Renal Block

Physiology Team

5th Lecture

Tubular secretion

This Lecture is Done By :

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From the previous lecture : tubular reabsorption

❖ Urea Reabsorption:

- Plasma urea concentration =15-40mg /100ml
- End product of protein metabolism
- It is the only waste to be reabsorbed, Creatinine and Phenol are not reabsorbed.
- 50 % is reabsorbed in PCT passively with water
- 50-60% excreted.
- ↓GFR (renal disease; low renal blood flow) → ↑urea concentration in plasma due:

– Reduction in urea filtration.

- More urea reabsorbed to blood due to slow flow rate of filtrate.

❖ Phosphate reabsorption

- Bones, teeth & skeleton = 80%
- Intracellular P =20%
- Plasma P= 1mmol/L freely filtered
- 1/3 of filtered P is excreted in urine
- 2/3 Reabsorbed co-transported with Na in PCT in luminal border (Na/Pi).
- It is increased by Vit D and decreased by Parathyroid Hormone

❖Bicarbonate reabsorption:

♠ 90% of filtered is reabsorbed in PCT

♠ Filtered $HCO_3^- + H^+ \rightarrow H_2CO_3$

♠ $H_2CO_3 \rightarrow H_2O + CO_2$ in the presence of carbonic anhydrase enzyme

- ♠ CO2diffuses into the cell + H2O →H2CO3
- ♠ H2CO3→H+ + HCO3
- ♠ HCO3 is reabsorped by simple diffusion
- ♠ H+is secreted in exchange for Na +

❖ Glucose reabsorption :

Glucose will be reabsorbed from the lumen to the epithelial cells by Na/G transporter or channel(SGLT 2) then it will leave the epithelial cells to enter Peritubular Capillary by protein carrier (GLUT 2) – (facilitated diffusion).

Tmax: The Maximum limit/rate at which a solute can be transported across the tubular cells of kidneys is called Tubular transport maximum
Tm for Glucose is 375 mg/min

Filtered Load = 125 mg/min (GFR x Plasma Glu)

Renal Threshold = the maximum level of Glu which above it the Glu will appear in the urine, that 200mg/dl

Tubular secretion

❖Tubular secretion:

From peritubular blood through peritubular space → renal tubular cell → tubular lumen.

Secretion:

- Passive NH3, salicylic acid
- Active :
  - ♠ Tubular maximum (Tm): creatinine; PAH .
  - ♠ No Tm: K; H .

Potassium:

- 67-90% of filtered K is reabsorbed (PCT) (solvent drag)
- K is secreted in DCT in exchange for Na and under the control of Aldosterone hormone .

♠ **What is the effect of increased dietary K intake On K excretion?**
K directly stimulates aldosterone secretion and leads to an increase in cell [K] in collecting duct principal cells. Both of these lead to enhanced secretion and, hence, excretion,of K.

Hydrogen:

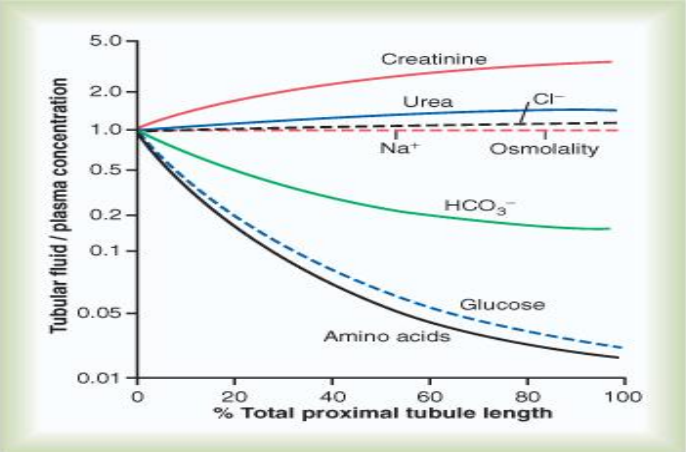
- Secreted in Proximal Tubule and Thick ascending LOH by Counter Transport with Na
- Secreted in DCT by H+ ATPase

❖ Changes in average Concentration of Different Substances at Different Points in Tubular System Relative to Glomerular Filtrate.

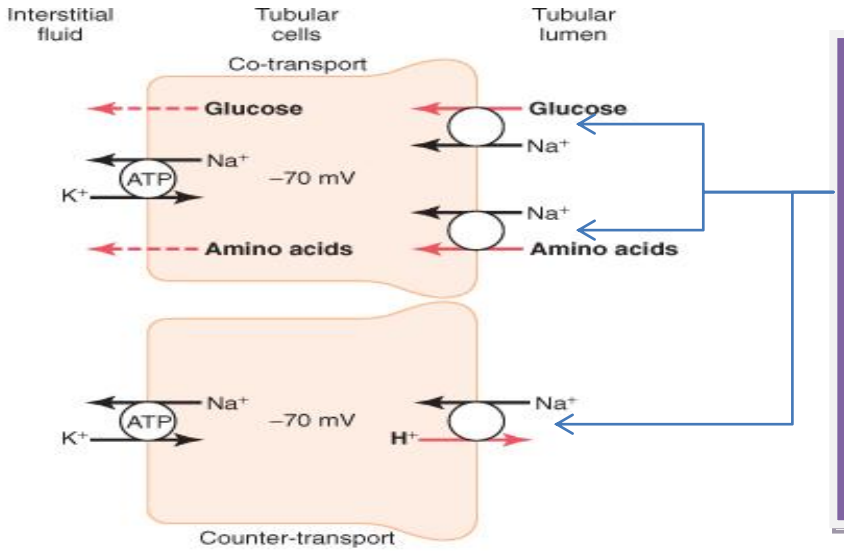
1- Proximal convoluted tubule (PCT):

Features of PCT:

- Many mitochondria (because it has more channel that act actively).
- Brush border multiplies the surface area about 20-fold. (so it reabsorbs 65% of the water)
- Tight junctions.
- Lateral intercellular spaces.



The main thing you should note in the picture above that , In PCT the osmolaloty does not change (isosmotic).



These channels are secondary active channels and they get the energy from NA/K Pump which is primary active and located in the basolatral membrane.

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Note: you must keep in your mind all of these channels and know where they are located. For example: Na/Glucose channel it is co-transporter and secondary active channel which located in luminal membrane.

2- Descending limb of loop of henle:

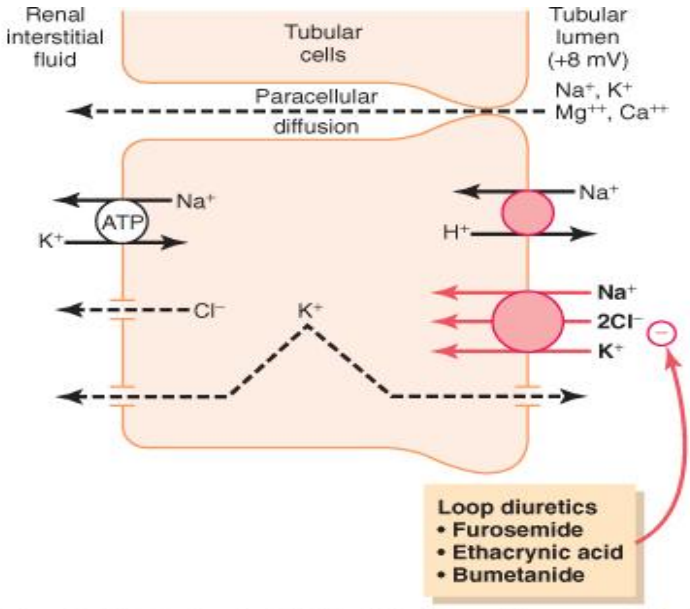
- ♠ Has Few mitochondria
- ♠ Flattened with few microvilli (Cells Simple Squamous Epithelial Cells).
- ♠ osmolality of filtrate increases(hypertonic) due to only water reabsorption, ↑ NaCl and ↑ Urea concentration in filtrate.
- ♠ Highly Permeable To Water But Not To Solutes.
- ♠ osmolality of filtrate increases gradually from 290 to 1200 mOsm/l at the tip of the loop.
- ♠ 15-20% of filtered water is reabsorbed

3- Thick ascending loop of henle and early duct:

♠ Cells are cuboidal epithelia.	♠ Water imperable
♠ Many mitochondria and microvilli, but fewer than in the proximal tubule.	♠ The THICK ASCENDING limb constitute 2/3 of ASCENDING LOOP OF HENLE
♠ Highly permeable to solutes,particularly NaCl,but not to water.	♠ Na/K ATPase in basolateral membrane
♠ Osmolarity drop from 1200 to 200mosm/l	♠ Filtrate diluted due to solute reabsorption not water(hypotonic).
♠ Na/K/2Cl reabsorption by co-transport (luminar)	♠ It is called the dilated segment of the loop.

- **Compression between the ascending loop of Henle and the descending loop of Henle :**

Ascending loop of Henle	Thick descending loop of Henle and the early duct
Has Few mitochondria	Many mitochondria and microvilli, but fewer than in the proximal tubule
Highly Permeable To Water But Not To Solutes	Highly permeable to solutes,particularly NaCl,but not to water.
15-20% of filtered water is reabsorbed	Water imperable
osmolality of filtrate increases from 290 to 1200 mOsm/l at the tip of the loop	Osmolarity drop from 1200 to 200mosm/l
Not permeable to solutes	Na/K/2Cl reabsorption by co-transport (luminar)
osmolality of filtrate increases(hypertonic) due to only water reabsorption, ↑ NaCl and ↑ Urea concentration in filtrate	Filtrate diluted due to solute reabsorption not water(hypotonic).
Flattened with few microvilli (Cells Simple Squamous Epithelial Cells).	Na/K ATPase in basolateral membrane



The thick ascending limb is very sensitive to diuretic drugs (Furosamide). These drugs are called "Loop" diuretics.

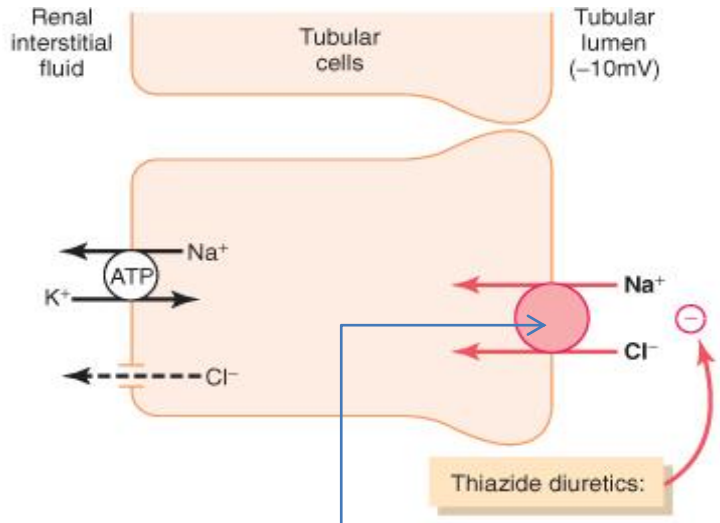
These diuretics block Na+-K+-2Cl⁻ co-transporter:

☒ Decreased NaCl reabsorption

☒ Isotonic fluid delivered to distal tubule instead of a hypotonic fluid.

☒ Increased fluid excretion "diuresis".

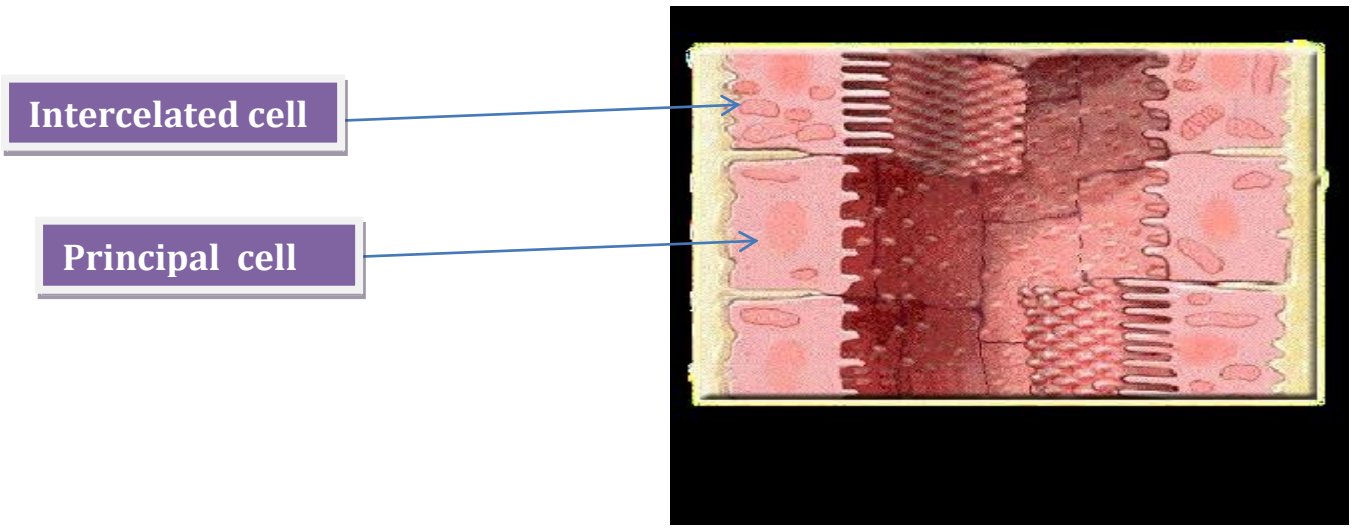
EARLY DISTAL TUBULE



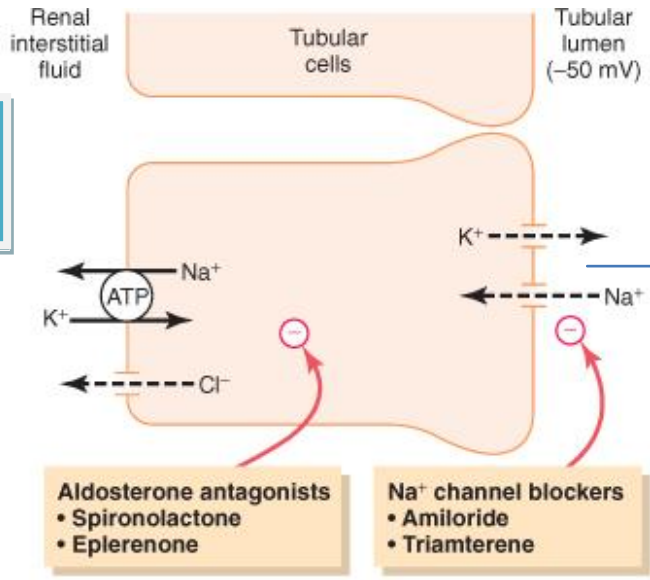
Mechanism of sodium chloride transport in the early distal tubule.

4- Late duct and cortical collecting tubule :

- Mitochondria and microvilli decrease
- Cuboidal cells are of two distinct functional types principal and intercalated cells.
- Principal Cells (Na Abs and ADH related Water abs)
- Intercalated Cells (Acid Sec and HCO3 Transport)
- Principal cells permeability to water and solutes is regulated by hormones (ADH will act on principal cells to make them permeable to water).
- Principal cells is responsible for water and salt reabsorption
- Intercalated cells secretion of hydrogen ions for acid/base balancing.
- 19% of filtered H2O is reabsorbed.
- 9% of filtered Na+ is reabsorbed in exchange of K+or H+.
- Cl^- also reabsorbed.

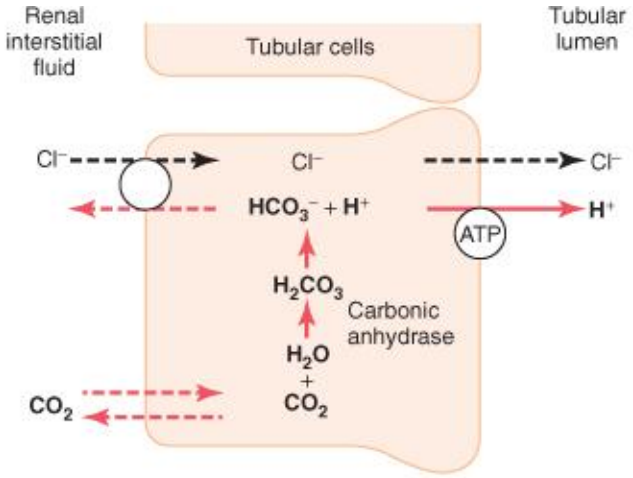


Principal Cell



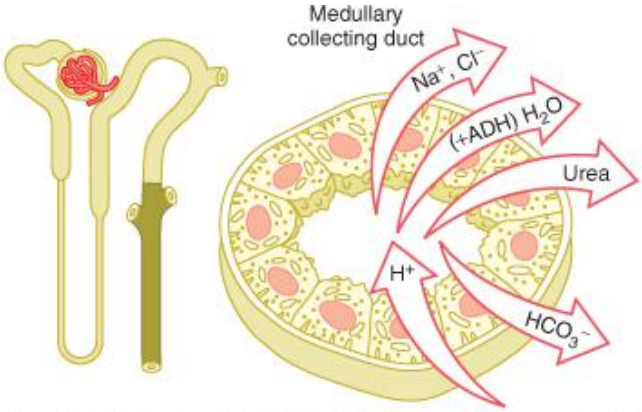
Site of action of aldosterone

Intercalated cell



5- Medullary collecting duct :

- Composed mainly by principal cells.
- Hormonally regulated permeability to water and urea.



*** In Collecting duct we find that:**

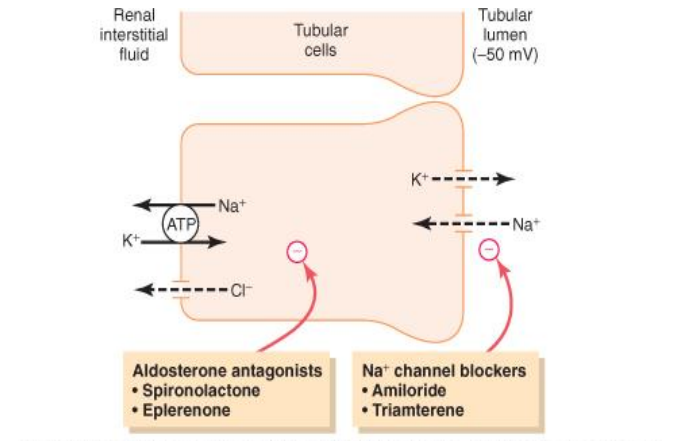
•Water permeable under ADH only .

•Urea is rebsorbed in the presence of ADH.

•Na reabsorbed in exchange for K under the influence of aldosterone.

What happens when we are fasting ?

Plasma concentration increases and this will stimulate ADH and permeability of water will increase so this will lead to more water reabsorption and small amount of urine secretion .



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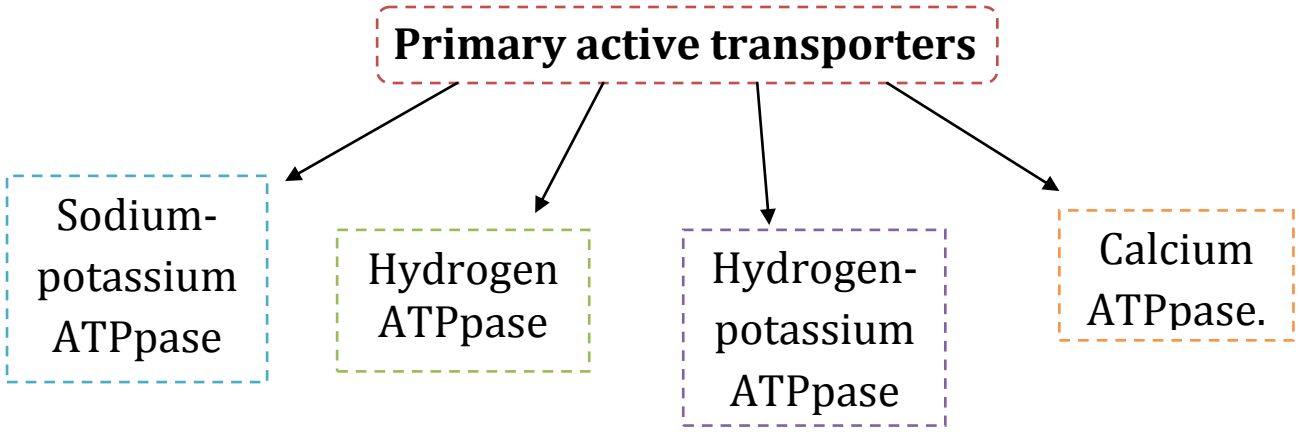
❖Transporters :

SITE	APICAL TRANSPORTER	FUNCTION
Proximal Tubule	•Na/Glucose CT •Na/Amino Acid •Na/H Exchanger	•Na & Glucose Uptake •Na & Amino Acid Uptake •Na Uptake and H Extrusion
Thick Ascending Limb	• Na, 2 Cl,, K CT •Na/H Exchanger •K Channels	•Na, 2 Cl, K Uptake •Na Uptake and H Extrusion •K Extrusion
Early Duct	NaCl CT	Na & Cl Uptake
Late duct Collecting Duct	Na Channel (ENaC)	Na Uptake

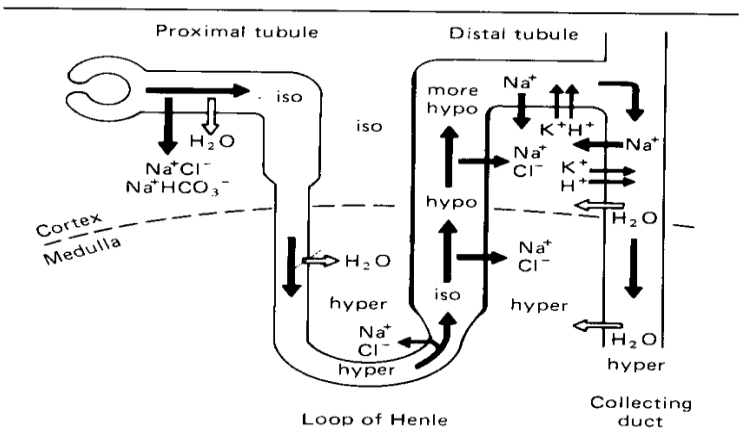


♠ Urea Recirculation:

- Urea is passively reabsorbed in proximal tubule.
- In the presence of ADH, water is reabsorbed in distal and collecting tubules, concentrating urea in these parts of the nephron.
- The inner medullary collecting tubule is highly permeable to urea, which diffuses into the medullary interstitium.
- ADH increases urea permeability of medullary collecting tubule.

❖ Osmolality of the filtrate along the nephron:

Osmolality of filtrate in PCT:	Osmolality of filtrate in Descending loop:	Osmolality of filtrate in Ascending Loop:	Osmolality of filtrate in Collecting Duct
similar to plasma ~290 mosm	graded ↑ in osmolality from 300 mosm. To maximum of 1200 mos. at the tip of loop	graded ↓ in osmolality1200-150	–↑ADH → ↑ water reabsorption →concentrate urine 1200 mosm./ –No ADH →no water reabsorption→dilute urine 50mosm
Due to reabsorption of equal portion of solute & water.	Due to only water reabsorption.	Due to only solute reabsorption.	Osmolality depend on ADH.



❖Bulk flow:

This occurs through the peritubular capillary walls, mediated by hydrostatic pressure & colloid osmotic forces.