

Pharmacology Team

introduction of diuretics

غير مطلوب لكن للفهم فقط

this part has been explained for us for about 1 hour
but it's just for your understanding
good luck all
and hope u benefit from our team

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Special thanx to Badra'a



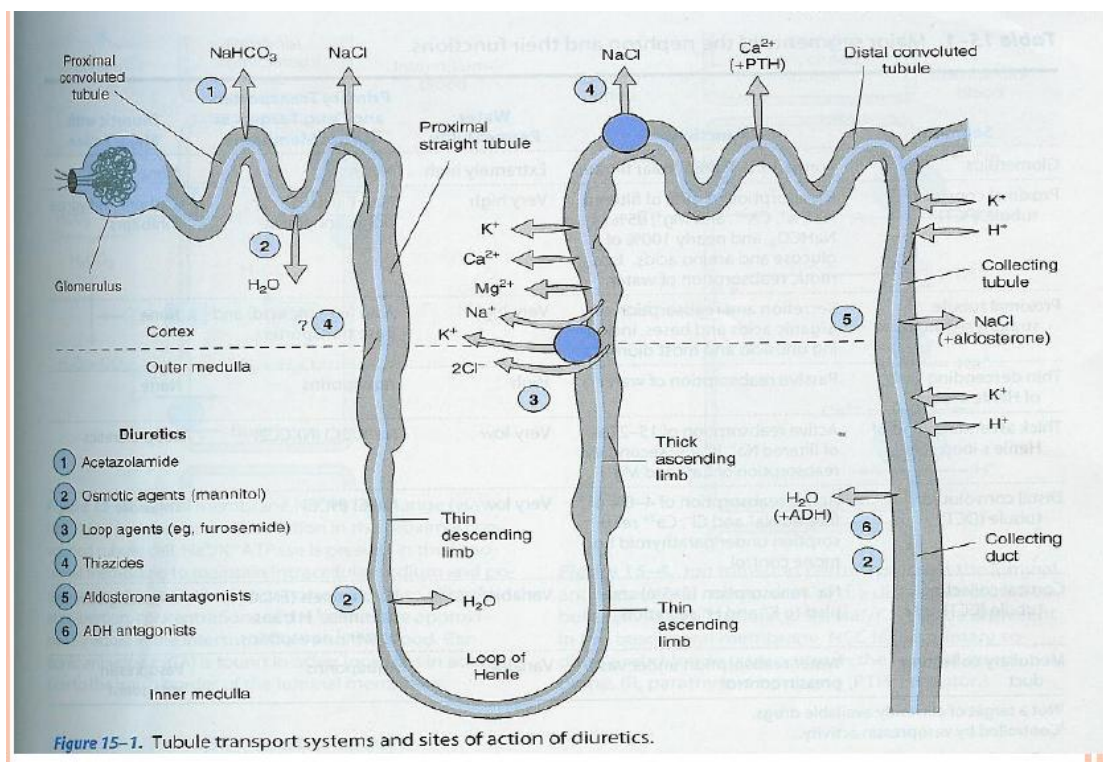
KIDNEY

oNephron is the unit of the kidney

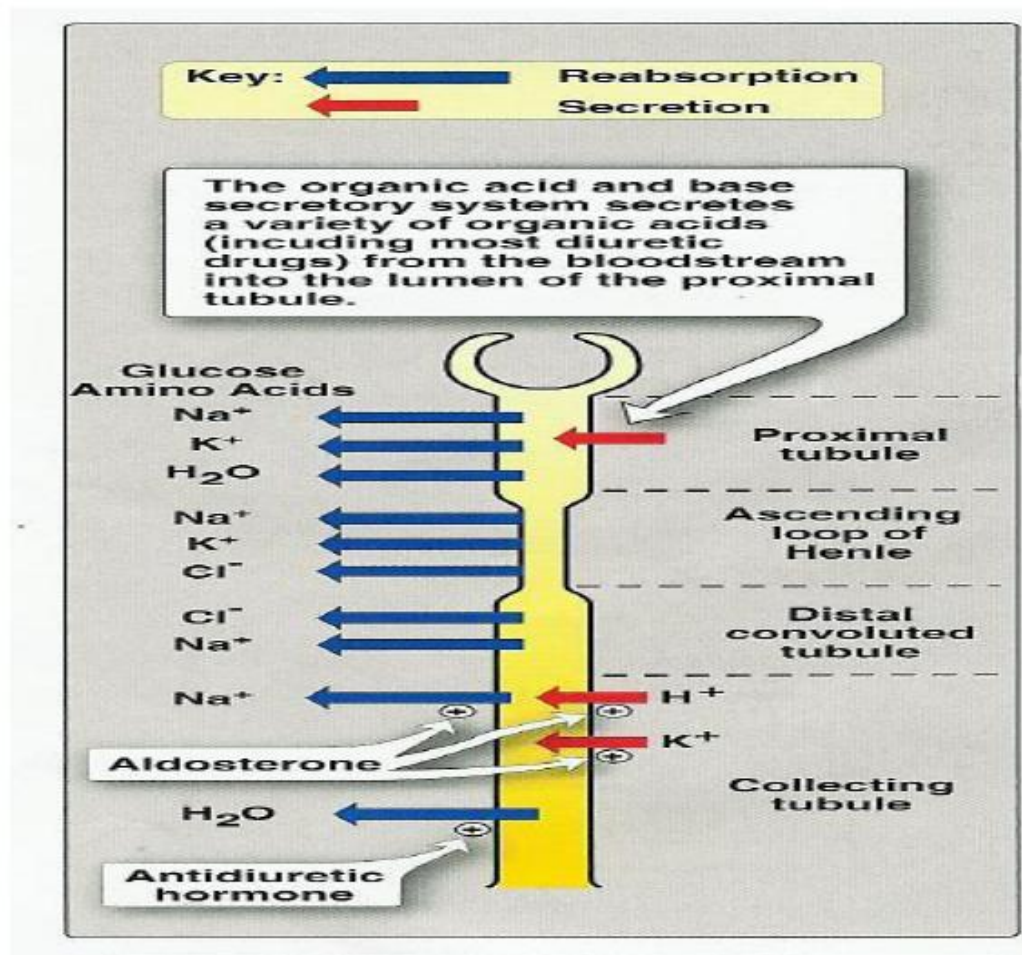
oIt is classified **structurally and functionally** into different zones:

- Glomerulus
- Proximal convoluted tubule
- Descending loop of Henle
- Ascending loop of Henle
- Distal convoluted tubule
- Collecting duct = Finally it gives urine

REGULATION OF FLUIDS AND ELECTROLYTES



SITES FOR SOLUTES AND WATER TRANSPORT ALONG THE NEPHRON



FUNCTION OF THE KIDNEY

oKidney is responsible for regulation of fluids and electrolytes

oIt controls: { volume of the urine
ionic composition of the urine

oKidney do its function through three processes

- •Glomerular filtration
- •Passive tubular reabsorption (passive : no energy, no carrier , it occurs according to different in concentration)

- • Active tubular secretion (Active : needs energy from ATP , needs carrier so it can be saturated "limited number of carriers")

❖ Glomerular filtration:

- **16-20 %** of blood entering the kidney **by renal Artery** is filtered (the coming of glomerouls is the filtrate)

• Filtrate contains glucose, amino acids, sodium bicarbonates, organic solutes and electrolytes as sodium, potassium, chloride.

(the high molecular weight can't filtrate so the drug which bind to plasma protein can't filtrate)

❖ Proximal convoluted tubule (PCT):

- Located in the cortex

- Responsible for reabsorption of [important]

→ • **all** glucose, amino acids, **100%**

→ • organic solutes

→ • electrolytes as (النسب لا تحفظ)

- sodium chloride (NaCl)(**66% of Na**) (**66% Na** which come back; as NaCl or NaHCO_3)
- Potassium (K^+ , **66 %**)
- sodium bicarbonate (NaHCO_3 , **85% by It self**)

- • NaHCO_3 is reabsorbed by action of enzyme carbonic anhydrase (*luminal membrane of proximal tubular cells*).
- $\text{NaCl} \rightarrow$ by Na,H transporter
Those transporters gives H and take Na
- • **water** is absorbed **passively following salts** to maintain osmolarity in tubular fluids (**60%**).
- • PCT is the site of organic acids or bases secretory systems

CARBONIC ANHYDRASE

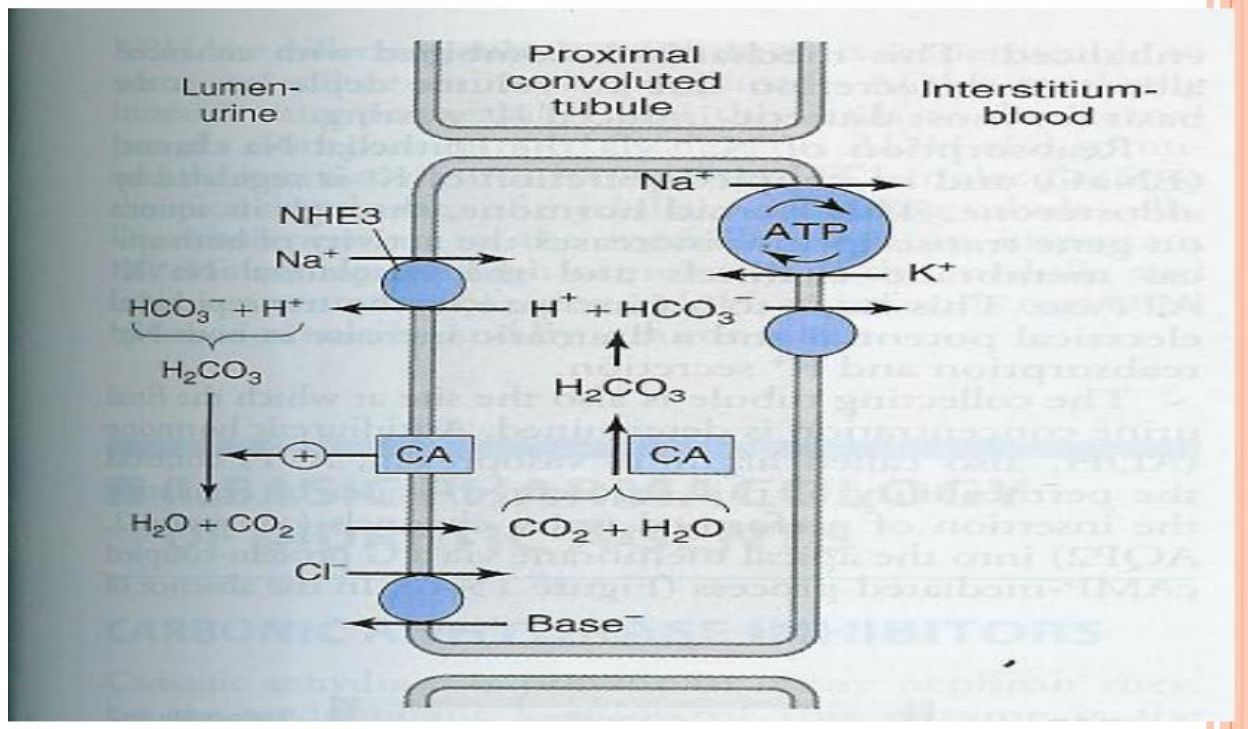


Diagram explanation

CA → carbonic anhydrase

CA : it is imp. To reabsorption of NaHCO₃

NaCl transport by Na , H transporter (in Na , H out)

(water follow solute when Na in ; the water go in also , so water absorbed passively)

*exchange between Na , H result in the H go out to the lumen; meets HCO₃⁻ in the filtrate result in H₂CO₃; then CA will work on it and degrade it to H₂O + CO₂ , CO₂ reabsorbed by diffusion in tubular cell meets H₂O and form again H₂CO₃ by CA and then it result of H⁺ & HCO₃⁻ which will go to interstitium blood)

SO CA is require For dehydration & rehydration Of H₂CO₃

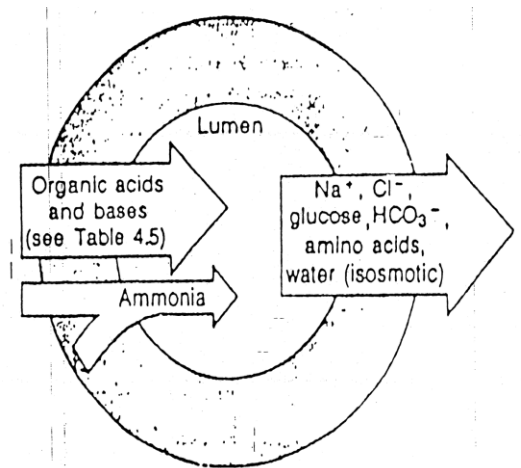
(ALSO there is exchange between NA, K in basolateral membrane by (Na , k transporter) so the Na can go to bl.)

(Diuretic drug will work in PCT is CA inhibitor which interfere with reabsorption OF NAHCO₃

NO drug can interfere NACL reabsorption)

Organic Acids Or Bases Secretory Systems

- **Organic base secretory system (ACTIVE)**
responsible for secretion of bases into luminal fluid
e.g. choline and creatinine
- **Organic acid secretory system (ACTIVE)**
responsible for secretion of acids into luminal tubular fluid
e.g. uric acid, NSAIDs, antibiotics and diuretics.
(NSAID: non steroidal Anti inflammatory drug like aspirin)
- are saturable (since this process active and needs carrier)



❖ Descending loop of Henle

- Located in the medulla

• **In thin descending loop of Henle:** water is reabsorbed by osmotic forces in hypertonic medullary interstitium (*counter current mechanism*)

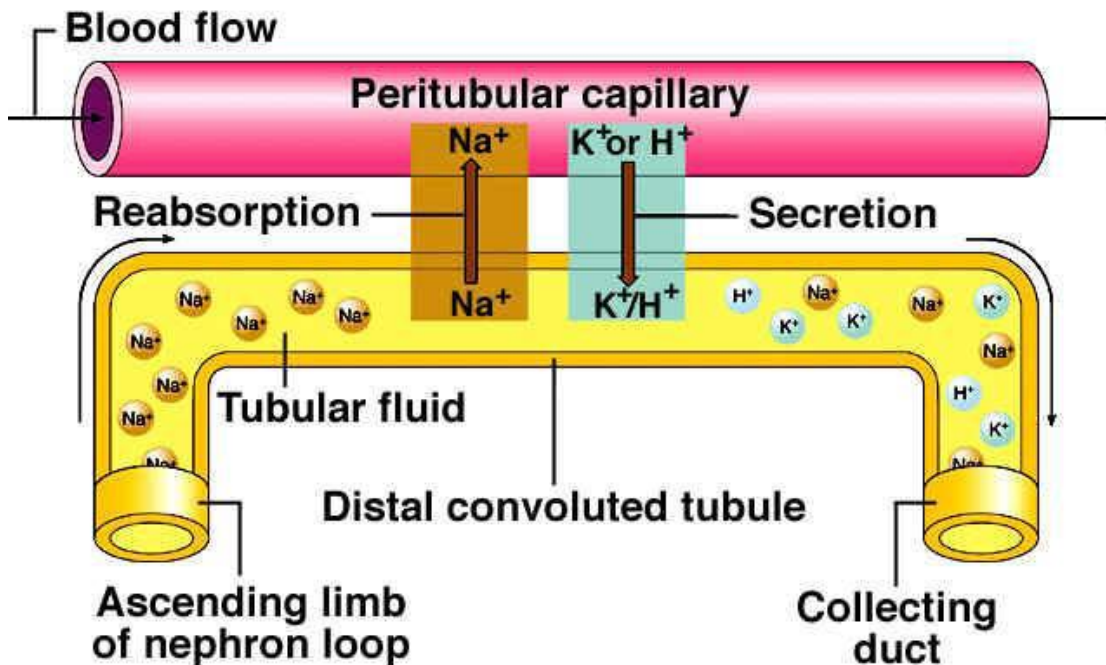
• The filtrate (isotonic) → **concentration of water = concentration of solute** becomes concentrated along this descending loop due to water reabsorption. يصير تركيزه عالي لان نفس الكمية من الماء و الملح تزيد

(Filtrate which come From PCT is isotonic, BUT in Descending loop of henle become more concentrated due to water reabsorption so less water = hyperosmotic)

• **Diuretics (*impermeant mannitol*)** (make the fluid more osmotic in D. loop of henle than the surrounding so the water can't reabsorbed)

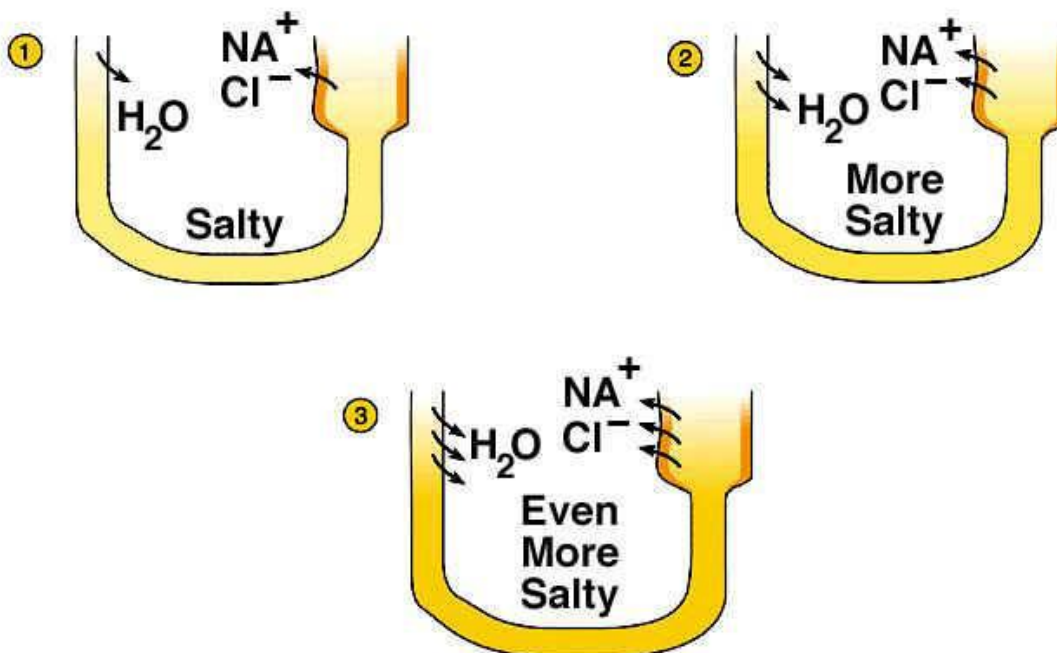
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Tubular Reabsorption and Secretion



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Countercurrent Mechanism



❖ Ascending loop of Henle

•Is impermeable to water (so no reabsorption of H_2O)

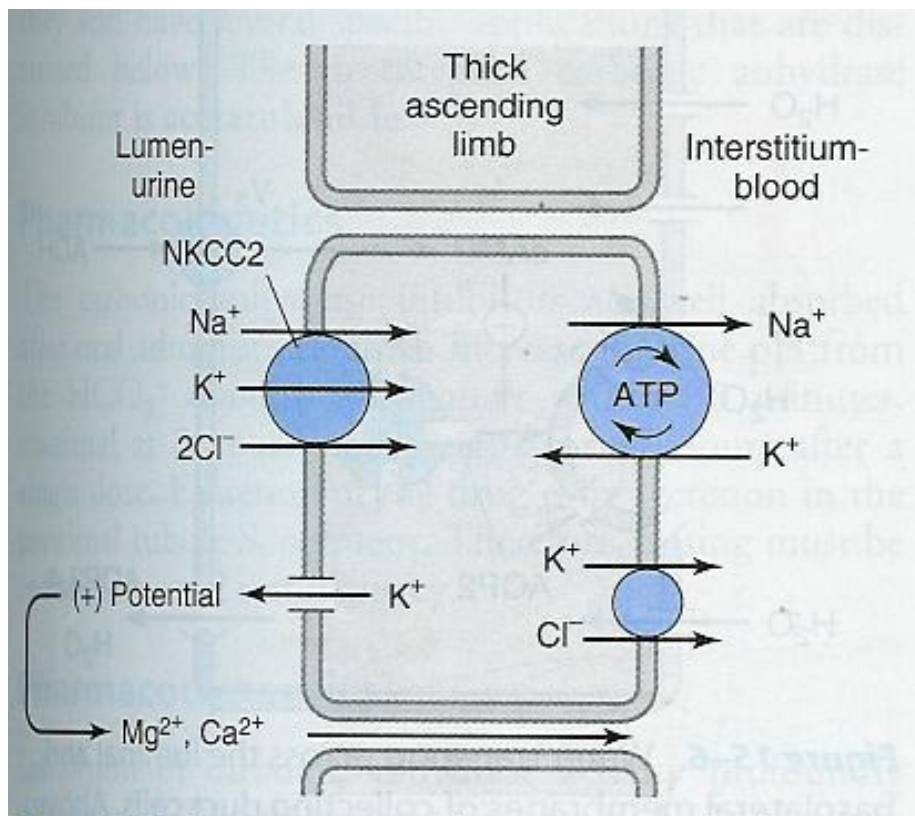
•**In Thick ascending loop of Henle (TAL)** is responsible for active reabsorption of Na, K and Cl (25% of Na) via transport system in luminal membrane called **$Na^+/K^+/2Cl^-$ -co-transporter**

•TAL is called the **diluting segment** (because of reabsorption Of electrolytes and the water still there)

•Ca and Mg enter the interstitial fluid via paracellular pathway **from lumen to bl** (by different in potential)

•**Loop diuretics** act on this segment to inhibit NaCl, Ca, Mg reabsorption

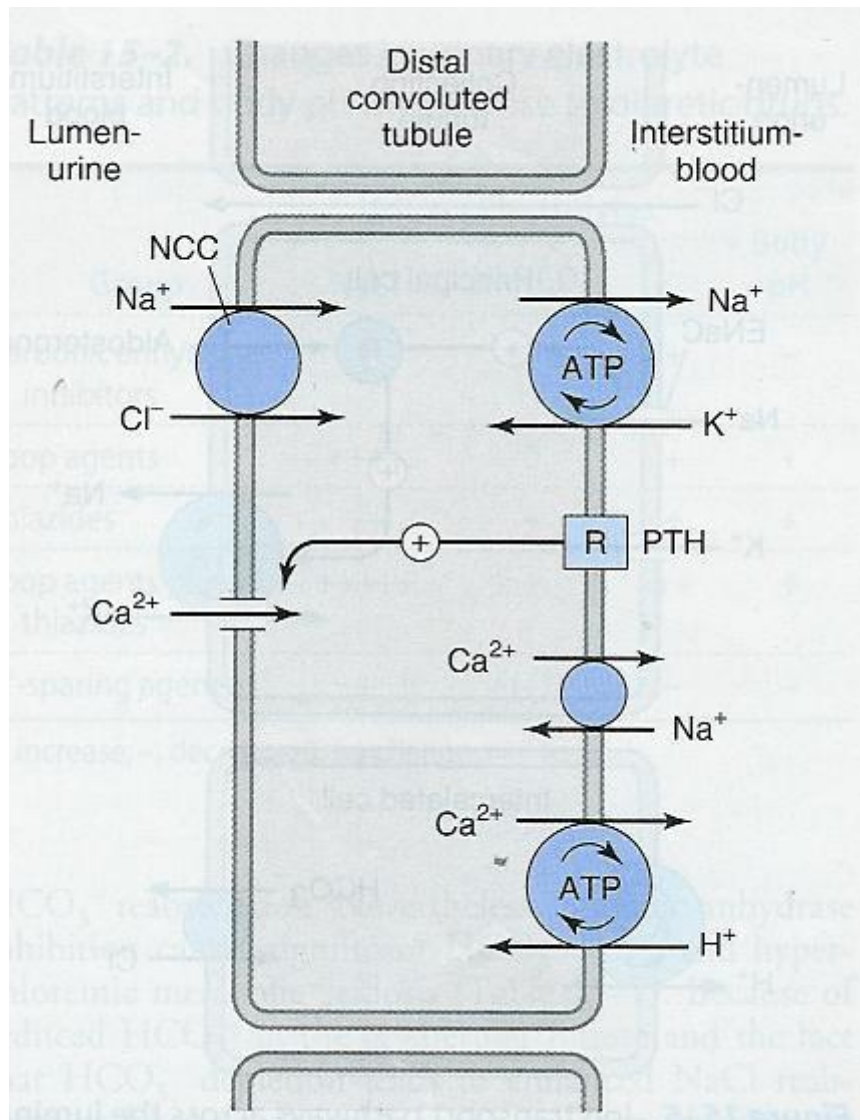
(the diuretic act on T. A. loop of henle is loop diuretic)



❖ Distal convoluted tubule (DCT)

- Is impermeable to water
- Responsible for **active** reabsorption of NaCl (10%) via transport system **Na/Cl transporter** in **luminal membrane** of
- Ca^{2+} **actively** reabsorbed via **Ca channel** and **Na/ Ca^{2+} exchanger** in basolateral membrane.

(diuretic here is **thiazide** which inhibit the NA/CL transporter)



❖ Collecting tubule

2 kinds of cells :

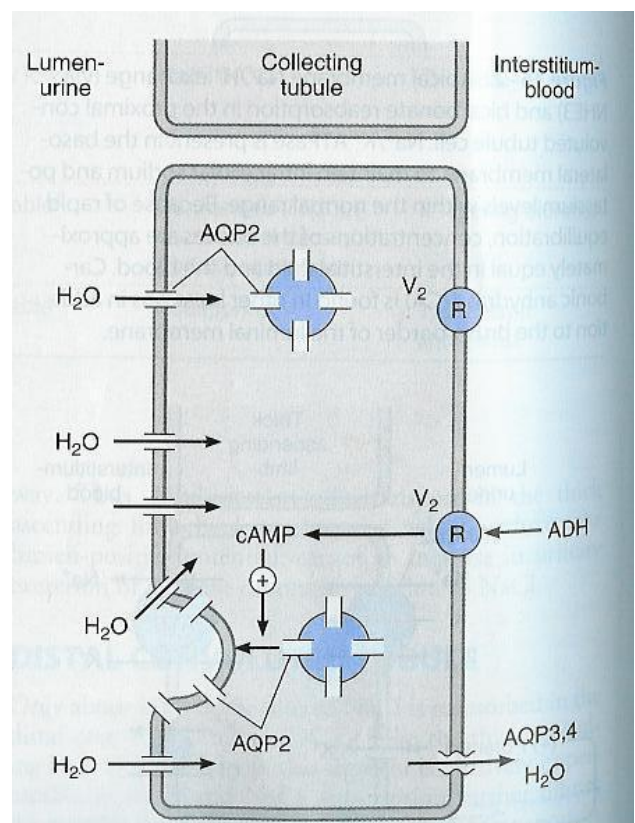
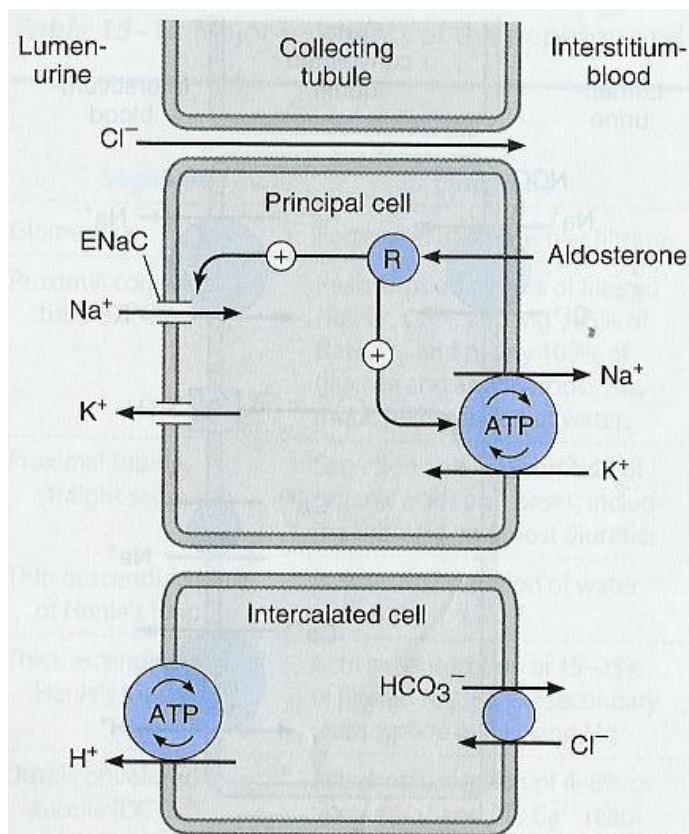
• **Principal cells** are responsible for reabsorption of Na (in exchange for K via Na/K-ATPase) and water

• **Intercalated cells** affect H secretion

• **Aldosterone receptors** located in the principle cells influence **Na reabsorption** and **K secretion**

(Aldosterone is one of the mineralocorticoid which cause salt & water retention & K secretion)

• **Antidiuretic hormone (ADH)** promotes reabsorption of water
It's function ↑ water absorption (water retention)



ADh increase formation H₂O channels (AQP2) *aqua porin transport* push the water to body

FUNCTION OF DIFFERENT PARTS OF NEPHRON

segment	Function	transporter	Diuretic drug
PCT	Reabsorption of 66% Na, K, Ca, Mg, 100% glucose and amino acids; 85% NaHCO ₃	Na/H transporter, Carbonic anhydrase enzyme	Carbonic anhydrase inhibitors
PST	Secretion and reabsorption of organic acids and bases	Acid & base transporter	None
TAL	Active reabsorption 25% Na, K, Cl Secondary reabsorption Ca, Mg	Na/K/2Cl transporter	Loop diuretics
DCT	Active tubular reabsorption of 5% Na, Cl, Ca	Na and Cl cotransporter	Thiazide diuretics
CCT	Na reabsorption K & H secretion	Na channels K & H transporter	K-sparing diuretics

PST : proximal straight tubules // k- sparing diuretics keep k in bl. Instead of being in urine.

PCT → proximal convoluted tubule

TAL → thick ascending loop of henle

CCT → Cortical collecting tubule

PST → proximal straight tubule

DCT → Distal convoluted tubule

TABLE 20.4 Functions of Nephron Components	
Part	Function
<i>Renal Corpuscle</i>	
Glomerulus	Filtration of water and dissolved substances from the plasma Receives the glomerular filtrate
Glomerular capsule	
<i>Renal Tubule</i>	
Proximal convoluted tubule	Reabsorption of glucose; amino acids; creatine; lactic, citric, uric, and ascorbic acids; phosphate, sulfate, calcium, potassium, and sodium ions by active transport Reabsorption of proteins by pinocytosis Reabsorption of water by osmosis Reabsorption of chloride ions and other negatively charged ions by electrochemical attraction Active secretion of substances such as penicillin, histamine, creatinine, and hydrogen ions
Descending limb of nephron loop	Reabsorption of water by osmosis
Ascending limb of nephron loop	Reabsorption of sodium, potassium, and chloride ions by active transport
Distal convoluted tubule	Reabsorption of sodium ions by active transport Reabsorption of water by osmosis Active secretion of hydrogen ions Secretion of potassium ions both actively and by electrochemical attraction
<i>Collecting Duct</i>	Reabsorption of water by osmosis