MEDICINE
KING SAUD UNIVERSITY

Physiology Team 436

Revised by
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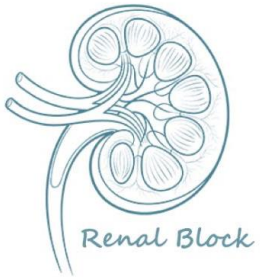
Renal Transport Process 2:Tubular Secretion



Red: very important.
Green: Doctor's notes.
Pink: formulas.
Yellow: numbers.
Gray: notes and explanation.

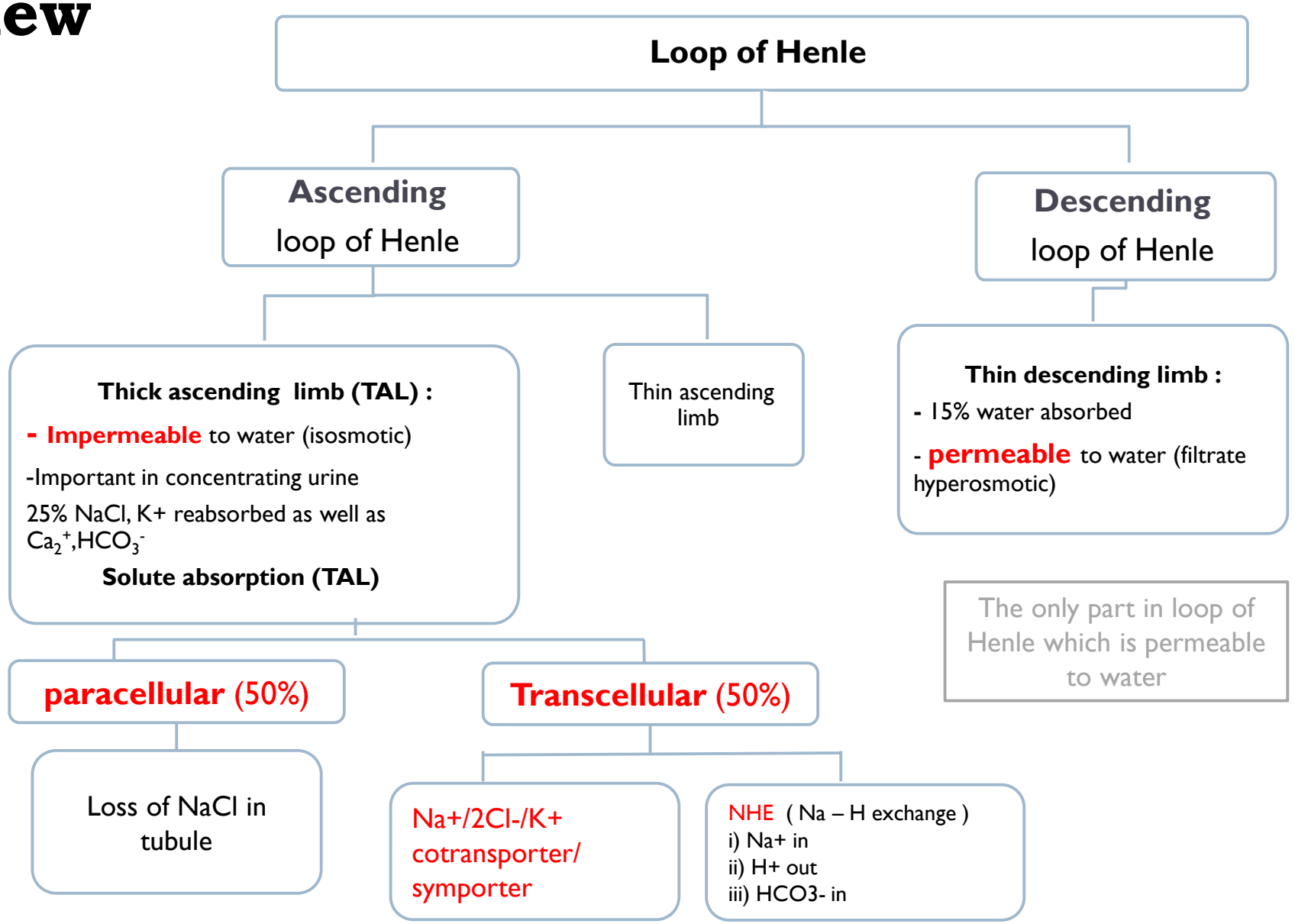
Physiology Team 436 – Renal Block Lecture 6

For further understanding please check our "Extra Notes" file which contains extra explanation from reference books.

Objectives

- Describe tubular secretion with PAH transport and 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 Na+ in the late distal tubules.

Overview



-Its important to know each segment of the nephron and the osmolality of the filtrate in it.
-Its important to know each segment of the nephron and what is it permeable and Impermeable to.

Loop of Henle

- **Thin descending limb :**
  - 15% water reabsorbed
  - **permeable** to water (filtrate **hyperosmotic**)
  to allow simple diffusion
- **Thick ascending limb :**
  - **Impermeable** to water *(isosmotic)* Thin Ascending Limb Hyposmotic
  -Important in concentrating urine (more details in next lecture)
  - 25% NaCl, K+ reabsorbed as well as Ca_2^+ and HCO_3^-

Mechanisms of Solute reabsorption (in TAL):

1- Transcellular needs to enter the cell (50%)

1) Na+/2Cl-/K+ cotransporter*/ symporter**

2) NHE (Na, H exchange)

Na+ in \ H+ out \ HCO3- in

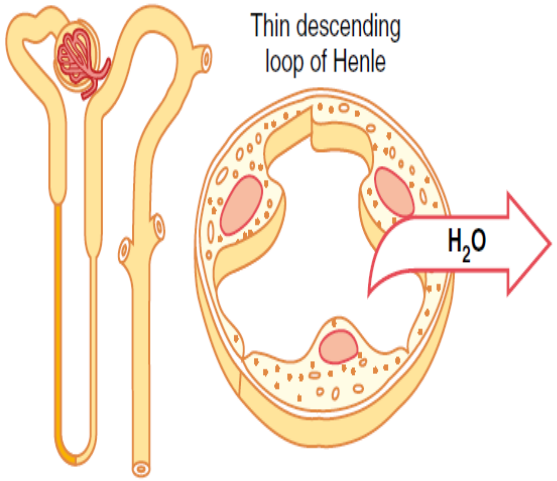
2- Paracellular (50%)

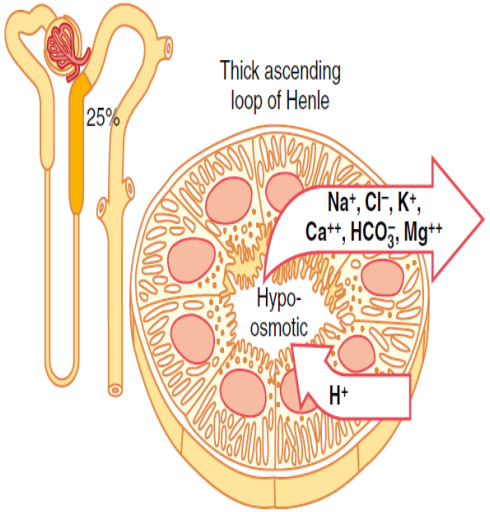
Loss of NaCl in tubule

Remember:

- the beginning of the loop of henle has a similar structure to PCT
- Tubular fluid reaches early segment of loop of henle as isotonic (equal in sodium and water)
- loop of henle has 3 segments 2 of them aren't permeable to water and one is (thin descending is permeable) (thin ascending and thick ascending aren't permeable)

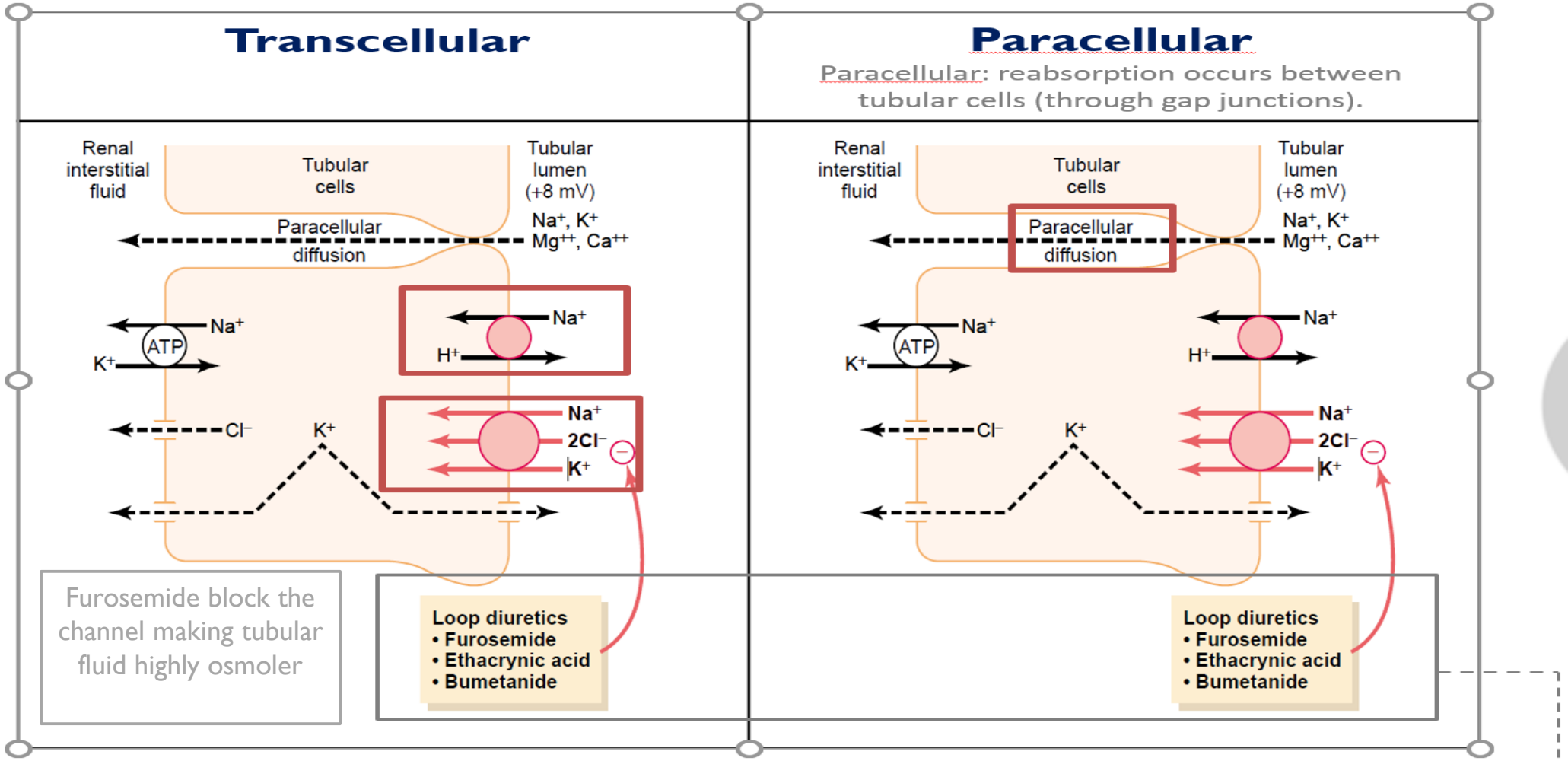
- The thick **ascending** limb reabsorbs 25% of NaCl and K, but the majority (70%) is reabsorbed in the proximal convoluted tubules. Transcellular is when ions enter the blood circulation after passing through tubular cells.
- Hydrogen secreted through the sodium hydrogen exchanger (NHE) is obtained from the dissociation of carbonic acid in the presence of carbonic anhydrase.





*means all of them enter together **all in same direction

Loop of Henle



Remember from pharmacology *loop diuretics mechanism *

The thick ascending limb of the loop of Henle is the site of action of the powerful *"loop" diuretics furosemide, ethacrynic acid,* and *bumetanide,* all of which inhibit the action of the sodium, 2-chloride, potassium co-transporter.

Loop of Henle

- Solute absorption (TAL):

1) Transcellular (50%)

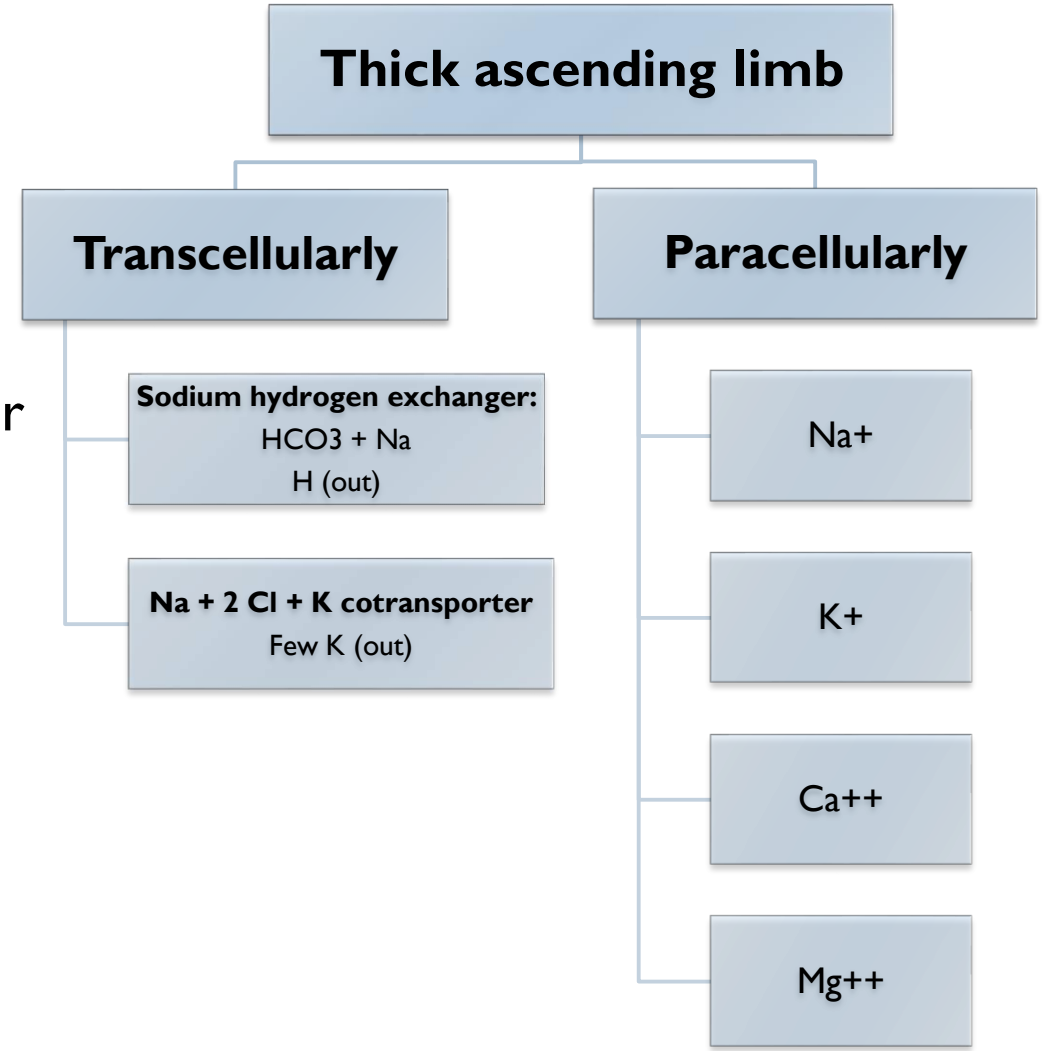
a) Na+/2Cl-/K+ cotransporter/ symporter

b) NHE

i) Na+ in

ii) H+ out

iii) HCO3- in



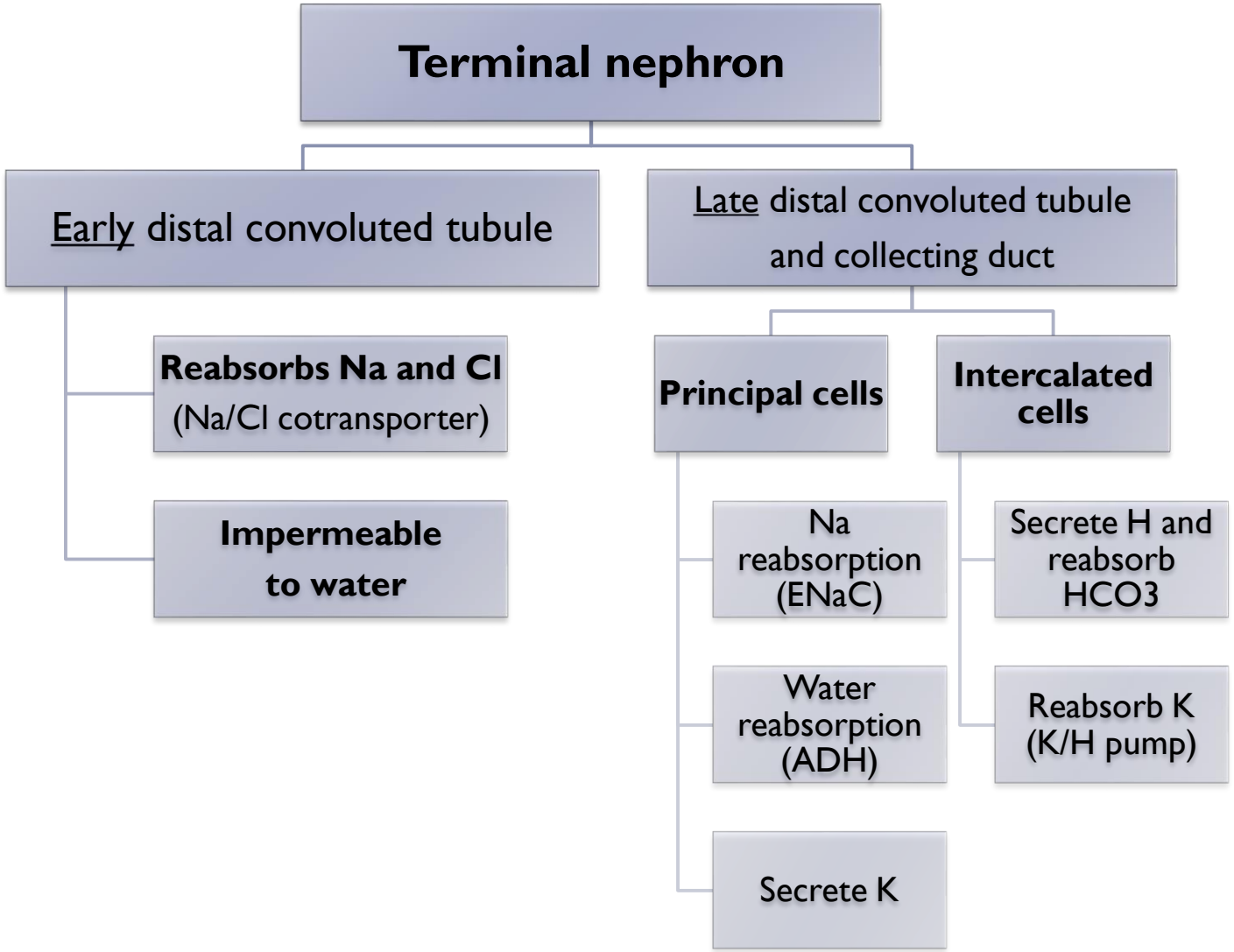
2) Paracellular (50%)

- Loss of NaCl in tubule

  ⇒ ↑ positive charge compared to blood drives absorption

NaCl moves from lumen to interstitium this leaves behind positive charged molecules, positivity will increase in tubular fluid so equilibrium must be met in tubular fluid → Ca K Mg follows NaCl

Overview


Terminal nephron
Early distal convoluted tubule
Late distal convoluted tubule and collecting duct
Reabsorbs Na and Cl (Na/Cl cotransporter)
Impermeable to water
Principal cells
Intercalated cells
Na reabsorption (ENaC)
Water reabsorption (ADH)
Secrete K
Secrete H and reabsorb HCO3
Reabsorb K (K/H pump)

Distal convoluted tubule (DCT) & collecting duct (CD)

- 7% NaCl reabsorbed مهمة النسبة ومقارنتها مع البروكسميل
- 8 – 15 % water reabsorbed *(needs ADH)*
- Some K^+, H^+ secreted *into* tubule

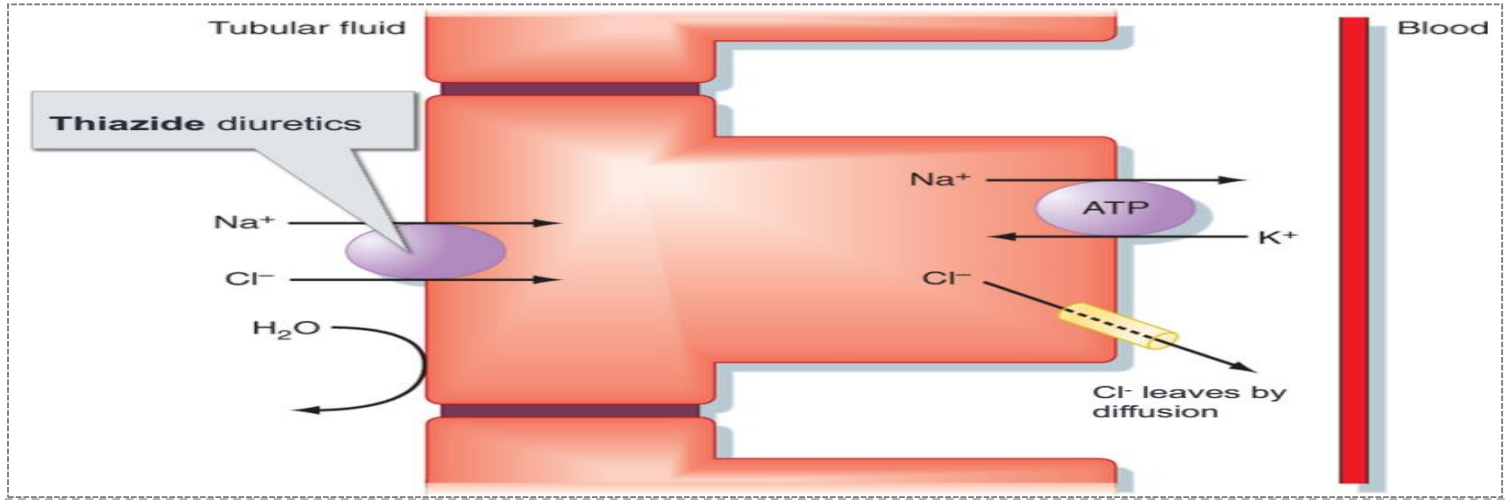
Early DCT

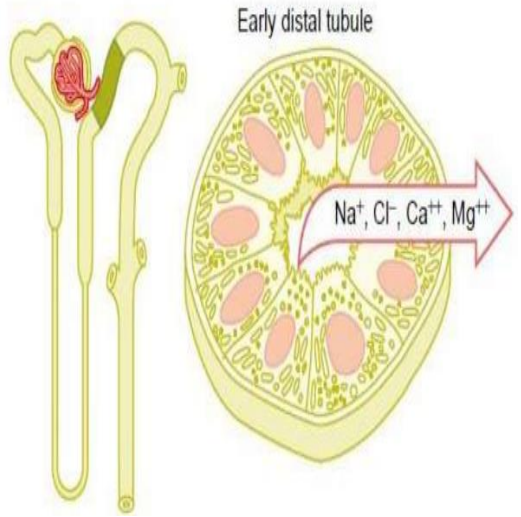
- Reabsorbs Na^+, Cl^-
- Impermeable to water.

Diuretics:

- Mannitol is a hyperosmolar material so it will attract huge amounts of water
- A less powerful diuretic is Furosemide (loop of henle)(blocks NKCC pump)
- Least powerful is thiazide (early DCT) (blocks Na Cl pump)

Thiazides are most commonly used in HTN





Distal convoluted tubule (DCT) & collecting duct (CD)

Late DCT

Principle cells:

- Reabsorb Na^+, Na+ diffuses via selective channels.
- Reabsorb water
- Secrete K^+ down the conc gradient

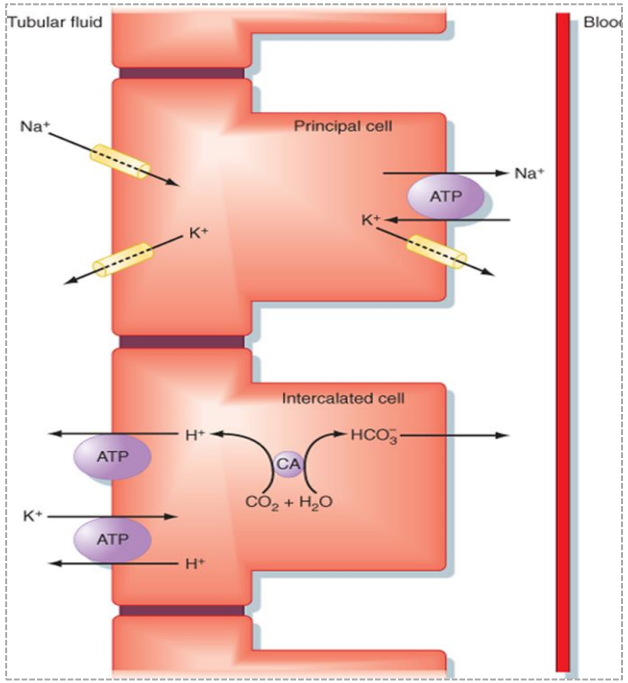
Intercalated cells:

- Secrete H+
- Reabsorb $HCO3^-$
- Reabsorb K^+ (by K, H exchanger)

this area is under control of hormones:

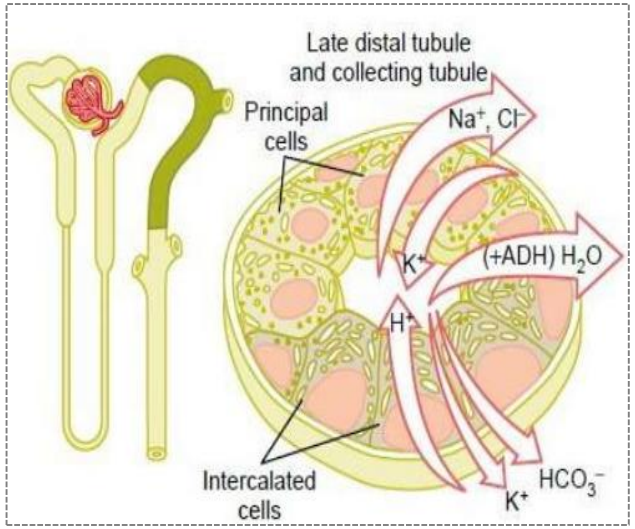
Aldosterone:

- ↑Na reabsorption by principle cells,
- ↑K+ secretion



➢Intercallated cells :

- if blood is acidic; reabsorbs bicarbonate secretes H .
- If blood alkaline; reabsorbs H secretes bicorbonate



Secretion is most at the distal end of nephron

➢Secretion in collecting duct is higher than secretion in DCT and so on…

- Principal and intercalated cells are both hormonally regulated.
- The intercalated cells reabsorb K by the K/H pump (active transport).

Factors Affecting Na Reabsorption

1. GFR: when increased causes an increase in filtration of Na which sensitise the macula densa.
2. Aldosterone.
3. Estrogen: Increase reabsorption of Na and decrease Na excretion.
4. Natriuretic hormone.
5. Osmotic diuresis (Increase Glucose, Mannitol and Urea) increase their conc. In the filtered load then causes a decrease in water reabsorption and Na.
6. Diuretic Drugs (Lasix)
7. Poorly reabsorbed anions causes retention of equal amount of Na.

1- More GFR > more filteration > more excretion
less GFR > less filteration > more reabsorption

2- Aldesterone secreted by adrenal gland in zona glomerulosa
Functions: Sodium/water retention and Potassium secretion

3-Estrogen: Why is there edema in pregnancy > elevated estrogen > increase reabsorption of Na

4- ANP's functions are opposite to aldosterone; sodium/water excretion and potassium reabsorption

5- Osmotic diuresis: increase osmolalrity of tubules > so they pull water with them (negative effect on reabsorption)

6- Lasix = furosemide

7- Anions negatively charged, so Na will be attracted to these anions in the tubules and won't be reabsorbed

Transport of potassium K+

- Most abundant cation (+) in the body
- 98% is intracellular [150mM]

Regulates intracellular function such as Cell volume, Acid/base status,

cell growth & division

- 3,500-4,000 mmol in blood. قليل ولازم يظل قليل ولا أدى الى اعراض خطيرة مميته منها اريثميا

- 2 % K extra-cellular [3.5-5mM]

This regulates membrane potentials in excitable cells and diffusion

potentials in transporting epithelia.

If extracellular K is increased massively or decreased → hyper-excitation / paralysis / arrhythmia

K+ Intake 80-120 mmol/day

Tissue damage leading to cell lysis increases plasma [K+]

Both extracellular [K+] and total body potassium are tightly regulated.

HOW?

- **INTERNAL DISTRIBUTION**

(This regulates extracellular [K+])

- **RENAL K+ EXCRETION**

(This regulates total body potassium)

Internal potassium distribution

Potassium content of average meal is 30-40 mmol.

This is *rapidly absorbed*.

Renal elimination is slow. It can take up to six hours eliminate this load.

If nothing happened then this absorbed load would cause Plasma [K+] to rise by 2-5 mmol which is potentially lethal.

Buffering of the load occurs by increased intracellular uptake via Na+/K+ pump into Skeletal Muscle, Liver, Bone RBCs etc.

Loss of K+ from exercising muscle can seriously increase plasma K+ ,trained athletes show accelerated uptake after exercise

Why can exercise increase plasma K levels?

- More action potentials > more K efflux
- some cells are damaged (not very common)

B-blocker are contraindicated in exercise > they increase K level (increase uptake of cells even more)

Renal excretion of potassium

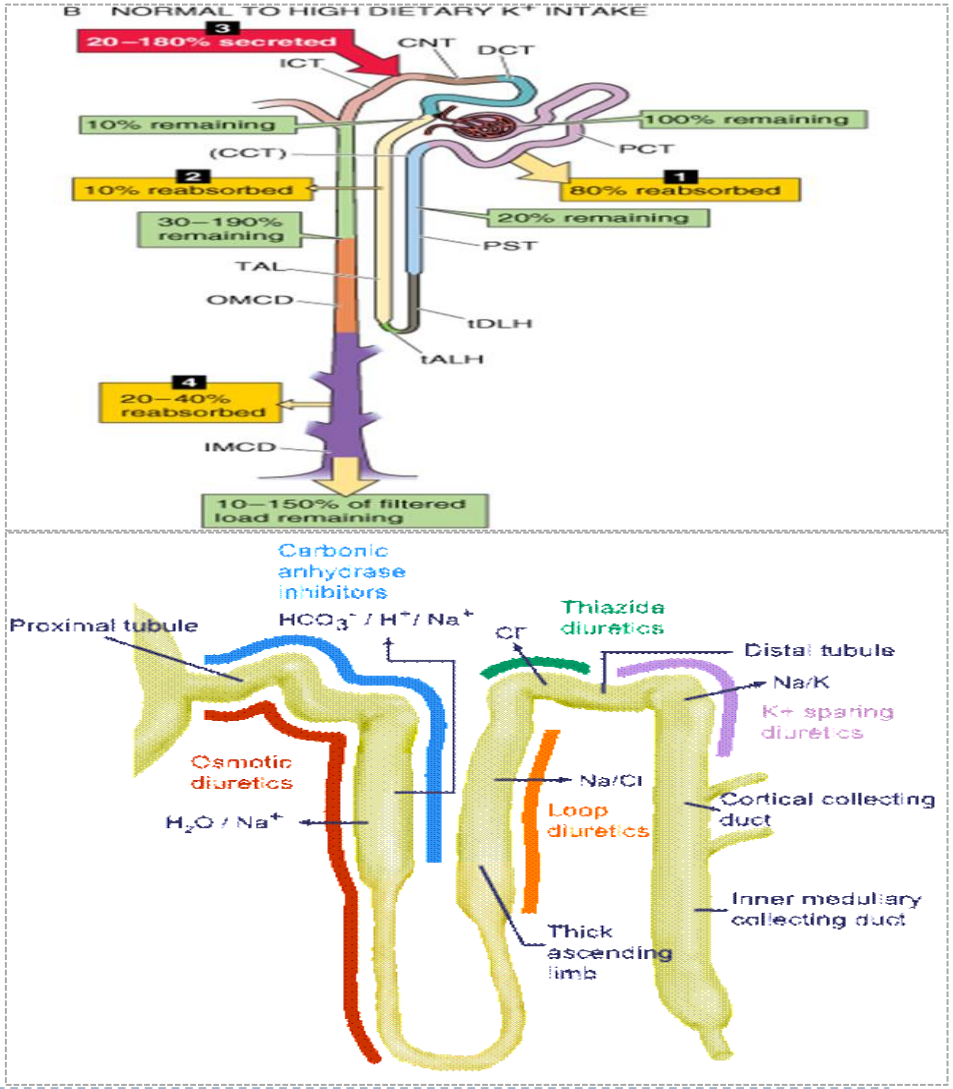
- 90-95% of Dietary K^+ excreted via the *kidneys* .
- 5-10% in *Sweat & Feces* (This is unregulated and may become significant in diarrheas).
- In normal individual intake is matched by excretion and potassium balance is maintained.
- Filtered load of potassium ~ 720 mmol/day .
- Bulk reabsorbed *by proximal tubule and loop of Henle*.

Renal K+ Transport mechanisms كلها اخذناها قبل بس هنا مرتبة للبوتاسيوم

- ✓ Cell membrane <u>transporters</u> :
- Na-K ATPase, H-K ATPase
- K^+ channels, K:Cl cotransport
- Na:K:2Cl cotransport

- ✓ K^+ is <u>Reabsorbed</u> in :
- PT (Proximal tubules) by solvent drag
- TAL (thick Ascending limb of loop of Henle) NKCC (luminal membrane)
- Intercalated cell in CCD (cortical collecting duct)

- ✓ K^+ <u>Secreted</u> in :
- Late distal tubule
- principal cells of late DT (Distal Tubules)
- CCD (cortical collecting duct)

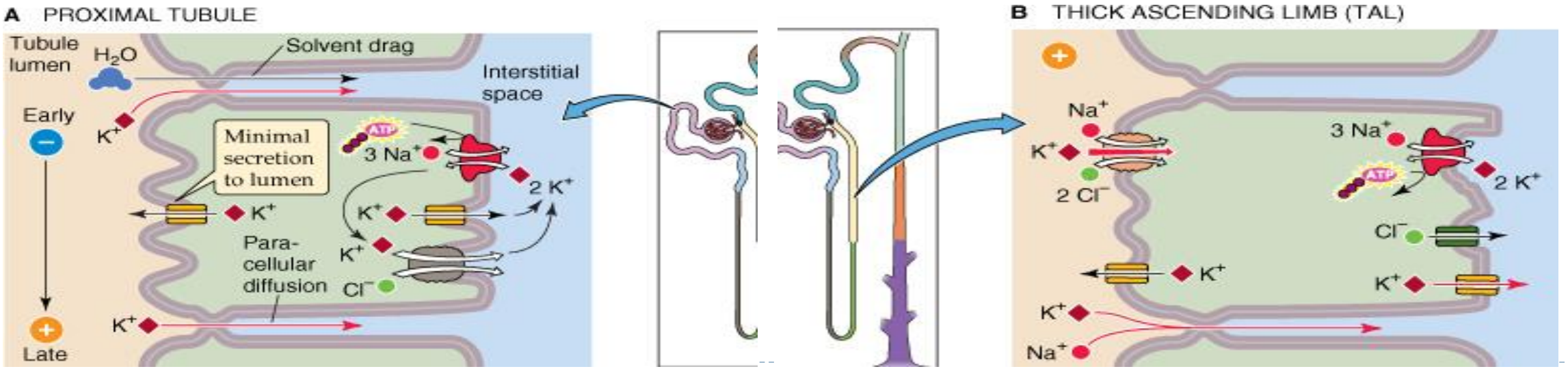


Renal K+ Transport mechanisms كلها إعادة

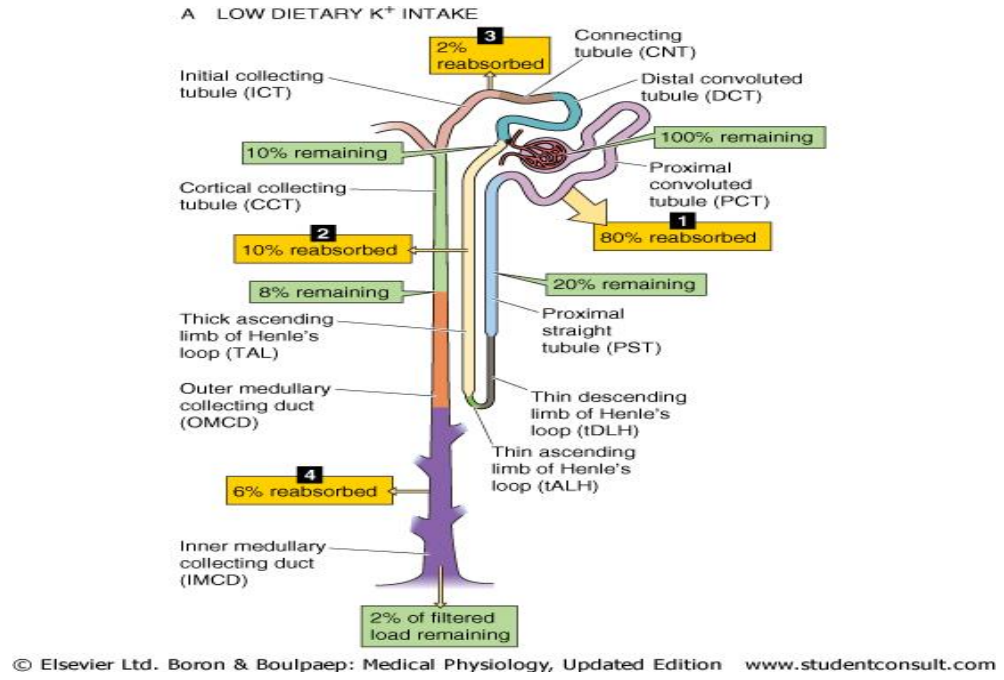
- **Proximal Tubule:** K^+ is absorbed by intercellular solvent drag whereby fluid movement driven by Na+ absorption entrains K^+ ions.في المحاضرة السابقة
- **TAL:** Na:K:2Cl in luminal membrane.
- **K:Cl** co-transport in Baso-lateral membrane
- **CD:**

-K reabsorption is by the intercalated cells via a luminal H-K ATPase.

-K+ secretion in the principal cells (via luminal K channels and basolateral Na-K ATPase).



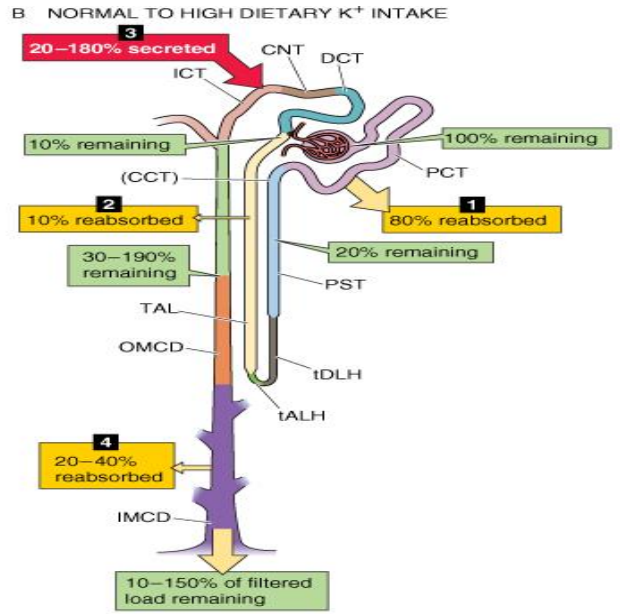
A) Low dietary K intake (not normal)



100% is filtered
80% is reabsorbed in PCT
10% reabsorbed in thick ascending
2% reabsorbed along the DCT
6% reabsorbed in medullary part of collecting duct
2% excreted

(notice how there's no secretion of potassium)

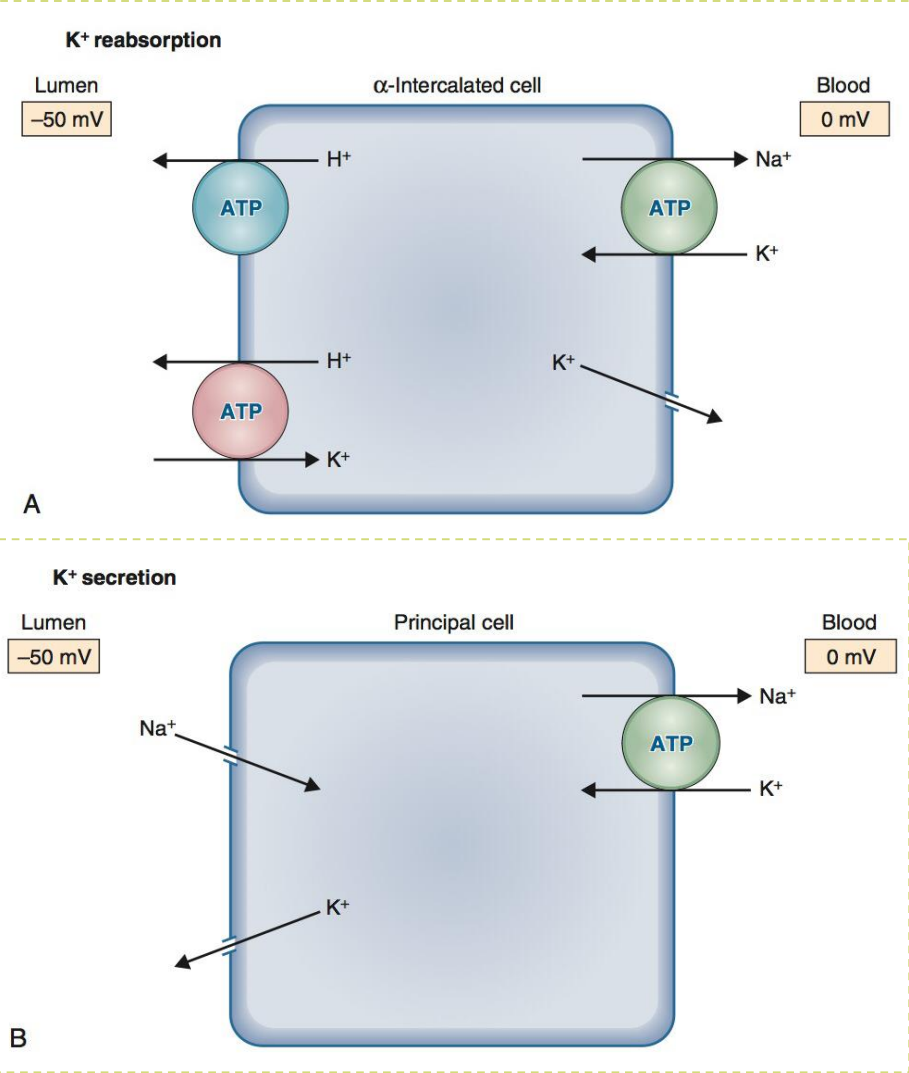
B) Normal to high K intake



100: filtered
80% is reabsorbed in PCT
10% reabsorbed in thick ascending
20-180 % secretion in Principal cells
20-40% reabsorbed in medullary collecting duct
10-150% eliminated in urine

20-180% is NOT a range (this Is just an example)

Renal K+ transport mechanism



When a person is on a low K+ diet

K+ reabsorption is by the intercalated cells via a luminal H-K ATPase (primary active transport)

K+ secretion in the principal cells (via luminal K channels and basolateral Na-K ATPase)

Factors affecting potassium secretion/reabsorption

Peritubular factors (change inside tubular cells.) (All **Increase** the secretion and excretion of potassium)		
1- Hyper-kalemia	2- Hyper-aldosteronism	3- Alkalosis
Increase K in tubular cell and incresase chemical grdient of K between tubular cell and tubular lumen which lead to increase in the secretion and excretion of K.	Increase aldosterone increases the secretion and excretion of K. (Its main action is reabsorbe Na and secretion of K)	Alkalosis=↑Ph=↓H ions Increase H-K exchange at basolateral membrane then increase in the secretion and excretion of K. فعشان ادخل هيدروجين لازم اطلع بوتاسيوم
Luminal factors		
Diuresis: increase volume of urine and decrease concentration of K in lumen which causes secretion via chemical gradient (increase secretion and excretion) (has a negative impact on sodium reabsorption)		
Increased urinary excretion of Na : increase in Na-K exchange at luminal membrane causes an increase in secretion and excretion of K. فإذا زاد اخراج الصوديوم لأي سبب راح يزيد معها اخراج البوتاسيوم		
Increased urinary excretion of bicarbonate, phosphate, sulphate and ketone acids: increase negativety of lumen then increase electrochemical gradient between cell and lumen بسبب الشحنة causes secretion and excretion of K.		

Secretion=from tubular sell to tubular lumen, excretion =get ride of it out the body

NaCl Transport along the Nephron (summary)

Segment	Percentage of Filtrate reabsorbed	Mechanism of Na+ Entry across the apical Membrane	Major Regulatory Hormones
Proximal tubule	67%	Na^+-H^+ antiporter, Na^+ symporter with amino acids and organic solutes, $1Na^+$-$1H^+$-2Cl--anion antiporter, paracellular	Angiotensin II , (Norepinephrine , Epinephrine) Dopamine ()= sympathetic
Loop of Henle	25%	$1Na^+$-$1K^+$-2Cl- symporter	Aldosterone, Angiotensin II
Distal tubule	≈ 5%	NaCl symporter (early) Na^+ channels (late)	Aldosterone, Angiotensin II
Collecting ducts	≈ 3%	Na^+ channels	(Aldosterone, ANP), BNP, urodilatin, uroguanylin, guanylin, (angiotensin II)

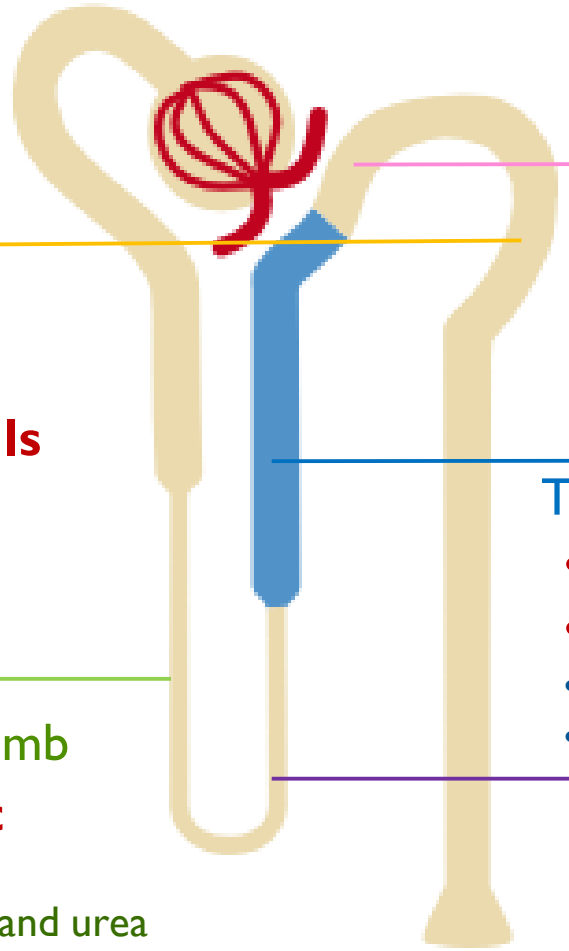
()*Prof. Mona Saied these are enough

Water Transport along the Nephron (summary)

Segment	Percentage of Filtrate reabsorbed	Mechanism of Water Reabsorption	Hormones That Regulate Water Permeability
Proximal tubule	67%	Passive	None
Loop of Henle	15%	Descending thin limb only; passive	None
Distal tubule	0%	No water reabsorption	None
Late distal tubule 20 and collecting duct	≈ 8% - 17%	Passive	(ADH, ANP), BNP*

*Prof. Mona Saied these two are enough

Summary



Late Distal Convoluted Tubule & Collecting Duct

- **Principal and intercalated cells**
- Permeable to H2O (ADH-regulated)
- Na, H2O, HCO3, K are reabsorbed
- K and H are secreted

Thin Descending Limb

- **Hyperosmotic**
- Permeable to H_20
- Permeable to NaCl and urea
- Solutes are secreted

Early Distal Convoluted Tubule

- Cortical diluting segment
- Impermeable to H_2O
- Na/Cl reabsorption

Thick Ascending Limb

- Isosmotic
- Load dependent
- Na, Cl, K, HCO3, Ca, Mg are reabsorbed
- H and K are secreted

Thin Ascending Limb

- Hyposmotic
- impermeable to H_20
- Permeable to NaCl

Thank you!

اعمل لترسم بسمة، اعمل لتمسح دمعة، اعمل و أنت تعلم أن الله لا يضيع أجر من أحسن عملا.

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Link to Editing File

References:

- Girls' and boys' slides.
- 435 Team.
- Guyton and Hall Textbook of Medical Physiology (13th Edition).
- Linda (5th Edition).

Special thanks to Team435's Leaders: Meshal Alhazmy & Khawla Alammari and members!