5&6. Tubular Reabsorption & Tubular Secretion

(TUBULAR PROCESSING)

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Recommended Videos!

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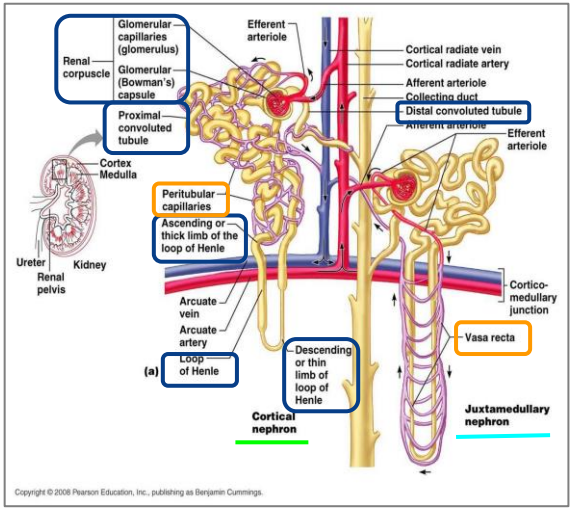
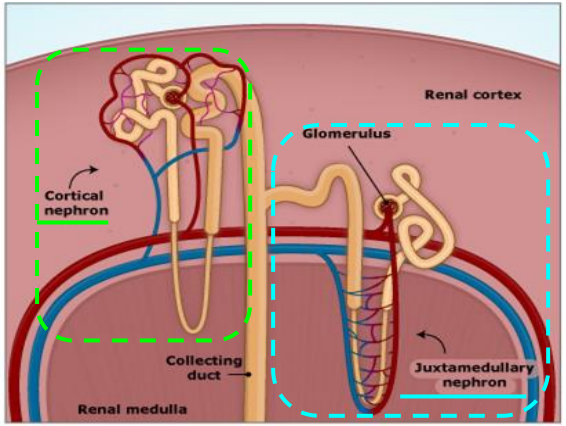
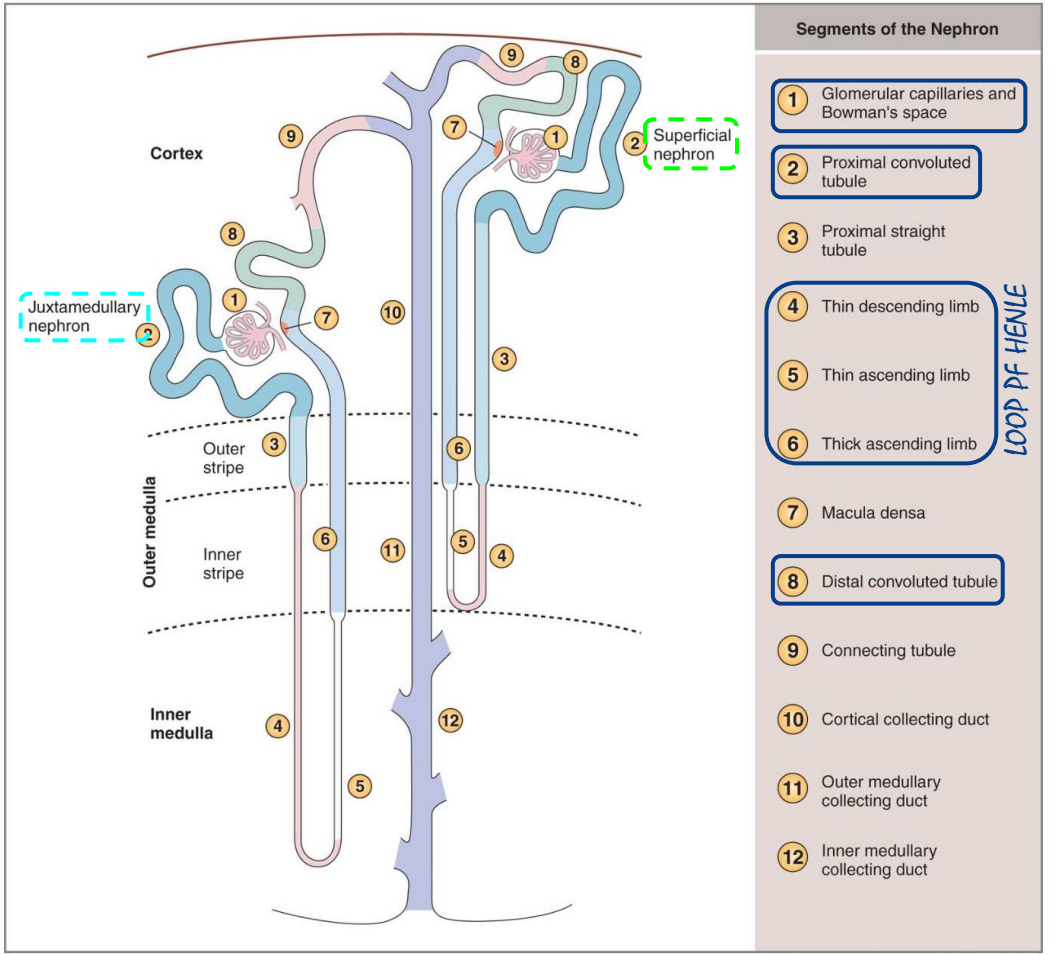
Juxtamedullary Nephrons VS Cortical Nephrons







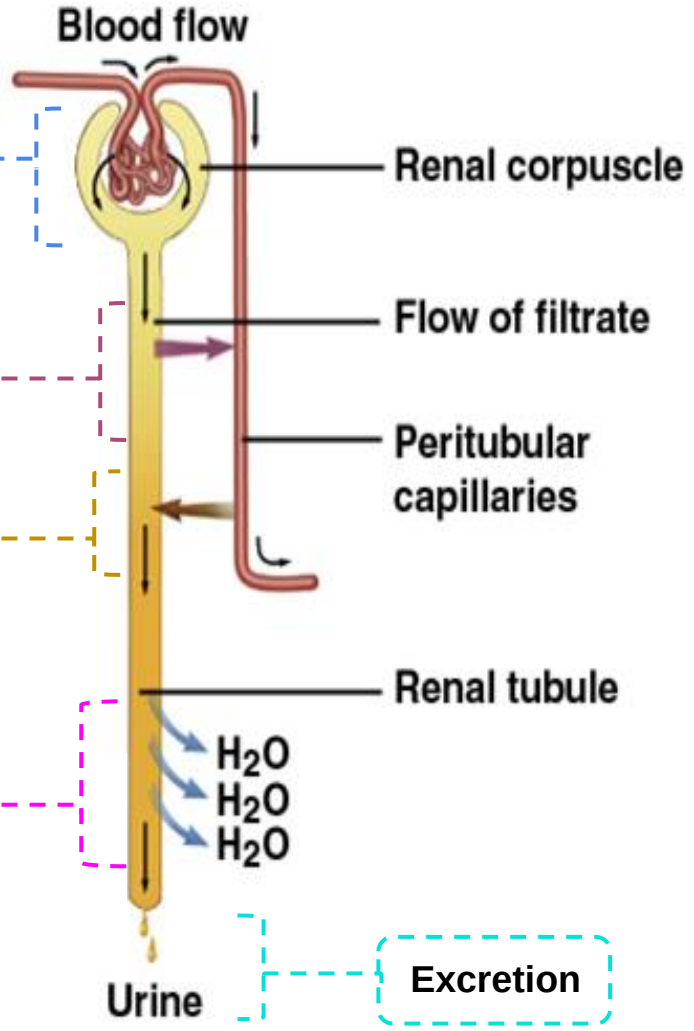
Steps of Urine Formation

① **Glomerular filtration**
Creates a plasmalike filtrate of the blood

② **Tubular reabsorption**
Removes useful solutes from the filtrate, returns them to the blood

③ **Tubular secretion**
Removes additional wastes from the blood, adds them to the filtrate

④ **Water conservation**
Removes water from the urine and returns it to blood, concentrates wastes



PLEASE CHECK THIS 2 MINS VIDEO

Introduction

Urinary Excretion = Glomerular Filtration **–** Tubular reabsorption **+** Tubular secretion.

TO RENAL TUBULE | TO BLOOD | TO RENAL TUBULE

✧ Tubular secretion means:

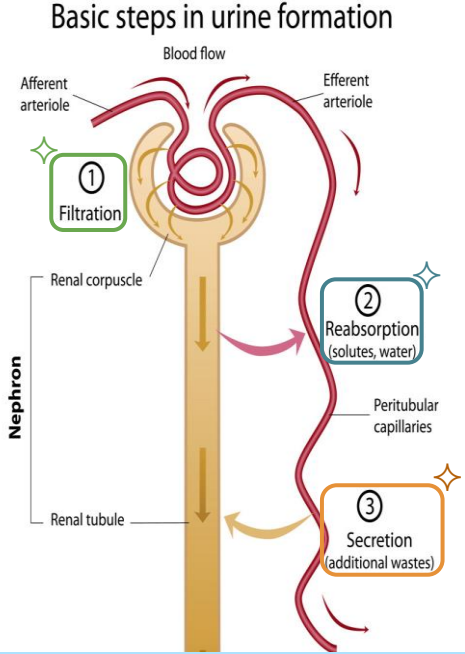
The net movement of solutes from peritubular capillaries into the tubules.

✧ Glomerular Filtration means:

Is the process by which the kidneys filter the blood, removing excess wastes and fluids into the tubules.

✧ Tubular reabsorption means:

Is the process by which solutes and water are removed from the tubular fluid and transported into the blood.

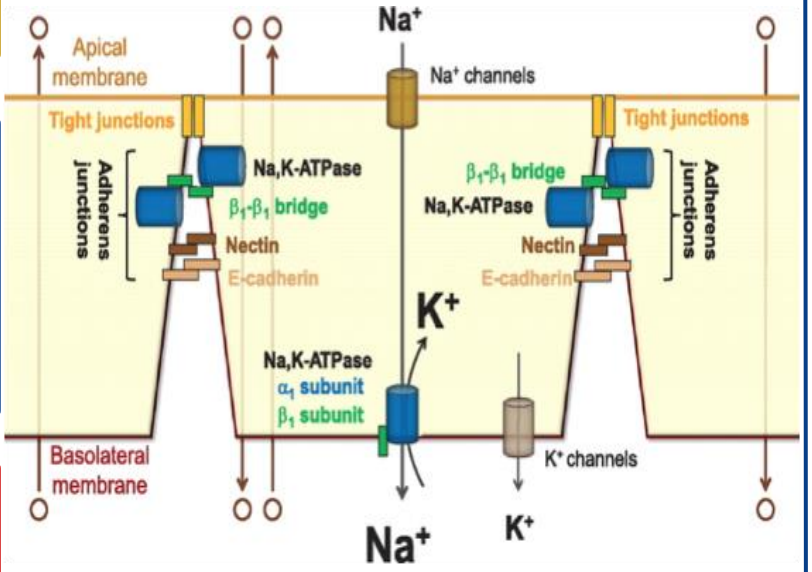


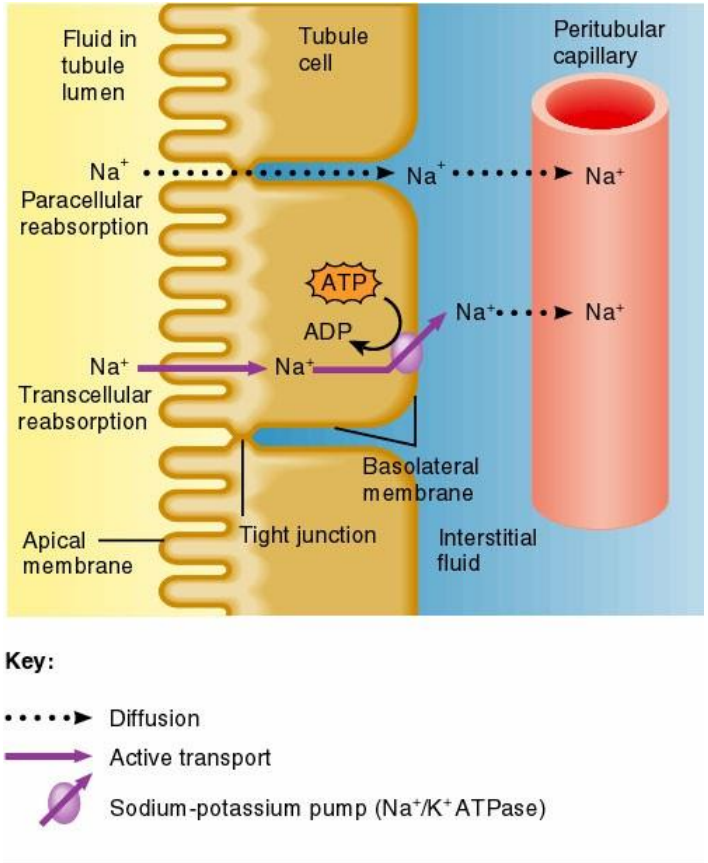
Reabsorption & Secretion

RENAL TUBULE

TUBULAR MEMBRANE

INTERSTITIAL SPACE





Routes of Entrance Substance Into Tubules

1- Glomerular filtration.

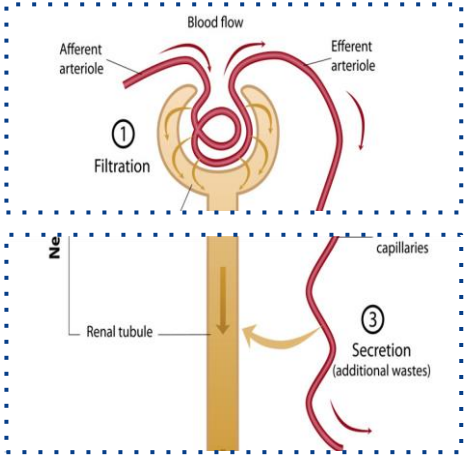
2- Secretion from the peritubular capillaries which occurs in two steps:

A. Simple diffusion

Of the substance from **peritubular capillaries into renal interstitium.**

B. Active or Passive Transport

Movement across the **tubular epithelium into the lumen**



Mechanisms of Tubular Transport:

* WILL BE DEFINED INDIVIDUALLY NEXT SLIDES

✧ Active Transport

- **Primary active transport:**

E.g. Na-K-pump, H+-pump.

- **Secondary active transport:**

E.g. Na-K-2Cl co-transport, glucose-sodium co-transport, amino acid-sodium co-transport.

✧ Passive transport:

- **Simple diffusion:**

E.g. Cl, HCO3-, urea.

- **Facilitated diffusion:**

E.g. glucose at the basal border.

✧ Osmosis

✧ Pinocytosis/ Exocytosis.

✧ Thus the molecules moves through **ion channels, transporters, pumps & exchangers.**

Active Transport

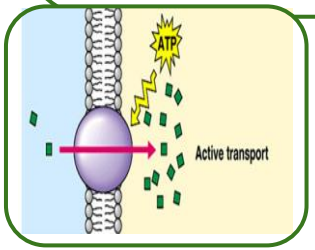
When a cell membrane moves molecules or ions "uphill" **against** an electrochemical gradient.

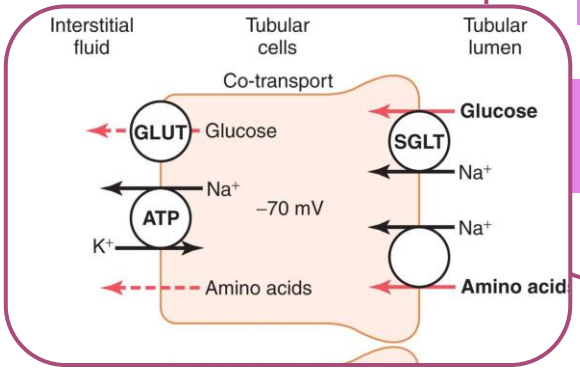
-CARRIER IN NEEDED AND AN ATP UTILIZATION-

Primary Active Transport

The energy is derived **directly** from breakdown of adenosine triphosphate (ATP) or of some other high-energy phosphate compound.

- Examples:
  - ✓ Sodium potassium ATPase
  - ✓ Hydrogen ATPase
  - ✓ Hydrogen potassium ATPase
  - ✓ Calcium ATPase.





Secondary Active Transport

The energy is derived secondarily from energy that has been stored in the form of ionic concentration differences of secondary molecular or ionic substances between the two sides of a cell membrane, created originally by primary active transport.

One of the substances (e.g., sodium) diffuses down its electrochemical gradient

↓

The energy released is used to drive another substance (e.g. glucose) against its electrochemical gradient

↓

Both bind to one carrier protein to be transported together.

Thus, secondary active transport does not require energy directly from ATP.

Active Transport cont.

Secondary Active Transport cont.

The direct source of the energy is that liberated by

↓

The simultaneous facilitated diffusion of another transported substance

Down its own electrochemical gradient

The electrochemical gradient for Na is maintained by **Na/K pump.**

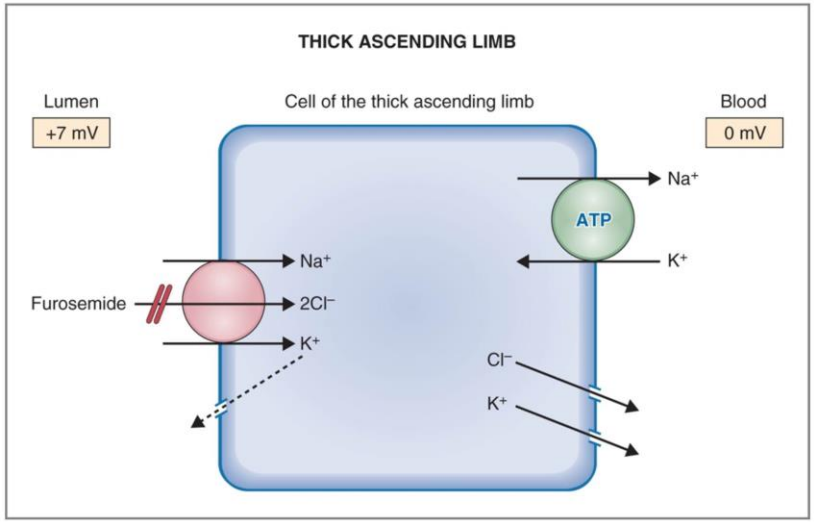
ANOTHER EXAMPLE OF A SECONDARY ACTIVE TRANSPORT IS

Na-K-2Cl Co-transport

In thick ascending limb of Henle.

RECALL FROM PHARMACOLOGY!

"loop" diuretics as furosemide, inhibits the action of theThis transporter



Secondary Active Secretion

This transport is mediated by specific protein in the brush border of the luminal membrane.

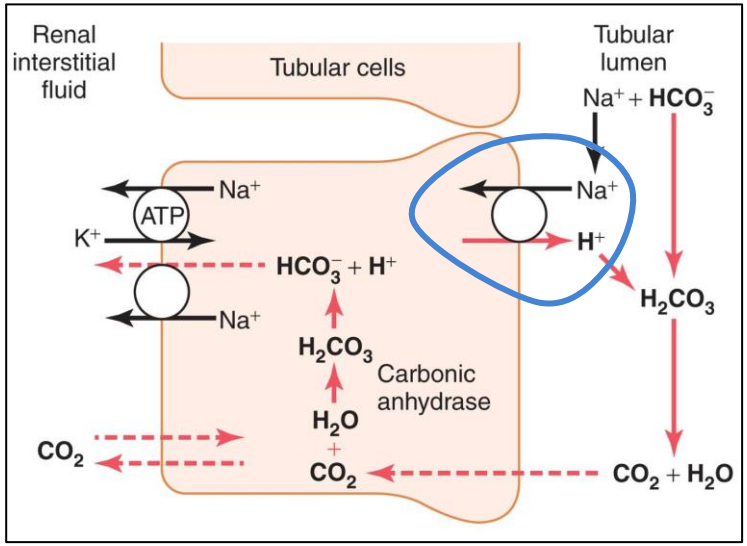
As sodium is carried inside this cell down its chemical

This will generate an energy and we will use it

To take out H+ outside of the cell in the luminal side

By a counter transport called Na+/H+ counter transport

It takes one sodium in and one hydrogen out

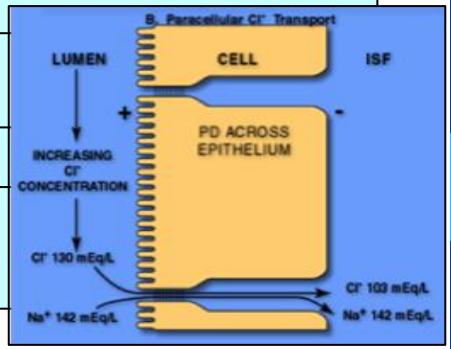


COUNTER TRANSPORT OR "ANTIPORT" MEANS CARRIED TO MOLECULE AGAINST EACH OTHER.

Simple Diffusion & Osmosis

Simple Diffusion (Passive Diffusion)	
Kinetic movement of molecules or ions occurs through a membrane opening or through intermolecular spaces without any interaction with carrier proteins in the membrane.	
Examples	Reabsorption of Chloride and Urea. -Negative ions such as chloride are transported along with sodium because of electrical potentials.- **Urea:** Inner medullary collecting duct, passive urea reabsorption is facilitated by specific urea transporters.

Osmosis	
✧ Transport of solutes out of the tubules makes their concentration inside the cells to decrease while increase in the renal interstitium. ✧ This creates a concentration difference that causes osmosis of water in the same direction that the solutes are transported, from the tubular lumen to the renal interstitium.	
Example	Water reabsorption is mainly coupled to sodium. ✧ Permeability differs through the nephron.
Route	Paracellucar via tight junctions (THEY'RE NOT MUCH TIGHT AS THEIR NAME INDICATES)
Effect of ADH Distal & collecting tubules-	Regulates the body's retention of water by acting to increase reabsorption in the collecting ducts of the nephron"



Transport Through
Proximal Convoluted Tubule (PCT)

Special Criteria for PCT Cells

- ✓ Highly metabolic cells (rich in mitochondria) "SUPPORT POWERFUL ACTIVE TRANSPORT PROCESSES"
- ✓ Rich in proteins carriers and channels.
- ✓ Wide surface area in the luminal side due to brush borders.

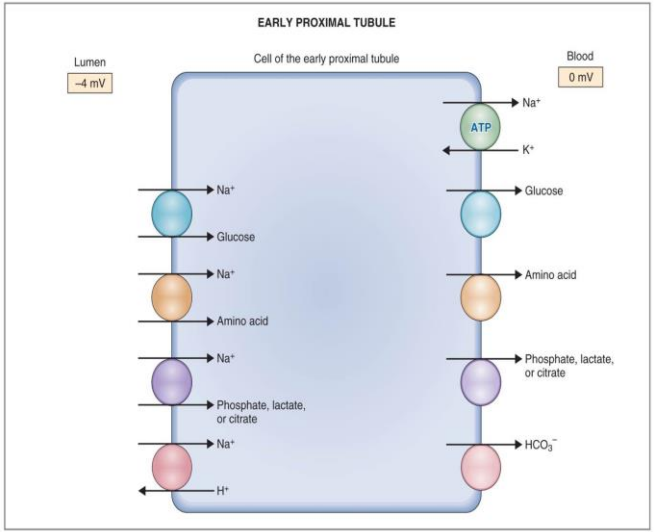
Normally, about 65 percent of the filtered load of sodium and water and a slightly lower percentage of filtered chloride are reabsorbed by the proximal tubule.

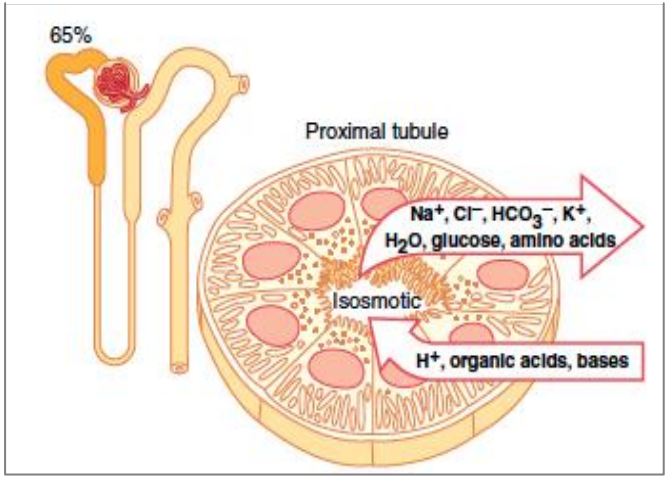
Solute reabsorption in the proximal tubule is **isosmotic**
(water follows solute somatically and tubular fluid osmolality remains similar to that of plasma = equal amount of solute and water are reabsorbed).

- ✧ 100% of glucose & amino acids is reabsorbed.
- ✧ 60-70% water and Na reabsorbed
- ✧ 90% of bicarbonate, calcium and K+ reansorbed.

The re reabsorption here = **Coarse adjustment** [1]

MEANING THAT WHATEVER THE CONDITION IS AND WHATEVER YOUR BODY NEED THIS REABSORPTION IS HAPPENING ALYWAYS!





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Transport Through
Proximal Convoluted Tubule (PCT) cont.

<table>
<tr><th colspan="2">Reabsorption</th><th>Secretion</th></tr>
<tr><td colspan="2">Transporters
1) Na+/K+ ATPase "NEEDED FOR DECREASING THE TUBULAR CELLS SODIUM"
2) Sodium glucose co –transporters.
3) Sodium amino acid co –transporters.
4) Sodium-hydrogen exchanger (counter-transport)
5) Sodium-chloride co-transport.</td><td rowspan="3">✧ Organic acids and bases:
✓ Bile salts.
✓ Oxalate.
✓ Urate.
✓ Catecholamines.
✧ Certain drugs:
✓ Penicillin
✓ Salicylates.</td></tr>
<tr><th>In the first half of the PCT</th><th>In the second half of the PCT</th></tr>
<tr><td>Sodium is reabsorbed by co-transport along with Glucose, Amino acid..etc</td><td>Sodium is reabsorbed with chloride. The second half has high concentration of chloride compared with early segment.
Because when sodium is reabsorbed ,it preferentially carries with it glucose, bicarbonate, and organic ions in the early proximal tubule, leaving behind a solution that has a higher concentration of chloride.</td></tr>
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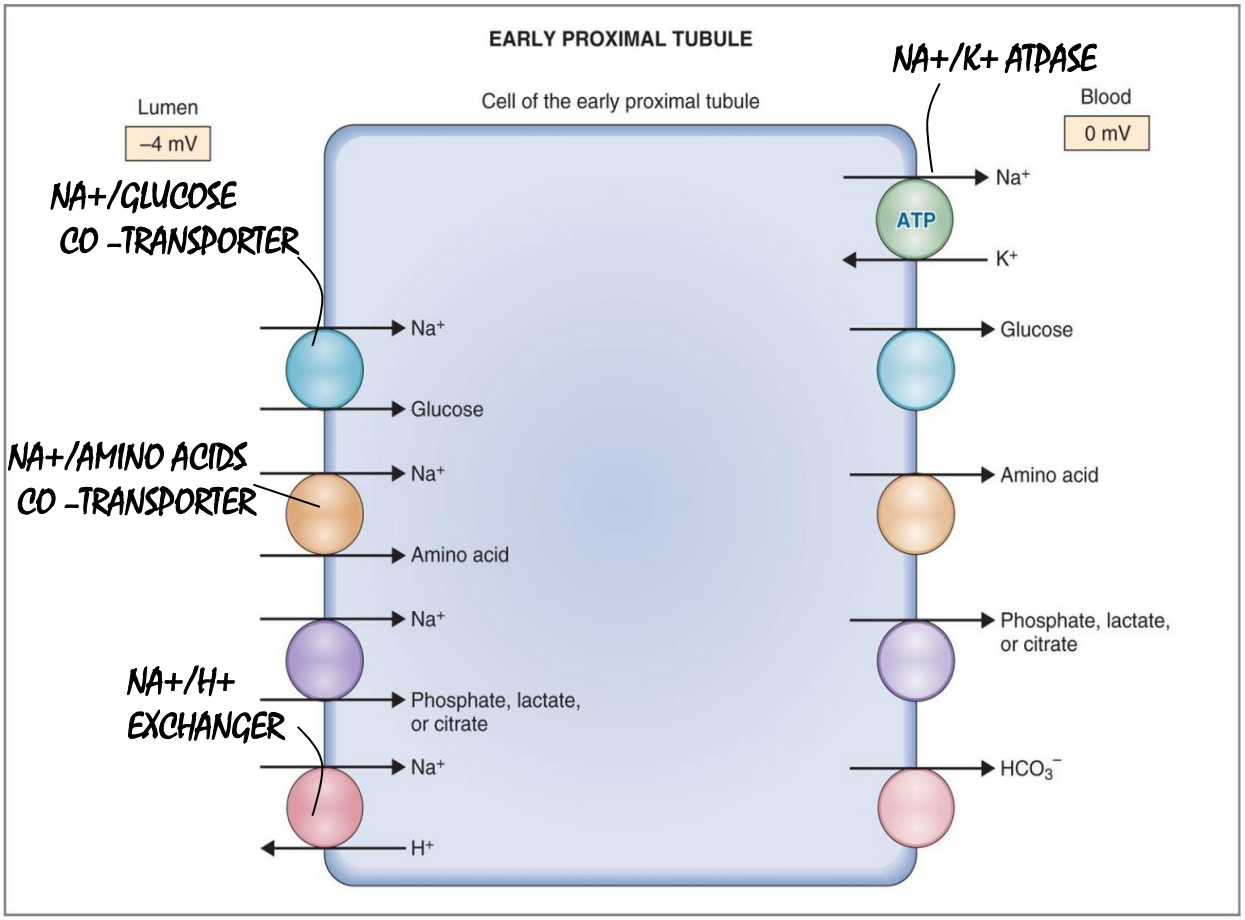
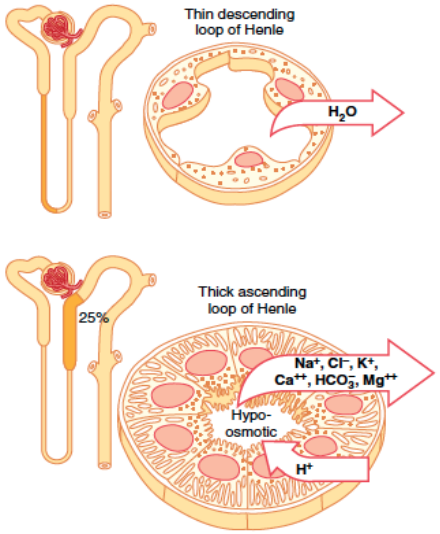
Transport Through
Proximal Convoluted Tubule (PCT) cont.



Transport Through Loop of Henle



Descending Loop of Henle

*H_2O permeable, allow absorption of 25% of filtered H_2O.
*Solutes (NaCl) impermeable.
Accordingly water leaves behind solutes increasing their concentration in tubular fluid thus osmolarity increases the fluid become hyper-osmolar.

Thin Ascending Loop of Henle

* H_2O impermeable
*Solutes (NaCl) permeable, absorbed passively.

Thick Ascending Loop of Henle

*Solutes (NaCl) permeable, allow 25% of the filtered sodium to be reabsorbed.
*H_2O impermeable → The filtrate becomes very dilute as it flows toward the distal tubule(hypo-osmolar fluid)

Special carrier the **1Na,2Cl,1K co-transport.**

"This co-transport protein carrier in the luminal membrane uses the potential energy released by downhill diffusion of sodium into the cell to drive the reabsorption of potassium into the cell against a concentration gradient"

- The filtrate is hypo-osmotic due to the absorption of solute without water.
- Significant paracellular reabsorption of cations, such as Mg++ ,Ca++ , Na+ , and K+ .

" there is a slight backleak of potassium ions into the lumen, creating a positive charge of about +8 millivolts in the tubular lumen. This positive charge forces cations such as Mg++ and Ca++ to diffuse from the tubular lumen through the paracellular space and into the interstitial fluid."

Transport Through
Distal Convoluted Tubule (DCT)

What happens here depends on hormonal control:

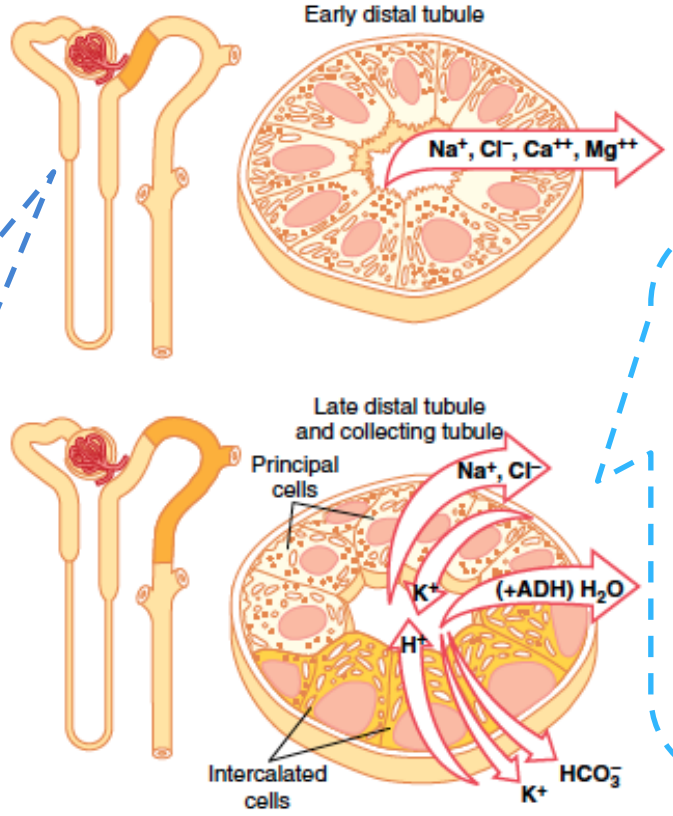
- **Aldosterone** — Reabsorb Na+ and secrete K+
- **ADH** (vasopressin) — Reabsorb water
- **Parathyroid Hormone** — Increases Ca++ reabosrption

Early Portion	Late Portion of DCT & Cortical Collecting Tubules	
	Principal Cells	**Intercalated cells**
*Fine adjustment of tubular filtrate takes place here according to body needs. * The first portion of the distal tubule forms the macula densa ➔ provides feedback control of GFR and blood flow in this same nephron. *Same characteristics as ascending limb of Henle: -H_2O Impermeable -Solutes (NaCl) permeable So it is called the diluting segment & the osmotic pressure of the fluid ~ 100 mOsm/L.	○ Absorb Na+ & H_2O ○ Secrete K	○ Absorb K+ ○ Secrete H+ Which is mediated by a **hydrogen-ATPase transporter.**
	Impermeable to urea	

Transport Through
Distal Convoluted Tubule (DCT) cont.

Early Distal Tubules

Approximately 5% of the filtered load of NaCl is reabsorbed here
The Na-Cl co-transporter moves sodium chloride from the tubular lumen into the cell ➔ and the Na/K pump transports sodium out of the cell across the basolateral membrane



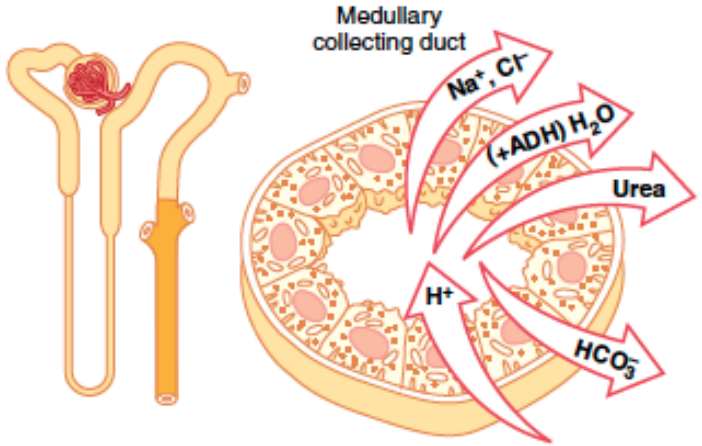
Late Portion of DCT & Cortical Collecting Tubules

The permeability water is controlled by the concentration of ADH

High levels of ADH
These tubular segments are **permeable to water**
Absence of ADH
They are virtually **impermeable to water.**

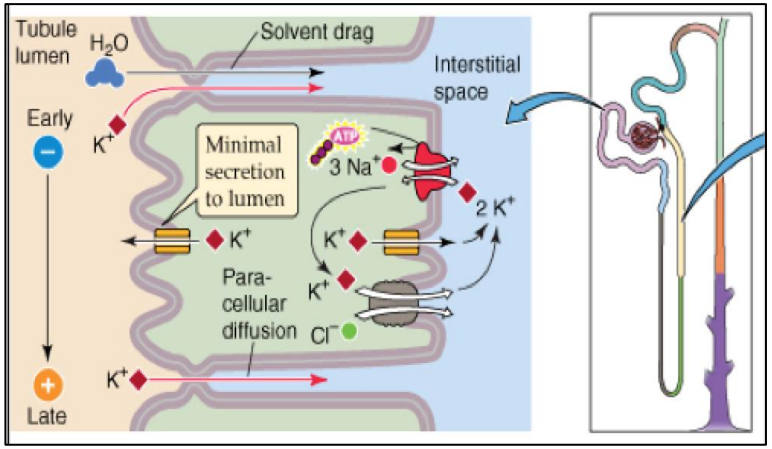
Transport Through
Medullary Collecting Ducts

Reabsorb <10% of sodium & H_2O.
The permeability of the medullary collecting duct to water is **controlled by the level of ADH.**
Highly permeable to urea Special urea transporters that facilitate urea diffusion across the luminal and basolateral membranes. Therefore, some of the tubular urea is reabsorbed into the medullary interstitium, helping to raise the osmolality (WE WILL TAKE THIS MECHANISM IN DETAIL IN LECTURE 7)
It has a role in acid base balance by secreting H+ against concentration gradient.
Final site for processing urine so determine final urine output of H_2O and solutes.

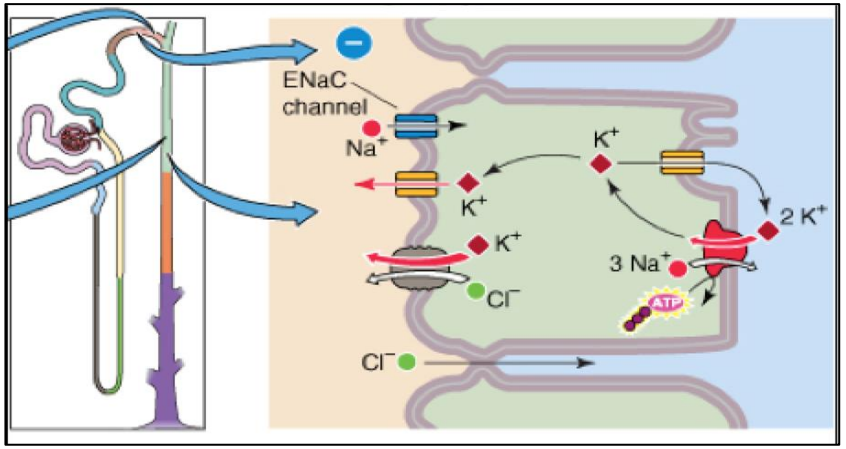


Potassium (K+) Handling

Notes	Reabsorption of K+	Secretion of K+
*K+ is the major cation in cells and its balance essential for life. *Small change from 4 to 5.5 mmoles/L will lead to hyperkalemia	Reabsorbed at **proximal tubules** largely **passive** and follows the movement of Na and fluid.	Occurs in **cortical collecting tubule (principal cells)**, and relies upon **active transport** across **basolateral** membrane and **passive exit** across apical membrane **into tubular fluid**.



Proximal convoluted tubules



Cortical collecting tubules

Reabsorption of Bicarbonate (HCO_3)

As we know that one of the essential products of our body which maintain alkalinity we have to reabsorb it!

Bicarbonate is freely filtered in the glomerulus **it moves to proximal convoluted tubule**

It will bind to H+ "Na+/H+ Counter transport"

Will convert into carbonic acid (H2CO3)

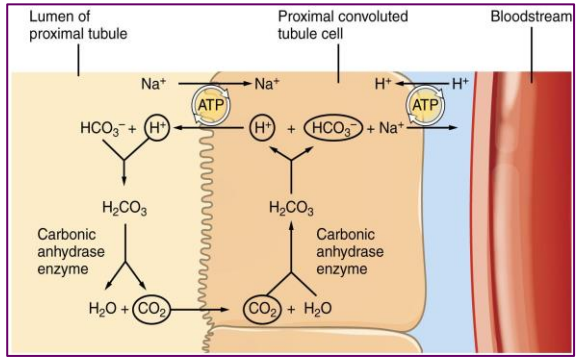
An enzyme called carbonic anhydrase will convert it to water (H2O) and carbon dioxide (CO2)

Carbon dioxide will move inside the cell because its lipophilic it will find a water inside the cell

Same enzyme will convert these two product into Carbonic acid (H2CO3)

Finally it will split into H+ & HCO3-

HCO3- has a basolateral receptor so **it will move into the interstitium.**

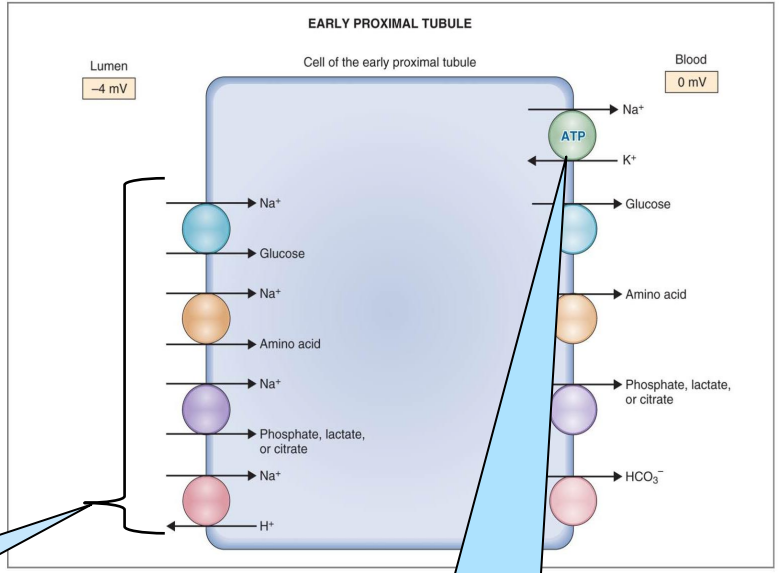


Soduim Absorption (Na+)

*Na & Cl reabsorption plays **a major role** in body electrolyte and water metabolism.

Na+ transport is also **coupled to the movement of H+, K+, glucose, amino acids.**

Mechanisms		
Active Transport	**Passive Transport**	**Co-Trasnport[1]**
Collecting tubules and ducts	Thin ascending limb	Thick ascending limb
Na+ is pumped into the interstitium by **Na+-K+ ATPAse**		



Na moves by exchanger co transport. which help in reabsorption of nutrients

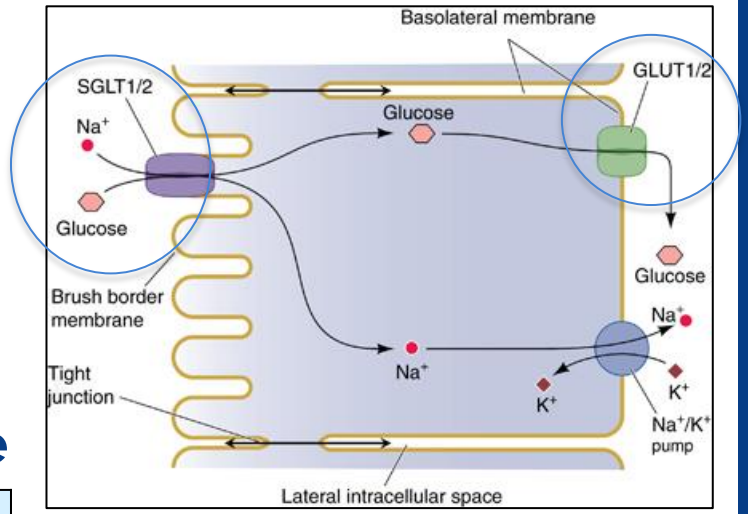
Na is pumped into the interstitium by Na/K ATPase

1: Co-transport is the name of a process in which two substances are simultaneously transported across a membrane by one protein, or protein complex which does not have ATPase activity

Glucose Absorption & Handling

Glucose absorption also relies upon the Na+ gradient. It is absorbed by Na-glucose co-transport.
Mostly at the proximal tubule.

Apical Membrane	**Na-Glucose co transporter** Rely uponNa
Basolateral Membrane	**Glucose transporters (GLUTs)** DoesNOT rely on Na



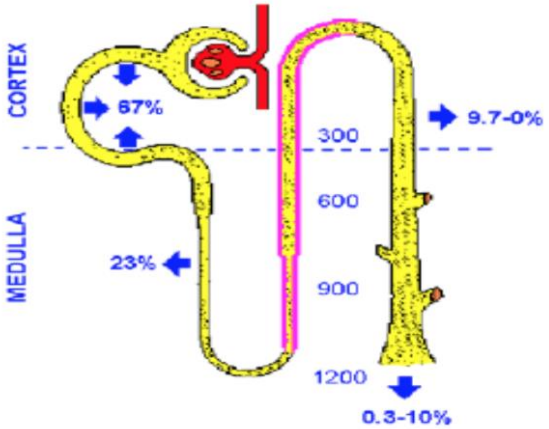
Tubular Transport Maximum for Glucose

Essentially (100%) all glucose is reabsorbed	
Tubular Maximal Transport	Men : 375 mg/min
	Women : 300 mg/min
Threshold	180 mg/dl
Handling of glucose is limited by saturation of the transport mechanism i.e. carriers	

Water Reabsorption

Percentages Of Reabsorbed Filtered Water Across The Nephron

Structure	Percentage
Proximal convoluted tubule	65 %
Descending loop of Henle	20 -25 %
Ascending limb	Zero
Distal tubules & collecting tubules	Under ADH control



Regulation of Tubular Reabsorption

There must be balance between glomerular filtration and tubular reabsorption.

"**Why?** because if you increase the glomerular filtration this mean that some of the important solutes will pass away and it won't reabsorbed because it runs too fast. In the other hand, if Glomerular filtration decreased this will accumlate the solutes and waste will be reabsorbed"

This balance will be controlled locally either by		
Hormonal Mechanisms		**Nervous Mechanisms**
Aldosterone	↑Na+ reabsorption and K+ , H+ excretion	Sympathetic ➔ Increases reabsorption of Na+
Ang II	↑ The synthesis of aldosterone	
ADH	↑Water reabsorption in distal segments	
ANP	↑Na+ excretion and diuresis.	
PTH	↑Ca reabsorption & ↓ PO reabsorption	

Glomerulotubular balance

Prevents Overloading of Distal Part When GFR Increases.

How?

Glomerulotubular balance ensures that a constant fraction of filtered load is reabsorbed by the PCT, even if the filtered load increases or decreases. This constant fraction (or percentage) is normally maintained at 65-67% of the filtered load.

Ang II = Angiotensin II
ADH = AntiDiuretic Hormone
ANP = Atrial Natriuretic Peptide
PTH = ParaThyroid Hormone

Regulation of Tubular Reabsorption cont.

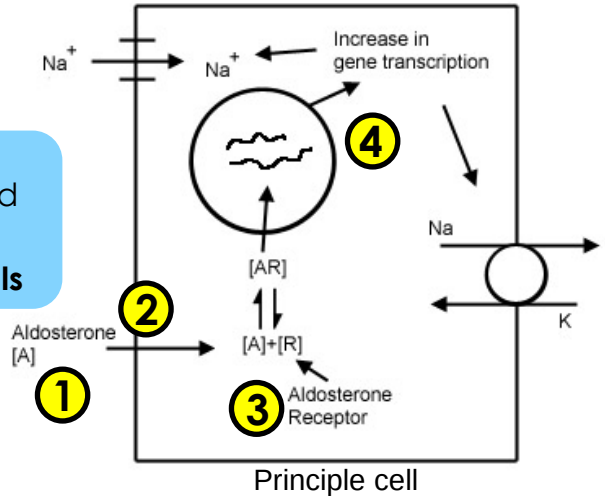
Peritubular Capillaries Reabsorption are regulated by Hydrostatic Pressure and Oncotic Pressure
How?
When we increase the **hydrostatic pressure** in the peritubular capillary ➔ Capillary will has a pressure more than the interstitium ➔ Will keep the fluid and the solutes in the interstitium➔Decreases reabsorption. When we increase the **oncotic pressure** inside the capillary ➔ Pull the water and the solutes toward it ➔Increases reabsorption.

Arterial blood pressure on Reabsorption Mechanism
An **increase in arterial blood pressure** will **decrease the reabsorption** mechanism
How?
As we mention before this is one of the mechanisms were hydrostatic pressure is more than interstitium pressure

Mechanism of Aldosterone Action

1. Aldosterone will be secreted in the blood stream
2. Penetrates the endothelium and the it will enter **The principal cells**
3. Binds to a receptor called " aldosterone receptor"
4. Signals go to the nucleus and produce mRNA for three genes that are responsible of the formation of

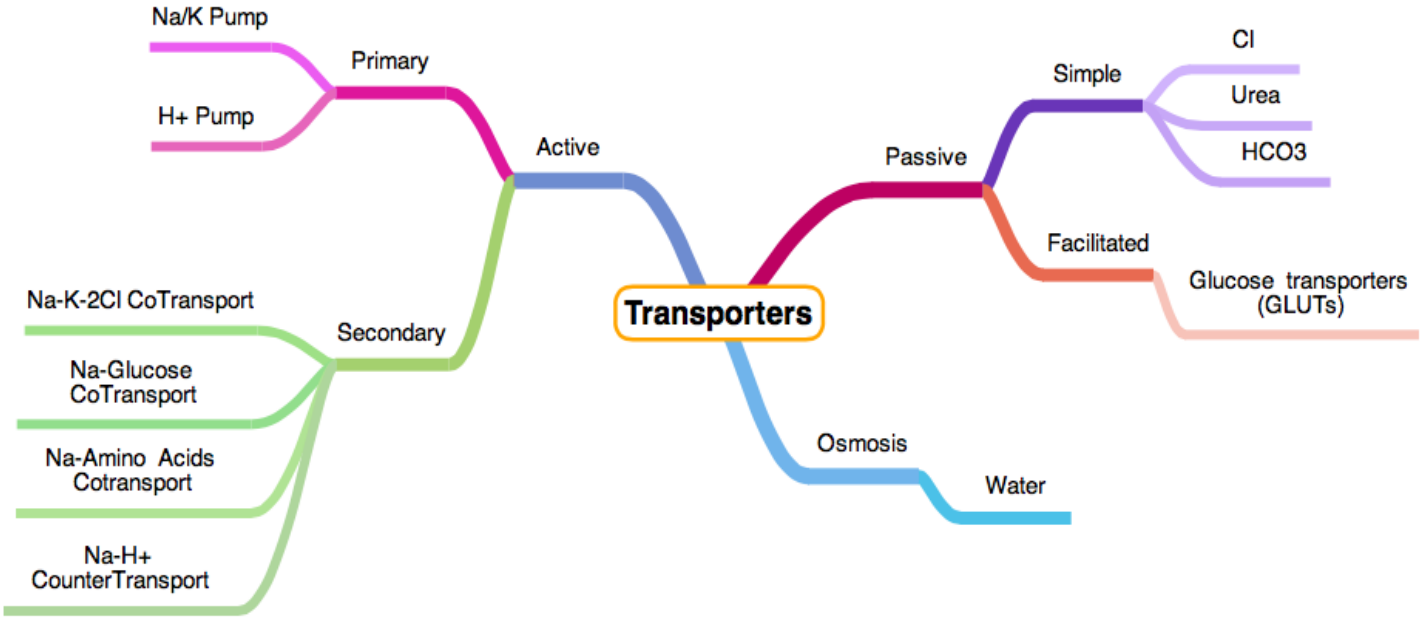
- **Na+/k+ pump**
  3 NA+ OUT
  2 K+ IN
- **K+ secreted channels**
- **Na+ reabsorbed channel**



Principle cell

Sodium will be in **low concentration inside the cell** comparing to outside → **Enhance reabsorption of Sodium**

Potassium will be in **high concentration inside the cell** comparing to outside → **Enhance secretion of Pottassium**



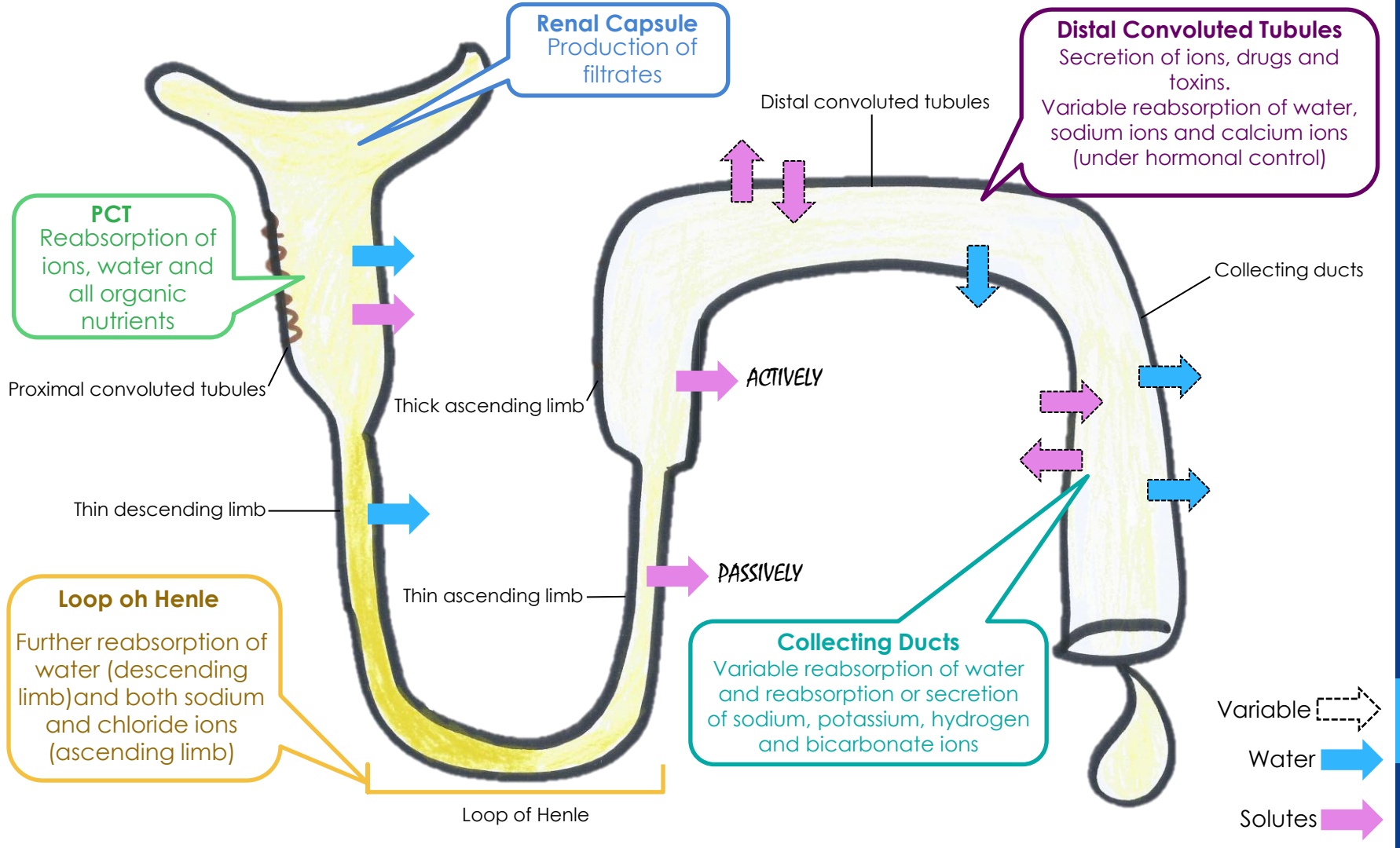
↑GFR	↑Absorption
↑Sympathetic	↑Na absorption
↑ADH	↑H2O absorption
↑Aldosterone	↑Na absorption + K excretion
↑ANP	↑Na excretion

Regulation of Tubular Reabsorption

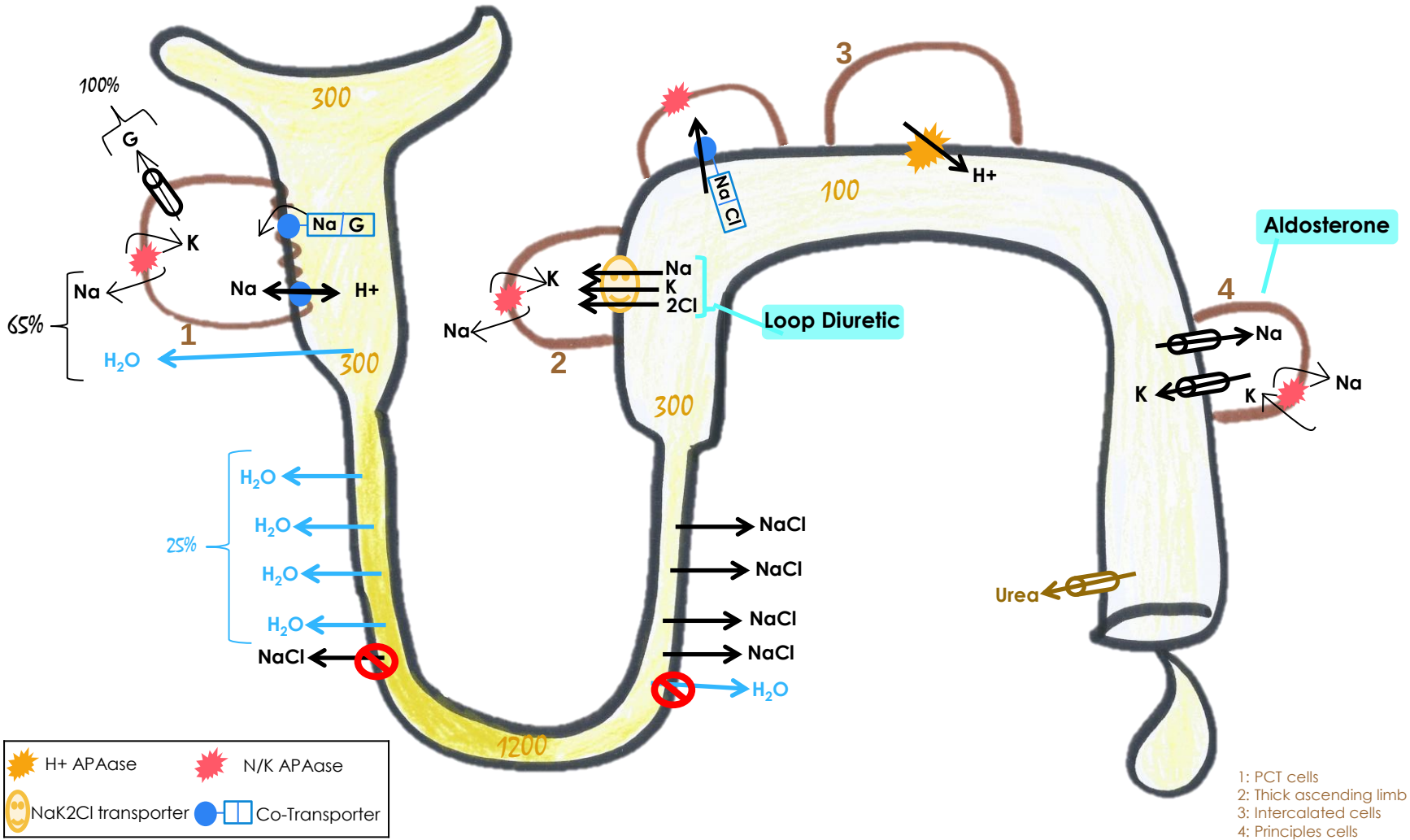
Summary

Structure	Transport	
	Reabsorption	Secretion
Proximal Convoluted Tubules	65% of Na and water 100% Glucose and amino acids	H+ Urea Ammonia
Descending Loop of Henle	25% of water	-
Thin Ascending Loop of Henle	Solutes (NaCl)	-
Thick Ascending Loop of Henle	Na , K and Chloride	-
Distal Convoluted Tubules	- Na in response to aldosterone - Water in response of ADH - Calcium in response of parathyroid hormone	K in response of aldosterone
Late Distal Tubule & Cortical Collecting ducts	**Principal cells**	
	Absorb Na+ & H2O in response of ADH	Secrete K
	Intercalated cells	
	Absorb K+ & HCO3-	Secret H+ and K in response of aldosterone
Medullary Collecting ducts	Water in response of ADH - Highly permeable to urea (To maintain osmolarity of medulla)	H+

Summary


Renal Capsule
Production of filtrates
Distal Convoluted Tubules
Secretion of ions, drugs and toxins.
Variable reabsorption of water, sodium ions and calcium ions (under hormonal control)
Distal convoluted tubules
PCT
Reabsorption of ions, water and all organic nutrients
Collecting ducts
Proximal convoluted tubules
Thick ascending limb
ACTIVELY
Thin descending limb
PASSIVELY
Thin ascending limb
Loop oh Henle
Further reabsorption of water (descending limb)and both sodium and chloride ions (ascending limb)
Collecting Ducts
Variable reabsorption of water and reabsorption or secretion of sodium, potassium, hydrogen and bicarbonate ions
Loop of Henle
Variable
Water
Solutes

Summary



1: PCT cells
2: Thick ascending limb cells
3: Intercalated cells
4: Principles cells

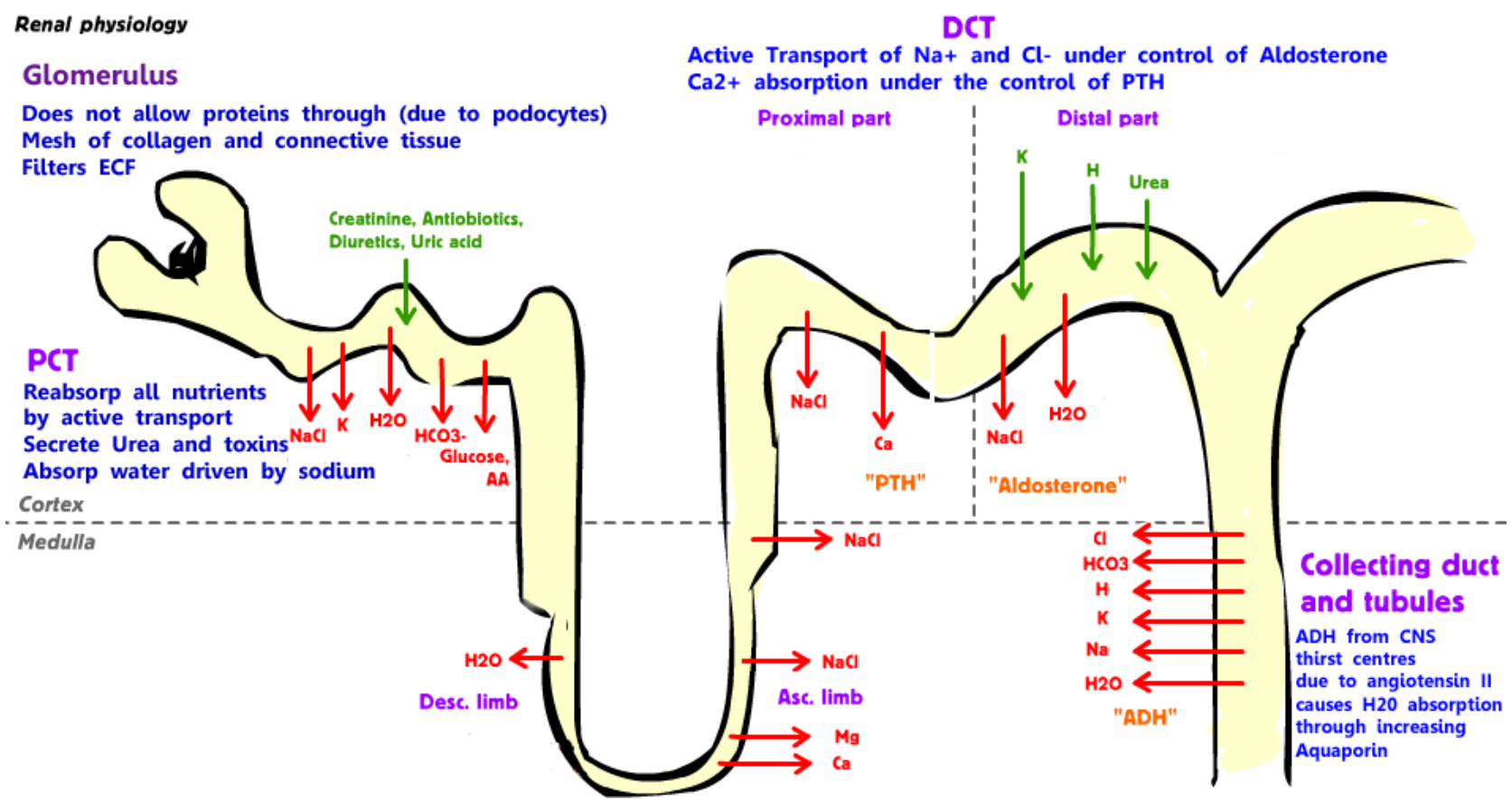
Summary

Glomerulus

Does not allow proteins through (due to podocytes)
Mesh of collagen and connective tissue
Filters ECF

PCT

Reabsorp all nutrients by active transport
Secrete Urea and toxins
Absorp water driven by sodium



DCT

Active Transport of Na+ and Cl- under control of Aldosterone
Ca2+ absorption under the control of PTH

Proximal part

Distal part

Collecting duct and tubules

ADH from CNS thirst centres due to angiotensin II causes H20 absorption through increasing Aquaporin

Loop of Henle

Thin Decending limb only reasorbs water
Thick ascending limb co-transports Na+ and CL- along with passive absorption of Mg and Ca

Summary

1- Which of the following transport Na through passive diffusion:

A.Collecting tubules
B. Collecting duct
C. Thin ascending limb
D. Thick ascending

2- Which of the following tubules never reabsorbs water?

A. Proximal convoluted tubule
B. Descending loop of Henle
C. Ascending limb
D. Collecting tubules

3- The reabsorption of amino acids mainly occur in the:

A. First half of PCT
B. Second half of PCT
C. Acsending part of loop of henle
D. Descending loop of henle

4- At plasma concentrations of glucose higher than occur at transport maximum (Tm), the

A. Clearance of glucose is zero
B. Excretion rate of glucose equals the filtration rate of glucose
C. Reabsorption rate of glucose equals the filtration rate of glucose
D. Excretion rate of glucose increases with increasing plasma glucose concentration

5- H+ ion is secretes in the distal tubules by which mechanism?

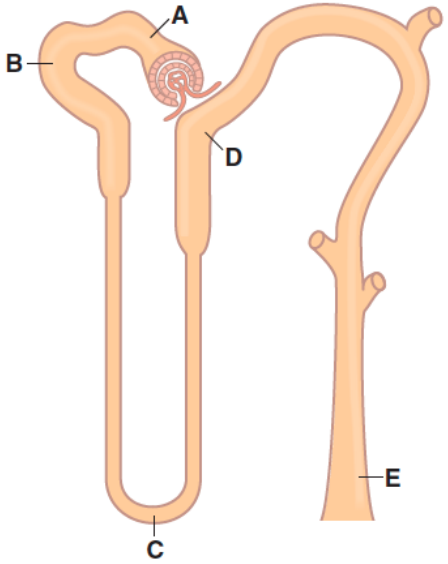
A. K+\H+ antiport
B. Na\H+ cotransport
C. H+ ATPase

6- Principal cells are responsible for reabsorption of?

A. Ca
B. Phosphrus
C. Hydrogen
D. Sodium

MCQs

The following figure applies to Questions 5–7.



7- At which nephron site does the amount of K+ in tubular fluid exceed the amount of filtered K+ in a person on a high-K+ diet?

A. Site A
B. Site B
C. Site C
D. Site D
E. Site E

8- At which nephron site is the tubular fluid/plasma (TF/P) osmolarity lowest in a person who has been deprived of water?

A. Site A
B. Site B
C. Site C
D. Site D
E. Site E

9- At which nephron site is the tubular fluid glucose concentration highest?

A. Site A
B. Site B
C. Site C
D. Site D
E. Site E

1.C
2.C
3.A
4.D
5.C
6.D
7.E
8.D
9.A

MCQs

1- What is the name of the enzyme that helps in Bicarbonate reabsorption?
Carbonic anhydrase

2- Where does the aldosterone synthesis?
Adrenal cortex

3- Tubular reabsorption regulated by two mechanism which is?
A) Hormonal mechanism
B) Nervous mechanism

4- What is the formula of urinary excretion?
Glomerular Filtration – Tubular reabsorption + Tubular secretion.

5- What is the energy source of sec. active transport?
From another active transporters "primary"

6- What is the function of the intercalated cells ?
Absorb K+ & secrete H+

7- What is the special carrier proteins found in thick ascending loop of henle?
Na,2Cl,1K co-transport

SAQs

THANK YOU FOR CHECKING OUR WORK!

BEST OF LUCK

Done By:

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