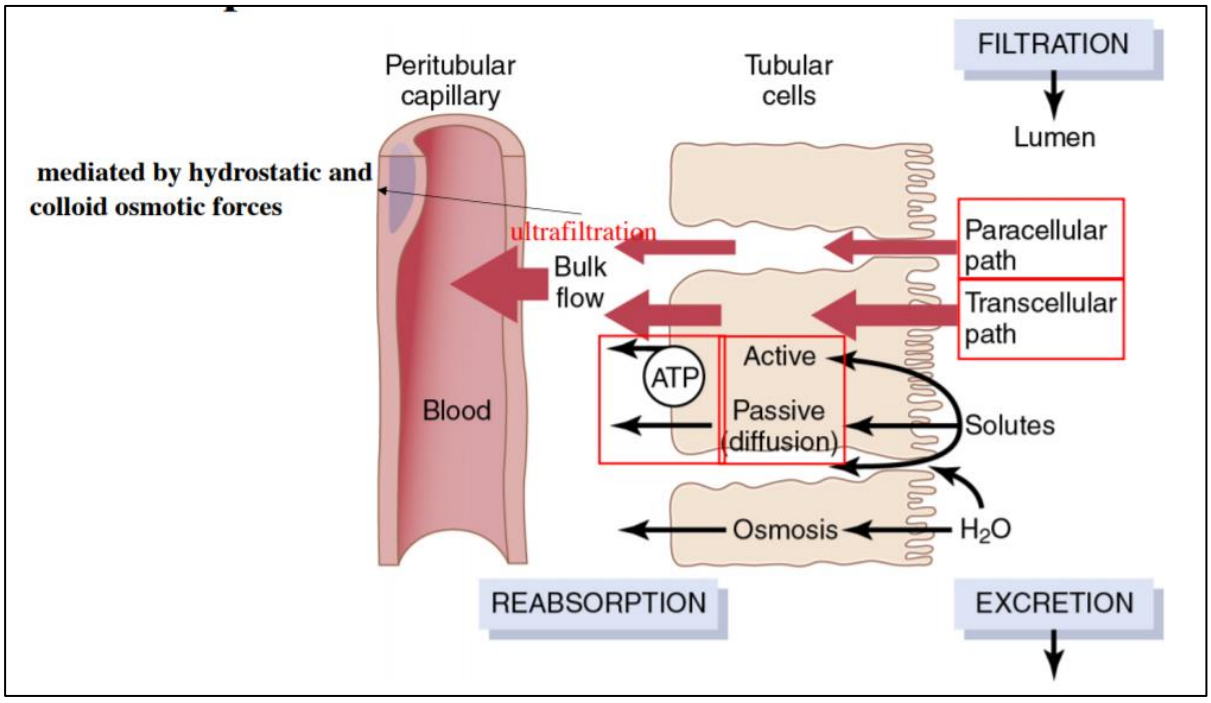
فاذا اي تغيير بيحصل فيهم ← رح يأثر بشكل كبير على ال excretion

excretion = filtration – Reabsorption + secretion

● Tubular reabsorption

- Highly selective
- Glucose and amino acids are completely reabsorbed
- Electrolytes are mostly reabsorbed but dependent on body needs
- Urea & creatinine poor absorption
- Tubular reabsorption includes passive and active mechanisms

● Reabsorption of Water and Solutes

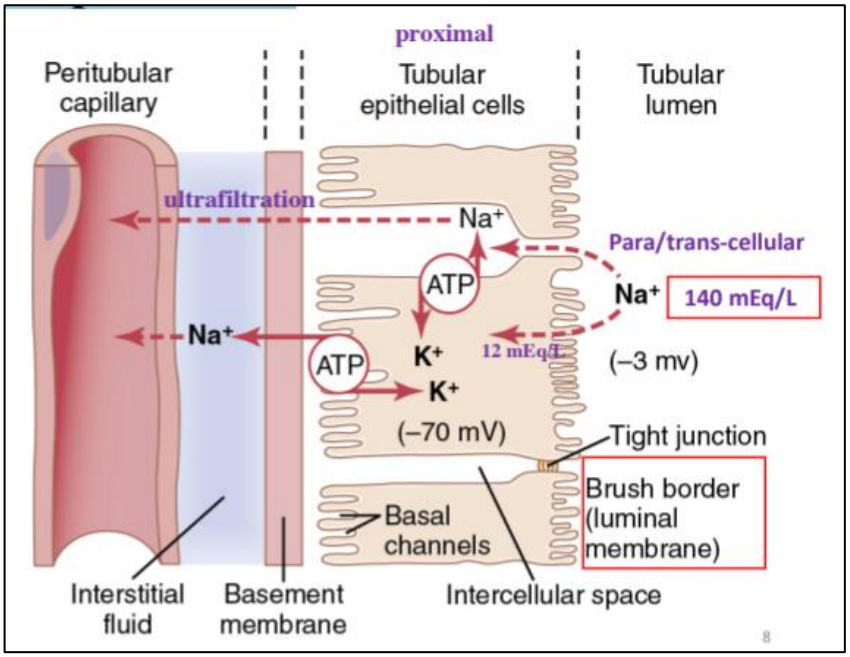


(this Figure) Reabsorption of filtered water and solutes from the tubular lumen across the tubular epithelial cells, through the renal interstitium, and back into the blood. Solutes are transported through the cells (**transcellular path) by passive diffusion or active transport**, or between the cells (**paracellular path**) by diffusion. Water is transported through the cells and between the tubular cells by osmosis. Transport of water and solutes from the interstitial fluid into the peritubular capillaries occurs by ultrafiltration (bulk flow).

ACTIVE TRANSPORT

- Moved against electrochemical gradient
- ATP-dependent
- Primary active transporters in kidneys:
  - Na-K ATPase
  - H-ATPase
  - H-K ATPase
  - Ca ATPase

Primary Active Transport of Na+



(this figure) Basic mechanism for active transport of sodium through the proximal tubular epithelial cell. The **sodium-potassium pump** transports sodium from the interior of the cell across the basolateral membrane, creating a low intracellular sodium concentration and a negative intracellular electrical potential.
(notice the difference of Na concentration between the lumen part (140 mEq/L) and the proximal part (12 mEq/L).)
The low intracellular sodium concentration and the negative electrical potential cause sodium ions to diffuse from the tubular lumen into the cell through the brush border.

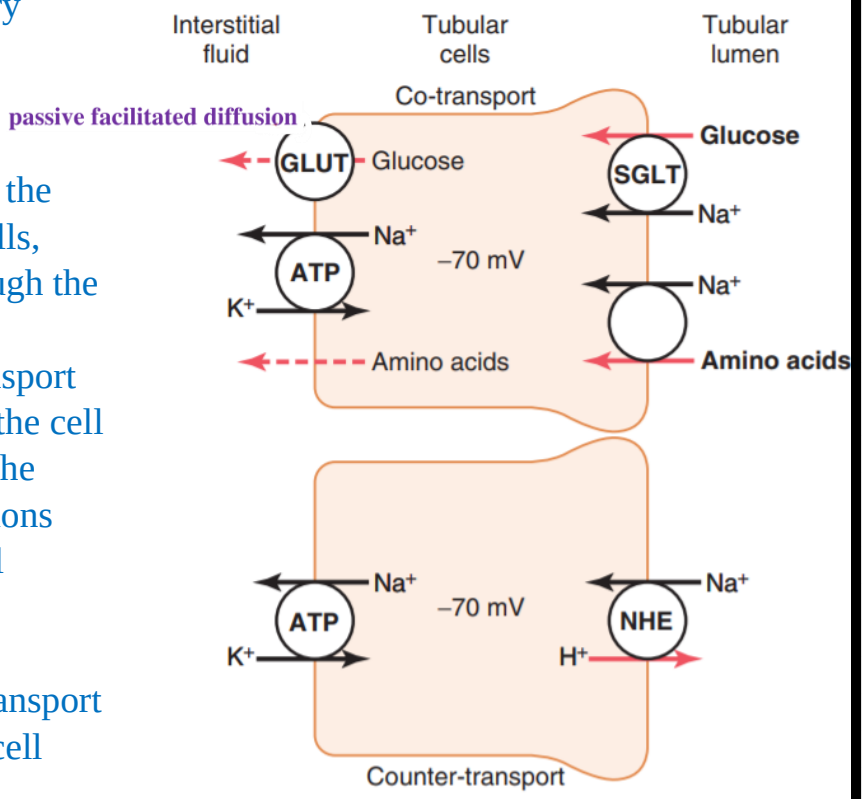
Passive diffusion of Na (Carrier proteins)

1) concentration gradient difference

2) -70 mV intracellular potential attracts positive Na

Mechanisms of secondary active transport.

(this Figure) Mechanisms of secondary active transport.
The upper cell shows the co-transport of glucose and amino acids along with sodium ions through the apical side of the tubular epithelial cells, followed by facilitated diffusion through the basolateral membranes.
The lower cell shows the counter-transport of hydrogen ions from the interior of the cell across the apical membrane and into the tubular lumen; movement of sodium ions into the cell, down an electrochemical gradient established by the sodium-potassium pump on the basolateral membrane, provides the energy for transport of the hydrogen ions from inside the cell into the tubular lumen.



Pinocytosis

• An **Active** Transport Mechanism for Reabsorption of Proteins

• Inside the cell, protein is digested into amino acids→ reabsorbed through basolateral membrane into interstitial fluid.

Transport Maximum

Some substances have a maximum rate of tubular transport due to saturation of carriers, limited ATP, etc.

• Transport Maximum: Once the transport maximum is reached for all nephrons, further increases in tubular load are not reabsorbed and are excreted.

• Threshold is the tubular load at which transport maximum is exceeded in some nephrons. This is not exactly the same as the transport maximum of the whole kidney because some nephrons have lower transport max's than others.

• Examples: glucose, amino acids, phosphate, sulphate

Glucose Transport Maximum

• Normally No glucose in the urine -all filtered

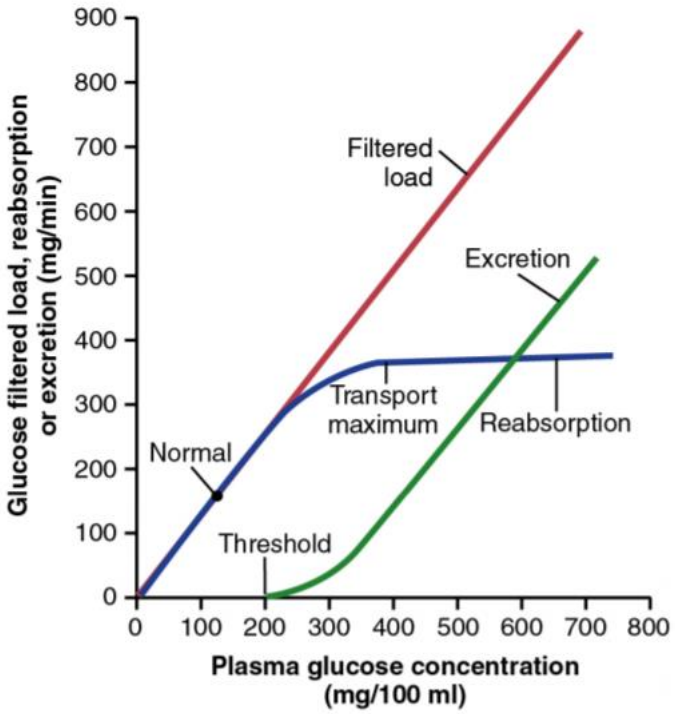
• glucose is reabsorbed in proximal tubule.

• When filtered load > Tm →urinary excretion of glucose

• Appearance of glucose in urine (at the threshold) occurs before transport maximum is reached.!! Why?

• not all nephrons have the same transport maximum for glucose→ some of nephrons begin to excrete glucose before others have reached their transport maximum.

• The overall transport maximum for the kidneys which is normally about **375 mg/min**, is reached when **all** nephrons have reached their maximal capacity to reabsorb glucose.



(this Figure) 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. The transport maximum is the maximum rate at which glucose can be reabsorbed from the tubules. The threshold for glucose refers to the filtered load of glucose at which glucose first begins to be excreted in the urine.

Reabsorption of Water and Solutes is Coupled to Na+ Reabsorption

• H2O is absorbed by osmosis through tight junctions

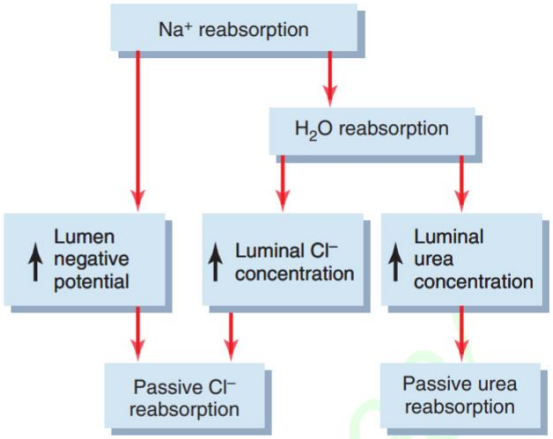
• Proximal tubules are highly permeable to water (Proximal tubules are always permeable for water)

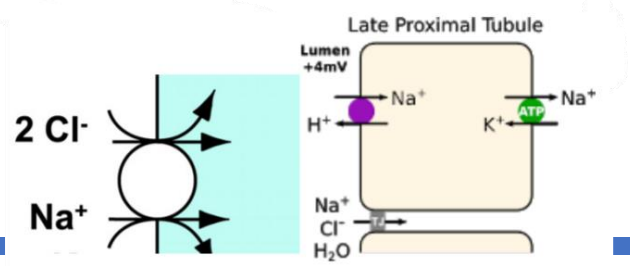
• H2O osmosis drag other solutes (Na, Cl, K, Ca & Mg) mainly in proximal T. Distally less permeable membrane & less surface area→ less solvent drag & osmosis

• Cl reabsorption (paracellular pathway) occurs via passive diffusion due to Na and water reabsorption

• Secondary active transport of chloride occurs a along with active transport of Na

• Urea is reabsorbed passively in the different segments of the nephron.





• Creatinine is large molecule and is essentially impermeant to the tubular membrane→almost none is reabsorbed

⬤Transport Characteristics of Proximal Tubule (PT)

• Proximal tubules have a high capacity for active & passive reabsorption→↑ mitochondria & extensive brush border on luminal side, extensive basal channels →↑ SA (Surface Area)

• PT reabsorb 65% of filtered Na, Cl, HCO3, & K

• Na is mainly reabsorbed by primary transport

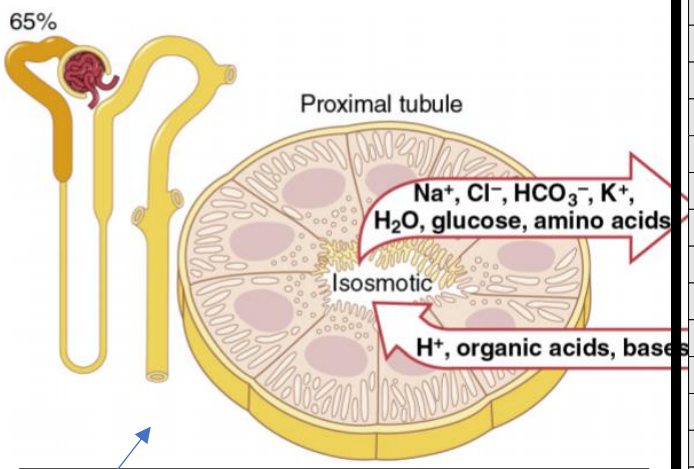
(GLU=Glucose) (AA=Amino Acids)

• In 1st ½ of PT→ Na, GLU& AA → COTRANSPORT

• In 2nd ½ of PT → low GLU& AA & high Cl →mainly Cl reabsorption by diffusion through intercellular j.

• Reabsorb all filtered glucose and amino acids

• Secrete organic acids, bases, & H+ into lumen.



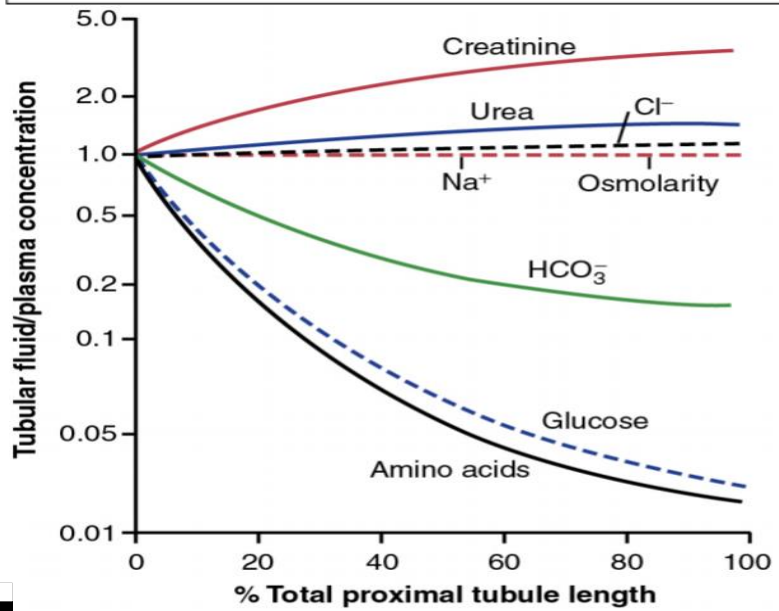
(this Figure) Cellular ultrastructure and primary transport characteristics of the proximal tubule. The proximal tubules reabsorb about 65 percent of the filtered sodium, chloride, bicarbonate, and potassium and essentially all the filtered glucose and amino acids. The proximal tubules also secrete organic acids, bases, and hydrogen ions into the tubular lumen.

• H+ secretion binds HCO3 → H2CO3→H2O +CO2

• Secretion of drugs (penicillin and salicylates),toxins, bile salts , ureat oxlate and catcholamines are secreted by the proximal tubule.

•PT is highly permeable to water thats why the reabsorption of solutes and water is occurring in the same rate (isosmotic)

Changes in Concentration in Proximal Tubule



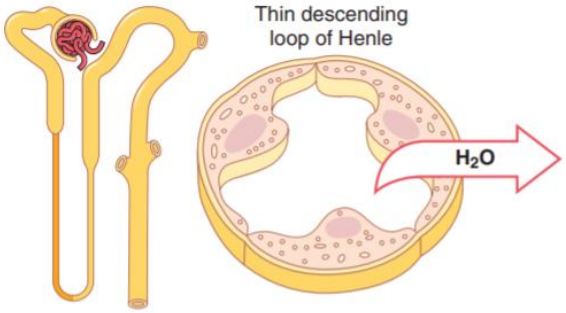
=1.0 concentration of substance in tubular fluid = concentration in plasma→High H2O permeability
<1 substance is reabsorbed> H2O
>1.0substance is reabsorbed < H2O or is secreted into the tubules.

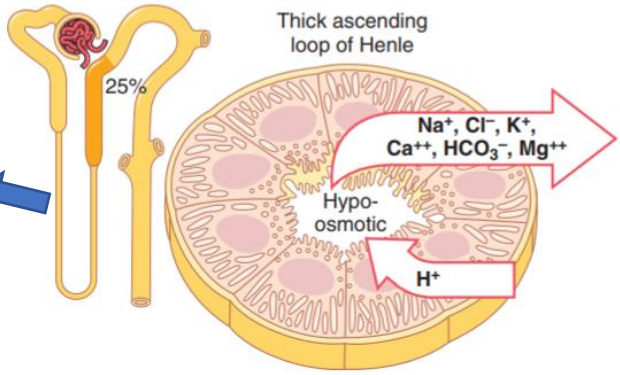
Transport characteristics of loop of Henle

3 functionally segments:

1- thin descending
2-thin ascending
3-thick ascending

thin epithelium
no brush borders
few mitochondria
minimal levels of metabolic activity





highly permeable to H2O
moderately permeable to most solutes

~ 25% of filtered load
• Reabsorption of
Na+, Cl- , K+, HCO3 - , Ca++, Mg++
• Secretion of H+
• not permeable to H2O
(hypo-osmotic)

Ascending segment of the ascending loop of Henle is virtually **impermeable** to water

•NaCl & K transport in thick

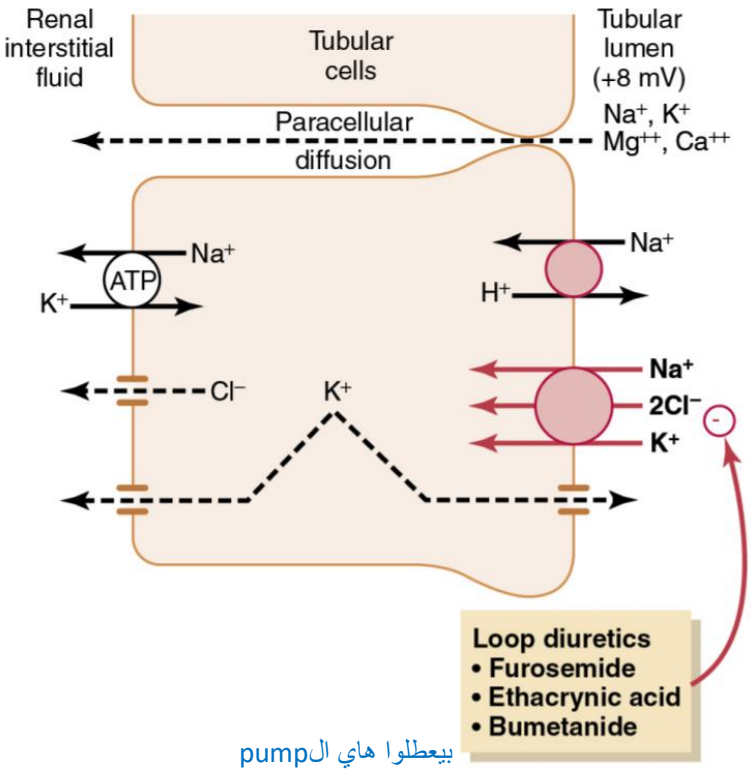
• ascending loop of Henle depends on Na+-K+ATPase

• In the epithelial cell basolateral membranes

• Pump →↓ intracellular Na→ favorable gradient for movement of Na from tubular fluid into cell.

• Movement of Na is mediated primarily by a 1-Na, 2-Cl, 1-K co- transporter

• Na-H counter-transport mechanism



بيعطلوا هاي الpump

Early Distal Tubule

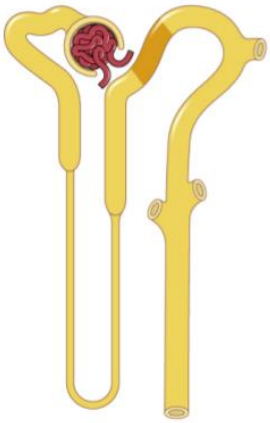
• Functionally similar to thick ascending loop

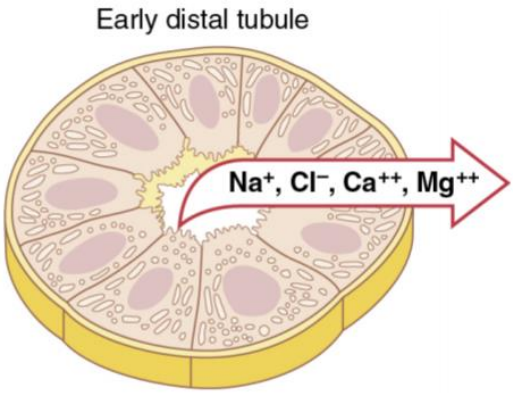
• Not permeable to water (called diluting segment)

• Active reabsorption of Na+, Cl- , K+, Mg++

•Early part contains macula densa (part of juxtaglomerular complex)& provides feedback control of GFR and RBF (Renal Blood Flow).

•The next part of the distal tubule is highly convoluted →reabsorbs most of ions& impermeable to water and urea.

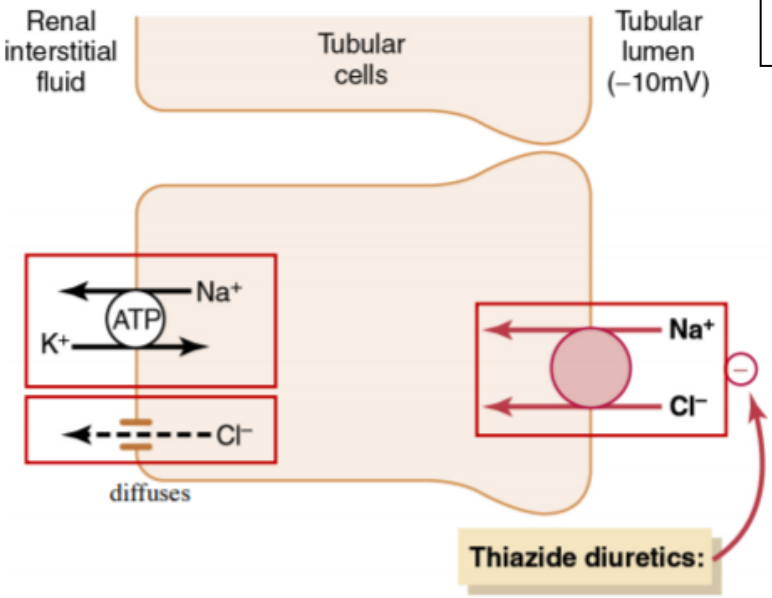




~ 5% of filtered load NaCl reabsorbed

• not permeable to H2O

• not very permeable to urea



←Mechanism of sodium chloride transport in the early distal tubule. Sodium and chloride are transported from the tubular lumen into the cell by a co-transporter that is inhibited by thiazide diuretics. Sodium is pumped out of the cell by sodium-potassium ATPase adenosine triphosphatase, and chloride diffuses into the interstitial fluid via chloride channels.

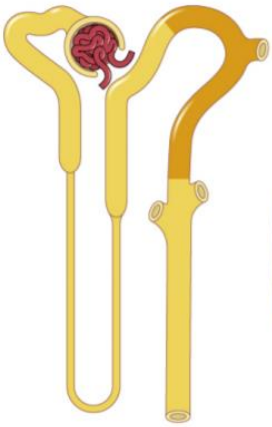
Late Distal Tubules and Collecting Tubules

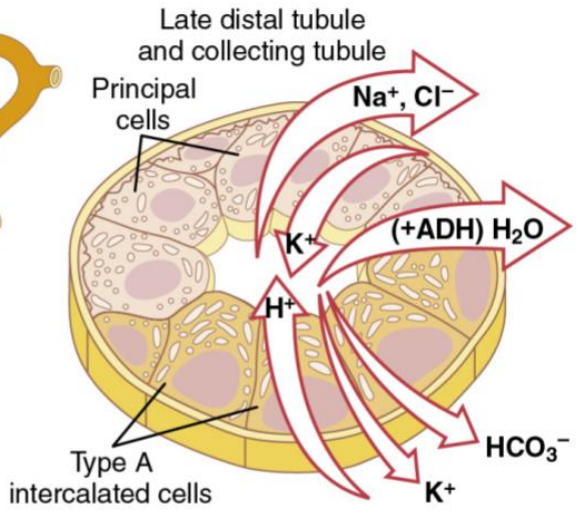
Late Distal Tubules and Collecting Tubules have similar functional characteristics

• permeablility to H2O depends on ADH

• not very permeable to urea

•The reabsorption of water from this tubular segment is controlled by the concentration of **antidiuretic hormone.**





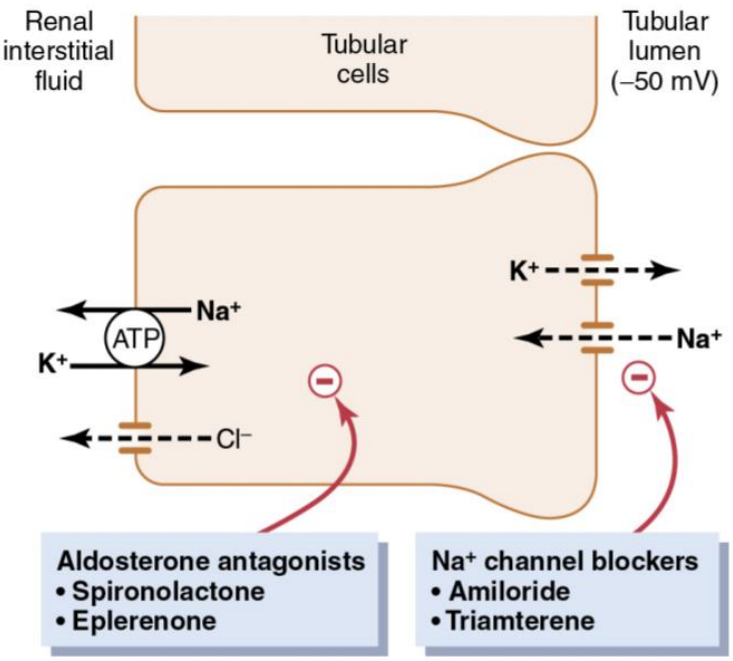
Principal Cells Reabsorb Na and Secrete K

• Depend on activity of Na+-K+ATPase pump basolateral membrane. Low intracellular Na→Na diffusion in+ high intracellular K →K diffusion OUT

• The principal cells are the primary sites of action of the K-sparing diuretics.

• Aldosterone antagonists inhibit stimulatory effects of aldosterone on Na reabsorption and K secretion.

• Na channel blockers inhibit the entry of Na into Na channels of →↓ Na that can be transported across the basolateral membranes by the Na+-K+ATPase pump.

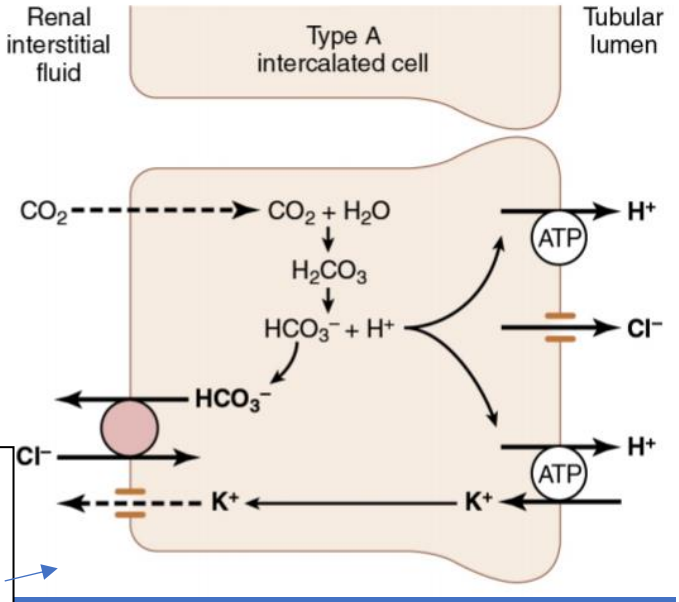


(this figure). Mechanism of sodium-chloride reabsorption and potassium secretion in the principal cells of the late distal tubules and cortical collecting tubules. Sodium enters the cell through special channels and is transported out of the cell by the sodium-potassium ATPase pump. Aldosterone antagonists compete with aldosterone for binding sites in the cell and therefore inhibit the effects of aldosterone to stimulate sodium reabsorption and potassium secretion. Sodium channel blockers directly inhibit the entry of sodium into the sodium channels.

Intercalated Cells Secrete H and Reabsorb HCO3 & K

Type A intercalated cells

• H secretion is mediated by a H-ATPase
• H is generated in this cell by the action of CA on H2O and CO2 to form H2CO3→dissociates into H & HCO3.
• H secreted into the tubular lumen, and for each H secreted, HCO3 becomes available for reabsorption across the basolateral membrane.

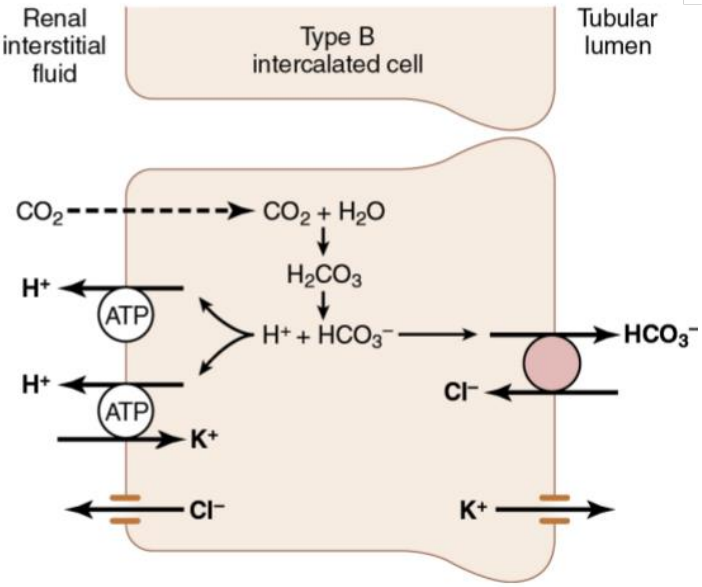


Type A cells contain hydrogen-ATPase and hydrogen-potassium-ATPase in the luminal membrane and secrete hydrogen ions while reabsorbing bicarbonate and potassium ions in acidosis.

Type B intercalated cells

• Functions is opposite to those of type A cells (in alkalosis)
• HCO3 to lumen
• H reabsorption via H-ATPase

In type B cells the hydrogen-ATPase and hydrogen-potassium-ATPase transporters are located in the basolateral membrane and reabsorb hydrogen ions while secreting bicarbonate and potassium ions in alkalosis.



Intercalated cells can also reabsorb or secrete K

Late distal tubule & cortical collecting tubule

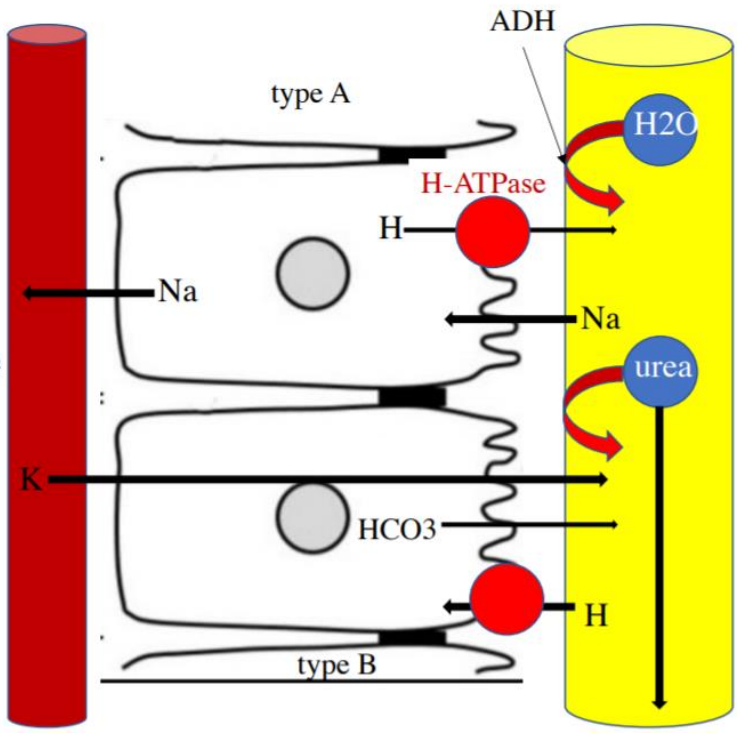
Functional characteristics:

1. impermeable to urea, some reabsorption of urea occurs in the **medullary** collecting ducts.

2. reabsorb Na→ controlled by hormones, especially **aldosterone**.

3. secrete K from peritubular capillary to lumen controlled by **aldosterone**

4. play a key role in acid-base regulation
-type A intercalated cells → secrete H by active H-ATPase mechanism in **acidosis**.
-type B intercalated cells secrete HCO3 and actively reabsorb H In **alkalosis**



5. controlling the degree of dilution or concentration of the urine →permeability to water is controlled by concentration of ADH/vasopressin.

↑ ADH → ↑ permeability

↓ADH → ↓ permeability

Transport characteristics of medullary collecting ducts

• Reabsorb <10% of filtered H2O & Na.

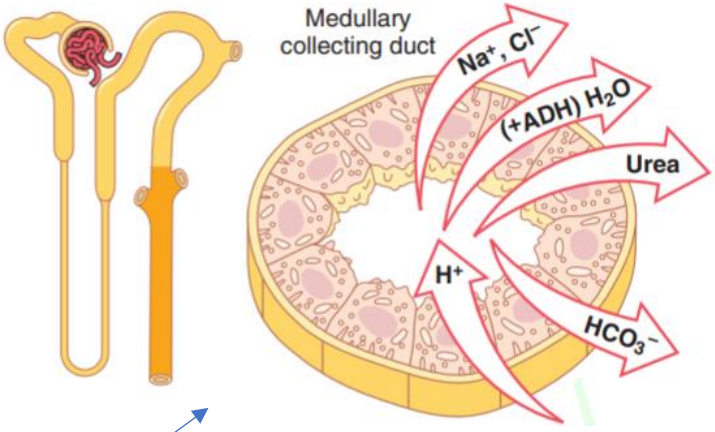
• The final site for processing the urine.

• Play an extremely important role in determining the final urine output of water and solutes.

• Its permeability to water is controlled by the level of ADH.

• permeable to urea→urea is reabsorbed into medullary interstitium →helping to raise the **osmolality** in this region of the kidneys and contributing to the kidneys' overall ability to form a **concentrated** urine.

• Secretes H against a large concentration gradient→ plays a key role in regulating acid-base balance



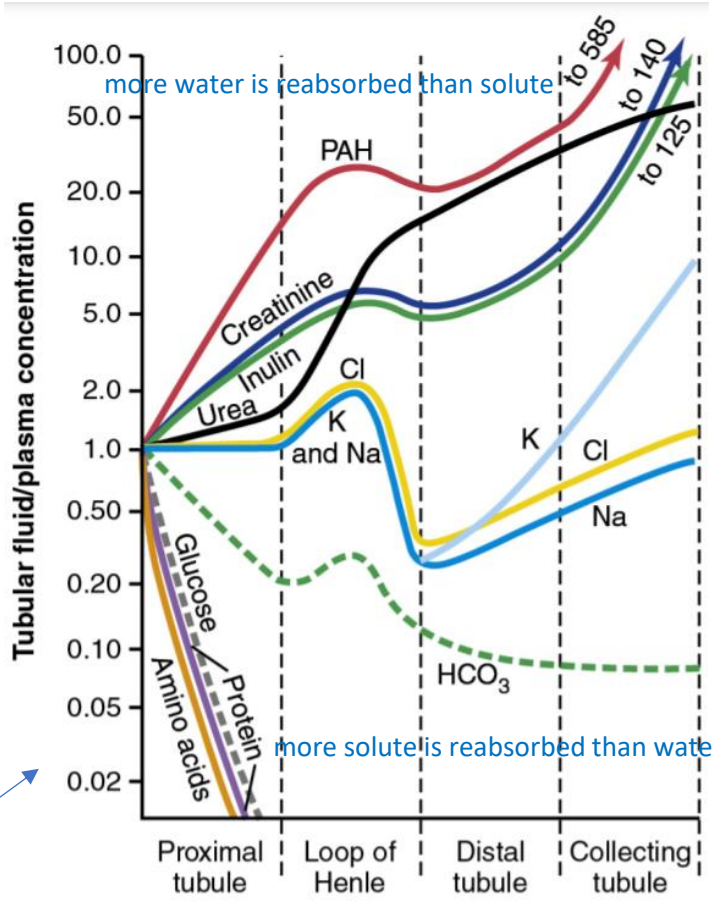
(this figure) Cellular ultrastructure and transport characteristics of the medullary collecting duct. The medullary collecting ducts actively reabsorb sodium and secrete hydrogen ions and are permeable to urea, which is reabsorbed in these tubular segments. The reabsorption of water in medullary collecting ducts is controlled by the concentration of antidiuretic hormone

concentrations of substances in the renal tubules

• Concentrations of solutes in different parts of the tubule depend on relative reabsorption of the solutes compared to water

• If water is reabsorbed to a greater extent than the solute, the solute will become more concentrated in the tubule (e.g. creatinine, inulin)

• If water is reabsorbed to a lesser extent than the solute, the solute will become less concentrated in the tubule (e.g. glucose, amino acids)



A value of 1.0 indicates that the concentration of the substance in the tubular fluid is the same as the concentration of that substance in the plasma. Values below 1.0 indicate that the substance is reabsorbed more avidly than water, whereas values above 1.0 indicate that the substance is reabsorbed to a lesser extent than water or is secreted into the tubules.

THANK YOU AND GOOD LUCK